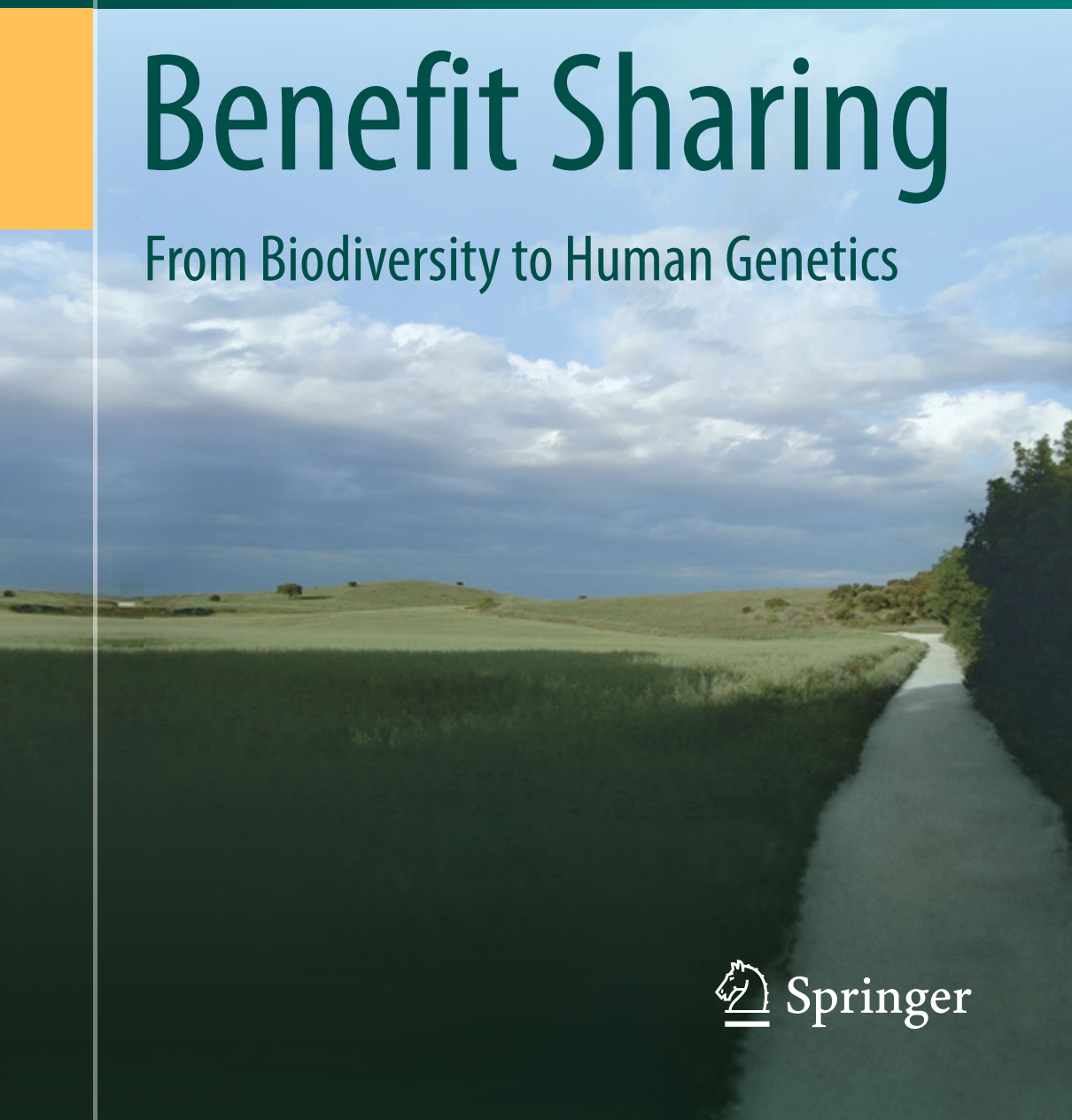
Doris Schroeder
Julie Cook Lucas
Editors

Benefit Sharing

From Biodiversity to Human Genetics



Springer

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To our Grandmothers
Apollonia Jungen, Wilhelmine Schröder,
Esther Coe and Edith Cook

Foreword

It was only just over a decade ago that the Council on Health Research for Development (COHRED) was attempting to raise awareness of the now well-known 90/10 gap—the fact that 90 % of medical research was being carried out into diseases affecting only (mostly the richest) 10 % of the world's population—and calling for a dramatic increase in the amount of research on the diseases affecting the world's poorest people. Since then, there has indeed been a rapid rise in the amount of biomedical research carried out in low-income settings. Much of this has taken the form of international collaborative networks, including private–public partnerships, addressing diseases, both communicable and increasingly also non-communicable, affecting the world's poorest people. Much of this research has been funded by charities such as the Wellcome Trust and the Bill and Melinda Gates Foundation. But this period has also seen an exponential rise in the amount of commercially funded research carried out in low- and middle-income countries by multinational pharmaceutical companies.

The rapid growth of biomedical research, both public and private, being carried out in low- and middle-income countries has led to an intensification of debate about the ethics and governance of such research. Perhaps surprisingly, a reasonable degree of international consensus has been achieved about many of the core requirements for ethical research. This includes the view that while there is much disagreement about its precise form and scope, valid consent is essential for research with competent adult participants; and the view that research participants should not, except in exceptional circumstances, be subjected to greater than minimal risk of harm.

There are, however, some aspects of international research ethics which continue to be the subject of a great deal of debate and disagreement. Broadly speaking, these relate mostly to an overarching question about the nature of the responsibilities of researchers and research institutions to research participants and 'communities' in which they carry out their research, over and above those of obtaining valid consent and minimising risk. What, for example, are the responsibilities of researchers to provide—or to avoid providing—benefits to participants and communities during the course of the research? And what are their responsibilities once the research has been completed?

Over the past decade, the analysis of the ethical features of various competing approaches to what has come to be known as 'Benefit Sharing' has emerged as one of the most important, vibrant and creative sites of both debate and public policy deliberation in international research ethics. Throughout this period, Doris Schroeder has consistently been one of the most perceptive thinkers on this incredibly pressing and difficult cluster of topics. Her work on definitions of 'Benefit Sharing', on the development of models of fair benefit sharing, and on the nature and scope of the benefit-sharing responsibilities of researchers in the public and private sectors has played an unmatched role in setting the international benefit-sharing agenda. In this impressive collection, which analyses examples of innovative benefit-sharing practice and provides a wide-ranging critical analysis of current thinking on benefit sharing, Doris Schroeder and Julie Cook Lucas offer an acute and perceptive assessment of the major and pressing challenges that need to be addressed in this area, and important signposts for how this task should be undertaken.

Prof. Michael Parker
Professor of Bioethics and Director of the Ethox Centre
University of Oxford
Oxford
UK

Acknowledgments

International research groups can be hard work. Or they can be exciting and enthusiastic, and lead to lasting collaborations and friendships. In 2006, the European Commission funded an international consortium to carry out a three-year research project called GenBenefit (Genomics and Benefit Sharing with Developing Countries—From Biodiversity to Human Genomics).[1] Luckily GenBenefit turned out to belong to the latter category, and many of the partners and advisors from Australia, Canada, France, Germany, Iceland, India, Italy, Kenya, Lithuania, Mexico, Nigeria, the Philippines, South Africa and the United Kingdom will stay in touch well beyond this publication.

We are grateful to the European Commission for granting the funding for our work, and to our project officer, Dr Dr René von Schomberg, for his committed and engaged interest. Additional funding was granted by the South African government's Department of Science and Technology, which seeks out promising European Union projects on topics relevant to the country. We would also like to thank the three anonymous reviewers for Springer, whose valuable recommendations we have endeavoured to take on board. Special thanks to our editor, Fritz Schmuhl, who not only attended our final project conference but has also gone to great lengths to support us, and in addition has shown considerable patience. Thanks also to his colleague Takeesha Moerland-Torpey for her valuable assistance with this book. Paul Wise, our Cape Town-based copy editor, has assisted us enormously with his eagle eye and sense of style.

We would like to acknowledge the invaluable input and understanding regarding indigenous matters provided by Prof. Jack Beetson. Dafna Feinholz (also a co-author) provided ongoing support and encouragement for the inclusion of a gender analysis in our benefit-sharing research.

In addition, a wide variety of people shared their experience and perspectives of benefit sharing with us in different ways. We would particularly like to

[1] Research leading to this book was undertaken as part of GenBenefit, a research project funded by the European Community's Sixth Framework Programme for Science and Society under Grant Agreement Number 036691. This book reflects only the authors' views, and the European Community is not liable for any use which may be made of the information it contains. The project website is at www.uclan.ac.uk/genbenefit.

acknowledge all of the research participants, interviewees and informants who took part in GenBenefit.

Thanks to the ethics committees that approved our research.

Thanks to Jane Kamene of the Kenya AIDS Control Project, University of Nairobi, for her research contributions, as well as for walking some of us through the Majengo slums when our taxi arrived at the wrong location.

He is unlikely ever to read this, but thanks also from the three Majengo interviewers (Fatima Alvarez Castillo, Pamela Andanda and Doris Schroeder) to our Nairobi taxi driver, Peter, who not only chauffeured us through the crammed, potholed streets of Nairobi safely and efficiently, but also reminded local girl Pamela that she should go easy on her two exhausted foreign colleagues. Though he is a co-author, thanks to Dr Joshua Kimani, without whom we would have returned on our long-distance flights without any results.

Thanks for input into our research from members of the Kalahari San communities, especially Collin Louw of the South African (SA) San Council, the Working Group of Indigenous Minorities in Southern Africa (WIMSA) and the Hoodia Trust, Mathambo Ngakaeaja of WIMSA Botswana and Andries Steenkamp of the SA San Council.

Thanks to Ambrose Rachier, at the time chair of the Kenya Medical Research Institute/National Ethics Review Committee, for an enlightening discussion and a subsequent presentation at one of our workshops.

Thanks to the co-chairs of the Working Group on Access and Benefit Sharing, UN Convention on Biological Diversity; Tim Hodges (also a co-author) and Dr Fernando Casas, for their interest and highly insightful input throughout the project.

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Thanks to Dr Judith Bwonya, at Kenya's Ministry of Medical Services, and her staff for inviting us to host a Capacity-Building Workshop on Benefit Sharing in Nairobi.

Thanks to Victoria Haraseb and Silke Felton of WIMSA for providing very useful information.

Thanks to the participants in the David C. Thomasma International Bioethics Retreat and its organizer, Prof. Tomi Kushner, whose unwavering interest in matters of benefit sharing has been remarkable over the years. Thanks also to the following speakers for accepting our invitations to present their high-profile research at our workshops: Prof. Gurdial Nijar Singh, Prof. Himla Soodyall, Prof. Anton van Niekerk, Prof. Raj Ramesar and Prof. Jon Altman.

The research for this book involved much travel and many meetings and events. In Cape Town we were ably supported by Fahdelah Hartley from the University

of Cape Town and Lynette Osiemo, who provided research assistance to Pamela Andanda. Carole Le May provided excellent operational and moral support in Montreal. Dr Keziah Nginya supported the interviews in Majengo with a smile and abundant local knowledge.

The authors of Chap. 7 would like to thank Ms. Tomme Young for her insights and Mrs. Yihong Hu, Director of the Bioresource and Biosafety Division, China National Centre for Biotechnological Development, Beijing, for additional information on the Chinese experience. Thanks are also due to John Herity, Balakrishna Pisupati and Sijmen E. Schoustra for their comments on an earlier draft and to Dr S. Rajasekharan of the Tropical Botanic Garden and Research Institute in Trivandrum, India, for his enlightening comments on the Kani case.

No research endeavour can succeed without the support of the hosting institution(s). At the University of Central Lancashire we are indebted to:

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- Cathy Lennon, our committed and very supportive former research assistant in the Centre for Professional Ethics.
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Doris Schroeder is grateful for the flourishing research environment provided by Queen's College, Melbourne, and its Master, Prof. David Runia, as well as the hospitality of Mrs. Gonni Runia. In the same setting, the Centre for Applied Philosophy and Public Ethics at the University of Melbourne has been a great place to work on this book when not at the University of Central Lancashire.

Finally, thanks to all our co-authors.

Contents

Contributors

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Gardar Arnason is an Assistant Professor at the Leibniz University of Hanover, Germany. He has a Ph.D. in Philosophy from the University of Toronto, Canada. He co-edited *Arguments and Analysis in Bioethics* (Rodopi 2010), *The Ethics and Governance of Human Genetic Databases*: *European Perspectives* (Cambridge University Press, 2007) and *Blood and Data*: *Ethical*, *Legal and Social Aspects of Human Genetic Databases* (Centre for Ethics and University of Iceland Press, 2004). His research interests include bioethics, neuroethics and the philosophy of science.

Fatima Alvarez Castillo is a University of the Philippines Centennial Professor in the Social Sciences. She teaches politics, research ethics and qualitative research methods. Her research is on a wide range of topics, but always deals with issues of justice, gender, equity and government accountability. She works with Civil Society Organizations in advocating for the rights of indigenous peoples and of women in poverty. Her published work includes *Conceptual Analysis*, *Critical Review of Policy*, and *Empirical Studies of Women's Health and Human Rights*. She recently led a two-year study that examined poor people's conceptions of poverty and deprivation in a project that sought to develop alternative indices of poverty that could truly reflect gender inequities. A particular focus of her research and publications in the past few years has been gender justice in health research.

Sachin Chaturvedi, Ph.D., is a Senior Fellow at the Research and Information System for Developing Countries (RIS), a Policy Research Institute in New Delhi, India. He works on key policy issues confronting the developing world, with a focus on trade, technology and innovation linkages. He was a Global Justice Fellow at the

MacMillan Center for International and Area Studies at Yale University, USA, where he worked on drug prices and issues relating to intellectual property rights. He is author of two books, has edited three volumes and has published several research articles and book chapters. His assignments have included working at the German Development Institute (2007), the Institute of Advanced Study in Shimla, India (2005), and the University of Amsterdam in the Netherlands (1996). He was a Member of the Committee of Experts set up by the Independent Group on South Asian Cooperation to evolve a framework of cooperation for the conservation of biodiversity in the region served by the South Asian Association for Regional Cooperation. He has worked closely with the World Bank and several UN agencies including the Economic and Social Commission for Asia and the Pacific, and the Food and Agriculture Organization. Currently he is leading the RIS work programme on emerging economies and their development cooperation polices, and is visiting professor at the Centre for Studies in Science Policy, Jawaharlal Nehru University, New Delhi.

Roger Chennells has been an Attorney in private practice in South Africa since 1980. Prior to 1990 most of his legal work involved representing and protecting those who opposed the apartheid state. After the emergence of a democratic state in the early 1990s, he began to represent indigenous peoples, initially in their struggles for the restitution of land and heritage rights. He assisted the San peoples with the formation of a regional organization to represent their rights in Botswana, Namibia and South Africa. During the United Nations International Decade of the World's Indigenous People, he became an advocate for the emerging intellectual property and heritage rights of indigenous peoples, representing indigenous groups elsewhere in Africa, as well as in Australia and Jamaica. In 2001 Roger was requested to help the San challenge the use of their traditional knowledge in the *Hoodia* patent granted to South Africa's Council for Scientific and Industrial Research. Roger continues to work with the San, and other indigenous peoples, and is currently studying for a Ph.D. at the University of Central Lancashire, UK, in the area of Benefit Sharing, funded by the Wellcome Trust.

Sara Crager did her undergraduate work in neuroscience at McGill University, Canada, before going on to complete an MD at Yale School of Medicine, USA. She is currently a Resident Physician in the Emergency Medicine Residency Program at the University of California, Los Angeles, USA. She has worked on several projects to improve access to health care, including directing a free clinic providing health care to underserved populations in New Haven, USA, as well as family planning education in Guatemala. She has also worked in various capacities on improving access to medicines, including leadership in the organization Universities Allied for Essential Medicines, co-leading a grassroots campaign to improve access provision for biologic medications in the 2010 United States Affordable Care Act, and involvement in civil society efforts to ensure access to medicines provision in the Intergovernmental Working Group on Innovation, Intellectual Property and Public Health convened by the World Health Organization. She has previously done basic science research in Malaria Vaccine Development, and has authored several papers on access to vaccines and other biologic medications.

Dafna Feinholz-Klip has a B.A. and an M.A. in Psychology and a Ph.D. in Research Psychology from the Universidad Iberoamericana, Mexico, and also a Master's in Bioethics from the Universidad Complutense, Madrid, Spain. She has studied at the Kennedy Institute of Ethics and the Harvard School of Public Health in the USA. Dafna has wide experience as a Member of Research Ethics Committees in Mexico and internationally. She was a member of the international team that wrote the World Health Organization's *Operational Guidelines for Ethics Committees that Review Biomedical Research* (2000) and was responsible for its translation into Spanish. She is founder and former Chairperson of the Latin American Forum of Ethics Committees for Health Research. She was Executive Director of the National Commission of Bioethics in Mexico for five years. In 2005 she represented Mexico at intergovernmental meetings of experts to finalize the *Universal Declaration of Bioethics and Human Rights* for the UN Educational, Scientific and Cultural Organization (UNESCO). She was Mexico's Representative at the Steering Committee on Bioethics of the Council of Europe. She is currently Chief of the Bioethics Section at UNESCO.

Véronique Fournier is a Cardiologist and a specialist in public health. She was Counsellor to Bernard Kouchner, France's Minister of Health (1998–2002), in charge of patients' rights and bioethics. She was delegated by him to investigate the field of clinical ethics, and to create the first clinical ethics service support in France. For this, she spent a year in the MacLean Center for Clinical Medical Ethics at the University of Chicago, USA. In 2002 she created the Clinical Ethics Centre, located at Hôpital Cochin, Assistance Publique, Paris, where she is the director. During the past ten years, her main fields of interest in clinical ethics have been end-of-life issues, issues raised regarding access to reproductive technologies, and more recently ethical questions surrounding ageing and the care due to old people, whether disabled and cognitively impaired or not. In 2009, she published *Le bazar bioéthique* (Ed Robert Laffont). She is a Member of the European Clinical Ethics Network.

Eugenijus Gefenas is an Associate Professor and Director of the Department of Medical History and Ethics at the Medical Faculty of Vilnius University, Lithuania. He is also a Director of the Lithuanian Bioethics Committee. Eugenijus graduated from the Medical Faculty of Vilnius University in 1983. He obtained his Ph.D. from Lithuania's Institute of Philosophy, Sociology and Law in 1993. He teaches bioethics at the Medical Faculty of Vilnius University and, together with colleagues from the Center for Bioethics and Clinical Leadership of Union Graduate College in the USA, co-directs the Advanced Certificate Program in Research Ethics in Central and Eastern Europe. In 2007 he was elected to the board of directors of the International Association of Bioethics. His international activities also include membership in the European Society for Philosophy of Medicine and Healthcare. In 2011 he was elected chair of the Council of Europe's Steering Committee on Bioethics. The areas of his professional interest include ethical, philosophical and policymaking issues related to human research, psychiatry and health care resource allocation.

Timothy Hodges is a career Canadian diplomat who focuses on environmental, benefit-sharing, economic and trade policy issues through institutions that include the UN General Assembly, G8, the World Trade Organization, Asia Pacific Economic Cooperation, the UN Convention on Biological Diversity, the UN Framework Convention on Climate Change, the UN Food and Agricultural Organization, the UN Educational, Scientific and Cultural Organization, the Organisation for Economic Co-operation, the Organization of American States and the North American Free Trade Agreement. His more recent assignments include serving as co-chair of the Ad Hoc Open-ended Working Group on Access and Benefit Sharing for the Convention on Biological Diversity. Following the adoption of the Nagoya Protocol on Access and Benefit Sharing, Timothy returned to the headquarters of Canada's Department of Foreign Affairs and International Trade, where he is currently senior advisor for the policy staff.

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Joshua Kimani is an Epidemiologist with a Medical Degree from the University of Nairobi, Kenya, and a Master's in Public Health from the University of Washington, Seattle, USA. He is currently the Clinical Director of the Kenya AIDS Control Project, a research unit housed within the University of Nairobi Institute of Tropical and Infectious Diseases. This unit has implemented numerous collaborative HIV research activities for the past three decades, led by investigators from the University of Nairobi and the University of Manitoba, Canada. The data generated is used for evidence-based programming, and has influenced HIV/AIDS management and policy formulation in the region for over 20 years. Kimani is currently spearheading the implementation of the *HIV Prevention/Care Program with Most at Risk Populations*, funded by the US Centres for Disease Control and the US President's Emergency Plan for AIDS Relief, which has so far enrolled 18,000 sex workers from Nairobi Province. Kimani's research interests include the epidemiology and immunobiology of sexually transmitted infections, mechanisms of HIV resistance, reproductive health issues among sex workers, microbicide studies, and HIV pre/post-exposure prophylaxis and treatment as prevention in HIV control. More recently he has become involved in global health ethics, genomics and malaria control in pregnant women.

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Miltos Ladikas, Ph.D., is a senior research fellow at the Centre for Professional Ethics, University of Central Lancashire, UK. He has held research positions at the London School of Economics and the Science Museum in the UK as well as the European Academy for Technology Assessment and the Karlsruhe Institute of Technology in Germany. His research background covers the areas of technology assessment, public perceptions of science and technology, ethics in science and technology policy, and science and development. He has coordinated a number of international research projects in these areas. He is currently the coordinator of Global Ethics in Science and Technology Policy, a project funded by FP7, the European Union's Seventh Framework Programme for Research.

Julie Cook Lucas is a Research Associate in the Centre for Professional Ethics, University of Central Lancashire, UK. After obtaining a B.A. (Hons) in English literature, Julie developed national women's health initiatives at the Health Education Authority of the UK's National Health Service (NHS) in the 1980s. She has more recently worked as an advocate and counsellor providing voluntary-sector women's mental health services, and as an elected community representative and health activist around reproductive health issues and user representation in NHS development. Julie ran award-winning health and environment campaigns for the Women's Environmental Network through the early 1990s, and co-founded the UK's first course on ecofeminism at Birkbeck College, University of London, in 1994. Her interests revolve around environmental issues, feminism and animal rights, and she has worked for a range of NGOs, including some in the anti-vivisection and pro-choice movements. Her postgraduate research in the Philosophy Department at the University of Lancaster (1995–1998) examined the tensions between activism and academia, and between theory and practice, in relation to the ecofeminist movement. She joined the Centre for Professional Ethics in 2005 and now works on a range of externally funded research projects in connection with health and global justice. She has published a number of papers on 'Benefit Sharing', with particular emphasis on gender issues.

Emezat Mengesha obtained a Ph.D. in Gender Equality and Sustainable Development Issues in Africa from the University of the Witwatersrand, South Africa, in 2009. She holds an LL.B. from Addis Ababa University, Ethiopia, and an LL.M. from the University of Pretoria, South Africa. Emezat is currently an Assistant Professor and the Director of the Institute for Gender Studies at Addis Ababa University. Emezat has extensive research experience on the socio-economic rights of women, as well as gender and development issues in the African context. Her research has a particular focus on the legal analysis of human rights instruments. She has produced

several research reports and publications in peer-reviewed journals and has worked as a consultant with both Local and International Organizations.

Vasantha Muthuswamy recently retired as Senior Deputy Director-General and Chief of the Division of Basic Medical Sciences, Traditional Medicine and Bioethics, and of the Division of Reproductive Health and Nutrition, at the Indian Council of Medical Research (ICMR). A Medical Graduate and Postgraduate in Obstetrics and Gynaecology, she has played a major role in the area of drug development, including traditional medicine, genetics and genomics. A World Health Organization (WHO) fellow at the Kennedy Institute for Ethics, Georgetown University, USA, she is recognized for her leading role in the issuing of the ICMR's *Ethical Guidelines for Biomedical Research on Human Subjects* in 2000, and the revised *Ethical Guidelines for Biomedical Research on Human Participants* in 2006. She was also involved in the development of the *Operational Guidelines for Ethics Committees that Review Biomedical Research* and the *Guidelines for Survey and Evaluation of Ethics Committees that Review Biomedical Research* by the Special Programme for Research and Training in Tropical Diseases of the United Nations (UN) Children's Fund, the UN Development Programme, the World Bank and the World Health Organization. She has been associated with national guidelines on research ethics in Nepal, Sri Lanka and the Maldives, and has been a member of many National and International Ethics Review Boards. She was the founding secretary of the Forum for Ethical Review Committees in Asia and the Western Pacific Region and is currently president of the Forum for Ethics Review Committees in India and chairperson of India's Forum for Medical Ethics Society.

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Doris Schroeder, Ph.D., was educated in Germany and the United Kingdom at postgraduate level in economics and management, and also in philosophy and politics. Her first career was in management, as a strategic planner for Time Warner. Her voluntary work includes 15 years for Amnesty International. She currently holds two appointments: Professor of Moral Philosophy and Director at the Centre

for Professional Ethics at the University of Central Lancashire and Adjunct Professor at the Centre for Applied Philosophy and Public Ethics (CAPPE), Charles Sturt University, Canberra, Australia. She was the principal investigator in two International Projects on benefit sharing, both of which led to books. The first was *Indigenous Peoples*, *Consent and Benefit Sharing*: *Learning Lessons from the San Hoodia Case* (2009, co-edited with Rachel Wynberg and Roger Chennells). This is the second.

Giorgio Sirugo earned an MD from the University of Pavia, Italy, and a Ph.D. in Human Molecular Genetics from the University of Strasbourg, France. He completed his post-doctoral training in Molecular Genetics at Yale University, USA. In 1999, he took a research clinician position at the Medical Research Council Unit in The Gambia, where he headed the Laboratory of Human Genetics and started the Gambian national DNA bank. In 2007 he was appointed Head of the Genetics Research Unit at San Pietro Fatebenefratelli Hospital in Rome, Italy, with a main research focus on genetic susceptibility to infectious diseases. He is a founding member of the African Society of Human Genetics.

Yeyang Su, MS, M.A., works at BGI (formerly the Beijing Institute of Genomics) in China as the secretary of its Institutional Review Board and a multidisciplinary researcher. Her research interest lies in the interactions between science and society, particularly in understanding how genetics and genomics shape the future of society and human beings, and how human beings react to such a revolution.

Huanming Yang, Ph.D., is Co-founder and President of BGI (formerly the Beijing Institute of Genomics), China, and is a former member of the International Bioethics Committee of the UN Educational, Scientific and Cultural Organization. He has recently been appointed to the International Research Panel of President Obama's Presidential Commission for the Study of Bioethical Issues.

Acronyms

ABS	Access and benefit sharing
AICRPE	All India Coordinated Research Project on Ethnobiology
ATSIC	Aboriginal and Torres Strait Islander Commission (Australia)
CBD	Convention on Biological Diversity
CIOMS	Council for International Organizations of Medical Sciences
COMPITCH	*Consejo Estatel de Organizaciones de Médicos y Parteras Indígenas Tradicionales de Chiapas* (Mexico)
CSIR	Council for Scientific and Industrial Research (South Africa)
ECOSUR	*El Colegio de la frontera Sur* (Mexico)
FPIC	Free and prior informed consent
FTA	Free trade agreement
GISN	Global Influenza Surveillance Network
HIF	Health Impact Fund
HUGO	Human Genome Organisation
ICBG	International Cooperative Biodiversity Group
IE	*Íslensk erfðagreining* (Iceland)
IGC	Intergovernmental Committee on Intellectual Property and Genetic Resources, Traditional Knowledge and Folklore
IHR	International Health Regulations
IPR	Intellectual property rights
ISR	International Sanitary Regulations
IUCN	International Union for Conservation of Nature
KEMRI	Kenya Medical Research Institute
MOU	Memorandum of understanding
NGO	Non-governmental organization
NIPRD	National Institute for Pharmaceutical Research and Development (Nigeria)
PROMAYA	Promotion of Intellectual Property Rights of the Highland Maya of Chiapas (Mexico)
QALY	Quality-adjusted life year
R&D	Research and development
SEMARNAP	*Secretaría de Medio Ambiente, Recursos Naturales y Pesca* (Mexico)

SMTA	Standard material transfer agreement
TBGRI	Tropical Botanic Garden and Research Institute (India)
TRIPS	Trade-Related Aspects of Intellectual Property Rights
UNEP	United Nations Environment Programme
WHA	World Health Assembly
WHO	World Health Organization
WIMSA	Working Group for Indigenous Minorities in Southern Africa
WIPO	World Intellectual Property Organization
WTO	World Trade Organization

Figures

Tables

Chapter 1
Benefit Sharing: From Biodiversity to Human Genetics—An Introduction

Doris Schroeder and Julie Cook Lucas

Abstract What happens when people hand over natural resources for scientific research or commercial use? And what *should* happen? This book raises fundamental questions about benefit sharing to provide orientation for policymakers, lawyers, ethicists and lobbyists on a topic of global concern.

Keywords Benefit sharing • Traditional knowledge • Human genetic resources

What happens when people hand over natural resources for scientific research or commercial use? And what *should* happen? This book raises fundamental questions about benefit sharing to provide orientation for policymakers, lawyers, ethicists and lobbyists on a topic of global concern.

Scientific research and associated commercialization have gone global in recent decades. While keen botanists might have travelled around the world for centuries amassing foreign treasures for Northern botanic gardens,[1] today's efforts are both more widespread and more systematic. For instance, in the ten years between 2000 and 2010, the export of raw agricultural materials from Africa, Asia, Central America and South America almost tripled (WTO 2012). At the same time, human tissue banks boomed.

> Biobanks have multiplied significantly since the 1970's, and have become integral to research facilities around the globe. The period 1990–1999 saw the most significant percentage increase, at 42%. Growth in 2000 to 2009 was almost as impressive, with a 36% increase in biobanks (ASD 2012).

[1] The growing critique of such activities is summarized in Shiva (1998).

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While some biobanks operate solely with national resources (e.g. the Icelandic biobank described in Chap. 5), many store human tissue and DNA samples from around the world.[2] In the area of plant resources, many seed banks have also been set up to preserve biodiversity. For instance, the Millennium Seed Bank at Kew Gardens in London, in collaboration with partners in 50 countries, aims to bank 25% of the world's wild plant species by 2020 (Kew n.d.).

It is within this context of global resource use, combined with claims about exploitation (Shiva 1991; Egziabher 1994; Nijar 1996; Srinivas 2008: 86), that discussions of benefit sharing need to be framed. The established meaning of 'benefit sharing' goes back to the adoption in 1992 of the international Convention on Biological Diversity (CBD), which aims to conserve biological diversity and facilitate its sustainable use through fair and equitable benefit sharing with resource providers (CBD 1992: article 1).

Today, the CBD has 193 parties and is considered a 'grand bargain', which aligned the national and regional self-interests of developed and developing nations. Developed nations focused on maintaining a high level of global biodiversity to protect ecological functions and to secure access to natural resources for future use. Developing countries lobbied for sovereignty rights to counter exploitation, rights which they secured for plants, animals, micro-organisms and related traditional knowledge within their boundaries (Schroeder and Pisupati 2010). Such natural resources now fall squarely under national sovereignty rights, and can only be accessed after prior informed consent has been obtained from providers on mutually agreed terms.

This book starts with discussions about benefit sharing related to biodiversity, but moves on to the as yet unresolved topic of benefit sharing in return for access to human biological resources. Human biological resources are excluded from the CBD, and no other legally binding international instrument regulates their management. The Declaration of Helsinki (WMA 2008) requires that the benefits of research be shared with clinical trial participants, and to a more limited degree with human sample donors. This type of benefit sharing is reminiscent of CBD requirements in that those who provide a resource are seen to deserve something in return (Schroeder 2007). However, the Declaration of Helsinki is not legally binding, and hardly any examples of successful benefit sharing exist in relation to its provisions.

In recent years, the term 'benefit sharing' has also been used in a much broader, more aspirational sense (EC 2012; see also Table 1.1). This is linked to human rights, for instance article 27(1) of the Universal Declaration of Human Rights, which proclaims that:

> Everyone has the right freely to participate in the cultural life of the community, to enjoy the arts and to *share in scientific advancement and its benefits* (UN 1948) (our emphasis).

The human right to share in the fruits of science is universal and does not require any contribution to that scientific advancement. While we fully support this universal human right, this book mostly deals with the established, narrower

[2] The American company Bioserve, for instance, holds samples from '120,000 patients on four continents' (BioServe n.d.).

Table 1.1 Main Governance Instruments for Benefit Sharing

Benefit Sharing (established sense)	Benefit Sharing (aspirational sense)
Convention on Biodiversity, 1992: United Nations (except USA). Includes national laws, e.g. Biodiversity Bill, India, 2002; Biodiversity Act, South Africa, 2004	*Universal Declaration of Human Rights,* 1948: United Nations
Declaration of Helsinki, 2008: World Medical Association. Includes national laws, e.g. Brazilian National Health Council resolution No. 196/96, 1996	*Universal Declaration on Bioethics and Human Rights,* 2005: UNESCO

meaning of benefit sharing: that those who have contributed resources to scientific research ought to receive benefits in return.

Accessing human biological resources can be highly contentious in many respects. In this book, we do not attempt to deal with all of the many ethical concerns that may arise. For instance, in 2010, the Havasupai Indians won a case against the Arizona State University, and were able to limit researchers' use of their blood samples (Harmon 2010). The case was successful because samples had been used outside the terms of the original consent agreement. A violation of informed consent is an ethical concern in addition to those regarding benefit sharing. Another even more high-profile project that became publicly controversial is the Human Genome Diversity Project. Many indigenous groups whose DNA was collected for the project were seriously disadvantaged, economically and socially, and concerns were raised about potential further discrimination against such groups (Dodson and Williamson 1999). The discriminatory use of genetic information is another serious ethical concern in addition to those regarding benefit-sharing requirements, and will not be dealt with in this book.

Chapter 2 by Arnason and Schroeder clarifies both the concept of benefit sharing and the related philosophical concepts of vulnerability, exploitation and undue inducement. The link between benefit sharing and exploitation is clear. If a resource is taken from its rightful holders without their consent and without mutually agreed terms, then exploitation has occurred, according to the CBD. Such exploitation is particularly problematic if it involves vulnerable populations. Moving from biodiversity to human genomics, this claim of exploitation has been countered by the 'undue inducement' argument. It is an established principle that human research participants should never be offered benefits for taking part in research, otherwise they might consent to participate against their better judgement. Notably, the more vulnerable a population is, the more of an inducement even the smallest benefit could be. Having charted the philosophical groundings of the debate by defining vulnerability, exploitation and undue inducement, the authors work towards resolving the tension between undue inducement and benefit sharing.

Chapter 3 by Andanda, Schroeder, Chaturvedi, Mengesha and Hodges provides an overview of the key international instruments and guidelines that make provision for benefit sharing. Legal documents are often categorized as either

binding or non-binding. With the exception of the CBD itself, most benefit-sharing provisions are non-binding, such as the Declaration of Helsinki (WMA 2008), the International Ethical Guidelines for Biomedical Research Involving Human Subjects issued by the Council for International Organizations of Medical Science (CIOMS 2002), the Statement on Benefit Sharing by the Ethics Committee of the Human Genome Organisation (HUGO 2000), the UN Educational, Scientific and Cultural Organization's Universal Declaration on the Human Genome and Human Rights (UNESCO 1997) and the same organization's Universal Declaration on Bioethics and Human Rights (UNESCO 2005), all of which are introduced in this chapter.

Chapters 4 and 5 present seven case studies to illustrate the challenges of benefit sharing, with examples from around the world. Lucas, Schroeder, Chennells, Chaturvedi and Feinholz outline indigenous peoples' rights in the context of access to plants, animals, micro-organisms and associated traditional knowledge, and discuss four paradigm cases.

In the Kani case (India), a benefit-sharing agreement was initiated voluntarily by researchers involved in the commercialization of Jeevani, a health product based on the Kani people's traditional knowledge. To their credit, the researchers instigated the benefit-sharing effort in the early 1990s, before any legal benefit sharing regime was adopted in India.

In the Niprisan case (Nigeria), a medicine was developed in Africa, based on African traditional knowledge, for the prophylactic management of sickle-cell disease. The licensing of Niprisan to a US company was the first instance of reverse transfer of medical technology in Africa. However, the case has been plagued by setbacks, both in terms of benefit sharing and in the marketing of the drug.

Much has been written about the International Cooperative Biodiversity Group project (Chiapas, Mexico), which remains deeply controversial. An international consortium established a research collaboration with Mexican communities and research partners to identify and evaluate bioactive agents from plants. The researchers promised a share of benefits to communities actively taking part in the research, as well as others. However, the proposed mechanisms for benefit sharing became a focus for resistance to the project, and, in the end, the project never got off the ground as the funder terminated the grant.

As in the Mexican story, the *Hoodia* case (southern Africa) has been discussed worldwide since first hitting the headlines in 2004 (see especially Wynberg et al. 2009). Traditional knowledge about the appetite-suppressant properties of the *Hoodia* plant led to an international rush to commercialize dietary supplements without any benefit sharing with the indigenous people. The legitimate licence holders, Pfizer and Unilever, later dropped out of product development, and the future of this high-profile case is still unclear.

These four cases from three continents serve as a guide when moving from benefit sharing regarding biodiversity to human genetics, In Chap. 5, Lucas, Schroeder, Arnason, Andanda, Kimani, Fournier, and Krishnamurthy analyse three further cases to illustrate the potential for exploitation and other associated ethical concerns when accessing human biological resources.

The deCODE genetics case (Iceland) presents the example of a biobank which planned to combine health data, genetic data and genealogical data to examine common diseases such as arthritis, stroke and schizophrenia (Kaiser 2002). The controversial plans required new legislation to combine this information, which raised many ethical concerns, particularly around consent and privacy. In 2003 the Icelandic Supreme Court concluded that the Act on a Health Sector Database violated the national constitution, and thus the biobank did not go forward in the intended form.

The Majengo sex workers case (Kenya) is about a long-standing research project into sexually transmitted diseases involving a large group of severely educationally and economically disadvantaged women from a slum called Majengo in Nairobi. The ongoing participation of hundreds of women over more than 20 years has contributed to experimental vaccine trials, and the research studies are continuing.

The final case, which involves avian flu virus samples (Indonesia), has succeeded in raising the concerns of a developing country at the international level. In 2006, the Indonesian government decided to withhold avian flu virus specimens from World Health Organization (WHO) laboratories in alleged violation of WHO regulations on public health emergencies. The country's health minister argued that any vaccines based on Indonesian samples would be unaffordable to the Indonesian population, and demanded a new benefit-sharing regime for virus sharing.

Chapter 6 analyses gender issues in benefit sharing. If benefit sharing is about justice, then it needs to be fair to both sexes. In the light of international commitments to women's rights, Lucas and Castillo examine international guidelines on benefit sharing for the extent to which they protect such rights. Through a discussion of illustrative cases, the chapter demonstrates how gender-based power imbalances can work against the implementation of guidelines and policies. The authors highlight the importance of developing benefit-sharing strategies, processes and mechanisms that are sensitive to power dynamics in local contexts.

Chapters 7 and 8 discuss the way forward for benefit sharing that relates to human biological resources. Two alternative approaches to the current legal vacuum are outlined. In Chap. 7, Chaturvedi, Crager, Ladikas, Muthuswami, Su and Yang advocate an inclusive approach to benefit sharing and argue that the CBD should be expanded to include human biological resources. They argue that current research and development do not respect the traditional differences between plant, animal and human-based resources, and that any attempt to regulate independently for human biological resources is destined to fail.

Chapter 8 by Schroeder, Gefenas, Chennells, Fournier, Feinholz and Sirugo considers the possibility of using ethics review as the main mechanism to achieve compliance with benefit-sharing requirements for human biological resources. Given that the Declaration of Helsinki is widely accepted globally, and that its benefit-sharing articles have been elaborated since 2000, the chapter investigates whether monitoring through research ethics committees could achieve justice for human sample donors. This chapter concludes the analysis of the specific,

established meaning of benefit sharing: those who contribute to scientific advancement are owed benefits in return.

Chapter 9 looks at the broader picture of injustice between developed and developing countries, focusing on the human right to the enjoyment of the highest attainable standard of physical and mental health.[3] The chapter introduces a reform plan (the proposed Health Impact Fund) to modernize and humanize the international intellectual property rights system, which, in its current form, is a significant obstruction to realizing the human right to health.

We hope that this book, and our conclusions as summarized in the final chapter, will serve as a helpful resource for policymakers, civil society and academics as we move forward to secure justice for all providers of biological resources.

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Chapter 2
Exploring Central Philosophical Concepts in Benefit Sharing: Vulnerability, Exploitation and Undue Inducement

Gardar Arnason and Doris Schroeder

Abstract The philosophical principle behind benefit sharing is simple. Those who contribute to scientific research ought to share in its benefits. This is a matter of justice. If benefit sharing does not take place, exploitation may have occurred. Such exploitation is particularly problematic if it involves vulnerable populations. To counter the claim that contributors to research ought to receive benefits, the spectre of 'undue inducement' has been raised: vulnerable populations should not be offered benefits for taking part in research, otherwise they might consent to participate against their better judgment – and the more vulnerable the population is, the more of an inducement even the smallest benefit could be. Global research ethics aims to avoid both the exploitation of research participants and undue inducement; as neither is morally acceptable. This chapter charts the philosophical groundings of the debate by defining vulnerability, exploitation and undue inducement. It concludes that in research which involves only minimal risk for participants, such as the donation of genetic samples, concerns about undue inducement are largely misplaced, and should not be used by researchers and funders to circumvent their clear benefit sharing responsibilities.

Keywords Benefit sharing • Exploitation • Vulnerability • Undue inducement

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2.1 Introduction

The topic of benefit sharing emerged towards the end of the 20th century. Today, it is frequently discussed at the highest levels of policymaking: the World Health Organization, the World Trade Organization and the World Intellectual Property Rights Organization. Yet its philosophical foundations and its relationship to other ethical concepts in scientific research, namely exploitation, vulnerability and undue inducement, are rarely discussed.

An example of end-stage renal disease and the availability of transplant kidneys can demonstrate these links. While dialysis can enhance survival for end-stage renal disease patients for a limited period, the health and well-being of humans is much better served with functioning kidneys. But the donation of a kidney by a living person to secure the health and well-being of another is only allowed in very limited circumstances, for instance as a gift to a close relative. In almost all countries, the sale of kidneys is forbidden because it is regarded as exploitative.

The horror of overriding the basic moral intuition that no human should be exploited as mere organ providers was a theme of the 2005 novel by Kazuo Ishiguro, *Never Let Me Go* (made into a film in 2010). The lives of Kathy, Ruth and Tommy are followed through childhood, adolescence and early adulthood. All three have been created (cloned, in fact) for one purpose: to provide organs to non-clones, or 'originals'. In the end, they all die as a result of these organ harvests. What makes the story particularly tragic is that Kathy, Ruth and Tommy experience human relationships in all their depth, with love and jealousy expressed through art, and yet they are resigned to their fate and do not try to escape even when opportunities arise, having been brainwashed into accepting their 'completion' (death).

No amount of monetary inducement could make up for such loss of life. If any were offered, it would be regarded as an undue inducement to participate in an ethically unacceptable activity. While the removal of one kidney is not generally life-threatening, countries that allow kidney donation for money are heavily criticized (Scheper-Hughes 2003), and it is not considered appropriate to discuss resources such as donated human kidneys in the context of benefit sharing. The fictional example in Ishiguro's novel follows the traditional lines of bioethical debate, but, as this chapter will demonstrate, the concept of undue inducement of research participants may look rather different in the context of donating human biological resources. While the protection of vulnerable populations from exploitation in scientific research must remain a focus of any action or debate in bioethics, it should not be employed as an easy excuse for researchers and their sponsors to avoid any kind of benefit sharing.

We shall explore benefit sharing and its relationship to the concepts of vulnerability, exploitation and undue inducement in more detail before returning to the donors of human biological materials such as DNA or blood (rather than kidneys).

2.2 Vulnerability

It is easy to agree that the characters in *Never Let Me Go* are vulnerable.[1] They are (cloned) children, later young adults, with no family, who are raised in institutions for the harvesting of their organs, one by one, until they die. However, agreeing on a definition of 'vulnerability' is not so straightforward. The two major problems as outlined in the academic literature, are, first, that the concept is vague and therefore lacks the specificity that an adequate definition requires,[2] and, second, that 'vulnerability' has been given increasingly broad interpretations over the years (Forster et al. 2001).

There is a sense in which all humans are vulnerable. None of us could survive as an infant without care, or in the desert without water. As Nancy Jecker notes: 'All persons are made of "flesh" not steel' (Jecker 2004, p. 60). However, in the context of scientific research involving human beings we need a narrower concept of vulnerability if it is to do any work in protecting research participants from exploitation.

The bioethicist Samia Hurst has compiled a list of cited examples of vulnerable groups in research from five sets of international guidelines for research ethics. Adjusting the list using the latest Declaration of Helsinki (2008), the examples include racial minorities, the economically disadvantaged, the very sick, the institutionalized, children, prisoners, pregnant women and fetuses, incompetent persons, persons susceptible to coercion or undue influence, junior or subordinate members of a hierarchical group (including medical and nursing students, subordinate hospital and laboratory personnel, employees of pharmaceutical companies, and members of the armed forces or police), elderly persons, residents of nursing homes, people receiving welfare benefits or social assistance and other poor people, the unemployed, patients in emergency rooms, homeless persons, nomads, refugees or displaced persons, patients with incurable diseases, individuals who are politically powerless, members of communities unfamiliar with modern medical concepts, and patients in emergency situations (Hurst 2008, p. 193).

There are concerns that these attempts to specify vulnerable groups in detail represents a possible over-extension of vulnerability which could lead, in the end, to no one qualifying for more protection than anyone else.

In this section we will suggest ways of addressing both the vagueness and the over-extension problem of vulnerability. In response to the first problem, we will provide a definition of 'vulnerability' in the context of scientific research. In response to the second, we will consider the conditions of vulnerability, in order to give a more precise description of the concept's application and extension in the context of human research.

The general meaning of the word 'vulnerability', as one finds it in dictionaries, is to be exposed to the risk of physical or emotional harm. Typical dictionary

[1] This section is based on Schroeder and Gefenas (2009).

[2] For examples of this complaint see, among others, Kipnis (2001), Ruof (2004), Levine et al. (2004), Rogers (1997), Shi (2001), Hurst (2008).

definitions have two features. First, there is an emphasis on the external element of vulnerability, namely the presence of a potential harm. Second, the potential harm is usually identified as either physical or emotional. However, in the research context, as we will see below, the definition requires either a wider understanding of harm, which *includes* violations of rights to well-being, autonomy and justice, or an acknowledgement of such violations *in addition to* harm.

In research ethics, one finds a notable definition of 'vulnerability' in the International Ethical Guidelines for Biomedical Research Involving Human Subjects of the Council for International Organizations of Medical Science (CIOMS 2002).

> 'Vulnerability' refers to a substantial incapacity to protect one's own interests owing to such impediments as lack of capability to give informed consent, lack of alternative means of obtaining medical care or other expensive necessities, or being a junior or subordinate member of a hierarchical group (CIOMS 2002).

The commentary on this guideline provides a corresponding description of vulnerable persons.

> Vulnerable persons are those who are relatively (or absolutely) incapable of protecting their own interests. More formally, they may have insufficient power, intelligence, education, resources, strength, or other needed attributes to protect their own interests (CIOMS 2002).

In contrast to the generic dictionary definition, the CIOMS description emphasizes what we might call the internal aspects of vulnerability, which may prevent some from protecting their interests as research participants. A complete definition of vulnerability needs to combine both the internal and the external aspects. This distinction between the two aspects is useful because it reminds us that vulnerability – and, by implication, harm – can be lessened or prevented on two fronts: reducing or eliminating the cause of the potential harm, and helping the vulnerable protect themselves. For example, where people are vulnerable to malaria, one could either fight the mosquitoes carrying the parasite or provide the vulnerable population with mosquito nets, repellents and medication, and with health care if they get infected. Ideally one would, of course, do both.

Before developing our definition further, let us point out another useful distinction: there is a difference between stating the meaning of a concept and setting out the criteria for its use. We might be clear about what vulnerability means, but still unsure about whether it applies to specific cases. The CIOMS formulation provides first a definition of 'vulnerability', namely a substantial inability to protect one's interests, and goes on to list some of the criteria for using the concept. So, according to the criteria, we can describe someone who cannot give informed consent, or who is a junior member in a relevant hierarchical group,[3] as vulnerable, but these are just some criteria for the use of the term 'vulnerability' and do not form part of its definition.

A first definition of 'vulnerability' could combine the external element of the dictionary definition and the internal element of the CIOMS definition.

[3] The examples cited are medical and nursing students, subordinate hospital and laboratory personnel, employees of pharmaceutical companies, and members of the armed forces or police.

To be vulnerable means to be exposed to the possibility of harm, while being substantially unable to protect oneself.

For someone to be vulnerable there must be relevant risk present. The mere absence of protection does not amount to vulnerability. For example, when we walk the streets of Paris or Berlin we may be unprotected against malaria, but we are not vulnerable to malaria, because there is no danger of contracting the disease. In the absence of relevant potential harm it makes no sense to speak of vulnerability. But even in the presence of relevant potential harm, or danger, we are not necessarily vulnerable. We might be travelling through a rural area in Africa, where malaria is prevalent, but enjoy the protection of prophylactic medication, bednets or immediate access to health care upon infection. In this case there is a general danger of contracting malaria in the area where we are travelling, but we have the best available protection. In order to account for both the external element (presence of potential harm) and the internal element (lack of relevant protection), our definition of vulnerability includes both the exposure to possible harm and the substantial lack of available protection.

However, the definition still needs some clarification for the research context. First, the external element seems too broad. We are all exposed to the possibility of harm, one way or another. No one is ever *completely* safe – not even Superman and other superheroes, otherwise there would be no thrill in watching them overcome adversaries. If everybody is vulnerable, then no one deserves special protection on the grounds of vulnerability. Hence, that cannot be what is meant by 'vulnerability' in the research context. When we talk about vulnerability, we are not talking about *any* possibility of *any* harm. When somebody leaves the house to take part in a research study, her purse might be stolen at a busy train station, but that is not what is meant here. We want the external element to be specific and relevant, so we will talk about a *significant probability* of an *identifiable* harm. The external element of our definition then reads:

To be vulnerable means to face a significant probability of incurring an identifiable harm…

The whole purpose of Kathy's, Ruth's and Tommy's lives is to be sacrificed for others. Hence we have a clearly identifiable harm (death through organ harvesting) and a significant probability of it occurring, given that powerful others are driving towards this harm.

Second, the internal element needs further explication. It is not clear what sort of ability we are talking about when we say that the vulnerable lack the ability to protect themselves or their interests. To take an example from the research context, a potential research participant who is illiterate would not be able to read an information

sheet provided before giving or refusing consent. That person is vulnerable. A potential research participant who is severely intellectually disabled might face the same problem; he might not be able to understand the information provided for consent and is therefore vulnerable as well. There is an important difference between the abilities of these two potential research participants, though. The illiterate research participant might be able to learn to read and would then no longer be vulnerable, or at least not in that respect. That person is *contingently* vulnerable: she lacks the means rather than the physical or mental abilities to protect herself.[4] The intellectually disabled research participant, on the other hand, is *intrinsically* vulnerable.[5] He truly lacks the (mental) ability to protect himself whatever alternative consent procedures are considered. We will reserve the word 'ability' for intrinsic abilities, and use the word 'means' for what determines contingent abilities, such as literacy, education, resources, and social and economic status. We will therefore rephrase the internal element of our definition to refer to the 'ability or means to protect oneself'. And now we can present our final definition of vulnerability.

> To be vulnerable means to face a significant probability of incurring an identifiable harm, while substantially lacking the ability or means to protect oneself.

Now that we have provided a definition of 'vulnerability', we turn to the possible over-extension of vulnerability. The World Medical Association's Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects, the Declaration of Helsinki for short, is the most important international guideline for the governance of ethical medical research. Following a revision of the Declaration of Helsinki in the year 2000 (the version prior to the current one), article 8 stated:

> Some research populations are vulnerable and need special protection. The particular needs of the economically and medically disadvantaged must be recognized. Special attention is also required for those who cannot give or refuse consent for themselves, for those who may be subject to giving consent under duress, for those who will not benefit personally from the research and for those for whom the research is combined with care (WMA 2004).

This article was heavily criticized for making everyone, and thereby no one, vulnerable. Forster et al. (2001) made this point very succinctly:

> The new declaration goes further [than the old one], making every conceivable person vulnerable, from patients with an illness, to those who cannot give consent, to healthy volunteers … The new declaration expands the category of vulnerability so broadly that it eliminates this category …; if everyone is vulnerable, no one is entitled to special protection.

Paragraph 8 was revised in 2008 to read (now as paragraph 9):

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[4] In this case, researchers are also in a position to empower her by, for instance, facilitating verbal, recorded consent, if this is acceptable to her.

[5] For a further discussion of this distinction see Silvers (2004, p. 56).

> Medical research is subject to ethical standards that promote respect for all human subjects and protect their health and rights. Some research populations are particularly vulnerable and need special protection. These include those who cannot give or refuse consent for themselves and those who may be vulnerable to coercion or undue influence (WMA 2008).

Through this latest revision, the Declaration of Helsinki's potential to overextend vulnerability has been at least partially reversed. The declaration does not provide a definition of 'vulnerability', but instead picks out two groups: those who cannot give or refuse consent and those vulnerable to coercion or undue influence. In doing so it leaves wide open the question of who is considered vulnerable and who is not.

Above we cited a list compiled by Samia Hurst of types of populations that could be regarded as vulnerable. The list gives some idea of the multiplicity of such groups. It also indicates a tendency to first identify vulnerable groups and then judge whether individuals are vulnerable on the basis of their membership of such a group, without identifying any specific potential harm. For example, an unemployed person in a welfare state such as Sweden is not generally vulnerable to exploitation in scientific research, whereas an unemployed person in Zimbabwe is very likely to be. The former does not face any particular risk of exploitation and is almost certain to enjoy the benefits which result from scientific research through national health care provision. The latter is much more likely to become a victim of exploitation because participation in scientific research might be his only avenue to access health care.

When we have to decide whether someone is vulnerable in the research context, rather than ask whether she belongs to any group previously identified as vulnerable, we should ask whether there is any substantial probability of identifiable harm to her, and whether there is a lack of ability or means for her to protect herself. We cannot list here every possible harm which could be incurred by participating in scientific research, but we can describe four basic markers for the occurrence of harm in the research context:

1. Unfavourable risk-benefit ratio
2. Breach of confidentiality or privacy
3. Invalid consent
4. Lack of access to the benefits of research.

The possible harm in question is not necessarily either physical or psychological. It is possible to exploit people without harming them physically or emotionally. It is even possible to exploit research participants without them knowing it, for example if they do not receive the benefits required by justice and fairness. Therefore we have to understand possible harm to include violations of rights to well-being, autonomy and justice.

Let us now look at each of the four markers. First, if there is an unfavourable risk-benefit ratio, the research participant is suffering harm or is placed at unnecessary risk as weighed against the potential benefits gained. (Here benefits are understood narrowly as the immediate personal benefits of participating

in particular research.) This may involve a direct, negative impact on well-being up to the point of injury or death. We take this marker to cover cases of certain and direct physical harm. Second, a breach of confidentiality or privacy can also have a negative effect on well-being, for example through stigma, embarrassment and developments such as paternity suits. The research participant's family relations, social relations, employment and insurance could also be negatively affected in some cases. Third, if consent is not obtained in a valid manner, for example because of deception, coercion or lack of information, the participant's right to autonomy has been violated. Lastly, lack of access to the benefits of research is a violation of the right to justice, which we will clarify further below.

To be vulnerable is especially problematic if another party is intent on exploitation. While the death of a young person through, say, an avalanche would be tragic, the death suffered by the characters in *Never Let Me Go* seems worse, because it can only happen through the presence and action of an exploiter.

2.3 Exploitation

The word 'exploitation' usually means taking advantage of something or someone to further one's own interests (Macklin 2003, p. 475).

In the context of this book, which deals with research involving human individuals or communities, particularly in developing countries, we are concerned with the exploitation of people. The exploitation of people is sometimes taken, even by definition, to be morally wrong. It is indeed very often unjust, unfair, harmful or plain wrong, although some argue that it can, in some situations, be morally neutral and permissible.[6]

What is problematic is that the injustice or immorality of exploitation in specific cases is often taken to be obvious: its wrongfulness is not analysed, explained or even described in any detail. This section seeks to answer two related questions. (a) What does exploitation mean in the context of research involving individuals or communities in developing countries? (b) What features or conditions make such exploitation a moral wrong?

In 1946, a team of US researchers deliberately infected 1,500 Guatemalans with syphilis, gonorrhoea and chancroid in order to test penicillin (Carroll 2011). Most of the experimental subjects were sex workers, orphans, prisoners and low-ranking soldiers. They were not told about the nature of the experiment and some were forced to participate. About 13% of those infected with syphilis were lost track of without receiving treatment and many of those who were treated were not cured. Some passed congenital syphilis on to their children. As research, this is as unethical as it gets. It is also a clear case of exploitation, although the direct harm and coercion are so shocking that the exploitative character of the case

[6] Joel Feinberg (1988, p. 14) gives a good example of morally neutral exploitation between humans: that of one driver following the lights of another car in dense fog.

may seem of secondary significance. Nonetheless, the research subjects were indeed exploited – the researchers used them to further their own interests – and it is easy to point out why the exploitation in this case was unethical: the research participants were coerced to participate, they were harmed and received little or no benefit, and the researchers treated them as mere means rather than as ends in themselves, as Immanuel Kant put it (1998 [1785], p. 45 [4:438]). The researchers took unfair advantage of the participants' vulnerabilities.

What is it, then, that distinguishes morally unacceptable exploitation? Some argue that exploitation is wrong because it is coercive (Schwartz 1995). If the only way for a pregnant woman in a developing country to access antiretrovirals in order to prevent the transmission of HIV to her unborn baby is to take part in a placebo-controlled trial,[7] despite the existence of a proven standard of care,[8] then one could say she has been coerced into enrolling.[9] Exploitation occurs here when one party takes advantage of another by making them an offer they cannot refuse; they are then coerced to accept simply because they lack alternatives. (We shall return later to the topic of lack of alternatives.) In the case of the penicillin research in Guatemala, the coercion extended to direct and physical force. Others argue that exploitation is wrong because it treats human beings as means rather than ends (Wood 1995), that is, it instrumentalizes them. Yet others claim that exploitation is wrong because it disadvantages the vulnerable (Macklin 2003, p. 475).

Learning from the above, political scientist Robert Mayer has presented a new analysis of exploitation, which we are going to use here (Mayer 2007). Mayer distinguishes three forms of exploitation.

In type 1 exploitation, exploiters fail to benefit other parties at all, even though they ought to. This type of exploitation is best exemplified in free riding. Free riders benefit from public goods, which are indivisible and non-excludable, without contributing their fair share. Usually this behaviour results in increased burdens on others and/or inferior public goods. For instance, somebody might evade taxes but still use health services funded through general taxation. The relative burden of financing the health service is then higher on others and/or the service is not as well resourced as it might otherwise be. Free riders thereby obtain wrongful gains (access to health care) when fairness requires that they ought to contribute to the costs of that public good.

In type 2 exploitation, exploiters do not benefit others sufficiently. In this case of exploitation an exchange takes place, but it does not benefit both parties fairly, and one party gains disproportionately. We can all imagine straightforward

[7] A placebo-controlled trial involves some participants being given a medicine with active ingredients, for instance a new drug against malaria, while others, known as the control group, are given a sham, a placebo treatment, which is expected to have no effect. Neither the participants nor the researchers know who has received which treatment until after the results are analysed.

[8] A proven standard of care is a treatment that already exists for the illness under consideration. Hence the ethical demand to test any new drug against an existing one that is known to be effective, rather than a placebo, is part of the 'standard of care' debate.

[9] For a discussion of the exploitative character of such studies see Annas and Grodin (1998).

instances of type 2 exploitation. Take, for instance, two children who merrily exchange stamps. One has a booklet detailing current trading prices, the other does not. Deliberately, the booklet owner offers a low-value, common stamp in exchange for a rare one. The ignorant child accepts. Exploitation has occurred. What makes this occurrence of exploitation easy to judge is (a) the existence of a booklet detailing the value of the exchanged goods, (b) the agreement that stamps are commodities and (c) the agreement that fairness requires equality of exchange value in this case. In scientific research, type 2 exploitation is more difficult to judge, as we will see below.

In type 3 exploitation, exploiters do not benefit others authentically. In this form of exploitation an exchange takes place as with type 2. But even though exploiters might give others what they want, the exchange does not genuinely benefit them. For instance, the purchase of heroin might be what buyers want, but they would nevertheless be harmed or degraded by the exchange when judged from a neutral standpoint. The exchange can be fair in terms of type 2 exploitation (e.g. the heroin is sold at market price), but it is nevertheless harmful to the buyer.

The three types of exploitation have one thing in common, namely the failure to benefit others as they deserve. Using a formulation by Robert Mayer (2007, p. 142), we can propose the following definition:

> 'Wrongful exploitation' is a failure to benefit others as some norm of fairness requires.

One important feature of this definition is that it is substantial as opposed to procedural. It appeals to fairness, or at least 'some norm of fairness'. Some critics claim that it is impossible to find a norm of fairness on which everyone will agree.[10] They in turn propose a *procedural* definition of fairness, according to which an exchange is not exploitative if, for example, the agents negotiate the exchange free of coercion and under perfect market conditions. There are two significant problems with such procedural definitions, though. First, it is not necessarily easier to develop and agree on a proper procedure than it is to develop and agree on a norm of fairness. In particular, perfect market conditions almost never hold in practice. Second, on the procedural view, no matter how unfair an exchange may appear to us, it will be impossible, *provided* that the proper procedure was followed, for us to criticize the exchange on the grounds of unfairness. This seems highly unsatisfactory. The proponent of a procedural definition of unfairness might reply that if the proper procedure is followed, the resulting exchange will not only be fair on procedural terms but will also agree with our

[10] See Richard Ashcroft's (2008, pp. 3–6) discussion of what he calls the 'undecidability presumption'.

intuition of fairness. But if that is the case, then we could just as well go with a norm of fairness based on our intuitive sense of what is fair. Hence the argument that a procedural account is superior to a normative one is not clear-cut.

Another important feature of the above definition, for our purposes, is that even consensual and mutually advantageous transactions can be wrongfully exploitative. This is important because many, if not most, scientific research in developing countries is of this sort. For example, consider again poor HIV-positive pregnant women in Africa who participate in trials for medication that is supposed to prevent transmission of the HIV virus to their babies. In these trials half of the women get the experimental drug, the other half a placebo. Testing the experimental medication against a placebo is both cheaper and scientifically more useful than testing it against standard therapy. Critics claim that the researchers are exploiting the women by giving half the group a placebo rather than the standard therapy; a procedure that would be deemed unethical in developed countries. The researchers, on the other hand, point out that these women would not have access to any therapy at all, experimental or standard, if it were not for the trials – and now they stand at least a 50% chance of getting the experimental medication. The women also agreed to participate, knowing that this would give them at least a chance of receiving an effective therapy, which they would not have had otherwise. In short, the participation is consensual and everybody benefits (or at least no one is worse off, apart from the disappointment of raised hopes).

So why is this still a case of wrongful exploitation? It is so because the researchers fail to benefit the women as fairness requires. It is unfair to the women to use a placebo, rather than the standard therapy, as an alternative to the experimental therapy, especially since the research is conducted against the background that the women are poor and lack access to health care. It has to be acknowledged that they are, at the very least, investing time and accepting inconvenience, but 50% of them receive nothing in return. One must therefore ask: 'What do the research participants deserve? What is fair benefit sharing?'

2.4 Benefit Sharing

The debate on exploitation and vulnerability has been going on for as long as the debate on research ethics. The debate on benefit sharing, however, is more recent. *Never Let Me Go* dramatically illustrates the concerns of the more traditional bioethics approach, which focuses on direct harm. In this chapter we are more interested in benefits (although the avoidance of harm must clearly remain the foundation for ethical research). With the rapid internationalization of research (Tangwa 2009, p. S17), even research participants who are not directly harmed or coerced can be exploited, in the sense of not receiving fair benefits.

Not involving human beings in research at all is obviously not an answer. Medical progress relies on scientific research. If nobody agreed to take the latest tuberculosis drug during an experimental phase, none of us would ever get access

to it. If nobody allowed their blood to be sampled for the latest strain of viruses, progress in the development of vaccines would be significantly hampered. People usually contribute to scientific research as altruists – that is, by acting for the benefit and in the interests of others (Scott and Seglow 2007, p. 1) – and do not expect any specific rewards in the form of benefit sharing. This is particularly the case for research which involves minimal risk and requires large numbers of participants, such as genetic research (Williams and Schroeder 2004). It has also been suggested that we have a duty of solidarity with others when it comes to health (Knoppers 2000), a 'duty to facilitate research progress and to provide knowledge that could be crucial to the health of others' (Berg and Chadwick 2001).

However, the potential exploitation of research participants in developing countries has cast doubt on the altruism and the solidarity model in scientific research (Schroeder and Lasen-Diaz 2006). John le Carré's 2001 novel *The Constant Gardener* (made into a film in 2005) held researchers responsible for the exploitation of naive research participants. In an article entitled 'A lot of very greedy people', Le Carré wrote:

> I had not been exploring Big Pharma for more than a couple of days before I was hearing of the frantic recruitment of third world 'volunteers' as cheap guinea pigs. Their role, though they may not ever know this, is to test drugs, not yet approved for testing in the US, which they themselves will never be able to afford even if the tests turn out reasonably safe (Le Carré 2001).

This picture shows a particularly ugly face of scientific research, which has been revealed in, for instance, the Trovan meningitis study in Nigeria (Macklin 2004, p. 99f), the proposed Surfaxin study in Latin America (Macklin 2004, p. 17f), and the child autopsy case in Malawi (Lemmens and Nwabueze 2007; Mfutso-Bengu and Taylor 2002). However, even if clinical trials in a developing country are carried out exactly as they would be in an affluent Northern country, a sense of exploitation can linger in poor settings. 'I have been used like a guinea pig, so how does he just leave me without compensation?' (Shaffer et al. 2006, p. 55) is how a Kenyan research participant reacted to the departure of doctors at the end of a research study.

The difference between showing altruism in scientific research in a developed country and doing so in a developing country is highly significant, as the following shows. The benefits of scientific research are various. For most citizens in affluent countries scientific research leads to

1. Ever increasing numbers of medical interventions to achieve and maintain health tailored to local health needs and, in principle, accessible to all.
2. Increased knowledge about human health made available to citizens through general education or health campaigns.
3. The availability of jobs in a high-tech industry (pharmaceutical research) and various related sectors (e.g. academia), and indirectly the very infrastructure and institutions that make such jobs possible.
4. Profits for commercially oriented research companies and the pharmaceutical production and retail industry (Schroeder 2008; Schroeder and Gefenas 2011, p. 4).

These benefits, largely taken for granted in developed countries, are often not available in developing countries. The further down the list one goes, the more restricted the availability of the benefit, even in affluent countries, but benefit 1, access to medical interventions, is generally available to all. Hence the term 'altruism' is misleading in the context of scientific research in most affluent countries, as those who contribute to research will always benefit at least their immediate communities.

Benefit sharing (or lack thereof) in scientific research becomes a pressing problem when human research participants contribute to research but derive no benefits at all, and in particular no access to successfully tested medical interventions. In a (hypothetical) worst-case scenario, a research participant in Malawi makes a contribution to bringing an intervention to market that is not tailored to her (local) health needs and would never be affordable to her in any case. She will obtain no knowledge or understanding of her own health condition and needs, the drug or related research outcomes. The research is carried out without local infrastructure improvements ('helicopter in and out' research), and all commercial profits derived will stay abroad.

The problematic aspects of this scenario apply whether the research participant is involved in a clinical trial such as the HIV transmission study or donated human biological samples. In either case a contribution to research is made by a member of an impoverished, vulnerable population without any benefit to herself. Such a scenario is impossible in affluent countries, and therefore to expect such altruism or solidarity routinely from research participants in poor settings is not appropriate. It is essential that feasible benefit-sharing frameworks be developed and that they apply both to research participants involved in clinical trials and to those who donate their biological samples.

The meaning of 'benefit sharing', then, is quite simple. Those who contribute to developments in science and technology ought to share in the benefits, so if those benefits are not shared with the contributors to scientific advancement, that advancement is exploitative. For instance, if the traditional knowledge of indigenous peoples is used in commercial applications without any benefit sharing, the indigenous group has been exploited. Likewise, if medical products are not reasonably available in developing countries where their safety was tested, research participants in those countries have been exploited (Hawkins and Emanuel 2008).

Here it is worth repeating why research participants may deserve something in return for their participation that is not due to those who do not take part in research. We are all human beings and, according to the Universal Declaration of Human Rights, all have a right to access to health care (UN 1948, article 25).

When we talk about fair benefits, we are referring to the principle of justice, a principle that comes in many forms. *Justice in exchange* establishes the fairness or equity of transactions. *Distributive justice* deals with the division of existing, scarce resources among qualifying recipients. *Corrective justice* rights a wrong that one has brought upon another, usually through a court declaring a remedy to correct the given injustice. *Retributive justice* establishes which punishment is appropriate for any given crime. (see Fig. 2.1).

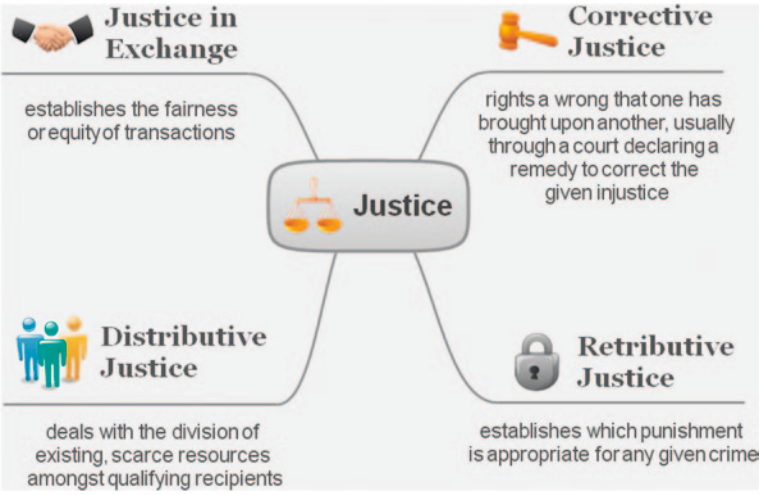

Fig. 2.1 Realms of Justice

According to human rights advocates, lack of access to health care is an injustice (Pogge 2008), and we agree with this assessment. However, as already noted in the introduction (see Chap. 1), this book focuses on the *additional* injustice of unfair exchange. While all human beings have the right of access to health care, a right that has to be resolved through distributive justice mechanisms, it is an *added* injustice to take something from someone without fair benefit sharing. The injustice here is type 2 exploitation, as described above. If no fair exchange occurs, the exploiting party gains disproportionately. Scientific research which uses resources from vulnerable populations in developing countries without providing local access to the resulting benefits, for instance, represents such exploitation.

This understanding of benefit sharing in terms of justice in exchange came to prominence with the adoption of the Convention on Biological Diversity in 1992 and the introduction of post-study obligations in the 2000 Declaration of Helsinki (see Chap. 3).

In many developing countries, research participants and their communities do not derive any of the benefits of scientific research, or do so to a very limited extent. Since it is exploitative to use individuals and communities for the creation of benefits without their receiving any of them, we must find ways to share the benefits of scientific progress in a fair manner with research participants (individuals and their communities).

A number of benefit-sharing schemes have been proposed. Some work on this subject has focused on profit sharing (see, for example, Barclay 2008), but, as the list below indicates, profit sharing is not the only available method of sharing the benefits of scientific research. In fact, while many people seem to associate benefit

sharing with profit sharing, the latter is only a minor component of the former and could be replaced with broader measures to avoid undue inducement (see below) without major difficulties.

The most comprehensive mechanism for the sharing of benefits from research is the access and benefit-sharing agreement in the framework of the Convention on Biological Diversity (CBD) now formalized as the Nagoya Protocol.[11] The protocol itself does not explicitly exclude human genetic materials from its scope, but such materials are already excluded by a prior agreement of the Conference of the Parties to the CBD (see Chap. 3, Sect. 3.2). As a result the Nagoya Protocol does not apply to medical or human genetics research directly.[12] Still, through its reference to human pathogens and relevant WHO regulations (see Chap. 3, Sect. 3.2.5), the Nagoya Protocol, together with the 2011 WHO Pandemic Influenza Pandemic Preparedness Framework (World Health Assembly 2011), could contribute to future discussions of benefit sharing in human medical research (see Chap. 8).

The principle for benefit sharing in the Nagoya Protocol is that

> benefits arising from the utilization of genetic resources as well as subsequent applications and commercialization shall be shared in a fair and equitable way with the Party providing such resources that is the country of origin of such resources or a Party that has acquired the genetic resources in accordance with the Convention. Such sharing shall be upon mutually agreed terms (CBD 2010a, article 5.1).

The protocol includes the following extensive, but not exclusive, list of potential benefits (CBD 2010a, annex):

1. Monetary benefits may include, but not be limited to:
   (a) Access fees/fee per sample collected or otherwise acquired;
   (b) Up-front payments;
   (c) Milestone payments;
   (d) Payment of royalties;
   (e) Licence fees in case of commercialization;
   (f) Special fees to be paid to trust funds supporting conservation and sustainable use of biodiversity;
   (g) Salaries and preferential terms where mutually agreed;

[11] The Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization to the Convention on Biological Diversity (CBD 2010a) was adopted at the tenth meeting of the Conference of the Parties to the CBD on 29 October 2010, in Nagoya, Japan. The access and benefit-sharing scheme formalized in the Nagoya protocol replaced the voluntary Bonn Guidelines on Access to Genetic Resources and the Fair and Equitable Sharing of the Benefits Arising out of their Utilization.

[12] The exclusion of human genetic resources is explicitly stated in the Bonn Guidelines (2002: paragraph 9), but not mentioned in the Nagoya Protocol itself. When the Nagoya Protocol was adopted, it was made clear that 'genetic resources' did not include 'human genetic resources' in decision I/5: 'The Conference of the Parties … [a]grees, bearing in mind decision II/11, paragraph 2, and without prejudice to the further consideration of this issue by the Conference of the Parties serving as the meeting of the Parties to the Protocol, that human genetic resources are not included within the framework of the Protocol' (CBD 2010b).

(h) Research funding;
(i) Joint ventures;
(j) Joint ownership of relevant intellectual property rights.

2. Non-monetary benefits may include, but not be limited to:

(a) Sharing of research and development results;
(b) Collaboration, cooperation and contribution in scientific research and development programmes, particularly biotechnological research activities, where possible in the Party providing genetic resources;
(c) Participation in product development;
(d) Collaboration, cooperation and contribution in education and training;
(e) Admittance to ex situ facilities of genetic resources and to databases;
(f) Transfer to the provider of the genetic resources of knowledge and technology under fair and most favourable terms, including on concessional and preferential terms where agreed, in particular, knowledge and technology that make use of genetic resources, including biotechnology, or that are relevant to the conservation and sustainable utilization of biological diversity;
(g) Strengthening capacities for technology transfer;
(h) Institutional capacity-building;
(i) Human and material resources to strengthen the capacities for the administration and enforcement of access regulations;
(j) Training related to genetic resources with the full participation of countries providing genetic resources, and where possible, in such countries;
(k) Access to scientific information relevant to conservation and sustainable use of biological diversity, including biological inventories and taxonomic studies;
(l) Contributions to the local economy;
(m) Research directed towards priority needs, such as health and food security, taking into account domestic uses of genetic resources in the Party providing genetic resources;
(n) Institutional and professional relationships that can arise from an access and benefit-sharing agreement and subsequent collaborative activities;
(o) Food and livelihood security benefits;
(p) Social recognition;
(q) Joint ownership of relevant intellectual property rights.

Not all of these benefits would be appropriate for benefit sharing in scientific research involving human participants, but the list gives a good idea of the diverse possibilities for the sharing of benefits, far beyond profit sharing.

Since the Nagoya Protocol excludes human genetic resources, there may be other more appropriate mechanisms for sharing the benefits of scientific research in general. More options and legal guidelines are discussed in Chap. 3.

What is important overall is that research participants who currently derive few or no benefits from scientific research should receive fair benefits for their contribution to research. This is a prerogative of justice in exchange. Benefit sharing then requires

the sharing of advantages derived from the use of resources with resource providers in order to achieve justice in exchange. This just exchange should focus particularly on the clear provision of benefits to vulnerable populations who may lack reasonable access to resulting products and services of scientific research. At the same time, the exchange should not *provide unethical inducements*. When research participants receive such benefits as health care or money, or even food, for their participation in research, the question arises whether those benefits constitute unethical or undue inducement, a sort of coercion or some other violation of their autonomy. We will conclude this chapter with a discussion of 'undue inducements'.

2.5 Undue Inducements

Can benefits provided under a benefit-sharing mechanism constitute 'unfair inducement'?[13] Let us return to Kazuo Ishiguro's novel. If Kathy, Ruth and Tommy had been fully informed of the consequences, and been asked as adults whether they wanted to donate their organs, and had then said 'yes', because, say, they had been offered a million dollars in return and three years to spend it, would this have been fair benefit sharing? No, clearly not. But would it be a case of undue inducement? It may seem so, for instance in the light of the warning against undue inducements in CIOMS guideline 7.

> The payments should not be so large … or the medical services so extensive as to induce prospective subjects to consent to participate in the research against their better judgment ('undue inducement') (CIOMS 2002: guideline 7).

On a second look, this example shows one way in which charges of undue inducements fail. The sort of radical organ harvesting practised on Kathy, Ruth and Tommy results in severe illness and ultimately death. Offering them money for their organs and suffering may be considered an additional wrong, but not offering them money does not make their contribution morally acceptable. The moral problem is the immense harm resulting from their contribution, and the issue of payment makes little moral difference.

First of all, as we have already made clear, benefit sharing is hardly ever about profit sharing – that is, about whether a million dollars change hands for a kidney, a liver or other organ. But more importantly, what makes sense for living organ donation or participation in certain clinical trials might not be the best basis for judging which benefits may be appropriate in return for taking part in genetic research or donating a blood sample. In the remainder of this section, we will explain why fear of undue inducement should not be allowed to defeat efforts to achieve fair compensation for research participants. Although the line between undue inducement and appropriate compensation may be a fine one, it should not

[13] This section is based on Arnason and Van Niekerk (2009).

stop researchers and their funders meeting their responsibilities to share benefits with research participants in developing countries.

So what exactly is the problem in the context of scientific research in developing countries? The following four claims capture most of what is considered problematic about inducements.

1. They jeopardize the voluntary nature of informed consent.
2. The research participant might accept a risk that would not otherwise be acceptable.
3. Research participants might participate in research against their better judgement.
4. The entire practice of rewards or inducements is alien to the noble ideals and altruistic intent of medical practice.

We will look at each of these in turn and will argue that not all inducements of any kind and any magnitude are problematic, provided that the research in question is otherwise ethical. We talk about 'inducements' here because that is the word commonly used when this problem is discussed, but what we have in mind is any kind of benefit provided to a research participant to satisfy some norm of fairness. The worry is that even if there is no intention to induce someone to participate in research, the benefits promised might still have the effect of an 'undue inducement'.

The first claim is that inducements can jeopardize the voluntary nature of informed consent. But why should inducements invalidate consent? The idea is that one may get an offer which one just cannot refuse, not because of any threats associated with the offer, but because the offer is so good that one cannot say no. Or one might be under so much pressure to accept the offer because of need (or greed), that it amounts to coercion. Consider, however, a gravely ill patient whose doctor suggests a life-saving operation. The patient might think that he does not have a choice; it is either the operation or death. In the mind of the patient there might be no true alternative to giving consent to the operation. But that does not diminish the patient's autonomy or invalidate his consent. In general, desperate need does not invalidate one's choice. If a person needs to sell his house because of financial problems, it would be wrong to prevent him from doing so. Taking away the choice, or an option, to alleviate a desperate need diminishes freedom rather than increasing it.[14]

The second concern is that the research participant might accept a risk that would not otherwise be acceptable. But the burden of assessing the risk of participating in research does not rest on the research participant alone. Any scientific research involving human participants must be assessed by a research ethics committee.[15] That committee must evaluate the risk-benefit ratio for participation in the research. If the risk-benefit ratio is significantly unfavourable for the research participant, then the study is considered to be unethical and must not be approved. This is one of the fundamental tasks of any ethical review of scientific research. If the risk involved in participating in a study is not acceptable, then the research is

[14] For a more thorough discussion of this argument see Wilkinson and Moore (1997, p. 377).

[15] See paragraph 15 of the Declaration of Helsinki (WMA 2004) and guideline 2 of the CIOMS guidelines (CIOMS 2002).

unethical and should not be conducted. Removing any elements of 'undue inducement' would not make such risky research ethical.

One might object that certain studies cannot get proper ethical review, especially in developing countries, where resources for ethical review are very limited and sometimes even completely absent (Schroeder and Gefenas 2011, pp. 6–7). In such a case the individual research participant has to carry the entire burden of evaluating the risk. But without proper ethical review a study simply should not be carried out. To proceed with it is unethical in itself. One might press this objection further and say that if scientific research is nonetheless to be carried out without proper ethical review, in those cases it would be unethical to offer any benefits that could amount to undue inducements. It is, unfortunately, true that scientific research is carried out in some developing countries without proper ethical review, in disregard of one of the most basic principles of research ethics. There is no purpose, however, in proposing ethical guidelines against inducements for participation in scientific research that is already blatantly unethical. If the researcher does not respect the basic principles of research ethics in the first place, further ethical guidelines are not going to make any difference. (We shall return to the problem of ethics review in developing countries in Chap. 8.)

So to answer the concern that the research participant might be induced to accept a risk which is otherwise unacceptable, we argue that this can only be so with a study that is already unethical because of an unacceptable risk-benefit ratio. It would be unethical to let people volunteer for such a study in any case, and removing 'undue inducements' does not make it any less unethical.

The third concern is that research participants might participate in research against their better judgement. This is a vague objection. It could mean that the inducement effectively invalidates the research participant's consent, but that is the first concern on the list above, and we have already discussed it. Inducing research participants to act against their better judgement might mean that they are induced to take unacceptable risks, but this is the second concern, and we have answered that as well.

Participating in research against one's better judgement might also mean that one does something one would not do otherwise. But this is to miss the point of incentives. Most employed people do things for a monthly pay cheque that they would not do otherwise. Or people might go to a restaurant they would not normally eat at if it offers two meals for the price of one. There is nothing inherently wrong about offering people incentives to do things they would not do otherwise – that is, not in the absence of an incentive.

The claim that research participants might act against their better judgement can also be interpreted as amounting to an empirical claim about human psychology. Large rewards could cloud our judgement: that is, if we are offered large inducements, then our judgement about the risks and benefits might be compromised. As an empirical claim, this requires an empirical answer. There have not been many studies on this topic, but the studies that have been conducted did not find that people became any worse at judging risks when they were offered large rewards for taking them (Bentley and Thacker 2004). The empirical claim that judgement of risk can be compromised by large rewards has therefore not been supported so far.

The fourth concern is that the entire practice of rewards or inducements is alien to the noble ideals and altruistic intent of medical practice. In developed countries, the provision of health care services and the conduct of scientific research are impossible without all sorts of market transactions. It is not clear why research participants ought to be excluded from that. Even if we want to defend the altruistic motivation for participating in research in developed countries, this approach is inappropriate in developing countries, as we have shown. It means that research participants in developing countries would have to carry the risks and burdens of participating in research, without having access to any of its benefits. This is simply unfair, and that is precisely why we need to find ways to design and implement benefit-sharing mechanisms for human research in developing countries.

Even if we accept that the possibility of undue inducements may be a concern, this would primarily be the case where there is a significant possibility of physical harm. One might, for instance, object to the selling of kidneys, not to speak of more radical organ donation, on the grounds that the donors (or, rather, sellers) are likely to ignore the risks when presented with the possibility of considerable financial gain. Although one can live with only one kidney, there are immediate and longer-term medical risks involved in kidney donation. In contrast, genetics research that physically requires nothing more of the research participant than a swab from the mouth involves minimal physical risk. If the tissue samples are also coded, or fully anonymized, then the risk to the research participants is negligible in the vast majority of cases.[16] Where the risk to the research participant is minimal, there can hardly be any issue of undue inducements (bearing in mind that some risks, such as stigmatization, may be difficult to quantify).

2.6 Conclusion

In the context of research in developing countries, benefit sharing is a central concern. As we have seen above, the problem arises when people participate in research without the possibility of deriving any benefits at all. They contribute to research without enjoying the benefits, which are made available to others who did not participate. This state of affairs constitutes an injustice; more precisely, it is a failure of justice in exchange. The research participants exchange their contribution for little or nothing at all. This state of affairs is *exploitative*. It is aggravated,

[16] The non-physical risks involved in these studies (in which only tissue samples and health data are collected from the subjects) include violations of privacy, such as sensitive information about the research subject finding its way to employers, insurers or law enforcement; stigmatization, for example research on an illness in a certain group leading to an association of the group with that illness; and distress or other psychological harm, when test results reveal, for instance, a significant medical problem or false paternity. Coding and, in particular, the anonymization of samples and data reduce most of these risks significantly. The collection of tissue samples and health data for databases, as well as the re-use of samples and data for purposes other than those originally intended, adds further risks and complications.

and indeed much more likely to occur, when the research participants are *vulnerable*. To correct the injustice, and thereby to prevent exploitation and protect the vulnerable, *benefit sharing* is required. Benefits must be shared with the research participants, if they would otherwise have no access to the products resulting from the research, or, in our case, if they lack access to health care. There is a worry, although we have argued that it is a misplaced worry, that such benefits may constitute *undue inducements* to participate in such research. This is how the concepts of vulnerability, exploitation, benefit sharing and undue inducements are related in the context of research involving human participants in developing countries.

The concepts of vulnerability and exploitation are both vague and morally charged. We should be careful about their use. We have suggested a relatively precise definition of 'vulnerability' in the hope of both clarifying the concept and avoiding its over-extension, which we have observed in recent years. According to our definition, to be vulnerable means to face a significant probability of incurring an identifiable harm, while substantially lacking the ability or means to protect oneself. When we talk about vulnerable research participants we need to be clear about what (sort of) harm they are vulnerable to. We have pointed out that one particularly important marker for harm in research is the research participants' lack of access to the benefits of research. This type of harm relates directly to exploitation. Following Robert Mayer's account of exploitation, we have defined 'wrongful exploitation' as a failure to benefit others as some norm of fairness requires. Wrongful exploitation is particularly wrongful when it involves a failure to benefit vulnerable people.

From these considerations, we have developed a normative concept of benefit sharing: those who contribute to developments in science and technology ought to share in the benefits. The worry that such benefits may constitute undue inducements to participate in the research cannot be ignored, but in research that involves minimal risk, this concern is largely misplaced and should not be used to avoid benefit sharing. The next chapter discusses some of the benefit-sharing options available.

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Chapter 3
Legal Frameworks for Benefit Sharing: From Biodiversity to Human Genomics

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Abstract The philosophical principle behind benefit sharing is simple. Those who contribute to scientific research ought to share in its benefits. This is a matter of justice. If benefit sharing does not take place, exploitation may have occurred. The term "benefit sharing" was popularized by the Convention on Biological Diversity (CBD), which was adopted at the Earth Summit in Rio in 1992. This chapter provides an overview of the key international instruments and guidelines that make provisions for benefit sharing. Legal instruments are often categorized as to whether they are binding or non-binding. With the exception of the CBD itself most benefit sharing provisions are non-binding. All other key instruments presented here – the Declaration of Helsinki, the CIOMS International Ethical Guidelines for Biomedical Research Involving Human Subjects, the HUGO Ethics Committee's Statement on Benefit Sharing, and UNESCO's Universal Declaration on the Human Genome and Human Rights, and Universal Declaration on Bioethics and Human Rights – are non-binding. Yet even when the law is clear and binding, compliance is not usually easily achieved. The access and benefit-sharing

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provisions of the CBD have been incorporated into national law in many countries world-wide, but success stories are still hard to find. It is hoped that the 2010 Nagoya Protocol to the CBD will address this shortfall for non-human biological resources. An example from Brazilian national legislation, which is discussed here, is encouraging in terms of achieving benefit sharing with those providing access to human biological resources. However at the global level, benefit sharing for human biological resources remains an unresolved and often contentious issue.

Keywords Benefit sharing • Post-study access • Convention on Biological Diversity • Declaration of Helsinki

3.1 Introduction

As benefit sharing is a relatively new philosophical and legal concept, it is important to understand its use in legal frameworks. This chapter provides an overview of the key international instruments and guidelines that make provision for benefit sharing. By doing so, the chapter serves as the basis for discussions of how current challenges in benefit sharing can be addressed.

'Benefit sharing' is a technical term that was popularized by the Convention on Biological Diversity (CBD) adopted at the 1992 Earth Summit in Rio de Janeiro, Brazil. The CBD was the first international treaty to recognize that the conservation of biodiversity is a 'common concern of humankind'. Today, its 193 parties cooperate to stop the destruction of biodiversity by attempting to ensure its sustainable use, and by requiring users of this natural wealth to share the benefits with those who provide access to biological resources. The resources covered by the CBD are animals, plants, micro-organisms and traditional knowledge.

The concept of benefit sharing is less established in the area of human biological/genetic research. It has made a cautious entry into international debates through the Declaration of Helsinki (2000), which aims to act against exploitation by prescribing a duty to assure research participants of access to successfully tested drugs or services after a clinical trial has been concluded. This approach avoids a situation in which research participants in developing countries have no access to a medical product they helped bring to market. The most recent revision of the Declaration of Helsinki (WMA 2008) has opened the possibility of benefit sharing through routes other than access to successfully tested interventions.

This chapter provides an outline of the main benefit-sharing provisions of the following instruments:

- The Convention on Biological Diversity (CBD 1992)
- The Declaration of Helsinki (WMA 2008)
- The Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines for Biomedical Research Involving Human Subjects (CIOMS 2002)

- The HUGO Ethics Committee's Statement on Benefit Sharing (2000a)
- The UN Educational, Scientific and Cultural Organization's (UNESCO's) Universal Declaration on the Human Genome and Human Rights (UNESCO 1997) and Universal Declaration on Bioethics and Human Rights (UNESCO 2005)
- The Brazilian national guidelines on post-trial obligations (National Health Council 1996, 1997, 1999, 2000, 2008) as an example of national law.

It is generally understood that ethical guidelines have no legal status, but it is important to note that in terms of the current legal literature, ethics guidelines are regarded as customary international law. To qualify as customary international law, an ethics guideline must be supported by the consistency and generality of being widely accepted as a practice (Brownlie 2003: 7). David Fidler's observation that government funding of national and international clinical trials reveals some general and consistent state practices which support the basic principles of ethical codes such as the Declaration of Helsinki and CIOMS guidelines supports this point (Fidler 2001: 326). In practice, however, there is still a considerable vacuum when it comes to the power and bite of international as well as national ethics guidelines. It has been argued that global bioethics has to contend with a regulatory crisis in terms of 'the persisting national public law silences and health inequities, especially in low-to middle income countries' (Merali et al. 2004: 692). Complications are often indicated by abstentions and protests by a number of states in the face of a practice that is followed by others (Brownlie 2003: 8). Most pertinent to the topic of this book is the withdrawal of the United States of America (USA) from the benefit-sharing clauses of the Declaration of Helsinki (more in Chap. 8). And, of course, persistent objectors cannot be made to comply with voluntary guidelines, which raises issues relating to the binding nature of customary international law.

We shall therefore start our discussion with the one international instrument on benefit sharing that is legally binding, namely the CBD.

3.2 The Convention on Biological Diversity

3.2.1 History

Until the late twentieth century, access to biological resources was generally regarded as a free-for-all (Schroeder and Pogge 2009). Typically, botanists or researchers from the North would obtain biological samples from countries in the South and use this biodiversity in scientific studies and product development. They were thus able to take resources out of their natural habitats without obtaining consent from, or sharing benefits with, states or local communities.

From the early 1970s, this approach to resource use across international borders was criticized heavily by activists around the world, Vandana Shiva (1991: 257), Pat Mooney (1969), Gurdial Singh Nijar (1996) and Tewolde Berhan Gebre Egziabher (1994) being among the most prominent. They criticized not only the

exploitative nature of taking resources without returning benefits, but also the related injustice of obtaining monopoly control over foreign resources through the international patent system.

For example, the neem tree has been used in traditional medicine in India, Sri Lanka and Burma for hundreds of years. Yet an international agrochemical business filed for a patent based on the neem tree's medicinal properties, involving samples from India, without disclosing this history of prior use. In 2005, Vandana Shiva and her supporters famously won a ten-year legal battle to revoke the patent (Sheridan 2005).

Before concerns over such exploitative use of developing country resources led to the adoption of the CBD, a different kind of benefit sharing was envisaged. Instead of relying on a common-heritage principle, which could be (and often was) equated with a free-for-all – first come, first served – the United Nations brokered two treaties about resource use, which specified that all of humanity had to benefit. Both the UN Agreement Governing the Activities of States on the Moon and Other Celestial Bodies (1979) and the UN Convention on the Law of the Sea (1982) made the principle of a fair common heritage explicit. These treaties declared that the seabed and the ocean floor, including its subsoil, as well as the surface and the subsurface of the moon, were not to become the property of any state, organization or individual. Instead, the use of their potential resources was to be carried out so as to benefit humankind as a whole.

However, in the 1990s the USA's Clinton administration undermined the common-heritage approach to resource use with a superseding agreement that opened seabed resources on a first-come-first-served basis without benefit-sharing requirements.[1] It is in this context that the CBD was adopted.

3.2.2 Objectives

The main response of the international community to concerns about the exploitation of developing country resources is the CBD, adopted at the Earth Summit in Rio de Janeiro, Brazil, in 1992 (CBD 1992). The adoption of the CBD is one of the great policy success stories of the twentieth century. After exceptionally wide processes of consultation, 193 parties have ratified this broad and participatory convention. Only Andorra, the Holy See, South Sudan and, notably, the USA have not, as at the time of writing.[2]

The CBD aims to achieve three objectives:

- The conservation of biological diversity
- The sustainable use of its components
- The fair and equitable sharing of the benefits arising out of the utilization of genetic resources.

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[1] This revision and the Clinton administration's role in imposing it are discussed in Pogge (2008: 131–132).

[2] http://www.cbd.int/convention/parties/list/

These three goals are closely interlinked and form a 'virtuous circle' of mutually reinforcing elements. The CBD regards the conservation of biological diversity as a common concern of humankind. Biodiversity is important in securing food supplies, sources of medicines and energy, and ecological balance, among other things. Yet the twentieth century witnessed the disappearance of species at 50 to 100 times the natural rate (European Commission 2010), and this may accelerate to 1,000 or 10,000 times by 2020 (Shanahan and Masood 2004). The threat is partly related to the increase in human numbers and partly to the 18-fold increase in industrial production over the past century.

In order to counter this threat and enable access to biodiversity for sustainable use (the second CBD goal), benefit sharing is essential. It is one thing to look after a resource for the general benefit of humankind, and quite another to do so when one stands to benefit oneself. By giving a large stake in the benefits that flow from natural resources to their custodians, one may hope to preserve the planet's biodiversity better than otherwise. Besides, in the context of increasing criticism from developing countries regarding the exploitation of their biological resources, it is much more likely that access for use will be granted if developing countries' concerns are addressed satisfactorily through access and benefit-sharing agreements. Consequently, the third principle of the CBD – the fair and equitable sharing of benefits from the use of genetic resources – is instrumental in achieving the first two goals.

According to the preamble to the CBD, biological resources fall under the national sovereignty of states. The sovereignty of states over their (natural) resources is fully affirmed in articles 2 and 15. Initially it was unclear whether human genetic resources were to be covered by the convention, with some negotiators in favour and some against their inclusion. This uncertainty was resolved in 1995, when the parties to the convention agreed to exclude human genetic resources from its scope.[3] Now specifically included in the CBD is 'any material of plant, animal, microbial or other origin containing functional units of heredity … of actual or potential value' (CBD 1992: article 2). Traditional knowledge associated with biodiversity is covered through article 8(j), which is the only provision in the CBD recognizing traditional knowledge. This provision was included as an acknowledgement that cultural practices of biodiversity conservation are embedded in the day-to-day life of indigenous and local peoples and are intrinsically linked to their communities. Article 8(j) emphasizes the need for parties to the CBD to initiate projects on capacity-building with indigenous and local communities.

As noted above, plants, animals, micro-organisms and traditional knowledge fall under the decision-making powers of national governments. Based on the sovereignty principle, each CBD party agrees to develop and implement national laws to govern access and benefit sharing with regard to non-human biological resources.

[3] 'The Conference of the Parties … [r]eaffirms that human genetic resources are not included within the framework of the Convention' (CBD COP Decision II/11, paragraph 2, http://www.cbd.int/decision/cop/?id=7084).

3.2.3 Access and Benefit-Sharing Articles

Three main CBD articles cover access and benefit sharing provisions: articles 8(j), 15 and 16.

Article 8(j):

> Each contracting Party shall, as far as possible and as appropriate … respect, preserve and maintain knowledge, innovations and practices of indigenous and local communities embodying traditional lifestyles relevant for the conservation and sustainable use of biological diversity and promote their wider application with the approval and involvement of the holders of such knowledge, innovations and practices and encourage the equitable sharing of the benefits arising from the utilization of such knowledge, innovations and practices (CBD 1992).

The CBD thus aligns with international efforts to strengthen the rights of indigenous peoples. Beyond genetic resources, the convention covers knowledge, innovations and practices of indigenous and local communities embodying traditional lifestyles. The provisions for prior informed consent and mutually agreed terms are especially important in the context of accessing traditional knowledge and will be described further below.

Article 15. Access to Genetic Resources:

1. Recognizing the sovereign rights of States over their natural resources, the authority to determine access to genetic resources rests with the national governments ….
2. Each Contracting Party shall endeavour to create conditions to facilitate access to genetic resources for environmentally sound uses by other Contracting Parties ….
4. Access, where granted, shall be on *mutually agreed terms* ….
5. Access to genetic resources shall be subject to *prior informed consent* …. [emphasis added] (CBD 1992)

The essence of benefit sharing in terms of the CBD is thus captured in two legal expressions: ‘prior informed consent’ and ‘mutually agreed terms’.

Prior informed consent needs to be obtained before any non-human genetic resource is accessed, according to the CBD, but its prominence in the literature is greatest in the context of traditional knowledge. Since the early 1990s, the concept of prior informed consent has been employed systematically in connection with indigenous peoples’ rights of self-determination. However, to date no definition of the term has been agreed internationally (Haira 2006: 6). The following definition is adapted from the medical context:

> Prior informed consent is the voluntary, uncoerced decision made by a subgroup that legitimately represents an indigenous community, on the basis of adequate information and deliberation, to accept rather than reject some proposed course of action that will affect the community (Schroeder 2009: 31).

Essentially, obtaining prior informed consent requires four steps (Schroeder 2009: 31):

- Legitimate authorization to consent
- Full disclosure of all the relevant information

- Adequate comprehension of the disclosed information on the part of the representatives
- A voluntary decision by the representatives to agree to the proposed course of action.

Table 3.1 sets out the main legal instruments and guidelines requiring prior informed consent from indigenous communities.

Mutually agreed terms – that is, agreement on the terms for the use of genetic resources and subsequent benefit sharing – must be reached between the users and the providers of genetic resources. The CBD does not give exact specifications or suggestions. Instead, article 15(7) requires that parties to the CBD

> shall take legislative, administrative or policy measures … with the aim of sharing in a fair and equitable way the results of research and development and the benefits arising from the commercial and other utilization of genetic resources with the Contracting Party providing such resources. Such sharing shall be upon mutually agreed terms (CBD 1992).

Given the wide variety of possible exchanges and mutually agreed terms, any imposition of specific systems would be too rigid. Mutually agreed terms could, for instance, also cover transfer of technology. However, given the importance of this topic to development and fair benefit sharing, it is also provided for in a separate article:

Article 16. Access to and Transfer of Technology:

> 1. Each Contracting Party … undertakes … to provide and/or facilitate access for and transfer to other Contracting Parties of technologies that are relevant to the conservation and sustainable use of biological diversity ….
> 2. Access to and transfer of technology … to developing countries shall be provided and/or facilitated under fair and most favourable terms…
> 5. The Contracting Parties, recognizing that patents and other intellectual property rights may have an influence on the implementation of this Convention, shall cooperate in this regard subject to national legislation and international law in order to ensure that such rights are supportive of and do not run counter to its objectives (CBD 1992).

Article 16 raises a long-standing problem for the CBD, namely the potential incompatibility of benefit sharing with the international intellectual property rights system, in particular the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement).

Table 3.1 International Legal Instruments and Guidelines Requiring Prior Informed Consent from Indigenous Communities

1989	Convention 169 on Indigenous and Tribal Peoples (International Labour Organization), entered into force 5 September 1991
1992	Convention on Biological Diversity (CBD), entered into force 29 December 1993
2002	Bonn Guidelines on Access to Genetic Resources and Fair and Equitable Sharing of the Benefits Arising out of their Utilization (Bonn Guidelines, non-binding)
2007	United Nations Declaration on the Rights of Indigenous People (non-binding)

3.2.4 TRIPS and the CBD

The TRIPS Agreement was negotiated in the 1986-94 Uruguay Round of multilateral trade negotiations by members of the World Trade Organization (WTO) and took effect on 1 January 1995. Essentially, it demands that standard types of intellectual property (trade marks, designs, copyrights, patents, plant breeder rights, geographic indications, trade secrets and circuit layout rights) be recognized and effectively protected through national law, whether the intellectual property right holder is a resident citizen or a foreigner within the country concerned. The aim of TRIPS was to provide strong intellectual property rights protection for innovators across the globe. Developed countries had one year to effect the necessary changes to national laws, developing countries and transition economies were given five years, and least-developed countries were allowed eleven years. In 2001, a further exemption was given, namely that least-developed countries had until 2016 to effect intellectual property legislation for pharmaceutical patents.

Benefit sharing is one of the main areas of contention between the CBD and the TRIPS Agreement. This was discussed in November 2001 at a ministerial conference of WTO members in Qatar. The resulting Doha Development Agenda required the Council for TRIPS to review the relationship between the two instruments (WTO n.d.: paragraph 19). The views of WTO members have differed significantly when it comes to assessing this relationship. The analysis from the WTO Secretariat (WTO 2006) identified four different groupings into which these views can be classified.

The main non-signatory to the CBD, the USA, sees no conflict between the TRIPS Agreement and the CBD and argues that the two are mutually supportive, provided national measures are taken to implement their mandates.[4]

Other countries, including India, South Africa, Brazil and Kenya, argue that there is an inherent conflict between the two, and that there is a need to review the TRIPS Agreement so as to remove conflicting provisions.[5] These countries have demanded that the TRIPS Agreement be amended to reflect the spirit and commitments of the CBD. In order to achieve this, it is recommended that disclosure of source and country of origin of any biological resource or traditional knowledge used in an invention be made mandatory while a patent application is being filed. The disclosure suggestion has been debated for more than ten years at the WTO, and strong opposition from a group of industrialized countries led by the USA has not diminished.

Between these polar positions on the relationship between the CBD and TRIPS are views that see no inherent conflict between the two, but believe that some form

[4] United States (IP/C/W/434). See also proposals from Australia, (IP/C/W/310) and Japan (IP/C/W/236). (Sources referred to in these notes with numbers commencing 'IP/C' are working documents of the Council for TRIPS.)

[5] African Group (IP/C/W/404); Kenya (IP/C/M/47); Brazil, India, Pakistan, Peru, Thailand and Venezuela (IP/C/W/429/Rev.1); India (IP/C/W/198).

of international action is required to achieve compliance with the CBD. Within this broad group, however, there are different views regarding prescriptions: one subgroup suggests action in relation to the intellectual property rights system, while the other has not committed itself to the position that TRIPS needs to be amended to promote the objectives of the CBD.[6]

The following box gives examples of measures taken by developing countries to protect their traditional knowledge and non-human genetic resources while the discussions at the WTO continue.

Box 3.1 Proactive Measures by Developing Countries to Protect their Traditional Knowledge and Biodiversity

Peru has established a National Antibiopiracy Commission (NAC) to identify, prevent and avoid acts of biopiracy, which involve biological resources of Peruvian origin and traditional knowledge of the indigenous peoples of Peru. The NAC has focused on identifying potential cases of biopiracy, as part of which it has looked for pending patent applications or patents granted abroad that seek to protect inventions apparently obtained from or developed on the basis of key biological resources including the traditional knowledge of Peru's indigenous peoples. Initially six biological resources of Peruvian origin are being monitored.

Similarly, India's Council of Scientific and Industrial Research (CSIR) has launched a Traditional Knowledge Digital Library (TKDL) project to codify and disclose writings in ancient Sanskrit scriptures from as far back as the twelfth century BC. With respect to TKDL Unani, a team of 30 Unani experts, information technology experts and scientists is currently working to develop a database of previously disclosed Unani literature. The project was launched in 2002. After completing 36,000 formulations in five international languages, significant work has been carried out on the Ayurvedic system of traditional medicine. This initiative is likely to be expanded to the Siddha system of traditional medicine in South Asia.

In China a traditional Chinese medicine (TCM) patent database has been launched. It is in both Chinese and English. The Chinese language version contains more than 12,124 deeply indexed records of TCM patent literature with 32,603 TCM formulas. The English language database is a demo version that was prepared for and demonstrated at the third session of the committee of WIPO, containing 1,761 records of TCM patent literature in English, with 4,177 TCM formulas. (For measures taken by Brazil, see conclusion of this chapter).

Source: Research and Information System for Developing Countries (2007).

[6] Australia(IP/C/M/48); Canada(IP/C/M/47); New Zealand (IP/C/M/47); Andean community (IP/C/M/37/Add.1, paragraph 231); Brazil(IP/C/W/228); China(IP/C/M/47, paragraph 57).

A number of CBD articles in addition to those described above support the convention's access and benefit-sharing provisions. Article 17 encourages the exchange of information from all publicly available sources, with an emphasis on the needs of developing countries. Such exchange may include information from technical, scientific and socio-economic research, training and surveying programmes, as well as the exchange of information on traditional knowledge. Article 18 further elaborates on possibilities for cooperation. It emphasizes the need for joint research programmes and joint ventures for the development of technologies. Article 19 focuses on biotechnology and requires contracting parties to adopt legislation to facilitate effective participation in biotechnological research activities by the providers of resources, in particular if those are based in developing countries. These articles include the proviso that access to and transfer of technology to the providers of genetic resources must be granted on mutually agreed terms. Finally, provisions concerning financial resources and financial mechanisms are dealt with in articles 20 and 21, which aim to ensure that developed countries supply part of the financial resources necessary for developing countries to fulfil their CBD-related obligations.

As the above discussion suggests, since 1993, when the CBD entered into force, its access and benefit-sharing provisions have gone largely unimplemented, cases of alleged 'biopiracy' of genetic resources (and associated traditional knowledge) have grown in number and the need for legal certainty and transparency has become more evident.

3.2.5 Nagoya Protocol

The most promising development on benefit sharing as governed through the CBD occurred in 2010 with the adoption of the Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization. The protocol was adopted on 29 October 2010 at the tenth meeting of the Conference of the Parties to the CBD (CBD 2010).[7] Adoption was achieved through a consensus decision among 193 countries, following some six years of intense, complex and fractious talks – which frequently pitted developed countries against developing countries, and providers of genetic resources against users of those resources.

The objective of the new treaty, reflecting the principal goals of the CBD itself, is the fair and equitable sharing of the benefits arising from the utilization of genetic resources, thereby contributing to the conservation and sustainable use of biodiversity.

At the core of the Nagoya Protocol is a set of interrelated provisions on access, benefit sharing and compliance (the so-called ABCs of access and benefit sharing).

[7] For the text of the decision adopting the protocol, see http://www.cbd.int/decision/cop/?id=12267.

Access measures are envisioned at the domestic level to create legal certainty, clarity and transparency, provide fair and non-arbitrary rules and procedures, create conditions to promote biodiversity-related research, and provide for the issuing of permits or the equivalent when access is granted.

Benefit-sharing measures focus on the fair and equitable sharing of benefits (both monetary and non-monetary) arising from the utilization of genetic resources, subject to mutually agreed terms. The protocol's compliance obligations require parties to take measures providing that genetic resources utilized within their jurisdictions have been accessed in accordance with prior informed consent and that mutually agreed terms have been established as required with the other party.

Another key requirement is for parties to take measures to monitor and enhance transparency regarding the utilization of genetic resources, including through designated checkpoints, and collecting information at any stage of research, development, innovation, pre-commercialization or commercialization. A range of specific responses are outlined, including cooperation in cases of alleged violation, opportunities for legal recourse and access to justice.

The Nagoya Protocol serves as both a regulatory instrument over genetic resources and an enabling instrument facilitating national governance, international cooperation and the augmentation of indigenous research capacities. These twin characteristics contributed to the complexity of its negotiation and render the protocol quite unique.

The protocol includes, as a key element, traditional knowledge associated with genetic resources, which is anchored in provisions on access, benefit sharing and compliance. Significantly, and despite some protracted resistance during much of the negotiation, the protocol's preamble references the UN Declaration on the Rights of Indigenous Peoples. In addition, one of the forward-looking aspects of the protocol is a new provision (i.e., one not found in the CBD) requiring each party to the instrument to take measures to ensure (for those indigenous and local communities that have established rights to grant access to genetic resources) the prior informed consent of such communities.[8]

According to Graham Dutfield (2011), article 10, under the heading 'Global Multilateral Benefit-Sharing Mechanism', will be the key to the success of the protocol.

> Parties shall consider the need for and modalities of a global multilateral benefit sharing mechanism to address the fair and equitable sharing of benefits derived from the utilization of genetic resources and traditional knowledge associated with genetic resources that occur in transboundary situations or for which it is not possible to grant or obtain prior informed consent. The benefits shared by users of genetic resources and traditional

[8] Since the protocol's adoption, a group of indigenous organizations has sent a submission to the executive secretary of the CBD secretariat outlining 'substantive and procedural injustices' (http://www.ubcic.bc.ca/files/PDF/NagoyaProtocol_IGCJointSubmission_060111.pdf) – for instance, the fact that 'excessive reliance on national legislation is likely to lead to serious abuses, in light of the history of violations' and the lack of 'full and effective participation' by indigenous representatives during the negotiations.

> knowledge associated with genetic resources through this mechanism shall be used to support the conservation of biological diversity and the sustainable use of its components globally (CBD 2010: 8).

Particularly noteworthy for the purposes of this book is the fact that the Nagoya Protocol refers to human genetic resources, namely human pathogens, in the introduction: '*Mindful* of the International Health Regulations (2005) of the World Health Organization (WHO 2007) and the importance of ensuring access to human pathogens for public health preparedness and response purposes' (CBD 2010: 3).[9] We shall return to this topic in Chaps. 5 and 8.

Likewise, it is significant that 'access to affordable treatments by those in need, especially in developing countries' is included in article 8 among the special considerations that must be observed when regulating access to genetic resources.

These provisions in the Nagoya Protocol represent the first cautious appearance of human genetic resources in the CBD since their exclusion in 1995. We shall now move on to the main international ethics guidelines that contain benefit sharing provisions.

3.3 Declaration of Helsinki

3.3.1 History

In 1926, doctors from several countries formed the Association Professionnelle Internationale des Médecins, an organization aimed at discussing the problems of practising medicine across borders. The organization suspended operations during the Second World War after achieving a membership of 23 countries. During the war, the British Medical Association became the new focal point for doctors who wanted to compare medical practice in different countries. Two conferences held in London initiated plans to form a new organization, which was to be called the World Medical Association (WMA). In 1947, the First General Assembly of the WMA was held in Paris, with founder members from 27 countries. In particular the atrocities committed in the name of medical research during the Second World War had prompted a renewed focus on collaboration across borders.

Work amongst the country delegations of the WMA culminated in the adoption of the Declaration of Helsinki.[10] The declaration is part of the international regime that governs medical research involving humans. Of course, other international

[9] This development, the mentioning of human pathogens in the Nagoya Protocol, marks a departure from the approach otherwise taken in CBD legislation, which since 1995 excludes material of human origin.

[10] It should be noted that prior to the Second World War, no international ethical standards existed to regulate research on human subjects. National standards were also scarce. For a detailed look at the history and development of the Declaration of Helsinki see Human and Fluss (2001).

and regional bodies have formulated guidelines based on the ethical principles that are contained in the declaration.[11] However, today the WMA represents physicians from 97 countries.[12] Hence, of those organizations currently involved in the formulation of guidelines, the WMA has by far the most reasonable claim to be taken seriously.[13]

Since its adoption, the Declaration of Helsinki has undergone a number of revision processes, the latest in October 2008. The current declaration directly addresses issues related to benefit sharing and post-study access to any products developed. The relevant paragraphs are discussed below.

3.3.2 Benefit Sharing in the Declaration of Helsinki

It is evident from the earlier discussion of the definition of benefit sharing (see Chap. 2) and the above account of the CBD that different types of benefit-sharing frameworks are currently in place. The prevailing approach to benefit sharing for providers of human biological resources such as DNA or blood samples is the prescription of post-study obligations. Essentially, these obligations (previously known as post-trial obligations) describe a duty to provide human research participants with access to a proven beneficial health care intervention after a study has been concluded. This means that in return for contributing to medical research, the research participants are meant to obtain access to any resulting products or interventions as a form of benefit sharing. Post-study obligations were first introduced in the Declaration of Helsinki in 2000, when the WMA General Assembly in Edinburgh adopted paragraph 30.

> At the conclusion of the study, every patient entered into the study should be assured of access to the best proven prophylactic, diagnostic and therapeutic methods identified by the study (WMA 2004b).

This early formulation of post-study obligations was restricted to patients and, by implication, to clinical trials involving volunteers in need of treatment. As a result, healthy volunteers who enrolled in clinical trials, as well as donors of biological materials, were excluded from benefit sharing. Both the limited scope and the rigidity of this approach were criticized (Schroeder 2008). For instance, if post-study access to a drug is the only way to avoid the exploitation of research participants, those who take part in studies that do not lead to the marketing of a

[11] See Andanda (2006: 60–61) for a detailed discussion of this regime.

[12] http://www.wma.net/en/60about/10members/20memberlist/index.html

[13] We agree with Udo Schuklenk on this claim. When comparing the Declaration of Helsinki with other influential guidelines, Schuklenk argues that 'an international consensus among smallish operators with impressive names is not a sufficient reason to do away with the authority of the WMA, which represents more members of the medical profession in one single country, let alone across the world, than the rest of the organisations and institutions mentioned … combined'. See Schuklenk (2004: 196).

drug (perhaps because it was found to be ineffective) are excluded from receiving any benefits. (We shall return to this in Chap. 8.)

In 2004, the WMA's General Assembly in Tokyo added a note of clarification on paragraph 30, which opened the way for other benefits instead of post-study access to successfully tested interventions.

> The WMA hereby reaffirms its position that it is necessary during the study planning process to identify post-trial access by study participants to prophylactic, diagnostic and therapeutic procedures identified as beneficial in the study or access to other appropriate care (WMA 2004a).

To reduce the rigidity of post-study access to successfully tested drugs, the phrase 'access to other appropriate care' was added. At the same time, the term 'patients' was changed to 'study participants', to allow for the inclusion of healthy volunteers. However, the term 'trial' was retained, thus limiting benefit sharing to those taking part in clinical trials. This changed in the 2008 declaration, adopted in Seoul, articles 14, 17 and 33 of which relate to benefit sharing.

Paragraph 14 of the 2008 version of the Declaration of Helsinki deals directly with the issue of broadening the scope of beneficiaries from clinical trial participants to study subjects and is therefore much clearer.

> The protocol should describe arrangements for post-study access by study subjects to interventions identified as beneficial in the study or access to other appropriate care or benefits.

It follows, then, that all medical research involving human subjects which needs approval from an ethics review body should describe, in its study protocol, post-study access to successfully tested interventions or other benefits. This implies that donors of biological samples could be included among the possible beneficiaries, as the scope is not limited to 'trials'.

However, such a formulation gives rise to a practical concern, namely that compliance with it could mean that *any* arrangement for post-study access would suffice, as long as it was detailed in the study protocol. Even the sentence 'There are no arrangements for post-study access,' could arguably be regarded as compliance in that, as long as study participants and ethics review bodies know that there is no provision for post-study access, sufficient compliance with paragraph 14 would have been achieved. Hence this obligation could be called informational rather than substantial, in which case it does not satisfy the wider demand for benefit sharing.

At first sight, this concern seems to be mitigated through paragraph 33 of the declaration.

> At the conclusion of the study, patients entered into the study are entitled to … share any benefits that result from it, for example, access to interventions identified as beneficial in the study or to other appropriate care or benefits (WMA 2008).

This paragraph implies that post-study obligations are a substantial rather than an informational demand for all medical research involving existing *patients*. However, that still seems to leave healthy volunteers and donors of human biological samples potentially excluded from any post-study benefits, as benefit sharing is only envisaged with patients, rather than all participants in medical research.

This would seem contrary to the spirit of benefit sharing as understood through the CBD, which aims to reward 'resource providers' in particular in order to avoid concerns about exploitation.

Here one needs to remind oneself of the purpose of benefit sharing for human genetic resources. As noted in Chap. 2's section on exploitation, formal benefit-sharing frameworks such as the CBD or the Declaration of Helsinki are only required where participants contribute to research but derive no benefits at all. In developed countries, medical research is covered by what we term a fair-exchange model. Human sample donors contribute to research and in return have access to increased medical interventions, tailored to local health needs, to achieve and maintain their health. Where this model fails, as it does in developing countries where the health infrastructure does not support broad access to health care, other solutions have to be found. In this regard, one could argue that such solutions are only required for vulnerable populations – and this is the approach taken by the Declaration of Helsinki through paragraph 17.

> Medical research involving a disadvantaged or vulnerable population or community is only justified if … there is a reasonable likelihood that this population or community stands to benefit from the results of the research (WMA 2008).

This means that when ethics review bodies are presented with proposed studies on vulnerable groups which do not fall under the category of 'patients', they still need to ensure that the research population or the wider community stand to benefit from the research. Hence, a study protocol which notes that there is no provision for post-study access or alternative benefits would be unethical, according to paragraph 17 (rather than paragraph 14), if it involved vulnerable populations. It is evident that the latest declaration is therefore comprehensive in its benefit-sharing clauses, in providing (somewhat intricate) frameworks on which arguments in favour of benefit sharing with donors of biological samples can be based.

3.3.3 Feedback on the Outcomes of Research

The 2008 Declaration of Helsinki includes one other new aspect which could be subsumed under benefit sharing, namely the requirement to provide feedback to participants.

The right to feedback on the outcomes of the research has been provided for in paragraph 33 of the declaration.

> At the conclusion of the study, patients entered into the study are entitled to be informed about the outcome of the study … (WMA 2008).

Failure to give feedback on the results or outcomes of the research (whether positive or negative) has been mentioned as one point of dissatisfaction with collaborative research in developing countries. An interview with the Kenyan National Ethics Review Committee revealed the level of concern. 'The individual [research participant] will never get to know what happened to the samples or

Table 3.2 Main Guidelines on Benefit Sharing with Human Research Participants

Guidelines	Issuing Body	Issued	Benefit Sharing
International Covenant on Economic, Social and Cultural Rights	UN General Assembly	1966	Article 15(b)
Declaration of Helsinki	WMA	1964/ 2008	Articles 14, 17 and 33
International Ethical Guidelines for Biomedical Research Involving Human Subjects	CIOMS	1982/ 2002	Guidelines 5(12), 10, 21
Convention on Human Rights and Biomedicine	Council of Europe	1997	Preamble
Statement on Benefit Sharing	HUGO Ethics Committee	2000	Entire document
Universal Declaration on Bioethics and Human Rights	UNESCO	2005	Article 15
International Declaration on Human Genetic Data	UNESCO	2003	Article 19
Operational Guidelines for Ethics Committees that Review Biomedical Research	WHO	2000	Guideline 6.2.3.10

what became of the whole study [emphasis added].'[14] This benefit-sharing provision of the Declaration of Helsinki could therefore address some of the concerns and dissatisfaction raised in the context of collaborative research in developing countries (Table 3.2).

3.4 CIOMS International Ethical Guidelines for Biomedical Research Involving Human Subjects

The Council for International Organizations of Medical Sciences (CIOMS) was established jointly by the WHO and UNESCO in 1949. It is an international, non-governmental organization which works on a non-profit basis. Its International Ethical Guidelines for Biomedical Research Involving Human Subjects is one of the most frequently quoted guideline documents on research ethics in the academic literature.

The current document (CIOMS 2002) consists of general ethics principles and 21 guidelines. The text was designed to assist in the definition of national research ethics policies, with particular emphasis on developing countries. In contrast to the Declaration of Helsinki, the CIOMS guidelines include a helpful and extensive commentary.

[14] Interview with a member of the Kenya Medical Research Institute (KEMRI) Ethical Review Committee quoted in Andanda and Cook Lucas (2007).

The guidelines acknowledge the central role and relevance of human rights instruments in the application of ethics to research on human subjects. They are non-binding and may therefore seem 'aspirational' in so far as they aim to draw the attention of sponsors, investigators and ethical review committees to the ethical implementation of research protocols. However, this impression may be countered with the claim made earlier in this chapter, namely that such guidelines can be regarded as customary international law. Scholars have lauded the CIOMS guidelines for encompassing the three basic principles of respect, beneficence and justice (King 1998: 187). The principle most relevant here is that of justice, which as King has proposed 'should be reflected … in the distribution of the benefits and burdens' (King 1998: 187). Responding to the demands of justice, the CIOMS guidelines give broad support for benefit sharing.

> In general, the research project should leave low-resource countries or communities better off than previously or, at least, no worse off. It should be responsive to their health needs and priorities in that any product developed is made reasonably available to them, and as far as possible leave the population in a better position to obtain effective health care and protect its own health (CIOMS 2002: 18).

The CIOMS guidelines that deal directly with benefit sharing are guideline 5 (paragraph 12), which focuses on the information given to research participants about post-study access to interventions; guideline 10, which focuses on post-study access to beneficial interventions, as well as responsiveness to local health needs; and guideline 21, which focuses on the provision of services that are necessary for making a beneficial intervention/product available. These guidelines are discussed below.

3.4.1 Post-study Access to Beneficial Interventions

Guidelines 5 and 10 are discussed together as they both deal with the issue of post-study obligations. Guideline 5 (paragraph 12) states that as part of the informed consent process, participants should be informed

> whether, when and how any products or interventions proven by the research to be safe and effective will be made available to subjects after they have completed their participation in the research, and whether they will be expected to pay for them; …

Guideline 10 deals with research in populations and communities with limited resources.

> Before undertaking research in a population or community with limited resources, the sponsor and the investigator must make every effort to ensure that:
>
> - the research is responsive to the health needs and the priorities of the population or community in which it is to be carried out; and
> - any intervention or product developed, or knowledge generated, will be made reasonably available for the benefit of that population or community.

This guideline should be read together with the commentary to guideline 12, which focuses on equity in the distribution of burdens and benefits. It emphasizes that 'no group should be deprived of its fair share of the benefits of research, short-term or long-term', and it notes that 'such benefits include the direct benefits of participation as well as the benefits of the new knowledge that the research is designed to yield'. In this regard, proponents of benefit sharing have argued that the

> establishment of clinical trial infrastructure, including training of local investigators … which would translate into much-needed research on diseases specific to developing countries at local level … should not be discounted (Tomossy and Ford 2006: 29).

These considerations of what may be considered as benefits in terms of post-study obligations are significant in the context of resource-poor countries where most patients 'may have only limited or even no access to healthcare' and may not have the voice to negotiate benefits (Zong 2008: 183).

Zong argues that 'there is an increasing consensus that, in principle, participants in developing countries should continue to receive benefits originating from the studies in which they enlisted beyond the research period'. She emphasizes that the consensus is mainly based on the ethical principles of beneficence and justice as reciprocity (Zong 2008: 188). However, Zong also observes that how far the obligations of beneficence and reciprocity extend to participants in developing countries remains contentious as there is no agreement on whether or not post-study provision should be mandatory in practice (Zong 2008: 189). The situation is made more complex by the fact that ethics committees and institutional review boards face dilemmas due to lack of consensus among guidelines. In addition, Phase I clinical trials, epidemiological studies, and research focusing on basic scientific knowledge do not easily translate into the development of new medicines and vaccines suitable for post-study provision (Zong 2008: 189; see also Nuffield Council on Bioethics 2005).

The commentary on CIOMS guideline 10 specifically mentions sponsors' responsibility to ensure post-study availability, but acknowledges the limitations of this in relation to studies which aim at generating scientific knowledge as opposed to a commercial product. In such cases, however, there should still be an assurance that the scientific knowledge developed will be used for the population's benefit. This means that the concept of 'benefits' should not be limited to access to commercial products, but rather extended to include all knowledge that is gained from research.

Further commentary on guideline 10 provides that it is unethical to conduct research in a particular country or community if there is good reason to believe that the intervention will not be made available to the local population. This provision is in line with the requirement that research be responsive to the needs – in particular, the health needs – of the participants and their communities. However, 'a rare exception' is made in relation to, for example, studies which are designed to obtain preliminary evidence that a drug or a class of drugs has a beneficial effect in the treatment of a disease that occurs only in regions with extremely limited resources, and which could not be carried out reasonably well in more developed communities. In such cases, the commentary indicates that 'research may be justified ethically even if there is no plan in place to make a product available to

the population of the host country or community at the conclusion of the preliminary phase of its development'.

The CIOMS guidelines focus on benefits to the community/country rather than just those for individual participants (CIOMS 2002: guideline 5, paragraph 11; guideline 10). This approach has caused uneasiness among stakeholders who find reference to 'community' rather nebulous, and the obligation that is imposed on sponsors too stringent. For instance, Bruce Innis, vice-president of clinical research and development at GlaxoSmithKline, argues:

> Our first concern is to be sure we have a clear contract with each volunteer in the study … This is a balanced discussion between potential volunteers being solicited and investigators who want to conduct the trial, the authorities who authorize the trial and the sponsors, whether they be academic institutions or private parties, developers and manufacturers. The community part is much more nebulous (Wolinsky 2006: 672).

3.4.2 Provision of Services that are Necessary for Making a Beneficial Intervention or Product Reasonably Available

The third of the CIOMS guidelines to deal with benefit sharing is guideline 21, concerning the ethical obligations of external sponsors to provide health-care services.

> External sponsors are ethically obliged to ensure the availability of:
>
> - services that are a necessary part of the commitment of a sponsor to make a beneficial intervention or product developed as a result of the research reasonably available to the population or community concerned.

The commentary on guideline 21 acknowledges that sponsors are not obliged to provide health care services beyond those necessary for the conduct of the research, and that such services are not a necessary part of their commitment to make available a beneficial intervention or product developed as a result of the research. However it emphasizes that it is morally praiseworthy to do so, and gives examples such as treating cases of an infectious disease contracted during a trial of a vaccine designed to provide immunity to that disease, or providing treatment of incidental conditions unrelated to the study.

The rather stringent requirements on sponsors of research have been criticized as too demanding (Emanuel et al. 2004: 935), perhaps surprisingly also by stakeholders from developing countries such as Uganda. Julius Ecuru, from the Uganda National Council for Science and Technology in Kampala, commented as follows on the Declaration of Helsinki and CIOMS:

> I think they are overly stringent when it comes to the obligation of the sponsors to provide the best proven care and research product to the host communities during and after the research. I could take that as a desirable standard, but not an absolute moral or ethical requirement without which research would not be allowed to proceed (Wolinsky 2006: 672).

Neither the Declaration of Helsinki nor CIOMS focuses especially on the providers of human genetic resources. There is, however, one document that does: the HUGO Ethics Committee Statement on Benefit Sharing.

3.5 HUGO Ethics Committee Statement on Benefit Sharing

The Human Genome Organisation (HUGO) is an international scientific body which aims at encouraging public debate and providing information and advice on the scientific, ethical, social, legal and commercial implications of human genome projects.

In its Statement on Benefit Sharing (2000a), the HUGO Ethics Committee made six recommendations:

1) that all humanity share in, and have access to, the benefits of genetic research.
2) that benefits not be limited to those individuals who participated in such research.
3) that there be prior discussion with groups or communities on the issue of benefit-sharing.
4) that even in the absence of profits, immediate health benefits as determined by community needs could be provided.
5) that at a minimum, all research participants should receive information about general research outcomes and an indication of appreciation.
6) that profit-making entities dedicate a percentage (e.g. 1% - 3%) of their annual net profit to healthcare infrastructure and/or to humanitarian efforts (HUGO Ethics Committee 2000a).

These recommendations are ambitious and far-reaching. Stating that all humanity should have access to the benefits of genetic research and that benefits should not be limited to the individuals who participate in research implies a very broad view of benefit sharing. This is also indicated in the suggestion that some health benefits ought to be provided even if the relevant research does not generate any profits, and that a percentage of annual net profits should be donated. As discussed in Chap. 2, benefit sharing can be derived from concepts of justice in exchange or distributive justice.[15] In this book we focus on the former, but it is worth noting that the HUGO Ethics Committee Statement on Benefit Sharing advocates the latter.

It is also worth noting that the requirement to share information with research participants and provide feedback on results was included in the HUGO statement as early as 2000. Such a requirement was only included in the Declaration of Helsinki in 2008 and is not discussed at all in the CIOMS guidelines. The requirement of prior discussion with groups or communities on the issue of benefit sharing shows some kinship with the CBD, as it implies both the obtaining of prior informed consent and the negotiation of mutually agreed terms, albeit less formally expressed.

[15] For a detailed discussion of these two concepts of justice in the context of benefit sharing, see Schroeder and Pogge (2009: 274).

While other guidelines and instruments that are outlined in this chapter *include* benefit sharing, the entire HUGO statement is focused on this issue. The statement is therefore very helpful in mapping out benefit-sharing options for the use of human biological resources. Most importantly, it provides useful discussions on extending the concept of benefit beyond therapeutic benefits for those participating in clinical trials. This is useful because, as mentioned above, many research settings are not linked to the clinical trial context. The case of the Majengo slum sex workers (see Chap. 5) is a good example. The Hugo statement is thus viewed by many scholars as a clear statement on benefit sharing in the context of human biological resources (see HUGO Ethics Committee 2000b; Knoppers et al. 2000; Weijer 2000).

3.5.1 Benefits and Beneficiaries

The concepts of property ownership and communities as beneficiaries are both controversial when used in the context of human biological resources. In this regard the HUGO statement's recognition that the human genome is a part of the common heritage of humanity that should benefit all humanity could be used to support an argument *against* benefit sharing for human biological resources. A plausible argument here would be that there is no sense of individual ownership in such resources that can be used to support a basis for sharing benefits with the donors. The unique situation is that

> increased knowledge concerning the molecular basis of human disease is in itself a benefit and this knowledge could, at a later stage, result in new therapeutic modalities. Progress in diagnostics and the prevention or treatment of disease is another benefit to society at large, as well as to patients and their families (Chadwick and Berg 2001: 319).

In the same vein, arguments have been put forward against benefit sharing with genetic sample donors, especially when it comes to the pharmaceutical industry funding genetic research.

Intuitively, sharing of economic benefits seems morally desirable, but it is also difficult to identify any specific reason why the pharmaceutical industry should be obliged to share their revenue from genomic research. The populations, families and individuals whose samples have formed the basis for new products and revenue, have not themselves done anything to make their samples 'valuable'. 'If anything, their samples have become valuable because of work conducted by scientists' (Chadwick and Berg 2001: 320).

Why, then, one could ask, has the CBD been adopted by 193 state parties? It demands exactly that – the sharing of benefits with resource (e.g. plant DNA) providers. However, here one could argue that beneficiaries (such as indigenous communities or governments) are rewarded for their contribution to resource management. Resource providers are at the same time owners, managers and/or custodians of genetic resources (IISD and Stratos Inc. 2007: 14). One cannot say the same about the donors of human genetic resources. In addition, the traditional

knowledge associated with non-human genetic resources has been passed down from one generation to the next, implying efforts of education.

The possibility of private ownership in bodily materials has not been developed, particularly in legal frameworks and systems, where a clear dichotomy exists between the ownership of human tissues and human tissue-related inventions, which are usually at stake when it comes to sharing benefits from human biological resources (Andanda 2008).

The dichotomy is based on the well-established legal principle that 'a thing which the legal system does not recognise as susceptible to ownership (a thing which is *res extra commercium*) will not be deemed an asset in that legal system' (Weisman 1993). The situation is compounded by the law's, particularly patent law's, 'traditional "proprietary" distinction between law and nature' (Pottage 1998: 749). Consequently, the settled legal position is that the object of a patent is to protect a technical disclosure rather than the proprietary rights of physical objects such as human tissues, organs or parts thereof. As a consequence, the property ownership argument has not found favour as a basis for benefit sharing with biological resource donors and there is currently no agreement within philosophy and law on how to move forward (Simm 2007a: 11).

In addition, Chadwick and Berg have identified two practical problems associated with sharing economic benefits with human resource donors. First, it takes a long time for a viable product to emerge and the beneficiaries for such products may not easily be reached at that stage. This problem, however, applies equally to benefit sharing in the context of the CBD. Second, benefit sharing could be seen as an attempt to buy people off, so they argue that the standard approach in research ethics, namely to protect individuals from harm, should not be replaced by a benefit-sharing model (Chadwick and Berg 2001: 320). This ethical argument *against* benefit sharing with the donors of biological resources is intriguing. We have already discussed the problem of undue inducement (see Chap. 2) and shall return to it in a later chapter (see Chap. 8).

It is interesting to note here, however, that the recommendation that all humanity share in and have access to the benefits of genetic research can be used to discredit the property argument as a basis for benefit sharing. The logical argument in this regard could then be: if all humanity shares in such resources, then there is no basis for the individual resource donors to lay claim to the benefits just because *their* resources have been used. A problem arises when one discusses the potential for exploitation, of course. In this context, one has to ask whether the act of donating samples does not entitle donors to share benefits on the basis of 'justice in exchange', assuming benefits are derived to which they have no access.

It may be argued that the HUGO statement can be used to support benefit sharing based on the notions of common property and distributive justice.[16] This approach might work in developed countries, where most people have access to a

[16] See a further explanation of the two notions in part 3.6 of this chapter, particularly where article 12(a) of UNESCO's Universal Declaration on the Human Genome and Human Rights (UNESCO 1997) is discussed.

health care system through which the envisaged benefits to the community would be channelled. However, there would be a practical problem in developing countries, where 'patients may have only limited or no access to healthcare' (Zong 2008: 188). Channelling benefits through the regular health care system in developing countries has therefore been argued not to be a viable option.

The HUGO statement puts forward some valuable considerations that could be used to address these problems.

> In the case of profit-making endeavours, the general distribution of benefits should be the donation of a percentage of the net profits (after taxes) to the health care infrastructure or for vaccines, tests, drugs, and treatments, or, to local, national and international humanitarian efforts (HUGO Ethics Committee 2000a).

It also recommends that benefits should not be limited to the individuals who participated in the research, thus emphasizing the principle of solidarity as a basis for sharing benefits. This principle is applied in contexts of group solidarity, such as participants in research, or among those who share genes, or by region, tribe or disease group.

The principle of solidarity is identified in communitarian discourses and is appropriate when focusing on a limited community or population. However, the approach can be difficult to reconcile with the focus on justice in exchange (see Chap. 2), which the HUGO statement also recognizes, terming it 'compensatory justice'. One example of the tension between the two is that

> benefit sharing as a compensation for voluntarily accepted risks necessarily excludes individuals and communities who would be included in the case of a solidarity-based benefit-sharing arrangement (Simm 2007b).

According to the HUGO statement, compensatory justice seems to be satisfied with 'the possibility of reimbursement for an individual's time, inconvenience and expenses (if any)' (HUGO Ethics Committee 2000a). The focus on community also applies, according to the statement, in cases where donors of an unusual gene benefit those with another disorder. Here, benefit sharing should also be independent of participation in research. The statement therefore, while mentioning compensatory justice, seems to be much keener on the principle of solidarity.[17]

3.6 UNESCO's Universal Declaration on the Human Genome and Human Rights (1997) and Universal Declaration on Bioethics and Human Rights (2005)

UNESCO was established on 16 November 1945. Its mission is to contribute to the building of peace, the eradication of poverty, sustainable development and intercultural dialogue through education, the sciences, culture, communication and

[17] For a detailed analysis of the concept of solidarity in the context of benefit sharing see Simm (2006).

information (UNESCO n.d.). Standard-setting is one of the organization's main constitutional functions. In this regard, the declarations adopted by UNESCO's General Conference promulgate principles and norms that are intended to inspire the action of member states in specific fields of activity (UNESCO 2007).

The declarations are legal instruments, promulgated in accordance with the procedure provided for under article IV, paragraph 4, of UNESCO's constitution (UNESCO 1945). It is important to note, however, that UNESCO's declarations are not legally binding as international law. This is evident from article 38(1) of the Statute of the International Court of Justice, which defines the scope of international law to include the following:

a. international conventions, whether general or particular, establishing rules expressly recognized by the contesting states;
b. international custom, as evidence of a general practice accepted as law;
c. the general principles of law recognized by civilized nations;
d. … judicial decisions and the teachings of the most highly qualified publicists of the various nations, as subsidiary means for the determination of rules of law (ICJ n.d.).

Faunce has argued, however, that 'such declarations can come to be accepted as representing international customary law if sufficient states implement them with the sense of being obliged to do so' (Faunce 2005), as we noted earlier.

The two declarations that are relevant to this chapter are the Universal Declaration on the Human Genome and Human Rights, adopted by the General Conference of UNESCO at its 29th session in 1997, and the Universal Declaration on Bioethics and Human Rights, adopted by the General Conference at its 33rd session in October 2005.

The specific articles in these declarations which address the issue of benefit sharing are outlined below.

3.6.1 Universal Declaration on the Human Genome and Human Rights

Article 12(a) of the 1997 declaration seems to embrace the idea of sharing benefits on the basis of common property and distributive justice.

> Benefits from advances in biology, genetics and medicine, concerning the human genome, *shall be made available to all, with due regard for the dignity and human rights of each individual* [emphasis added] (UNESCO 1997).

This article implies that benefits from advances concerning the human genome are considered common property and as such should be made available to all. The additional point that there should be due regard for the dignity and human rights of each individual brings the notion of distributive justice into play. This means that, apart from considering all human beings to be beneficiaries of such advances, each individual's needs ought to be considered in turn on the basis of the principle of distributive justice.

Article 19(a)(iii) puts the obligation of making benefits available into an international context.

> In the framework of international co-operation with developing countries, states should seek to encourage measures enabling … developing countries to benefit from the achievements of scientific and technological research so that their use in favour of economic and social progress can be to the benefit of all … (UNESCO 1997)

3.6.2 Universal Declaration on Bioethics and Human Rights

The adoption of this declaration in 2005 generated a lot of debate from critics who argued that it had not been preceded by adequate consultation of stakeholders and that public comment had not been solicited (Macpherson 2007).

One of the aims of the declaration, as stated in article 2(f), is

> to promote equitable access to medical, scientific and technological developments as well as the greatest possible flow and the rapid sharing of knowledge concerning those developments and the sharing of benefits, with particular attention to the needs of developing countries … (UNESCO 2005)

Article 15(1) advocates sharing of the benefits of research within the international community, but emphasizes the need to share benefits with developing countries. It further suggests forms that benefits could take.

> Benefits resulting from any scientific research and its applications should be shared with society as a whole and within the international community, in particular with developing countries. In giving effect to this principle, benefits may take any of the following forms:
>
> (a) special and sustainable assistance to, and acknowledgement of, the persons and groups that have taken part in the research;
> (b) access to quality health care;
> (c) provision of new diagnostic and therapeutic modalities or products stemming from research;
> (d) support for health services;
> (e) access to scientific and technological knowledge;
> (f) capacity-building facilities for research purposes;
> (g) other forms of benefit consistent with the principles set out in this Declaration.

The article has been criticized for neglecting 'to address the unique duties of profit-driven sponsors or the challenges to identifying or sharing benefits in resource-poor nations' (Macpherson 2007: 589). This criticism does not, however, take into account the nature of the declaration and the role of UNESCO, which do not warrant the inclusion of such details in the article. Stakeholders are left free to determine how to deal with specific issues that they may encounter in different situations. At the same time the article does provide some guidance on what can be considered benefits.

Article 21(4) is particularly relevant to negotiating benefit sharing in transnational collaborative research. It provides that 'when negotiating a research agreement, terms for collaboration and agreement on the benefits of research should be established with equal participation by those party to the negotiation' (UNESCO 2005).

3.7 Brazilian National Guidelines on Post-trial Obligations

In addition to the international guidelines outlined above, some countries (e.g. Brazil, Uganda and India) have introduced binding national law on benefit sharing with human research participants. The Brazilian legal provisions on post-trial obligations are described here as an example of such national measures.

3.7.1 Brazil's National Health Council

In 1996, the Brazilian National Health Council issued a resolution (No.196/96), which emphasized the importance of post-study obligations. According to this resolution, research undertaken on Brazilian subjects *must* result in benefits for them.

> Research involving human subjects, regardless of the field of knowledge, must … ensure the research subjects the benefits resulting from the research project, in terms of social return, access to procedures, products or research agents … (National Health Council 1996: article III.3(p))

Through this resolution, the Brazilian government imposes a substantial obligation to provide post-study access to drugs and other successfully tested medical interventions. It was initially unclear on whom the obligation rested, but this was clarified later (see below).

The resolution also requires research involving human subjects

> to guarantee that, whenever possible, research in communities is translated into benefits whose effects continue to be felt after the research is concluded. The project must analyze the needs of each of the members of the community and existing differences among them, and make clear how such differences will be respected … (National Health Council 1996: article III.3(m))

Such research must also

> guarantee the individuals and communities where the research was undertaken a return on the benefits obtained in the research. When it is really beneficial to foster or encourage changes in practices or behaviors in the interest of a community, the research protocol must include, whenever possible, provisions to communicate such benefits to the individuals and/or communities … (National Health Council 1996: article III.3(n))

Section IV of the resolution, which sets out the terms of the freely given and informed consent to be obtained from research subjects, states that they must be informed of

> any foreseeable risks or discomfort to the subject, as well as benefits that might reasonably be expected, associated with participation in the research … (National Health Council 1996: article IV.1(a))

One could assume here that the term 'benefits' includes post-study benefits, but this is not explicit. An explanation of potential benefits (e.g. of a therapeutic or diagnostic nature) is, however, always part of an informed consent process. In addition, the resolution requires research subjects to be informed about

> medical follow up and care to be provided to the subjects of research, as well as the identity of those responsible for such actions … (National Health Council 1996: article IV.2(d)).

Again however, this is not explicitly linked to post-study access to successful medical interventions, given that some trials include medical follow-up or care as part of the research.

A year later, the National Health Council issued a supplementary resolution (No.251/97), which focuses on new pharmaceutical products, medicines, vaccines and diagnostic tests. This 1997 resolution clarifies who should meet the obligation for post-study access.

> Access to the medicine being tested must be assured by the sponsor or by the institution, researcher, or promoter, if there is no sponsor, in the event its superiority to the conventional treatment is proven (National Health Council 1997: article IV.1(m)).

Brazilian legislation is very clear about benefit sharing. Research sponsors (or other specified groups) have an obligation to provide Brazilian research participants with post-study access to drugs which were tested on research subjects in Brazil (assuming, of course, that the results of the trials confirmed their safety and efficacy). The more general demands in the 1996 resolution – that there should be a return of benefits to communities where research takes place, covering issues drawn as broadly as 'social return, access to procedures, products or research agents' (National Health Council 1996: article III.3(p)) and 'changes in practices or behaviours' (National Health Council 1996: article III.3(n)) – which also considers people's different needs, mean that these more general benefit-sharing obligations are due not only to individual research participants but to the wider community as well.

Since then the National Health Council has issued two more resolutions which are relevant here, Resolution No. 292/99 and Resolution No. 304/00.

Resolution 292/99 (National Health Council 1999) covers research with foreign cooperation. According to article II, it is mandatory for any research involving foreign collaborators

> II.1 – to prove the Brazilian participation and to identify the co-responsible national researchers and institutions; and
> II.2 – to set forth the responsibilities, rights and obligations through an agreement of the parts involved [in the research] (National Health Council 1999: article II).

The burden and benefits of research involving foreign cooperation must be distributed fairly, according to article IV, and details must be described in protocols for submission to ethical review. One could say that the resolution sets a broad requirement for equal partnership, as opposed to narrow benefit sharing, after foreign research has been concluded.

Following on from this requirement, Resolution 404/2008 issued in 2008[18] pronounces most clearly on post-study obligations by noting the following:

[18] Thanks to Bruno Schlemper Junior for providing an up-date on Brazilian national legislation to DS.

> Regarding the access to health care: In the end of the study, all the participating patients must have been ensured the access to the best proven prophylactic, diagnostic and therapeutic methods identified by the study (National Health Council 2008).

Resolution 304/00, issued in 2000 (National Health Council 2000), covers research involving indigenous peoples. Combining requirements in the CBD about free, prior informed consent from local and indigenous communities with the mechanisms available through ethics review, Article IV of this resolution requires research protocols to describe the following items:

> (1) a commitment to obtain the consent of the communities involved and a description of the process of obtaining this consent;
> (2) a description of the process of obtaining and recording the Terms of Free and Enlightened Consent, demonstrating the adequacy [of the process] to the cultural and linguistic particularities of those involved (Albert 2005: 167).

However, instead of combining free prior and informed consent with strict requirements for benefit sharing that may arise from the utilization of resources (often involving patenting), the Brazilian National Health Council opted to forbid patenting in research involving indigenous populations.

> It will be considered ethically unacceptable to patent, by somebody else, chemical products and biological material of any kind, obtained from researches with indigenous peoples (National Health Council 2000: article III(4)).

In this way, the Brazilian government pre-empts the difficulties described above about making the CBD compatible with the TRIPS Agreement by forbidding any patenting at all.

3.8 Conclusion

On the basis of this chapter one might argue that benefit sharing for human genetic resources is an under-regulated area. Legal documents are often categorized as to whether they are binding or non-binding. On such a simplified appraisal, only the CBD (1992) and the Brazilian government's national guidelines on post-trial obligations (National Health Council 1996, 1997, 1999, 2000, 2008) fall into the binding category. All other key legal instruments presented in this chapter – the Declaration of Helsinki (WMA 2008), the CIOMS International Ethical Guidelines for Biomedical Research Involving Human Subjects (2002), the HUGO Ethics Committee's Statement on Benefit Sharing (2000a), UNESCO's Universal Declaration on the Human Genome and Human Rights (1997) and the same organization's Universal Declaration on Bioethics and Human Rights (2005) – are non-binding.

As we have seen, however, international ethics guidelines are regarded as customary international law when they have been used generally and consistently in support of prescribed practices. For example, the practice of obtaining informed consent prior to involvement in medical research is widely accepted on the basis of non-binding ethical guidelines.

What is important is *clarity* in law, whether in binding conventions or in customary international law. In this respect, the clarifications and additions regarding post-study access that have been provided in the Declaration of Helsinki since 2000 are commendable. The rigidity of insisting on post-trial access to drugs and services (as in the 2000 version) considerably limited the potential for benefit sharing. In particular for the donors of genetic samples, the chances of receiving access to a successfully tested product were minimal, given the vagaries of medical research and the limited possibility that any specific research would lead to a marketed product.

Yet even when the law is clear, compliance is not easily achieved. It is here, one hopes, that the Nagoya Protocol has significantly enhanced the CBD, at least for non-human genetic resources. Requiring greater legal certainty and transparency on benefit sharing for providers and users of such resources was one of its main aims (CBD 2010: 1). To realize this aim, the protocol requires all parties to ensure, within their jurisdictions, that users of genetic resources comply with the CBD. While many parties have already adopted national legislation to govern access and benefit sharing for non-human genetic resources, the following example from Brazil shows that a tightening up of procedures and follow-up on compliance may be necessary.

Brazil implemented a comprehensive biodiversity law in 2001, nine years after the Earth Summit in Rio de Janeiro. Yet, from 2002 to 2009, the relevant authority obtained only 33 applications to access genetic resources (of which 15 were renewals) and two applications to access traditional knowledge associated with genetic resources (Kleba 2011). Only when the Brazilian authorities started tracking the use of genetic resources through the application of patents or the registration of new drugs did the extent of non-compliance become obvious. This tracking, combined with the imposition of fines and other penalties, had an almost immediate effect. In 2010 alone, more than a hundred new applications to access genetic resources were filed with the relevant authority (Kleba 2011). One would hope that the Nagoya Protocol leads to similar approaches and successes in other countries, especially biodiversity-rich ones. Whilst the example from Brazil is encouraging in terms of achieving benefit sharing for access to non-human resources at least in the medium term, benefit sharing for human resources is less promising.

More detailed legal and practical challenges will become clearer in the next two chapters, which review a number of benefit sharing cases that have come to international attention.

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Chapter 4
Sharing Traditional Knowledge: Who benefits? Cases from India, Nigeria, Mexico and South Africa

Julie Cook Lucas, Doris Schroeder, Roger Chennells, Sachin Chaturvedi and Dafna Feinholz

Abstract Benefit sharing is a relatively new area in international law, given that the Convention on Biological Diversity (CBD) was only adopted in 1992. However, the history of formal benefit-sharing agreements between the users and the providers of traditional knowledge goes back beyond the adoption of the CBD. This chapter outlines indigenous peoples' rights in the context of access to plants, animals, micro-organisms and associated traditional knowledge, and discusses four paradigm cases: The Kani people (India); Niprisan (Nigeria); the International Cooperative Biodiversity Group project (Mexico), and the San/*Hoodia* case (southern Africa). These cases straddle the historical boundary between unregulated and regulated access to non-human biological resources, and are thus highly instructive in terms of lessons learned, best practice and emerging policy challenges for the access and benefit sharing regime of the CBD.

Keywords Benefit sharing • Traditional knowledge • Indigenous peoples Kani • Niprisan • Maya ICBG • San-*Hoodia*

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4.1 Introduction

Benefit sharing is a relatively new area in international law, given that the Convention on Biological Diversity (CBD) was only adopted in 1992. It is essential to consider the earliest, most important cases of benefit sharing in order to provide examples of good practice and identify common concerns.

The best-researched and best-documented cases to date focus on benefit sharing for access to traditional knowledge. This chapter therefore begins with a short reminder of indigenous peoples' rights in this context before proceeding to outline four paradigm cases: the Kani case (India), the Niprisan case (Nigeria), the International Cooperative Biodiversity Group case (Mexico) and finally the *Hoodia* case (southern Africa). Viewing these cases through the lens of CBD legal requirements for access and benefit sharing reveals a range of emerging policy challenges, which will be outlined.

We shall summarize concerns and examples of best practice emerging from the above cases, in preparation for the subsequent chapters, in which we suggest ways forward for benefit sharing involving human biological samples.

4.2 Traditional Knowledge and Benefit Sharing

It is uncontroversial to assert that the right of property forms an accepted part of international law. Most property rights depend for their enforceability on the status and reach of prevailing international law, as well as the local or domestic laws of the holders of such rights. However, until the late twentieth century, the development of international law and practice effectively excluded the previously silent constituency known as 'indigenous peoples'. Since the early 1970s the profile of the indigenous peoples' movement has risen as an increasingly vocal constituency serious about articulating and protecting their distinct rights *inter alia* to culture and intellectual property (Hodgson 2002: 1040).[1] In the subsequent three decades particular rights of indigenous peoples have emerged and crystallized.[2]

The cosmology largely shared by indigenous peoples clashes squarely with that of the dominant Western states across a number of fracture lines. At the heart of

[1] According to Berlin and Berlin (2004: 482), 'The Barbados Conference of 1971 was crucial to the increased concerns of the international community on the nature of indigenous peoples' problems.'

[2] Before the long-awaited UN Declaration on the Rights of Indigenous Peoples was adopted on 13 September 2007, the only substantive international law on the distinctive rights of indigenous peoples was the International Labour Organization Convention 169 of 1989, Article 15 of which requires signatory states to safeguard indigenous peoples' rights to natural resources, while Article 13(1) requires states to respect the 'collective' aspects of indigenous peoples' relationship to their lands. As discussed in Chap. 3, the Nagoya Protocol to the CBD makes specific reference to the UN Declaration on the Rights of Indigenous Peoples.

the conflict are different notions of how the world should be and, in particular, the degree to which humankind should exploit nature in the interests of economic growth. The relationships between intellectual property, biogenetic resources and traditional knowledge have become 'politicised' (Dutfield 2004), with dividing lines drawn between governments, non-governmental organizations (NGOs) and traditional advocates on a number of terrains.[3] The most important of these terrains for our purposes are the United Nations Convention on Biological Diversity (1992), the Bonn Guidelines on Access to Genetic Resources and Fair and Equitable Sharing of the Benefits Arising Out of their Utilization (Bonn Guidelines 2002), the Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization (CBD 2010) and the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPs agreement) (1994).[4]

The CBD has been described in detail in Chap. 3. Article 8(j) (CBD 1992) is the most important source of rights for indigenous peoples in the convention, requiring state contracting parties to:

1. respect, preserve and maintain knowledge, innovation and practices of indigenous and local communities embodying traditional lifestyles relevant for the conservation and sustainable use of biological diversity,
2. promote the wider application with the approval and involvement of the holders of such knowledge, innovations and practices, and
3. encourage the equitable sharing of the benefits arising from the utilization of such knowledge, innovations and practices.

Article 15 of the CBD (1992) is explicit regarding rights and access to non-human genetic resources. It recognizes the sovereignty of states over their natural resources, and provides that access to these resources shall be subject to the prior informed consent of the provider state, as well as based upon mutually agreed terms in order to ensure the sharing of benefits arising from the commercial or other utilization of such resources. Some indigenous activists strongly criticize the fact that the CBD places sovereignty over biological resources in the hands of states, rather than in those of the indigenous peoples, whose rights under Article 8(j) are far more vague (Harry 2005).

In 2002 the CBD contracting parties operationalized the above provisions by adopting the Bonn Guidelines, which were designed to assist parties in developing overall access and benefit-sharing (ABS) strategies, and to help them when establishing legislation and policy measures. The emphasis of the Bonn Guidelines is

[3] Other early important agreements are the 1976 International Convention on Economic, Social and Cultural Rights, which provides that state parties to the covenant 'recognize the right of everyone to enjoy the benefits of scientific progress and its applications', the International Undertaking on Plant Genetic Resources for Food and Agriculture (1983), later superseded by the International Treaty on Plant Genetic Resources for Food and Agriculture (2001), and the UPOV convention (International Convention for the Protection of New Varieties of Plants 1991).

[4] The TRIPS agreement is administered by the World Trade Organization (WTO).

on the obligation upon *users* to seek *prior informed consent* from *providers*, *prior* to access and benefit-sharing measures. These guidelines were adopted unanimously by 180 countries, which gives them an indisputable authority as evidence of international will. In August 2002 this international will was reinforced by the World Summit on Sustainable Development, which called on all countries to negotiate an 'international ABS regime to promote … the fair and equitable sharing of benefits arising out of the utilization of genetic resources' (UN 2002: Resolution 2: Plan of Implementation, para 44(o)), as recalled in the Preamble to the Nagoya Protocol. Indigenous critics again pointed out that indigenous peoples' rights remained vulnerable, being subject to the national sovereignty of states over natural resources, as set out in national laws (Harry 2005).[5]

In this context, indigenous peoples have challenged the intellectual property rights and patent systems as being incompatible with their collectively owned, shared knowledge systems. At various forums they assert the iniquity and inability of intellectual property rights to safeguard their rights, and call on states to develop *sui generis* – in other words, specially designed – methods of traditional knowledge protection (Correia 2001: 11–14). Indigenous peoples issued a statement entitled 'No to Patenting of Life' in opposition to the TRIPS agreement, adding:

> Patenting and commodification of life is against our fundamental values and beliefs regarding the sacredness of life and life processes, and the reciprocal relationship, which we maintain with all creation (Tauli-Corpuz 2003: 25).[6]

Those who reject commodification do not limit themselves to TRIPS. They also argue that because indigenous knowledge is sacred, fair and equitable benefit sharing is impossible under 'the prevailing paradigm of privatization and commodification of nature and knowledge', as implied in the CBD (Sridhar et al. 2008). From this perspective, it is argued that CBD-style benefit sharing is dead (Sharma 2005: 1), even before it has begun, and that the 'most sweeping biopiracy coup occurred in 1993, when the CBD came into force and thereby legalized "recognition" of national sovereignty over genetic resources' (Ribeiro 2005: 49). If indigenous peoples accept the prevailing paradigm and collaborate with the propatents CBD approach, then 'their current way of living and their culture will be destroyed in the long run' (Sharma 2005: 1).

At the other end of the spectrum, the CBD itself, signed by 193 parties, claims exactly the opposite, namely that it will 'sustain the rich diversity of life on earth'.[7] It implicitly assumes that the benefits of natural resources should be

[5] As discussed in Chap. 3, the 2010 Nagoya Protocol includes a new provision (see Art 6.2) that requires parties to take appropriate measures to ensure the consent of indigenous and local communities to access genetic resources, where their rights over the genetic resources are established in domestic law. This provision cannot however have any impact on access and benefit sharing arrangements in circumstances where the indigenous and local peoples do not have such established legal rights.

[6] See also Tauli-Corpuz (2002).

[7] First description of CBD aims on running banner on CBD official website, http://www.cbd.int/.

shared equitably among humankind and that the proviso of prior informed consent is sufficient to avoid the desecration of sacred knowledge, concern about which is one of the strongest arguments against commodification.

The history of formal benefit-sharing agreements between those who would utilize traditional knowledge for product development and the holders of traditional knowledge (indigenous peoples) goes back beyond the adoption of the CBD in 1992. These 'transitional' cases, which straddle the boundary between unregulated and regulated access to biological resources, are highly instructive in terms of lessons learned, best practice and emerging policy challenges. One of the best-known benefit-sharing cases to date is also one of the earliest, which began outside the remit of the CBD in the late 1980s.

4.3 The Kani Case (India)

The story of the Kani access and benefit-sharing agreement began in April 1987, when a scientist from the All India Coordinated Research Project on Ethnobiology (AICRPE)[8] arrived in the forests of the Agasthyar hills in southern India to seek permission in accordance with local custom from the Mottu Kani (head of the Kani tribe) to launch an expedition into the forests.[9] The tribal head, Adichan Kani, deputed a team of three Kanis to accompany the expedition as guides. The full team, led by the chief coordinator of the AICRPE, Dr P. Pushpangadan, arrived in the forests in December 1987.

Within a few days, the scientists noticed that they were feeling more tired and fatigued than their Kani guides. After much urging, the guides revealed their secret, namely that they regularly chewed fruit from a plant that imparted this vitality and rejuvenation. They were reluctant to share this information because members of the Kani tribe considered the knowledge sacred and not to be disclosed to others. The scientists took samples for phytochemical and pharmacological study at the Regional Research Laboratory in Jammu, which coordinated the AICRPE project. The investigations confirmed the presence of certain glycolipids and non-steroidal polysaccharides with immuno-enhancing and anti-fatigue properties. The plant was *Trichopus zeylanicus travancoricus*, which the Kanis call Arogyappacha (meaning 'source of evergreen health'). Detailed phytochemical and pharmacological investigations pursued at the Regional Research Laboratory have since led to the filing of five patents.

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[8] The AICRPE was launched by the Department of Science and Technology in 1982. It soon joined the Ministry of Environment and Forests, with a mandate to develop several interdisciplinary teams across the country to document the multidimensional perspectives of tribal lives: their culture, beliefs and knowledge systems that promote sustainable resource management.

[9] The project coordinator, Dr S. Rajasekharan, met the Mottu Kani from the Chonampara tribal settlement, Kootur Thiruvananthapuram district, in April 1987 (personal communication from Dr S. Rajsekharan).

In 1990, Dr Pushpangadan moved from the laboratory to become director of the Tropical Botanic Garden and Research Institute (TBGRI) in Thiruvananthapuram, Kerala. The research on Arogyappacha moved with him, and as it progressed, two of the three original Kani guides were included in the team as paid consultants.[10] Eventually this project led to the development of a product called Jeevani, which was ready to be marketed by 1994, just as India became one of the first countries to sign and ratify the CBD.

Kani tribe members used the fruit of the plant, but for strategic reasons of year-round availability and sustainability, Jeevani was developed from its leaves. Only about 15% of the plant was used for the final product, which also contained other ingredients based on existing Ayurvedic knowledge and wisdom. In November 1996 the TBGRI transferred the technology to the Arya Vaidya Pharmacy, based in Coimbatore, one of the largest Ayurvedic manufacturing companies in India, against a licence fee of Rs. 1 million (approximately US$28,000) and royalties of 2% at ex-factory sale.

At the time there was no precedent for sharing these profits with the tribal community. However, Dr Pushpangadan had been closely involved in the national and global discussions on the protection of the indigenous knowledge system which preceded the CBD, and he was actively involved at international forums for the cause. By 1995 the provisions of Articles 15 and 8j of the CBD were directly applicable, and this supported the case for benefit sharing for Jeevani, even though India's national legislation in the form of the National Biodiversity Act was not enacted until 2002.[11] Dr Pushpangadan was able to act as a link between these developing processes and the TBGRI. His involvement facilitated an agreement in September 1995 that the proceeds would be shared equally between the research institute and the tribal community. This honoured the AICRPE's original verbal agreement with the Kani (a formal benefit-sharing agreement took effect in 1996).

The executive committee of the TGBRI suggested transferring the money to the Scheduled Castes and Scheduled Tribes Development Department in Kerala, but the Kanis vehemently opposed the idea. The TBGRI was reluctant to transfer the money directly into their hands, because of serious levels of alcohol misuse in the community, and, in the absence of any formal domestic benefit-sharing regulations, the expert consensus was that a trust for the tribal community should be established to receive the funds. The Kerala Kani Samudaya Kshema Trust[12] was

[10] During the intensive research stage from 1992 until 1998, the TBGRI kept the two guides in the research loop as ethno-medical experts with a standard payment on a monthly basis for their two visits a week to the TBGRI. The fee was Rs. 3000 (approximately US$80) per month between 1993 and 1998 (personal communication from Dr S. Rajsekharan).

[11] The National Biodiversity Act received presidential assent in 2003 and was followed by the formulation of the Biological Diversity Rules in 2004 to provide the necessary statutory and administrative mechanisms at national level to realize the Act's objectives. The relevant documents are available at the website of India's National Biodiversity Authority: http://www.nbaindia.org/publications.htm.

[12] *Samudaya* means 'community' and *kshema* means 'welfare'.

registered in November 1997, to regulate and direct the inflow of money. The main objectives of the trust are as follows[13]:

- Addressing the welfare and upliftment of the Kerala Kani tribal community
- Formulating and implementing necessary development projects (including research projects)
- Documenting and protecting the knowledge of the Kani tribal community.

The secretary of the Scheduled Castes and Scheduled Tribes Development Department was emphatic about ensuring that the trust should be representative. He called a meeting of all the factions of the Kani tribes on 21 January 1999 at Kottur. All Kani members present suggested to the secretary that the money should be transferred to the trust. Accordingly, an amount of Rs. 519,062 (approximately US$12,000) (50% licence fee and 50% royalties) was transferred to the trust (No 109/97) on 22 February 1999 (Equator Initiative 2002).

A second phase of benefit-sharing negotiations in 2004 was more transparent and democratic in nature, including Kani people in the decision-making process rather than just as recipients of benefits, both by formalizing the presence of the trust representatives in the new negotiation process and by including two representatives from the Kani Trust on the seven-person business management committee at the TBGRI, which agreed to set minimum conditions for the access and benefit-sharing arrangement. This process led to a second benefit-sharing agreement in 2006 with an increased share of the profits for the Kani (in both absolute and percentage terms).

As this account shows, the original Kani benefit-sharing agreement was initiated voluntarily by the researchers involved, with the general support of the Kani people (or at least some of them), before there was any legal regime or obligation governing access and benefit-sharing arrangements in India. However, this process did not happen in isolation. It was part of a growing movement towards binding international frameworks in this area. This, in turn, was based on earlier developments in the 1970s and 1980s, both in India and worldwide, towards the protection of indigenous peoples and their traditional knowledge systems. The commitment of certain key individuals to these processes was essential to the outcome in this case. It is noteworthy and commendable that prior to domestic or international legislation, the research institute involved decided to share proceeds equally with the indigenous community.

This is not to say, however, that criticisms of the Kani benefit-sharing agreements since the CBD are irrelevant. The initial consent phase involved very few community members, and this later became divisive. The Kani Trust is in principle open to all for involvement in decision-making, but membership has not expanded sufficiently to achieve a genuinely fair and equitable sharing of benefits. Limited efforts at the initial stage to make the trust more representative are partly responsible for this, but there have been more far-reaching criticisms, for instance on gender issues (see Chap. 6).

[13] Personal communication from Dr Rajsekharan.

While it is undoubtedly true that the funds distributed through the Kani Trust have helped alleviate poverty in the Agasthyar hills through a variety of programmes, the beneficiaries are still limited to small numbers across this very poor community.

In terms of wider benefits, however, as well as broader issues of the conservation of biological diversity, there have been some important developments. When the technology was transferred to Arya Vaidya Pharmacy for commercial production, the company faced a raw material crisis: the Kerala Forest Department (responsible for the protection and conservation of forests, including the regulation of the transit of forest produce) refused to allow the tribal community to pluck the leaves of the plant. Their concern was that the unscientific harvesting of leaves could cause the extinction of the plant. Later, with the intervention of the TBGRI, cultivation of *T. zeylanicus* was ensured and training was provided to several Kani tribe members under the Integrated Tribal Development Programme of the Directorate for Tribal Welfare. This programme provided 50 Kani families Rs. 1,000 each to cultivate the plant (Gupta 2004). As part of the new arrangement, the Kerala Forest Department and the TBGRI have worked together to develop mechanisms for periodically assessing the production and cultivation practices among the Kani tribes; the department allows cultivation of Arogyappacha within the tribal areas and has also permitted the collection of leaves from outside the core area of the reserve forest. This capacity-building exercise in order to ensure the sustainable use of *T. zeylanicus* is a good fit with the provisions of the CBD (Tables 4.1, 4.2).

Despite being a transition economy, India is renowned for its capacity to manufacture drugs and health products. That is how the entire process, from learning about traditional knowledge to bringing Jeevani into pharmacies and shops, could take place within one country. This is most definitely not the norm, and the CBD's access and benefit-sharing requirements are often seen as most pressing when partners from different countries or even continents are involved. One very interesting case of this kind took place in Nigeria, initially without any external involvement, and later with assistance from a US company (Table 4.2).

Table 4.1 Time Line and Details of Kani Case

Date	Details
1987	Research expedition into forests of Agasthyar hills
1994	Jeevani ready to be marketed
1996	TBGRI and Arya Vaidya Pharmacy negotiate first benefit-sharing agreement, valid for seven years, which enters into force 10 November 1996. Licence fee of Rs. 1,000,000 (US$28,000) agreed, royalties to be paid at 2% for 10 years
1997	Kerala Kani Samudaya Kshema Trust registered
1999	Rs. 519,062 (US$12,000) (50% licence fee and 50% royalties) transferred to trust
2001	First election of Kani Trust
2006	Kanis, TBGRI and Arya Vaidya Pharmacy negotiate new agreement (yet to be implemented) valid for seven years: licence fee Rs. 2,000,000 ($42,000). Royalties to be paid at 4% for 10 years

Table 4.2 Good Practice, Criticisms and Challenges of Kani Case

Good Practice	Criticisms	Challenges
Ongoing development of more transparent and democratic mechanisms (improved representation of Kani in second agreement negotiations; co-option of women to trust executive committee to improve gender balance)	Initial access to traditional knowledge provided by individuals without community consent Late involvement of wider Kani community in decision-making No initial role for Kani women in trust decision-making	Involving very poor rural community spread over wide geographical region in decision-making
Generous, forward-looking decisions by research leaders involved	No diversification of products; Jeevani remains only product based on Kani traditional knowledge	Compliance: American products do not generate royalties (Chaturvedi 2007: 16)
Trust fund contributions to community hall, local employment and transport improvements		General CBD challenge that commodification is allegedly not compatible with sacredness of traditional knowledge
One of few success cases of the CBD to date that do generate income through benefit sharing		Ensuring sustainable supply of resources and guarding against overharvesting

4.4 The Niprisan/Nicosan Case (Nigeria)[14]

Sickle-cell disease is a genetic blood disorder affecting red blood cells. These cells become sickle-shaped and have difficulty passing through smaller blood vessels, resulting in damage to the tissue that cannot be reached. Approximately 70% of sickle-cell disease patients (12 million people) live in Africa. Infant mortality from the disease is around 8%, and the chance that babies who have inherited the disorder will survive to the age of five in rural areas is only 20% (Effiong 1982).

Until recently, only palliative measures were available for affected patients. Consequently, most died early from microbial infections or related complications. Undoubtedly, sickle-cell disease is a major public health problem in sub-Saharan Africa, where it is endemic. Those who survive early childhood mortality suffer from cycles of excruciatingly painful crises, interrupted educational careers and social discrimination.

[14] The description of the Nigerian case is based on a report written by Prof. Charles Wambebe for the GenBenefit project (Wambebe 2007).

Niprisan is a very effective medicine developed in Africa for the prophylactic management of sickle-cell disease based on traditional knowledge.[15] Like the Kani case, this case from Nigeria spans the period around the adoption of the CBD.

In 1992 research collaboration commenced between the Nigerian National Institute for Pharmaceutical Research and Development (NIPRD) and a traditional health practitioner, Rev. Paul Ogunyale, to develop a medicine to treat sickle-cell disease. The research built on the indigenous medical knowledge and practice of the practitioner and his family. Sickle-cell disease was the priority disease targeted by the NIPRD for the development of new medicines at this time. The CBD had not yet been adopted, but it was already clear to the NIPRD, partly owing to the acknowledged distrust of biomedical researchers among traditional health practitioners, that it needed to establish a legal basis for the scientific and clinical assessment of the herbal medicine [derived from *Piper guineense* seeds, *Pterocarpus osum* stem, *Eugenia caryophylum* fruit and *Sorghum bicolor* leaves (Wambebe 2006)].

The NIPRD and the traditional health practitioner therefore signed a memorandum of understanding in terms of which the research process was to be transparent, fair and equitable. There was no model for such an MOU, but the World Intellectual Property Organization (WIPO) provided various resource materials which enabled the NIPRD to start developing a unique MOU for research collaboration between scientists and traditional health practitioners. This agreement is regarded as the first of its type in the world, and it was subsequently adopted by both WIPO (Wambebe 1999) and the World Health Organization (WHO) (WHO 2004; see Appendix 1).

The goal of the MOU was to establish clear provisions on the responsibilities of the parties involved and the potential benefits, and a formula for equitable benefit sharing of any commercial product arising from the collaboration. It was developed ten years before the adoption of the Bonn Guidelines, yet would fulfil several of its requirements regarding mutually agreed terms (Bonn Guidelines 2002: paragraph 43), as well as those of the Nagoya Protocol (CBD 2010: Annex, Monetary and Non-monetary Benefits), by including the traditional health practitioner as an active member of the research team in collaboration and

[15] Xechem Nigeria, producers of Nicosan, list the medicine's benefits as follows:

1. It is used for prophylactic management of sickle cell disease (SCD).
2. It has potent anti sickling effect on sickled erythrocytes, obtained from patients with SCD and on transgenic mice that produced human sickle hemoglobin, thus useful in preventing painful crisis experienced by SCD patients.
3. It reduces hypoxic stress experienced by SCD patients (due to trapping of sickle cell in lungs), drastically.
4. It removes the incidence of blood transfusion in SCD patients.
5. It prevents clinical sequel (i.e. painful crisis).
6. It prevents ocular damage (http://xechemnigeria.com/products.htm).
   In Phase IIa clinical trials, between 73% and 80% of patients did not experience any crisis during the study period, and a majority gained weight to the extent that, for example, school attendance improved (Wambebe 2006).

co-operation with specific responsibilities around the supply of raw plant materials for product development, and as an author of all publications, while acknowledging his right to continue using his own medical knowledge independently. However, this had limited impact upon the subsequent negotiations to license the rights to develop the promising new drug, under the trade name Nicosan, to the US-based, Indian-owned company Xechem International. The entire research team at the NIPRD, including the traditional health practitioner, was excluded from these negotiations, which were undertaken by NIPRD management.

The outcome of this process was that, in terms of the MOU, the traditional health practitioner was entitled to a share of a good faith payment (US$115,000), plus 10% in perpetuity of the royalties which the NIPRD would receive from the licensee (7.5% of gross sales).[16] However, despite Xechem's prompt payment of its obligations to the NIPRD, no monetary benefits have been received by the traditional health practitioner (or, since his death, by his trust), which raises concerns about the monitoring and enforcement of such agreements, even where they are of a model status.

With regard to benefit sharing, it has been suggested that by virtue of their status as indigenes of Oyo town, the community where Rev. Ogunyale lived should also have benefited from the commercialization of Niprisan. However, this was not considered during the negotiations (Wambebe 2007: 13). Another area of concern regarding sharing the benefits of this research relates to clinical trials for Niprisan carried out by the NIPRD with sickle-cell disease patients in two Nigerian cities. The price of the drug, when it entered the market as Nicosan, was not affordable for poor sickle-cell disease patients. Therefore, as has been noted retrospectively (Wambebe 2007: 13–14), since the cooperation of trial participants had been needed to generate valuable clinical data, it would have been appropriate for the licensee to make provision for a supply of Nicosan to those participants for life, either free or at a much reduced fixed rate that any of them could afford (for example, US$1 per month's supply). In fact, the duty to provide patients with access to the medicine for which they have been study participants has been enshrined in the Declaration of Helsinki since 2000 (WMA 2000: paragraph 30) (for current requirements see Chap. 3).

The significance of the Niprisan/Nicosan case is that the project was initiated and executed by African scientists working in Africa at a time when international provisions for benefit sharing regarding commercial products derived from indigenous medical knowledge were unavailable. The licensing of Niprisan to a US company was the first case of reverse transfer of medical technology (medicine) in Africa, and expanded interest in investigations based on African medicine. The subsequent bankruptcy of Xechem, however, prompted the Nigerian government to terminate the licence agreement. In March 2009 it was announced that the NIPRD was taking over production of the drug in Nigeria. This was welcomed as a good development for the country, with the potential for poor patients to access the drug

[16] A royalty of 7.5% falls within the global practice range (Ten Kate and Laird 1999: 68).

cheaply (Hassan 2009). However, the factory closed in late 2009. By mid-2010 supplies were exhausted, and at the end of the year it was reported that 'despite promises by the Nigerian government that it would restart production, the drug is currently unavailable', and the NIPRD's research into the development of other drug candidates from traditional remedies had ceased (Ndhlovu 2010).

In March 2012 however, after much negotiation, the Nigerian Federal Ministry of Information announced that NIPRD was about to resume commercial production of Niprisan in Nigeria once a Memorandum of Understanding had been signed between the various interested parties.

The Director–General of NIPRD, Professor Karniyus Gamaniel, stated that the 'most critical challenge facing the institute today is funding' (Federal Ministry of Information 2012). Nevertheless, the most enduring component of this programme remains the strengthening of research capacity in Nigeria (Tables 4.3, 4.4).

Table 4.3 Time Line and Details of Niprisan/Nicosan Case

Date	Details
1992	Research project commences based on MOU with traditional health practitioner
1994	Phase I clinical trials conducted at NIPRD in Abuja with healthy volunteers (Wambebe 2008)
1996	Phase II clinical trials commence in patients with sickle-cell disease at Army Base Hospital, Yaba, Lagos, Nigeria
1997	Phase IIb clinical trials commence in patients with sickle-cell disease at NIPRD Clinic, Abuja, Nigeria
1998 to 2000	Through grant from United Nations Development Programme, Niprisan patented in Nigeria, USA, England, India and 42 other countries in Europe, Africa, West Indies and Americas (Wambebe 2008)
2002	Licence granted to Xechem for exclusive global manufacture and marketing of Niprisan
2002	Rev. Ogunyale dies
2005	Both US Food and Drug Administration and European Medicines Evaluation Agency give treatment 'orphan drug' status, qualifying it for financial incentives to produce drugs considered too expensive or unprofitable to develop (Hassan and Scott 2008)
2006	Nicosan receives approval from Nigerian National Agency for Food and Drug Administration and Control in March 2006 and, according to Xechem, is first produced two months later (6 July 2006) 'on a limited basis' (Hassan and Scott 2008)
2006	Manufacturing plant at Abuja commissioned by US-based firm
2008	Xechem International files for bankruptcy protection in the United States (Hassan 2008)
2009	Nigerian government withdraws Xechem's licence and announces that NIPRD will take over production in Nigeria (Hassan 2009). Xechem liquidated. Factory subsequently closes (Abutu 2010)
2010	Supplies are exhausted and drug becomes unavailable (Abutu 2010)
2010	Research and development of Niprisan at NIPRD cease (Ndhlovu 2010)
2012	Resumption of commercial production announced (Nigerian Federal Ministry of Information)

Table 4.4 Good Practice, Criticisms and Challenges of Niprisan/Nicosan Case

Good Practice	Criticisms	Challenges
Treatment developed by African scientists based on African traditional knowledge for neglected disease	Benefit-sharing negotiations excluded traditional knowledge holder	To date, no royalty sharing with traditional knowledge holder as agreed in MOU shows the challenge of enforcement
Comprehensive MOU developed and later adopted by WIPO and WHO	Post-study obligations to clinical trial participants according to Declaration of Helsinki not honoured	Bankruptcy of licensee
Strengthening of pharmaceutical research and manufacturing capacity in Nigeria	Drug price outside reach of poor patients	Lack of capacity of local companies to produce drug despite considerable local investment
		Should wider community where traditional knowledge holder lived share in the benefits?
		General CBD challenge that commodification is allegedly not compatible with sacredness of traditional knowledge

In the Niprisan/Nicosan case, the pre-CBD legal emphasis was on the protection of traditional knowledge *as distinct from* environmental concerns and the sustainable use of biodiversity. The potential impacts of the research into and production of Niprisan/Nicosan were not addressed in the MOU. The advent of the CBD in 1992 – with its three core objectives of the conservation of biological diversity, the sustainable use of its components, and the fair and equitable sharing of the benefits – represented a codification of increasing global concerns about the interlinked nature of the issues at stake, and had a major impact, intentionally, on research agendas. One of the most interesting and controversial benefit-sharing stories from this transitional period comes from Mexico.

4.5 The Chiapas Case (Mexico)[17]

In late 1998, a five-year research project funded by the International Cooperative Biodiversity Group (ICBG) programme, a consortium of US federal agencies, began in the central highlands of Chiapas, Mexico, one of the richest and most endangered biodiversity regions on earth. In the wake of the CBD, 'Drug Discovery and

[17] This case study draws upon Feinholz-Klip, Barrios and Cook Lucas (2009).

Biodiversity among the Maya of Mexico' had the bold purpose of excelling as a model of plant bioprospecting in an indigenous territory in a difficult social and political climate. It contained a benefit-sharing package, an 'elaborate informed-consent protocol' (Rosenthal 2006: 123), terms to share intellectual property rights over any resulting patents, and provisions to safeguard Maya medicinal knowledge from patenting by carefully classifying it as 'prior art'. Nevertheless the project foundered in a mire of opposition and regulatory chaos, and was abandoned in 2001. Much has been written about the failure of the Maya ICBG, as the project became known, but this story still has lessons to teach about the impact of CBD provisions on researchers and vulnerable communities, as well as what can happen during transitional periods. The CBD was in force at the international level by 1998, when the project began, but relevant domestic Mexican legislation was not yet in place. Meanwhile, NGOs and others were referring to the new CBD safeguards while simultaneously trying to resist the commodification of traditional knowledge, which should allegedly not be for sale.

The Maya ICBG aimed to identify and evaluate bioactive agents from plants found in Chiapas to discover which of these were of immediate health significance and potential economic value to the local population. The intention was to develop local capacity for the sustainable management and production of plants for local medicinal use and for global markets, and to enrich knowledge about the flora of the highlands, including through innovative publications in local languages. The project was led by a US-based professor of anthropology who had been conducting research among the Maya for 40 years. Project partners were a Mexican research centre, *El Colegio de la frontera Sur* (ECOSUR), and Molecular Nature Ltd, a small for-profit natural products discovery company based in the UK. Capacity-building for the local research institutions, as well as among Maya collaborators, was a core component of the project, which viewed the indigenous highlanders as major stakeholders.

The Maya ICBG intended highland people across the entire region to have an equal share of the benefits, whether communities actively took part or not. The project secured this through the innovative establishment of PROMAYA (Promotion of Intellectual Property Rights of the Highland Maya of Chiapas, Mexico), a non-profit organization established to administer the indigenous community's share (25%) of the 1% of any total pharmaceutical profits that the research consortium would receive. However, despite proposed indigenous representation on PROMAYA, it became a core focus of resistance to the project as it exemplified the top-down approach of the research community towards the highland population. The initial consortium did not include any Maya representation: for the Maya ICBG, bringing the Maya people to the table as 'a full partner in our activities' (Berlin et al. 1999: 143) was not a precondition but a *goal* of the project. In fact PROMAYA never actually met, as the project did not run long enough to generate funds for it to distribute.

To understand the representation issues at stake, it is important to be aware of the history of the region. The Maya civilization in southern Mexico and Central America was devastated by Spanish colonizers in the 1500s. Since constitutional reform in 1917, however, the land rights of the original occupants have been officially recognized. Today, in the wake of the 1994 Zapatista uprising, around 900,000 people speaking four Maya languages live in the highland Chiapas region

of Mexico, a militarized, volatile area with extreme levels of poverty. The Maya population is not formally represented in the region by a single socio-political body, but there are a number of dynamic and sometimes conflicting forms of organization, increasingly connected with national and international networks. At the time the Maya ICBG began its work, the concept of community in Chiapas was highly contested, which fuelled later criticism of the project locally, nationally and internationally.

In the post-CBD but pre-Bonn Guidelines environment, the Maya ICBG consciously proceeded on the basis that CBD Articles 15 and 8j required consent for the use of genetic resources to be obtained from the local community (see Berlin and Berlin 2004; Berlin and Berlin 2003, especially 631–632), and interpreted this as referring specifically to a recognized, existing Mexican socio-political unit (Berlin and Berlin 2002).[18] So the researchers invited authorities and members of local hamlets in the study area on tours of the herbarium and the laboratories, presented a play in native languages explaining the project, provided multi-language materials and followed up expressions of interest in hamlet assemblies, in a process leading to hamlet-level written consent agreements.

On the basis of consent from a number of hamlets, the project made the first permit application for biotechnology collections in Mexico (Rosenthal 2006: 124) to the Mexican Department of the Environment, Natural Resources and Fishing (*Secretaría de Medio Ambiente, Recursos Naturales y Pesca* – SEMARNAP). However, existing domestic regulatory frameworks were inadequate to respond to this request. While legal provisions existed for the collection of plant material for scientific purposes, there were none for the collection of material for potential commercial exploitation, and in the absence of any clear regulations, the scientists became embroiled in lengthy negotiations as different parties interpreted the law in line with their own interests.

Concerns about the process of initiating the research and exclusion from it were first raised by the local healers and midwives organization, the Organization of Indigenous Physicians of the State of Chiapas (*Organización de Médicos Indígenas del Estado de Chiapas* – OMIECH). They in turn mandated the Chiapas Council of Traditional Indigenous Doctors and Midwives (*Consejo Estatel de Organizaciones de Médicos y Parteras Indígenas Tradicionales de Chiapas* – COMPITCH) to take the matter up on their behalf. COMPITCH asked communities not to participate in the project until the situation was clarified, and also requested support from an international NGO, the Rural Advancement Foundation International (RAFI).[19] Legal questions were raised about the validity of the ham-

[18] The term 'prior informed consent' is implied in Article 8(j) of the CBD, which requires contracting parties to obtain 'the *approval and involvement* of the holders of such knowledge' (emphasis added), but it was not until 2002 that the Bonn Guidelines expressly set out this requirement and provided detailed guidance on how to meet it.

[19] RAFI, an international NGO with a history of advocating against biopiracy and opposing bioprospecting, has since changed its name to Action Group on Erosion, Technology and Concentration (ETC Group). (See http://www.etcgroup.org/.)

let-level agreements, and concerns were expressed about the quality of the information which had been provided to obtain communities' consent. Wider objections were raised regarding the commodification of collectively owned knowledge, and there were also concerns about the fairness of the tiny share of profits that the Maya stood to receive collectively.

An acrimonious and very public debate ensued amid questions of proprietary versus public knowledge, as well as issues concerning the legal and social legitimacy of local communities' control over their biological resources. Researchers, NGOs and governments, as well as indigenous people, were all struggling to come to terms with the risks and benefits of life after the CBD, and to position themselves in relation to the unfolding debates and conflicts. In 2000 SEMARNAP denied the research permit application from the Maya ICBG on the basis that consent had not been obtained at the appropriate community level. ECOSUR tried to modify the project and include as a fourth member a widely representative indigenous organization which could conduct an appropriate informed consent process. However, the highly charged situation was in danger of affecting ECOSUR's other research efforts, as well as its role and influence in developing national bioprospecting regulations. ECOSUR therefore withdrew from involvement with the Maya ICBG in October 2001, on the grounds that conditions were not in place in Mexico for the project to be seen as both legal and legitimate. Without a local research partner, the funder terminated the project grant (Rosenthal 2006: 124).

This case study shows that even the best intentions of researchers and funders are not sufficient for successful benefit sharing, in particular when representation issues are not resolved and the legal situation is uncertain. The Chiapas case can be seen as representing a crisis of transition: whereas researchers saw the CBD as providing clear rules and a structured licence to operate, some NGOs criticized it as 'the most sweeping biopiracy coup …, [which] legalized "recognition" of national sovereignty over genetic resources' (Ribeiro 2005: 49) (Tables 4.5, 4.6).

The Maya ICBG remains deeply controversial. Events were significantly influenced by the involvement of international NGOs and other organized social networks, which exposed the general mistrust between Mexican institutions and the indigenous people. The central role of NGOs, along with the difficulties caused by a domestic legal and policy vacuum and disagreement over who constituted the relevant communities, are all echoed in probably the most well-known benefit-sharing case of them all – that of the San *Hoodia*.

Table 4.5 Time Line and Details of Chiapas Case

Date	Details
1998	Five-year research project begins
1999	National and international concerns first expressed
2000	Bioprospecting permit requested from SEMARNAP (later denied)
2001	Mexican research partner withdraws
2001	Funder withdraws grant and project is abandoned

Table 4.6 Good Practice, Criticisms and Challenges of Chiapas Case

Good Practice	Criticisms	Challenges
Innovative process of providing information to/obtaining consent from local population	Insufficient Maya involvement	Operation in volatile, poverty-stricken, militarized area
Effort to collect and publish knowledge in order to prevent future patents	Royalties unsatisfactory for provision of traditional knowledge and plant resources	Serious regulatory uncertainty, particularly regarding domestic legislation and requirements for obtaining prior informed consent
Partnership with local research institute		General CBD challenge that commodification is allegedly not compatible with sacredness of traditional knowledge
Establishment of non-profit organization to administer indigenous community's share of benefits		

4.6 The San *Hoodia* Case (Southern Africa)

4.6.1 The First Hoodia Benefit-Sharing Agreement: CSIR

This case is about the San peoples of southern Africa (also known as Bushmen) and a succulent plant called *Hoodia*. Botanically, the *Hoodia* is a stapeliad belonging to the Apocynaceae family (Glasl 2009: 302). The San's use of *Hoodia* dates back centuries. The stems and the sap of this succulent plant, growing freely in the Kalahari desert, were a substitute for food and water during hunting expeditions. This caught the interest of a research organization which realized that the plant's appetite-suppressant qualities could be highly useful in products for the anti-obesity market.

The San are generally regarded as having lived longer continuously in one location than any other population in history (Stephenson 2003: 21; Lee et al. 2002). At about the time European settlers were landing at the Cape in South Africa, the San occupied an area stretching from the Congo Zambezi watershed in Central Africa to the Cape, and numbered about 300,000 (Lee 1976: 5). The San today number approximately 100,000, and live mainly in Botswana, Namibia and South Africa, with scatterings of populations in Angola, Zimbabwe and Zambia.[20] After centuries of genocide and marginalization, leading to loss of land and

[20] San NGOs estimate the populations as follows: Botswana, 55,000; Namibia, 35,000; South Africa, 8,500; Angola, 3,000; Zimbabwe and Zambia, unknown (KFO 2006).

consequently large-scale loss of culture and identity, they occupy an unchallenged niche as the poorest of the poor in these countries (Suzman 2001).

Today, while a minority of San live in villages on their own land,[21] most reside in conditions of abject poverty on land to which they have no rights or traditional claim. Living in small rural villages in regions dominated by more powerful African cultures, in sterile government resettlement villages, or as labourers working on commercial ranches, they inhabit an uneasy twilight zone between their former traditional ways and the modern world.

In 1996, San leaders formed the Working Group for Indigenous Minorities in Southern Africa (WIMSA), their own umbrella organization, charged with uniting and representing the interests of San communities from Botswana, Namibia and South Africa. Regular meetings were held across national boundaries, and, at its general assembly in 1998, WIMSA secured a significant early achievement with a unanimous decision, subsequently confirmed on many occasions, that San culture and heritage was a collective asset, owned by all San across all boundaries. Heritage was understood to encompass all tangible and intangible aspects of culture, traditional knowledge, rock art, myths and music. This important policy decision was to be of great significance when the San later came to negotiate their rights in the *Hoodia* case.[22]

The Council for Scientific and Industrial Research (CSIR) is a South African research institute, one of the largest in Africa. In 1963, following leads in documented research related to the traditional use of the *Hoodia* species as an appetite and thirst suppressant (White and Sloane 1937), the CSIR began confidential research and trials to investigate and isolate the active ingredients. Tests were initially inconclusive, and were suspended until 1982, when they resumed with the benefit of new technology (Wynberg 2004).[23] By 1995 the first patent application had been lodged in South Africa (South African Patent No 983170), followed over the next few years by a succession of progressive international patent applications.[24] It is worth noting that no domestic access and benefit-sharing laws or frameworks were in place in South

[21] The approximately 4,000 !Kung of the N=a Jaqna conservancy (formerly West Bushmanland) in Namibia, 5,000 Jun/uasi of the Nyae Nyae (formerly East Bushmanland) in Namibia and 800 = Khomani San of the Northern Cape, South Africa, have secured rights to live on their traditional land.

[22] The Nagoya Protocol now recognizes in general (Annex 1) that innovative solutions are required to address benefit sharing in circumstances where traditional knowledge occurs in transboundary situations, as well as requiring parties to cooperate, with the involvement of indigenous and local communities, in circumstances where the same genetic resources are found within the territory of more than one party (Art 11.1).

[23] Rachel Wynberg (2004: 854–858) provides a detailed discussion of the ecology and use of *Hoodia*, and of the species' commercial development, the details of which are beyond the scope of this discussion.

[24] UK patent GB 2338235 and World Patent WO 98/46243 covering 'pharmaceutical compositions having an appetite suppressant activity', including 'raw materials, active substances and mode of action'.

Africa in 1996 when the CSIR patented a utility patent[25] (generally referred to as the P57 patent) relating to the active appetite suppressant ingredients of the *Hoodia*.[26]

In 1997 the CSIR signed a primary licensing agreement with Phytopharm, a small British company specializing in the development of phytomedicines, that would enable further development and commercial exploitation of the P57 patent. In 1998 Phytopharm sublicensed the right to develop and commercialize the P57 patent to US drug manufacturer Pfizer. This set of licensing agreements was meant to provide the CSIR, as patent holder, with a guaranteed stream of future payments based upon the progressive development of the patent as a drug or medicine (milestone payments) and finally upon commercial results (royalties).

In June 2001 the San first ascertained, through an article printed in the UK *Observer* newspaper (instigated by Biowatch, a South African NGO specializing in issues of environmental biodiversity), that San traditional knowledge relating to the *Hoodia* plant formed an essential component of the CSIR patent. There had been no attempt at consultation by the CSIR. In fact, Phytopharm's chief executive, Richard Dixey, was quoted as having been told by the patent holder, the CSIR, that the San 'no longer existed' (Barnett 2001). The fact that no efforts were made to obtain prior informed consent was in:

> flagrant disregard of the International Labour Organization's Convention 169, an international agreement for the protection of indigenous peoples' rights; the letter and spirit of the CBD; the African Union's Model Law for the Protection of the Rights of Local Communities, Farmers and Breeders and for the Regulation of Access to Biological Resources …; and the Bonn Guidelines on Access to Genetic Resources and Fair and Equitable Sharing of the Benefits Arising out of their Utilization (Wynberg and Chennells 2009: 101).

The international news coverage spurred the CSIR into action. Because the San had already begun to articulate and advocate for their rights to land and culture through WIMSA, they were prepared to start negotiations with the CSIR. WIMSA mandated South African San leaders to register a San Council and to negotiate with the CSIR on behalf of all San peoples. This council met frequently to receive specialized training in the field of intellectual property and to hold consultative workshops with their communities before and during the negotiations. San negotiators decided at an early stage of the negotiations that it was not in their interests to challenge the patent, and adopted the more pragmatic approach of opting for a potential share of benefits.

After two years of negotiations the San and the CSIR signed a benefit-sharing agreement in March 2003 in terms of which the San were to receive 6% of the CSIR's royalties from licensees and 8% of milestone payments. The outcome was hailed as a success for the CBD in the international media, and the case has not been out of the limelight since.

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[25] A utility patent, as opposed to a plant or a design patent, is any new or useful process… or any useful improvement thereof. The patent must comply with the three requisites of non-obviousness, novelty and usefulness.

[26] The P57 patent is a complex and broad patent, which includes the method of extracting the active principle, being the 'appetite suppressant agent'.

The first setback for the San became public a few months after the agreement was concluded. As part of a company restructure, Pfizer elected to withdraw from the venture and return the licence to Phytopharm (Phytopharm 2003). Phytopharm subsequently entered into a sublicence with international food giant Unilever, with a new vision of developing the P57 technology into a food supplement as opposed to a clinical drug. The second setback occurred in December 2008, when Unilever and Phytopharm announced a mutual termination agreement. As a result, the patent rights once again reverted to Phytopharm. This news was unexpected, as Phytopharm had noted the successful progression to stage three of product development with Unilever in September 2007, which meant that the final stage before regulatory approval had been reached (Glasl 2009: 301–302).

Meanwhile, in the expectation that millions of South African rands, or even US dollars, would flow into the Kalahari, the San *Hoodia* Benefit Sharing Trust was formed in 2005 by the San and the CSIR in accordance with South Africa's Trust Act. This trust was intended to be a stable institution that would receive and distribute *Hoodia* royalty money among the San. To date, the trust has received two major payments, one milestone payment each from Pfizer (R259,660 in 2000 = $40,000 US) and Unilever (R309,423 in 2005 = $28,000 US). The disappointment in the San community over the *Hoodia* agreement illustrates one of the major pitfalls of CBD benefit sharing, namely the raising of unrealistic expectations. Only a fraction of research projects in the health care sector ever lead to marketable products that may result in royalty payments. However, in contrast with the Kani, the San have negotiated a subsequent benefit-sharing agreement with commercial *Hoodia* farmers, and others covering different plants have since followed.

4.6.2 *The Second Hoodia* Benefit-Sharing Agreement: *Hoodia* Growers

Between 2001 and 2005 the international market for *Hoodia* exploded, with literally hundreds of dietary products being advertized on the Internet and appearing on pharmacy shelves. Most products were of dubious authenticity and no distributors had made benefit-sharing arrangements with the San (Glasl 2009: 305). Poaching and illegal harvesting of wild *Hoodia* were widespread, and farmers planted hundreds of hectares in expectation of the boom that was to follow. Legislation in South Africa was one step behind, and the listing of *Hoodia* in Appendix II of the Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES) in order to control the unbridled commercial trade was only effected in October 2004 (CITES 2004),[27] too late to save many wild *Hoodia* populations.

[27] This listing established a standardized international trading framework and monitoring regime for *Hoodia*. See Wynberg (2004: 854).

The San were approached by a group of *Hoodia* growers (the South African *Hoodia* Growers Association) who were cognizant of their obligations to share benefits with the San under the CBD. In March 2006, an agreement was concluded allocating the San an effective 6% of the value of *Hoodia* sold by South African *Hoodia* growers. After a further year of negotiations between the San, the South African *Hoodia* Growers Association and another substantial group of *Hoodia* growers (the Cape Ethno-botanical Growers Association), as well as the provincial environmental government agencies (being the bodies responsible for all growing and CITES permits), a comprehensive benefit-sharing agreement was concluded between the San and the newly formed Southern African *Hoodia* Growers Association on 15 March 2007.

This agreement, which initially brought the San a modest R24 per dried kilogram of *Hoodia* exported (to be renegotiated after one year, in the light of unpredictable prices), had the aim of securing a transparently managed *Hoodia* market, with all role players committed to best practices as set out in the agreement. The San peoples were to provide two directors out of the seven that would run the organization. The agreement, although negotiated in South Africa, was drafted in such a way as to welcome and enable the participation of *Hoodia* growers from neighbouring Namibia and Botswana in due course. However, the bureaucratic difficulties of government approval being required for any benefit sharing have prevented this second agreement from generating any income for the San so far: at the time of writing, having become dormant, it is awaiting renegotiation. It is worth noting that during 2009, the San reached agreement with the Nama people in Namibia, who are also acknowledged holders of traditional knowledge regarding the *Hoodia*, on the terms of their sharing of the benefits of *Hoodia* sales in that country. They concluded a benefit-sharing agreement with the *Hoodia* Growers Association of Namibia on 8th December 2010, along the lines of the precedent set in South Africa.

4.6.3 Analysis of the San Hoodia Case

As many analyses of the case have described (Wynberg 2004: 859–864), the negotiations between the CSIR and the San secured the 'consent' of the San *ex post facto*, which could wryly be termed 'post-informed consent'. On a formal level, the 2003 benefit-sharing agreement between the San and the CSIR was legally concluded with the South African San Council, thereby securing consent. However, upon analysis of the situation behind the discreet veil of the formal legal agreement, and of the differentiated, scattered and vulnerable state of the San peoples, one can reasonably ask at what stage the community could be said to have fully consented.

WIMSA has a constitution that complies with Western notions of governance and accountability, demonstrating the democracy, transparency and fiscal responsibility that donor funders expect of their beneficiaries. The WIMSA board of trustees is elected from the San leadership of each country – currently only South

Africa, Namibia and Botswana are effectively organized – and all important policy decisions are taken by the General Assembly, a meeting of representatives from San communities in all three countries. Implementing cooperative governance is a major challenge to the egalitarian San. Community meetings have been documented (Hitchcock and Biesele 2002: 14) at which literally hundreds of people have participated and attempted to employ the traditional consensus style of decision-making. As Ariel Salleh has pointed out, 'indigenous people who now enjoy the privilege of sitting on deliberative committees are expected to obey ostensibly universal – but really Eurocentric – terms of reference' (Salleh 2009: 10).

The contrast is particularly obvious when employees from large corporations or research institutes negotiate with indigenous representatives.[28] In corporate hierarchies, decision-making usually involves a few individuals and does not entail a wider consultation of stakeholders. Decisions are routinely made by highly educated personnel in positions of power who are well versed in the legalities and implications of their decisions. By contrast, decision-making in traditional indigenous communities such as those of the San often involves many community members, typically with little knowledge of the technicalities and legal implications of their decisions. Discussions are seldom limited to a single event, but rather unfold over time in conversations among friends, relatives and neighbours. In the case of the San, decisions are taken by consensus, which is reached when significant opposition no longer exists. When these decisions are taken to a boardroom table during benefit-sharing negotiations, the decision-making abilities of indigenous negotiators are compromized by both time frames – for example, the CSIR needed an urgent resolution to satisfy Pfizer, the main licensee at the time – and a relative lack of experience and knowledge on the part of their rural constituency.

There is no obvious solution to this dilemma. Investors are unlikely to allow years for community consultation processes to run their course, and are more likely to drop a particular research lead than compromise their own processes. On the other hand, the imposition on traditional communities of the rapid decision-making processes favoured by industries is both ethically unacceptable and impracticable, as the process has to be led by highly-trained professionals. In the San case, the tensions about time frames were further aggravated by the insufficiency of financial resources to fund meetings, obtain additional advice and hone negotiating skills, all vital elements of effective decision-making under such circumstances.

One could ask who is responsible for securing these components. In the San case, the CSIR invested in facilitating San representation and decision-making capability. This was necessary for the San to reach the negotiating table in the first place and then to achieve an agreement, which was essential for the CSIR. However, potential commercial partners cannot routinely be expected to invest considerable amounts of time and money in sustained capacity-building to enable community representatives to become equal partners in negotiations, a process

[28] This paragraph and the next draw on Wynberg, Schroeder, Williams and Vermeylen (2009).

which would inevitably raise questions about the legitimacy of any resulting agreements. The time lost through investing in this way could have cost the CSIR its chances to secure a licensing agreement with a very attractive licensee (Pfizer). In addition, one might well ask whether capacity-building and education are not the responsibility of national governments. A partial solution has been found in South Africa, where the Biodiversity Act (Republic of South Africa 2004) now locates support for consultations firmly with the South African government, in order to ensure that benefit-sharing agreements are negotiated on an equal footing. Assuming this support is adequate, the decision-making processes of traditional knowledge holders and those of bioprospecting partners could become more compatible in future.[29]

That San leaders were able to conclude a successful benefit-sharing agreement at all was thanks to the fact that they had already built a sufficiently coherent structure, based upon sound and abiding principles, which aimed at benefiting all San. The San, as a party to this complicated set of legal relationships, seem to have succeeded in articulating and securing their CBD-related rights over a sustained period. What may have helped is that NGOs and advisers[30] were in a long-term relationship with the San. The legal advice given to the San was embedded in the principles of San development organizations, and was therefore, to a degree, sensitive to the complexities of this particular community.[31] The lesson learned by the San was that it is possible to negotiate binding agreements even in the absence of an enabling domestic legal environment. The South African Biodiversity Act was signed into law in June 2004, but the regulations guiding its application only entered into force in April 2008. Hence it was not available to guide either of the San *Hoodia* benefit-sharing negotiations. The general principles of international law flowing from the CBD guided the parties in all the negotiations referred to here, and they were able to reach binding agreements despite the fact that there were no precedents, nor binding domestic law. This is evidence of the power and ability of negotiating parties to meet each other, to establish rules of engagement, to commit to acting in good faith, and to attempt to strike a balance encompassing the long-term requirements of divergent parties. However, as the Chiapas case above has shown, it is essential that the communities involved have a representative governance structure that is credible to all parties. The *Hoodia* story bears this out.

To date, the domestic legal and policy environment in the countries that grow *Hoodia* is still inadequate in many ways. South Africa, Botswana and Namibia do

[29] The Nagoya Protocol addresses these issues in Article 21, on awareness raising around traditional knowledge associated with genetic resources, and more extensively in Article 22, (Capacity), specifying the involvement of indigenous and local communities in capacity building and development as well as support for identifying their capacity needs and priorities, with a view to enhancement.

[30] WIMSA, the South African San Institute (SASI) and the Kuru Family of Organizations.

[31] Interestingly the Nagoya Protocol attempts to capture this idea via for example Article 21.

not yet have a coherent joint framework of law and policy reflecting the prescriptions of the CBD relating to the *Hoodia* and to benefit sharing. The governments of South Africa, Namibia and Botswana are the three Southern African Development Community states which share the *Hoodia* genetic resource, and are therefore interlinked in the manner in which they interpret and implement their rights and obligations under Article 15 of the CBD. Currently these three countries differ significantly in how, and to what extent, they have implemented their duties to require prior informed consent relating to access to genetic resources from 'indigenous and local communities', the obtaining of 'mutually agreed terms' and benefit sharing with such communities. Of course, it may be particularly difficult to come to agreements when the traditional knowledge holders reside in several countries and the relevant resource, in this case a plant, also occurs across those borders.[32]

International NGOs opposing biopiracy and the patenting of life forms have approached the San through their lawyer[33] (both in advance of the benefit-sharing negotiations and subsequently) to offer support should the San decide to oppose 'patents on life' and challenge the patent. As this chapter has already noted, some activists criticize the CBD as yet another Western imposition tantamount to biopiracy. The *Hoodia* case illustrates the difficulties indigenous peoples can face when deciding whether or not to commodify their knowledge. In this context, it is important to note that it is not for policymakers, academics, activists, lawyers or other outsiders to decide whether traditional knowledge should be commodified in given circumstances or not. This decision has to rest with those directly concerned, but they should be assured of sufficient time to gather information, and to build capacity and knowledge, in order to be able to act appropriately and independently. In the case of *Hoodia*, the San decided to accept the patent and negotiate benefits, rather than attack the validity of the patent. But the pros and cons of commodification are local choices that cannot be made universally, and communities that categorically refuse to share their knowledge need to be sure that they will be heard and respected. The CBD's provision for prior informed consent is therefore paramount: it must be taken seriously and strengthened (Tables 4.7, 4.8).

Today, the San *Hoodia* case still captures the imagination of CBD negotiators, academics and the media, although the expected millions have not materialized and may never do so. Few other cases have started as dramatically as the *Hoodia* case did, with a pronouncement that the San were extinct, or have experienced so many ups and downs. One hopes that future benefit-sharing agreements involving the San will be more successful in terms of income generation, being set in a clearer legal framework since the South African Biodiversity Act entered into force.

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[32] See note 22 regarding ways the Nagoya Protocol addresses these transboundary issues.

[33] Roger Chennells.

Table 4.7 Time Line and Details of San *Hoodia* Case

Date	Details
1996	CSIR registers patent (P57) in South Africa followed by patent application worldwide in subsequent years
1997	CSIR signs licensing agreement with UK research company Phytopharm enabling Phytopharm to research further and develop P57 patent
1998	Phytopharm further sublicenses rights to develop and exploit P57 to Pfizer
2001	Article in UK *Observer* announces development of P57 patent, and quotes Phytopharm chief executive officer as saying that San are to the best of his knowledge 'extinct'
2001	San inform CSIR through their lawyer that they intend to claim their legal rights
2003	San and CSIR sign benefit-sharing agreement in South Africa
2003	Pfizer returns licence to Phytopharm
2004	South African Biodiversity Act signed into law by President Mbeki
2004	Phytopharm announces that it has sublicensed the P57 commercialization rights to Unilever, which intends to develop an appetite suppressant energy bar
2005	San *Hoodia* Benefit Sharing Trust elected, formed and registered
2007	Second benefit-sharing agreement signed between San and Southern African *Hoodia* Growers Association with approval of South African government, allocating San approximately 6% of revenue from sales of *Hoodia*
2008	South African Biodiversity Act enters into force in April
2008	Unilever returns licence to Phytopharm, which has since held discussions with other interested partners
2009	San reach agreement with Nama peoples in Namibia, so that joint benefit-sharing agreement can be negotiated with *Hoodia* growers in Namibia as well as South Africa
2010	San conclude a benefit-sharing agreement with the *Hoodia* Growers Association of Namibia

Table 4.8 Good Practice, Criticisms and Challenges of San *Hoodia* Case

Good Practice	Criticisms	Challenges
One of few agreements which have generated funds, though much less than anticipated	Benefit share too low	Unrealistic expectations
Existing structures were used to great benefit to provide legitimate negotiators	In violation of indigenous peoples' rights, no consent was obtained from San prior to registration of patent	Serious problems with over-harvesting during *Hoodia* boom
Cross-border cooperation between San and Nama		Cross-border residence of owners of traditional knowledge
Agreement achieved in initial absence of a legal framework		Severe compliance issues as *Hoodia* products enter world market without any benefit sharing
		General CBD challenge that commodification is allegedly not compatible with sacredness of traditional knowledge

4.7 Conclusion

The CBD was adopted 20 years ago, and examples of productive, long-term benefit sharing with the providers of non-human genetic resources and associated traditional knowledge are still almost non-existent. Even the famous San *Hoodia* and Kani agreements have generated significantly more unrealistic expectations than income for their beneficiaries. In the Kani case, however, income has been provided over the longer term, and in the case of the San population, further, non-*Hoodia*-based agreements have been concluded.[34] In marked contrast, the Niprisan and Chiapas cases never generated royalty income for their traditional knowledge holders and local communities.

It is important to make two points, though. First, the success of benefit sharing cannot be measured exclusively in terms of royalties. In particular, local capacity-building should not be underestimated. In the Niprisan case, the development of a comprehensive MOU, which was later adopted by WIPO and the WHO for use in other contexts, demonstrates the potential impact of such advances. Pharmaceutical research and manufacturing capacity in Nigeria was also strengthened considerably in this case. While it is disappointing that production of the sickle-cell anaemia drug developed from local traditional knowledge has met so many obstacles to being produced in Nigeria at affordable prices, it is encouraging that a drug for a major neglected disease was developed in Nigeria and approved for sale in the first place, and there are hopes that it may return to market.

Second, even though the CBD was adopted in 1992, many signatory countries still lack national legislation to facilitate the process of obtaining prior informed consent and negotiating benefit-sharing agreements, while other countries have only adopted such legislation in recent years. (For instance, the South African Biodiversity Act was adopted in 2004.)

Involving poor rural communities in procedures to obtain prior informed consent and agree on benefit sharing is difficult in any circumstances. However, often the boundaries of the community are not clearly defined. Who, for example, are the traditional knowledge holders? And even where they are clear enough, additional problems of the legitimacy of representation, competing groups, capacity to negotiate and the incompatibility of Western and traditional law systems become apparent.[35] In the Chiapas case, for example, good intentions for mutually beneficial bioprospecting which involved the local community innovatively from the start led to one of the least successful cases to date.

Even if all of these problems are resolved, others can occur later in the benefit-sharing process. This applies in particular to compliance issues, and to the possibility of overharvesting resources. In the Kani case, an American company produced a higher-priced product in competition with Jeevani, and was not legally

[34] Roger Chennells.

[35] For a more in-depth discussion of the challenges in benefit sharing with traditional knowledge holders, see Wynberg, Schroeder and Chennells (2009).

challenged. In the San case, the international market was flooded with *Hoodia* products of dubious quality, which ignored the existing benefit-sharing agreement and almost led to the disappearance of wild *Hoodia* in the Kalahari.

Given all these challenges after 20 years of legal regulation, it does not come as a surprise that benefit sharing for access to *human* genetic resources, which does not benefit from a binding international convention, is at least as difficult to secure, as we shall see in the next chapter.

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Chapter 5
Donating Human Samples: Who Benefits? Cases from Iceland, Kenya and Indonesia

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Abstract Benefit sharing involving human genetic resources is an unresolved topic. Some argue that participation in scientific research should always be altruistically motivated, which is how access to human genetic resources has historically been governed in affluent nations. However, uncritically transferring the altruism model to developing countries leads to the emergence of serious exploitation issues. This chapter illustrates the potential for exploitation and other associated ethical concerns through a discussion of three cases: The Icelandic deCODE biobank for genetic research; the sex workers from Nairobi, Kenya, whose samples are used for ongoing HIV/AIDS research; and the Indonesian government's

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decision to withhold virus samples from the World Health Organization in order to achieve fairer benefit sharing. Public attention is captured more easily by global pandemics, but the case of the Nairobi sex workers illustrates that the exploitation issues raised on the international stage by the Indonesian government are not limited to virus sharing. A framework for equitable access to human genetic resources is urgently needed, but in order to ensure justice, this needs to be accompanied by sustained attention to benefit sharing.

Keywords Benefit sharing • Icelandic biobank • Majengo sex workers • Indonesian virus samples • Exploitation • Human genetic resources • HIV/AIDS

5.1 Introduction

Since the adoption of the Convention on Biological Diversity (CBD) in 1992, benefit sharing for traditional knowledge as well as non-human biological resources has been discussed widely. In Chap. 4, we introduced examples of good practice as well as outstanding challenges. By contrast, benefit sharing involving human genetic/biological resources is a topic which is essentially unresolved. As the CBD specifically excluded human resources from its remit in 1995 (see Chap. 3), these remain in a legal vacuum, as far as international, binding legislation is concerned.

It could be argued that participation in medical research should only ever be altruistically motivated: that those who contribute to research act for the benefit and in the interests of others, and do not expect any specific rewards in the form of benefit sharing. This is particularly pertinent for research which involves minimal risk and requires large numbers of participants, for example in recruitment of participants to the growing number of biobanks,[1] or in genetic research (Williams and Schroeder 2004; Merchant 2005: 168, note 56). Some even maintain that people *should* participate in such research, as human beings have a duty of solidarity with others when it comes to health (HUGO Ethics Committee 2000a) or, in other words, a 'duty to facilitate research progress and to provide knowledge that could be crucial to the health of others' (Berg and Chadwick 2001). We will see in Chap. 8, however, that this model, which is widely accepted in affluent nations, cannot be transferred to developing countries without the emergence of serious exploitation issues. Some form of benefit sharing for human biological resources

[1] For example, the UK Biobank, a research project which collects health, medical and lifestyle information from large numbers of people, together with blood, saliva and urine samples in order to track participants' long term health, states in its information letter to potential participants, 'Taking part is not intended to help you directly, but it should give future generations a much better chance of living their lives free of diseases that disable and kill.' http://www.ukbiobank.ac.uk/docs/participantinviteletter.pdf.

therefore needs to be agreed upon to avoid the exploitation of vulnerable populations. The cases described here illustrate the *potential* for exploitation, as well as associated ethical concerns, being the prime motivator for the discussion and adoption of benefit-sharing requirements.

We shall introduce three relevant cases: The Icelandic deCODE biobank for genetic research, the sex workers in Nairobi, Kenya, whose samples are used for HIV/AIDS research, and the Indonesian government's decision to withhold virus samples from the World Health Organization (WHO) in order to achieve fairer benefit sharing.

5.2 DeCODE Genetics' Biobank (Iceland)

On 26 August 1996, the research company deCODE genetics Inc. was incorporated in Delaware, USA. A wholly owned subsidiary, Íslensk erfðagreining, was established later that year in Reykjavík, Iceland. The company was founded under the leadership of Kári Stefánsson, an Icelandic medical doctor and (at the time) professor at Harvard, with US$12 million in funds from American venture capital firms.

The aim of deCODE genetics is to conduct population genetics research on common diseases in the Icelandic population, and to use the results for the development of treatments and diagnostic tools. The Icelandic population is claimed to be of great value for genetics research because of the population's (alleged) genetic homogeneity, good medical records and extensive genealogical records.[2] One of deCODE's key goals was the construction of a population database in Iceland that would combine health data, genetic data and genealogical data from the entire population. The database was intended to be the main resource for deCODE's own research, but it would also be made commercially available to other researchers, companies and organizations.

In February 1998, deCODE concluded a five-year agreement with pharmaceutical giant Hoffmann-La Roche, which was expected to yield more than US$200 million for deCODE. According to a Roche press release, Roche would 'provide the Icelandic people free of charge with pharmaceutical and diagnostics products that emerge from the collaboration' (Roche 1998). Two subsequent agreements between deCODE and Roche confirmed the assurance of free medication and diagnostic products for Icelanders, if developed through the company's collaboration (Potts 2002).

In order to construct its database, deCODE planned to collect data from medical records in a new 'Health Sector Database'. The Health Sector Database would provide the medical data, which would then be combined with two further databases, one containing genetic data and another genealogical data. The genetic and genealogical databases could be easily constructed, the first by collecting

[2] For a further discussion of the homogeneity of the Icelandic population, see Árnason (2004).

biosamples from patients (with some sort of informed consent given) and the second by collating public genealogical records. The Health Sector Database, however, was more difficult, because the company would need access to confidential medical records. Therefore deCODE proposed new legislation which would allow the construction of the database with an exclusive operating licence granted to an unnamed company (which would naturally be deCODE).

The Act on a Health Sector Database (No. 139/1998) was passed by the Icelandic parliament on 17 December 1998, after extensive debate in parliament and society at large, and in the face of immense opposition from doctors, scientists and the organized opposition group Mannvernd (although the majority of the public supported deCODE and the Act).[3] The most controversial aspect of the Act was the implied 'presumed consent'. Data relating to individuals would be included in the database on the assumption that they did not object. Those who did not want to take part would have to make this wish explicit and opt out. Many physicians were reluctant to cooperate with deCODE and give the company access to the medical records of their patients. The Icelandic Medical Association was also opposed to the Health Sector Database, and received support from the World Medical Association regarding its concern about the ethical issues, in particular those relating to consent, and the standard requirement that research participants should be able to withdraw their participation.

In January 2000, despite the protests, deCODE genetics was granted an exclusive operating licence for the Health Sector Database for 12 years, and a separate agreement was concluded between deCODE and the Minister of Health that the company would pay the state an annual fee of 70 million kr. (close to €1 million at the time) for its licence, as well as 6% of profits, up to a maximum amount equivalent to the annual fee.[4] In addition, deCODE was to pay all costs incurred by the database, such as those of the monitoring institutions. The annual fee and share of profits was to be used for the health care system and for research, and can be considered benefit sharing. Interestingly, this falls within the (non-binding) benefit-sharing recommendations of the Human Genome Organisation (HUGO) Ethics Committee Statement on Benefit Sharing, which suggests that in the case of profit-making endeavours, the general distribution of benefits should be the donation of a percentage (recommendation 6 suggests 1%–3%) of the

[3] *Mannvernd* means literally 'human protection'. Although Mannvernd calls itself, in its full name, the 'Association of Icelanders for Ethics in Science and Medicine', it is specifically the 'organized opposition to the Icelandic government's Act on a Health Sector Database', according to its website (http://www.mannvernd.is). Its members are primarily medical doctors, scientists and academics. Mannvernd and its individual members were highly active and visible during the parliamentary debates on the Health Sector Database Act in 1998 and, to a lesser extent, during the following three or four years, as the association encouraged people to opt out of the database.

[4] 'Samkomulag á milli heilbrigðis- og tryggingamálaráðherra og Íslenskrar erfðagreiningar ehf. í tengslum við útgáfu rekstrarleyfis til gerðar og starfrækslu gagnagrunns á heilbrgiðissviði' [Agreement between the Minister of Health and Insurance and Íslensk erfðagreining (deCODE) in relation to a licence to operate a health sector database], signed 21 January 2000 by the Minister of Health, Ingibjörg Pálmadóttir, and Kári Stefánsson, CEO of deCODE genetics Inc. Available (in Icelandic only) at http://www.mbl.is/serefni/decode/ (see articles 4 and 6).

net profits (after taxes) to the health care infrastructure or for vaccines, tests, drugs and treatments, or to local, national and international humanitarian efforts (HUGO Ethics Committee 2000b).

However, to date the Health Sector Database has not materialized, because the Icelandic Supreme Court stopped its development. In 2003, the court came to the conclusion that the Act on a Health Sector Database violated the Icelandic constitution by not sufficiently protecting the right to privacy.[5] By ruling that the Act was in conflict with the constitution, the judgment declared invalid the legal framework for deCODE's plans to collect data from medical records in a centralized database. There had already been signs that deCODE had lost interest in constructing its database: in November 2002 deCODE had indefinitely postponed relevant negotiations with Iceland's largest hospital, the National University Hospital (Sigurdsson 2003). With the Supreme Court's decision it became clear that the database would most likely never be established. No attempt was made by deCODE or the government to revise the legal framework to remove the conflict with the constitution. If there had been any interest in reviving the project, such a revision would certainly have been feasible.

Nevertheless, deCODE continued to conduct genetic studies within the Icelandic population, and it did meet some research milestones set in its first agreement with Roche, though at a considerable financial loss.[6] The failure to make a profit caused financial difficulties for deCODE, aggravated by the fact that their operating funds had been handled by Lehman Brothers, a bank that lost substantial funds in failed investments. By November 2008 deCODE was practically bankrupt. The Icelandic government was unable to provide support, as it was also struggling financially, following the collapse of Iceland's main banks. A year later, in November 2009, deCODE filed for bankruptcy protection and started liquidating its assets. deCODE's key operating subsidiary, Íslensk erfðagreining, was sold to a group of investors, but it is still operating under the name of deCODE genetics, and, although the company has a new CEO, Kári Stefánsson remains on board as executive chairman and president of research (Carmichael 2010).

There are few international laws or regulations, if any, that apply to the Icelandic database. The CBD and the Bonn Guidelines exclude human genetic resources, as noted at the outset (Bonn Guidelines 2002). UNESCO's Universal Declaration on the Human Genome and Human Rights, adopted by the General Conference of UNESCO at its 29th session on 11 November 1997, does apply, in particular via a range of clear statements regarding informed consent,[7] but includes

[5] It decided in the case of *Gudmundsdóttir v. the State of Iceland* (No. 151/2003), that the daughter of a deceased man could prevent his health information from being entered into the Health Sector Database. For a good analysis of the judgment, see Gertz (2004).

[6] Apparently deCODE only received US$74.3 million out of the expected US$200 million (see Sigurdsson 2003).

[7] For example: 'In all cases, the prior, free and informed consent of the person concerned shall be obtained. If the latter is not in a position to consent, consent or authorization shall be obtained in the manner prescribed by law, guided by the person's best interest' (UNESCO 1997: article 5(b)).

only vague general references to sharing the benefits of genetic research so that they are available to all.[8] UNESCO's Universal Declaration on Bioethics and Human Rights, adopted by the General Conference of UNESCO at its 33rd session on 19 October 2005, also applies to this case, but again it is vague on the sharing of benefits 'with society as a whole and within the international community' through any of a number of generalized forms, the most relevant of which in this case are the 'provision of new diagnostic and therapeutic modalities or products stemming from research' and 'access to scientific and technological knowledge'.[9]

Although the database itself never materialized, the case of the Icelandic database is significant from the perspective of benefit sharing. Benefit sharing was barely an issue at all in the debates and discussions in Iceland, but two specific benefit-sharing agreements were negotiated: one between deCODE and Roche for free pharmaceutical and diagnostic products for the Icelandic population, and the other between deCODE and the Ministry of Health as part of the operating licence.

There is no *requirement* for benefit sharing of any kind in the Act on a Health Sector Database, but article 4 implicitly leaves benefit sharing to negotiations with the licensee: 'The minister [of health] and licensee may agree on further payments to the Treasury, which shall be devoted to promoting the health service, research and development' (Icelandic Parliament 1998: article 4). The Icelandic population was expected to enjoy various other indirect benefits as a result of deCODE's operations in Iceland and the database in particular. These included economic benefits, jobs created in the biotechnology sector, an improved research environment for genetics and medicine in Iceland, and attracting talented Icelandic scientists back home from abroad. And, of course, Icelanders expected to have access to the medications resulting from the research through the national health service.

Given that Iceland is, notwithstanding its recent economic crisis, a wealthy Western nation, with universal health care coverage providing heavily subsidized or free medication to citizens, it is perhaps surprising that deCODE negotiated benefit sharing at all for the Icelandic population. One possible explanation for Roche's generosity is the fact that deCODE's database would allow it to track the use of Roche's free products in Iceland, and closely monitor their effectiveness and reported side effects in a population that, in most cases, would be considerably larger and easier to manage and monitor than those available for post-marketing (Phase IV) trials. deCODE wanted to create 'a totally informative population with which … to model both disease and *host-drug interactions*' (emphasis added) (Gulcher and Stefánsson 1998: 526). In this context, the promise of free drugs was criticized, although it aligns with the requirements of the Declaration of Helsinki

[8] 'Benefits from advances in biology, genetics and medicine, concerning the human genome, shall be made available to all, with due regard for the dignity and human rights of each individual' (UNESCO 1997: article 12(a)). '[D]eveloping countries [should] benefit from the achievements of scientific and technological research so that their use in favour of economic and social progress can be to the benefit of all' (UNESCO 1997: article 19(a)(iii)).

[9] UNESCO (2005), article 15, specifies examples of sharing benefits of scientific research in general.

relating to post-study obligations (see Chap. 3). For instance, one of deCODE's founders, physician Ernir Snorrason (who left the company and became one of its main critics), wrote a letter to the parliamentary committee on health as the Health Sector Database Bill was being debated in parliament, arguing that free medications would harm patients' health, as older, well-known drugs would be replaced by free medications fresh from clinical trials with little-known side effects. (Some side effects emerge only once a drug is on the market and in wide use.) Ernir Snorrason suggested that Roche wanted to use the Icelandic population to test drugs for efficacy and side effects (Snorrason 1998).

An affluent, democratic country such as Iceland, with a high level of education and universal health care, may seem far from vulnerable to exploitation. But even in this case there are issues of vulnerability and potential exploitation to consider. One issue concerns the so-called 'presumed consent' policy for the Health Sector Database. Instead of the entity proposing the tests seeking informed consent from research participants, as is the rule for human genetic research, every resident in Iceland who used medical services was to be included as a research participant in the database, unless he or she signed a document to opt out. This policy is problematic for a number of reasons, but especially for failing to protect vulnerable individuals. In particular, those who would normally not be allowed to participate in research because they are legally incapable of giving informed consent would be included in the database by default. Many patients with mental illness or serious physical illness, and those suffering from drug or alcohol abuse, would be doubly vulnerable: their conditions make them less able to inform themselves and to make or act upon a decision on whether to opt out, even though they may have a greater interest in opting out, because their medical information is more sensitive than that of most people.

It could therefore be reasonably argued that these vulnerable citizens would be exploited simply by the inclusion of their data in the Health Sector Database. Their data would be used to benefit others without any assurance that they had considered the proposal and decided not to opt out. More likely, their ignorance of the database or their inability to withdraw from it might explain their 'presumed consent'. In this sense, their participation would benefit the researchers, the pharmaceutical companies conducting the studies and the commercial company operating the database. The latter would obtain substantial medical data which would usually be unavailable were informed consent required. As a result, these vulnerable individuals could be exposed to risks which they could avoid more easily if informed, rather than presumed, consent was required.

Vulnerability and potential exploitation are concerns not only at the level of individuals, but also at the level of the population. Many of these vulnerabilities were discussed during the debate on the Health Sector Database in Iceland. First, in general, privacy concerns have a low priority in Iceland, although the debate about the database increased public awareness of privacy issues in medicine and medical research. Second, the Icelandic public consider scientists and physicians very trustworthy, a situation which can facilitate potential exploitation.[10] Third,

[10] For a general discussion on this issue, see Andanda (2005).

the democratic process and public institutions are vulnerable to manipulation because the culture of both politics and public institutions is characterized by nepotism: favours to family, friends and political allies often outweigh standard procedures, regulations and even the law. This vulnerability is often blamed on the small size of the population, only about 317,000 (Wade 2009: particularly 25–26; Vaiman et al. 2010: 370; Bergmann 2010). Fourth, there was a significant power imbalance between the corporations (deCODE and Roche) on the one hand and the population on the other.

This power imbalance was based on four key advantages of the corporations: funds, political power, scientific authority and economic rationality. Regarding funds, deCODE had the financial means to stage an advertising and public relations campaign to win over the population. For example, the company ran full-page advertisements in the main Icelandic newspapers and toured Iceland with town-hall style meetings to sell the idea of the Health Sector Database to the public. As for political power, deCODE had very close ties to the conservative Independence Party, which was in power in Iceland at the time. In February 1998, when deCODE and Roche signed their contract, David Oddsson, then Iceland's prime minister, passed the pen between the representatives of the two companies. Later that year, Oddson's centre-right coalition in parliament passed the Health Sector Database Bill as law. The initial version of the Bill was drafted by deCODE and faxed to the Ministry of Health on 14 July 1997. Concerning scientific authority, deCODE presented the Health Sector Database plans as a major scientific undertaking which was very likely to result in major contributions to scientific and medical progress, and downplayed their commercial aspects. Although the opposition to the project was led by medical doctors and scientists, who had some scientific authority of their own, they were discredited as being merely envious rivals of deCODE's founder, Kári Stefánsson. Finally, the company and its supporters appealed to economic rationality, when deCODE promised to create jobs in technology, science and medicine, and bring to Iceland investment capital and research funding. In his speech during the signing of the deCODE–Roche contract, Prime Minister David Oddsson compared the economic benefits of deCODE's cooperation with Roche both to a good fishing season and to an aluminum smelter, the twin cores of Iceland's manufacturing and export.[11]

These vulnerabilities made it easier for the corporations to gain access to the population in an attempt to use it for commercial gain by turning it into a genetics laboratory, with the acceptance of the majority of the population and its political representatives. Although the project to establish the Health Sector Database eventually failed, this was not because of resistance within the population, let alone any concerns about exploitation. A combination of scientific

[11] For a detailed discussion, see Jóhannesson (1999).

and financial reasons had taken the steam out of the project, with the result that it did not have enough momentum to get past the legal setback discussed above.

The Icelandic case gives rise to more questions than answers. What is a fair reward for a genetic resource, when that resource is a human population? deCODE is a private, American corporation. It was to have rights to sell information from the database to other corporations or institutions (with certain limitations). In this setting, many object to the commercialization and corporate control of medical data – that is, of what is seen as confidential personal information (see, for example, Rose 2001). Who can decide to commercialize and sell such a resource, and through what process? This case involves deep ethical and political issues, not least regarding how the decision can be made to subject the population to this sort of research, and whether the population can be sensibly said to have agreed or consented to the research (Tables 5.1 and 5.2).

The Icelandic case shows that in the absence of an international legal regime, even an affluent society whose parliamentary representatives have discussed access and benefit-sharing requirements for a particular case in detail can fail to achieve agreement. The following case is even more extreme, in that it spans a much longer time frame and involves a highly marginalized, disadvantaged population in a developing country.

Table 5.1 Time Line and Details of Icelandic Case

Date	Details
26/08/1996	deCODE genetics Inc. established in Delaware, USA
late 1996	deCode subsidiary Íslensk erfðagreining established in Iceland. Its primary objective: to create and operate a centralized health sector database for the whole nation, and use it on a commercial basis for research in population genetics
Feb 1998	deCODE signs agreement with Hoffmann-La Roche claimed to be worth about US$200 million. (Ultimately only US$74.3 million was paid to deCODE)
17/12/1998	Act on a Health Sector Database (No. 139/1998) passed by Icelandic parliament
22/01/2000	Íslensk erfðagreining/deCODE granted exclusive operating licence for the Health Sector Database
14/10/2002	Negotiations between deCODE and Iceland's largest hospital about Health Sector Database postponed indefinitely
27/11/2003	Icelandic Supreme Court decides that Health Sector Database Act violates Icelandic constitution's protection of privacy, marking end of Health Sector Database project
17/11/2009	deCODE files for bankruptcy protection. Íslensk erfðagreining (deCODE's core business) sold but keeps operating under name of deCODE genetics

Table 5.2 Good Practice, Criticisms and Challenges of Icelandic Case

Good practice	Criticisms	Challenges
Extensive debates about project in media, parliament and society	Poor quality of social debate (poorly informed, biased and aggressive)	Encouraging open, informed and fair debate in society, as a democratic requirement
deCODE was to pay Icelandic treasury annual fee for operating database, and share of profits. Funds were to be earmarked for health care, research and development	Potential stigmatization of population (for example, if research found certain genetic diseases to be more common in Iceland than elsewhere)	General challenge that human genetic resources should not be commercialized
Whole community would share in benefits	'Implied consent' or opt-out policy disadvantages vulnerable populations	Stability and predictability of benefit-sharing outcomes when reliant upon private companies (bankruptcy of deCODE mirrors problems in Nicosan case, see Chap. 4)
	'Implied consent' or opt-out policy violates Icelandic constitution and major ethical guidelines	Absence of international legal regime
	Concerns whether free medications are a form of benefit sharing or an attempt to turn population into a laboratory, with benefits accruing to industry	Uncertainty about data privacy, and about who gets access to and control over data. deCODE's exclusive rights to health data prevent other researchers from accessing data

5.3 HIV/AIDS Research and the Majengo Sex Workers (Kenya)

AIDS is one of the most devastating illnesses the world has ever faced and "remains one of the world's most serious health challenges" in 2012 (UNAIDS 2012: 8). The number of people living with HIV in 2011 was estimated at 34.0 million (UNAIDS 2012: 8). Despite the gradually falling incidence of HIV, Sub-Saharan Africa remains the region most heavily affected, accounting in 2011 for 71% of all new HIV infections (UNAIDS 2012: 11), 70% of AIDS-related deaths (UNAIDS 2012: 12), and 69% of all people living with HIV (UNAIDS 2012: 8). 44% of the latter do not have access to the antiretroviral drugs that have contained the disease in the developed world (UNAIDS 2012: 51).

Despite decades of research activity, scientists are almost no closer to producing a vaccine against HIV infection today than they were in the 1980s. The main ray of hope for developing a vaccine was provided by the 'Nairobi prostitutes',

as they have become known among AIDS experts (Associated Press 1997; Carlin 2003). They are a large group of educationally and economically disadvantaged women from a slum called Majengo in Nairobi's Pumwani District, who resort to commercial sex work to earn a living.[12] They have attracted the attention of the international community since the early 1990s through their involvement with a clinic originally established in the slum to study sexually transmitted diseases.

With the emergence of HIV, researchers wanted to find out if the virus could be found among the women already involved in the studies. The clinic has now been going for over 25 years and the cohort of research participants has been growing steadily as staff and peer leaders have helped with the recruitment process.[13,14]

5.3.1 The Research Projects

In the late 1980s, Canadian infectious disease scientist Francis Plummer first noticed something perplexing[15] among a group of 2,000 Nairobi sex workers enrolled in a study regarding sexually transmitted diseases (STDs).[16] Approximately 5% of these women had repeatedly tested negative for HIV infection, despite their high-risk behaviour (Bower 1998), according to the research team. Some of them had experienced hundreds of unprotected exposures to the AIDS virus over a decade without showing any signs of HIV infection (d'Adesky and Jeffreys 1999). The researchers were interested in two main issues, as described in an interview with a senior University of Nairobi scientist:

> [O]ur interest at that particular time … was to really try and understand two things: … how the immune system is behaving among women who are exposed to HIV and are not getting infected … that was one … and the second interest was to look at those who are already infected; what happens to HIV when these women get recurrent sexually transmitted infections? So we were looking at viral loads, earlier on before many people started doing viral load, and looking at when there is a STI [sexually transmitted infection] how does the viral load behave?[17]

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[12] See Andanda (2009) for a discussion of the women's vulnerability.

[13] Interview with University of Nairobi researcher, GenBenefit, April 2007.

[14] The interviews quoted in this chapter were conducted as part of the GenBenefit project. Clearance was granted by the University of the Witwatersrand's Human Research Ethics Committee (Non-medical), Protocol Number 61110, and the Kenya Medical Research Institute's National Ethical Review Committee, reference number KEMRI/RES/7/3/1.

[15] This phenomenon was first described by Plummer at an international AIDS conference in Berlin in 1993 (Altman 1993).

[16] The cohort of female sex workers was established by Elizabeth Ngugi and colleagues from the University of Nairobi and the University of Manitoba (see Jeffreys 2001).

[17] Interview with a University of Nairobi researcher, GenBenefit, April 2007.

These original studies are now considered to be foundational in understanding the epidemiology of HIV, and the risk factors associated with its spread (Bandewar et al. 2010). Since 1998, researchers from the universities of Oxford, Nairobi and Manitoba (Canada) have been collaborating on a project to develop a vaccine against HIV based on the immunological protection mechanisms found in these sex workers. The partnership currently includes the UK Medical Research Council, the International AIDS Vaccine Initiative[18] and the Uganda Virus Research Institute.

An early study which followed 424 sex workers between 1985 and 1994 established that a small proportion of highly exposed individuals have a natural protective immunity, which means that they seem to be resistant to HIV infection (Fowke et al. 1996). Subsequent studies aimed to clarify the nature of the women's immune response, as this 'has significant implications for vaccine design' (Rowland-Jones et al. 1998a). A 1998 study established that the Nairobi women's resistance could not be accounted for by various mechanisms suggested so far (Fowke et al. 1998).

An immunological evaluation in a further study established that the HIV-resistant women possessed high levels of a type of white blood cell known as cytotoxic T lymphocytes, or killer T-cells, which showed an HIV-1 specific response. The women's killer T-cells were able to target particular proteins produced by the HIV virus quickly, before the virus could take hold, and this protected them against HIV-1 infection (Fowke et al. 2000). This provided the researchers with a new understanding, on which subsequent vaccine development was based (Bower 1998; Rowland-Jones et al. 1998b; Kaul et al. 2001a).

Vaccine trials started in 2001 and proceeded through Phase I and II clinical trials.[19] However, in 2004 it was announced by the Oxford-Nairobi team at an international AIDS vaccine conference in Switzerland that the vaccine had failed to offer sufficient protection against HIV infection.[20]

A study conducted in Nairobi between 1996 and 2000 noted that 11 of the women who had been classified as HIV-1-resistant had seroconverted.[21] This

[18] Founded in 1996, the International AIDS Vaccine Initiative (IAVI) is a global not-for-profit, public-private partnership, with a mission to ensure the development of preventive AIDS vaccines that are not only safe and effective, but also accessible to all people http://www.iavi.org/Pages/home.aspx.

[19] Phase I trials are the earliest human tests in the life of a new drug. They involve few people and check for safety, side effects and efficacy. This information is used to establish the dose which will be used in the next stage of testing. Phase II trials are carried out in larger groups of volunteers, to establish more about efficacy, dosage and side effects.

[20] Initial analysis showed that although the vaccine was safe and well tolerated, only 20% of the volunteer participants had shown a potentially protective stimulated T-cell response after receiving the vaccine, and even that response was at a lower rate than desired (Okwemba 2004; Waldholz 2004).

[21] After initial exposure to any agent, it takes time for antibodies to develop. At some point after initial HIV infection, seroconversion occurs. (Usually this takes a few weeks to a few months.) This means there is now a detectable level of antibodies to HIV in the blood, and a person will test (sero)positive for HIV.

aroused concern, as well as scientific interest as to whether their immunity was waning. A key finding in this study was that the women's seroconversion was correlated with a reduction in sex work: that is, a break in sex work was associated with a loss of the immune responses which were protecting them against the HIV virus. The study therefore drew some important conclusions for vaccine development (Kaul et al. 2001b: 3). Attention shifted to the factors that led to seroconversion and what could be learned from this for vaccine development (Kaul et al. 2001c). Subsequent studies on the long-term survivors have suggested new directions in HIV research (Fang et al. 2004: 697).

Other studies, which used the women's genetic samples, have focused on genetic variation in order to determine susceptibility to HIV-1 infection (Ji et al. 2004). Genetic studies have provided new insights with regard to the factors associated with resistance to infection by HIV-1[22] and more studies are under way, which could contribute to the development of a vaccine against HIV.

Follow-up studies of 850 women in Majengo are currently being conducted as part of the ongoing collaborative project by researchers from the universities of Nairobi and Manitoba.

5.3.2 The Research Participants

The sex workers who live and work in Majengo often have no other income or support, live in small tin shacks, work well into middle age and have dozens of clients every day, as the payment from each is very low (Lavery et al. 2010: 1; Carlin 2003). In addition to poverty, social circumstances such as the loss of parents to HIV/AIDS, domestic violence or the need to provide for extended families may force them into sex work.

As sex work is illegal in Kenya, the women are not organized in brothels and usually work independently and compete with one another. Remnants of colonial policies, 'when sex workers were imported into Kenya from Tanzania by the British government for its soldiers' (Bandewar et al. 2010: 3), still lead to racial divisions today.

The women's extreme socio-economic disadvantage, in conjunction with the poorly funded health care system, means that they are unable to access quality health care in any other way than through involvement in the research clinic.

As for benefit sharing, the original, routine issues of negotiation and decision-making related to the Majengo research studies only involved researchers and administrators from the relevant universities and institutions. There was no formal inclusion of representatives of the sex workers. The volunteer (sex worker) participants themselves

[22] For example: 'This study adds IRF-1, a transcriptional immunoregulatory gene, to the list of genetic correlates of altered susceptibility to HIV-1. This is the first report suggesting that a viral transcriptional regulator might contribute to resistance to HIV-1' (Ball et al. 2007: 1091).

have at all stages given individual consent to their participation in the ongoing studies, which use their blood, cervical, vaginal and saliva samples.[23] However, they have retained no right of ownership over any donated samples or knowledge accrued from them, and therefore no negotiating rights regarding any subsequent developments.

5.3.3 The Legal Situation

Research involving human subjects is bound by various international guidelines, most prominently the Declaration of Helsinki (WMA 2008) and the Council for International Organizations of Medical Sciences (CIOMS) guidelines (CIOMS 2002). These are not enforceable legal instruments, but constitute the most authoritative statements on medical ethics, influencing the formulation of international, regional and national legislation and professional practice. The legal situation with regard to benefit sharing for human biological resources is discussed in Chap. 3. In relation to the Majengo case, the national law of Kenya and UN guidelines that apply to HIV/AIDS research are also relevant.

Although Kenya has put regulations in place to govern access to non-human genetic resources and subsequent benefit sharing, currently no such policy or regulations exist for the use of human genetic resources (Minister for Environment and Natural Resources 2006).[24] However, in 2005 Kenya developed national Guidelines for Research and Development of HIV/AIDS Vaccines (Ministry of Health 2005) in response to the Majengo case. Although the sex workers have not themselves been involved in vaccine trials, the guidelines are relevant because the women's research participation led to the development of experimental vaccines. The guidelines provide an enabling framework for addressing issues of financial compensation for participants through material transfer agreements and research and development agreements. It has been argued that benefit-sharing agreements could effectively be incorporated into the cooperative research and development agreements (Ministry of Health 2005: 44 section 8.3; see also Andanda 2008: 173). The agreements would then be binding and enforceable in domestic law.

Paragraph 4.2 of the Kenyan guidelines, which stipulates the terms of reference for science and ethics committees in the country, requires such committees to verify the ethical integrity of HIV/AIDS vaccine trial protocols in accordance

[23] Issues have been raised concerning the difficulties of communicating adequate information for obtaining meaningful consent from potential participants, given the difficulties of translating complex concepts into languages that may not (yet) have the linguistic resources to communicate those. '[T]he moment you begin to talk about even translating into a language that the subject, the participant understands, you find that most words do not exist here … so there is a problem of the concepts' (interview with Kenya Medical Research Institute (KEMRI) Ethics Committee member, GenBenefit, Nairobi, April 2007).

[24] Interview with an official at the Ministry of Health (MoH), Kenya, GenBenefit, April 2007.

with internationally accepted ethical guidelines, such as the Ethical Considerations in HIV Preventive Vaccine Research of the Joint United Nations Programme on HIV/AIDS (UNAIDS). This guidance document (UNAIDS 2000) is not legally enforceable, but Guidance Point 10 stipulates: 'The research protocol should outline the benefits that persons participating in HIV preventive vaccine trials should experience as a result of their participation. Care should be taken so that these are not presented in a way that unduly influences freedom of choice in participation' (UNAIDS 2000: 44) (see also Chap. 2). The commentary on this Guidance Point lists what may be considered to be *minimum* benefits for participants in HIV preventive vaccine trials in terms of health care.

Some of the activities related to the conduct of HIV vaccine trials should benefit those who participate. At a minimum, participants should:

- have regular and supportive contact with health care workers and counsellors throughout the course of the trial
- receive comprehensive information regarding HIV transmission and how it can be prevented
- receive access to HIV prevention methods, including male and female condoms, and clean injecting equipment, where legal
- have access to a pre-agreed care and treatment package for HIV/AIDS if they become HIV infected while enrolled in the trial
- receive compensation for time, travel and inconvenience for participation in the trials, and
- if the vaccine is effective, develop protective immunity to HIV.

However, these are not, strictly speaking, benefits that are derived *from* the research, which could then be shared with the participants, but simply benefits that may be derived *from participating in* vaccine research, in line with current agreed international standards of ethical conduct in medical research. As we will see below, most of these 'benefits' have been, and continue to be, available to the women in the Majengo studies.[25]

5.3.4 Current Benefits

The main benefit received by sex workers who are involved in the research projects today is access to health care. In the early 1980s, the Majengo sex workers could only access health care from the Special Treatment Centre in Nairobi (the popularly named 'Casino Clinic' because of its proximity to a local casino).

[25] This was confirmed by a University of Nairobi researcher, as well as some of the Majengo participants. It is important to note that this has been a major factor in the women's (continuing) involvement: 'I expected treatment, free of charge. Every time I fall sick I come here for treatment and it's free.'; 'It is their treatment, they give us free medicine because of the nature of our work' (GenBenefit interviews, Nairobi, April 2007).

The services were poor and care providers discriminated against the sex workers (Bandewar et al. 2010: 4).

Since the research team established a clinic in the slums of Majengo, the quality of services has improved vastly. The sex workers now have non-discriminatory access to full health care within walking distance. Since 2005, the women have also been able to access a comprehensive care package, which includes antiretroviral treatments. This package has led to a marked reduction in morbidity and mortality. At the same time, it has reduced the number of orphans and decreased the number of HIV transmissions in the wider community.

In addition to these direct benefits in terms of health care, from the mid-1990s the dedicated clinic environment has offered a 'safe haven', which has enabled the women to share their experiences with one another in a respectful environment. This has allowed them to form new relationships, social networks and a sense of solidarity and belonging, creating a 'sex workers community'. This has helped unite the sex workers in, for instance, a 'no condom, no sex services' campaign (Bandewar et al. 2010: 6).

In addition, international exposure as a result of the research publications has brought an increased level of attention to the case that may eventually help safeguard the women's rights to any benefits that might accrue from the ongoing research activities. In recent times their representatives have been invited as stakeholders whenever Ministry of Health officials discuss the needs of most-at-risk populations, thus moving to integrate their representation into formal consultations and decision-making processes.

The increased engagement between the health care personnel and the sex workers has also led to important insights for the researchers regarding the costs and benefits of targeted HIV prevention interventions and which community engagement exercises can be employed successfully. It has been demonstrated, against expectations, that with the right motivation a highly disadvantaged and poor population can cope with the demanding rigours of antiretroviral treatments and can achieve the same adherence levels as the general population. This unforeseen outcome of the research studies is of great significance – and benefit – to all those living with, or working with those living with, HIV/AIDS, irrespective of the quest for a successful vaccine.

5.3.5 Analysis of the Majengo Case

Traditionally, donors of samples used for scientific research do not have a direct stake in future benefits. As previously noted, altruistic donation of samples is frequently taken for granted. However, the traditional assumption that 'the donors of genetic material used in research act altruistically and are entitled to no property rights or direct benefit-sharing in the fruits of the research' (Marchant 2005: 153) is 'under assault from several directions simultaneously' (Marchant 2005: 159). In particular, this traditional handling of resource samples

has been increasingly criticized in the context of the potential exploitation of research participants in developing countries (Schroeder and Lasén Diáz 2006; see also Sheremeta 2003). Wider issues of benefit sharing with the Majengo participants have been raised (Andanda 2004) in the general context of CBD-style benefit sharing in cases of non-human genetics, and in particular following publicity regarding an alleged dispute between researchers from the Universities of Oxford and Nairobi over a patent application related to the HIV vaccine.[26] According to some media reports, the Majengo women themselves have also raised issues related to benefit sharing (Okwemba 2000). The main issues in this context are:

- How to decide on appropriate benefits
- Representation issues in benefit sharing negotiations/agreements
- The fear of undue inducement or problems with informed consent
- Export of samples.

5.3.5.1 Appropriate Benefits and Representation Issues

Benefit sharing in the context of the CBD is often assumed to mean monetary royalties from marketed products. Benefit sharing in the case of post-study obligations in medical research is normally assumed to mean access to marketed products. Yet, in both areas, alternative benefits are feasible. Under the CBD, benefits are usually negotiated case by case. Hence there are no legal requirements for any particular kind of benefit: outcomes depend on the particular negotiations. Likewise, the Declaration of Helsinki and similar guidelines recognize that in some cases alternative benefits might be more appropriate than access to successfully tested health interventions; otherwise research participants involved in studies, such as those in Majengo, which do not lead directly to a particular product or intervention would simply not benefit at all (see also Chap. 8).

The following list (which is not exhaustive) gives examples of benefits which satisfy current standard benefit-sharing requirements *in addition* to royalties (CBD context) and straightforward post-study access to products:

[26] Details came to public attention through the media, where an alleged patent dispute between the Universities of Nairobi and Oxford was first discussed in 2000 (Turner 2000). It was reported that disagreements arose when University of Nairobi scientists protested that their partners at Oxford had patented the HIV vaccine development process without acknowledging them (Daily Nation 2001). This dispute was resolved after 'intense' negotiations (Turner 2000) which resulted in a new memorandum of understanding between the parties. The 30-page memorandum was in force from 1 October 2001 to 30 September 2004. Although it provides that the collaborators will be joint applicants for, and owners of, rights, titles and interests in inventions and/or patents arising from the research, and that research benefits will be shared equally between them, it does not mention how the researchers would compensate the Majengo women who provided so many of the resources leading to the vaccine development (AAVP 2002).

- Feedback to participants (Declaration of Helsinki) (WMA 2008: article 33)
- Access to health care for participants to ensure the safe conduct of research and adherence to post-study obligations (CIOMS 2002: guideline 21)
- Support for local health services, including health infrastructure (HUGO Ethics Committee 2000b)
- Access to scientific and technological knowledge (Universal Declaration on Bioethics and Human Rights) (UNESCO 2005: article 2f, 15e)
- Capacity-building facilities for research purposes (Universal Declaration on Bioethics and Human Rights) (UNESCO 2005: article 15f, 24.2).

The sex workers do benefit from feedback and the provision of health care, as well as health education campaigns and the availability of a functioning health infrastructure. But who decides whether this is appropriate, or enough? Some of the Majengo women have a very clear sense of what additional benefits there should be. Unsurprisingly, many of the sex workers want to leave their dangerous profession. During our research a young sex worker asked: 'Is there any way you can help us to fend for ourselves and get on in life like others? That would be good.'[27] Over the past 15 years the clinic has made efforts to help some leave sex work. However, these initiatives have not been successful, due to inadequate business skills, the poor state of the economy in Kenya and lack of experience: 'We are doctors and poorly equipped to help effect transition for sex workers into other trades.' [Joshua Kimani].

Interestingly, one of the most serious problems in decision-making for CBD-style benefit sharing in non-human genetics (as discussed in Chap. 4), – namely, who can legitimately represent a community – would not be as problematic in urban Majengo. As an outcome of the long-standing research study, the sex workers regularly elect peer leaders who have represented their interests in discussions with the clinic management and researchers, and more recently in consultations with government agencies.

More broadly, though, there are important questions about who should be included in the group that qualifies for these benefits. The sex workers enrolled in the study? Sex workers in the Majengo slum in general? Sex workers in Kenya? The whole Majengo community? The entire nation?[28]

When trying to resolve issues of representation and appropriate benefits for this case, we have to conduct our discussion in the wider context of benefit sharing as established by relevant ethical guidelines. For instance, the UNAIDS guidance document recommends that any successful HIV vaccine should be made available not only to clinical trial participants but also to 'other populations at high risk of HIV infection' (UNAIDS 2000: 13). As Majengo sex workers undoubtedly constitute such a group, this means that if a vaccine were developed, the women should

[27] Interviews with Majengo participants, GenBenefit, Nairobi, April 2007.

[28] Some of the sex workers have pointed out that benefit sharing via national governments would be complicated by the fact that some of them are migrants from Tanzania or Uganda. Additional questions around benefits for the families of deceased participants have also been raised by several parties (see GenBenefit 2009).

receive it on the basis of their need (risk), regardless of their involvement in the research studies which brought it about. However, even if one were optimistic about achieving compliance with the UNAIDS guideline, access to successfully marketed products is not the only question on the topic of appropriate benefits. The main problem is of a different nature: should the donors of biological samples be able to negotiate for benefits on a case-by-case basis with the users of those resources? If they did, would this not violate all guidelines on research ethics, because the prospect of freely negotiated benefits would, in fact, present an undue inducement to participate? This leads us to the next point.

5.3.5.2 Undue Inducement/Informed Consent

A common concern related to participation in medical research is whether offering benefits to research participants is an inducement which threatens informed consent (Grady 2001; Simm 2007: 11–12). A senior Kenyan ethicist has noted that 'poverty is a great factor and sometimes militates against voluntary consent'.[29] As we have observed above, some international guidelines accept that research participants may receive free medical services, and even encourage the idea. However, they also note that these should not be 'so extensive as to induce prospective subjects to consent to participate in the research against their better judgment' (CIOMS 2002: guideline 7) and that '[b]enefits should not constitute improper inducements to participate in research' (UNESCO 2005: article 15).

Prostitution is a criminal offence in Kenya, and the age of consent is 18. The UNAIDS guidance document notes clearly that '[p]ersons who engage in illegal or socially stigmatized activities are vulnerable to undue influence' and argues that legal or social status may limit a person's ability to provide valid informed consent (UNAIDS 2000: Guidance Point 13). The sex workers are known to be discriminated against in other health facilities, and this paradoxically compromises the issue of informed consent in Majengo. Who would not enrol in a research study to obtain free and non-discriminatory health care in a secure setting, given that there is no alternative?

For the sex workers themselves, the prospect of free health care is clearly perceived as a major benefit of participation in the studies: 'I agreed because when I am sick they help me a lot and when my immunity is down they will also help me.'[30] '[I agreed] because I did not have money to go to hospital so if they gave me medicine … I thought it was better and my body can help other people by the research.'[31]

This demonstrates that the provision of health care in return for research participation can compound people's vulnerabilities (see Andanda and Cook Lucas 2007). The Majengo case illustrates that the tension between benefit sharing and

[29] Interview with KEMRI Ethics Committee member, GenBenefit, Nairobi, April 2007.

[30] See Footnote 27.

[31] Ibid.

undue inducement is not always easily resolved (see Chap. 2). Indeed a senior Kenyan ethicist has commented:

> Most people think that our commercial sex workers have been exploited. They have been used and in the end there was no benefit from that. Society may benefit from the alleged resistance. … we can say the whole world will benefit, but is that enough to these ladies who have been attending the clinic since 1985?[32]

The discussion about undue inducement will be revisited in Chap. 8.

5.3.5.3 Export of Samples

The final concern is the use of samples abroad. In common with many developing countries, Kenya does not have the capacity for scientific analysis of many of the

Table 5.3 Time Line and Details of Sex Worker Case

Date	Details
1984	Cohort of female sex workers established in Nairobi to study STDs
1985	Majengo sex workers' clinic established in Pumwani Division, Nairobi, with comprehensive STD care and prevention services
1985	First-generation HIV testing kit used to test samples from the sex workers. Many test positive for HIV, changing the focus of the research programme
1988–1993	Natural history study of HIV initiated, and efforts to enrol sex workers into the cohort scaled up. Approximately 5% of sex workers enrolled in the study repeatedly test negative for HIV infection, despite their high-risk behaviour
1993	Announcement of natural resistance to HIV in some of these women raises hopes of a vaccine
1996	Results from study officially published in peer-reviewed journal. The scientific world searches for an HIV vaccine
1998	International collaboration begins between Universities of Oxford, Nairobi and Manitoba towards an HIV vaccine based on the immunological protection mechanisms found in these sex workers
1996–2000	Ongoing studies reveal late seroconversion in some of the women who had been classified as HIV-1 resistant. This catalyses further research
2001	Vaccine trials start and proceed through Phase I and II clinical trials
2004	Vaccine trials abandoned, as the vaccine offered insufficient protection against HIV infection (Follow-up studies of 850 women in Majengo are being conducted as part of the ongoing collaborative project by researchers from the Universities of Nairobi and Manitoba.)
2005	Free antiretrovirals (ARVs) become part of Majengo sex workers' clinic comprehensive standard of care and prevention services
2005–2010	All HIV-infected sex workers enrolled in the Majengo sex workers' clinic who qualify for ARV are initiated on therapy. Reduction in both morbidity and mortality noted. Studies continue on single nucleotide polymorphisms to explain HIV resistance among sex workers

[32] See Footnote 29.

Table 5.4 Good Practice, Criticisms and Challenges of Sex Worker Case

Good practice	Criticisms	Challenges
Comprehensive health care package for participants	Some might regard comprehensive health care as undue inducement	Identification of who should benefit if product is marketed
Feedback to participants	Research involves vulnerable participants	Absence of binding international legal regime
Ongoing effective community engagement strategy between sex workers and researchers, e.g. through peer representation and consultation meetings	Problem of stigmatization of research population because sex work is illegal in Kenya	Building further in-country research capacity
Improved representation of sex workers, e.g. at government consultations	No involvement of sex workers in initial decisions about benefit sharing (e.g. contract between Nairobi and Oxford)	
Improving research capacity in Kenya	No specific commitment made to ensure post-study access to developed products	
	Export of samples for analysis due to lack of local capacity	

samples provided in the Majengo study. This means that in 'most cases … the samples or the materials are taken out of the country … [and] when these materials are gone we never get to know what happens to these things.'[33]

Kenya's guidelines on HIV vaccines research address this issue superficially: 'No biological material transfer shall be done without informed consent of the trial participants' (Ministry of Health 2005: 41 section 7.3).[34] However, while it is very easy for individual participants to agree to their samples being transferred abroad for analysis, or to consent to the transfer of material for (potential) commercial development, this is not equivalent to the country having control over the samples. The real issue arises when the issue of exploitation becomes pressing at a community or country level. This will be discussed next with our final case study (Tables 5.3 and 5.4).

[33] Ibid.

[34] 'Material transfer' here refers to the transfer of materials or specimens to another party.

5.4 Avian Flu Virus Samples (Indonesia)

Avian flu (H5N1 influenza type A) is a contagious viral disease, most likely to affect birds. The most dangerous form of avian flu spreads very rapidly and can cause almost 100% mortality among birds within 48 hours. On rare occasions, the virus can cross the species barrier and infect humans, although human-human transmission is very rare.[35] As for age distribution, the majority of human avian influenza cases, unlike seasonal influenza cases, are found in those below 25 years of age. The disease became an international problem in the late 1990s and, since then, the human death toll has been worst in Indonesia (Table 5.5).[36,37]

Table 5.5 Avian Flu: Human Death Toll by Country, 2003 – June 2011

Indonesia	146	Cambodia	13	Nigeria	1
Vietnam	59	Azerbaijan	5	Pakistan	1
Egypt	48	Turkey	4		
China	26	Lao	2		
Thailand	17	Iraq	2	Total	324

Data: World Health Organization[38]

The WHO collects virus samples for distribution to affiliated laboratories in an effort to monitor and assess the risk posed by avian flu and other similar infectious diseases, to detect mutations and to develop vaccines targeted to specific strains.

Indonesia reported its first human case of avian flu in July 2005, and continued to report an average of five new cases per month from September 2005 to May 2007 (Sedyaningsih et al. 2008: 483). From 2005 to 2006, Indonesia shared by far the largest number of virus specimens with WHO laboratories, including the U.S. Centers for Disease Control and Prevention in Atlanta, Georgia, and Hong Kong University.[39] This was in accordance with the WHO regulations on public health emergencies of international concern (WHO 2005b). However, towards the end of 2006, Indonesia lost trust in the WHO system and decided to withhold its samples (Sedyaningsih et al. 2008).

Various factors, according to Indonesian officials, led to the breakdown of trust: individuals who were outside of the WHO system were given access to samples that Indonesia sent to the WHO; laboratory results involving the Indonesian

[35] http://www.who.or.id/avian/index.php

[36] As of August 2010 there had been 139 deaths recorded in Indonesia out of a total 168 cases (http://www.who.int/csr/disease/avian_influenza/country/cases_table_2010_08_31/en/index.html).

[37] See Footnote 35.

[38] http://www.who.int/csr/disease/avian_influenza/country/cases_table_2011_06_3/en/index.html

[39] http://www.who.int/csr/disease/avian_influenza/country/en/

samples were presented at international meetings with little or no notification to the Indonesian government; and papers based on the use of the samples were written without genuine opportunities to include local collaborators as co-authors (Sedyaningsih et al. 2008: 485). This was in contravention of the WHO's own policy, published in March 2005, regarding the sharing of influenza viruses or specimens with the potential to cause human influenza pandemics, which stated that 'the designated WHO Reference Laboratories will seek permission from the originating country/laboratory to coauthor and/or publish results obtained from the analyses of relevant viruses/samples', and that there 'will be no further distribution of viruses/specimens outside the network of WHO Reference Laboratories without permission from the originating country/laboratory' (WHO 2005a).

Subsequent reports confirmed that members of the WHO Global Influenza Surveillance Network (GISN) routinely shared information derived from virus specimens with firms that were outside of the network, and that some GISN member institutions and private firms filed patent applications using that information (Hammond 2009; WIPO 2007; Sedyaningsih et al. 2008: 486). Indonesian officials argued that allowing pharmaceutical companies (who were not members of the WHO) to have access to the Indonesian samples was not only (again) in contravention of the WHO's policy regarding virus sharing, but also an indication of the grave unfairness of the system. As Endang R. Sedyaningsih et al. (2008: 486). put it:

> Disease affected countries, which are usually developing countries, provide information and share biological specimens/virus with the WHO system; then pharmaceutical industries of developed countries obtain free access to this information and specimens, produce and patent the products (diagnostics, vaccines, therapeutics or other technologies), and sell them back to the developing countries at unaffordable prices. Although it is general knowledge that this practice has been going on for a long time for other major communicable diseases – not just for avian influenza – the fear of potential pandemic influenza has magnified this gap.

Following Indonesia's decision to stop sending samples, the policy that permission should be sought prior to distributing any samples to entities outside of the WHO was overridden by the WHO's executive board meeting in January 2007. The new WHO recommendation stressed countries' responsibility to share their specimens or viruses without imposing 'agreements or administrative procedures that may inhibit the proper functioning of the WHO GISN, including in particular the timely sharing of material and information and the achievement of the Network's objectives' (Sedyaningsih et al. 2008: 486; WHO 2007b).

Appealing to all members of the WHO in 2007, the organization's director-general, Margaret Chan, said that cooperation was crucial to combating a pandemic: 'International public health security is both a collective aspiration and a mutual responsibility' (WHO 2007c: 3). Referring to its specific situation, the Indonesian government noted that the CBD gave sovereignty over biological resources to national governments, a principle which they upheld on behalf of their populations, and that national law required a standard material transfer

agreement (SMTA)[40] for shipment of materials outside the country (Sedyaningsih et al. 2008: 487).

Aware of the problem since 2006, the WHO issued a report on 'Best practice for sharing influenza viruses and sequence data' in January 2007 (WHO 2007a). The report emphasized that the 'timely sharing of influenza viruses and the associated genetic and antigenic information is essential for developing the diagnostic tests, vaccines, and strategies necessary to protect populations' (WHO 2007a: 1). However, it also recognized that developing countries carried a disproportionate disease burden without the appropriate means to protect their populations' health, a clear sign of vulnerability (see Chap. 2). For this reason, it noted, it was important that the 'benefits derived from this global system [of virus sharing], including better access to influenza vaccines, must be shared (WHO 2007a: 2).

Following a two-day meeting organized by the WHO in Jakarta in March 2007, the Indonesian government resumed sending occasional virus samples to the WHO (Revill 2008). This decision followed agreement among members of the WHO 'on a timetable to make the changes necessary to accomplish … [the] objective of achieving equitable and affordable access to vaccines for developing countries around the world' (Wulandari and Pathoni 2007).

In April 2011, after four years of negotiations, the WHO's Open-Ended Working Group of Member States on Pandemic Influenza Preparedness reached agreement on an alternative framework for influenza virus sharing. The Pandemic Influenza Preparedness Framework (also called PIP Framework), ratified by the WHO at the May 2011 World Health Assembly (WHA), is meant to be responsive to the concerns raised by the Indonesian government (WHO 2011a). Importantly, it recognizes the 'sovereign right of States over their biological resources' (WHO 2011a: PP11). To protect this right, the framework includes the requirement for two binding SMTAs (WHO 2011a: paragraph 5.4). The first SMTA applies to institutions within the GISN and contains terms and conditions which prohibit laboratories from making intellectual property claims in relation to the samples shared with them. In this regard, the first SMTA does not impose any requirements for benefit sharing but rather ensures that no relevant patents are being applied for. The second SMTA applies to those outside the GISN system and imposes two benefit-sharing conditions, selected from a list of options which include: giving developing countries 10% of the resulting vaccines and/or anti-virals; selling 10% of these at an affordable price; or granting manufacturing companies within developing countries licences to produce vaccines or antivirals at affordable royalties, or royalty-free (TWN 2011b; WHO 2011a).

On the whole, the framework is 'an important step forward towards a system for the sharing of influenza viruses and resulting benefits'. In particular, it is 'a milestone as it obliges pharmaceutical industry and other entities (that benefit from the WHO virus sharing scheme) to engage in sharing of benefits (TWN 2011a). In particular, the binding language and the compulsory nature of SMTA 2 is to be welcomed (Wilke 2011).

[40] An SMTA is a legal contract that governs the transfer of materials – typically biological materials – between two parties. An SMTA specifies the rights and obligations of provider and recipient, binding both to certain terms and conditions of transfer.

5.4.1 Benefit Sharing for Influenza Viruses

In 1951, the United Nations adopted the International Sanitary Regulations (ISR) through the Fourth WHA. The ISR had two aims: to prevent the international spread of designated infectious diseases, and to set requirements for the reporting and notification of disease cases. The regulations were designed to ensure maximum security against the international spread of diseases with minimum interference in world traffic. In 1969, the ISR were revised and renamed International Health Regulations (IHR).[41] The current regulations aim to avoid acute public health crises by preventing the spread of global disease (WHO 2008).

Two schools of thought have interpreted the current IHR in conflicting ways (Fidler 2008) when commenting on Indonesia's actions (Sedyaningsih et al. 2008: 489). The first school of thought argues that compliance with the IHR requires the timely sharing of biological samples without any preconditions. The second school of thought argues that the IHR does not require the sharing of specimens with the WHO, but only the sharing of public health information. In the former case, Indonesia would have to send swabs, endotracheal aspirates, lung biopsies etc. to the WHO. Supporters of this view maintain that the sharing of information alone is not an effective means to realize the global health aims of the IHR and that:

> surveillance for aetiological agents that may cause a PHEIC [Public Health Emergency of International Concern] can only be conducted if countries share samples in a 'timely and consistent' manner, without 'preconditions' (Sedyaningsih et al. 2008: 484).

In the second scenario, facts about cases, strains, locations etc. would suffice. Proponents of this view argue that the IHR does not require the sharing of specimens and that the CBD gives nation states sovereignty over biological resources. This scenario is closer to the position taken by Indonesia.

The situation was clarified in May 2007 through a statement from the WHA, which recognized 'in particular, the importance of international sharing, with WHO Collaborating Centres, of clinical specimens and viruses as a contribution to assessment of the pandemic risk' and asked member states to support the 'timely sharing of viruses within the [WHO's] Global Influenza Surveillance Network' (WHO 2007d). At the same time, the WHA also recognized 'the sovereign right of States over their biological resources' and recalled the Jakarta Declaration on Responsible Practices for Sharing Avian Influenza Viruses and Resulting Benefits, which demanded an end to exploitative practices (WHO 2007d: 1–3).

It is worth noting that the Indonesian government made no attempt to justify its actions through appeals to international ethics guidelines governing medical research, such as the Declaration of Helsinki. As noted in Chap. 3, article 17 of the Declaration of Helsinki maintains: 'Medical research involving a disadvantaged or vulnerable population or community is only justified if … there is a reasonable likelihood that this population or community stands to benefit from the results of

[41] The IHR in their current version, which came into force on 15 June 2007, are legally binding on 194 countries.

the research' (WMA 2008). It is clear that this article is relevant to the Indonesian sample donors, particularly in relation to demands for research benefits for the community. However, Indonesia chose the CBD as its point of reference. Although the CBD excludes human biological resources from its remit, it is part of the framework of international law and has led to some benefit-sharing agreements.

The point Indonesia has made through its actions is that when developing countries share virus samples that are critical to the development and production of vaccines and/or antivirals, these donor countries are mostly excluded from resulting benefits. As noted earlier by Sedyaningsih et al. (2008), any resulting vaccines are sold at a high price and so are largely unavailable to those living in developing countries such as Indonesia. Furthermore, in contrast to many developing countries, developed countries have the funds necessary to obtain supplies of limited vaccines through pre-purchase agreements with manufacturers. As Caplan and Curry (2007) have noted:

> Indonesia is basically correct: pandemic vaccines that are in development and early testing … are largely already obligated by contract to a limited group of national governments. That list does not include Indonesia or developing nations in general.

These sorts of benefit-sharing issues are highly relevant to global public health. In practice, the timely delivery of samples to the WHO, which is necessary to protect global public health, cannot be separated from the development of meaningful benefit-sharing measures, particularly when vulnerable populations are involved. As the Indonesian case illustrates, as long as sample donors continue to lack access to the benefits that result from their participation in research, their continued participation in such research is precarious. The governments of developing countries may withhold samples when the research process is regarded as exploitive or unfair to their citizens. At the same time, it would have been difficult, without the Indonesian virus samples, to monitor avian flu properly and to develop an effective vaccine. Global public health would have been at significant risk (Tables 5.6 and 5.7):

> Virus sharing is a critical part in the global effort for pandemic preparedness and global health security. Hence, the global community should continue the efforts to create a mechanism for virus access and benefit sharing that is accepted by all nations (Sedyaningsih et al.: 484).

Table 5.6 Time Line and Details of Avian Flu Case (WHO 2011b)

Date	Details
2005	IHR adopted by WHO regarding international sharing of biological samples in a health emergency
Mar 2005	Indonesia reports its first human H5N1 case, and begins to send virus samples to WHO laboratories in Jakarta and Hong Kong
Jul 2005	H5N1 cluster erupts in Indonesia
Late 2006	Indonesia learns from a journalist that an Australian pharmaceutical company is developing a vaccine based on samples shared with them by the WHO and subsequently stops virus sharing

(continued)

Table 5.6 (continued)

Date	Details
Jan 2007	WHO issues 'Best practice for sharing influenza viruses and sequence data'
Feb 2007	High-level WHO delegates attempt to resolve virus and benefit-sharing issues, but Indonesia does not resume sharing viruses with WHO
Mar 2007	Indonesia agrees to resume sharing viruses (MacKenzie 2007)
May 2007	WHA resolution 60.28 stipulates a series of actions to promote 'transparent, fair and equitable sharing of the benefits arising from the generation of information, diagnostics, medicines, vaccines and other technologies', while maintaining the 'timely sharing of viruses and specimens'(WHO 2007d). An interdisciplinary working group is convened to review and reform the global virus sharing system
Jul-Aug 2007	Working group fails to reach consensus
Nov 2007	The Intergovernmental Meeting on Pandemic Influenza Preparedness: Sharing of Influenza Viruses and Access to Vaccines and Other Benefits fails to reach a solution, but provisionally agrees on an interim statement admitting a 'breakdown of trust' in the existing system and the need to take urgent action toward agreement on a detailed framework
Feb 2008	Indonesia resumes sending occasional samples to WHO (Revill 2008)
May 2009	WHA resolution 62.10 urges the facilitation of 'a transparent process to finalize the remaining elements [of the virus and benefit sharing framework], including the Standard Material Transfer Agreement (SMTA)' (WHO 2009)
May 2010	WHA resolution 63.1 urges continued 'work with Member States and relevant regional economic integration organizations, on the Pandemic Influenza Preparedness Framework for the Sharing of Influenza Viruses and Access to Vaccines and Other Benefits', and the undertaking of 'technical consultations and studies as necessary' to support this work (WHO 2010)
Apr 2011	The WHO Open-Ended Working Group on Pandemic Influenza Preparedness for the Sharing of Influenza Viruses and Access to Vaccines and Other Benefits reaches agreement on terms and conditions that will govern the sharing of influenza viruses and other benefits
May 2011	At the WHA meeting, the WHO ratifies Pandemic Influenza Preparedness Framework for the Sharing of Influenza Virus and Access to Vaccines and Other Benefits

Table 5.7 Good Practice, Criticisms and Challenges of Avian Flu Case

Good practice	Criticisms	Challenges
Indonesia was the first country to draw significant international attention to potential exploitation of biological sample donors, leading to a WHO working group, which contributed to the PIP Framework	Withholding samples, thereby potentially endangering global public health Ongoing export of samples due to lack of local research capacity	Absence of binding international legal regime to address withholding of samples

5.5 Conclusion

It is commendable that agreement has been achieved on an alternative framework governing virus sharing, which ensures that virus donors and their communities should receive at least some benefit in return. However, early critics of the new framework have noted that it fails to establish genuine fairness and equity in virus sharing. This is largely because most of the outcomes for developing countries are inadequate to protect people in those countries from avian flu, and because they are optional rather than mandatory forms of benefit sharing. The Third World Network, for example, notes that 'the Framework does not go far enough to secure from the industry and other entities a reasonable level of benefits nor are there mandatory commitments to share knowledge, technology and know-how with developing countries on the production of vaccines, and other products' (TWN 2011b). Hence sample donors drawn from vulnerable populations may still not have access to the results of the research they contribute to. From a 'justice in exchange' perspective on benefit sharing, such access is necessary in order to avoid exploitation (see Chap. 2).

The Indonesian case shows that the lack of legal instruments governing access and benefit sharing for human biological resources is a pressing concern in a world where international consortia need to work together to monitor and protect global public health. In January 2010, the Indonesian health minister, Dr Endang Rahayu Sedyaningsih, said: 'We still insist that the responsibility to share viruses should be on an equal footing with the benefits we receive' (IRIN 2010). Indonesia is not the only country to be hit by a flu epidemic and then later demand a better benefit-sharing regime in return for access to resources. In 2009, Mexico was hit by the swine flu virus (H2N1). Commenting at the 126th session of the WHO's executive board in January 2010, the Mexican government noted that cooperation was essential to combat swine flu. However, it also noted that even with a mechanism for sharing viruses, there had not been a sharing of benefits. 'We have limited stock of vaccines and only a few countries have access to it' (TWN 2010). The Mexican government added that it was essential for an agreement to be reached on benefit sharing.

Every new global health crisis makes it clearer that despite the exclusion of human biological resources from the CBD, a solution to the question of access to those resources and the sharing of benefits from them will have to be found. In this context, the WHO initiative, which has resulted in a new framework on virus sharing to protect global public health, is a first step towards a global resolution. At the same time, it is noteworthy that the Nagoya Protocol (see Chap. 3) makes reference to the need to ensure access to human pathogens (such as influenza viruses) for public health purposes. This indicates that a more inclusive approach to access and benefit sharing for genetic resources may be possible in the medium-term future (see also Chap. 7).

However, while public attention is captured more easily by global pandemics, the case of the Nairobi sex workers illustrates that the exploitation issues noted by the Indonesian government are not limited to virus sharing. Chapters 7 and 8 outline policy responses to the current gap in the global legal framework governing access and benefit sharing.

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Chapter 6
Fair for Women? A Gender Analysis of Benefit Sharing

Julie Cook Lucas and Fatima Alvarez Castillo

Abstract If benefit sharing is about justice, then it needs to be fair for both sexes. This chapter provides a gender analysis of benefit sharing. Five cases are presented, from Kenya (Nairobi sex workers), Nigeria (NIPRISAN), southern Africa (San/Hoodia), India (Kani people), and Iceland (deCODE biobank), to show the ways in which women are politically marginalized, and the implications of this for genuine fairness in benefit sharing. In the light of international commitments to women's rights, international guidelines on benefit sharing are examined for the extent to which they protect such rights. Seeing how gender-based power imbalances on the ground can work against the implementation of guidelines and policies demonstrates the importance of strategies, processes and mechanisms that are sensitive to power dynamics in local contexts. The chapter concludes that all guidelines and policies for benefit sharing should explicitly require women's meaningful participation in all phases of decision-making, and should include examples of the kinds of mechanisms that will enable women to have an effective voice.

Keywords Benefit sharing • Gender • Indigenous peoples • Women's rights • Justice • Women's representation

> Women's empowerment and their full participation on the basis of equality in all spheres of society, including participation in the decision-making process and access to power, are fundamental for the achievement of equality, development and peace …(UN 1995: Beijing Declaration, paragraph 13).

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6.1 Introduction

For this chapter, five very different benefit-sharing cases have been analysed (drawn from Chaps. 4 and 5), and it is evident that gender is a real concern for fair benefit sharing. In all of these cases women were, and continue to be, marginalized in key decision-making bodies and processes that have negotiated for and implemented benefit-sharing agreements. This situation obtains regardless of the many differences between the societies where the cases are located, for example in levels of socio-economic and political development.

This chapter provides a gender analysis of benefit sharing. We show the ways in which women are politically marginalized and the implications of this for genuine fairness in benefit sharing. International guidelines on benefit sharing are examined for the extent to which they provide adequate protection for women's rights in the light of international commitments to such rights. The principle of gender justice is used as a guiding principle for evaluating whether or not benefit sharing is truly just and fair. The chapter concludes with some specific recommendations for how women's political participation in benefit sharing might be improved significantly.

6.2 Gender-Based Vulnerability and Women's Political Marginalization

Vulnerability has been defined as exposure to probable harm without the capability or means for protection (Schroeder and Gefenas 2009). A gender analysis of vulnerability shows that in a hierarchically sexist society[1] gender exposes women to the risk of political marginalization and deprives them of the capability or means for protecting their interests (Alvarez-Castillo, Lucas and Cordillera Castillo 2009). The marginalization of women in public decision-making takes place in all types of societies. The degree and features of marginalization have similarities as well as differences, but all have the same effect: women have less voice in processes that affect them. This is clearly seen in the experiences of women in benefit sharing in the five cases analysed here, where the most significant and common

[1] A '*hierarchically* sexist society' is equivalent to a patriarchal society, as defined by Karen Warren: 'As I use the term, "patriarchy" is the systematic domination of women by men through *institutions* (including policies, practices, offices, positions, roles), *behaviors*, and *ways of thinking* (conceptual frameworks), which assign higher value, privilege, and power to men (or to what historically is male-gender identified) than to that given to women (or to what historically is female-gender identified) …. What characterizes the position of women under patriarchy is not that women have no power, valued status, prestige, or privilege; they do…. What characterizes women's position is the varying degrees and ways women, as a group, are excluded from political and economic institutions of power and privilege …. [W]hat women under patriarchy have in common, as a group, is less institutional power and privilege than men' (Warren 2000: 64).

barrier to women's involvement is their marginalization in decision-making processes.[2]

In terms of simple numbers men dominated all the benefit-sharing decision-making bodies and the negotiations with outside parties in all five cases. Women from the relevant communities were in some cases not included in any research-related negotiations.

The female sex workers In Majengo, Nairobi, (see Chap. 5) have been identified elsewhere as a multiply vulnerable community in terms of a host of international ethical guidelines (Andanda and Lucas 2007: 18). They are the main sources of the biological materials for the HIV/AIDS research programme, but historically have been completely excluded from the research negotiations (beyond giving their individual consent to participate).

> [R]outine issues of negotiation and decision making related to the conduct of research studies only involved researchers and administrators from the relevant universities and institutions …. There was no formal inclusion of representatives from the sex workers in any of the negotiations (Andanda and Lucas 2007: 9).

It is clear that they have no right of ownership to any knowledge generated by the studies that have used their medical data, blood and other bodily samples for 25 years, or to ownership of any knowledge that will be generated by the research programme, including a vaccine, if one is ever developed (Andanda and Lucas 2007; see also Andanda 2009). Currently, as discussed in Chap. 5, they do not even have a clear right to free access to such a vaccine, should one be developed. This is despite the significance of their contribution to HIV research.

> The few sex workers who have not also seroconverted over the years, despite repeated exposures to HIV, have provided the scientific world with a natural model of HIV resistance, affirming that a HIV vaccine is a reality if we had the right tools to unravel the mysteries.[3]

In the Nigerian case, (see Chap. 4) the use of traditional knowledge was mediated through one individual male traditional health practitioner, Rev. Ogunyale, who was the only community representative involved in the negotiations (Wambebe 2007). Before Rev. Ogunyale died he set up a foundation to receive his royalties from the benefit-sharing agreement. It is recognized however that most traditional medical practitioners are elderly women.[4] It is therefore reasonable to assume that as a group women made a substantial historical contribution to the development of the traditional knowledge and technology within Nigeria that eventually resulted in Niprisan/Nicosan, and yet this role is not recognized in the benefit-sharing agreements.[5]

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[2] This analysis is based on Alvarez Castillo and Lucas (2009: 141).

[3] Personal communication from Dr Joshua Kimani, November 2010.

[4] Personal communication from Charles Wambebe, June 2008.

[5] Concern has been expressed that benefit sharing should have taken place with the wider community in which Rev. Ogunyale lived (Wambebe 2007: 13) (Lucas et al. Chap. 4).

In the other cases, even where women have been included they have had far less influential roles than men.

In the San-*Hoodia* case, (see Chap. 4) only men were directly involved in the original negotiations with South Africa's Council for Scientific and Industrial Research (CSIR) and the other parties, including the *Hoodia* growers' groups. The direct participation of women leaders, who constituted a very small minority in the relevant meetings, took place only at a much later stage in the process, when some key decisions had already been taken. Once agreements had been reached on benefit sharing (e.g. royalties), the San-*Hoodia* Benefit-Sharing Trust was formed by the San and the CSIR to receive and allocate the money among the San people. At the time of writing, only one of the seven elected San trustees is a woman.

It has been suggested that some benefit-sharing funds have been used specifically to benefit women. For example, in the allocation of the money from the Kani trust fund, (see Chap. 4) some has been set aside for the daughters of a woman who was killed by an elephant, and some for the family of another woman who committed suicide. The key informant (a woman) cited these examples as evidence that women do participate in decision-making and that women's needs are taken care of in the benefits distributed by the Kerala Kani Samudaya Kshema Trust.[6] However, a gender analysis suggests that this reflects thinking that conflates the interests of children with those of their mothers, on the assumption that mothers do not have interests distinct from those of their children. Empirical evidence actually indicates that the Kani women have many urgent needs of their own, for example around reproductive health care, which is illustrated by high abortion rates and low contraceptive use (Menon 1999). We would argue that better representation of women in the decision-making process about distributing monetary benefits from the trust could improve the targeting of funds, the better to address women's actual needs.

In the Icelandic case, (see Chap. 5) there was less female than male participation in the widespread public debates over the deCODE project.[7] Women constituted only one quarter of the members of the parliament that passed the Act on a Health Sector Database for the deCODE project[8] (Table 6.1).

It is significant that this marginalization of women in negotiation and decision-making is commonly found in all five cases despite fundamental differences between these societies in the nature of socio-economic and political developments within them. For instance, the San (southern Africa) and Kani (India) are indigenous societies that are in the process of being integrated into the market economy, while the Majengo (Kenya) and Nigerian societies are already so

[6] Apart from the trust fund, the Tropical Botanic Garden and Research Institute has also implemented capacity building for women. This includes an entrepreneurship development programme, the establishment of cooperative societies and self-help groups, and marketing strategies (personal communication from Dr Sachin Chaturvedi, October 2007).

[7] Data provided by Gardar Arnason, GenBenefit project meeting, Paris, 7 July 2008.

[8] In Iceland's 1997 election, the percentage of women elected to parliament was 25.4% http://data.un.org/Data.aspx?d=MDG&f=seriesRowID%3A557.

Table 6.1 Five Benefit-Sharing Cases: Women's Representation in Formal Benefit-Sharing Decision-Making

Benefit Sharing Case	Number of Women in Formal Benefit-Sharing Decision-Making Bodies
Kani (India) (Alvarez Castillo and Lucas 2009: 160)	Kerala Samudaya Kshema Trust Executive Committee, which administers benefit-sharing income: o 1997–2008: 1 woman in 11-member committee o 2008 to present: 2 women in 11-member committee (co-opted members as no women candidates stood for election)
San (South Africa) (Alvarez Castillo and Lucas 2009: 159)	Working Group of Indigenous Minorities in Southern Africa, which mandated South African San Council to undertake benefit-sharing negotiations: o 2001–2002: none South African San Council, which negotiated benefit-sharing deal: o 2001–2003: none San-*Hoodia* Benefit-Sharing Trust, which administers benefit-sharing income: o 2005 to present: 2 out of 9 elected trustees
Nigeria (Niprisan/Nicosan)	A benefit-sharing agreement was negotiated between the National Institute for Pharmaceutical Research and Development, representing the government, and a sole male traditional health practitioner. There was no body that represented such practitioners
Kenya (Majengo) (Alvarez Castillo and Lucas 2009)	This case is unique in that it only involves women. However, given the traditional nature of the scientific research project, no benefit-sharing agreement has been negotiated with the community of participants
Iceland[9]	The Act on a Health Sector Database was passed by a parliament 25% of whose members were women

integrated, but face huge problems of socio-economic inequalities and political instability. Iceland, by contrast, is a developed, capitalist-industrialized society with a strong welfare system and guaranteed political freedoms.

The differences between these societies, in terms of their respective socio-economic, cultural and political situations, are reflected in the degree and manifestations of gendered inequality within them. For instance, negotiations on benefit sharing were monopolized by men in the Nigerian and Kenyan cases, while women had a much higher level of formal participation in Iceland (although they were still in the minority). These differences are exemplified by the very low percentage of women in parliament in Kenya and Nigeria compared to Iceland (Table 6.2).

The specific differences between women's broader political participation in the larger societies, is then reflected in the degree of women's involvement in benefit-sharing negotiations within these societies. This is perhaps an unsurprising result.

[9] http://data.un.org/Data.aspx?d=MDG&f=seriesRowID%3A557

Table 6.2 Comparison of Women's Parliamentary Representation

	Iceland	Kenya	Nigeria
% of parliamentary seats occupied by women[10]	35 (2000) 43 (2010)	4 (2000) 10 (2010)	3 (2000) 7 (2010)

However, knowing that the gender dynamics of specific benefit-sharing cases tend to reflect the overall political situation in the region, those striving to develop truly fair benefit-sharing processes would do well to pay close attention to the political context.

6.3 The Question of Gender in Indigenous Societies

The presence of gender hierarchies in indigenous societies exemplified by male domination of the political domain has been observed in both the San and Kani societies, but is a relatively recent development that is closely linked to the dominant mode of production and division of labour (Kelkar and Nathan 1991; Watanabe 1968; Leacock 1983).[11]

In early indigenous societies that engaged in food gathering or horticulture as the main economic activity, men and women worked together (Shanthi 1999; Hitchcock et al. 2004), and their economic and social roles were frequently interchangeable. The division of labour was flexible, both economically and socially, and women's work was valued as much as that of men.

The experience of the Kalahari San is illustrative. Gendered structures were institutionalized when they shifted from foraging-hunting societies to sedentary settlements. In the sedentarization phase of societal transformation, the economic division of labour changed, primarily as a result of the introduction of animal husbandry and men taking jobs on cattle farms. Men acquired livestock and gained more control over these new economic resources. Previously women's economic contribution had been valued equally with that of men, but in this altered societal phase, women's work was frequently of lower economic value (Felton and Becker 2001).

The gendered social division of labour became rigid, with men less involved in child caring and household chores, and women's autonomy and influence eroded. This was exacerbated by the loss of mobility in the fixed settlements and the emergence of economic differentiation between individuals. The approach of external agents such as development workers and state agencies was to deal with men as the heads of households, which further weakened women's economic and social status. For example, agreements were made with men, and the men were given

[10] http://data.un.org/Data.aspx?d=MDG&f=seriesRowID%3A557

[11] The emergence of a specific mode of production in early societies was influenced by the interactions of factors such as the natural environment, the food sources, climate, technology, population size, material culture and social organization.

cattle on the assumption that they were the family heads, while women were allotted small livestock, such as goats (Sylvain 2006).

> The processes through which men gained control over material and non-material resources and enhanced their influence and power within their communities were matched by women's loss of resources, power and influence. These developments were not merely of a structural nature. They were incorporated in San male and female identities (Becker 2003: 16).

Among the San men, there may currently be no pronounced hierarchy in political decision-making and in class differentiation (Chennells 2007: 16), but between men and women, gendered post-colonial hierarchical changes in relationships have been significant. Men began to dominate the public domain and women's participation in political affairs has dwindled (Sylvain 2006: note 26).

6.4 Benefit-Sharing Guidelines Through a Gender Lens

We shall now look at the existing major international guidelines that contain provisions on or have relevance to benefit sharing (see also Chap. 3).

We examine the Convention on Biological Diversity (CBD 1992), the Bonn Guidelines (2002) and the Nagoya Protocol (CBD 2010), the Declaration of Helsinki (DOH) (WMA 2008), the 2002 Council for International Organizations of Medical Sciences International Ethical Guidelines for Biomedical Research Involving Human Subjects (CIOMS 2002) and the HUGO Ethics Committee Statement on Benefit Sharing (HUGO Ethics Committee 2000) in the light of the following questions:

- Are women's rights to free and prior informed consent (FPIC) recognized and protected?
- Are women's rights to fair benefit sharing protected? If so, how?
- Are women's rights to fair participation and representation in negotiations and decision-making recognized and protected?

6.4.1 Free and Prior Informed Consent

Informed consent is a concept drawn from medical ethics, where it means the 'voluntary, uncoerced decision, made by a sufficiently competent or autonomous person on the basis of adequate information and deliberation, to accept rather than reject some proposed course of action that will affect him or her' (Gillon 1985: 113).

In the context of access to biodiversity and benefit sharing, prior informed consent means the voluntary, uncoerced decision made by a group that legitimately represents a community, on the basis of adequate information and deliberation, to accept rather than reject some proposed course of action that will affect the community, *before that course of action begins* (Schroeder 2009: 31).

HUGO, CIOMS, the Bonn Guidelines and the DOH all appeal to the concepts of free prior informed consent, fairness and mutuality.

It is in the process of obtaining the FPIC of research participants that the opportunity for negotiating and deciding on benefit sharing mostly exists. HUGO recommends prior discussion with groups or communities on the issue of benefit sharing, but, like the other guidelines, is silent on women's participation. CIOMS addresses the process of obtaining free and prior informed consent, especially in cultures where decisions by elders or leaders tend to prevail over individual decision-making. We believe this has clear relevance to women in some societies, but again this is not brought out in the guidelines, except in gender-neutral terms (CIOMS 2002: guideline 4, commentary).[12]

6.4.2 Benefit Sharing

All the guidelines contain provisions stipulating that research subjects or study populations (DOH, CIOMS) or those who are the sources of biological materials and knowledge (CBD for non-human materials only, HUGO) should benefit in some meaningful way from the research study or its outcome (see Chap. 3). However, ensuring that women in the community or population get a fair share of the benefits is not explicitly mentioned (see Alvarez-Castillo and Feinholz 2006).

6.4.3 Participation and Representation in Decision-Making

During the long development of the CBD, there was much emphasis on the role women play globally in biodiversity management and protection, and how their priorities support those of the International Union for Conservation of Nature and Natural Resources (see, for example, IUCN 1988: recommendation 17.13). This perhaps explains why the CBD is the only relevant set of guidelines that explicitly mentions women's participation. In the *Preamble*, it states:

> Recognizing also the vital role that women play in the conservation and sustainable use of biological diversity and affirming the need for the full participation of women at all levels

[12] For example, in a study regarding gender, consent and research participation in Pakistan, 44% of respondents believed it was important or essential for the researcher to involve the family members or elders of an adult potential study participant in the process of obtaining informed consent. If the research participant was a woman, 60% of the respondents felt it was essential that the father's or, in the case of a married woman, husband's permission be sought before approaching the woman. Where there was a difference of opinion between the study participant and the father or spouse, 74% felt that the opinion of a male participant should prevail, but if the study participant was a woman, then only 53% of respondents felt that her opinion should be honoured. There was no significant difference in the opinions expressed between male and female respondents (Jafarey 2006).

> of policy-making and implementation for biological diversity conservation … (CBD 1992: preamble).

The CBD has been criticized for the failure of the 2002 Bonn Guidelines to follow through on gender issues (see Alvarez-Castillo and Feinholz 2006: 114). However, by way of progress towards recognizing these concerns, the more recent 2004 CBD Akwé: Kon voluntary guidelines (for impact assessments regarding proposed developments impacting sacred sites or indigenous lands) echoes the CBD preamble, and actively recognizes gender considerations both in its general structure and in a number of its articles, explicitly recommending, for example, the:

> [e]stablishment of effective mechanisms for indigenous and local community participation, including for the participation of women … in the impact assessment processes … (CBD 2004: procedural consideration 8(c)).

Even more significantly, the Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization to the Convention on Biological Diversity, which opened for signature on 2 February 2011,[13] not only reiterates the CBD's original general position regarding women, but does so specifically in relation to benefit sharing:

> *Recognizing also* the vital role that women play in access and benefit-sharing and *affirming* the need for the full participation of women at all levels of policymaking and implementation for biodiversity conservation …(CBD 2010).

The protocol includes two articles specifically referring to the need to emphasize the identification and enhancement of the capacity needs and priorities of women. Article 22 states:

> As a basis for appropriate measures in relation to the implementation of this Protocol, developing country Parties, in particular the least developed countries and small island developing States among them, and Parties with economies in transition should identify their national capacity needs and priorities through national capacity self-assessments. In doing so, such Parties should support the capacity needs and priorities of indigenous and local communities and relevant stakeholders, as identified by them, emphasizing the capacity needs and priorities of women (CBD 2010: article 22.3).
>
> Measures … may include … [s]pecial measures to increase the capacity of indigenous and local communities with emphasis on enhancing the capacity of women within those communities in relation to access to genetic resources and/or traditional knowledge associated with genetic resources (CBD 2010: article 22.5j).

Article 25 stipulates that in providing guidance in respect of the financial mechanism related to capacity-building and development for developing country parties:

> the Conference of the Parties … shall take into account … the capacity needs and priorities of indigenous and local communities, including women within these communities (CBD 2010: article 25.3j).

These are welcome developments, but as the following discussion indicates, the gap between goodwill and implementation is huge.

[13] The protocol was adopted on 30 October 2010 at the tenth meeting of the Conference of the Parties to the CBD (2010).

6.5 Explicit Protection for Women

In our examination of the five cases, we found that the actual – though frequently invisible – dynamics of power relations between men and women often obstruct the process of women's inclusion in formal negotiations and decision-making on benefit sharing. Women were marginalized in community consultations among the San and in Iceland. In the Kani case, women did not actually get their 'fair share' of the benefits accruing to the community in general. This indicates that, in fact, the benefit-sharing arrangements were not fair and equitable at all.

It seems, therefore, that generalized provisions on free prior informed consent, fairness, mutuality and benefit sharing (such as we find in HUGO, CIOMS, the DOH and the Bonn Guidelines) often fail in practice to ensure that women are treated fairly. There are three core reasons for this:

- Where the vulnerability of a group or community is homogenized (as in the existing guidelines), the hidden or invisible structures and practices in communities that create further vulnerabilities specific to women might be ignored. For example: 'Women bear a disproportionate burden of the world's poverty. Statistics indicate that women are more likely than men to be poor and at risk of hunger because of the systematic discrimination they face in education, health care, employment and control of assets. Poverty implications are widespread for women, leaving many without even basic rights such as access to clean drinking water, sanitation, medical care and decent employment. Being poor can also mean they have little protection from violence and have no role in decision making' (UN Women 2008). While there is a growing awareness of the vulnerability of poor communities to exploitation in research, the additional and specific vulnerability to exploitation of women *within* those communities will be missed until it is simultaneously recognized that poverty is also gendered.
- There is an assumption that prior discussion with the community automatically includes the women, but this is not borne out by empirical research.
- The expectation that when a community shares in the benefits, women will get their fair share, is unrealistic in many cases.

There is a clear danger that a gender-blind approach to decision-making for benefit sharing can reinforce existing discrimination against women in community practice.

6.6 Gender Justice: Interrogating Free Prior Informed Consent, Justice and Fairness

It is clear that all the major international guidelines have used the concepts of free prior informed consent, justice and fairness without adequate attention to their implications for women. We argue that an understanding of justice and fairness

which is uninformed by and insensitive to women's realities could in fact be worse than neutral, and actually mask (and therefore collude with) inequity and discrimination against women.

Inequity and discrimination against women are often found in personal and family relations (the private sphere), which are commonly ignored in guidelines and processes that seek to promote justice and fairness. Equally, the problems of injustice and unfairness are commonly seen to be largely located in society broadly (the public sphere), without regard to the fact that all persons are gendered social beings, and that their public personality is a reflection of power relations in their private life.

Women's freedoms are circumscribed by everyday patriarchal norms, practices and structures in society. Men are freer than women, even if they belong to the same social class or ethnic group. Women's freedom to speak in political gatherings is circumscribed by cultural norms and traditions, as exemplified by the San women's situation:

> [A]lthough we have traditionally our ways of making decisions there are certain skills needed before a San woman joins the mainstream, talks about issues openly … And when there were meetings women culturally were not talking openly; they were supposed to just listen. So many of the San women have still that cultural practice and in most cases they are shy to talk in front of many people.[14]

There is clear evidence that in various types of societies, women are either absent from or silent in such gatherings.[15] It might seem like common sense to interpret their silence as assent, but this is not always appropriate.

What initially seems just and fair to a researcher or to sponsors of research, or to men in the community, could therefore be unfair and unjust to women. The exclusion of women from bodies that are supposed to represent the whole community is patently unjust and unfair. According to the evidence, any assumption that these bodies represent women effectively, or that women are included in community consultations, is erroneous. However, such thinking becomes a self-fulfilling prophecy: if no attention is paid to the circumstances on the ground that prevent women from representing themselves or participating in these processes, then there appear to be no barriers to their participation, and therefore no mechanisms are developed to overcome these unacknowledged barriers. The Nagoya Protocol has now formally recognized the need to address such issues, but it is too soon to make any assessment of its impact.

In the past two decades, a number of strategies have been tried in order to end gender discrimination, one of which is gender mainstreaming.

> Mainstreaming a gender perspective is the process of assessing the implications for women and men of any planned action, including legislation, policies or programmes, in all areas and at all levels. It is a strategy for making women's as well as men's concerns and experiences an integral dimension of the design, implementation, monitoring and

[14] Personal communication from Victoria Haraseb, July 2008.

[15] For example, this is the experience of women in pastoralist and rural societies in Africa (see Kipuri and Ridgewell 2008; IFAD 2004).

> evaluation of policies and programmes in all political, economic and societal spheres so that women and men benefit equally and inequality is not perpetuated. The ultimate goal is to achieve gender equality (UN 1997).

But attention has also been drawn to the inadequacies of gender mainstreaming; it has been claimed that one of the ways in which gender mainstreaming has been officially interpreted is:

> [T]o ensure that the implementation of programmes, processes, and mechanisms are inclusive of women's participation and responsive to poor women's needs *only in so far as to encourage and sustain their involvement without any real policy impact* (Francisco and Antrobus 2009: 157) (our emphasis).

Therefore the alternative concept of 'gender justice' is now being increasingly employed by activists and academics who wish to create a strong enough sense of, or adequately address, the ongoing gender-based injustices from which women suffer (Mukhopahyay 2007).

Gender justice is a principle that recognizes women's socially disadvantaged position (Mahowald 2000) and seeks to correct this imbalance through various avenues of policy and action. To promote gender justice is to work for the redress of inequalities that victimize women and also to address the accountability of individuals and institutions when, by omission or commission, they contribute to the maintenance of such inequalities (Goetz 2007). An example is in the discussion of general ethical principles that precedes the CIOMS guidelines:

> Sponsors of research or investigators cannot, in general, be held accountable for unjust conditions where the research is conducted, but they must refrain from practices that are likely to worsen unjust conditions or contribute to new inequities (CIOMS 2002: 18).

In implementing this kind of recommendation, careful attention should be paid to the power dynamics in the particular group, including those that have an impact on women's right to participate fully. Researchers and sponsors of research therefore have a responsibility to devise appropriate strategies, in partnership with women (and members of other groups) who, through tradition and practice, are often discriminated against. In benefit sharing, this means working for the protection of women's equal rights to full and autonomous participation in decision-making, including decisions pertinent to the allocation and use of the benefits.

A study by the United Nations Environment Programme (UNEP) explores the links between actual community best practices for distributing benefits in 14 communities:

> Women play varying roles in the respondent communities. In most, they are active in the decision-making and implementation activities, sometimes anchoring the major activities of the groups …. Whatever their role, women are no longer considered to hold inferior positions within their societies. They have equal claim to wages and shares. Many of the women-headed groups said that the early days in the groups' existence were very difficult. The members of the groups were met with often harsh opposition when they ventured out, be it for conservation-related or economic activities. An illustrative case is that of Asociación de Mujeres, where the women faced stiff resistance from the men of the community when they embarked on fish-processing activities. In sharp contrast to that difficult start, however, they now have a working value-addition agreement with the local fishermen's group (Suneetha and Pisupati 2009: 27).

6.7 How Many Women are Enough? Issues Around Women's Representation

> [T]he Universal Declaration of Human Rights affirms the principle of the inadmissibility of discrimination and proclaims that all human beings are born free and equal in dignity and rights and that everyone is entitled to all the rights and freedoms set forth therein, without distinction of any kind, including distinction based on sex (UN 1979: preamble).

The UN Fourth World Conference on Women held in Beijing in 1995, reiterated that:

> the human rights of women and of the girl child are an inalienable, integral and indivisible part of universal human rights (UN 1995: Chap. 1, paragraph 2).

In recognition of the CBD's commitment to the role of women in the conservation of biological diversity, the Organization of African Unity (OAU), now the African Union, included in its model law to regulate access to, and benefit sharing for, non-human genetic resources the aim of achieving women's 'full participation at all levels of policy-making and implementation in relation to biological diversity, and associated knowledge and technologies' (OAU 2000). Unfortunately the model law did not incorporate any mechanisms to achieve this, and it needs to be asked – how many women constitute 'full participation'?

Women's specific rights to equal participation and representation are enshrined in a variety of UN covenants that most governments have ratified. For example, the 1979 Convention on the Elimination of All Forms of Discrimination against Women (CEDAW) sets as one of a state's responsibilities:

> to embody the principle of the equality of men and women in their national constitutions or other appropriate legislation if not yet incorporated therein and to ensure, through law and other appropriate means, the practical realization of this principle … (UN 1979).

One of the areas of concern identified at the UN Fourth World Conference on Women in 1995 in Beijing was the under-representation of women in decision-making processes. Despite increased democratization over the preceding decade, it was recognized that there had been little progress in improving the participation of women in decision-making through the attainment of political power or by achieving the target endorsed by the United Nations Economic and Social Council of having 30% of decision-making positions in the hands of women by 1995.[16]

> While it is true that no definite relationship has been established between the extent of women's participation in political institutions and their contribution to the advancement of women, a 30% membership in political institutions is considered the critical mass that enables women to exert meaningful influence on politics (EC 2008).

[16] '*A critical 30% threshold should be regarded as a minimum share of decision-making positions held by women at the national level.* Few countries have reached or even approached this target, recommended in 1990 by the UN Commission on the Status of Women ….The Report recommends that each nation identify a firm timetable for crossing the 30% threshold in some key areas of decision-making. The 30% threshold should be regarded as a minimum target, not as the ultimate goal' (UNDP 2005).

At the end of 2006, almost all of the 20 countries that had achieved the critical mass of 30% had implemented some form of quota system to proactively reduce the obstacles to women entering politics at the national level. While the efficacy of quota systems is controversial, an example of their successful use comes from Norway, where the government imposed a minimum of 40% on the female membership of boards in both public and private companies. With sanctions for non-compliance, this resulted in female representation in the boardroom rising to 34% by 2007, 10% ahead of any other European country (EC 2008).[17]

With two women among nine Hoodia trustees, that committee has slightly less than 25% female membership, which some might consider a reasonable proportion, but the women are still decisively in a minority. It is important to remember that many of the bodies involved in benefit sharing negotiations and decision-making are quite small. The Kani Trust, for example, has only 11 members (so even the two co-opted women give it only a 19% female membership). In such small groups, the precise number of women becomes very important in terms of appropriate representation: increasing the number of women from three to four in a working group of seven people, for example, could shift the dynamics significantly.

At the 1995 Beijing Conference, 189 states adopted the Beijing Platform for Action, which is considered a milestone in the enforcement of women's rights across the world. One of the areas for action was Women in Power and Decision-Making, in relation to which the platform recommends two strategies: 'Take measures to ensure women's equal access to and full participation in power structures and decision-making' and 'Increase women's capacity to participate in decision-making and leadership'. Both should be addressed by 'Governments, national bodies, the private sector, political parties, trade unions, employers' organizations, research and academic institutions, sub-regional and regional bodies, and non-governmental and international organizations'.[18]

It therefore seems that there is general international agreement on these goals and requirements are in place for active measures to be taken by all sectors to

[17] By 2011 this figure was 40.2% (Lord Davies of Abersoch 2011: 24). Several EU member states have recently started to act in this area and have introduced legally binding quotas for company boards. This includes Belgium, France, Italy, the Netherlands and Spain, with Denmark, Finland, Greece, Austria and Slovenia adopting rules on gender balance for the boards of state-owned companies. The European Commission is currently considering whether or not to impose quotas and legislation across European Member States. The European Commission Vice-President for Justice, Fundamental Rights and Citizenship, Viviane Reding, launched a public consultation in March 2012 to identify possible action at EU level (Reding 2012). A 2011 report Women on Boards (Lord Davies of Abersoch 2011) for the UK Government published a roadmap for UK plc businesses to achieve 25% female representation on boards by 2015, relating this clearly to questions of corporate governance.

[18] The Platform for Action outlines 12 critical areas of concern where the violation of women's rights and gender inequality persist, and proposes strategic objectives and actions for each (see UN 1995).

achieve them. Again, this specifically includes most, if not all, parties to proposed benefit-sharing arrangements (i.e. 'the private sector… research and academic institutions').

Because women's subjective consciousness and objective life situation have generally marginalized them from public politics, it is essential that strategies, processes and mechanisms be empowering for women, and give them space and time to speak their mind, ask questions and think things over. Instead of (or as well as) big public meetings, small conversation groups for women only could be organized, facilitated by women. These are small but important steps that could eventually result in women gaining self-confidence and skills in political matters.[19]

There are many examples around the world of relevant programmes that could provide resources and models for interested parties to follow. The emphasis of UNIFEM (the women's fund at the United Nations) has been on knowledge-sharing and capacity-building in making indigenous women aware of their rights as contained in the legal frameworks of their countries. Training in human rights, leadership and participation has been successfully carried out throughout the Andean region, for example (see UN Women 2004). In 2006, Alliances for Africa funded the Women in Governance and Decision Making capacity-building initiative in Imo State, south-east Nigeria (evaluated by the British High Commission), which was designed to contribute to the broader goal of empowering, in particular, grassroots and urban poor women and advocating their full participation in governance and decision-making processes and structures (Alliances for Africa 2006). In January 2007 the Minister of Canadian Heritage and Status of Women announced a funding programme for Aboriginal women's organizations 'to support the full participation of Aboriginal women in consultations and decision-making processes' (Canadian Heritage 2007). In Cambodia the World Bank has funded a programme to conduct public forums and training sessions to enhance women's leadership in decision-making at the local commune level (CPWP 2007). Increasingly, there are also specialist regional organizations dedicated to these kinds of approaches to the issue, such as the Gender Training and Development Network, based in Nigeria, which carries out community-based research and

[19] For a discussion of appropriate strategies to facilitate women's participation in practice, see Alvarez-Castillo and Feinholz (2006: 117–118). Such initiatives can have unanticipated benefits. For example, when GenBenefit researchers met the women's leaders in Majengo, Nairobi, in September 2007, they noted a sense of empowerment and solidarity among the women. During the meeting one of the authors (Fatima Castillo) shared with them a problem faced by women in sex work in other countries, which is that customers refuse to use condoms – and women who insist on condoms often lose their customers because the men simply go to other women who agree to sex without a condom. The Majengo women said that in their group, customers like these were refused, and there was an agreement among the women in Majengo that not one of them would cater to such a customer. The result is that sex workers' customers in Majengo have to use condoms, which reduces the risk for women of contracting sexually transmitted infections. See also Lavery et al. (2010).

training on a broad range of gender issues in the areas of leadership, governance and development policy.[20]

In its assessment of the contribution of 14 benefit-sharing enterprises to communities' well-being, the UNEP report cited earlier assigns scores to each community's achievement of its basic needs. Under the category of 'Equity in transactions' (part of 'Belonging needs'), indicators include gender equity under both economic activity and leadership. Thirteen of the communities had made 'much improvement' with regard to the involvement of women in leadership, meaning that women now occupied at least 25% of leadership positions *as a result of the benefit-sharing enterprise* (Suneetha and Pisupati 2009: 35–39). The report is intended to provide input to help policymakers understand the basic principles that apply in benefit-sharing practice at the local level, in order to make provisions and policies both relevant and possible to implement. This evidence of how benefit-sharing processes can start to work to empower women, even where gender has not been foregrounded as an issue, indicates that there is both will and potential at ground level towards achieving gender justice in benefit sharing. The process of building on this existing capacity could be meaningfully supported through requirements for gender justice within benefit-sharing guidelines, such as those now contained in the Nagoya Protocol, which the UNEP study suggests would be implementable within communities in practice.

6.8 Imposition of a Western Gender Framework as a Further Injustice?

Jeanne Simonelli and Duncan Earle discuss the importance of researcher reflection on gender issues in their account of obtaining consent for anthropological studies among indigenous peoples in Chiapas, Mexico:

> [T]he majority of the men had closed themselves up for yet another meeting, this one private. We had hung out waiting, where else but in the kitchen. Most of the women were either there or arrived shortly afterwards, and before we knew it, there was a meeting happening to the sound of making tortillas and gurgling babies. The meeting was very animated; everyone opined.
>
> 'Is the other meeting in the house just for the men?'
>
> Luz, one of the leaders, responded casually, 'Yes, they have a meeting with themselves now, and we have ours too; and then later we meet together. Everyone has a chance to speak of how they see things.'
>
> We realized then how we had jumped to conclusions about gender inequality, not respecting the indigenous idea about complementary opposition that precedes the dynamic union, how both segregating and integrating are part of their process of consensus. (Simonelli and Earle 2003: 82).

It is sometimes claimed that imposing Western ideas of gender equality on other cultures, especially indigenous peoples, is just another example of cultural

[20] http://www.scidev.net/en/announcements/gender-training-and-development-network-web-resources.html.

imperialism, rather than a liberatory strategy. It is crucial to be aware of such issues, as well as of cultural forms according to which, for example, women may not be able to speak about issues relating to (particular) land or resources, not because of sexist silencing, but owing to traditionally gendered sacred responsibilities, in terms of which such issues are literally not their business. This is particularly an issue for some Australian Aboriginal societies:[21]

> In many cases knowledge and the resulting power was gender-specific. Thus there were men's sites and there were women's sites, and the traditional owners, whether they be female or male, had sole decision-making powers over those areas (Gale 1990).

However, many of the rights under discussion here are already incorporated into the political agendas of indigenous peoples. For instance, the first three (of 16) leadership priorities specified by two Yukon Aboriginal women's summits held in November 2007 were:

1. Include the voices of female Aboriginal Elders as advisors in meetings that involve First Nation people.
2. Increase representation of Aboriginal women in decision-making positions in governments, corporations and nonprofit organizations.
3. Increase representation of Aboriginal women at decision-making tables dealing with water, land and traditional knowledge (YACWI 2008).

A 'key message' produced by this summit was: 'Encourage and support Aboriginal women to take on decision-making and political leadership roles' (YACWI 2008).

The relevance of these priorities to benefit sharing is obvious. Likewise, based on a 2003 review of the Aboriginal and Torres Strait Islander Commission (ATSIC, the statutory authority established by the Australian federal government in 1990 as an expression of its self-determination policy for Aboriginal and Torres Strait Islander peoples), indigenous advocates in Australia are currently proposing 'improved gender representation in any new representative structure' (Davis 2008: 6):

> The evidence from ATSIC's own evaluation confirms what many women know, that men can never adequately and effectively represent the unique and diverse interests and needs of women (Davis 2008: 8).

The ATSIC women's committee, Kungkala Wakai (Our Women's Voice), argued that the result of women's under-representation was a lack of attention to women's issues, as well as to those affecting other minority groups (youth, the homeless, etc.), and that:

> a key objective of any new arrangements should be equal representation of women in terms of membership of regional councils, the proportion of regional council chairs, and in the proportion of commissions on the ATSIC board. That is, 50% of these officials should be women. Putting in place a mechanism to achieve this may or may not have broad community acceptance, but it is nevertheless one way of addressing the marginalization of women in Indigenous affairs (Kungala Wakai 2003).

[21] We are grateful to Jack Beetson for this point (GenBenefit Dissemination Conference: Montreal, 6 November 2009).

In response to questions about how to approach this issue, San leader Victoria Haraseb has suggested that women ought to be asked about it.[22] In other words, the appropriate strategy for research design is to engage with the women in the community, starting from where they are (including their consciousness), and not where the researchers are coming from, thus avoiding the imposition of a Western gender perspective at the outset. Such inclusion would also support those indigenous women who wish to resist bioprospecting research in their territories, and incursions into their intellectual and cultural heritage, by giving them a powerful setting in which to say 'no', if that is what they wish.[23]

6.9 Conclusion

A truly just and fair sharing of benefits should make sure that women are treated equally with men. 'Equality' here is understood as simple equality between men and women that takes differences into account (Molyneux and Razavi 2002). This requires attention to both the outcome and the process of benefit sharing. As an outcome, just and fair benefit sharing is where women are allocated their rightful share; as a process, it ensures that women fully participate at all levels and in all aspects of the (often protracted) negotiation and decision-making process.

In order to achieve this, guidelines and policies on benefit sharing in research need to be re-examined from a gender perspective. This process should be informed by evidence about how women are being unjustly treated in current benefit-sharing arrangements (see, for instance, Alvarez Castillo and Lucas 2009: 141). Seeing how gender-based power imbalances can work against the implementation of guidelines and policies on the ground demonstrates the importance of strategies, processes and mechanisms that are sensitive to power dynamics in local contexts.

In order to carry out the international will expressed above, all guidelines and policies for benefit sharing should *explicitly* require women's meaningful participation in *all* phases of decision-making, starting (as much as possible) with the formulation of the research design through to the signing of agreements and the allocation of benefits with minimum, appropriate and measurable indicators. The definition of meaningful participation should be contextualized in, *but not bound by*, cultural, social, political and economic practices and relationships. This is because these practices and relationships could be the sources of inequality and women's exclusion, as shown in the case analysis.

In addition, guidelines and policies should include examples of the kinds of mechanisms that will enable women to fully participate and have an effective voice. These could, for instance, be modelled on the appendices to the Nagoya

[22] Personal communication July 2008 in relation to the skills building needs of San women.

[23] See NGO Forum 1995.

Protocol, with lists of mechanisms that might be included, but should not be limited by that model. We would suggest the following principles:

- Aim for women to have equal membership of bodies that negotiate or make decisions (in light of the fact that 30% is recognized as a critical mass threshold where women's presence *begins* to have an effect, but may in practice, in a smaller group, mean only one or two persons).
- Set up negotiating and decision-making bodies for women only, if that is what women prefer. These could then feed into other bodies.
- Hold consultations separately for women, and feed the outcome back to the negotiating or decision-making body, in order to ensure that women's views become part of the agenda and are a basis of decisions made.

Ultimately, of course, international guidelines and policies can only change reality on the ground if governments and other local stakeholders seriously and consistently create the necessary mechanisms through practical, implementable, local processes. International, national and local bodies, as well as researchers, should be accountable for the exclusion and discriminatory treatment of women in benefit sharing, as in other areas of their work.[24] Research ethics committees should look for appropriate provisions in study protocols, and in progress and final reports from researchers. Study sponsors should also take more responsibility for this matter.[25]

It is no simple, linear process for women to recognize their gendered selves and represent themselves in decision-making on benefit sharing in the exercise of their agency. The interconnectedness of structures, subjectivity and context makes this a difficult, complex enterprise. Guidelines that seek to protect women's rights in benefit sharing, while morally compelling, are not sufficient to bring this about.

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[24] For an interesting discussion see Lavery et al. (2010).

[25] For example the European Commission includes an optional 'consideration of gender aspects' in research funding applications under Framework 7, currently expressed as **'**an indication of the type of actions that will be undertaken during the course of the project to promote gender equality in the project, or in the specific research field…. The gender dimension of the research content should also be considered' (EC 2010: 31).
These kinds of mechanisms could be used more widely to consider research *content* in more detail. For example, the Research Council of Norway regards it as 'essential that gender perspectives are given adequate consideration in the research projects' it funds, and states that 'consideration will be given to whether the research projects have taken such perspectives adequately into account' (Research Council of Norway 2003).
In a recent development, point 4 of the Manifesto for Integrated Action on the Gender Dimension in Research and Innovation (2011) launched at the 1st European Gender Summit in November 2011, wishes to: 'Consider "whether, and in what sense, sex and gender are relevant in the objectives and methodology of the project" to ensure excellence in research. This key question must be asked by researchers, research funders, evaluators, reviewers and journal editors. Evidence demonstrates that the assertion that science is gender neutral is not the case. When gender is not taken into account, research often results in different health and safety outcomes for women and men. Researchers also need to question how to ensure that the products and services they help develop benefit both women and men.' The Manifesto is the product of extensive public consultation and discussion and was presented to the EC Commissioner for Research, Innovation and Science, Maire Geoghegan-Quinn on December 16th, 2011.

There is perhaps a greater probability of achieving concrete gains in the prevention of exploitation at the grassroots level, where there is an urgent need to explore alternative ways of strengthening the protective capacities of vulnerable people. Nevertheless, guidelines, despite their limitations, can be tools for women to use in advancing their rights, and can also serve as a moral force for the state and other committed parties.

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Chapter 7
Promoting an Inclusive Approach to Benefit Sharing: Expanding the Scope of the CBD?

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Abstract The Convention on Biological Diversity (CBD) is a major international agreement to ensure the conservation of biological diversity, the sustainable use of various components of biological diversity, and fair and equitable access and benefit sharing of advances arising from the use of related genetic resources. The CBD excludes human genetic resources. In light of the rapid advances in biotechnology, genetic resources are increasingly being utilised by different types of users and in different industries. This usage is not confined to plants, animals or micro-organisms but includes human genetic resources and sometimes a mix of such resources. In the absence of any international agreement, various national governments are framing their own rules and guidelines. This patchwork of regulation may eventually impede global research efforts. This chapter argues that the CBD is qualified to be the central agency at the global level for the advance of broader benefit sharing frameworks. By implication, the scope of the CBD should be expanded to include human genetic resources.

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7.1 Introduction

Even by the most conservative estimates, the global debate on access and benefit sharing (ABS) for biodiversity has been going on for 20 years. Despite the high global stakes of this debate and the adoption of the Nagoya Protocol to the Convention on Biological Diversity (CBD) in 2010, there is no clear pathway for its resolution in sight. ABS is one of the major stumbling blocks in the stalled negotiations on trade-related aspects of intellectual property rights (TRIPs) at the World Trade Organization (WTO), and its current fluid state internationally is the source of different, and at times contradictory, approaches at national levels. In the medium to long term this may adversely affect research and technology transfer prospects. The absence of clear international guidelines further complicates global research initiatives as national governments evolve their own ABS frameworks.[1] This situation is frustrating for negotiators, disheartening for non-governmental organizations (NGOs) and other civil society organizations, and disappointing for many others involved in the process.

The CBD's Ad Hoc Open-Ended Working Group on Access and Benefit Sharing concluded its work with the adoption of the Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization at the tenth meeting of the Conference of the Parties to the CBD (COP 10) in Nagoya, Japan, in October 2010.[2] The deliberations of the CBD have thus far, however, overlooked technological trends in the realms of synthetic biology and pharmacogenomics, and these may undermine the relevance of the definitions currently being employed by negotiators for 'biological resources'. One of the factors that may be responsible for this approach is the continued compartmentalization of the CBD and the World Health Organization (WHO), which are independently discussing ABS issues with little input from each other. One can observe some movement towards more collaboration, but it is not enough.

[1] Glowka (2008) calculates that more than 60 countries have established their own ABS regimes.

[2] After nearly 20 years of negotiations, 193 governments adopted the 'historic' Nagoya Protocol as a supplementary agreement to the CBD. It provides a transparent legal framework for the effective implementation of one of the three objectives of the CBD: the fair and equitable sharing of benefits arising out of the utilization of genetic resources. The instrument outlines legally binding international rules for sharing benefits from resources (including traditional knowledge) used in food, pharmaceuticals, cosmetics and other products. The protocol was open for signature at the United Nations Headquarters in New York from 2 February 2011 until 1 February 2012 and will enter into force on the 90th day after the date of deposit of the 50th instrument of ratification, acceptance, approval or accession (CBD 2010, see also Chap. 3).

The Nagoya text does refer to human pathogens and provides a way for some human genetic resources eventually to be included in the CBD. The protocol has added the following text in Annex 1:

> Mindful of the International Health Regulations (2005) of the World Health Organization and the importance of ensuring access to human pathogens for public health preparedness and response purposes… (CBD 2010).

The key question appears to be how biological (genetic) resources are defined. Is it possible to continue the customary approach of separating ABS regimes for plants and traditional plant-based community knowledge from leads based on human genetics research? It is currently unclear how benefits would be distributed in cases where products are derived from a combination of human genetics research and community-based knowledge of plants, despite the increasing frequency of such combinations.

The decision by the second meeting of the Conference of the Parties to the CBD in 1995 (CBD 1995a) not to include human genetic resources under the purview of ABS appears to have been made with the understanding that, unlike plant-based resources, human genetic resources would always remain removed from the sphere of commercial gain (Nijar 2009). Subsequent trends in the patent regime, however, increasingly reveal a pattern of commercial gain becoming inextricably involved with human genetics research (Hopkins et al. 2007). This is a major departure from the premise on which the Human Genome Project was launched. Since the establishment of the Human Genome Project and the identification of genes in human DNA which play a role in human diseases and disorders, a long moral and political battle has been fought over the extension of intellectual property rights to information contained in human genetic material (Papaioannou 2008) (see also Caulfield 2006; WHO 2009a).

The estimated total of 26,000 to 30,000 genes in the human genome includes approximately 3,000 to 5,000 targets that are potentially amenable to pharmacological interventions. Within the *in vitro* diagnostic industry, molecular diagnostics is the fastest-growing segment. The market for molecular diagnostic products has surged from US$50 million to over US$1 billion in the United States in little more than a decade and, it is anticipated, will reach US$35 billion globally by 2015. The US demand for *in vitro* diagnostic products is growing by an estimated 6.1% annually (Visiongain 2009).

This raises the question: does the continued exclusion of human genetic resources from the CBD remain a viable proposition? Is it not possible to have an international ABS understanding regarding human genetic resources, as we now have for plant genetic resources? Are human genetic resources not part of genetic resources? These are some of the issues we attempt to address in this chapter. Section 7.2 examines the concept of genetic diversity and the evolution of the idea in the context of the CBD, and Sect. 7.3 gives a detailed account of the impact of new technologies on the use of human genetic resources. Section 7.4 looks into instances of ABS in human genetic resources, and the final section suggests possible ways forward.

7.2 ABS Debate

At the eighth Conference of the Parties to the CBD (COP 8), held at Curitiba, Brazil, from 13 to 17 March 2006, it was decided that the negotiations on an international ABS regime should be completed by COP 10, scheduled to meet in 2010. And indeed, the negotiations did result in the adoption of the Nagoya Protocol in October 2010. However, the ABS debate is still raging simultaneously in various major intergovernmental forums, such as the World Intellectual Property Organization (WIPO) and the WTO, where these issues are being tackled in different ways and from widely diverse perspectives, with the result that the agencies concerned are all going in different directions – and, at times, in circles.

The centrifugal force needed to break out of these circles is likely to come once something that should have been done initially is achieved: namely, defining clearly the terms being used in this debate in order to resolve many of the current ambiguities (Pisupati 2008; Schroeder 2007). It is evident from the history of the CBD that as the end of the original negotiations approached, definitions were problematic and, in fact, became an impediment to the conclusion of the CBD itself. Rather than resolving this issue, the negotiators instead agreed to remove the problematic definitions, or let them remain vague. For example, no further effort was made to clarify the definition of 'conservation of biological diversity'. The adoption of the relatively weak definition '"technology" includes biotechnology' was a way to avoid controversy on the definition of this critical concept and many others.

In this section, we explore a number of cases that are relevant to our current concerns regarding ABS. We examine the debate on what is covered by the definition of 'biological diversity' and how this question is being addressed by different organizations. Another important aspect of this debate is the determination of how benefits may best be distributed and how the proper recipients of these benefits will be identified, but a discussion of these issues is beyond the scope of this chapter.

7.2.1 Concepts and Coverage

It is important to understand the definitions adopted by the CBD in order to appreciate the broader implications for our current concerns regarding ABS. It should be recognized that the focus of the CBD as originally proposed was significantly broader and more comprehensive than it became later, after an extremely wide process of consultation. When the Conference for the Adoption of the Agreed Text of the Convention on Biological Diversity met in Nairobi in 1992, the document had already gone through three meetings of technical experts and seven negotiating sessions, held between November 1988 and May 1992. This process was led by the General Council of the United Nations Environment Programme (UNEP), initially through the Ad Hoc Working Group of Experts on Biological Diversity (between November 1988 and July 1990), followed by the Ad Hoc Working Group of Legal

and Technical Experts (between November 1990 and March 1991). This group was eventually renamed the Intergovernmental Negotiating Committee for the CBD.

At the Nairobi conference in 1992, three resolutions were passed, of which Resolution 2 was articulated in a very broad framework:

> Further recognizing that the preparation of biological diversity country studies is the first systematic attempt to assist countries in establishing baseline information on their biological diversity and is the basis for national action programmes on conservation of biological diversity and the sustainable use of its components … (CBD 2005: 404).

Resolution 2 also suggested that the CBD Secretariat would identify components of biological diversity that were of importance for conservation and sustainable use, including the collection of data needed for effective monitoring, upon request from the national governments, and while doing so would also evaluate potential economic implications. The text consistently referred to 'biological' and 'genetic' resources. Nowhere did it confine itself to plant-based components of biological or genetic diversity. In Resolution 3, however, while identifying the work agenda, the conference narrowed this definition to 'plant genetic resources for food and sustainable agriculture' (CBD 2005: 407) and further:

> Recognize[d] the need for the provision of support to the implementation of all activities agreed upon in the programme area on conservation and sustainable utilization of plant genetic resources for food and sustainable agriculture and in the programme area on conservation and utilization of animal genetic resources for sustainable agriculture in the Agenda 21 proposed to be adopted at the United Nations Conference on Environment and Development in Rio de Janeiro (CBD 2005: 408).

This narrowing of the focus of the CBD was contested by some member countries. The definition of biological resources was one area where a lack of initial consensus about the scope of the CBD was evident in individual country submissions to the process. For instance, in the early stages of drafting, Peru observed that:

1. Article 2 lacks a definition of the term 'conservation of biological diversity,' which should cover the preservation or integral protection, maintenance, sustainable use and recovery of its components.
2. In Article 19, paragraph 3, there is no express mention of the human being within the scope of this paragraph, that is, the protection of the human being from the adverse effects that may be produced by living organisms modified by biotechnology (CBD 2005: 392).

Biological Diversity

It is evident from the literature that approaches to defining the scope of this concept have remained ambiguous. The four major concepts that appeared in the 1970s and 1980s – biological diversity, biological resources, genetic diversity and genetic resources – were never fully defined or adopted. The expression 'genetic diversity' appears in the Stockholm Declaration (1972), the World Conservation Strategy (1980), the International Union for Conservation of Nature (IUCN) General Assembly Resolution (1984) and the Protocol Concerning Mediterranean

Specially Protected Areas (1982) (Van Heijnsbergen 1997: 261). The classic example is the report of the UN Conference on the Human Environment (1973) that refers throughout Recommendations 35 to 45 to the need to preserve the world's genetic resources, yet in Recommendation 40 uses the term 'genetic diversity', where the subject to be protected is referred to as 'genetic resources' (Van Heijnsbergen 1997). The International Undertaking on Plant Genetic Resources (FAO 1983) refers to genes as part of 'genetic diversity'. In this context, Bergman (1986), as quoted in Van Heijnsbergen (1997), observes that biological diversity includes much more than genetic diversity.

In this section we will emphasize those issues that were suspended at the time of the final adoption of the CBD, and have since failed to be successfully resolved. There are three important definitions with regard to biological diversity, biological resources and genetic material.

The concept of biological diversity initially arose in a resolution of the IUCN's General Assembly in 1984, the main purpose of which was to address the conservation of wild genetic resources (Van Heijnsbergen 1997). A commentary on this from the IUCN (Miller et al. 1984) argues that 'biological diversity covers all life forms, with their manifold variety, which occur on earth'. Almost the same concept of biological diversity was articulated at the 17th session of the General Assembly of IUCN and 17th technical meeting at San José, Costa Rica in 1988. The first draft of what would later become the Convention on Biological Diversity provided the definition:

> [B]iodiversity comprises the sum total of plant and animal species in the world today and exists at the level of individuals, populations, species, communities and ecosystems and applies to the genetic diversity they contain and to their relationships and interactions between them.

However, the final draft produced by the 17th meeting was more limited in its approach:

> Biological diversity means the genetic variation represented by the aggregate of species living in the world, or in respect of any State or area, by the aggregate of indigenous species living in the territory of that State (Van Heijnsbergen 1997: 198).

The June 1989 draft of the biological diversity treaty returned to species diversity and presented a very broad concept of biological diversity. This approach was consistently present until the Nairobi conference for the adoption of the agreed text of the Convention on Biological Diversity in February 1992 (UNEP 1992). At this conference the distinction between variety and variability was dropped and only variability remained (Van Heijnsbergen 1997).

Article 2 of the CBD, Use of Terms, states that:

> For the purposes of this Convention:
> '*Biological diversity*' means the variability among living organisms from all sources including, *inter alia*, terrestrial, marine and other aquatic ecosystems and the ecological complexes of which they are part; this includes diversity within species, between species and of ecosystems.

> '*Biological resources*' includes genetic resources, organisms or parts thereof, populations, or any other biotic component of ecosystems with actual or potential use or value for humanity. …
> '*Genetic material*' means any material of plant, animal, microbial or other origin containing functional units of heredity (CBD 1992: article 2).

Annex I of the CBD proposes a number of explanations relevant to identification and monitoring. It is important here to note that Annex 1 also identifies 'genomes and genes of social, scientific and economic importance' to be monitored (CBD 1992: annex I).

Access

When deciding to open negotiations on the CBD, the UNEP Governing Council specifically mandated that the convention should be 'broad in scope' (Miller et al. 1984). The implications of this were most evident in the early stages of negotiating; for instance, in early drafts the concept of 'access' was included, but only in the context of the promotion, funding and access of researchers. Researchers were to get 'priority access' to the wildlife of other countries, but first they had to get permission. Virtually from the moment this statement was drafted, most of the pre-discussion team was opposed to it, as they believed that requiring permission would give developing countries a monopoly on wildlife. There were others in the early negotiations, however, who argued that developing countries would not agree to the convention without some recognition of their rights. This marked the beginning of ABS.

The expression 'access' remained in the UNEP document, but now with a focus on access to 'biodiversity' or 'genetic materials' (a term originally defined to mean essentially 'biological specimens'). The first UNEP meeting in 1989 was attended by invited experts and called an 'expert group'. It discussed and then abandoned the idea of the 'rationalization' of existing conventions, but continued to focus on the protection of wild genetic material, protected areas, the concerns of an advisory committee on the conservation of biological diversity in situ, and 'ecosystems' relevant to wild genetic material. Regarding ABS, only the phrase 'any material of plant, animal or microbial origin' was used. This draft did not distinguish between biological resources, genetic resources and biological diversity; all were included in ABS.

At the same time, the concept of benefit sharing entered the negotiating arena. The initial focus was on the transfer of technology, and many discussions were held to identify which technologies should be transferred and how. This was intended not to be solely conservation technology, but also to include technologies that could enable developing countries to get a higher level of value from the sustainable use of their biological resources. At the time, there were some detailed discussions on 'biotechnology', and many attempts were made to define this term in detail, but a definition was never actually adopted, and as a result the term was not included in the final draft of the CBD.

Towards the end of the formal negotiations (a few months before the UN Conference on Environment and Development, also known as the 'Rio Earth

Summit', from 3 to 14 June 1992), the term 'genetic resources' was substituted for the original expression 'biological resources' or 'genetic material'. The negotiators were under significant pressure to finalize the draft in time for the summit, so all definitions and concepts that were still controversial were either deleted or cut down to the lowest common denominator (i.e., language that was acceptable to everyone but generally legally ambiguous). For this reason, there was little discussion of the definition of 'genetic resources'. The process of proposing and adopting a definition was simply aimed at cutting down the language to the point that no party found it objectionable. Because the negotiations were at a very late stage, it appears that no scientists or experts in biotechnology were consulted and no detailed analysis of the potential administrative and political interpretations of the term was undertaken.

Exclusion

The decision of the second meeting of the Conference of Parties of the CBD (1995a) not to include human genetic resources in the definition of biological resources was based on very limited discussion. One of the official COP2 meeting documents (CBD 1995b), which would have given rise to the explicit (negative) reference in the COP2 decision, contains the following discussion, which may help contextualize the evolution of this idea. (This quotation includes the related footnote.)

> **4. Human genetic resources**
>
> 64. Medical researchers are increasingly interested in the diversity of the human gene pool as a source of valuable scientific and medical information. The genetic material found in human beings is 'genetic material' as defined under the Convention, in that it is material of animal origin containing functional units of heredity. The collection and analysis of samples of human genetic material from many different ethnic groups around the world could provide insight into the evolution of the human species as well as the nature of human susceptibility and resistance to diseases.[43] This value for humanity indicates that these samples constitute genetic resources – genetic material 'of actual or potential value' – again fitting a definition under the Convention. Yet from the history of its negotiation, it is clear that the Convention was not formulated with human genetic resources in mind.
>
> The collection and use of human genetic resources raises difficult ethical and political issues. For example, the direct, physical interest of affected individuals in their own genetic resources argues strongly for extensive consultations with affected citizens. Given all the serious concerns surrounding this issue, the Conference of the Parties may wish to study the question of human genetic resources and the Convention on Biological Diversity to determine how it may be approached by the Conference of the Parties.

[43] See Anna Maria Gillis, 'Getting a Picture of Human Diversity: Population geneticists and anthropologists plan to use variation in human genes to get a sense of Homo sapiens History,' *BioScience* 44:8 (994); Mary Claire-King, *Celebrating Identity and Diversity: The Human Genome Diversity Project* (testimony to the U.S. Senate Committee on Governmental Affairs, April 26, 1993) (CBD 1995b).

As is evident from the above, during its evolution the CBD went through a complex and arduous negotiation process that oscillated between the need to be all-inclusive of relevant concepts and, at the same time, specific about their

meanings and functions within the convention. Nowhere is this tension more apparent than in the definitions of 'biodiversity' and 'access', and the inclusion/exclusion criteria, which provide a good insight into the issue of human genetic resources within the scope of the CBD.

7.2.2 ABS Issues in International Negotiating Forums

ABS has emerged as an important policy option for addressing concerns regarding biopiracy and related issues. As is clear from Table 7.1, it was and is being discussed by a large variety of organizations.

While some individual nations have come to a decision regarding formulating a policy on the issue of ABS, no international agencies have done so. This includes WIPO, UNEP, the United Nations Food and Agriculture Organization (FAO), the World Medical Association and the United Nations Educational, Scientific and Cultural Organization (UNESCO). This does not imply a lack of interest in the subject, as the many ongoing debates in various international forums attest, but rather an inability to achieve consensus on basic facts related to ABS issues and how these relate to international treaties. The differences in opinion between developed and developing countries are again evident, and are the main reason behind the continuing deadlock.

The situation is nowhere more apparent than at the negotiations of the TRIPS Agreement of the WTO. The TRIPS negotiations have become the main international stage for contentious debates on ABS, not least because WTO treaties include strong enforcement rules that make them akin to international law. In the

Table 7.1 ABS Discussions in Global Processes

Food and Agriculture Organization	Commission on Genetic Resources (ongoing)
Food and Agriculture Organization	International Treaty on Plant Genetic Resources for Food and Agriculture (Rome, 2001)
World Trade Organization	TRIPs (ongoing)
Convention on Biological Diversity	Nagoya Protocol (2010)
Antarctic Treaty System	Bioprospecting in Antarctica (1999)
World Intellectual Property Organization	Intergovernmental Committee on Intellectual Property and Genetic Resources, Traditional Knowledge and Folklore (2001)
General Assembly of United Nations	United Nations Informal Consultative Process on Ocean Affairs and the Law of the Sea (UNICPOLOS) (2001) and Ad Hoc Working Group on Biodiversity Beyond the Limits of Any National Jurisdiction (2004)
World Summit on Sustainable Development	International Regime on ABS (2002)
United Nations	Declaration on the Rights of Indigenous Peoples (2007)

Source: Glowka (2008)

effort to make the TRIPS Agreement an instrument of international legislation on property rights that does not disregard the issue of biopiracy and works in accordance with the CBD provisions, ABS is seen as the missing link that would both enhance the functioning of TRIPS and promote the values of the CBD.

A strong alliance among developing countries, including the Africa group and the group of 17 Like-Minded Megadiverse Countries (which includes India, China, Brazil, Bolivia, Colombia, Cuba, the Dominican Republic, Ecuador, Peru and Thailand), has requested the introduction into the TRIPS Agreement of a mandatory requirement to disclose the origin of biological resources and/or associated traditional knowledge used in inventions for which intellectual property rights are applied. In a case where the country of origin of biological resources is identified in the patent application, applicants would have to provide information that includes evidence of compliance with the applicable legal requirements in the providing country for prior informed consent and for access and fair and equitable benefit-sharing (WTO 2006b). This amendment would incorporate into TRIPS the ABS objectives as developed in the CBD, thereby making the two treaties compatible. In the absence of proper consent or authorization for the use of resources, the country of origin could claim law infringement and apply for the patent to be revoked.

The main opponent of incorporating ABS provisions into TRIPS is the United States, followed by Japan and, to some extent, the European Union and Australia. The US has argued against changing the status quo of patent approval in TRIPS, asserting that the prerequisites for granting a patent (novelty, non-obviousness and utility) represent the only lawful arrangement and any other addition would complicate matters unnecessarily (RIS 2007).[3]

These opponents are not, however, against ABS rules per se. They argue that the value of ABS is best governed by means other than intellectual property laws, such as contracts, conservation laws and export controls, that responsibility for keeping track of the use of genetic resources lies with the countries that provide them and not the patent offices of other countries, and that requiring additional disclosure would increase the costs of research because of the record keeping required, thereby reducing research and increasing the cost of products. They maintain that the purpose of TRIPS is to establish minimum levels of intellectual property rights protection and not to specify contractual obligations regarding access to genetic materials in other countries' territories.

The arguments against the incorporation of ABS in TRIPS are technically valid, but proponents of such a move argue that perhaps this misses the point. In new submissions, developing countries (e.g. WTO 2006a, 2006c, 2008) are adamant that ABS is a key issue in protecting intellectual property rights and that without the amendment there is an apparent contradiction between TRIPS and the CBD. To

[3] Patent revocation can only occur on the following grounds: that the invention for which patent protection is sought is not new, lacks true innovation or is not capable of industrial application, or that the application does not disclose the invention in a manner sufficiently clear and complete for the invention to be carried out by a person skilled in the art.

clarify this point, Peru has submitted a dossier of cases of patent applications that are based on the country's biological resources without proper acknowledgement (WTO 2007a).

A robust debate continues, with new submissions in the WTO TRIPS Council for and against the amendment proposal. On the main arguments, both sides remain unmoved. Norway has sided with developing countries on the issue (WTO 2006d: WT/GC/W/566), while Japan has proposed as a compromise the creation of a global database on traditional knowledge that can be easily accessed by patent officials (WTO 2007b). It remains to be seen which argument will prevail, but the alliance of developing countries on this issue is impressive in its depth and strength.

It is also extremely important to stress that the understanding of the term 'biological resources' by the countries that have initiated the amendment proposal includes human genetic resources. Although this issue has not yet been at the centre of negotiations (presumably because the CBD is seen to cover the definitions of relevant terms adequately), developing countries have made it clear that 'human genetic resources' are not to be excluded from the amendment. In their own words:

> Taking the above definitions into account, we can see that biological resources may refer to something that exists in the natural or crude form and to the whole organism including human beings … (WTO 2006a).

No other international forum has taken up the issue of ABS with such force and intensity as the WTO. ABS tends otherwise to be a side issue on the main agenda or a formal discussion point for peripheral initiatives that deal with capacity-building and technology transfer.

At WIPO, for instance, a stage for a similar debate on intellectual property rights commenced officially with the establishment of the Intergovernmental Committee on Intellectual Property and Genetic Resources, Traditional Knowledge and Folklore (IGC) in 2000. The IGC mandate is to develop, first, 'guidelines, and model intellectual property clauses for contractual agreements on access to genetic resources and benefit-sharing, taking into account the specific nature and needs of different stakeholders, different genetic resources, and different transfers in different sectors of genetic resource policy', and, second, 'appropriate provisions or guidelines for national patent laws which facilitate consistency with measures of States concerning access to genetic resources and which are consistent with existing international intellectual property standards' (WIPO 2001). It has agreed upon principles for the development of guidelines for intellectual property aspects of ABS with regard to genetic resources, but has fallen short of developing a legally binding international instrument, owing to limitations in the WIPO remit to develop such instruments. The work of the IGC continues along these lines.

The debate on ABS in UNEP, on the other hand, focuses on more practical aspects of the issue. UNEP follows the CBD closely and is the designated global agency for ABS under the CBD processes. The organization is working with national, regional and global stakeholders to aid the formalization of ABS management systems. These include support for the ongoing finalization

of negotiations for the international regime on ABS, and support to national and regional capacity-building efforts to help stakeholders appreciate the relevance of ABS issues and the need to address them within ecosystem management options. Along these lines, UNEP has undertaken a series of capacity-building programmes, mainly in Africa, based on the recommendations of the voluntary Bonn Guidelines, which were adopted by the Conference of the Parties to the CBD in April 2002, with the aim of helping countries achieve CBD objectives, and have since been superseded by the Nagoya Protocol. These programmes mainly deal with legal aspects of ABS, analysing national capacities, initiating training programmes and promoting regional cooperation.

The issue of ABS has also been debated at the FAO. Although it is not in the mandate of the FAO to establish guidelines on ABS matters, these issues were deemed important enough to be incorporated into the organization's International Code of Conduct for Plant Germplasm Collection and Transfer (1993). The code sets out the responsibilities of collectors, donors, sponsors, users and curators of plant genetic resources. Among these responsibilities, curators are to:

> take practical steps, inter alia by the use of material transfer agreements, to promote the objectives of this code including the sharing of benefits derived from collected germplasm by the users with the local communities, farmers and host countries… (FAO 1993: article 13.3).

The international debate on ABS issues has therefore proven to be one of the most complex aspects of negotiations in international forums outside the CBD, particularly in so far as it relates to the inclusion or exclusion of human genetic resources.

7.2.3 ABS and WHO

The WHO is a late entrant into the debate on ABS. It was only at the 60th session of the World Health Assembly (WHA), WHO's supreme decision-making body, from 14 to 23 May 2007, that the issue of ABS came up in a major way. Within the framework of the International Health Regulations (WHO 2005), the WHA adopted Resolution 60.28 (WHO 2007a, 2007b). The work relating to the resolution was undertaken at the intergovernmental meeting and the open-ended working group.

The importance of WHA Resolution 60.28 in the context of the CBD is that it acknowledged the sovereign right of states over their biological resources. This was a marked departure from earlier practices; for more than 50 years, the WHO's Global Influenza Surveillance Network of laboratories, including its collaborating national influenza centres, H5 reference laboratories and other expert laboratory reference centres, had been sharing samples without clear obligations. The issue came to the fore in 2007, when Indonesia refused to share its samples with the WHO and observed that it was not fair to pass on ownership of samples to the WHO collaborating centres without getting any benefit from the resulting papers

or patents (*Nature News* 2007). Indonesia pressed for a material transfer agreement (MTA) that would allow research use, but give Indonesia sovereign ownership of its samples, apart from access to vaccines emanating from its samples (Siti 2007) (see also Chap. 5).

The concern basically comes from a growing trend in biomedical research involving the patenting of viruses (Table 7.2) that has triggered a major debate in various groups (Regalado 2003). Experts such as Richard Gold have argued for reforms of the patent system, particularly in the context of the patenting of the SARS virus (Gold 2003). Similar views have come from Peter Yu (2003). In this context, the debate on the TRIPS Agreement's article 27.3(b) on the lack of harmonization over the criteria of novelty and 'inventive steps' has remained inconclusive.

Some progress has been made with the WHA's adoption in 2011 of the Pandemic Influenza Preparedness Framework. As described in more detail in Chap. 5, WHA resolution 62.10 urged the facilitation of 'a transparent process to finalize the remaining elements [of the virus and benefit sharing framework], including the Standard Material Transfer Agreement' (WHO 2009b). One year later, WHA resolution 63.1 urged continued 'work with Member States and relevant regional economic integration organizations, on the Pandemic Influenza Preparedness Framework for the Sharing of Influenza Viruses and Access to Vaccines and Other Benefits', and the undertaking of 'technical consultations and studies as necessary' to support this work (WHO 2010). Finally, in April 2011, the WHO Open-Ended Working Group on Pandemic Influenza Preparedness for the Sharing of Influenza Viruses and Access to Vaccines and Other Benefits reached agreement on terms and conditions that will govern the sharing of influenza viruses and other benefits, and these were approved in May 2011 by the WHA.

Table 7.2 Examples of Virus-related Patents

Patent	Applicant	Concept	Application
US Patent 6,528,066 4 March 2003	University of Iowa	First known mutant chicken-pox virus	May be useful for potential new diagnostic test for chicken-pox
US Patent 414319 28 April 2006	Rabinowitz, Joseph E. (Carrboro, NC, US), Samulski, Richard Jude (Chapel Hill, NC, US), Xiao, Weidong (Jenkintown, PA, US)	Viral vectors and methods of making and administering the same	The parvoviruses of the invention provide a repertoire of vectors with altered antigenic properties, packaging capabilities, and/or cellular tropisms as compared with current AAV vectors
US Patent 4,983,387 31 July 2001	Zimmerman, Daniel H. (Bethesda, MD) Sarin, Prem S. (Gaithersburg, MD)	Modified HGP-30 peptides	Forms part of the core of the AIDS virus for a potential vaccine against AIDS

Sources: WHO (2009a), Regalado (2003)

Thus we see that ABS has also been a major issue in WHA negotiations in respect of human virus research, a fact that was reflected in the addition of the text referring to human pathogens in the CBD ABS decision adopted at COP 10 in Nagoya in October 2010.

7.3 New Technologies that Blur Traditional Boundaries

After this historical overview, this chapter now approaches its main argument for expanding the scope of the CBD to include human genetic resources, namely the practical impossibility of separating the origins of genetic resources in the innovation process. The lines between human genetic resources and those covered by the CBD are becoming increasingly blurred. Drug development is already inextricably integrating the use of these resources into the same discovery programmes, and even into the same molecules.

The publication of the human genome in 2000 led to a plethora of ideas as to the use of the emerging information on genetics in diagnosis and treatment of human diseases and the creation of new diagnostic and therapeutic tools.[4] The earliest and most obvious applications of genome research are tests for genetic disorders, but less obvious diagnostic uses may prove at least as important (e.g. in forensics to establish identity). Genome research also holds the promise of identifying genes expeditiously, making a genetic approach attractive as the first step in the study not only of complex diseases, but also of normal biological functions and of human diversity. Identifying relevant genes gives investigators a molecular handle on problems that have previously proven intractable.

One distinctive aspect of the genome project was its explicit attention to technology development in addition to basic science. The development of new biological methods, instruments, automata and robots, as well as other new technologies, became an explicit objective. An unprecedented commitment to supporting research on the ethical, legal and social implications of human genome research has been a key feature of the project since its earliest phases. Existing genome research focuses on ties to industry, with plans to locate genes through mapping techniques and an eye to drug discovery through collaborative research. Identification of relevant

[4] In the scientific community this initial optimism has waned, since it has proved more difficult than first anticipated to connect one gene to one trait. There is an emerging view that the way genes interact may be more important, and might even be essential in predicting the effect of a certain allele (form of a gene). This means that the entire genetic background of a gene determines its effect and/or function. A gene found in a person from South Asia may very well not have the same effect when introduced into a person from South America, or even someone from another ethnic group in South Asia. This will affect the speed of discovery and perhaps the effectiveness of therapeutic use. So, although it may take longer than first thought, the approach of using genetic information to find novel therapies is still promising.

genes has many possible uses, including the determination of potential drug targets, the use of a gene itself as a therapeutic agent (gene therapy), controlling the expression of a gene, and using a gene product as a protein therapeutic.

Private investments necessitated a means to stake claims in this territory, which have taken the form of patents or trade secrets. These claims necessarily changed the complexity of research, altering the rules by which materials and data were exchanged. The seriously conflictual nature of this issue came to the surface in the international controversy provoked by US patent applications on thousands of human DNA sequences filed by the National Institutes of Health in 1991, where opponents to these applications made ethical claims about direct links between human genes and human dignity (United States Congress 1994).

It is evident, however, that DNA is a universal genetic code, and it will be difficult, if not impossible, to distinguish human genes from those derived from other organisms. While it is obvious that the human genome in aggregate contains the instructions for creating a human – instead of a monkey or nematode or yeast – it is equally clear that very few, if any, genes are exclusively human in origin. A classic 1975 paper by King and Wilson showed that the average protein sequence differed by only 1% between humans and pygmy chimps and the difference at the DNA level was only slightly greater than 0.3938% (King and Wilson 1975). The obvious implication is that humans differ more in the parameters of gene expression than in the genes themselves. Furthermore, with the advent of human-animal, human-microbe and human-plant chimeric proteins, which involve creating synthetic genes combining genetic material from humans with that of other species, these distinctions become extremely difficult to delineate on a purely practical basis.

These increasingly molecular-based approaches have made target-based drug discovery easier than was the case with the traditional *in vivo* approach. This is not surprising, considering the superiority of molecular approaches in screening capacity and the ability to define rational drug discovery programmes. In part, these ideas have helped to re-evaluate the enormous costs involved in the drug discovery process and have streamlined the strategies being employed by pharmaceutical and biotechnology companies. Constantly improving genomics technologies, such as ribonucleic acid interference, have satisfactorily validated targets that would have taken much longer (and cost more) with traditional transgenic technologies. Drug targets identified by these techniques involving human genetic resources could end up being the basis for drug discovery programmes using molecules isolated from plant sources (Table 7.3).

Molecular diagnostics is the fastest growing segment of the *in vitro* diagnostics industry. In little more than a decade, the clinical market for molecular diagnostic products has surged from US$50 million to over US$1 billion in the United States, and it is likely to reach US$35 billion globally by 2015. These astonishing exponential figures are an indication of the profitability of the molecular diagnostics market. A major proportion of this may be attributed to advances in genetics, genomics and proteomics. Driven by perceived commercial benefits, pharmaceutical companies are increasingly interested in developing tests that can eventually be used to individualize the prescription of their drugs (Mancinelli et al. 2002).

Table 7.3 Examples of the increasingly inextricable utilization of plants, human genetic resources and microbes in drug development

Use of human genetic resources	Example	Covered by CBD?[5]
Drug target	A genetic study conducted by Swedish scientists using samples from different ethnic groups in Africa implicated C-reactive protein as a potential target for an adjunct treatment for malaria. An unrelated study by Japanese scientists has suggested that the compound AHCC isolated from shiitake mushrooms native to East Asia lowers levels of C-reactive protein	Partially (para. 13.7)
Vaccine target	A large number of studies use samples from individuals living in Africa and other malaria endemic regions to identify potential candidate antigens for malaria. A novel way of administering malaria vaccine antigens through the consumption of transgenic tomatoes was suggested	Partially (para. 43.3)
Antibodies	During the avian influenza pandemic, samples taken from Vietnamese survivors by scientists in the US were used to identify antibodies that could be used to design antibody-based therapies for the treatment of H5N1 infections. Technologies for creating recombinant antibodies are becoming increasingly sophisticated, and using these kinds of samples to guide the development of antibody-based therapeutics is likely to have increasing importance. Such antibodies would often be produced through the use of microbial cells. These antibodies can also be used to guide the selection of avian influenza virus antigens for use in vaccines	Partially (para. 13.2)
Chimeric proteins	A strategy seen with increasing frequency in anti-cancer drug development is the creation of chimeric proteins that combine a human protein with a plant toxin into a single molecule that selectively kills cancer cells; the expression of these protein constructs thus involves both human genetic material and plant genetic material	Partially (para. 43.3)
Gene therapy	A major strategy for gene therapy is to insert a human gene into a virus, which will then deliver the gene to human cells; these virus constructs thus contain both human genetic material and viral genetic material	Unclear (para. 13.2)
Diagnostics	Genetic diagnostics are becoming an increasingly important area, as can be seen in the example of Herceptin and HER2/neu. Creation of genetic diagnostics relies on the identification of important polymorphisms, and there are a large number of studies in many different ethnic populations all over the world to identify these polymorphisms for use in potential diagnostics. A study by a group in France compared alleles that predispose to rheumatoid arthritis across ten different ethnic populations from 17 countries	Unlikely (para. 13.2)

Sources Israelsson et al. (2009), Yanagimoto et al. (2008), Perlaza et al. (2001), Chowdhury and Bagasra (2007), Khurana et al. (2009), Ben-Yehudah and Lorberboum-Galski (2004), Barnetche et al. (2008), http://www.fusionantibodies.com//index.cfm

[5] References in this column are to the annex to the CBD (2009), which begins on page 6 of that document.

Take the case of Herceptin, which is indicated for metastatic breast cancer, and also gained approval in the UK for early-stage breast cancer in 2006. Herceptin treatment is seriously considered only when a patient scores within a particular range on a diagnostic test that selectively identifies a subgroup of breast cancer patients who may maximally benefit from Herceptin and, equally importantly, those for whom Herceptin will not be useful. Herceptin is the epitome of personalized medicine in its fundamental approach, providing the appropriate drug to the appropriate patient and at the appropriate dosage – thus improving considerably the safety and well-being of the patient (Madsen 2004).

This is an area where sequence data from the Human Genome Project, and the subsequent Human Proteome Project, is making an enormous impact. As long as there is a demand in discovery research for the identification of key genes involved in common disease aetiology, this area of the market is likely to grow. Information on key genes involved in drug metabolism or transport has also been exploited for pharmacogenomic studies. This is an area where pharmaceutical companies, in their quest for safer, more efficacious and more cost-effective medicines, require indicative answers as to how subjects are metabolizing or excreting drugs to discover if there may be genetic reasons for medicinal effects on humans. Again, the indications are that tools for pharmacogenetics will potentially provide rich pickings for the diagnostic market.

Hence human genetics and genomic studies have resulted in widespread global collaborative studies (see also Majengo sex worker case in Chap. 5), with the transportation of human biological materials across continents and between academic institutions and commercial organizations underlining the ongoing ethical debates over the ownership of material, informed consent, material transfer agreements, and ABS. A number of instances have surfaced in which the collection of such material has been undertaken without informed consent, and these are barely the tip of the ABS iceberg, as we show below.

7.3.1 Developing Country Experiences

India

Being a country rich in biodiversity, India attracts global interest in the genetic diversity of its anthropologically well-defined populations, including a number of tribal groups. This has not only global evolutionary implications, but also potential applications in pharmacogenetics for personalized medicine. India's strength in the area of drug development complicates the situation, especially with the existence of Indian biobanks as national repositories of biological samples, which gives rise to issues of privacy protection and confidentiality. When international collaborative studies are conducted, the main concerns are exploitation, stigmatization, ownership, MTAs and benefit sharing, especially when a gene-based product is likely to be commercialized eventually. Biopiracy is even more worrying in a

developing country that has appropriate ethical guidelines and regulations in place, but lacks proper implementation mechanisms to monitor misuse.

The potential for obtaining valuable information which may result in academic laurels or commercial benefits is leading to increasing instances of biopiracy. Of late, more and more instances are coming to light of guidelines being flouted by researchers associated with foreign investigators who are funded by agencies that in their own countries are required to adhere strictly to high ethical standards concerning human research.

For instance, samples from two Indian tribes were subjected to genetic analysis without permission being obtained from the local authorities concerned. This situation arose in relation to a study funded by the US National Institutes of Health, the European Commission and the Estonian Medical Research Council and published in the *American Journal of Human Genetics* (Kivisild et al. 2003). It listed 18 authors from seven institutions in six countries. It was not clear who had given permission to collect the samples, nor was any Indian institution or author acknowledged for any kind of collaboration. The article mentions that informed consent was obtained. On enquiry however, the European Commission could only provide the information that the samples had been collected 25 years previously and kept in the archives of one of the collaborators. Considering that even today the concept of informed consent is still not understood by many Indian patients or volunteers, particularly those from the tribal populations, the possibility of having obtained valid informed consent 25 years ago is highly questionable.

Later, a number of further articles on the genetic make-up of Indian tribes were published by the same team in the *European Journal of Human Genetics* and *Current Biology* (See Cardaux et al. 2003, 2004) but this time with the name of an Indian investigator and institution that had contributed the samples. However, it appears that approval from the authorities concerned was not obtained for sending the samples abroad for the study. The issues of prior informed consent, ownership of the biological material, appropriate MTA and ABS remained unattended to. The onus of vigilance about this in collaborative studies falls on the editorial boards of journals and the ethics committees of the developed world's partner institutions (The Hindu, 2006). However, as the next chapter explains (Chap. 8 on ethics review), these parties may, for a variety of reasons, fail to ensure that such issues are addressed.

China

The controversial case of Harvard researcher Dr Xu Xiping, who took and exported millions of DNA samples from poor areas in Anhui province, central China, sparked heated international, national, and local debates on bioethics issues such as informed consent and benefit sharing. This episode came to light in 1999, when Dr Gwendolyn Zahner, a former faculty member at the Harvard School of Public Health, exposed the unethical conduct in Dr Xiping's research programme. These debates led to in-depth discussions on the protection of vulnerable participants in biomedical research, and on the pursuit of best practices in informed

consent procedures and mutually beneficial models of international scientific cooperation (Sleeboom-Faulkner 2005).

One of the outcomes is China's 1998 Interim Measures for the Administration of Human Genetic Resources. This crucial set of regulations underscores the importance of the ethical and scientific review of international cooperative projects that involve exporting human genetic resources from China or importing them into the country. Yihong Hu, the divisional director of Bioresource and Biosafety at the China National Centre for Biotechnological Development, explicated the function of the Chinese Human Genetic Resources Management Office at the fourth Bionet workshop, entitled 'Biobanking and personal genomics: Challenges and futures for EU–China collaborations', held in April 2009, in Shenzhen, China:[6]

- Drafting the implementation details and documents, coordination and supervision of the implementation of this approach
- Management and registration of important family genealogy and special genetic and specific areas of genetic resources
- Administrative approval of international cooperation projects on human genetic resources
- Acceptance of applications for the export of human genetic resources
- Other tasks related to human genetic resources management (Hu 2009).

Since the launch of the interim measures, every international cooperative project that involves the transportation of genetic resources across Chinese borders must apply for permission from the Human Genetic Resources Management Office. An expert panel was established to review the applications according to both scientific and ethical considerations. From January 1999 to April 2009, the office received 303 applications and rejected 59 of them. Taking into account the advancement of biomedical research and emerging issues in benefit sharing and intellectual property, the office has been consulting with international and national experts since 2005 in order to revise the *Interim Measures*.

The current regime, however, does not necessarily cover all international cooperative projects. Exceptions can occur in the case of research that involves investments by a foreign institution or company, but is conducted in China. For example, a large-scale epidemiology project, led by a researcher at a prestigious UK university, was successfully launched in China in 2004 without reporting to the Human Genetic Resources Management Office (see www.ckbiobank.org). Although the study collects and stores blood samples and extensive health-related data, it does not actually export any 'human genetic resources' out of China. While there is every reason to believe that the research being approved by the university ethics committee and Chinese partner institutions is appropriately obtaining informed consent from participants, this kind of research alerts the office to potential loopholes in the current regulations. How to protect research participants effectively

[6] http://www.bionet-china.org

and efficiently, while promoting genuine international cooperative biomedical and pharmaceutical research, therefore remains a major issue.

7.4 ABS in Human Genetic Resources

Notwithstanding the complexity of identifying the origin of the 'biological resources' that constitute the raw material and the focal point of ABS guidelines, there is growing acceptance that some kind of benefit sharing should take place when human genetic material is involved (Schroeder and Lasen-Diaz 2006). We can find examples of this in international debates and guidelines, as outlined in Chap. 3. For instance, the Statement on Benefit Sharing by the Hugo Ethics Committee (2000), the WHO report *Genetic databases: Assessing the benefits and the impact on human and patient rights* (WHO 2003) and the UNESCO Declaration on Human Genetic Data (UNESCO 2003) have forcefully called for benefit sharing with participating populations in genetic studies. What constitutes benefit sharing in such cases is widely debated, as it may vary depending on the needs, values and cultural parameters in a given case. What is clear, however, is that benefit sharing is considered a key aspect of research involving human beings and human genetic material. Yet, because there are currently no legally binding obligations requiring ABS agreements to be concluded in such cases, there is little evidence that this is actually done in any formal or meaningful manner anywhere in the world. While research groups prefer to offer participating individuals in research studies (which are usually of a clinical nature) free health care as a 'benefit' (see Chap. 5), formal arrangements between the parties appear to be rare.

One exception is the formal benefit-sharing agreement that involved a genetics research company, a drug manufacturer and the government of Iceland. In this case the research company planned to develop a database of the Icelandic population to identify particular genetic polymorphisms that could eventually lead to drug development. Interestingly, the plans for the database were ruled unconstitutional, partly on the basis of issues of informed consent and privacy, and the result of the remaining scientific collaboration so far has been disappointing, with no commercial developments. The case, which is described in detail in Chap. 5, has nevertheless opened up new perspectives on ABS agreements in terms of basic research in population genetics studies.

7.5 Exploring the Way Forward

The CBD is an important global agreement that provides national sovereignty over the biological resources found within national geographical borders, and spells out that any commercial benefit derived from these resources should, among other things, acknowledge the supplier country and/or indigenous and local

communities for their conservation efforts, and also recognize any prior knowledge about a resource's potential utility. This is a commitment incorporating the principles of fairness and equity. It needs to be appreciated that the CBD is fundamentally an effort to protect the world's biodiversity and to ensure the conservation of all the varied components of the earth's biological resources, which must include all species. Sustainable use of the various components of biological diversity, with fair and equitable ABS arising from the use of such genetic resources, is an institutional objective towards that goal. This focus of the CBD qualifies it to be the central agency at the global level to evolve broader frameworks for ABS.

The ABS mechanism is also being discussed at the WHO, largely in the context of the sharing of viruses for vaccine development, which resulted in the adoption of the Pandemic Influenza Preparedness Framework in 2011. It would be extremely useful if the WHO and CBD would work together more closely and generate common ABS guidelines. It is evident from the technological trends in various streams of biomedical research that clearly delineating the precise sources of a drug will become increasingly difficult as greater convergence is achieved between plant and human genetic resources in drug targeting, selection and development. This will require a far more refined and focused ABS regime. The efforts to address unresolved elements of ABS continue at CBD meetings (Balmford et al. 2005), but certain issues remain outside the scope of the CBD due to its non-inclusive approach to biodiversity. The fact that many of the important human genetic resources for drug development come from indigenous communities makes this a matter of even greater concern (Hammond and Mayet 2009).

The proliferation of patents involving human genetic resources is a case in point. From 1980 to 2005 nearly 15,603 patent families[7] claiming human DNA sequences were filed (Hopkins et al. 2007). Of these, nearly 5,669 were filed at the world's three leading patent offices, namely the US Patent and Trademark Office, the European Patent Office and the Japan Patent Office (Hopkins et al. 2007). The growing realization of this valued resource for technology (and product) development has received varying responses from national governments. For example, the Indian Ministry of Health and Family Welfare has already issued guidelines restricting the transfer of biological material for collaborative research subject to the approval of institutional review and ethics committees (GOI 1997). These guidelines also discuss the exchange of biological material for commercial purposes and stipulates that approval is on a case-by-case basis with a three-month lead time (GOI 1997). China's National Office of Administration on Genetic Materials has been revising the 1998 regulation on the administration of genetic material, which specifically regulates the export and import of genetic material (including human genetic resources) in that country. The office has also been concerned with the way ABS is defined and how best to ensure justified benefit sharing in international collaborative studies.

[7] A patent family comprises all the patent applications and granted patents resulting from a specific invention.

This could eventuate in a huge cobweb of national statutes that may seriously hamper international drug development efforts. It is necessary to consider whether international technology efforts using biodiversity can work effectively if there are diverse kinds of national legislation determining the nature and focus of ABS, as opposed to a single clear and transparent system facilitating global drug development efforts. It seems, therefore, that an international comprehensive ABS regime is urgently needed.

Further research in this field should address issues such as who the beneficiaries of such arrangements would be, how they should be identified, and how the benefit sharing would be effected. The extent of benefit sharing also needs to be defined, and a strategy for doing so elucidated: whether it is to be achieved by a share in the profits from the drug, fixed royalties, or else free or low-cost access to drugs, for example. How would ABS be accomplished for human genetic resources when the source is mixed or unknown? Since implementing benefits from human genetic resources, unlike plant genetic resources, would require not only highly advanced technology but also huge capital inputs, global arrangements for ensuring cost-effective access to medicines will have to be viewed as a priority. This may also require re-evaluating the way in which we cover human genetic research databases or population databases in this context.

At the practical level, administrative challenges will certainly arise from the inclusion of human genetic resources in ABS regimes. This will raise a multitude of issues that require us to draw upon the experience of expert institutions in the field and to consult with diverse stakeholders.[8] Chapter 8 begins this process by bringing to bear the experience of those involved with international research ethics.

Whichever route the inclusion of human genetic resources in ABS regimes might take, it must be evident from this chapter that it is becoming increasingly important to consider the inclusion of human genetic resources in international treaties that deal with biodiversity issues. To exclude such resources from these agreements for the sake of simplicity merely weakens those instruments by excluding a crucial area, potentially with major repercussions in science, the economy and society. It is our common position that this should not happen, and we heartily support the wording of the Nagoya Protocol on ABS, which takes the first step towards inclusion.

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[8] See Hodges and Casas (2008) for the need to involve industry in this process.

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Chapter 8
Realizing Benefit Sharing: Is There a Role for Ethics Review?

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Abstract The donors of human genetic resources deserve benefits in return for their contribution to scientific research. In the context of developing countries this claim holds as a matter of justice. But how can this demand be realised and implemented? This chapter looks at the role of ethics review as a possible benefit sharing mechanism. In particular the promising role of research ethics committees in monitoring the Declaration of Helsinki's post-study obligations is considered. However, a range of obstacles are identified, which would have to be overcome before ethics review could reliably achieve justice for the donors of human genetic resources in developing countries. These issues are addressed in specific recommendations. The

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chapter concludes that the provision of health care, however extensive, in return for the donation of human genetic resources does not represent undue inducement, but rather fair benefit sharing.

Keywords Benefit sharing • Research ethics • Developing countries • Post-study access • Declaration of Helsinki

8.1 Introduction

'The arc of the universe is long, but it bends towards justice.' This is how Martin Luther King Jr. expressed his hopes for the future. Of course, justice does not arrive of its own accord. Four years after receiving the Nobel Peace Prize in 1964 for his non-violent work to advance civil rights King was assassinated. Today, there is a black President of the United States, giving an indication that some of King's dreams of justice have been realized. However, when we turn to international justice, we note that the US is one of a handful of countries[1] that are not parties to the international Convention on Biological Diversity (CBD). In the previous chapter, an expansion of the CBD was suggested in order to achieve justice for donors of human genetic resources.[2] This chapter will explore the potential for utilizing the existing, well-established system of ethical review to advance benefit sharing.

How does one protect human research participants from harm and exploitation? Four basic markers for the occurrence of harm in the research context can be distinguished (see Chap. 2).

1. Unfavourable risk-benefit ratio
2. Breach of confidentiality or privacy
3. Invalid consent
4. Lack of access to the benefits of research.

Exploitation is mainly relevant to the fourth marker and equates to 'a failure to benefit others as some norm of fairness requires' (Mayer 2007: 142) (see Chap. 2). Ethics committees have increasingly taken on the responsibility of preventing such exploitation. They appear in two main varieties: clinical ethics committees have been in existence since the early 1960s, mostly to support staff, patients and families in making end-of-life decisions, while research ethics committees have been in existence since the late 1960s (see below) to govern research involving human participants (Aulisio 2003: 841).[3]

[1] Three exceptions at the time of writing are Andorra, Holy See (Vatican) and South Sudan.

[2] By human biological resources, we mean human biological samples collected for genetic studies and related data.

[3] For more on clinical ethics committees see McGee et al. (2001), Kuczewski (2004), Slowther (2007) and ASBH (1998).

Research ethics committees are most relevant to this chapter. Their primary role is to decide whether a particular research project is ethical or not by reviewing its study protocol. Such committees usually comprise scientists, professionals and lay people supported by an administrator. Standard questions for such a committee would be:

- Are the research participants appropriately informed?
- Is the balance of risks and benefits posed by the research fair and reasonable?
- Are the research participants likely to be worse off for participating in research? If so, does their consent represent a sufficient protection of their interests (or are they being exploited)?
- Is the research likely to be useful and informative? (Ashcroft 2007: 684)

Ethical review generally follows a particular pattern. Study protocols are received from researchers, and are then reviewed by a single member, a small consultation team or the full ethics committee. Applications may be approved at that point; if not, they are returned to the applicant with queries before being reconsidered and finally approved or rejected. The legitimacy of ethics committees derives from the fact that they are lawfully established and adhere to a process of deliberation as a diverse group of experts (including lay people) who reach consensus after discussion (Garrard and Dawson 2005: 423). While review requirements differ between (and sometimes within) countries, Fig. 8.1 shows the most basic steps.

In assessing whether a protocol is ethically acceptable, research ethics committees refer to international guidelines (e.g. the Declaration of Helsinki), national guidelines (e.g. UK Medical Research Council guidelines) and national law (e.g. National Health Council of Brazil resolutions). A research ethics committee therefore seeks to protect the interests of research subjects by ensuring compliance with ethical guidelines. Many countries (e.g. the US and the UK) have made it a criminal offence to start medical research without ethical approval from the relevant research ethics committee. This, de facto, gives ethics committees the role of a regulatory authority, a position with 'immense power over the research that is carried out' (McGuinness 2008: 695).

The Nuremberg Code (1949)[4] and the World Medical Association's Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects (1964) placed responsibility for safeguarding research participants on the investigator. In 1975, however, the Tokyo revision of the Declaration of Helsinki introduced ethics committee review of research as its second basic principle (Levine 1995: 2312):

> The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol which should be transmitted to a specially appointed independent committee for consideration, comment and guidance (WMA 1975).

[4] The Nuremberg Code of 1949 is a set of principles and rules to be observed when undertaking research with human participants. It was developed after the Nuremberg trials in 1946 and 1947 of Nazi doctors who had committed atrocities against concentration camp internees as part of medical research. It was superseded by the Declaration of Helsinki in 1964 (see Chap. 3).

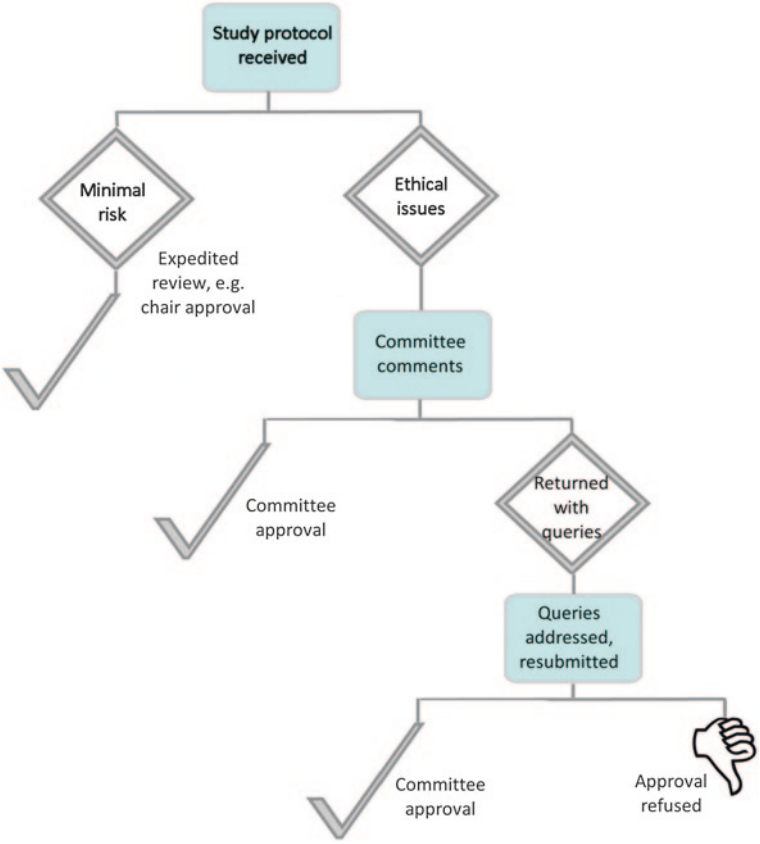

Fig. 8.1 Simplified Ethical Review Process

Since 1975, repeated revisions of the Declaration of Helsinki have specified in increasing detail what is implied by ethics committee review. Principle 15 of the current (2008) declaration reads:

> The research protocol must be submitted for consideration, comment, guidance and approval to a research ethics committee before the study begins. This committee must be independent of the researcher, the sponsor and any other undue influence. It must take into consideration the laws and regulations of the country or countries in which the research is to be performed as well as applicable international norms and standards but these must not be allowed to reduce or eliminate any of the protections for research subjects set forth in this Declaration. The committee must have the right to monitor ongoing studies. The researcher must provide monitoring information to the committee, especially information about any serious adverse events. No change to the protocol may be made without consideration and approval by the committee (WMA 2008).

Until the end of the twentieth century, ethics committee review concentrated on pre-start approval, but nowadays it is increasingly seen as a process that does not stop until the research has been completed. For instance, funding bodies such

as the Economic and Social Research Council in Britain see monitoring as a minimum ethics requirement. The council's Framework for Research Ethics includes the following:

> Procedures for institutional monitoring should be in place. Universities and other research organisations should establish appropriate procedures to monitor the conduct of research which has received ethics approval until it is completed, and to ensure appropriate continuing review where the research design anticipates possible changes over time that may need to be addressed (ESRC 2012: 5).

It would therefore be feasible for ethics review of a research project to continue up to the point at which it may be possible to determine whether vulnerable research participants, especially in developing countries, have benefited from taking part in research. To complement Chap. 7, which recommended expanding the provisions of the CBD to include access and benefit-sharing arrangements for human biological resources, we will ask:

> Could research ethics committees ensure compliance with post-study obligations (a form of benefit sharing), in order to avoid burdening medical research with further governance structures?

Before answering this question, it is worth revisiting and strengthening a claim made earlier (see Chap. 2), namely that the developing world should be treated differently from the developed world when it comes to the governance of human biological resources. The alleged altruism shown by European DNA donors, for instance, cannot be expected of donors from developing countries without perpetuating exploitative relationships.

8.2 Benefit Sharing Versus the Altruism or Solidarity Model

For decades human tissue has been provided voluntarily by individuals for research purposes, in most cases without any expectation of benefit. The case of blood donation in the United Kingdom for blood transfusions and research purposes is a case in point (Keown 1997). This altruism is also apparent among research participants in developing countries. In interviews undertaken with sex worker participants enrolled in long-term HIV/AIDS research in Majengo, Nairobi (see Chap. 5), one respondent said:

> On my faith … they can get a cure from my blood and it can help the whole world. So that is why I gave myself. Even if I am infected…I am ready because I agreed to collaborate in the research.[5]

This respondent donated her blood to help the whole world. However, international ethics guidelines (see Chap. 3) now *require* benefit sharing with research

[5] Interview with Majengo participant in GenBenefit project, April 2007.

participants. To recap, paragraph 14 of the Declaration of Helsinki (WMA 2008) requires as follows:

> The protocol should describe arrangements for post-study access by study subjects to interventions identified as beneficial in the study or access to other appropriate care or benefits.

Hence, every research project which is presented for ethics approval must outline in its protocol how it will deal with post-study obligations. This is particularly important in the case of vulnerable populations, which is why the Declaration of Helsinki (WMA 2008) adds in paragraph 17:

> Medical research involving a disadvantaged or vulnerable population or community is only justified if … there is a reasonable likelihood that this population or community stands to benefit from the results of the research.

The question arises: why should humans not be able to donate their tissue for the good of the world, without requiring burdensome and bureaucratic arrangements for post-study access to benefits? It seems that most people who provide blood or samples for research in the developed world are content to do so purely on the assurance that the tissue supplied will be utilized for the betterment of humankind. Why then should individuals from the developing world expect any more from the same transaction? No work is involved in producing DNA, nor do donors incur significant risks in donating samples. One could say that we need to draw upon the altruism of humankind to ensure the provision of resources that are so important for health research (Berg and Chadwick 2001: 320).

Altruism, which in its broadest sense means promoting the interests of another (Scott and Seglow 2007: 1), is an interesting concept. Under scrutiny it reveals complex questions about morality. For example, to donate one's blood or organs with the proviso that they can *only* be given to those of one's own race would be altruistic, but morally questionable. A UK government investigation found it 'abhorrent' that a hospital had accepted an organ donation on condition that it benefited a white patient (BBC 2000). Hence, acts of altruism might not always be as morally pure as they appear at first sight.

The eighteenth-century political economist Adam Smith maintained that egoism or self-interest would lead to general welfare, stating that it was not 'from the benevolence of the butcher, the brewer or the baker that we expect our dinner, but from their regard to their own interest' (Smith 1976: 26f). On the other hand, French philosopher Auguste Comte, who coined the term 'altruism' in the early nineteenth century, believed that promoting other people's interests meant that morality triumphed over egoism (Scott and Seglow 2007: 15). Immanuel Kant provided useful guidance on the motives behind altruism. He distinguished beneficence (*Wohltun*), which is understood as doing good, from benevolence (*Wohlwollen*), which is understood as wishing well. Beneficence is then benevolence in action; acting in accordance with a 'maxim of making others' happiness one's end' (Kant 1996: 452). While this might appear noble in essence, the motive Kant provided for beneficence is actually close to self-interest. He claimed that one would not want to live in a world where those in need were not supported or

assisted, simply because one might require similar assistance from others in the future.

This scenario of individuals mutually acknowledging their human needs and subsequent duties has been called the duty of mutual aid (Herman 1993). In this context, reciprocity and expectations are important. Such reciprocity protects the altruist, even though it might provide a less than perfectly noble motive for her good deeds. Reciprocal altruism is performed in the hope of obtaining a future reward, for instance in the form of assistance, and is therefore something of a hybrid between altruism and self-interest.

Reciprocity was examined by Marcel Mauss in his classic 1950 anthropological study *The Gift* (2002). Mauss examined gift-giving in ancient times and in more recent Roman, Jewish, Germanic and other Indo-European societies. The seemingly ubiquitous practice of gift-giving existed separately from commercial transactions in all these societies. He defined a gift as 'a voluntary, unrequited surrender of resources' (Mauss 2002: 3). The apparent generosity of the gifting practices seemed to indicate very high levels of solidarity, charity and trust. However, Mauss famously concluded that in all such societies there were no free gifts. The giving of gifts engaged the giver and the receiver alike in finely woven, if implicit, obligations and commitments that reflected and resonated with the institutions of the day. Morality did not seem to enter the transaction, and the society's (unwritten) norms and expectations framed what was required in certain circumstances. Mauss established that the entire notion of a free gift was based upon a misunderstanding of the nature of such a transaction, and concluded that a gift that expected no return, that did nothing to enhance solidarity, was a contradiction in terms (Mauss 2002: xii). His work encourages us to consider that material items, whether sold or given, always retain something of the identity of the giver, and often require reciprocation in some form.

The work of Richard Titmuss added significantly to the understanding of altruism. In his book *The Gift Relationship* (1997) he attempted to counter policies that promoted the commodification of human blood. His primary aim was to advocate voluntary blood donation, which allowed people the moral choice to give blood as a 'symbolic gift of life to an unnamed stranger' (Titmuss 1997: 140). What might be regarded as particularly altruistic was that the gift of blood was to unknown individuals. Hence, it was not given to those in close relationships to whom, in Mauss's societies, one might turn in times of need. The only reward for the donors was the knowledge that they had contributed to the public good.

One of Titmuss's most powerful arguments was that the opportunity to behave altruistically was an essential human right. He believed that specific instruments of public policy were able to harness and encourage that crucial element of altruism in opposition to the 'possessive egoism of the marketplace' (Titmuss 1997: 59). His plea was that people should be enabled to choose to give to unnamed strangers, and not be 'constrained by the market' (Titmuss 1997: 310). However, whether the donation of blood is a true gift that expects no return, or instead creative altruism that fosters a sense of belonging to a community of assistance, is difficult to establish (Scott and Seglow 2007: 111).

Titmuss's plea has been echoed in more recent appeals for altruistic donation (or solidarity) in the context of genetic research. Kåre Berg and Ruth Chadwick talk about a 'duty to facilitate research progress and to provide knowledge that could be crucial to the health of others' (Berg and Chadwick 2001: 320). Solidarity and equity are suggested as frameworks or paradigms in which the emphasis is on the duty of individuals and communities to participate in health research for the benefit of others. This approach might, however, contradict the post-study obligations outlined in paragraphs 14 and 17 of the Declaration of Helsinki (WMA 2008), as quoted above, given that these require benefit sharing.

Berg and Chadwick give two main reasons for preferring a solidarity framework over benefit sharing. First as noted above, no work is required to produce DNA or blood:

> The populations, families and individuals, whose samples have formed the basis for new products and revenue, have not themselves done anything to make their samples 'valuable'… If anything, their samples have become valuable because of work conducted by scientists (Berg and Chadwick 2001: 320).

Second, 'the emphasis on distribution of benefits might be seen not as an exercise in … justice, but as an attempt to buy people off' (Berg and Chadwick 2001: 321). The implication of 'buying people off' is that providing specific benefits to donors would entail the risk of unduly influencing individuals to participate in research. Such undue inducement is prohibited by almost all ethics guidelines, as is the commodification of the body (i.e. the possibility of obtaining money in return for body parts or bodily tissue).

It is difficult to see how the first point could be justified morally. At first it appears as if it might be based on John Locke's widely accepted labour-desert theory. He argued in the seventeenth century that ownership can be achieved if one mixes one's labour with otherwise unowned objects. In the *Second Treatise on Civil Government* he writes: 'As much land as a man tills, plants, improves, cultivates, and can use the product of, so much is his property' (Locke 1690: Chapter V, 'Of Property', section 32). For instance, if one looked after raspberry bushes on unowned land, one might be able to declare ownership of the bushes after a period of time. But the basis for Locke's theory is his belief that we all own our individual bodies. Hence, the labour of geneticists is not mixed with *unowned* objects. Besides, if the samples were not valuable in themselves, there would be no interest in obtaining them. Assuming that value is only added later is reminiscent of debates prior to the adoption of the CBD. Vandana Shiva (2005: 15) wrote in this context:

> [It is assumed] that prior to prospecting, the resources of desire were unknown, unused and without value. Using terminology derived from earlier 'prospecting' for minerals and fossil fuels, 'bioprospecting' obscures the fact that living resources are not non-renewable and are not without value prior to exploitation by global commercial interests for global markets.

Hence, to assume that value is only created through doing something with a resource, as scientists might, risks falling back into pre-CBD exploitative practices in relation to accessing the resources of developing countries. With the adoption of

the CBD, it has been legally accepted that natural resources in developing countries are not unowned, only to become valuable with added (Western) labour. The fact that nobody has 'made' their own DNA is not therefore in itself an objection to benefit sharing.

The objection to benefit sharing which arises from prohibitions against undue inducement and commodification of the body is more serious. At the same time, it must be understood that benefit sharing does not mean handing over cash for DNA samples, which could be regarded as straightforward commodification. The CBD's Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization (see Chap. 2) lists considerably fewer monetary than non-monetary benefits. The latter include collaboration in scientific research, collaboration in education and training, institutional capacity-building, access to scientific information, contributions to the local economy, research directed towards priority needs, such as health and food security, livelihood security benefits and social recognition.

This brings us to an important point that helps us explain why research participants in the developing world should be treated differently from those in developed countries in relation to the governance of human biological resources. DNA donors from Northern countries generally benefit automatically from education and livelihood security benefits. Those contributing to medical research in the North can usually rest assured of (see Chap. 2):

- Access to ever-increasing numbers of medical interventions to achieve and maintain health, which are tailored to local health needs and (in principle) accessible to all
- Increased knowledge about human health, which is made available to citizens through general education or health campaigns.

Hence, the 'altruistic' donor in the North could be regarded as part of a community which offers a fair exchange model to such donors. People experience a tangible form of reciprocity for their participation in the complex social and economic network encompassed by the health care system, reminiscent of a Maussian society, ensuring the fairness of the entire exchange. Assured of far more than the mere cup of tea and biscuit traditionally received by blood donors since Titmuss's time, individuals from affluent countries might appear to be acting out of solidarity with their group, but their ostensible altruism is strongly bolstered by the fact that their contribution is virtually risk-free, and reciprocation is provided through the assurance of fair compensation via the health care system.

It is still the case that others may free-ride (type 1 exploitation, see Chap. 2) on the willingness of research participants to donate their time or even take risks. In this regard, Berg and Chadwick (2001) are right to appeal for more solidarity within communities. But it would be highly exploitative to demand such solidarity from donors who are outside the fair exchange model and who contribute their DNA without receiving *any* benefit in return. Participants from an impoverished developing country are assured of none of the above benefits, and the use of their donated genetic material for the benefit of affluent, distant strangers deserves

critical attention, which returns us to the question: could research ethics committees ensure compliance with post-study obligations (a form of benefit sharing), in order to avoid burdening medical research with further governance structures?

As African bioethicist Godfrey Tangwa notes:

> In medical research the principle of justice demands fairness in the treatment of individuals and communities and the equitable distribution of the burdens and benefits of research. This has important implications for such issues as … post-study benefits, and long term access or distribution of the benefits of the study. These are the issues, which preoccupy every research ethics committee sitting to review a health research protocol in Africa today (Tangwa 2009: S5).

When assessing the question of how justice might be secured within current regulatory frameworks, it is essential to distinguish between two types of benefit-sharing arrangements which have different compliance challenges associated with them. First, we shall consider obstacles to enforcing post-study obligations which aim to provide a successfully tested health care intervention to research participants after the study has been concluded. We term this duty 'post-study access'. Second, we shall analyse obstacles to enforcing the provision of benefits not directly linked to the study, such as access to health care, support for the local health infrastructure or health information campaigns. These will be referred to as 'other benefits'. We shall discuss first the challenges that apply to both benefit-sharing types, and then those that apply exclusively to either type.

8.3 Post-study Access and Other Benefits

The following challenges to implementing a benefit-sharing framework of post-study obligations apply both to giving research participants access to successfully tested interventions and to the provision of 'other benefits'.

8.3.1 Whose Duty?

The Declaration of Helsinki does not specify whose obligation it is to discharge post-study obligations. Is it the duty of individual researchers? After all, they are the interface between sample donors on the one hand and research studies on the other. They are also the ones with the most to gain, aside from research participants. Unlike physicians, whose prime duty is the promotion and safeguarding of patient health, researchers have potentially competing obligations to their sponsors, as well as aspirations to achieve scientific progress.

While the Declaration of Helsinki clearly stipulates that '[i]n medical research involving human subjects, the well-being of the individual research subject must take precedence over all other interests' (WMA 2008: paragraph 6), such 'other interests' cannot be ignored altogether. What is, however, identical in the two relationships – that

between doctor and patient and that between researcher and research participant – is that trust plays a major role and the relationship is often highly personal.

The breaking off of a relationship between researcher and research participant can be very difficult, even traumatic. If, as is frequently the case in the developing world, participation in a research study is the only way to access health care, then the end of a study implies the end of health care. In particular, researchers working with AIDS patients often find it difficult to withdraw in the knowledge that those patients are likely to die from a treatable disease (Shapiro and Benatar 2005: 45). Needless to say, the sense of abandonment for the research participant is even stronger, especially when the study provided the only access to health care. In the worst cases, the end of the research results in death.

It is in this context that post-study obligations to research participants are advocated. Focus group research conducted among patients, clinical researchers and research administrators in Kenya showed that all stakeholders believed strongly that researchers had a long-term obligation to participants. 'The rationale behind this belief – whether fear of death, inability to continue therapy, or an ethical obligation – warrants attention' (Shaffer et al. 2006: 55). Focusing on the ethical obligations, one would argue that research participants, having contributed to the advancement of knowledge, deserve some benefit in return. This aligns with the argument for non-exploitation as advocated throughout this book.

Importantly, though, a number of participants in the focus groups noted specifically that the loss of access to health care would result in a general loss of trust between research participants and researchers, potentially making the community unwilling to participate in research at all (NBAC 2001: 59). Both sides consider it unacceptable to abandon, at the end of a study, research participants who are in dire need of medical attention.

In terms of who has how much invested in the relationship, it might therefore make sense to allocate post-study obligations to researchers. However, these could also be among the duties of research funders and sponsors, who, one would assume, are best placed to find the resources to discharge such obligations.

One of the few countries with binding national law on post-study obligations is Brazil (see Chap. 3). In 1997, a resolution by that country's National Health Council set the following stipulation:

> Access to the medicine being tested must be assured by the sponsor or by the institution, researcher, or promoter, if there is no sponsor, in the event its superiority to the conventional treatment is proven (National Health Council 1997: article IV.1(m)).

The Declaration of Helsinki lacks a similarly clear assignment of duties to a specified group. One might argue that this allows the flexibility needed in guidelines that must apply all over the world. In practice, however, this flexibility is partly responsible for the ineffectiveness of the guideline and the concomitant lack of good practice examples for post-study obligations. If the commitment to benefit sharing re-emphasized in the 2008 Declaration of Helsinki is to be effective, then research ethics committees need to know whose duty it is to provide access to successfully tested interventions or 'other benefits' in order to ensure compliance.

8.3.2 Insufficient Capacity for Review

Concerns about workload and personnel resources are factors that detract from the effectiveness of research ethics committees even in affluent settings (Schuppli and Fraser 2007). It is therefore not surprising that ethics committees in developing countries often lack the resources to give adequate attention to ethical review. A study published in 2009 that examined the effectiveness and training needs of African research ethics committees concluded that the 'major constraints identified are shortage of resources and inadequate training of the ERC [ethical review committee] members' (Nyika et al. 2009: 193). The study also summarized the constraints hindering the adequate review of study protocols in African settings. Table 8.1 lists the constraints in order of perceived gravity: that is, the first constraint is the one noted by the highest number of respondents.

Other studies have also shown that 'the capacity to conduct ethical review in developing countries needs to be developed or enhanced' (Hyder et al. 2004). Evidently, insufficient resources, lack of expertise and so on can render the protection of human research participants unreliable or even non-existent. Under these circumstances, it is unlikely that research ethics committees in developing countries would be in a position to enforce the requirement of benefit sharing. In order to carry out this task, they would need investment in both infrastructure and training. As the next subsection will show, this issue is particularly problematic when research ethics committees in the country of the research funder or sponsor are likely to ignore the obligation. Encouragingly, though, a funding stream from the European and Developing Countries Clinical Trials Partnership is successfully funding the establishment of new ethics committees in Africa and capacity-building for existing committees.[6]

Table 8.1 Constraints on African Research Ethics Committees

Insufficient resources
Expertise on ethical review lacking
Pressure from researchers
Lack of active or consistent participation by members
Lack of recognition of importance of committee functions
Lack of support from institute concerned
Insufficient independence
Pressure from sponsors
Unequal treatment of applicants in review

Source Nyika et al. (2009) (modified)

[6] See the partnership's website at http://www.edctp.org.

8.3.3 US Withdrawal from Post-study Obligations

The previous chapter suggested that an expansion of the provisions of the CBD to include human biological resources would close an important gap in the international legal framework. It would establish an *inclusive* approach to biodiversity, both human and non-human, bring legal clarity to a contentious area and, most importantly, provide a way forward when a spectrum of genetic resources are used by various industries (e.g. when a product is developed using plant and human genetic resources).

As noted in the beginning of this chapter, the US is virtually the only country that is not a party to the CBD. At the same time, the US is the leading innovation economy in the world. For instance, the *2011 World Intellectual Property Indicators* showed that 24% of all patents world-wide were granted by the US Patent and Trademark Office (WIPO 2011). In 2008, however, the US government effectively opted out of the Declaration of Helsinki when the US Food and Drug Administration discontinued its reliance on the declaration and issued independent Guidelines for Good Clinical Practice. The new guidelines omit the two standard benefit-sharing principles of the Declaration of Helsinki, namely post-study access to successfully tested interventions and the requirement that research, particularly in developing countries, must benefit local communities and be responsive to local health needs (Kimmelman et al. 2009). This means that US government requirements for the treatment of research participants are now in direct conflict with the prescriptions of the Declaration of Helsinki (aside from the fact that the US is not a party to the CBD).

This development could mean that US research ethics committees (or institutional review boards) will in general put less pressure on researchers to describe compliance with post-study obligations in study protocols than their international counterparts that fully subscribe to the Declaration of Helsinki. While this is a serious concern, resource provider states are not entirely powerless in relation to compliance where they rely on ethics review. US researchers, like any others, require local ethics review in order to access human genetic resources. Such local ethics review (for instance in Kenya, Thailand or Bolivia) can, if well informed and decisive enough, provide approval only on condition that benefits to research participants and local communities are explicitly articulated. This strategy presents a distinct advantage over CBD expansion. In fact, strong ethics committees or national legislation in developing countries (see for instance Brazil's benefit-sharing legislation as outlined in Chap. 3) can enforce benefit-sharing compliance *now*, without additional legal frameworks.

8.3.4 Timeliness of Research

A related advantage of utilizing ethics review to achieve benefit-sharing compliance is that the procedure needs to be undertaken by researchers in any case. For instance, informed consent documentation and risk-benefit ratios will always be checked by an ethics review committee whether or not benefit sharing is *also* regulated through independent mechanisms. Adding benefit-sharing information to that

already required in the protocol in terms of the Declaration of Helsinki puts only a limited extra burden on the existing approval process.

Assuming that benefit-sharing requirements for human research participants were to be regulated through the CBD framework, another approval process would have to be added. According to Laird and Wynberg (2008), '[t]he negotiation of consent and benefit sharing agreements between those who access and those who provide non-human genetic resources takes on average 1–2 years and sometimes longer' This would be a significant additional burden with considerable impact on the timeliness of research. Especially in health research, such delays can be highly detrimental to global public health and individual patients.

8.4 Post-study Access

The constraints we have listed so far concern enforcing the provision of post-study access to successfully tested interventions and 'other benefits'. However, some challenges are limited to ensuring post-study access.

8.4.1 Unrealistic Timeframe for Post-study Access

By the time a post-study obligation becomes relevant, some of the researchers involved are likely to have left the study site and even the country. In 'helicopter research' (flying in and out of locations, for instance in a current epidemic), researchers leave as soon as the data is obtained. Many research units have long-standing collaborations with host countries, but some do not, leaving research ethics committees with no recourse to researchers after the completion of their study. In any case, it takes on average a decade to bring a drug to market (Trade and Industry Select Committee 2002). To be required to return to participants a decade after the study to see whether they are in need of the developed intervention is rather unrealistic and cumbersome to say the least. More importantly, for the purposes of this chapter, it would be highly unrealistic to expect research ethics committees to ensure compliance ten years after a project's completion.

8.4.2 Inbuilt Unfairness in Post-study Access: The Research Participant

Research ethics committees aim to protect *all* human research participants from exploitation, not just some.

Failure rates in drug development are extremely high. Of those developments that make it into clinical trials, 38% fail Phase I (safety), 60% of the remainder fail

Phase II (basic efficacy), 40% of the rest fail Phase III (comprehensive efficacy) and 23% of those still in the running will not be approved by the relevant health agency (Lowe 2004). As a result, the chances for any individual participant that the particular research she or he was involved in will actually lead to a marketable product are very slim, particularly for donors of biological materials in the early phases of research, and participants in Phase I and II drug trials.

Even if post-study access could be assured a decade after a study's completion, it would only benefit those research participants lucky enough to have been part of bench-to-bed research which overcame all hurdles smoothly. But since those whose participation shows that a product is unsafe or not efficacious contribute as much to medical research as their luckier counterparts, one cannot argue that only the latter are entitled to benefit sharing – and there is no way to predict which participants will fall into which category. By the time a research ethics committee can establish which participants will not have an option of post-study access, it is likely to be too late to ensure any other benefits either. The committees are therefore restricted in their ability to provide equitable protection for *all* research participants.

A related problem is that of involvement in basic research, which is not likely to lead directly to any new medical interventions. In this case, however, research ethics committees could opt for the choice of 'other benefits' from the start.

8.4.3 Inbuilt Unfairness in Post-study Access and Possible Side Effects

It has been argued that imposing post-study obligations on researchers or their sponsors could mean that developing country research focused on local health needs would not be undertaken due to prohibitive costs (Brody 2002: 2857; McMillan and Conlon 2004: 206). One could respond with Solomon Benatar that '[r]equiring greater sensitivity to the plight of the poor and some degree of solidarity with them is not an excessive moral requirement' (Shapiro and Benatar 2005: 42).

However, this could mean that attempts to achieve compliance with the benefit-sharing regulations of the Declaration of Helsinki in order to achieve justice for resource providers in line with the CBD might be self-defeating. Currently, the demand to provide post-study access to successfully tested interventions applies equally to researchers who are using charitable funds to develop drugs for neglected diseases that only exist in, say, South East Asia, and pharmaceutical companies running clinical trials in developing countries for diseases that are prevalent and widespread in the North. However, the former is arguably not a case of exploitation, whereas the latter could be. Benefit sharing is intended to be an instrument to mitigate such exploitation. Yet if the mechanism is so coarse that it makes valuable (and arguably non-exploitative) research prohibitively costly, then enforcing benefit sharing through ethics review could undermine global efforts to realise access to locally tailored health care. In this case, the global injustice in

terms of access to health care could deepen rather than lessen, and concentrating on smaller details could cause the bigger picture to be overlooked.

Based on the three challenges to post-study access discussed above, one could venture that 'other benefits' may be a more promising and consistent benefit-sharing tool for research ethics committees to require.

8.5 Other Benefits

In practice, when benefit sharing is addressed through ethics review, 'other benefits' are generally thought to be a more realistic arrangement than post-study access. The most common example of this type of benefit sharing is access to health care during a study, as was and is the case for the Majengo sex workers (see Chap. 5). However, there are two problems here.

First, the latest (2008) Declaration of Helsinki may inadvertently have restricted the use of 'other benefits' as a benefit-sharing mechanism. The 2004 declaration required study protocols to include information on post-trial access or 'other benefits', and imposed no restrictions on what might constitute 'other benefits'. It did not exclude, for example, health care during or after a study. By contrast, paragraph 33 of the 2008 declaration states:

> *At the conclusion of the study*, patients … are entitled … to share any benefits that result from it, for example, access to interventions identified as beneficial in the study or to other appropriate care or benefits' (WMA 2008: paragraph 33) (our emphasis).

This formulation aligns with the general usage of terms, as one usually speaks of *post*-study obligations. However, it means that comprehensive health care delivered *during* a study, even a longitudinal study, is no longer included under 'other benefits' as a benefit-sharing mechanism.[7] Yet many of the Nairobi sex workers interviewed in the course of our research indicated that access to health care was an important benefit they received in return for donating samples (see Box 8.1).

Box 8.1 Comments from sex workers in Majengo on the provision of free health care[8]

- I don't pay for the medicine, I don't do anything with respect to them, but they give me medicine. When I get some little ailment, they help me.
- I came and joined the clinic and I have been helped a lot. I used to have

[7] Of course, one could argue that comprehensive health care during a study offers too little in terms of benefit sharing. However, where comprehensive health care is offered to study participants and their families, sometimes for decades, as is the case with some Nairobi sex workers, the fair exchange model available to donors from affluent countries is being approximated.

[8] Interviews with Majengo research participants, GenBenefit, April 2007.

bad headaches, you know when your immunity goes down you get other ailments and they are worse than normal … but once you know your status you can come and be treated quickly before it gets worse… So I'm grateful to this clinic, it has done us a lot of good.

- Yes, treatment. I get it for free; if they want to carry out some research and they need blood they give us bus fare because the appointed day may come to take your blood or urine sample and you may not be able because you don't have bus fare.
- I expected treatment, free of charge. Every time I fall sick I come for treatment and it's free.
- They just passed by telling people on the streets, and I learned there is a clinic for helping people to detect diseases and in return they use your blood for research. We agreed that it is OK.
- You see, they usually check us down there to see how we are getting on; you could be developing something. So you get to know about it early enough and save yourself. That for me is a benefit.
- No, I did not expect money or such things, just treatment.
- They give us free medicine because of the nature of our work. If you have a problem they help you.
- Because that is what I need. That is what is important, they give me what I would otherwise not be able to get [treatment].
- I was told I would get benefits of [testing for and treatment of] communicable diseases. If I am found with them, I would be treated, there is a doctor here, and there is medicine…
- Yes, I am satisfied because when I come here I get a cheerful doctor who I can confide in without fear and tell her about my pains, and when I have problems there is a counsellor I can go and talk to and [s]he counsels me until I am satisfied… I like this clinic because since we realized the benefits of the clinic, we try to bring many people so that they too can benefit. And the benefits I get from this clinic have also helped me in doing my work. I can protect myself against infections according to how we are advised at the clinic and I also teach others so that they can protect themselves too.
- We have a very nice doctor, sisters, they all welcome us in the clinic.
- For me I see that the benefits I would expect is treatment because whatever kind of sickness I get I am treated. So this clinic has a lot of benefits.
- I don't think there should be any other kind of benefits … we are given free medicine, free treatment.
- I think it's forever, because there are some women I have heard saying they have been here since 1986. So it can go on forever, that is so long as you are going to sponsor it [Interviewer: So you will be getting these free services forever?] Yes, hopefully! God willing. [Laughter].
- I don't know what I will do if they close down.

If the emphasis in the Declaration of Helsinki is on *post*-sharing of benefits, some of the challenges of securing post-study access (for example, the unrealistic timeframe) would now also apply to 'other benefits'. In other words, if only those benefits delivered *after* a study is completed count towards benefit sharing, seeking compliance through an ethics review committee could become difficult, as the committee usually ceases its monitoring work once the research is complete.

Second, offering access to health care as a benefit to participants could violate undue inducement prohibitions, a topic we have considered before (see Chaps. 2 and 5). When undertaking research on economically disadvantaged or otherwise vulnerable populations possibly suffering from hunger or malnutrition, and lacking access even to elementary health care, any prospect of health care (for example, a general check-up as part of being enlisted in a study) can be regarded as an undue inducement. It is no surprise that UNESCO's Universal Declaration on Bioethics and Human Rights includes two requirements of benefit sharing: first, that '[b]enefits resulting from any scientific research and its applications should be shared with society as a whole and within the international community, in particular with developing countries', but, secondly, that those '[b]enefits should not constitute improper inducements to participate in research' (UNESCO 2005: article 15).

Some international guidelines, such as the International Ethical Guidelines for Biomedical Research Involving Human Subjects issued by the Council for International Organizations of Medical Science (CIOMS), accept that research participants may receive free medical services. However, CIOMS also notes that these services should not be 'so extensive as to induce prospective subjects to consent to participate in the research against their better judgment' (CIOMS 2002: guideline 7). And research has shown – unsurprisingly – that the need to access medical services can amount to pressure to join research studies in developing countries. One cannot reliably determine how many participants actually take part 'against their better judgement', but it is clear that many feel they effectively have no choice. As one of the Majengo research participants said, 'I don't know what I will do if they close down.'

When 347 Ugandan parents with children enrolled in a malaria study were asked whether they had felt coerced to join, more than half said they had 'felt pressure to enrol their children because of the child's sickness' (Pace and Emanuel 2005). As Annas and Grodin (1998) have formulated it,

> in the absence of health care, virtually any offer of medical assistance (even in the guise of research) will be accepted as 'better than nothing' and research will almost inevitably be confused with treatment.

Ironically, strict prohibitions against undue inducement lead to a rather paradoxical result. The poorer a community is, the smaller the benefits that can be offered without potentially exercising undue influence on the decision to participate. The conflict here occurs because participants are meant to be protected against undue inducement on the one hand and exploitation on the other. Yet limiting benefit-sharing possibilities gives research sponsors who outsource research to developing countries a convenient 'ethical' argument for limiting the benefits to

study participants (Ballantyne 2008: 190). As long as this paradox remains unresolved, ethics committees will not be in a position to decide definitively whether the 'other benefits' in a given case constitute benefit sharing or an undue inducement. This makes it extremely difficult for committees to play their governance role successfully.

The authors of this chapter are continuing their research on the potential tension between benefit sharing for human genetic resources and undue inducement. They are already satisfied, however, that it is possible to provide benefit sharing while avoiding undue inducement. The commodification of the body can indeed open up further opportunities for exploitation, especially in developing countries. An example would be paid surrogate pregnancy, when Indian mothers, for instance, carry babies for affluent mothers in the North (Taneja 2008). But such commodification can be avoided by prohibiting one-to-one financial gain from a research transaction. If individual donors for DNA were given no cash except for legitimate expenses, the risk of undue inducement would be much reduced.

What, then, might legitimate benefit sharing that avoids undue inducement look like? Here it is important to look at two of the main reasons for legislating against undue inducement (see Chap. 2): namely, that research participants might accept a risk (usually to their health) that would not otherwise be acceptable, and that they would then participate in research against their better judgement.

It has already been noted that the donation of human genetic resources carries minimal risk and imposes a minimal burden.[9] Hence, the foundation of the undue inducement principle does not apply to access to genetic resources in the same way as it applies to enrolling in Phase I clinical trials. If risk reduction can only be achieved by restricting benefits to research participants (as, for instance, in burdensome, risky trials involving healthy volunteers), minimal risk studies can concentrate more on benefit sharing than misplaced concerns about undue inducement. Access to health care for research participants and their local communities is therefore the ideal benefit to be shared with the donors of human biological resources. Through such benefit sharing, they would come one step closer to the fair exchange model that exists between medical researchers in the North and their research participants. Global research without borders would then contribute to global justice without borders when it comes to access to health care. At least *some* additional access to health care, *some* new health care facilities and *some* health care training and education could be achieved this way.

At the same time, it is essential to note that benefit sharing cannot resolve deep-seated issues of distributive injustice or human rights issues that render national governments unable to respect, protect, and fulfil the human right to access to health care. For this reason, we shall present in Chap. 9 an example of a reform plan that provides a way forward for increasing the availability of life-saving medicines for the poor, with the potential to close the health care gap between developing and developed countries.

[9] Some exceptions, as outlined in Chap. 2, would have to be dealt with separately, for instance where blood might have sacred meaning.

8.6 Conclusion

Can compliance with benefit-sharing obligations as outlined in the Declaration of Helsinki be achieved through ethical review? As we have seen, the obstacles are manifold. In particular, post-study access does not seem to be a promising scenario, given the unrealistic timeframes and the potential for injustice. 'Other benefits' are a more realistic option, in particular the provision of comprehensive health care during long-term studies. In order to strengthen the capacity of ethics review to ensure benefit sharing, we submit the following recommendations:

- Research ethics committees and other parties need to know whose duty it is to discharge post-study obligations. This could be specified in the Declaration of Helsinki. Specification in national law (as in Brazil) is another possibility. Solutions should be integrated with local health systems in developing countries so that research sponsors and local authorities understand their specific roles in providing health care to populations.
- Effective research ethics committees require adequate resources, training and time to fulfil their important roles. As studies have shown, this cannot be taken for granted in developing countries. There is already a pressing need to facilitate

> innovative ways of offering training and education in research ethics. As well as supporting and enhancing current training programmes it will be essential to build up a cadre of trainers located in developing scountries, as well as establishing a process of mentoring for local ethics committees (Bhutta 2004).

- In addition, further ways of providing financial support to ethics committees in developing countries need to be found.
- Applying post-study obligations to all types of research without further refinement would be unlikely to achieve broad acceptance of the duties entailed and may even lead to new injustices, in particular if valuable publicly funded research tailored to Type III diseases[10] were abandoned in developing countries. Such research could attract exemptions or waivers from post-study obligations, as they already comply with fairness requirements.
- The tension between benefit sharing and undue inducement needs to be resolved for developing countries. The ideal solution would be the global success of the fair exchange model between the health care industry, human research participants and national governments: human research participants show solidarity with others (Knoppers 2000; Berg and Chadwick 2001) by taking part in medical research and are rewarded, like their fellow citizens, with the fruits of medical progress, generated through industry and partly funded through national governments. In such circumstances, concerns about undue inducements would be restricted to substantial monetary rewards and other excessive remunerations.
- However, as long as this ideal solution remains no more than an aspiration, ways must be found to avoid the exploitation of research participants in

[10] Type III diseases are those that occur exclusively or overwhelmingly in poor countries.

developing countries. One such way is to promote access to health care, as well as health care training and education, as a standard and legitimate means of sharing benefits for research involving minimal risk. To substantiate this recommendation, one could argue that CIOMS supports it indirectly.

> When research interventions or procedures that do not hold out the prospect of direct benefit present more than minimal risk, all parties involved in the research – sponsors, investigators and ethical review committees – in both funding and host countries should be careful to avoid undue material inducement (CIOMS 2002: guideline 7, commentary).

- In other words, concerns about undue inducement – which essentially aim to avoid a situation where participants take risks with their health, against their better judgement, in order to qualify for a benefit – are much less problematic when a research intervention poses only minimal risk (for example, sample donation). In such cases, the provision of health care (however extensive and for however long) should not count as an undue inducement. On the contrary, it should count as desirable benefit sharing.
- Overall, it is important not to lose sight of the bigger picture when discussing benefit sharing. Research sponsors and funders are, after all, not the main duty bearers for providing health care to those who cannot afford it. It is essential to support and strengthen the capacity of national governments to discharge their duties with regard to the right to health. Such support efforts should go far beyond the monitoring of post-study obligations through research ethics committees and concentrate on other factors, for instance the fact that – with reference to the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) and free trade agreements (FTAs) – 'TRIPS and FTAs have had an adverse impact on prices and availability of medicines, making it difficult for countries to comply with their obligations to respect, protect, and fulfil the right to health' (Grover 2009: paragraph 94). The next chapter will introduce a reform plan which aims to contribute a part-solution to this problem.
- Last, but not least, Martin Luther King's country of birth, the United States, should be put under pressure for opting out of the benefit-sharing frameworks of the CBD and the Declaration of Helsinki.

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Chapter 9
Beyond Benefit Sharing: Steps Towards Realizing the Human Right to Health

Aidan Hollis, Thomas Pogge and Doris Schroeder

Abstract Benefit sharing provides an answer to a very specific problem; namely the exploitative use of Southern resources in Northern research and development. Its emergence in the context of the export of plants, animals and micro-organisms for commercial use in more affluent countries emphasises concerns regarding justice in exchange; those who contribute a resource, often in the context of medical research, need to receive something in return. This is a narrow view of justice, which does not address wider issues. All human beings have a right to the enjoyment of the highest attainable standard of physical and mental health; in short, a right to health. This *universal* right is not promoted through the targeted returns of benefit sharing. The lives that may be saved because research participants obtain access to health care through benefit sharing does not even begin to tackle broader injustice issues, as for example, those related to the international intellectual property rights (IPR) system. This chapter introduces a reform plan to modernise and humanize the IPR system: the Health Impact Fund. Whilst a single reform plan cannot deliver on the ambitious goal of providing health care to all globally, it is important to remember that the demand for benefit sharing emerged in the context of extreme global disparities in wealth. In an ideal scenario, where the human right to health was fully realised, benefit sharing might even be safely replaced with the altruism model of research participation.

Keywords Human right to health • Benefit sharing • Health Impact Fund • Intellectual property rights • Access to medicines

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9.1 Introduction

Throughout this book we have discussed the concept of benefit sharing: its origin, its development and its application. Particular instances of benefit sharing usually take place in the context of very specific research endeavours. Possible benefit-sharing arrangements with research participants are determined by the provisions of the Convention on Biological Diversity (CBD 1992) or the Declaration of Helsinki's post-study obligations (WMA 2008).

Providing health care is a feasible benefit-sharing mechanism for highly vulnerable populations involved in minimal-risk research (see Chap. 8), as in the case of the Majengo sex workers, who can access life-saving medicines in return for contributing to medical research.

However, while much may be hoped for from medical research (e.g. a vaccine against HIV), benefit sharing is no more than a tool to guard against the specific exploitation of the small number of participants who contribute to that research (see Chap. 5); it can never provide a strategy to address urgent global health needs or resolve deep-seated problems of global distributive justice (see also Schroeder and Pogge 2009). To address those issues, much more ambitious and visionary plans need to be promoted.

'Faced with what is right, to leave it undone shows a lack of courage.' These words are attributed to Chinese thinker and philosopher Confucius (551–479 BC) Yet knowing that a state of affairs is wrong does not make the best way forward obvious. For instance, there is broad agreement that the premature, avoidable death of children is a catastrophe.[1] In Sub-Saharan Africa, one in every eight children dies before the age of five, often due to avoidable causes such as pneumonia, malaria, diarrhoeal diseases or birth complications. By comparison, in industrialized countries one in 167 children dies before turning five.[2] Likewise, the death of 10 million people each year because they do not have access to existing life-saving drugs is entirely unacceptable and one of the ethical challenges of the twenty-first century (Grover 2009). But how can these problems best be addressed?

The right to health[3] was incorporated into international law in 1948 when the governments of the world came together and asserted in the Universal Declaration of Human Rights that each and every human being

> has the right to a standard of living adequate for the health and well-being of himself and of his family, including food, clothing, housing and *medical care* and necessary social services, and the right to security in the event of unemployment, sickness, disability, widowhood, old age or other lack of livelihood in circumstances beyond his control [emphasis added] (UN 1948: article 25(1)).

[1] For a philosophical discussion of obligations towards the poor, see Pogge (2008).

[2] http://www.childinfo.org/mortality.html

[3] This chapter uses 'the human right to health' to mean 'the right of everyone to the enjoyment of the highest attainable standard of physical and mental health' (ICESCR 1966: article 12).

Yet, more than 60 years later, millions of people, including children, still die because they do not have access to health care. The Universal Declaration of Human Rights itself is non-binding on states, which means, one would imagine, that it would take *binding* human rights legislation to make a genuine impact. However, such international legislation already exists, and was adopted several decades ago. In 1966, the social security and welfare rights quoted above from the Universal Declaration of Human Rights were affirmed by article 12 of the *binding* International Covenant on Economic, Social and Cultural Rights, which requires that the

> States Parties to the present Covenant recognize the right of everyone to the enjoyment of the highest attainable standard of physical and mental health (ICESCR 1966).

Thus, the covenant commits states parties to strive for the highest attainable standard of health for citizens within their borders – and state obligations do not stop at the border. In article 2, the covenant affirms the responsibility of each state party

> to take steps, individually and through international assistance and co-operation, especially economic and technical, to the maximum of its available resources, with a view to achieving progressively the full realization of the rights recognized in the present Covenant (ICESCR 1966: article 2).

This covenant has been broadly adopted since 1966,[4] in addition to other treaties and agreements. Table 9.1 summarizes the main international legal instruments governing the human right to health.

While avoidable deaths of children have declined by around 35% in the past 20 years, 21,000 children under five still die every day.[5] Enshrining a human right in law is clearly not enough; the right to health has not been realized in recent decades – at least, not for everyone. Canadian research has confirmed that the ratification of human rights treaties 'is not a good indicator of the realization of the right to health' (Palmer et al. 2009: 1,987):

> Data for health (including HIV prevalence, and maternal, infant, and child [<5 years] mortalities) and social indicators (child labour, human development index, sex gap, and corruption index), gathered from 170 countries, showed no consistent associations between ratification of human-rights treaties and health or social outcomes (Palmer et al. 2009: 1,987).

If, then, leaving undone what is right indicates a lack of courage, what might Confucius expect us to do in these circumstances? To remain inactive about the avoidable deaths of millions of people every year is clearly not an acceptable option. But no single reform or tool can resolve problems of such magnitude as the lack of access to health care worldwide. As the preamble to the Universal Declaration of Human Rights states,

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[4] Only two major states are not parties to the covenant; the United States of America (see also their non-ratification of benefit sharing frameworks, Chap. 8) and South Africa. http://treaties.un.org/Pages/ViewDetails.aspx?src=TREATY&mtdsg_no=IV-3&chapter=4&lang=en.

[5] http://www.childinfo.org/mortality.html

Table 9.1 Legal Instruments on the Right to Health

Government obligations: domestic	Government obligations: international
Universal Declaration of Human Rights, article 25(1)	Declaration of Alma-Ata, article II
International Covenant on Economic, Social and Cultural Rights, article 12	UN Committee on Economic, Social and Cultural Rights E/C.12/2000/4, General Comment No.14
Convention on the Elimination of All Forms of Discrimination against Women, article 12	Millennium Development Goals 4, 5 and 6
Convention on the Rights of the Child, article 24(1–3)	Convention on the Rights of the Child, article 24(4)

> every individual and every organ of society, keeping this Declaration constantly in mind, shall strive by teaching and education to promote respect for these rights and freedoms and by progressive measures, national and international, to secure their universal and effective recognition and observance (UN 1948).

States are the primary duty bearers for respecting, promoting and fulfilling the human right to health, but it is also important for every individual and organ of society to strive towards improvements (Schroeder 2011). One key measure is the commitment to universal health insurance that includes necessary medicines (WHO 2012a). However, universal health insurance does not solve the problem of ensuring either the availability of or access to health care: there needs to be a commitment to adequate financing of the insurance and health systems.[6]

Also, insurance can create a special problem in the realm of innovative pharmaceuticals. If all patients are insured, and there is adequate financing of the system, then any supplier with a monopoly will have an incentive to increase prices. Therefore insurance can aggravate the exercise of market power. At the same time, where there is no universal insurance, monopolist providers may have incentives to price high in order to maximize their profits from a small number of wealthy patients, leaving poorer patients without any access to the drug at all. In either situation, it is clear that there is a need for an appropriate mechanism for ensuring wide access to the drug, while also providing revenues adequate to support innovation for the future.

In the remainder of this chapter, we shall discuss one specific reform plan, the Health Impact Fund (HIF), as an example of a visionary idea which would help fulfil the human right to health globally by addressing these complex problems of supporting innovation, availability, and access to new medicines.

[6] Insurance may be universal with respect to the population, but cover a very limited range of services.

9.2 Intellectual Property Rights and Global Public Health

According to the World Health Assembly,

> current incentive systems fail to generate enough research and development, in either the public or private sectors, to address the needs of developing countries (WHO 2012b: 24).

By 'incentive systems', the World Health Assembly means mechanisms to finance research and development into health care products and health care services. The main incentive system today is the international system of intellectual property rights (IPR) and, in particular, patents.

9.2.1 Incentive Systems: International Intellectual Property Rights

Intellectual property rights give innovators private property rights over creations of the mind. While property rights over land and tangible goods such as houses and farm animals have been part of human practice for a long time, intellectual property rights are a relatively recent phenomenon dating back only as far as the nineteenth century. One of the earliest protected drugs, for instance, was aspirin, first sold in 1899 (Dutfield 2009: 13).

Today, in all fields of innovation, from books to practical applications such as cutlery trays in dishwashers or cancer treatments, intellectual property rights are protected by national and international legislation. What this means in practice is that the originator of an idea applies for state protection through, for instance, a patent. Once obtained, the patent allows its holder to stop others from using the idea for a specified time, unless they pay a mutually agreed licence fee. Table 9.2 describes standard types of intellectual property as protected through national and international legislation.

Some products require considerable investment in research and development but are then easily copied by others who did not contribute to the development costs (e.g. medicines). There is an understanding that such innovations can only be made cost-effective when developers have the chance to recoup their investment costs during a monopoly interval (typically 20 years). As economists phrase it:

> The economic purpose of patents is … to bar entry of copy products for the term of the patent, to provide the innovator firm with an opportunity to price above the marginal cost and thereby recoup R&D [research and development] expense, in order to preserve incentives for future R&D (Danzon and Towse 2003: 185).

It is assumed that without such legislation, fewer new drugs would be produced, fewer cinematic films made and fewer inventions brought to market. Property rights to creations of the mind were therefore introduced in order to enable innovators to charge high mark-ups on their products. While this mechanism can facilitate and accelerate the development of science in affluent settings, it has

Table 9.2 Types of Intellectual Property

Type	Description	Example
Trademark	Typically a logo, word or phrase to distinguish one's product from someone else's	Mercedes-Benz three-pointed star
Design	Typically a shape or pattern, which gives one's product its unique appearance	Coca-Cola contour bottle
Copyright	Typically original material in the arts, media or computer programming	Harry Potter books
Patent	Typically a product, substance, method or process which is newly invented and useful	Clinical trials data
Data protection	Data on drug safety and efficacy submitted to regulatory authority	Driverless car
Plant breeder rights	New varieties of plants	New plant variety that is not eligible for a patent
Geographic indication	Protected link between a product and its local territory	Champagne
Trade secrets	Information one does not want to become public knowledge, usually protected through confidentiality agreements	Google's search algorithm
Circuit layout rights	Typically layout for computer chips	Computer chips

not been successful in the context of medical research in developing countries. According to the UN special rapporteur Anand Grover, nearly 30% of the world population do not have access to life-saving medicines:

> Nearly 2 billion people lack access to essential medicines. Improving access to medicines could save 10 million lives a year, 4 million in Africa and South East Asia. The inability of populations to access medicines is partly due to high costs…. TRIPS [Agreement on Trade-Related Aspects of Intellectual Property Rights] and FTAs [free trade agreements] have had an adverse impact on prices and availability of medicines, making it difficult for countries to comply with their obligations to respect, protect, and fulfil the right to health (Grover 2009).

As Grover points out, TRIPS and FTAs[7] are partly responsible for the lack of access to products of medical research in developing countries. TRIPS is an agreement negotiated by members of the World Trade Organization (WTO) which took effect on 1 January 1995 and requires signatories to institute a systematic and predictable system of protection for intellectual property. In essence, it rolls out strong

[7] Free trade agreements are usually bilateral agreements between two countries (often with the United States as one partner), which remove all trade barriers, such as import tariffs, for trading partners. We will concentrate here on intellectual property rights.

patent protection (as previously available in most affluent countries) on a global scale. Developing countries were given until 2000 or 2005 (depending on the country) to bring national legislation in line with WTO demands, with least-developed countries given until 2006 to effect the changes, although the time frame was later extended to 2013. A specific proviso was added for pharmaceutical patents, for which least-developed countries only need to institute full protection by 2016. The WTO took this measure in view of the concern that patents on pharmaceutical products could impede access to life-saving drugs by poor patients in developing countries. While debate over exactly how TRIPS should be implemented continues, there has been further strengthening of intellectual property rights through bilateral trade agreements that include 'TRIPS-plus' provisions (Smith et al. 2009).

The World Health Assembly has criticized current pharmaceutical research and development incentives on two main grounds relating to the needs of developing countries. First, TRIPS enables patentees to price new products out of the reach of the poor, as noted above. Second, diseases that predominantly affect the poor attract insufficient research investment because costs are unlikely to be recouped through sales. In the words of the World Health Organization's Commission on Intellectual Property Rights, Innovation and Public Health:[8]

> For developing countries, where the demand is weak – but not the need – there is little incentive to develop new or modified interventions appropriate to the disease burden and conditions of the country. This economic reality introduces an important gap in the innovation cycle: either no products exist in the first place, or if they do, then there is often disproportionately small effort, globally, to make them more effective and affordable in poorer communities. Broadly speaking, the innovation cycle does not work well, or even at all, for most developing countries (WHO 2012b: 25).

Figure 9.1 illustrates the imbalance between global health needs and pharmaceutical sales. The United States has less than 5% of the world population, but its patients and consumers are responsible for almost 40% of all pharmaceutical sales worldwide. By contrast, Asia, Africa and Oceania (including Australia) combined have about 73% of global population, but represent less than 15% of global pharmaceutical sales.

The imbalance between global health needs and pharmaceutical sales is attributed partly to an overemphasis on intellectual property rights as the main incentives mechanism in scientific research. TRIPS has been heavily criticized by developing country policymakers and thinkers. This is reminiscent of pre-CBD debates about the exploitation of developing country resources. For instance, as Vandana Shiva summarises,

> nature's diversity and the diversity of knowledge systems are undergoing a major process of destabilization with the expansion of patents and IPRs into the domain of biodiversity via the Trade-Related Aspects of Intellectual Property Rights (TRIPs) agreement of the World Trade Organization. The whole notion of TRIPs has been shaped by the objectives and interests of trade and transnational corporations. Through the instrument of TRIPs, transnational corporations have posed a potential threat to the biological and intellectual

[8] The commission was established in 2003 and later superseded by the Expert Working Group on Research and Development.

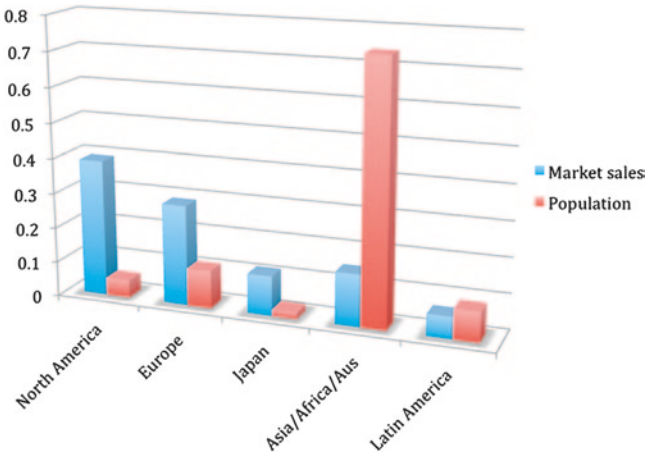

Fig. 9.1 Pharmaceutical Sales and Population Shares by region, 2010. *Sources* UN (2012), IMS Health (2011)

> heritage of our diverse communities by appropriating and privatizing their knowledge. For these commercial interests, biodiversity itself has no value; it is merely a raw material for the production of commodities and for the maximization of profits (Shiva 2007: 309).

While non-human biological resources are now protected through the CBD, such protection is still lacking for human biological resources. In this regard, TRIPS is criticized both as a tool for the exploitation of developing country resources and as a hindrance to realizing the universal human right to health. One visionary way of reforming this system in order to make life-saving medical products available to all is the Health Impact Fund Reform Plan.

9.3 The Health Impact Fund Reform Plan

Proponents of a Health Impact Fund (HIF) seek to complement the international intellectual property rights system by adding an alternative reward mechanism. Instead of recouping research and development costs through high monopoly prices, patentees would price their health products and services at the lowest feasible cost of manufacture and distribution, and be rewarded from the HIF according to the health impact of those products and services around the world. The HIF would be a second, optional reward system offering payments to patentees of new drugs which are sold globally at cost. It would be designed to offer payments based on the therapeutic impact of the drugs or vaccines, thus giving innovators efficient incentives to develop drugs that maximize health gains (Banerjee et al. 2010).

The basic idea behind the HIF is simple. The primary responsibility of pharmaceutical innovators is to develop medicines which save lives, reduce suffering and

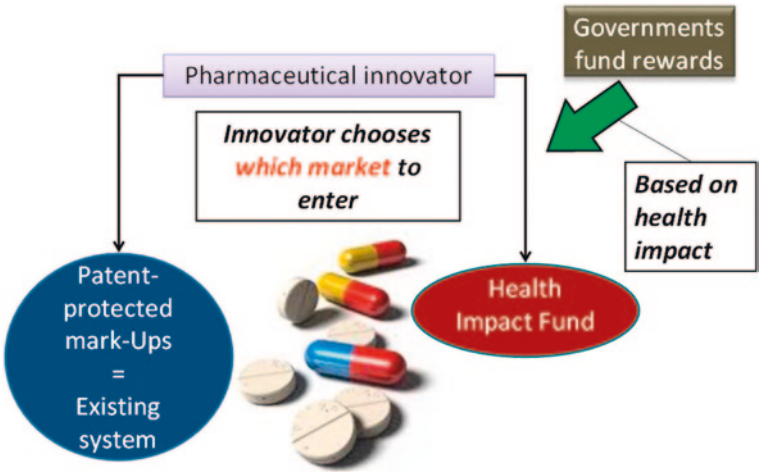

Fig. 9.2 The Health Impact Fund

improve public health (Hunt 2009: paragraph 35). Pharmaceutical companies respond to incentives. Current incentives for innovators – above all, patents – do not align fully with their primary task. Pharmaceutical research is currently concentrated on diseases and ailments of the rich; considerable funds are spent on marketing and litigation (see below) and only a limited match is achieved between research and the *global* disease burden. The HIF, by linking rewards for innovation to an effect on the global disease burden, would aim for a better match. Only innovators who make a positive impact on the global disease burden could be rewarded through this alternative system. Figure 9.2 illustrates the HIF reform plan.

The HIF would be funded by governments and make annual payments to pharmaceutical innovators who sell their patent-protected product at a price equal to the lowest feasible cost of production and distribution.[9] The basis on which rewards would be paid would be the measured health impact of the product. Such impact could be measured in terms of 'quality-adjusted life years' (QALYs), a standardized measure for assessing health interventions.[10] Thus the health impact of a drug could, for example, be approximated as the number of units sold multiplied by the estimated incremental QALY benefit per unit. With this basic idea, the HIF seeks to remove or ameliorate the problems of the current international intellectual property rights system set out in Table 9.3.

[9] The price could be set in various ways. If, for example, manufacture of the product was allocated by tender, the innovator (or owner of the rights to the product) could then sell the product on at the price paid for its production, without any mark-up. Alternatively, and depending on the degree of competition in production, the HIF might determine the price by estimating the cost of production (see Hollis 2009).

[10] Other measures are possible. For example, Michael Selgelid (2008) suggests that the DALY (disability-adjusted life year) approach might be preferable for the purposes of the HIF in that it quantifies relief from the burden of disease.

Table 9.3 Health Impact Fund Interventions in Relation to Intellectual Property Rights System

Problem of IPR System	HIF Intervention
Detrimental effects on the health of the poor	
The current incentives system for pharmaceutical research neglects the interests of the global poor in two ways. First, new products are priced beyond the reach of the poor. Second, research neglects diseases concentrated among poor populations because sales to this group are unlikely to be high enough to cover the research and development costs	The chief strengths of the HIF are that it would make all registered products accessible to poor patients from the beginning, and create an incentive to develop new medicines with large measurable health impacts, especially in areas where patent incentives are weak
A bias towards maintenance drugs	
Under the current system, it is more profitable for a pharmaceutical innovator to develop symptom-relieving maintenance drugs rather than cures or, especially, vaccines (which yield the least profit relative to their health impact)	The HIF would provide an unbiased incentive system, rewarding all products at a consistent rate according to their health impact
Paying lawyers rather than innovators	
Effective patent protection relies on the costly expertise of lawyers at all stages of the process, from negotiating a patent to litigating in its defence. In addition, lawyers' expertise is required when defending a firm against other companies' claims of patent infringement. Litigation costs per defended patent are on average £0.2–1 million in the UK and £1–2 million in the USA (Greenhalgh and Rogers 2007: 561)	One of the attractive features of the HIF is reduced patent litigation expenses so that innovators' profits can be re-invested or returned to shareholders
Excessive marketing	
Given the high mark-ups to be achieved in pharmaceutical markets, innovators find it worth their while to spend considerable funds on marketing, which includes influencing health practitioners to prefer one out of a class of essentially equivalent products. This drains funds away from research on current and future health needs	In the same way as the HIF would reduce litigation costs, it would also reduce marketing costs. Persuading physicians to prescribe one product rather than another would be profitable only if that product brought superior therapeutic outcomes, since the reward is based on the incremental benefit compared to pre-existing therapies

(continued)

Table 9.3 (continued)

Problem of IPR System	HIF Intervention
Counterfeiting and its consequences	
The large profit margins that can be achieved on pharmaceutical products encourage the illegal manufacture and sale of counterfeit medicines that lead not only to complications for patients, but in the medium term also to drug-resistant strains of diseases	Since counterfeiting is a criminal activity in most jurisdictions, the risk is worth taking only if a high mark-up on production costs can be earned. HIF-supported products would be sold without mark-up and therefore unlikely to attract counterfeiters
The 'last mile' problem	
Pharmaceutical companies have poor incentives to promote the optimum use of their medicines and to ensure that their drugs reach those, and only those, who need them. In terms of company profits, the interest of the company stops when the medicine has been sold over the pharmacy's counter[11]	Pharmaceutical innovators would have incentives to contribute their expertise and inventiveness toward resolving any local health infrastructure problems that might impede the health impact of their products

[11] The 'last mile' problem is about getting drugs to patients in settings with inadequate health infrastructures. It is particularly troubling in the poorest countries, where medical resources are stretched very thin and it may be difficult or impossible for patients to obtain accurate diagnoses or treatment in hospital. Rural populations are often very poorly served by health care personnel. Compounding this set of problems, pharmacies may not exist or may not stock needed drugs.

How can some of the practical difficulties in the way of implementing the HIF be overcome? It has been estimated that the HIF would require annual committed funding of at least $6 billion, and this amount would have to be guaranteed many years into the future in order to provide innovators with certainty of income. This minimum level is necessary to avoid excessive volatility in the reward rate and to realize economies of scale in health impact assessment. The HIF would also require an administrative structure to ensure that registered products are sold at or below cost and to calculate their rewardable health impact.

Like the exploitation of monopoly rights under the current intellectual property rights system, the HIF would enable payouts over a period of years. For example, a new pharmaceutical product might earn annual payments from the HIF for its first ten years of use. An extended payment period is important since it smoothes the payment stream and gives innovators an incentive to promote their products to ensure that they are widely used by those who can benefit.

The WHO expert group commented on the HIF as follows:

> We considered that the ideas underpinning the HIF were of interest and that, if successfully implemented, it would address many of our criteria. The proposal addresses directly intellectual property management issues in that it seeks to incentivize R&D relevant to the disease burden in developing countries, while also facilitating access to these products by making them more affordable. However, we considered that in practice implementation of the HIF would be problematic on a number of grounds – particularly uncertainties about whether a sufficiently reliable measurement of health impact could be achieved in the circumstances prevailing in developing countries (WHO 2012b: 55).

For the HIF to become a reality, the plan needs to be examined, refined and presented in more detail. Most importantly, the health impact metric has to be worked out and tested in several country pilot studies. It has been stated that ‘access to medicines has become the test above all others by which the rich world will be judged in its dealings with the poor’ (Horton 2002). The HIF is one example of a fair and cost-effective way of stimulating research and development of life-saving medicines and making them accessible to all.[12]

9.4 Conclusion

> When it is obvious that the goals cannot be reached, don’t adjust the goals, adjust the action steps (Confucius).

Realizing the human right to health globally seems to be such a goal – one that is aspirational, even utopian, but not realistically achievable just yet. However, if one bears in mind the advice of Confucius, one can focus on the steps towards the goal.

Benefit sharing with the donors of human biological samples is indeed a very limited and indirect contribution to realizing the human right to health, but it is an

[12] For more information on the HIF, see http://www.healthimpactfund.org.

important step towards eliminating exploitation in scientific research, which has been rightly criticized by developing countries for decades. It is a step which demonstrates – like the global (apart from the US) adoption of the CBD – a willingness to negotiate international agreements based on considerations of justice. Yet a lot more needs to be done, in particular improving the current system of providing incentives to pharmaceutical research, which, as the World Medical Association and the World Health Organization have noted, fails to deliver on the health needs of developing countries.

In this chapter, we have introduced one possible reform of the international intellectual property rights system: the Health Impact Fund. Clearly, a single reform plan on its own cannot achieve the ambitious goal of providing health care to all, globally. However, it is important to examine such broad, ambitious reform plans in the context of discussions on benefit sharing because, in an ideal situation, the full realization of the human right to health could make benefit sharing redundant. As is currently the case in affluent countries, patients and healthy volunteers could promote scientific progress by donating their samples freely in return for a functioning health care system that gives everyone access to medicines, health care personnel and education. To impose post-study obligations in such circumstances would unnecessarily burden the research enterprise in a setting where the fruits of science are available to all.

On the other hand, it is important to remember, while considering reform plans, that this ideal scenario is currently no more than a distant aspiration, and that benefit sharing is, at least for now, here to stay as an essential mechanism that helps avoid the most blatant exploitation in scientific research in developing countries.

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Chapter 10
Towards Best Practice for Benefit Sharing Involving Access to Human Biological Resources: Conclusions and Recommendations

Doris Schroeder and Julie Cook Lucas

Abstract Scientific advancement without benefit sharing is unjust. Those who believe that every human being has a right to share in the fruits of science will apply this claim universally. While we fully support the universal human right to benefit from scientific research, there is an urgent need to deal with the potential exploitation of resource providers and research participants. Therefore, in this book we have taken a narrower position: those who *contribute* to the advancement of science need to receive a *benefit in return*. This chapter gives our conclusions and recommendations.

Keywords Benefit sharing • Human Genetic Resources • Justice • Developing Countries • Traditional Knowledge

10.1 Introduction

Scientific advancement without benefit sharing is unjust. Those who believe that every human being has a right to share in the fruits of science will apply this claim universally.[1] While we fully support the universal human right to benefit from scientific research, there is an urgent need to deal with the potential exploitation of

[1] Article 27(1) of the Universal Declaration of Human Rights (UN 1948) reads: 'Everyone has the right freely to participate in the cultural life of the community, to enjoy the arts and to share in scientific advancement and its benefits.'

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resource providers and research participants. Therefore, in this book we have taken a narrower position: those who *contribute* to the advancement of science need to receive a *benefit in return*.

Access and benefit sharing in relation to plants, animals, micro-organisms and associated traditional knowledge is governed by the Convention on Biological Diversity (CBD 1992). In October 2010, the 193 parties to the CBD agreed the Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization to the Convention on Biological Diversity (CBD 2010). While it is by no means a foregone conclusion that the benefit-sharing spirit of the CBD can be realized through the Nagoya Protocol, it is still a landmark agreement as it operationalizes equity demands. The third objective of the CBD, 'the fair and equitable sharing of the benefits arising out of the utilization of genetic resources' (CBD 1992: article 1), has at last been given an international framework committing parties to its realization, thereby promising greater legal clarity for both users and providers of biological resources. It is now up to the 193 parties to implement the Nagoya Protocol coherently within national law.

Equal legal clarity does not exist for the donors (providers) of human biological materials, which are not covered by the CBD or any other binding legal instruments. In this book, we have looked at this legal vacuum and discussed many of the unresolved issues facing policymakers and researchers. The concluding chapter draws together our recommendations.

Box 10.1 Definitions

Vulnerability
To be vulnerable means to face a significant probability of incurring an identifiable harm, while substantially lacking the ability or means to protect oneself.

Exploitation
Wrongful exploitation is a failure to benefit others as some norm of fairness requires (Mayer 2007: 142).

Benefit Sharing as Justice in Exchange
Research participants who will derive few or no benefits from the results of scientific research should nonetheless receive fair benefits for their contributions. Benefit sharing thus requires the sharing of advantages derived from the use of resources with the resource providers in order to achieve justice in exchange. Such an exchange should focus particularly on the clear provision of benefits to vulnerable populations who may lack reasonable access to the resulting products and services. At the same time, the exchange should not entail unethical inducements.

10.2 Benefit Sharing as a Tool

The main focus of this book is justice, especially justice for resource providers. Justice is an ethical principle apparent in most cultures and throughout history. But benefit sharing has no such prominence: it is a relatively new ethical concept going back no further than the late 20th century, and is not comparable to justice in scope or nature. Justice is an ideal, a desideratum that we strive for, and benefit sharing is simply a principle used as a tool to achieve that ideal. To be considered just, the users of resources have to return some benefits to resource providers. That, in a nutshell, is benefit sharing. In an ideal world, we would all freely exchange resources to everybody's benefit. That this is not possible today is due to the extreme disparities in wealth and life chances that characterize any comparison between Northern and Southern countries – disparities that are, in turn, partly due to the related history of colonialism. In this global economic and political context of prior exploitation and continuing disparities, benefit sharing is being mooted as one way to achieve justice for the providers of resources.

The problem with trying out tools is that it can take a long time to refine them to such a degree that they achieve their purpose. On an optimistic reading, this is what is now happening with CBD-type benefit sharing. More than two decades after the adoption of the CBD, few examples of successful benefit-sharing yet exist. We have discussed several benefit sharing cases in this book, none of which were unproblematic (see Chap. 4). One can hope, though, that the legal clarity provided by the Nagoya Protocol will pave the way for future successes.

The benefit-sharing tool most relevant to the donors of human biological resources (as well as other research participants, such as those taking part in clinical trials) is the principle of post-study obligations. The Declaration of Helsinki is the most influential of all the international research ethics guidelines and has included a reference to such obligations since 2000. Providing post-study access to successfully developed interventions (or making alternative benefits available to research participants) is what benefit sharing requires.

However, a tool is only useful if the user knows how to handle it. Judging from the dearth of successful examples in either the academic literature or policy debates, the tool of post-study obligations is not useful as it stands. Providing post-study access to successfully tested medicines or interventions for study participants is a logistically complicated, risky measure in the quest for justice. As we have shown (see Chap. 8), a range of arguments can be raised against the usefulness of this tool for human research participants. Frustratingly, several problems were also identified regarding the provision of alternative benefits. Table 10.1 summarizes some of the main challenges identified.

It is clear that the proposed mechanism of benefit sharing for human research participants requires further refinement before it can achieve its purpose, which is to increase equity between partners (the affluent Northern users of resources and the poorer Southern providers of those resources).

Table 10.1 Challenges for Post-Study Obligations

Post-Study Access	Alternative Benefits
The delay between a study and the availability of a successful intervention makes post-study obligations unwieldy	Alternative benefits might violate prohibitions against undue inducement and the commodification of the human body
Those taking the highest risks (clinical trial stage 1) have the lowest likelihood of receiving interventions because of the low success rate in pharmaceutical product development	Alternative benefits require a process of negotiation for the most appropriate benefits. This poses challenges of determining whom to negotiate with and of studies possibly being delayed
The Declaration of Helsinki does not specify whose duty it is to discharge post-study obligations	
The Declaration of Helsinki treats every study alike – whether it is, for example, a publicly funded investigation of tuberculosis or a commercially funded effort to research Alzheimer's disease	
The US Food and Drug Administration's decision in 2008 to opt out of the benefit-sharing requirements of the Declaration of Helsinki and prioritize its own more limited guidelines has had a widespread impact on research governance	
Important research on diseases of the poor might not be undertaken if bureaucratic and financial burdens increase further	
Post-study obligations can be regarded as a reactive attempt to address the most blatant exploitation, when the human right to access to health care should be tackled in a much more systematic manner	

In the context of donated human biological resources, alternative benefits are the more promising benefit-sharing tool. Post-study access to a successfully developed product might make ethical sense, for instance, for HIV-positive patients testing a new antiretroviral drug. However, the donation of biological resources occurs so early in the research process, and may be related to so many different interventions and uncertain future outcomes downstream, that returning benefits in the form of access to successful products may be unachievable, even with the best of intentions. With this tool as the means, too many donors would still receive no benefit at all.

One might argue that the Indonesian case discussed in this book (see Chap. 5) demonstrates that post-study access is precisely what is owed to Southern providers of resources. However, a closer look shows that the problem is more complex.

10.3 Benefit Sharing Versus the Human Right to Health

The Indonesian case (see Chap. 5) shows that while human biological resources can be used in the development of new products (e.g. a vaccine), these products may not be accessible to the local populations that contributed to the research. This was the argument used by the Indonesian government when withholding avian flu samples from World Health Organization (WHO) laboratories.

Indonesian virus samples were going to contribute to the development of a vaccine, yet Indonesians would not be able to afford the resulting product. As it happened, the Indonesian government made reference to the CBD rather than the post-study obligations of the Declaration of Helsinki when justifying their actions. This suggests that expanding the CBD to include human biological resources could be one way forward towards achieving benefit sharing. We shall return to this below.

However, the Indonesian case also shows that arguments about justice get very complicated if one moves from specific justice in exchange between researchers and their research participants or sample donors to generalized questions of distributive justice between North and South. The Indonesian government did not demand access to the avian flu vaccine for individual donors of biological samples, as they were already affected by the disease,[2] but instead insisted on affordable access to the vaccine for the entire population.

This is a perfectly legitimate demand, especially since all human beings have a right to the enjoyment of the highest attainable standard of physical and mental health (ICESCR 1966). But it is not a narrow justice-in-exchange demand, as we have discussed it in this book. All human beings deserve access to health care, but justice in exchange for the donors of biological materials is an additional issue in the context of exploitation. This has an important implication, namely that benefit sharing for individual research participants should not be conflated with efforts to secure the human right to health for all.

Discussions of benefit sharing should never act as window dressing, or distract from broader, more visionary attempts to secure access to health care for all. Benefit sharing is a tool to prevent the exploitation of resource providers, not a tool to realize the human right to health. This book has introduced the proposed Health Impact Fund as an example of a reform plan that aims to improve the availability of and affordable access to life-saving medicines. **It is important that reform plans aimed at improving access to health care for all globally be pursued and supported alongside efforts to secure case-by-case justice for resource providers through benefit sharing**.

10.4 What Benefits?

If benefit sharing for the donors of human biological resources is meant to focus on ‘alternative benefits’, as we have suggested above, what should these alternative benefits look like? What benefits will ensure that the exploitation of donors is avoided? Unsurprisingly, there is no easy answer. The issues are not only about process (e.g. whose voices need to be heard when decisions about benefit sharing are made) but also about substance (e.g. whether royalties from product sales are

[2] The Indonesian case demonstrates that access to successfully tested interventions is a very crude tool for sharing benefits with the donors of biological resources. For the individual donors of avian flu samples in Indonesia, access to the vaccine would have come too late.

a suitable benefit). Answers must also cover a myriad of cases ranging from, say, a Swiss patient who allows a blood sample taken for necessary diagnostic tests *also* to be used for genetic research, to a Kalahari bushman whose one-off mouth swab is used for scholarly research into ancestry tracing, and to large populations of donors who take part over many years in a genetic research programme in which their genetic profile is linked to their health profile.

For all donors whose human right to health is secured through comprehensive, well-funded national health services, we firmly support the solidarity or altruism model in the governance of human biological resources. **Contributing voluntarily to medical research through an act that presents minimum risk and minimum burden when the individual donor and/or the donor's community is likely to benefit from the research outcomes does not warrant additional benefit-sharing arrangements**. Access to ever-expanding collectively funded possibilities to secure physical and mental health is a sufficient return for sample donation. **In affluent settings, we therefore do not recommend 'alternative benefits' for sample donation, apart from feedback on the research project.**

But only a minority of the seven billion people living today are in the fortunate position of having their health care needs met through communally funded systems such as national health services. When those who are less fortunate take part in medical research that is unlikely to benefit them directly, exploitation can occur. It is this exploitation that benefit sharing tries to avoid.

However, **not all research conducted in developing countries and funded by affluent nations is exploitative or warrants benefit sharing.** For instance, a charity may fund genetic research into tuberculosis with the aim of developing cheaper, more effective, shorter-term treatments. If successful, this research could be highly beneficial for a developing country. **As long as any resulting product is marketed within the donors' country at an affordable price, the solidarity or altruism model is applicable, and alternative forms of individual benefit sharing are unnecessary.**

The scenario of locally relevant research funded publicly or through a charity stands in marked contrast to the Indonesian case discussed in Chap. 5. The Indonesian government noted that Indonesian samples were being used to develop a product to benefit, almost exclusively, citizens in affluent nations. When such asymmetry between contribution and benefit occurs, benefit sharing is necessary. But what alternative benefits are appropriate in such cases? We turn to process recommendations below, focusing on gender issues, but we begin with substantive answers.

It is important to distinguish between benefits for research participants and benefits for the host community. Below we refer to one policy option, CBD expansion, which could improve the handling of host community benefits. However, this book has focused on research participants, so let us first look at benefits suitable for them.

One of the cases discussed in this book, that of the Majengo sex workers in Kenya, does offer an example of alternative benefits. The main benefit the sex

workers receive in return for donating a range of biological samples is access to health care for themselves and their immediate families over considerable periods (see Chap. 5). Research into the case has noted the following:

- Longer-term access to comprehensive health care is highly valued by the sex workers, for whom this would otherwise be unobtainable.
- Providing access to health care is a feasible means of benefit sharing, as the benefit is congruent with the setting. Medical researchers are much better equipped to provide health care than to implement other kinds of benefits, such as improved employment or livelihood opportunities.[3]
- Longer-term access to health care approximates the ideal scenario described for affluent nations (altruistic donation in return for the realization of the human right to health), which must remain the aspiration for all. This benefit-sharing measure therefore harmonizes with the broader, urgent pursuit of access to health care for all, while leaving the altruism model of medical research substantially intact.

The Majengo sex workers' project has been going on for decades, and many of the sex workers have contributed to research for a considerable time. A long-term relationship, such as this one, between a research project and a local population increases the feasibility of providing health care as an alternative benefit.

We recommend long-term relationships between research projects and research participants, and we believe that the provision of longer-term access to health care should be the default benefit-sharing option for vulnerable populations in developing countries who donate biological samples and take part in associated health research.[4]

10.5 But What About Undue Inducement?

All major ethics guidelines prohibit undue inducement, and many prohibit any commercialization of the human body. Undue inducements, such as payments, are said to jeopardize the voluntary nature of informed consent and thereby invalidate it. Also, such payments might induce research participants to accept unreasonable risks or burdens against their better judgement. **We categorically do not recommend cash for DNA.**

In the context of guarding against undue inducement for the donation of human biological samples, we are on safe ethical ground when we recommend access to health care as the default benefit-sharing option. There are two mutually reinforcing

[3] In our interviews in Majengo the sex workers told us that help finding alternative employment would be a desirable benefit. However, as one of the doctors explained, medical staff are ill-placed to provide such help.

[4] For instance, the donation of DNA for genotype research could be linked with research into the phenotype (which might require information about lifestyle).

reasons for this. First, the minimal risk and minimal burden involved in donating human biological resources invalidates any risk-related argument against inducements. Second, the prohibition of undue inducement is designed to avert actions that are prejudicial to the donor's health, and providing access to health care in a setting where it is not otherwise available is generally the opposite: it is *conducive* to health. It is only in specific cultural contexts that the promise of health care might give rise to unacceptable risks or burdens, such as in communities for whom blood is sacred[5] or where potential discrimination, privacy or racial stereotyping are concerns (Kowal 2012). **We recommend further research into cases where the promise of health care might induce research participants to violate cultural prohibitions.**

To recap, **concerns about undue inducement are much less problematic when a research intervention poses only minimal risk and minimal burden. In such cases, the provision of health care (however extensive and for however long) should not count as an undue inducement.** On the contrary, it should be seen as desirable benefit sharing.

10.6 Achieving Compliance Instead of Paying Lip Service

Benefit sharing has been accepted as a principle in many ethics guidelines, both national and international (see Chap. 3). This acceptance is linked not only to the international standing of the CBD, but also to the inclusion of benefit sharing in the Declaration of Helsinki (WMA 2008) since 2000 and in UNESCO's Universal Declaration on Bioethics and Human Rights (UNESCO 2005) since 2005. However, the presence of benefit sharing as a principle in ethics guidelines does not automatically lead to its realization. In fact, the dearth of good-practice examples could almost lead one to conclude that the principle is being paid no more than lip service with regard to human research participants, be they clinical trial participants or, in particular, donors of biological resources.

With human biological resources excluded from the scope of the CBD, there is no binding international legislation that covers benefit sharing for human sample donation. The fact that international ethics guidelines such as the Declaration of Helsinki are not legally binding is not in itself an insurmountable obstacle, as such guidelines, if applied generally and consistently in support of prescribed practices, can gain the status of customary international law. For example, the practice of obtaining informed consent before undertaking medical research is widely accepted on the basis of non-binding ethical guidelines.

There is one recent development signifying progress towards securing justice for the donors of human biological samples, and it follows the Indonesian government's

[5] Tensions between Western researchers and the Havasupai Indians were made public in a case brought by the tribe against Arizona State University. One of the reasons given for the claim of exploitation was that blood is sacred among the Havasupai (Harmon 2010).

withholding of avian flu samples. In 2011, the WHO adopted a framework governing virus sharing which ensures that virus sample donors and their communities should receive at least some benefits in return for their contribution to science. The Pandemic Influenza Preparedness (or PIP) Framework (World Health Assembly 2011) aims to protect global public health *and* ensure benefit sharing, and is a first step towards a more just situation in the field of international virus exchange. It is also worth noting that the Nagoya Protocol refers to human pathogens such as influenza viruses and thereby combines questions of access to human and non-human genetic resources. This indicates that **a more inclusive approach to access and benefit sharing for genetic resources may be possible in the medium term**.

10.6.1 Expanding the scope of the CBD

In Chap. 8, a group of influential authors suggest expanding the scope of the CBD to include human biological resources. They give four reasons for this recommendation:

1. In order to foster an inclusive, legally predictable approach to all biological resources, these should come under one umbrella regulation, namely the CBD.
2. There is no legally binding international instrument that covers human biological resources. Instead of developing a new regime, it would be better to extend an already existing regime, using experience and established mechanisms.
3. In the absence of a legal instrument, countries are taking unilateral steps to protect human biological resources, with potentially grave consequences for international collaboration. For instance, the Indian Ministry of Health has issued guidelines restricting the transfer of biological material for collaborative research, and the Chinese Human Genetic Resources Management Office has recently revised China's policy regulating the export and import of human genetic material across Chinese borders. As more countries establish their own national regulations, the difficulties facing global research collaboration involving human genetic resources will increase exponentially.
4. More and more, science is using a mixture of resources to develop innovations. As a result, it becomes increasingly difficult to separate animal, plant and micro-organisms from human biological resources to pursue separate benefit-sharing agendas. The only pragmatic solution is to cover all such resources under one framework.

As noted earlier, the benefit-sharing principle is a tool to achieve justice in a specific context; it is not desirable in and of itself. The CBD was adopted because the use of biological resources was being pursued unsustainably – first come, first served – rather than for the greater benefit of humankind. The CBD was one attempt to stem the tide of Northern exploitation of Southern resources. It may yet be necessary to do the same for human biological resources, and it remains to be seen whether the Nagoya Protocol will yield significant success stories in benefit sharing. Meanwhile, alternative approaches can be developed to benefit sharing for human biological resources. What could such alternative approaches be?

10.6.2 Compliance Through Ethics Committee Review

Since 2000, the Declaration of Helsinki has required benefit sharing with clinical trial participants. In 2004 the declaration extended this requirement to study participants from vulnerable populations, which includes human sample donors. Relevant ethical guidelines thus do exist. A mechanism for achieving compliance exists too, namely research ethics review. Yet, as noted above, very few benefit-sharing success stories, if any, have emerged involving human sample donors. The following recommendations are aimed at making the ethics review process stronger in the area of benefit sharing.

Effective research ethics committees have an important role and require adequate resources, training and time to fulfil it. As studies have shown, these cannot be taken for granted in developing countries. There is already a pressing need to facilitate innovative ways of providing those countries with training and education in research ethics, as well as supporting and enhancing current training programmes. A network of trainers located in developing countries must be built up, and a process established for mentoring local ethics committees. In addition, further ways of providing financial support to ethics committees in developing countries need to be found.

Ethics committees need very specific guidelines, or access to a range of clear case descriptions and success stories, in order to be able to assess whether a study protocol sufficiently protects human research participants against exploitation. More importantly, though, the Declaration of Helsinki is too vague on one particular aspect of this issue: research ethics committees and other parties need to know whose duty it is to discharge post-study obligations. The researcher's? The sponsor's? The funder's?[6] **We recommend that in its next revision, the Declaration of Helsinki specify whose obligation it is to provide post-study access to successfully tested drugs or alternative benefits**.

As noted above, not all research undertaken in developing countries is exploitative. **Applying post-study obligations to all types of research without further refinement would be unlikely to achieve broad acceptance of the duties entailed and may even lead to new injustices**, in particular if it led to the abandonment of valuable publicly funded research tailored to diseases prevalent in developing countries. Such research could perhaps qualify for exemptions or waivers from post-study obligations, if it already complied with fairness requirements, as suggested above.

Research ethics committees may need further guidance on how to assess a study protocol to ensure that the general benefits to a community warrant the waiving of post-study obligations in favour of the solidarity model. Minimum requirements for such waiving are: that local researchers had input into the

[6] The CIOMS International Ethical Guidelines for Biomedical Research Involving Human Subjects (CIOMS 2002) specifically mention sponsors and investigators as duty bearers, with the main emphasis on the sponsors.

research agenda, that the research is tailored to local research needs, and that the resulting product or intervention will be made available at affordable prices in the host country.

10.7 Women and Benefit Sharing

Fair benefit sharing has a process element and a substantive element, as noted above. Our main recommendation – that access to health care is a reasonable benefit in return for the donation of human biological samples – is a substantive recommendation. Suggesting how women should be integrated into decision-making processes would be a procedural recommendation. But first, a clarification is necessary. Benefit-sharing discussions are heavily influenced by policy-makers, practitioners and academics working on CBD-related issues. The CBD, in many instances, requires case-by-case benefit-sharing negotiations between those who access resources and those who provide such access. Usually the resource providers are groups, for example a group of traditional knowledge holders, such as the San of southern Africa in the *Hoodia* case described in Chap. 4.

Traditionally, research governed through the Declaration of Helsinki or similar ethics guidelines had no community negotiation element at all. Autonomous choices, it was assumed, were to be made by each individual (often a patient), who had to decide whether to take part in a research study after informed consent procedures started by another individual (usually a doctor or medical researcher). Negotiations about benefit sharing were not, and are not today, a part of informed consent processes. One could describe these processes as 'take it or leave it' with regard to benefits offered and obtained. This approach has seen some changes in recent years, especially in certain African and South American countries, where, *in addition* to informed consent obtained from an individual, obtaining permission from community leaders has become a more common requirement. Diallo et al. (2005) describe it thus:

> The realization of the need for community consent, or more accurately community permission, for research has occurred relatively recently. Practical experience with it is scarce. … The process [of obtaining community permission] had 6 steps: (1) a study of the community, (2) an introductory meeting with leaders, (3) formal meetings with leaders, (4) personal visits with leaders, (5) meetings with traditional health practitioners, and (6) recognition that obtaining permission is a dynamic process. … Far from competing with the individual informed consent process, the process of obtaining community permission both initiated and facilitated the process of disclosure for individual informed consent.

We support the approach of Diallo et al. to obtaining community permission and would like to concentrate here on the involvement of women. Ensuring that benefit sharing is fair to women requires attention to both the outcome and the process. In a just and fair outcome, women would be allocated their rightful share of benefits and assured of full participation at all levels and in all aspects of the decision-making process. In addition to the policies outlined in Chap. 6 increasing international

attention is being paid to such concerns. For example, the *World Development Report 2012: Gender Equality and Development* identifies four priority areas for policy going forward, one of which is 'shrinking gender differences in voice and agency within society' (World Bank 2011: xiii). The report recommends policies to address the combined influence of social norms and beliefs, women's access to economic opportunities, the legal framework, and women's education and skills, and to increase women's voice in society. We would like to add our voices to these calls.

Chapter 6 examined several cases and showed that women did not participate fully in any of the benefit-sharing arrangements there. **Guidelines and policies for benefit sharing should explicitly require women's meaningful participation in all phases of decision-making**, from the formulation of the research design (as far as possible) to the allocation of benefits, with minimum, appropriate and measurable indicators. The definition of 'meaningful participation' should be contextualized in, but not bound by, cultural, social, political and economic practices and relationships. This is because these practices and relationships could be the very sources of inequality and women's exclusion.

The guidelines and policies should include examples of the kinds of mechanisms that enable women to participate fully and have an effective voice. The full set of principles we would propose is available in Chap. 6, but we reiterate the main ones here:

- Aim for women to have equal membership of bodies that negotiate or make decisions (taking into account that 30%, though recognized as the 'critical mass' at which women's presence begins to have an effect, may, in a smaller group, mean only one or two persons).
- Hold consultations separately for women, and feed the outcome back to the negotiating or decision-making body, in order to ensure that women's views become part of the agenda and of the basis on which decisions are made.

Ultimately, of course, international guidelines and policies can only change reality on the ground if governments and other local stakeholders take them seriously and consistently create the necessary mechanisms through practical, implementable, local processes. International, national and local bodies, as well as researchers and funders, should be accountable for the exclusion and discriminatory treatment of women in benefit sharing, as in other areas of their work. Research ethics committees should look for appropriate provisions in study protocols, and in progress and final reports from researchers.

10.8 Conclusion

This book has traced the story of benefit sharing as it developed in the context of non-human biological resources, now extended into international research ethics arenas.

What is the way forward for benefit sharing? An important task for academics, practitioners and policy-makers who believe in benefit sharing as a means to protect human research participants (clinical trial participants and donors of human

biological samples) from exploitation is **to collect, critically investigate and disseminate accounts of both successful and unsuccessful cases.** Only by building on an evidence-based body of knowledge and practice can we move from theoretical understandings of fair benefit sharing and abstract conceptions of justice to better practice which benefits real people.

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