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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