Chapter 1
Sustainable Development for the Health-Care Industry: Setting the Stage

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Human Society Has Always Been Focused on Health

Health has been a topic of paramount importance and an integral part of fighting for one's subsistence along with an overlapping with the search for food and shelter, and interestingly it has progressively superseded wealth as a topic of interest. Evidence to that is the Google Ngram chart of the number of books addressing health versus wealth as a core topic; one can only notice that since the 1800s, health-focused books have always outnumbered those related to wealth by anywhere between 10 and 20 % up until the 1920s. From the beginning of the twentieth century, the number of books focused on health skyrocketed (with an acceleration since the 1970s) and the lead of health over wealth as a literature topic is now close to five-fold as expressed in total number of books.[1]

[1] https://books.google.com/ngrams/graph?content=health%2C+wealth&year_start=1800&year_end=2000&corpus=15&smoothing=3&share=&direct_url=t1%3B%2Chealth%3B%2Cc0%3B.t1%3B%2Cwealth%3B%2Cc0. Accessed 6 July 2014.

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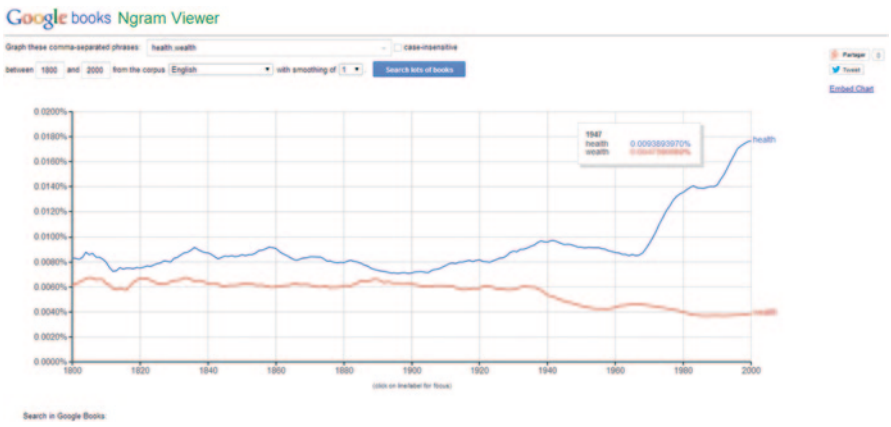


The progressive structuring of human society has led to an organization of more effective care procurement so as to contribute to a healthier society, along with the organization of education and other public services. In this context, the search for medical interventions has progressively evolved from empirical to experimental and scientific, and the life science industry has progressively emerged from the capitalistic efforts to streamline the search for innovative interventions addressing increasingly complex, unmet medical needs.

This evolution has spawned a fully structured industry segment, entirely organized around its capabilities to generate innovation, to protect it with the relevant intellectual property rights, to manufacture its assets in reproducible and high-quality manner, and to commercialize them while complying with a complex set of regulations and guidelines. The industry is nowadays much less driven by its manufacturing capabilities and supply-chain savvy (with the exception of very specific market segments, such as vaccines and some biological products) but rather by its R&D prowess and its superior capabilities to engage with its stakeholders during the latter part of the life cycle of its products, from late stage development to regulatory, then through market access to commercialization.

The Mission of the Health-Care Industry

The health-care industry'ts mission to focus on generating innovative products and solutions, both therapeutic and preventive, for the benefit of the populations around the world, addressing varying types and magnitudes of unmet medical needs, which vary considerably across countries and at times within countries has evolved as pivotal in its strategic roadmap. These geographical differences are not only a source of complexity in the management of the R&D portfolio of the health-care industry and its commercialization policies but also an opportunity to differentiate from competition and to create a form of competitive advantage.

Yet, contrary to the situation in a number of industry segments, the entire value chain of the health-care industry is subject to a large and ever-increasing number of regulations. As an example eloquently described in the guidelines of the Inter-

national Federation of Pharmaceutical Manufacturers Association (IFPMA), the industry should enforce strict principles of ethical conduct, ensure execution of high standards of manufacturing practices and quality assurance, provide contributions to the overall expertise, and foster collaborative relationships and partnerships with the various stakeholders dedicated to the improvement of public health.[2]

The discoveries of the health-care industry have contributed to changing the face of our world, and the impact has been extremely visible from the demographic perspective, along with the access to clean water and better food, the life expectancy in the developed countries has more than doubled in the last century. This substantial impact on demographics has happened simultaneously to a number of other changes contributing to increasing life expectancy, ranging from better sanitation to access to safer food without supply limitations, and to better living conditions as a whole. As a consequence, the population has been aging and the health-care issues that were linked to the previous societal conditions have progressively given way to more chronic conditions related to aging and to a more sedentary lifestyle. The search for solutions to the ailments linked with modern life in mature economies has evolved accordingly and the R&D efforts focusing on conditions such as hypertension, diabetes, depression, and cancer, to cite only a few, have progressively superseded the search for solutions against infectious diseases in the development programs of the health-care industry.

Simultaneously, a number of initiatives driven either by public authorities or NGOs such as patient associations or international organizations have ensured that the ailments afflicting small patient populations or lower-income regions or countries receive sufficient attention and R&D funding. Nowadays, the majority of leading health-care companies has some form of R&D program dedicated to the neglected conditions and/or "diseases of the South."

It is therefore obvious that the health-care industry's mission is aligned with societal ambitions for a healthier and more sustainable world (Mistra Pharma 2009).

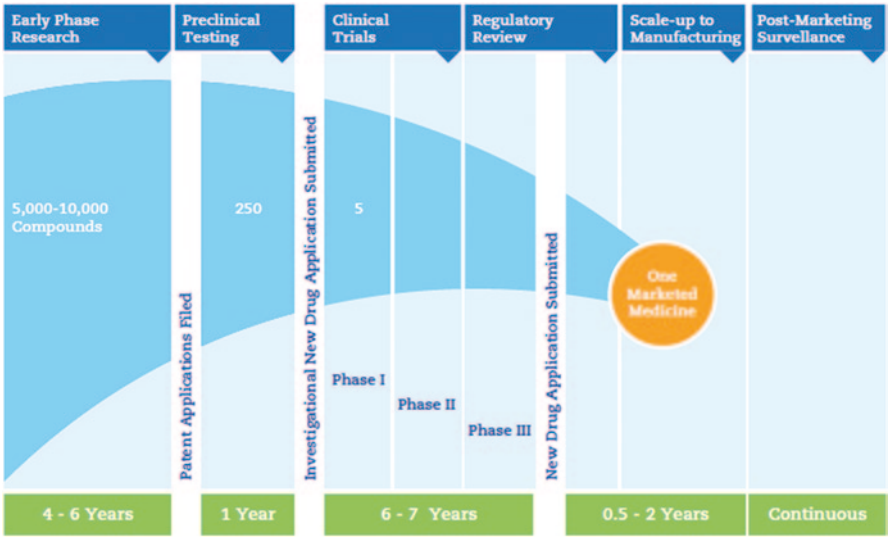
The Life Cycle of Pharmaceutical Products

The health-care industry is working with constrained resources and therefore prioritizing and making R&D choices which are driving the focus of its portfolio. Such arbitrages are not always well understood by the lay public which has sometimes diverging aspirations which it conveys through various media, ranging from the classical tools in democracies, such as voting all the way to the virtual world of social networks. Thus, it is the balance of the perception between these sometimes opposite goals and more specifically the emerging gap between public health objectives and individual expectations, which is increasingly shaping the agenda of the various stakeholders with which the life science industry is interfacing.

[2] http://www.ifpma.org/about-ifpma/welcome.html. Accessed 6 July 2014.

Understanding the arbitrages, often referred to as "portfolio management," which the health-care industry has to perform, one has to consider the main characteristics of the life cycle of pharmaceutical products in terms of duration, attrition, and protection.

The development of innovative medical solutions is a long and expensive process, fraught with a high failure rate, in spite of the large number of companies investing in R&D, from the large pharmaceutical conglomerates to the smaller R&D only, biotechnology companies. The development of a novel compound takes, on an average 10–12 years (and sometimes much more), and for several thousands of compounds that are tested during the early development, only a few hundred reach preclinical stage, a handful make it to clinical development, and a few of them reach commercialization stage. Although the probability of success varies according to the type of novel entity, they remain generally low (see chart).[3]

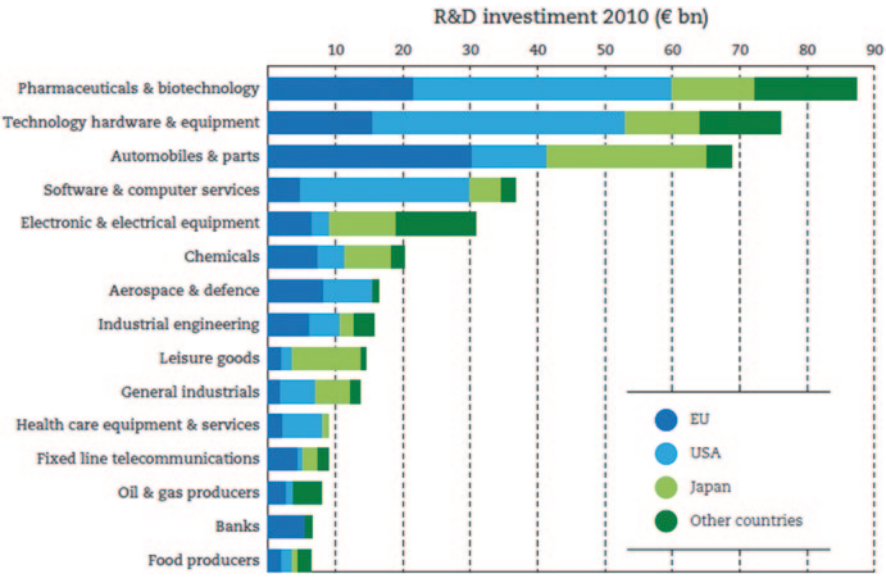


The R&D process of the life science industry has always been marked by high failure rates. From several thousand compounds analyzed during the early phase of exploratory research, a few hundred reach preclinical testing phase, only a handful enter the clinical trials stage, and a small number successfully go through the entire clinical development and regulatory review process. The health-care industry is the largest industry sector in terms of R&D spending (see chart)[4] and yet, its R&D productivity has been declining in recent years despite the so-called biotechnology

[3] IFPMA Facts and Figures 2012.

[4] http://www.ifpma.org/fileadmin/content/Publication/2012/IFPMA_CorpBrochureWEBVERSION.pdf. Accessed 6 July 2014.

bubbles.[5] The IFPMA reported in 2010 that the pharmaceutical and biotechnology industries had R&D investments of more than US$ 85 billion (IFPMA 2012) with US$ 48.5 billion R&D investments reported by PhRMA members (PhRMA 2013).



The decline of R&D productivity, both qualitatively and quantitatively, has been extensively commented and attributed to a combination of factors, such as increasing complexity and number of molecular targets, as fundamental science is now more precise; the evolution of the discovery process from random to target based; the larger knowledge gap between fundamental science (proteins, receptors, etc.) and therapeutic applications (hence, the emergence of "translational medicine" as a science); more complex medical needs that need addressing; harder to understand pathological mechanisms of the diseases; increasing difficulties to translate fundamental research into medical discoveries; rising hurdles to identify responder populations; tightened regulation to assess drug safety and more complex evidence demands from authorities; and as a consequence, an increased complexity and cost of clinical development programs, etc. (Paul et al. 2010). Over the years, the focus of R&D has evolved toward specialty care, capitalizing on the progress made by fundamental research in very selected disease areas, with smaller but much better defined target patient populations. Nowadays, the largest number of R&D projects

[5] http://www.fda.gov/AboutFDA/WhatWeDo/History/ProductRegulation/SummaryofNDAApprovalsReceipts1938tothepresent/default.htm. Accessed 6 July 2014.

is found in the field of oncology, while the cardiovascular segment is getting much less attention and central nervous system diseases even less so.[6]

Further, the industry is adamant to protect its rare assets as tightly and effectively as possible, in order to balance the staggering R&D costs with a commercialization period under some form of exclusivity.

The Mega Trends Which Affect the Health-Care Industry

During the past decades, health-care expenses have increased steadily despite numerous attempts to curb or limit their growth. The health-care spending is currently representing a very large share of the real economy expressed in terms of GDP. In most countries of the Organization for Economic Cooperation and Development (OECD), this share is growing at such a pace and up to such a level that it is challenging the sustainability of the health-care systems (World Economic Forum 2013). With the exception of the USA where health-care expenses represent a staggering 18% of GDP, most developed countries are investing 10% or more of their real economy in health care.[7] In emerging economies, the cost of health care is driving difficult trade-offs: When faced simultaneously with the emergence of diseases which are frequent in mature economies (such as hypertension, diabetes, dyslipidemia, depression, or cancer) while still dealing with remaining diseases typical of the emerging world (diarrheal or respiratory infectious diseases such as cholera, typhoid fever, rotavirus diarrhea, or tuberculosis), the public health decision makers are driven to tough choices to allocate their health-care priorities and resources. In addition, these emerging countries are often facing infrastructure challenges to invest in both the management of the wide scope of medical conditions, and in the construction of a robust, efficient, and accessible primary care infrastructure, including the brick-and-mortar components of hospitals and dispensaries and the human component of properly trained health-care providers.

While the emerging countries are facing these difficult investment choices, the mature economies, which are crippled by their economic debt also face tough trade-offs to drive the mutation of the health-care infrastructure and deal with the public expectation for efficient and personalized care procurement.

In this context, the health-care industry is often considered as one of the key drivers of the progression of the health-care costs, although the share of the total health-care costs represented by medications and devices in the total amount of health-care expenditures is usually comprised between 15 and 20% depending on the countries. The question therefore becomes one of understanding where the actual drivers of the bulk of the health-care expenditures are and what could be done to manage those effectively.

The health-care spending keeps increasing as it is driven by the “cost disease” as described by William J Baumol (2012), as health-care procurement is a very labor-intensive activity.

[6] Scrip Research and Pharmaprojects 2013 Citeline.

[7] http://stats.oecd.org/Index.aspx?DataSetCode=SHA#. Accessed 6 July 2014.

The key tenet of the book is that all services that consume personnel are condemned to see their cost rise at a rate significantly greater than the economy's rate of inflation because the quantity of skilled labor required to produce these services is difficult to reduce. It is especially the case in health care as automation or standardization is not always possible, and also since labor-saving productivity improvements occur at a rate well below the average for the economy (due to the increasing use of skilled labor, from an ever-increasing number of health-care providers, always more skilled and specialized). The authors underscore that the enduring stagnancy of the productivity has imposed a cost history of constant rise to the corresponding services. Every patient has to be examined individually; the patient is subject to specific examinations, possibly by a different health-care provider of different specialties until the diagnosis is firmly established, the course of treatment is decided, and a successful outcome is reached. Therefore, at every step of the patient's journey, there is the intervention of one or more health-care provider whose role, due to the evolution of science and the better understanding of the disease and their treatments, is ever more specialized. These well-trained, high-quality resources are therefore very expensive. The honorarium of health-care staff is subject to increases like salaries without much productivity gains, since by definition a diagnosis is personalized to each patient case. One could argue that automation and productivity gains are happening in other quadrants of health-care procurement chain such as biological or radiological examinations, yet the benefits of such gains are more than offset by the increasing sophistication and number of said examinations.

The authors also point that a simple way to slow down the increase of the costs is to shift some of the labor from the supplier to the consumer. This is already visible in developed countries, e.g., increase in the share of the health-care costs borne by the patients or increasing accountability of the patients in the execution of prevention measures.

They point to the absolute necessity for the high-tech firms to keep investing in the innovation that drives productivity growth. We can observe such initiatives all along the R&D and manufacturing value chain in the health-care industry. They argue that the rising cost of innovation can lead to fiscal strategies "that reduce investment in R&D, thereby further impairing R&D productivity. This in turn can impede overall productivity growth."

They are also arguing against cost controls (even though these are very often the staple of the public health policy in most economies) as such controls lead to the deterioration of the quality of the services and possibly worse to their partial or total disappearance. They are explicitly stating that "crude attempts at budget reductions or price controls in health spending are unlikely to be effective, equitable, or efficient." On the evaluation of health-care interventions (and these include the use of medications, devices, etc.), the authors argue that measuring them in terms of quality-adjusted productivity gains is not appropriate, and that the adequate criteria would be to measure labor-saving or cost-saving enhancements of productivity. In other words, the ability to induce a change in the way care is delivered.

Lastly, regarding global governance and equitable access to care (such as investing in emerging countries), the authors argue that "foreign aid that simply buys

health products and services in developing countries might crowd out local government health spending and distort national priorities," hence calling for a different approach to expanding access to care.

The trend of the share that health-care costs represent in the real economy is worrying for the public authorities because the growth in health spending has always outpaced that of the GDP, especially during economy downturns. What is even more worrying is the absence of correlation between health-care expenses and quality of care[8] and that has drawn the authorities' attention on the efficiency of care procurement. It has also been attracting the lay public's attention on the broad—and not always well-defined—topic of the value for the individual. This lack of correlation between the magnitude of investments and the quality of care procurement is also stretching to the relationship between the health expenditure and the degree of satisfaction that consumers have with their health-care systems.

The absence of a solid correlation between investments in health care and quality of care is triggering a host of activities driven by the authorities across all countries to search for efficiencies, looking for benchmarks from abroad to identify more effective ways to utilize health-care resources. The authorities are also concerned by the poor correlation between health-care spending and patient satisfaction[9], as the topic is politically loaded and oftentimes central to electoral programs. From the patient's perspective, the increasingly ubiquitous availability of information and the behavioral evolution toward challenging both the medical and the public authority are fueling mounting patient-driven challenges.

In addition, the life science industry has to cope with other global macro trends that affect its relationship with its ecosystem and stakeholders.

First, the shift of economic power to emerging markets is driving global economy growth and the rise of other health-care expectations while the developed countries are struggling with debt. Therefore, in both cases, social, political, and economy pressures result in investments in health-care infrastructure and increasing price pressure on medical interventions. The mature economies are looking for more cost-effective ways to utilize their health-care resources without raising public concern over care rationing. The emerging economies have to arbitrate between health-care priorities and invest in infrastructure to ensure the proper level of care coverage, access, and quality. In the first instance, the health-care industry has to find the right balance between innovation and the price it charges for the said innovation so as to generate an economic and social surplus for the health-care system. In the second instance, the industry has to balance its portfolio to ensure its adequacy with the local epidemiology and public health priorities.

Second, the emerging markets will represent the largest share of the growing cohort of health-care consumers, thanks to the swelling of the ranks of the middle class, driven by the economic growth. Simultaneously, these numerous and eager health-care consumers will increasingly live in urban areas; as a consequence, they will have easier access to care procurement as well as to health information, leading to an increase in qualitative and quantitative demand and in the challenge of the medical and public authorities. The flipside of the increase of the urban popu-

[8] Euro Health Consumer Index Report 2009.

[9] Analysis of data from WHO, The Commonwealth Fund, Frontier Centre.

lation will also take the form of a less-active lifestyle and evolution of the dietary regimens, resulting in an increase in incidence of the chronic diseases linked to sedentary behaviors as well as to a greater exposure to poorer air quality, which will trigger a higher incidence of respiratory conditions.

Lastly, whether in developed countries or increasingly in emerging ones, we are looking at shifting demographics with aging populations (also a consequence of the previous trends, better economic status contributing to aging) which will increase health-care demands in relation to the growing incidence of chronic diseases and organ failures linked to ageing.

The health-care industry has always been paying close attention to those trends and they contributed largely to the R&D orientations as well as to the definition of business development and geographical expansion priorities.

Societal Expectations for Personalized Medicine

Besides these economic and demographic trends, one has also to consider the impact of societal evolutions.

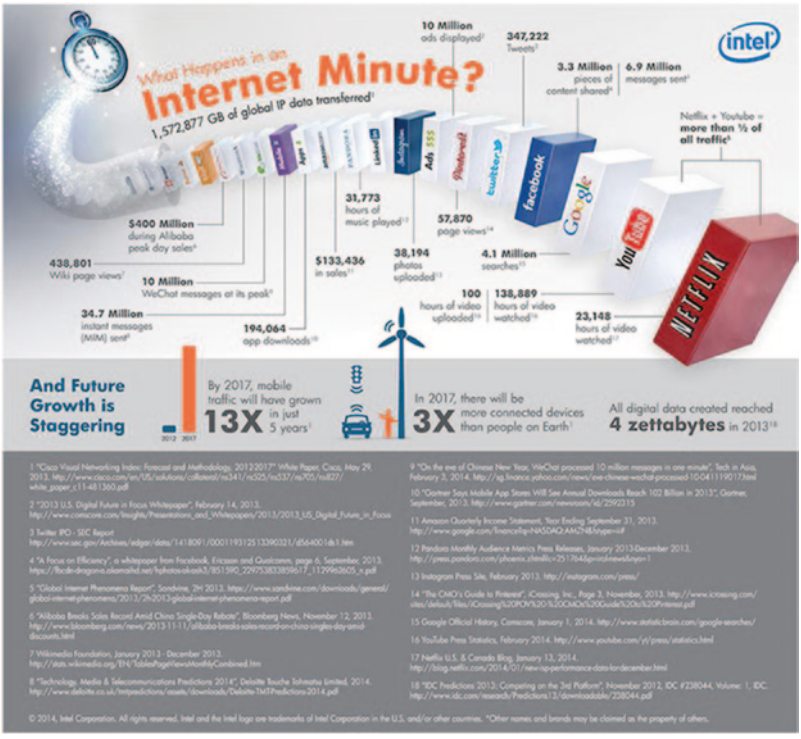
In recent years, the combination of education and access to information and mobility has contributed to the growing sense of self over that of the community. While such a trend can be welcomed from the perspective of consumer goods, as it creates opportunities for market segmentation and creation of value propositions matching more closely to the expectations of the customers, it comes with a number of hard to manage consequences in the field of health care.

For instance, when it comes to immunization, we have been witnessing the progressive evolution of resistance against immunization recommendations. Case in point is the growing number of parents who refuse to immunize their children against infectious diseases because they do not perceive those as a threat while they are worried about potential adverse events—some immediate, but most importantly the deferred, longer term ones—linked to vaccine administration. Vaccines are meant to protect against infectious, transmissible diseases; it is therefore of the utmost importance for the public health authority to ensure an adequate coverage in order to block transmission of said diseases. Typically, coverage of 80 % or more of any population is considered as an adequate threshold to block the transmission of diseases such as influenza. Because it is so important to reach such high coverage rates of the target population, all the stakeholders involved in executing immunization campaigns are striving to ensure adherence to the immunization calendars or guidelines. Thus, the goal is to mobilize a large enough share of the population to undertake a medical intervention on an otherwise healthy group of subjects, using a standardized medical intervention. The resistance to the recommendations is often stemming from the fear of safety issues as much as from a less precisely defined concern over such "one-size-fits-all" medical interventions. In fact, in an era where patients are expecting customized solutions, the very standardized nature of the immunization recommendations is negatively striking the chord of individualism, resulting in skepticism and sometimes resistance.

The growing magnitude of this societal trend has consequences for the stakeholders involved in the design and in the execution of health-care policies. For all the stakeholders, the ever more assertive attitude of patients has been considered very seriously and patient centricity has taken center stage in the past decade. Almost every life science company is claiming in its mission statements that the patient is central to its strategy and driving the focus of its strategic activities, from the priorities of the R&D investment, to the quality of manufacturing, and to the content and quality of the information flows in the context of the commercialization of its products. Such statements related to patient centricity are now so ubiquitous that they are hardly differentiating and it is important to look beneath the surface of the glossy corporate brochures and press releases to assess the reality of patient centricity, and how it translates in the real life of these corporations.

Patients are first and foremost people, living in an information age, accelerated by mobility, in which data are ubiquitous, where access to media is easy, and yet where understanding of available information is leaving room for improvement and is extremely uneven across population subgroups depending on the level of education and command of health-care matters.

It is commonplace to say that what happens in an Internet minute is staggering[10]. People access a deluge of data (including that related to health care) under various forms and from a multitude of sources, accelerated by the connectivity between devices.



[10] https://image-store.slidesharecdn.com/561a0856-b834-11e3-a614-22000a9780da-original.jpeg. Accessed 1 June 2014.

In this context, not one stakeholder can master the full scope of the information flows to build a comprehensive, reliable, and accurate representation of what is broadcasted on a given health-care topic. Subsequently, taking into consideration the voice of the customer is commensurately difficult, in light of conflicting priorities as described below, and compounded by expanding expectations for more effective and better-profiled care procurement. Overall, the difficulty is simply finding what the real voice of the customer is.[11]

As new generations reach adulthood and working age, customers of the health-care system as well as health-care providers are increasingly "born digital"; Internet, e-books, and social networks are all part of the standard tools that they are familiar with and which are an integral part of their daily functioning[12]. As the generations that are defined as "digital natives" grow up and reach the level of influence, starting from voting age all the way to positions of authority, one is witnessing drastic changes in information management practices and we are likely to see a parallel evolution of the way public health priorities are determined and addressed.

When looking at the number of articles published on health-care topics per year from 1970 to 2010, one notices a steady increase of the number of publications over 40 years, with the rate of increase becoming more pronounced from the beginning of the 2000s.[13] This surge in the number of publications is obviously the combined result of intensive research efforts and of the sharing of scientific knowledge. The sheer volume of information that is created is triggering a growing challenge for the human cognitive capacity, due to the exponential increase of both the number of sources and of their complexity, when these are needed for quality clinical decision making.

As the diagnosis of patients and the decision regarding the best course of action to follow are both becoming more complex, so is the task of the various stakeholders aiming at providing reliable, trustworthy, and most importantly understandable information, both to the practicing medical community and to the lay public. Evidently, the same difficulty is amplified downstream at the patient level, since the patient facing health-care providers often do not have enough time or the adequate educational skills to communicate effectively with the patients, most of the latter lacking the relevant educational background to approach data in a discerning manner and to form a relevant and scientifically sound opinion on their own.

The DNA of the Health-Care Industry: Evolving Management of Innovation

The concern for the life science industry is that the return on its R&D investment has eroded despite sustained spending in terms of percentage of total revenues (and the nominal amount of said R&D spend had increased, commensurately to the turn-

[11] Economist Intelligence Unit Survey, July 2012.

[12] http://mashable.com/2013/12/21/technology-age-comic/. Accessed 1 June 2014.

[13] Online searches at PubMed http://www.ncbi.nlm.nih.gov/pubmed. Accessed 1 June 2014.

over of the health-care industry) reflecting the lower outputs in new molecular entities, as well as the more limited volume and value sales for each new entity which addresses more targeted patients' populations. Yet the industry maintains its R&D investment, as the analysis of the evolution of approvals by regulatory agencies (FDA and EMA) indicate that innovation is driving sales, albeit at a lower rate of return. It is expected that this trend will continue, as indicated by a pool of evidence ranging from the declarations of the CEOs of the health-care companies, as well as by the sustained flow of investment by venture capitalists and capital developers in innovation-focused start-ups.

The maintenance of the R&D investment should not hide the substantial shift in the mix of projects, in terms of disease areas, and precisely defined patient populations. Even the latest development candidates addressing widespread conditions such as dyslipidemia are subject to a clinical development, resting on a larger number of clinical trials, each of them addressing smaller, well-targeted, and defined patient sub-populations, rather than larger scale clinical studies including less-precisely profiled patients.[14] Evidently, the nature and structure of such clinical studies is driven by the evolution of science as well as of the request for specific types of supportive evidence from the authorities. As the drug candidates address chronic diseases in the management of which the patient attitude is a contributing factor to the treatment outcome, the design of the clinical trials is starting to take this dimension into consideration.[15]

The narrowing of the patient populations initiated by the more precise, science-based profiling is further enhanced by the behavioral dimensions. As the societal trends have evolved and care procurement has grown more customized, these emerging individualized approaches lead patients to expect a fully personalized approach, fueling further the search for information.

What personalized—or "customized"—medicine is should be better defined, as well as the expectations of the patients, and the consequences for the industry. This author has been already writing on this topic[16]. Could medicine be customized, like the newer generations of cars, fully tuned to the customer liking (color, decoration, and features), the women's bracelets with a unique selection of charms, the decoration of our homes, the attention that we get when we meet our private banker of when we flash any frequent user membership card, etc.? In actuality, patients increasingly want medicine to be fully tailored to one individual, and in many instances, they are ready to foot the bill (at least partially) to an extent commensurate to the level of personalized attention that they get. It will probably be analyzed over time if this is a consequence of the societal evolutions or of the technological leaps that are pushing ever further the boundaries of the understanding of the pathologi-

[14] http://www.scripintelligence.com/home/ACC-PREVIEW-What-drug-trials-will-be-hot-in-Washington-DC-350858. Accessed 19 July 2014.

[15] http://www.scripintelligence.com/home/Healthcare-2030-facing-up-to-a-pharma-future-346693. Accessed 17 July 2014.

[16] http://brainfoodtv.com/personalized-medicine-who-needs-it-and-what-for/#.U8qQ6LHmcSQ. Accessed 15 July 2014.

cal mechanisms underlying the medical scourges that affect human beings, down to details specific to an individual.

Beyond the expectations of the individuals, the reality of the procurement of care is still a far cry from truly personalized medicine. In the earlier article referenced above, this author has argued that there's a substantial gap linked to the false belief prompted by the buzz on personalized medicine which is falsely leading people to believe that we are seeing already personalized care procurement, whereas we are actually looking only at increasingly precisely profiled medicine, yet still far from a genuinely individualized medicine.

Within such an evolving societal context, the health-care industry has to evolve so as to ensure the sustainability of its innovation-based model.

Sustainability and Pharmaceutical Products: Role in Human Health (Mistra Pharma 2009)

As characterized by several authors, a sustainable society is managing economic, environmental, and social issues in a long-term sustainable way. More specifically, a sustainable society must have a health-care system that is resting on similar principles, including the use of pharmaceutical products. This implies that the entire life cycle, from development and manufacturing to consumption and disposal of pharmaceuticals must be sustainable. These requirements for sustainability apply, whether the health-care solutions are produced locally or imported, as the responsibility for using sustainable products applies globally, irrespective of national regulations or borders (Wennmalm et al. 2010).

For instance, in his book entitled The Soul of Capitalism (Greider 2003), William Greider argues that goods-producing activities that generate increased economic output do not necessarily generate what the society wants and needs. The impact being that social trust is among the casualties of work when ownership is distanced and depersonalized from its real-world meanings and therefore insulated from the real-world consequences. Overall, he pleads for trustworthy financial firms, accountable business organizations, new patterns of ownership and governance, and new mediating institutions.

The author encourages an ethic of shared responsibility between consumer and producer as he argues (convincingly) that corporate governance is a central variable in the ecological crisis. He recommends that corporations develop the capacity and culture to tell the truth (yet without linking this capacity with value creation, or some other means to incentivize corporations and their shareholders to embrace the concept). He argues that effective corporate governance recognizes that motives of self-interest and social obligation are compatible and mutually reinforcing (here again, the link with value created and thus shareholder opinion/orientation remains to be demonstrated).

The notion of individual versus collective benefit surfaces through a discussion on the issue raised by corporate privileges damaging the interests of individual per-

sons. This notion is well understood by health-care companies, as it is the basis of most "health technology assessment" discussions with the authorities.

The author argues that a "new social corporation" should have the following founding principles:

- Producing real new wealth
- Achieving harmony with nature (apparently defined as the corporation ecosystem)
- Having governance mechanisms to ensure participatory decision making and equitable adjudication of inevitable differences (note: some legal dispositions in Europe about company profit sharing schemes are already in existence)
- Undertaking concrete covenants with the communities that also support it
- Promoting unbounded horizons for every individual within it (hence all the regulations on employee training, career advancement, etc., yet used in a discriminative way for obvious reasons)
- Designing a culture that encourages altruism
- Committing to defending the bedrock institutions of the society (in that case, the US, hence defined as viability of family life, integrity of representative democracy, etc.).

The author makes a brief set of comments on the pharmaceutical industry, blaming it for riding free on the public funding (NIH research) to develop patented medicines and deriving profits from this IP protection through inflated prices (note: it is accurate that drug prices in the USA are the highest in the world). The point would gain in accuracy if it was distinguishing between investments in research versus in development and acknowledging the development risk and costs, as well as the recent regulations encouraging generics, reference pricing, the use of health economics to measure the cost-effectiveness of drugs and determine their prices and reimbursement, etc. Also, some of the author's suggestions have since been put into legislation (e.g., Sunshine Act, protection of whistleblowers, etc.).

An interesting question is that should the corporations be more farsighted in focusing on what society wants and needs for its distant future, it would require a more precise definition of these needs and wants, and it would require to define these as goals for corporations, among other financial (and more short-term) goals. The "sustainable development" question is "are these reconcilable?" The author argues at several points that top-down change is not possible (i.e., legislation-driven) but that grassroots approaches (experiments undertaken by entrepreneurs) are mandatory, subsequently disseminated via compelling stories. Consistent with the notion of "stories", he mentions "indicators" which "work in two relatively invisible dimensions: individual consciousness and social process." And this analogy to "viral change" has also to be put in perspective with the recommendation for mediating institutions, likely assuming that corporations will not be accountable right away and will need time to regain trustworthiness.

The process of using social indicators to construct social narratives applies the principles of ecology to human systems (economy and community), to suggest so-

lutions: what has to be altered to restore the balance to the ecosystem (a form of homeostasis) and, thus, its sustainability.

Pharmaceutical Products and Contribution to Global Health: Global Health Requires More than Better Drugs

Since the beginning of the industrial age of the health-care industry, the level of consciousness to the sustainability issue has been evolving progressively. Evidence to that is the series of "Pharma Future" reports which have been addressing various aspects of the matter over the past 10 years.

The first such report, "Pharma Futures 1," was issued in 2004 to present the conclusions of a scenario planning exercise executed by the industry and its investors. The exercise was stemming from the early conclusions that the business model of the health-care industry had to evolve in light of the mounting challenges, both internal (such as the R&D drought) and external (such as the financial constraints weighting on most health-care systems; Pharma Futures 1 2004). The report identified an imbalance between the short-term shareholder perspective and the long-term value of research for the other industry stakeholders and highlighted seven key findings. First, the impact of the emerging markets was deemed underestimated, and this proved a very accurate prediction as these countries are now central to the development strategy of the industry. Second, the sustainability of the industry value was described as strongly correlated to issuing innovative therapies, and this finding has also been reinforced by recent analyses. Third, the authors estimated that the industry was in need for a more "adaptive, flexible, and open minded leadership…to signal to the investors the need to change; which has been echoed in several publications, including from this author. Fourth, the ability to change successfully was attributed to seizing the "first mover advantage," yet history has demonstrated that the first mover were often the industry stakeholders, starting by the regulatory authorities. Fifth, the perennial issue of trust was underscored, albeit from the perspective of the investors' confidence that the industry can deliver sustainable shareholder value. Sixth and linked to the first finding, the authors doubted that market-based solutions will help meet the access needs in poorly developed countries; the evolution of specific industry policies has demonstrated that much work remains to be done, but that some market-based solutions such as tiered pricing are indeed proving extremely effective to solve affordability and access issues. Lastly, the growing power of the health-care consumer was highlighted as a driver of awareness and of increased transparency.

The second report addressed a number of critical questions pertaining to "market access," including the mutations of the landscape of payers and also the access to emerging countries, and how the industry could manage its productivity more effectively. This scenario planning exercise is focused on visioning the environment and the health-care ecosystem in which the products under development at the time of the analysis will be launched. The analysis encompassed the projection of the

trends as well as their societal consequences and went on to elaborate further on how the industry and its shareholders should address them in a balanced way that would preserve the expectations of financial return of the investors while meeting the expectations of society. As a consequence, the initiative also focused on the need for the industry to communicate clearly and transparently on its strategies to manage these challenges to investors, as well as how investors should signal what needs to be brought to their attention (Pharma Futures 2 2007).

The report reinforced the earlier conclusions of the importance of R&D, when it was already obvious that the technological advances and the sustained investment were not necessarily translating into greater output of novel therapies. It also underscored the need for the industry to respond efficiently to increasing demands for evidence supporting pricing and reimbursement, therefore supporting the value proposition for products addressing predominantly chronic diseases. And the report echoed again the opportunity for growth embedded in emerging economies, provided the industry can address specific public health needs in an affordable manner, working in close partnership with the governments and the civil society.

Unlocking these opportunities was described as raising several challenges, most of which are still current, 7 years after the report has been published. The industry was expected to transition its portfolio to more targeted products requiring an extensive collaboration with a broader range of stakeholders from development to commercialization, and this prediction has proven extremely accurate. As a consequence, R&D was anticipated to be reorganized to eliminate redundancies and ensure a balanced portfolio in terms of types of innovation and probability of success of the programs, including unmet medical needs with a limited commercial potential. Meanwhile, the industry was expected to take a balanced approach on pricing of new products, hence managing successfully to navigate the payers' willingness to pay while ensuring that it is perceived as a trusted partner, hence demonstrating that it adds value to the health-care system. Thus, the industry should be able to contribute to implementing policies through collecting data throughout the entire product life cycle from the perspective of health outcomes as well as health-care system efficiency and societal expectations. In emerging economies, the challenge will include adequate pricing—and once again, this has been successfully achieved through policies such as tiered-pricing—while preventing negative repercussions on more affluent markets and maintaining an open dialogue with local stakeholders to secure the relevant foundational level of trust.

The third report is focused on a pool of opportunity that the industry has been contemplating for its contribution to economic and population growth, namely the middle-income countries including China, India, and Brazil. The purpose of the initiative was to analyze the connections between the public health objective of improving outcomes in these countries, and sustainable pharmaceutical business models. The core topic was affordability, and how the industry should balance its profitability objectives with the markets' willingness and the ability to pay for health-care interventions. It was recognized that the two should be aligned for the industry to perform in a sustainable manner (Pharma Futures 3 2009).

These emerging markets were described as complex from the cultural, ethnic, and economic perspectives, and presenting infrastructure and urbanization challenges; nowadays, these drivers of complexity remain the same, albeit under evolving proportions, hence requiring specific skills and investments. Although affordability was described as a key issue, time has shown that economic growth has spawned the swelling of the middle class which can afford more expensive care, and tilted the gradient of affordability-driven access in the right direction. Lack of proper infrastructure, inadequate access to care in the rural areas, and complex relationships with the local governments often mean that emerging markets are not entirely accessible by the international health-care companies. The topic of the social contract was raised and especially the expectation that life-saving drugs would be made available to all patients who need them, meaning that the privately held industry would be asked to solve the issues of the public health sector through developing innovative business models and ensuring that its shareholders understand the long-term value embedded in such initiatives.

More specifically, it was identified that investors need improved visibility on the opportunities in emerging markets and the expected return on invested resources with agreed-upon, forward-looking performance indicators. Meanwhile, health-care companies need a greater flexibility in their infrastructure and approaches to pricing and distribution, up to the development of hybrid solutions supported by financing vehicles combining philanthropic and mainstream venture capital. The industry has to ensure that its products meet actual health-care needs in an affordable and accessible manner. Overall, the conclusions advocated enhanced communication as a foundation for accountability and transparency.

Nowadays, most companies have a clear "north–south" policy including a pricing component, often referred to as "tiered pricing," by which the price of a medication is adjusted to the economic status of the countries. This question of affordability is not anymore confined into emerging countries, as indicated by the recent rows over the price of oncology products in the USA[17,18] or over the price of hepatitis C medications both in the USA and in Europe[19,20,21].

Elaborating further on the question of affordability, the fourth report is focused on "shared value," defined as the need for the health-care industry to rebuild its social contract with society at large. The report elaborated further on the shrinking R&D output and the difficulty to meet all patient needs in a context of overburdening debt that reduces the willingness and ability to pay for innovation, which is

[17] http://www.nytimes.com/2012/11/09/business/sanofi-halves-price-of-drug-after-sloan-kettering-balks-at-paying-it.html?_r=0. Accessed 15 Aug 2014.

[18] http://www.cancerletter.com/articles/20130628_2. Accessed 15 Aug 2014.

[19] http://www.nytimes.com/2014/08/03/upshot/is-a-1000-pill-really-too-much.html?abt=0002&abg=0. Accessed 15 Aug 2014.

[20] http://www.webmd.com/hepatitis/news/20140714/high-cost-hepatitis-c-drug-sovaldi-investigated. Accessed 15 Aug 2014.

[21] http://www.techtimes.com/articles/12045/20140805/sovaldi-hepatitis-c-drug-at-84–000-per-treatment-course-sparks-healthcare-concerns.htm. Accessed 15 Aug 2014.

a major concern for shareholders focused on the return on their investment. This central question is still burning today and is likely to remain so for the foreseeable future (Pharma Futures 4 2011).

The report highlighted the delicate R&D balance to be achieved between addressing chronic conditions and finding new solutions against resistant infectious diseases and underscored the unique capabilities possessed by the industry to translate fundamental science into approvable products, building on its network of relationships and on its vast knowledge of the diseases. The R&D challenge was—once again—described as one of efficiency since the R&D output kept declining since earlier reports. The attrition was correlated to five drivers: industrialization, duplication, risk aversion, consolidation, and regulatory requirements. As the industry adopted industrial techniques to screen and develop drug candidates, it biased its skills pool away from pharmacology and physiology and lost proximity with integrated biology and experimental medicine. Also, the generalization of the industrial techniques triggered a focus of the industry on the same few leads, resulting in numerous "me too's" and lots of areas of unexplored medical needs, especially for conditions lacking good biomarkers. As the shareholders are keeping a close eye on the return on their investment, the industry grew a tendency to focus more on validated targets, opting for predictable returns, further reinforcing the focus on the same targets and shrinking the breadth of the R&D portfolios. This was further accelerated by the wave of mergers and acquisitions, leading to a global decline in R&D productivity. Finally, the ever more stringent regulatory demands, fueling an increase of the cost of the clinical development and of the risk of failure, drove the industry to make difficult choices to prioritize their lead candidates; and the ensuing rationalization is further fueling the investors' concerns that the R&D strategies may not yield the expected return.

The question of R&D productivity is connected to that of return on R&D investment through the broad question of the value of innovation, for which the surrogate marker is the payers' willingness to pay. As the payers are operating under growing financial constraints and are increasingly concentrated and using more sophisticated methodologies to track outcomes, the industry has faced commensurately increasing resistance to pay for marginal innovation and had to polish her health economic capabilities to substantiate genuine value propositions, reinforcing the decision-making role of the payer over that of the prescriber. The business model of the industry has evolved to place greater emphasis on evidence of value, further fueling the industry's tendency for risk aversion as it has to collaborate with an expanding scope of stakeholders, including better informed and more demanding patient groups. As the report puts it, *"This could evolve into a 'Shared Value' model in which the social contract is renewed to the mutual benefit of industry and society"*.

The report highlighted a number of recommendations, for each type of stakeholder.

Government agencies are expected to provide a clear sense of direction through a health-care strategy and to create the conditions for discussions about future health policies. They should highlight areas of unmet medical needs and facilitate R&D

portfolio orientation choices through enhanced multilateral collaborations, and consistent health, regulatory, and reimbursement policies.

The regulators, including agencies tasked with performing the assessment of novel health-care solutions, and payers are expected to collaborate and harmonize assessment criteria, engage in a dialogue with the other stakeholders to provide guidance, and explore alternative mechanisms of pricing and reimbursement. The dialogue with the industry is especially critical to ensure that all patient needs are addressed, irrespective of the magnitude of the commercial opportunity.

The health-care industry has a commensurate and correlated set of obligations, revolving around the revamping of its business model, the redefinition of its core competencies, the clarity of its strategic roadmap towards investors, the accuracy, transparency, and reliability of its communication and overall the need to be bolder in its search for pools of opportunity, hence in the way it prioritizes and allocates its resources. The improvement of the R&D process is pivotal and is resting both on expanding capabilities for external collaborations and streamlining internal processes to attract and retain key talents. Further, the industry should rebuild the social contract through a collaborative approach to value, building on engagement with the relevant stakeholders all along the life cycle of the novel drug.

The investors are expected to continue to fund the early stage of drug discovery, often through start-ups and biotech companies and to be prepared to fund innovative risk-sharing models. The dialogue with the industry should encompass both the full breadth of the R&D portfolio and the choice of R&D model, to have a comprehensive view of the drivers of the return on R&D investment.

The latest report published in 2012 extends this analysis by broadening the dialogue with other key stakeholders including payers, regulators, and societal and government experts. The report analyzes new market access trends (including the new regulations driving pricing and reimbursement) and the connection with innovation and productivity, and is essentially reinforcing the notions of integration that were present in the previous reports (Pharma Futures 5 2012).

The report underscores the importance of the health reforms, especially the indicators of accountability and health outcomes as essential tools to improve productivity and the greater importance placed on the patient as the pivot to determine clinical effectiveness and value for the health-care system. These reforms have an impact on pharmaceutical R&D, regulatory, market access and commercialization as they promote an approach based on more real-life evidence, generated at the patient level of by the patient herself. They create the conditions for "adaptive licensing," hence a step-wise and dynamic process towards the building of evidence of value rather than a binary one, and for in-depth collaborations along the key decision points, from the nature of the supportive data, to the access to innovation and to the pricing or reimbursement of the said innovation. The support of the investors is expected when they understand that such approaches open the possibility for earlier cash flows, and reduced regulatory and reimbursement risks.

Such a systemic approach will require transparent communication and frequent collaboration as a prerequisite for mutual understanding and trust building and as a way to overcome internal resistance and behaviors built over the past decades.

The same concepts have been the focus of a landmark article published in the Harvard Business Review by Michael Porter and Mark Kramer (Porter and Kramer 2011).

The authors are pointing that the business world has been criticized as a major cause of social, environmental, and economic problems and that companies are accused of prospering at the expense of their communities, resulting in an erosion of trust and in the enactment of policies that undermine competitiveness and sap economic growth. Further, they point that the companies are a major part of the problem, especially as they are focusing on the near-term financial returns rather than on the longer-term picture. The solution could rest in developing "shared value," i.e., financial value for the corporations and simultaneously value for society. Redefining R&D and the approach to the markets, availability and affordability, and supportive collaborations are at the core of the recommendation. The authors are mentioning a number of initiatives and argue that "shared value could reshape capitalism and its relationship to society." That would lead to the identification of new pools of potential for the companies and to the creation of a new set of competitive advantages, provided the companies evolve their set of skills and the authorities take a more educational and collaborative approach to regulation.

The perspective on shared value is evidently bordering that of protection of assets through intellectual property rights. As these have been blamed for being the obstacle to greater access to care and shared value, especially in emerging economies, authors such as Charles Leadbetter (Leadbetter 2009) have been suggesting solutions to address this specific question. The book tenet is about the value of "we" versus "I," or in other words, the new culture of sharing information and the value it creates in society at large and more specifically for some types of businesses. Regarding the health-care industry, it provides suggestions related to sharing knowledge for medical development and mentions Victoria Hale, who created the Institute for One World Health. The concept is to get pharmaceutical and biotech companies to donate patents and discoveries that they do not intend to develop and commercialize, but which may be of medical interest for the developing world. The institute subsequently assembles the right capabilities (scientific, financial) to develop these discoveries and bring them to where they bring value. This type of initiative raises the key question of ownership (not only objects but also knowledge, know-how, etc.) and drives home the point that "collaborative innovation invariably requires a form of shared ownership."

Sustainable Concerns All Along the Life Cycle of the Health-care Industry

As previously described, the health-care industry is one of long innovation cycles, resulting in a life cycle of 10–12 years or over, along which the question of green and sustainable pharmacy is always present (Kümmerer and Hempel 2010): Within recent years, pharmaceutical compounds have come under increasing scrutiny as

contaminants of the environment and the issue of sustainable chemistry has gained momentum. The combination of the two is referred to as sustainable pharmacy, which is addressing environmental, economic, and social aspects of pharmacy.

The environmental dimension spans the entire life cycle of any pharmaceutical entity. It evidently included all the manufacturing questions, including the resources and energy consumption, and also the issues related to waste during the synthesis and production of an active pharmaceutical ingredient. Furthermore, it also considers the compounds themselves and aims to improve the biodegradability of the compounds after their human or veterinary use into the environment so as to reduce the risk caused by persisting chemicals. The approach also focuses on all the players along the prescription and dispensing value chain, as physicians, pharmacists, and patients respectively prescribe, dispense, and consume medications in a way that has a bearing on their presence in the environment. The question is to review their behaviors and assess how these could be more virtuous and contribute to more efficient use of pharmaceuticals with less environmental burden and less risk for drinking water. The book "Sustainable Pharmacy" addresses all these issues and is a pivotal piece dealing with this important topic.

The economic and social dimensions are multifaceted insofar as they tend to be polymorphic, depending on the geography and on the nature of the health-care ecosystem. Irrespective of the economic status of the said ecosystem, several authors have already elaborated on the importance of sustainable development and international collaboration in shaping the future of health-care systems, and how adequately funded R&D will assist in tackling current and predicted challenges (World Health Summit 2012). Across the entire wealth spectrum, the common challenge is the efficient management of scarce resources, ensuring that the gains of medical progress benefit as many people as possible. Related important topics span "priorities for research, public and private sector partnerships, intellectual property rights, regulatory procedures for health products, conventions on biomedical research and development and the place of information technology in health care systems".

> One of the biggest challenges for health in the globalized world is the privatization of the health sector and the lack of access of the poor to quality health services. Sima Samar (Chairperson of the Afghan Independent Human Rights Commission)

The challenge of managing diseases in modern environments is evidently an evolving one, as life expectancy has continued to rise steadily. Longer life expectancy, as well as unhealthy diets and sedentary lifestyles, has resulted in the global predominance of noncommunicable diseases as both the leading cause of death and of disease burden. Serious socioeconomic consequences can now be seen in both developed and developing countries, the latter often facing difficult arbitrage for resource allocation as they often have to deal simultaneously with the remnants of infectious diseases that are the hallmarks of poorer economies. These new issues are present on the global health agenda, alongside neglected diseases as well as future pandemics, for more balanced governance towards a healthier planet.

Public health interventions need to be designed and implemented taking into consideration research and innovation, as well as delivery of and access to that in-

novation, and capacity building and collaboration. As research is increasingly complex and technical, influencing policy and health-care practice requires transformation into usable information and a focus on a needs-driven research approach rather than market-driven approach, as it has been highlighted in the Global Strategies and Plan of Action of Public Health, Innovation, and Intellectual Property. Yet and as illustrated by the following quote, these matters go beyond the current scope of intervention of the health-care industry and require a broader collaborative approach, across different industry segments and coordinated by the public authority.

> To develop the political will for a health policy based on scientific data; in the tobacco epidemic, what works and what doesn't work has been proven for decades—it only requires political will to act in the short, medium and long-term interests of the health of the people. Judith Mackay (Senior Advisor, World Lung Foundation)

This is all the more important as the correlation between health and wealth has long been established, not only for emerging economies. Authors have described the impact of global financial crisis on health systems as "catastrophic" and are calling for more cooperation between the public and private sectors, and for sustaining investment and financing in health and social structures to maintain stability and security as well as to improve performance. This is the dimension where behavioral economics and the insights derived from data on consumer and lifestyle behaviors are expected to influence research and policy direction. As a consequence, drug development and usage will also be influenced, and this is already visible through new drug registration approaches (see interview of Richard Barker and the topic of adaptive licensing).

In the lower-income markets, access to health care—where available—has always been an issue, whether related to affordability, or awareness, and lower education level. As Severin Schwan (CEO, Roche Group) said "Lowering or removing these barriers is a shared responsibility, one that must be pursued more creatively and intensively in collaboration with health-care stakeholders worldwide—including governments, health-care providers and industry." Nowadays, all pharmaceutical companies have developed a strategic agenda for such sustainability initiatives in which educating health-care providers is a pivotal component. In addition, global health education will be essential to drive the required behavioral and consumption changes to maintain efficient health systems. As described in the previously referenced publication, "changing patterns of health threats in the twenty-first century such as those due to population movements and financial flows require a transformative educational approach of health professionals that are better attuned to the pressing needs for both global awareness and local sensitivity." The health-care industry is ideally positioned to contribute to the success of such educational initiatives as it hosts skilled resources and the knowledge of the patients and the diseases.

> It is against such a backdrop that one of the biggest challenges we face is getting people to work together—across agencies, governments, disciplines, and other boundaries, as well as changing human behavior. Although individual countries may be able to successfully develop strategies to counter some of the above, many global health issues defy borders and would require a collective strategy if we are to be successful. John Wong (Vice Provost (Academic Medicine) of the National University of Singapore)

As mentioned earlier, future success hinges upon collecting and analyzing massive amount of data and deriving actionable insights across the entire spectrum of health-care research, policy, and practice. The successful management of this information value chain will impact all the areas of health governance, research and innovation, politics and economics, as well as the education of health-care professionals and of the general population.

Factoring in all the above dimensions is an integral part of the strategic thinking in the health-care industry, all along its own value chain.

R&D

Much has been written about the evolution of the R&D output over the past decades and the conundrum that it represents for the health-care companies, the regulatory authorities, the payers, and the investors alike. The chapters presented in this book provide both an authoritative review and a fresh perspective of the critical topics of R&D productivity and patient centricity.

The chapter by *A. Schuhmacher* provides a comprehensive overview of the drivers of R&D sustainability. It analyzes where the pharmaceutical industry stands today in terms of innovation process and describes the drivers of the erosion of R&D productivity. Exploring the consequences of reduced R&D efficiency is then leading the author to recommend growth options to maintain sustainability for the health-care industry in the future, focusing on R&D-driven innovation.

In the chapter consolidating her executive insights, *K. Fischer* is demonstrating that capturing the patient voice early on in the development cycle is crucial to drug effectiveness. Based upon "real life" tradeoffs that patients are making around their treatments, she presents ways of using this data to improve the process of drug development, hence challenging the existing codes of practice, regulatory guidelines—originally designed to protect the patient—to ensure that their very importance voice is heard.

Another fascinating account of what can be accomplished when the industry gears itself properly to work more closely with the patients or the NGO representing them is given in the chapter presenting the interview of *S. Vink*. The insights are particularly relevant to the management of clinical development but also to global corporate governance as they address the need to evolve management practices, towards a long-term strategic orientation, openness to real-world data and responsiveness to societal pressure. The industry will need to flex its procedures, to open up to broader collaborative approaches and to foster a company-wide orientation towards innovation.

In the realm of R&D, other publications have addressed the broad topic of drug design and of "green chemistry," especially as compounds used in human medicine can cause adverse environmental effects. It is therefore argued that drug design should include consideration for environmental risk. In Sweden, systems for classification of drug environmental risk and hazard have been used for several years.

Although environmental data on human drugs are often missing, or reveal unfavorable environmental properties, it is argued that the pharmaceutical companies should highlight environmental precaution when designing new drugs (Wennmalm et al. 2008). Since chemical products are the main emissions of the pharmaceutical industry, it is difficult to hold them back efficiently. Very often they are not fully degraded to innocuous byproducts and unknown transformation products are formed in the environment. Publications have referenced case studies from industry, such as Taxol, Pregabalin, and Crestor, illustrating how a multidisciplinary approach to green chemistry has yielded efficient and environmentally friendly processes (Dunn et al. 2010). Therefore, according to the principles of green chemistry, the functionality of a chemical should not only include the properties of a chemical necessary for its application but also easy and fast degradability after its use. Authors advise taking into account the full life cycle of chemicals to lead to a different understanding of the functionality necessary for a chemical, factoring in its environmental properties. Several examples underline the feasibility and the economic potential of this approach, called benign by design (Kümmerer 2007).

This concept requires information on a compound's biodegradability to be available at an early stage, even before synthesis. Computer models for predicting biodegradation, therefore, are increasingly important, and various approaches to predict aquatic aerobic biodegradation have been critically reviewed from a user's point of view. The scientific debate addresses the fundamental problems in modeling biodegradation, as well as more general issues in modeling of compound properties by quantitative structure–property/activity relationships (Rücker et al. 2012).

The topic of preservation of natural resources has also been addressed in connection with R&D, exploring the connections between biodiversity, biotechnology, and sustainable development by examining the drug discovery process and agricultural improvements for better nutrition. Examples of ventures include the famous agreement between Merck & Co. and Costa Rica's National Institute for Biodiversity (INBio) and suggest policy options for potential host countries. The issues of costs, scientific and resource requirements, and economic prospects of different drug development models are also explored, as well as the combination of biodiversity and biotechnology to establish a sustainable agriculture. The authors have also delineated the legal ramifications of intellectual property rights, fair compensation for indigenous knowledge, and different contractual arrangements and more broadly how to assess biodiversity's economic value which could become the "green gold" and new competitive advantage for some countries (Pan American Sanitary Bureau 1996).

Manufacturing and Supply Chain

The sustainability of the production of human pharmaceuticals is multifaceted and includes topics that are common across to other industry sectors such as manufacturing constraints, concerns regarding the environment, knowing and managing the risks, wastewater treatment and energy consumption, as well as matters fully specific to the health-care industry such as technology transfer and north–south policies.

There is an abundant literature related to managing the risks for the environment and it is placed high on the agenda of the authorities. For instance, the US Environmental Protection Agency has released a list of 134 chemicals to be screened for their potential to disrupt the endocrine system of humans and animals, hence potentially affecting growth, metabolism, and reproduction.[22] Intensive research on pharmaceuticals in the environment started several years ago and a vast amount of literature has been published. The input and presence of active pharmaceutical ingredients (APIs) and their evolution in the environment remain of high interest. With the advent of proper measurement tools, it has been found that environmental concentrations can cause effects in wildlife and the question of mixture toxicity has gained more attention. Since work has been done in the field of risk assessment and risk management, the focus has been on raising discussions to influence policies in order to better manage risks (Kümmerer 2009b).

Energy saving has also received much attention, in the context of large manufacturing restructuring plans. One such example is Pfizer Germany GmbH's SPRING & E-MAP (Strategic Plant Restructuring & Energy Master Plan) project in Freiburg, Germany. The facility has won the Sustainability award in the 2011 Facility of the Year Award competition sponsored by ISPE, INTERPHEX, and Pharmaceutical Processing magazine.[23]

The pharmaceutical industry supply chain is subject to the Implementation Guidance Document (the Guidance Document) which conveys the spirit and intent of the Pharmaceutical Industry Principles for Responsible Supply Chain Management (the Principles) by providing a framework for improvement and examples of business practices and performance related to the principles.[24] This comprehensive document includes a description of the management systems required, such as the legal requirements, the tools of risk management, the required documentation, training and competencies and the need for continual improvement. The ethics section describes the principles of business integrity and fair competition, the identification of concerns, the principles of animal welfare and the privacy rules. The labor section contains a number of elements that are not specific to the health-care industry such as child labor, nondiscrimination and fair treatment, and the health and safety section expands on general topics such as worker protection, as well as on some that have aspects fully specific to the nature of the pharmaceutical products such as process safety, emergency preparedness, and hazard information. Evidently, the document elaborates on environmental protection, especially on the management of waste, emissions, and spills.

Technology transfer plays a pivotal role in the sustainable development activities related to the manufacturing of pharmaceutical products. As a matter of fact, trans-

[22] EPA to evaluate 134 chemicals for endocrine disruption http://www.environmentalleader.com/2010/11/17/epa-to-evaluate-134-chemicals-for-endocrine-disruption/. Accessed 10 Nov 2013.

[23] Pfizer discusses its strategic plant restructuring & energy master plan. http://www.environmentalleader.com/2011/04/11/pfizer-discusses-its-strategic-plant-restructuring-energy-master-plan/. Accessed 10 Nov 2013.

[24] Implementing the pharmaceutical industry principles for responsible supply chain management, pharmaceutical supply chain initiative. http://www.pharmaceuticalsupplychain.org/downloads/psci_guidance.pdf.

ferring technology contributes to improving the health of recipient countries' populations by facilitating access to innovative medicines and vaccines and strengthening local care procurement capacity. Such initiatives are usually part of broader programs including education of patients and populations at risk, and by conducting R&D on diseases specific to the developing world (IFPMA 2011).

Technology transfer is an accelerator of economic development as it allows emerging countries to access know-how and equipment relevant to the production of advanced health-care solutions. Once production is localized in an emerging market, it improves availability, access, and reliability of supply and creates high-tech job opportunities, therefore it contributes to improving the health and social status of the recipient country.

Many pharmaceutical companies have engaged successfully in technology transfer initiatives, including an educational component targeting the local health-care community and sometimes support to bettering the care procurement infrastructure. The importance of transferring technologies for medical products is recognized in the Global Strategy and Plan of Action on Public Health, Innovation, and Intellectual Property Rights of the World Health Organization (WHO). The technology transfers require a suitable local industrial partner to host the transferred technology. In addition, key success factors that have been described include a viable and accessible local market; political stability, good economic governance; clear development priorities; effective regulation; availability of skilled workers; adequate capital markets; strong intellectual property rights (IPR) and effective enforcement; and quality and duration of the relationship between industry and government.

Local governments create favorable conditions to attract technologies in demand by local manufacturers and evolve processes so as to foster mutual recognition of regulatory decisions. Technology transfer initiatives are also facilitated when they provide policy support for the development of a local private sector. Authorities in high income countries engage in educational initiatives to increase the technical expertise of the emerging countries regulators with the new technologies, while donors from developed economies provide funding for health care in the developing economies as a platform for development.

The IFPMA member companies are committed to transferring new technology and the relevant know-how and to delivering corporate social responsibility programs that offer products and specialized knowledge and skills contributing to economic development and public health of the recipient's country.

Licensing and Market Access

The current model for developing new drugs is becoming unaffordable, since costs to research and develop new drugs are steadily increasing, resulting in higher prices and mounting concerns among payers about affordability and cost-effectiveness and threatening access to novel therapies (Barker 2010). Obtaining a market authorization and a price or reimbursement has always been regarded by the industry as

a complex process fraught with risks, prior to commercialization. The probabilities of success being variable, pharmaceutical manufacturers are usually planning for lengthy and complex negotiations. As the access to innovative medicine can be substantially delayed, the authorities have been taking this question very seriously.

Published literature has described the traditional drug licensing approaches as being based on binary decisions, insofar as at the moment of licensing, an experimental therapy is presumptively transformed into a vetted, safe, and efficacious therapy. Recently designed adaptive licensing (AL) approaches are based on stepwise acquisition of evidence, with iterative phases of data gathering and regulatory evaluation. The purpose of the approach is to align the content of the market authorization more closely with patient needs, and to enhance access to new technologies and to the evidence required to support medical decisions. Whether adaptive licensing is an evolutionary step or a transformative framework, it will inevitably require legislative action to create the conditions for routine implementation (Eichler 2012).

It is critical to understand the far-reaching implications of such adaptive approaches, since their implementation will impact the entire life cycle (research and clinical development, licensing, and market access) and require a wider breadth of collaboration by involvement of all stakeholders including the industry, regulator, payers/providers, and the research community. When successfully implemented, these approaches yield a specific clinical development plan that provides a staged access to evidence on risk versus benefit, subsequently enabling a faster review and expedited authorization in a well-defined group of patients. Along the clinical development and the commercial life of the product, the monitoring of "real-life" effectiveness and safety provides further evidence, driving the license adaptation.[25] The debate on adaptive licensing is still current, but the consensus among stakeholders is that the concept emerged from the necessity to react to the evolving pharmaceutical and economic context and that it should be pivotal to the future of pharmaceutical development and licensing by offering options for more flexible, adaptive, and collaborative design of the development and approval process (Barker and Garner 2012).

The concept of adaptive licensing and the consequences for the industry in terms of implementing a genuinely patient-centric strategy are described in the chapter by *R. Barker*. One of the most striking insight is that the industry appears as more conservative than the regulatory authorities when it comes to exploring new licensing routes and that a change of mindset is needed as much as an evolution of the industry's organization.

The required evolution encompasses a greater integration of industry functions along the product life cycle, the focus on better-profiled patient populations, taking into consideration both the clinical and behavioral dimensions, and a commitment to deliver the expected outcomes.

The chapter authored by *S. Chundru* provides the perspective on such regulatory matters from the perspective of the manufacturers originated in emerging countries.

[25] Strategy for UK life sciences-one year on, Project Director: Dr Sarah Garner. http://casmi.org.uk/adaptive-licensing/ (2012). Accessed 23 Mar 2014.

The author calls for a greater integration of the regulatory requirements in the clinical approach to licensing as well as for an improved harmonization of regulations across Western regulatory bodies which play a decisive role in sizing the business opportunity for emerging market industry players.

Consumption of Health-Care Products: Use, Access, and Disease Management

Towards the end of the life cycle of a pharmaceutical product, during the commercialization phase, the way the drugs are used is potentially raising sustainability questions ranging from disease management to elimination in the environment, the latter sharing roots with issues raised during research, development, and commercialization: since pharmaceuticals can be environmental pollutants, they require responsible use as much as novel testing and manufacturing approaches (Juniper 2013).

Regarding disease management, the chapter by *F. Barei* raises the key question of the cost at which the desired outcomes can be obtained. She underscores the pivotal role of education in evolving the health-care systems and of the broad span of supportive innovation, from the products' pharmaceutical presentation to the exploration of new business models, aiming at improving the patient's experience through convenience and adherence. She also underscores the foundational role of health-care IT and patient data.

The executive insights provided by *V. Simons* are especially relevant to understanding the patient perspective on sustainable health care in a patient-centric society. He addresses the topic from the dual perspective of the patient and the founder of a patient association aiming at educating consumers most at-risk from a diagnosis of prostate cancer, informing the community on other diseases and conditions of negative impact, motivating consumers to make informed choices as to health-care and lifestyle management, laying the foundation for ongoing health-care information dissemination and interaction between the community and medical centers and creating an interactive network to maximize broad scale, mass communications of actionable health messages.[26] He provides examples of partnerships which contributed to improve drug development and industry processes, and also access to care, by focusing on the patient perspective.

Understanding the question of elimination of medications: The primary route by which active ingredients from human pharmaceutical products enter the environment is excretion in urine and feces. Besides, the disposal of unwanted, leftover medications by flushing into sewers also adds to environmental pollution but is considered to be of a lesser importance. Authors have argued that understanding these secondary routes is important from the perspective of preventing such pollution, because actions can be designed more easily for reducing the environmental

[26] http://www.theprostatenet.org/aboutUs.html. Accessed 15 Aug 2014.

impact of active ingredients compared with the route of direct excretion (via urine and feces). The expected benefits should include the reduction of the incidence of unintentional poisonings of humans and animals, and the improvement of the quality and cost-effectiveness of health care, since the unintentional exposure to active ingredients for humans via these routes is possibly more important than exposure to residues recycled from the environment in drinking water or foods (Daughton 2009, Daughton et al. 2009).

A review of the challenges posed by antibiotics in the aquatic environment is an illustration of the magnitude of the issue and of its far-reaching implications. Antibiotics have been used extensively for decades, yet the existence of these substances in the environment has gained attention only recently, with a detailed assessment of the environmental risks they may pose. Within the last decade, an increasing number of studies covering antibiotic input, occurrence, fate and effects have been published, but there is still a lack of understanding and knowledge about antibiotics in the aquatic environment despite the numerous studies performed. Important questions are still open, especially the risks associated with antibiotics presence in the environment, such as bacterial resistance (Kümmerer 2009a).

Even the prescribed use of pharmaceuticals can result in unintended, unwelcomed, and potentially adverse consequences for the environment and for those not initially targeted for the treatment. Depending on the nature of the active ingredient, medication usage frequently results in the collateral introduction to the environment of the said active ingredients or bioactive metabolites, and reversible conjugates. As mentioned earlier, imprudent prescribing and noncompliant patient behavior drive the accumulation of unused medications, which can pose major public health risks from diversion as well as risks for the environment when disposed inappropriately. The prescribers very seldom incorporate consideration of the potential for adverse environmental impacts into daily prescribing practice. Prescription guidelines could encourage the selection of medications possessing environment-friendly excretion profiles and the prescription of the lowest effective dose suiting the patient needs, reducing the incidence of adverse drug events and lowering health-care costs. It is argued that the prescriber needs to be cognizant that the "patient" encompasses the environment and other "bystanders," and that prescribed treatments can have unanticipated, collateral impacts that reach far beyond the health-care setting (Daughton et al. 2013).

Examples of initiatives of health-care companies taking the broader perspective of the patient in the environment have been published, such as GlaxoSmithKline's recycling of asthma inhalers. The initiative targets the collection of 100,000 used respiratory inhalers through a program to make new household products, such as plastic hangers and plastic flowerpots.[27] Also, Johnson & Johnson had 30 products in its Earthwards portfolio of environmentally conscious health-care and pharmaceutical products in 2010; it added 19 products to the range in 2011. In 2012, J&J

[27] GlaxoSmithKline aims to collect 100,000 inhalers. http://www.environmentalleader.com/2012/10/25/glaxosmithkline-aims-to-collect-100000-inhalers/. Accessed 10 Nov 2013.

was halfway towards its goal of having 60 products in the line by 2015.[28] Companies are also benefiting by leveraging "green" products as part of their payer value proposition. For instance, 35% of hospitals surveyed switched suppliers to gain access to sustainable health-care products; according to a 2012 report by Johnson & Johnson that finds hospitals to be placing greater emphasis on "green" products used in patient care and throughout the facilities such as cleaning products (Johnson & Johnson 2012).

Beyond the questions raised by the individual use of medications, the pharmaceutical companies have created competitive advantages by addressing unmet medical needs and access to care in low- and middle-income countries (Peterson et al.). The execution of this strategy often rests on partnerships, such as the 213 programs (recorded from 2003 to 2010), in the fields of HIV/AIDS, tuberculosis, malaria, and tropical diseases as well as other health needs, including preventable diseases, child and maternal health, chronic diseases, and additional health initiatives. The research-based health-care industry contributes to strengthening overall health care by implementing access and capacity-building programs in developing countries (IFPMA 2010).

The insights presented in the chapter transcribing the interview of *E. Pisani,* Director General of IFMPA, help put things in the global perspective by underscoring the pivotal value of global partnerships in the virtuous circle of reinforcing both health and wealth.

Global health partnerships play a pivotal role in meeting many of the most critical health needs of low- and middle-income countries[29]. Global health partnerships (GHPs) have evolved to become an effective vehicle for collaboration to address global health challenges. The BSR report summarizes the contribution of GHPs to meeting global health needs with a focus on low- and middle-income countries and provides perspectives on how to increase the impact and scale of GHPs going forward, based on interviews with leaders from the private sector and stakeholder groups, an assessment of more than 220 partnerships, a survey of pharmaceutical industry executives, and a multi-stakeholder roundtable convened in Geneva in December 2011.

Examples include the HIV/AIDS partnerships aiming at creating pediatric treatment centers, training health-care professionals, and working with community implementation partners to reduce stigma, promote prevention, increase rates of diagnosis, and to assist patients to comply with treatment regimens. The report also highlights Malaria-focused partnerships—and others focused on tropical diseases—which are facilitating technology transfer agreements (see the above section, related to R&D) for research on new compounds, training community health workers, providing education and outreach on prevention, enabling donations and differential pricing arrangements for no- and low-cost medication, and providing professional

[28] Johnson & Johnson expands green product range. http://www.environmentalleader.com/2012/03/02/johnson-johnson-expands-green-product-range/. Accessed 10 Nov 2013.

[29] Working toward transformational health partnerships in low and middle income countries, BSR; 2012.

education and best practice sharing for health-care professionals and policy makers. Among the partnerships surveyed, those focused on HIV/AIDS represent 20%, malaria accounts for 14%, and neglected tropical diseases for 16%, hence a total of 50% of the total partnerships surveyed. Only 14% of all GHPs focus on noncommunicable diseases. Concurring with this analysis, input from stakeholders and companies alike confirm that there is an increasing need for GHPs to focus on the unique challenges presented by NCDs in developing countries.

The chapter presenting the highlights of the interview with *F. Bompart* provides a detailed account of the tools that are part of the corporate responsibility programs, such as tiered pricing in the specific context of a malaria-focused initiative, and explores the recent evolutions since the early programs which were derived from HIV politics and market dynamics.

As the needs of the emerging countries are evolving, partnerships also target noncommunicable diseases and contribute to primary health systems that provide the foundation for diagnosis and continuous care across a range of chronic diseases. For instance, regarding diabetes and cardiovascular diseases, insufficient capacity of primary health systems poses a critical challenge to diagnosis and patient management. In the absence of a robust primary care system, populations are often underdiagnosed and untreated until the disease state generates complications, and requires more challenging (and expensive) treatment regimens, and raises the threat of reduced life expectancy.

The disease areas addressed by partnerships are broad, and the challenge for companies investing in such partnerships is to evolve so as to address the epidemiology shift towards chronic, noncommunicable diseases. More specifically, much remains to be accomplished in terms of addressing diagnosis, treatment, and managed care for such diseases in low-resource environments. At the same time, companies must maintain the legacy partnerships (e.g., HIV and malaria) where continued investment is critical to ensuring long-term disease control. This prioritization is required as well as an overall increase in allocated resources.

The challenges for companies (and the expectation of shareholders) are to identify indicators allowing measuring the impact of such initiatives. Tracking medical outcomes is often difficult due to lack of data and analytic resources both at the local level as well as within NGOs involved, let alone identifying overarching impact such as workforce productivity. Some of these challenges were attributed simply to a lack of resources allocated to unlocking this difficult puzzle. More development work is needed to expand the set of indicators and generate insights on the total impact achieved by partnerships. In the long-run, impact measurement should move from measurement of activity indicators (e.g., number of physicians trained) to highlighting performance indicators on wellness and life expectancy.

High-impact partnerships (or "transformational partnerships") are described as cutting across therapeutic areas, building primary-care systems, and developing local capacity for prevention, diagnosis, and treatment across a full range of diseases.

For the time being, most partnerships involve a single company working with a variety of partners, including NGOs, governments, and academics. These partnerships have made significant contributions to global health in terms of the range of

perspectives and diverse approaches to global health challenges. The specific challenges posed by non-communicable diseases raise the prospect of a higher proportion of partnerships involving several research-based companies to capitalize on a broader range of expertise and assets, most importantly funding, products, R&D capabilities, and skills and time of dedicated staff. Funding from companies is not fully addressing health-care needs in low- and middle-income countries, and the concern is that the public funding is declining throughout the world, further fueling the debate about the role of the private sector in driving global health outcomes. When corporate strategic orientations are aligned with the need to increase investment in partnerships, there are opportunities to develop innovative approaches for internal resources in ways that build local capabilities and simultaneously serve the company's increasing need to increase its intimacy with local markets.

Global Corporate Governance

As argued by Ian Davies, "By building social issues into strategy, big business can recast the debate about its role" (Davis 2005). The UN Global Compact requested to evaluate the potential for corporate responsibility initiatives to stimulate a transition to more sustainable forms of development by linking to wider policy frameworks.[30] Sustainable development in both the developed and developing world revolves around the common fundamental themes of advancing economic and social prosperity while protecting and restoring natural systems. For the time being, the majority of initiatives have focused on transferring knowledge from the developed to the developing world, yet there is an increasing body of evidence suggesting that indigenous knowledge from developing countries can contribute to the global dialogue, especially in the critical fields of water and energy. Case studies demonstrate that, with relevant analysis and quantification, insights can be adapted for transfer throughout the developed and developing world in advancing sustainability, especially the integration of natural processes and material flows into the anthropogenic system. As the global trend of urbanization accelerates, innovations applied to water and energy are expected to fundamentally shift the type and efficiency of energy and materials utilized to advance prosperity while protecting and restoring natural systems (Mihelcic et al.). Interestingly, despite a growing number of bold and visionary companies making considerable achievements, the overall corporate impact on critical sustainability issues—such as sanitation, health care and climate change—has been limited. The key will be to scale up corporate responsibility initiatives to make a greater contribution to addressing global challenges.[31]

[30] Gearing Up: From corporate responsibility to good governance and scalable solutions, http://www.sustainability.com/library/gearing-up?path=gearing-up#.UTYBhYlespo. Accessed 23 Mar 2014.

[31] Issue Brief: Progressive alliances, scaling up corporate responsibility to address global challenges http://www.sustainability.com/library/issue-brief-progressive-alliances#.UTYAn4lespo. Accessed 23 Mar 2014.

The chapter authored by *G.C. Chen* investigates how the biomedical enterprises transform their strategic goals to fulfill the mission of sustainability and addresses the need of a customized framework for biomedical enterprises. Based on an analysis of the current practices on the issues of sustainable development relative to the size of the corporations, the author provides recommendations about how to improve strategies for sustainable development.

The perspective from a health-care company based in a mature market is captured in the chapter by *V. Logerais*. She places the topic in perspective with both the moral obligations and the regulatory constraints weighing on the business and highlights the steps taken by the company to define the scope of its accountabilities and the operational implications. These include the environmental impact of the products and their manufacturing, purchasing principles compliant with fair trade guidelines, and a societal policy targeting the company employees. The chapter provides a clear example of an integrated company policy towards sustainable development that is relevant to the strategic situation and orientations.

A review of existing corporate sustainability policies demonstrates that companies are investing strongly as they generate evidence that such investment creates significant shareholder value, in a measurable way. The following examples focus on health-care companies.

In 2011, GlaxoSmithKline has set a target to achieve carbon neutrality across its value chain by 2050, as part of a new environmental strategy launched in the company's 2010 corporate responsibility report. The carbon neutrality target means that within 40 years, there will be no net greenhouse gas emissions from GSK's raw material sourcing, manufacturing, distribution, product use and disposal, the company said. It has set interim targets to reduce its carbon footprint by 10% by 2015 and 25% by 2020.[32]

In 2010, Pfizer reported average savings of US$ 1.4 million annually between 2004 and 2009 by installing energy-efficient light fixtures, timers, and occupancy sensors at all of its Kalamazoo, Mich., facilities. Savings in 2009 alone tallied US$ 2.6 million.[33]

Also in 2010, the campus of Janssen, Division of Ortho-McNeil-Janssen Pharmaceuticals, Johnson & Johnson flipped the switch on the largest solar panel array in New Jersey—as well as the largest solar installation of any site among the Johnson & Johnson family of companies.[34]

Novo Nordisk commented in its 2010 integrated annual report on the outcomes of sustainable initiatives that it exceeded long-term targets for reducing CO2 emissions, water consumption, and total energy consumption, while increasing its work-

[32] GlaxoSmithKline sets carbon neutrality goal for 2050 http://www.environmentalleader.com/2011/03/30/glaxosmithkline-sets-carbon-neutrality-goal-for-2050/. Accessed 10 Nov 2013.

[33] Energy-efficient measures saves Pfizer $ 2.6M in 2009 http://www.environmentalleader.com/2010/10/07/energy-efficient-measures-saves-pfizer-2-6m-in-2009/. Accessed 10 Nov 2013.

[34] Johnson & Johnson COMPLETES LARGEST SOLAR PANEL ARRay in NJ http://www.environmentalleader.com/2010/09/22/johnson-johnson-completes-largest-solar-panel-array-in-nj/. Accessed 10 Nov 2014.

force by 8% and sales by 12% in 2009. The company reduced CO2 emissions by 32% and water consumption by 20% in 2009.[35]

In 2009, Eli Lilly, reportedly reached its energy goal 2 years early in the context of a long haul program, improving its energy intensity (energy used per dollar of sales) by more than 35% and cutting its absolute energy use by 5.8% from 2004 to 2008. Over the same period, the company also cut its absolute greenhouse gas (GHG) emissions by 4.4%.[36] In the same year, Pfizer announced in its corporate sustainability report that it achieved three of its four public environmental goals to reduce emissions, also from a long-term initiative. The company exceeded its goal to reduce greenhouse gas (GHG) emissions by 35% on a relative basis from 2000 to 2007, cutting emissions by 43% in 2007 and an additional 20% over 2007 to 2008.[37]

A broad and benchmarked perspective is provided by consultancies that are conducting research and comparing company programs. Bristol-Myers Squibb and Sanofi-Aventis earned the two highest scores in the pharmaceutical sector for sustainability reporting, according to a 2009 report from the Roberts Environmental Center.[38] In the 2012 issue of the report, the highest marks went to Merck, Amgen and Abbott[39], indicating that the momentum is gaining the entire industry but that much remains to be done, since some of the score vary very substantially between the top and the bottom performers.

Conclusion

Health-care markets are evolving under demographic and economic pressures. In mature markets, patients navigate highly complex provider and payer systems with limited control on health-care quality and outcomes, as reflected by the absence of correlation between spending and patient satisfaction and outcomes. In developing markets, patients have limited—yet growing at varying paces—awareness, access, and ability to pay for health care. The per capita health-care spending is directly correlated to GDP growth, driving significant expansion of health-care markets

[35] Novo Nordisk Cuts CO2 Emissions by 32%, Water Use by 20% http://www.environmentalleader.com/2010/02/08/novo-nordisk-cuts-co2-emissions-by-32-water-use-by-20/. Accessed 10 Nov 2013.

[36] Lilly meets energy-efficiency goals ahead of schedule. http://www.environmentalleader.com/2009/10/23/lilly-meets-energy-efficiency-goals-ahead-of-schedule/. Accessed 10 Nov 2013

[37] Pfizer exceeds emissions reduction goals, misses clean energy target. http://www.environmentalleader.com/2009/10/07/pfizer-exceeds-emissions-reduction-goals-misses-clean-energy-target/. Accessed 10 Nov 2013.

[38] Bristol-Myers Squibb, Sanofi-Aventis tops pharmaceutical sustainability report. http://www.environmentalleader.com/2009/12/15/bristol-myers-squibb-sanofi-aventis-tops-pharmaceutical-sustainability-report/?graph=full&id=1. Accessed 10 Nov 2013

[39] https://www.claremontmckenna.edu/roberts-environmental-center/wp-content/uploads/2014/02/Pharmaceuticals2012.pdf. Accessed 15 Aug 2014.

in emerging countries. The largest part of health-care spending (estimated around 50 % by 2020) will be driven by providers and services, while the industry will represent about 10 %. The pools of profitability will progressively shift from prescription drugs to other product segments and to health-care delivery, and these shifts will be different by region.

The health-care industry needs to identify which businesses are attractive for major or new investments, in a sustainable manner. Sustainable growth in the health-care industry has already been extensively investigated and analyzed and this has left a trail of publications which focus primarily on R&D productivity (especially the ability to maintain a stream of innovation to replace the top selling drugs which lose exclusivity, the management of the R&D risk through a balanced portfolio, etc.), on tight management of the cost structure (particularly for those health-care industries which are capital intensive, such as the biopharmaceutical industry), on commercial effectiveness (for instance looking at the evolution of the marketing mix and the shift in analytics and marketing tactics to maximize return on promotional investments), etc.

The topic of sustainable development raises additional questions, some being specific to the health-care industry such as:

- The preservation of rare natural resources (leading to questions such as equitable prospecting of specific plants, sourcing, and respect of biodiversity)
- The performance or eco-efficiency (which can be specific to the health-care industry for its most capital-intensive segments such as the biological produced at large scale, such as vaccines)
- The environmental effects (especially pollution and hazards created by the handling of toxic or infectious materials, at industrial scale)
- The capacity issues in relation to the size of the medical need and/or of the market demand (leading to issues of access to care, especially in low- to middle-income markets)
- The recycling strategies for biopharmaceutical processes
- The private–public partnerships to address global health crises, and which have a bearing on the image management policies (especially in a global context of a growing challenge of the "for profit" model of the health-care industry)

The products researched, developed, manufactured, and commercialized by the health-care industry focus on improving the health of patients and populations, and regulations are applied to ensure the security of the end users and the sustainability of the health-care systems. The standardization of health-care products (both small molecules and biologicals) is de facto a driver of sustainable development, insofar as the search for reproducibility drives manufacturers away from the variability-induced extraction of compounds from natural resources towards, the use of materials of animal origin, etc., towards better defined chemical synthesis or bio-fermentation processes.

Overall, the entire value chain of the health-care industry should be engaged in the execution of the corporate strategic goals aiming at enhancing sustainability. Among the levers allowing to balance decisions related to risk management with

long-term shareholder value and business sustainability, patient centricity along the entire life cycle, integration of data and company functions, and engagement and collaboration with a broader scope of stakeholders have been demonstrated to be the most effective.

We expect that the present book will encourage academics, industry specialists, and representatives of the civil society to devote further attention to research on performance indicators generating supportive evidence of long term, shared value of sustainable development endeavors.

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