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Policy Principles to Promote Biotechnology

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Biotechnology Industry Organization

2013 Policy Principles to Promote Biotechnology

Biotechnology helps societies solve old problems in new ways.

Through the science of using living cells and the discovery of new molecules, biotech innovation provides societies with innovative means to address their most urgent needs: fighting disease, feeding the hungry, and improving the environment.

Biotechnology is:

In **QATAR**, fruit grows in the desert. The government's Biotechnology Center collaborated with a privatecompany, to **convert desolate salt flats irrigated with treated sewage into an agricultural oasis**. They did it by applying a special fungus that enhances the ability of plant roots to absorb water. Qatar, which imports 90% of the food it consumes, hopes **this public-private partnership might bolster food production**

Scientific American Worldview, p.72

(i) revealing the genetic origins of diseases – such as cancer, multiple sclerosis, and diabetes – to find new methods and products to detect and treat them;

(ii) boosting agricultural crop yields and reducing the environmental impact of farming; and

(iii) enabling manufacturing processes that reduce waste, minimize water use, prevent pollution, and curb greenhouse gas emissions.

Biotechnology differs from other traditional forms of technology in that it harnesses the power of living systems and organisms to develop new, useful, and sustainable products. Biotechnology employs living cells to create new and more effective treatments of disease. It enables plant cells to be modified more rapidly and precisely than traditional plant breeding, thereby increasing agricultural productivity and reducing the use of synthetic pesticides. Biotechnology is the industry of the future.

Developing biotech products is scientifically demanding, capital-intensive, time-consuming, and involves significant commercial risk. Securing the benefits of biotechnology requires a policy environment that enables scientists, businesses, investors, and regulators to work together to discover, develop, and bring to market innovative biotech products. Such an environment should:

(i) facilitate research cooperation among private, non-profit, and governmental organizations;

(ii) protect intellectual property rights to attract the private investment necessary to support biotech innovation;

(iii) provide a transparent and predictable regulatory approval process for new biotech products that is science-based and internationally recognized; and

(iv) maintain transparent, non-discriminatory, competitive, and commercially viable markets for biotech products.[1]

Countries all over the world are recognizing the importance of biotechnology to their economies, the health and well-being of their citizens, their food supply, and their ability to generate clean energy. Nearly every major country has adopted programs to generate a homegrown biotechnology sector and the well-paying jobs it supports.[2] This paper draws its recommendations in part from countries' best practices in building their biotech sectors.

[1] For biotech pharmaceuticals, the process for determining government reimbursement levels should recognize the objective value of such products.

[2] Scientific American Worldview: A Global Biotechnology Perspective, http://www.saworldview.com/; "The Biopharmaceutical Research and Development Enterprise: Growth Platform for Economies around the World," Battelle Technology Partnership Practice. May 2012.

1 Research Collaboration

MALAYSIA'S biotech sector is growing at 16% annually. In 2005, the government launched its National Biotechnology Policy. It created a "Bill of Guarantees" for biotech companies, ensuring IP protections and freedom to import capital and labor. It also created the "BiotechCorp," a convenient one-stop shop for biotech companies which provides funding and assistance with IP, immigration, regulation, and employment matters. The **number of biotechnology firms is now expected to double to 400 in three years.**

Scientific American Worldview 2012, p.12

While biotech innovation may begin in the laboratory of a university, government agency, or private company, its ultimate success often requires these three institutions to collaborate in order to develop innovations and bring them to market. Governments can facilitate collaboration by funding basic research and by adopting legal frameworks that (i) clearly define ownership of the intellectual property rights in the products of government-funded research, and (ii) enable those rights to be transferred from public institutions to the private sector so new innovations can promptly be applied to contemporary medical challenges. Countries that adopt effective models of research cooperation not only spur innovation at home but also attract partners from the world's most prestigious research institutions, creating a powerful incentive for their scientists and researchers who are working abroad to return home.

Government Support

Governments can advance domestic biotech industries by funding university research facilities, government laboratories, private companies, or a combination of all three, depending on their individual circumstances. Beyond basic research, governments might also choose to offer fiscal incentives to companies that develop biotech innovations and bring them to market.[3] They can do this by supporting entrepreneurial and investor incentives such as grants for small businesses or tax credits for therapeutic discoveries.[4] By providing seed funding, and leveraging funds from other sources, governments can lay the foundation for so-called "biotechnology clusters," which are incubators for the growth of biotechnology sectors.[5]

Technology Diffusion

An enabling policy environment will also allow governments, universities, and the private sector to combine their scientific knowledge, capital, and commercial expertise to develop and bring to market the products of government-funded research. To facilitate these partnerships, governments should establish a legal framework that enables public sector patent holders to transfer technologies to private companies. The best frameworks:

(i) accord universities and public institutions maximum flexibility to license inventions to attract both research and commercial collaborators;
(ii) define the legal rights and responsibilities of patent-holders so that they can effectively manage the technology; and
(iii) allow governments to use inventions for their own purposes while protecting innovator rights.

SINGAPORE is a biotechnology leader in part because of its ability to commercialize university and government research. Over the last decade, the National University of Singapore and the government's Agency for Science, Technology, and Research have **filed nearly 2000 patents worth hundreds of millions of dollars** and sold them to industry, fueling biotechnology growth and financing further research.

Pugatch Consilium, June 2012, p.52

[3] In all cases, government support should be available on terms that are non-discriminatory and consistent with international trade and investment norms.

[4] See, e.g., Therapeutic Tax Credit and SBIR program.

[5] Provide citation for biotechnology clusters and their role in economic development.

2 Intellectual Property Rights

After **JORDAN** implemented strong IP protections, including data exclusivity, the **number of drug launches more than quadrupled.** For the first time, multinational biopharmaceutical firms began holding clinical trials in Jordan, giving birth to the contract clinical research industry. Now, **pharmaceuticals are Jordan's highest value-added export industry** and meet roughly half of total domestic demand for medicine.

United States Trade Representative Fact Sheet 2004; Pugatch Consilium, June 2012, p.50

Biotech innovation is helping feed the hungry, fuel the economy, and heal the sick. This innovation requires significant investment and involves substantial commercial risk. In the case of biopharmaceuticals, the average total cost and total time to develop a new product is $1.2 billion and more than ten years.[6] Only one out of every ten biopharmaceutical discoveries is successfully developed and commercialized. Often, biotech products fail in the period after a concept is proven and before regulatory approval is received because companies are unable to attract the investor resources necessary to fund clinical trials.

This is why protecting intellectual property is essential. Investors will fund capital-intensive biotech innovation only if they are confident that, if a product beats the odds and makes it to the market, they will realize a positive return on their investment. This requires effective intellectual property rights protection, from the discovery of the innovation, through its development, regulatory approval, and commercialization. According to an investor survey, 100 percent of venture capitalists said "strong patent protection" is "essential" for consideration of funding for biotech companies.[7]

Patent Term

Most countries provide a patent term of 20 years from the date the application is filed, although the effective term for most inventions is approximately 17 years due to patent processing delays. In the case of biopharmaceuticals, however, the effective term of protection is in fact often much shorter – only 7 to 10 years – due to the additional time required to fully develop and obtain regulatory approval for the product. Some countries restore the patent terms for biotech products to offset time lost in the regulatory review process, equalize patent terms between biologic and other inventions, and encourage investment in the biotech sector.[8] The relatively short effective patent term for biotech medicines underscores the need for high-level protection while the patent remains in effect.

Data Exclusivity

Before a biopharmaceutical company can make a product available to patients, it must conduct extensive analytical, preclinical, and clinical research tests to prove to regulators that the product is safe and effective. These tests account for more than 90 percent of private sector research and development funding on biopharmaceuticals.[9]

[6] Tufts Center for the Study of Drug Development, Impact Report, Volume 8, Number 6, November/December 2006. In 2010, the global biopharmaceutical sector raised over $36.2 billion in financing and spent $67.4 billion on research and development on more than 400 investigational drug products and vaccines. See Biocentury: The Bernstein Report on Biobusiness, January 5, 2011. *http://www.biocentury.com/Data/StaticContent/ContentFiles/010611bo.pdf*; PhRMA 2011 Profile, April 2011, *http://www.phrma.org/sites/default/files/159/phrma_profile_2011_final.pdf*.

[7] Need citation for this.

[8] Australia, Israel, Japan, Korea, the United States, and many EU countries provide for patent term restoration. Often the length of the extension is based upon the length of time between the date of filing a patent application and the date a product receives regulatory approval.

[9] Avik S.A. Roy, "Stifling New Cures: The True Cost of Lengthy Clinical Drug Trials," Project FDA Report No. 5, March 2012, at 2, http://www.manhattan-institute.org/pdf/fda_06.pdf.

[10] This undisclosed or otherwise confidential data may include the originator's laboratory, pre-clinical and clinical data, such as: information regarding product indications, efficacy, tolerability and safety, pharmaco-kinetics, drug interactions, side effects, contra-indications, precautions, warnings, adverse effects, dosage, and product administration.

While the data generated by such work is proprietary to the biopharmaceutical company, it must be submitted to the appropriate regulatory agency to obtain marketing approval for the drug. [10]

In order to encourage companies to invest the substantial resources necessary to generate this data, many governments agree not to use it to approve identical or similar products for a limited period of time.[11] In some countries, such as the United States, the length of this so-called "data exclusivity" period is longer for biologics (12 years) than for small molecules (5 years). The reason for this longer period is that patents for biologics tend to be narrower (and therefore less protective of the patent holder's rights) because they pertain to a complex product produced under very specific circumstances. Because of their complexity, it is difficult to produce a precise replica of a biologic but easier to produce a highly similar product, that may not infringe upon the original.[12]

Data exclusivity also creates an incentive for large biotechnology companies to collaborate with smaller companies that would otherwise be unable to generate the testing data necessary to launch innovative biopharmaceuticals in multiple markets, especially developing markets. Such partnerships can provide the resources necessary to speed up patients' access to these innovative therapies.

[11] The following countries, for example, maintain data exclusivity periods: Europe (10 yrs); Japan (8 yrs); China (6 yrs); Australia, Brazil, and Mexico (5 yrs); the United States (12 yrs for biologics and 5 years for other pharmaceuticals). The value of protecting data submitted to gain marketing approval for pharmaceutical products is recognized by the WTO Agreement on Trade-Related Intellectual Property Rights, which obligates WTO member to protect against the unfair commercial use of such data.

[12] See Henry Gr. Grabowski, "Data Exclusivity for Biologics: What is the Appropriate Period of Protection?", AEI Health Policy Outlook No 10, September 2009, http://www.aei.org/article/health/healthcare-reform/data-exclusivity-for-biologics-what-is-the-appropriate-period-of-protection/.

3 Regulatory Approval

Last year, **KENYA** adopted biosafety regulations clarifying the regulatory environment for growing biotech crops. This made it significantly easier for Kenyan scientists to work with international NGOs and companies to establish biotechnology centers, train Kenyan scientists, and **develop biotech crops tailored to Kenyan needs**, such as drought-tolerant maize and virus-resistant cassava.

Scientific American

Biotechnology products are rightly subject to rigorous regulatory standards and must be shown to be safe and effective before they can be placed on the market. Governments can promote innovation and ensure the safety and efficacy of biotech products by creating regulatory review processes that are science-based, transparent, and time-limited.[13] Such processes provide the legal certainty necessary to bring innovative products to market, promote consumer confidence, facilitate scientific dialogue between industry and regulators, avoid unnecessary delay, and enable regulators to make the most informed decisions.

Biopharmaceutical Regulation

Biopharmaceutical regulation is divided into three phases:

(i) preclinical
(i) clinical and
(iii) post-marketing approval.

Preclinical Testing

The first phase (referred to as the preclinical phase) of testing occurs in the laboratory. The regulatory regime should require a biotech product to be tested in systems that can

(i) predict the overall effects of the product on humans;
(ii) establish the value of its therapeutic effects as compared to any harmful effects; and
(iii) optimize the dosage, frequency, and means for administering the product.

These systems involve humanely testing products on appropriately-selected animals and increasingly use sophisticated replications of human tissues and cells as well as computer simulations.

Clinical Trials

Once a product has cleared the preclinical phase, a regulatory regime should require the product to be tested on humans. Governments will want to ensure that clinical trials are designed and conducted in an ethical and scientifically sound manner that minimizes the risk to human study participants. Regulatory authorities, in cooperation with biotechnology companies, should adopt guidelines for the conduct of clinical trials that protect patients, uphold high ethical standards, and produce reliable results.[14]

Governments may consult, for example, the Declaration of Helsinki, the Good Clinical Practices developed through the International Conference on Harmonisation (ICH-GCP), as well as established industry practice and legal standards.
Governments and biopharmaceutical companies should assure the well-being of research participants regardless of where clinical trials take place. No matter what population is the subject of clinical trials, research, data collection, or analysis, all parties must ensure that each research participant is protected and valued. Participants throughout the world deserve equal protection based on the same fundamental ethical principles.

[13] See annexes on Clinical Trials, Biosimilars, Agricultural Products, and Industrial and Environmental products.

[14] An example of clinical trial guidelines is set forth in Annex A.

Post-Marketing Reporting

Once a product has been approved and is on the market, countries should establish mechanisms to track adverse reactions and assess differences in individual patient responses.

Regulation of Biosimilar Products

Special regulations are required for the approval of biopharmaceuticals that are similar to other biopharmaceuticals that have already been approved. These regulations will differ from those applied to generic pharmaceuticals.

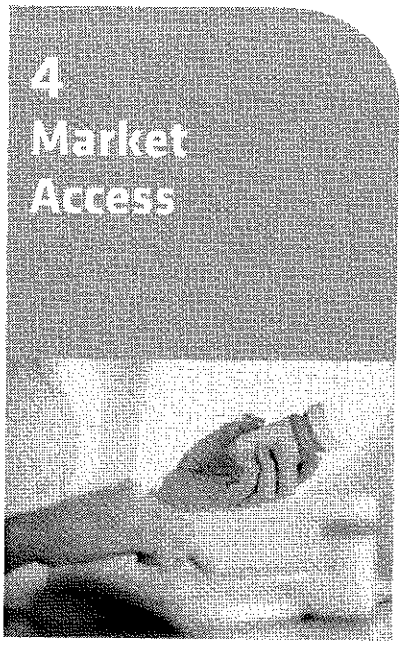
"Generics" is the term used to describe identical copies of traditional, "small molecule" pharmaceutical products (so-called because of their relative structural simplicity). Because these products are identical to the innovator product, regulators may rely on the finding of safety and efficacy of the innovator product to approve the generic version. For many biologics, however, it is currently impossible for a different manufacturer to replicate precisely the cellular or molecular processes that the original manufacturer used to produce the innovator product because biologics are so complex. Rather than produce a "generic," subsequent manufacturers instead produce a "biosimilar" product that is similar but not identical in structure and function. The biosimilar product will invariably differ from the innovator product to some extent, and even relatively minor differences can impact the safety or efficacy of such products for particular patients. Regulators, therefore, cannot rely exclusively on the data supplied by an innovative biologic to approve a biosimilar. Some governments have developed regulations that permit a biosimilar to be approved and placed on the market with less clinical data than the innovator, but that also take into account the differences between the biosimilar and the originator product.[15]

International Regulatory Cooperation and Harmonization

In designing regulatory regimes, governments can refer to internationally-recognized regulators and organizations for guidance.[16] While no two national regulatory systems are identical, countries should strive to adopt "best practices" described above and align their systems and standards with those adopted by internationally recognized regulators and organizations. This will help ensure that drugs developed and approved in the domestic market are also accepted in global markets, creating new opportunities for local biotech innovators to expand and grow.

[15] See annex for examples of biosimilar regulation in different jurisdictions.

[16] In particular, governments may wish to refer to the World Health Organization (WHO), the International Conference on Harmonization (ICH), the European Medicines Agency (EMA), and the U.S. Food and Drug Administration (FDA).



Biotech companies are more likely to invest in, develop, and launch products in markets that are competitive, transparent, and non-discriminatory.[17]

In many markets, governments are significant (if not dominant) purchasers of biologics and other pharmaceuticals; therefore, in order to maintain an environment that incentivizes risk-taking investments in biotechnology, offers patients access to the best quality care, and ensures government funds are spent appropriately, government reimbursement policies and procedures should take into account the following principles:[18]

(i) The decision whether to reimburse a new biopharmaceutical, or a new use for an existing biopharmaceutical, and the amount of such reimbursement should:

- be made within a specified period of time that facilitates patient access to novel therapies, based on transparent, non-discriminatory criteria, and subject to appeal;[19]
- give patients and doctors flexibility and choice, recognizing that not all patients react the same way to particular medicines; and
- take into account the effect of reimbursement decisions on the willingness of innovators to develop and bring products to market in a country.

(ii) Governments should adopt reimbursement methodologies that appropriately value the objectively demonstrated therapeutic benefit of a pharmaceutical.

(iii) Some governments consider cost-effectiveness when deciding whether to list a pharmaceutical for reimbursement. They should not use such analysis when comparing two interventions because, although the cost of a medicine may be readily apparent, its benefits are harder to measure accurately.[20] If a government still chooses to compare interventions based on cost-effectiveness, they should realize that:

- a new drug might allow for the avoidance of other, more costly, health care services (e.g., hospitalizations, surgery, and nursing care);
- a new drug can generate economic productivity gains by allowing individuals to manage better their medical conditions, achieve better health outcomes and a higher quality of life, and remain in or return to the workforce;
- comparative effectiveness studies cannot accurately assess the value of pharmaceuticals that target rare or orphan diseases as well as severe, rapidly progressive, or life-threatening diseases due to the vulnerabilities, small size, heterogeneity, and other characteristics of these patient populations; and
- a new drug may offer benefits even when it is similar to an existing drug if it is more effective for some patients than the existing drug.[21]

[17] This section pertains only to biopharmaceuticals, not to other biotech products.

[18] See reimbursement annex.

[19] A detailed set of procedural protections and other reimbursement principles are set forth in Annex B.

[20] For an explanation of the problems with this approach, see BIO, "The Complexities of Comparative Effectiveness," October 25, 2007, http://www.bio.org/articles/complexities-comparative-effectiveness.

[21] For an example of why this is the case, see Thomas J. Philipson, "Blue Pill or Red Pill: The Limits of Comparative Effectives Research," Project FDA Report No. 4, June 2011, http://www.manhattan-institute.org/html/fda_04.htm.

The annexes lay out more detailed recommendations and "best practices" for the implementation of these policy principles.

Annex A

Guidelines for Conduct of Clinical Trials

- Before a trial is initiated, foreseeable risks should be weighed against the anticipated benefit for the individual trial subject and society. A trial should be initiated and continued only if the anticipated benefits justify the risks.
- The rights, safety, and well-being of the trial subjects are the most important considerations and should prevail over the interests of science and society.
- The available nonclinical and clinical information on the product should be adequate to support the proposed clinical trial.
- Clinical trials should be (i) scientifically sound, (ii) described in a clear, detailed protocol approved by the regulator, and (iii) conducted in compliance with that protocol.
- The medical care given to, and medical decisions made on behalf of, subjects should always be the responsibility of a qualified physician or, when appropriate, a qualified dentist.
- Each individual involved in conducting a trial should be qualified by education, training, and experience to perform his or her respective tasks.
- Freely given informed consent should be obtained from every subject prior to clinical trial participation.
- All clinical trial information should be recorded, handled, and stored in a way that allows its accurate reporting, interpretation and verification.
- The confidentiality of records that could identify subjects should be protected, respecting privacy and confidentiality rules in accordance with applicable regulatory requirement(s).
- Investigational products should be manufactured, handled, and stored in accordance with applicable good manufacturing practice. They should be used in accordance with the approved protocol.

Annex B

Principles for Reimbursement

Procedural Protections

When considering proposals to list a new biopharmaceutical or new indication for reimbursement, or in setting reimbursement amounts, governments should:

- consider proposals within a specified time interval that promotes patient access to novel therapies;
- ensure that the procedures, methodologies, and principles used to assess proposals are disclosed and are fair, reasonable, and non-discriminatory;
- provide applicants timely opportunities to submit comments and respond to questions;
- provide applicants detailed written information regarding the basis for deciding whether to list the pharmaceutical product and the amount of reimbursement;
- provide written information to the public regarding their decisions while protecting business' confidential information; and
- establish an independent review process that the applicant or patients may invoke to reconsider the decision whether to list the pharmaceutical or the amount of reimbursement.

Reimbursement Conditions

Any conditions on reimbursement should be reasonable and should take into account the best interests of the patient. Restrictions on reimbursement should be strictly based on sound science and best medical practice, rather than on short-term cost considerations.

Risk-Based Contracting

Risk-based contracting and other alternative pricing schemes may be appropriate in circumstances when there is a need to balance uncertainty with patient access. These agreements should not be used solely as a way for the payer to contain costs, but rather must be intended to increase patient access and further innovation. Additionally, the terms of these contracts, such as implementation, measurement, and adjudication, must be agreed upon by both payer and manufacturer and must balance the risk between both parties rather than shifting risk solely to the manufacturer.

Pharmaceutical Budgets

When developing pharmaceutical spending budgets, governments should:

- consider the level of pharmaceutical spending in relation to other healthcare spending, taking into account that pharmaceutical spending reduces spending on other, more expensive health care services while boosting worker productivity; and
- provide long-term predictability that future reimbursement levels will be sustainable, given that biotech products take years to develop.

Conclusion

Biotechnology innovation–the union of scientific discovery and capital–can flourish in a supportive research and regulatory environment. These key policy principles will help facilitate the discovery, development, and commercialization of biotech products that will fight disease, feed the hungry, and improve the environment.

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