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The Future of Plant-Derived Vaccines

Ethical considerations for biotechnology

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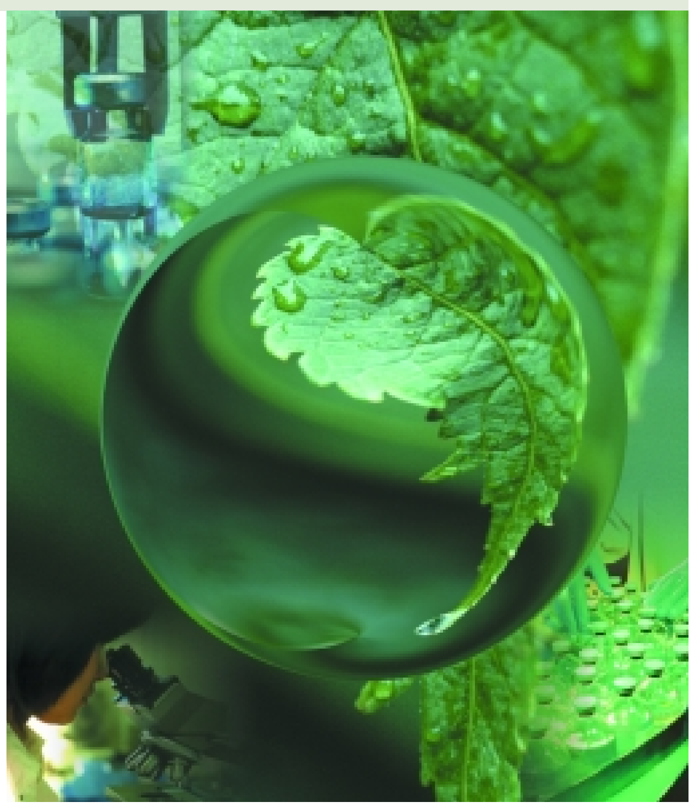
Biotechnology's Global Context

Few will deny that biotechnology can play a role in improving human health. What is controversial is the extent of biotechnology's role, and to what degree societies should come to rely on biotechnology to solve problems that may have other solutions. This debate has two aspects, one technical, the other ethical. On the technical side, biotechnology is obviously not a monolithic instrument, but is made up of thousands of biotechnolog*ies* that are responses to a wide range of problems at varying levels of efficacy. There are biotechnologies that solve old problems by supplanting less efficient technologies, some that compete with other current solutions, others that fill gaps where no biotechnology exists, and there are technologies that improve life even though no particular problem has been identified.



The ethical side of the controversy surrounding the use of biotechnology stems from a simple fact: biotechnologies do not specify their own social application conditions. If a technology's intended effects are to be realized, technical conditions arising in different contexts must be met. Such considerations are always relevant, but they differ from considerations about which contexts are most socially relevant, how and when a technology should be used, who will control the technology and who will profit from it. Careful assessment and subtle judgment about these social application conditions are preconditions for the ethically defensible deployment of new biotechnology.

Clearly, the technical and ethical aspects of biotechnology must be in synergy if biotechnology is to be expected to dramatically improve human health. Nowhere are these improvements needed more than in the world's poorest countries in which one-third of humanity has no access to proper sanitation and one-fifth earn less than a dollar a day. Mark Malloch Brown, administrator for the United Nations Development Programme (UNDP), has observed that new technologies that will improve the living conditions of people in developing countries are those that are practical and context-relevant, inexpensive and applicable to the real causes of suffering.[1] The UNDP report notes that biotechnology development in key sectors such as food, medicine and information systems could be highly relevant and useful to poor countries. Specific examples include vaccine development and delivery systems, techniques for diagnosing infectious

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diseases and for improving environment quality using low-input or bioremediative crops.[2]

The technical feasibility of these new technologies is not at issue, but the feasibility of managing social application conditions of technology is in doubt. The problem, according to Ismail Serageldin, is that so much of cutting-edge science and technology never reaches the vast majority of people who need it the most.[3] Noting the same difficulty, Alan Leshner observes: "In many cases, the solutions already exist. The problem stems from the failure to develop adequate scientific and technological co-operation and the infrastructure needed to ensure that poorer countries can sustain science- and technology-based progress over time."[4]

Leshner and Serageldin are referring to the growing biotechnology divide between those with capacity for domestic biotechnology innovation and those who are dependent on unsustainable technology transfer from donors.[5] The larger issue is that transfer of biotechnology and biotechnology capacity strengthening are equally prone to implementation hazards. Biotechnologies will be relevant and useful to poor countries only if these hazards are identified, managed and reduced. In other words, the social application conditions for new biotechnology must be brought into synergy with the biotechnology.

Plant-Derived Vaccines

Historically, the transformation of plants initially focused on input traits such as herbicide tolerance, then moved to the inclusion of value-added characteristics such as nutritional enhancements. The use of plants as bioreactors represents the third generation of plant biotechnology where the focus is on the output of specific molecules produced efficiently and inexpensively by plants.[6] Plant molecular farming is a suite of techniques that enables the production of valuable biological molecules in plants. Molecules of value in industrial applications such as plastic precursors, fuels or other industrial chemicals represent one class of plant-derived products, whereas pharmaceuticals, nutraceuticals and vaccines constitute another group.[7, 8]

Diseases such as cholera, enterotoxigenic *E. coli*, and hepatitis B are serious infectious diseases, particularly in regions with poor health care and sanitation. For example, hepatitis B is 100 times more infectious than HIV, its oncogenicity is second to tobacco, and it is widespread with as many as two billion suspected infections and 500 million acute cases.[9] While the amelioration of the systemic causes of high infection rates in developing countries remains the ultimate objective, the demand for effective, safe and inexpensive vaccines persists everywhere. Plant-derived vaccines have been developed for the diseases mentioned, and they possess a number of advantages.[10, 11] These include having a lower barrier to entry of their production compared with pharmaceutical manufacturing, the possibility for *in situ* production, no cold-chain requirements, and no injections, which are themselves responsible for the spread of many other infectious diseases and over a million deaths each year. So numerous are the benefits of plant-derived vaccines that it is hard to see how they could fail to be developed for use around the world.

Challenges

Of course, some concerns about the technical feasibility of plant-derived vaccines can be raised. For example, one might wonder if mucosal immunogenicity would work appropriately and for enough vaccine types, or if plant glycosylation patterns are potentially allergenic. Neither question appears to strike a fatal blow against the technology at this time. Turning to the social application conditions for plant-derived vaccine technology, however, there are at least three hazards that could have serious impact on their implementation.

Informed Consent — Standard practice in developed countries requires consent from the person to be vaccinated, either directly or by proxy through a parent or guardian. The same requirement ought to persist in developing countries, and will to the extent that the normal conditions of consent (free choice, and rational use of and access to relevant information) can be satisfied. Since plant-derived vaccines are a novel technology, their short- and long-term effects on large populations are unknown. The technology may be regarded as therapeutic or preventative, but it has an experimental dimension that must be acknowledged when seeking informed consent. Equally, it remains to be decided whether plant-derived vaccines will be used in mass immunizations where the attenuation of standards for individual consent must be justified, or if the pattern will be individual immunizations that have high consent standards attached.

Agricultural Risks — Crop plants are well studied and are hence appropriate systems for developing new biotechnologies. Yet as the case of ProdiGene demonstrates, the use of crop plants requires the segregation of production and processing lines to keep modified plants out of the food system. Modified plants must also be shown to pose no threat to the environment, particularly in the agro-ecosystems where they will be produced. Solutions to these problems are often feats of technical imagination, and include the use of abandoned mines for physical biocontainment, induced hybrid sterility for biological containment, and colour differences in the plants for visual segregation. Yet in the absence of systematic regulation tailored specifically for the plant-made products sector, the spectre of contaminated food and environmental risks will persist.

Intellectual Property Regulation — Most scientific research and technical development of plant-derived vaccines currently takes place in the developed world. This may also be the regulatory environment through which the technology passes, and is most likely to identify the regimes under which the intellectual property will be protected. Protection must also be sought in developing countries to prevent illegal copying, but not all countries have intellectual property regulation and even when they do, it may not be harmonized with that of developed countries. The case of "golden rice" raises the further possibility that implementing plant-derived vaccines in areas with unharmonized intellectual property regimes or in areas unable to afford licences may require many donated patent rights. Clearly, then, intellectual property for plant-derived vaccines will have to be carefully negotiated.

A Role for Ethics

Pessimism paints the following picture: Plant-derived vaccines are not implemented anywhere

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because they are judged to be a form of experimental medicine that fails tests for informed consent; they pose intolerable threats to agriculture and to the environment; and the inter-jurisdictional intellectual property issues are insurmountable. Must the future of plant-derived vaccines turn out this way? One might equally paint the opposite picture in which the hazards inherent in the social application conditions of new biotechnology are identified and managed in an ethically defensible way. Perhaps plant-derived vaccines will then paradigmatically demonstrate the potential for good when biotechnology and ethics work synergistically.

Some might argue this vision of the future is too optimistic — it is just wishful thinking to believe that this scenario will unfold. Indeed it will not if it is thought that it will come about by accident. What is required is the catalyst of proactive new technology assessment that critically examines risks and benefits of technologies in the intended contexts of use.[12] Proactive engagement of these issues arrests technological determinism in which technical application conditions are primary, and social application conditions for new technology are secondary if not simply sidelined. New technologies like plant-derived vaccines have to be integrated into tremendously complex social situations. These technologies must undergo sustained analysis and, where appropriate, there must be corresponding intervention through public engagement, regulatory change and policy reform at national and international levels.[13] Programmatic research of this kind, sketched briefly here for the case of plant-derived vaccines, is a precondition of socially responsible, ethically defensible new biotechnology introductions.

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