

Needed: models of biotechnology intellectual property

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Although never uncontroversial, intellectual property rights in biotechnological innovation are once more the focus of intense debate. The debate has yet to reach any result, largely because of several important errors in the way that various disciplines approach it. These errors include making assumptions without empirical basis and conflating various intellectual property regimes. What is needed is a transdisciplinary integrated method to correct these errors. Such a method can be implemented through the construction of alternative models of intellectual property protection designed to balance the various social, ethical and economic constraints that affect biotechnology.

Published online: 31 May 2002

Biotechnology patents are back on the negotiating table. A group of developing countries has proposed, for example, that the World Trade Organization (WTO) should loosen trade rules contained in the Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPs). They argue that nations ought to be able to issue compulsory licenses over patented inventions as well as permit importing of cheaper versions of an invention from low-priced markets. The impetus for this proposal is the behavior of pharmaceutical companies in enforcing their patent rights in the face of the AIDS crisis in much of the developing world. Meanwhile, the French government is refusing to implement part of the European directive on the legal protection of biotechnological inventions: that provision requiring the granting of patents over human genetic material [1]. This follows years of problems in passing and then implementing the directive [2].

Controversies over biotechnology patents have never really gone away. Proposals by African countries that would virtually eliminate patents over biological materials [3] and recent concerns in France and Canada about access to genetic tests for predisposition to breast cancer [4,5], center on biotechnology patents. The academic literature also points to significant concern in relation to the effects that biotechnology patents have on health care, biodiversity and environmental safety, the sharing of benefits arising from research, and the discovery and dissemination of new agricultural and health-enhancing products and processes [6–11]. Similarly, researchers are only just beginning to understand the links between patent

rights and financial investment in the biotechnology industry of developing countries [12,13].

Tragedy of errors

Although laudable, this increased public and academic interest in biotechnology and intellectual property rights is too often premised on several fundamental errors. One of the reasons for this is that although researchers in various fields (including law [2,6,9,10], ethics [7,9,14,15] and economics [11–13,16–30]) have begun to examine the effects of intellectual property rights on biotechnological research and innovation (nationally and internationally) their work has been largely accomplished in isolation from the other fields. Second, despite the assumption within intellectual property systems that they are necessary to encourage research and development, there is only a modest body of empirical evidence to support this in the biotechnology industry [16–18]. Outside of law, we see a third error. Disciplines often confound and conflate different intellectual property rights. For example, despite the substantial theoretical and practical differences between the different intellectual property regimes, there is a tendency to focus on patent rights to the exclusion of other important intellectual property rights such as trade secrets, copyright and database protection. Fourth, most studies ignore the way the biotechnology industry actually uses intellectual property rights and enters into licensing arrangements [13,16,27,30].

Ultimately, these errors result from our fundamental lack of an integrated, transdisciplinary methodology to understand and analyze the social, ethical and economic impact of intellectual property rights. The effect of these errors is to skew discourse in favor of one or another position with respect to biotechnology intellectual property without sufficient empirical or analytical support. These methodological lacunae lead to distorted ethical, legal, management and economic research practices and results. Consequently, intellectual property policy and regulation are severely compromised.

Complexity and compromise

The complex nature of intellectual property rights, differences between the intellectual property regimes of different countries and the impact that international trade law has on intellectual property systems create difficulty for those proposing solutions. Nevertheless, addressing the identified errors will result in better and more fruitful ethical, legal, economic and managerial analysis of intellectual property rights in biotechnological innovation, both nationally and internationally.

Some scholars have made suggestions as to how to alter current intellectual property systems to account for the ethical, social and economic particularities of biotechnology. These efforts are, however, fairly limited in effect. For example, Merges and Nelson

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have argued that more attention ought to be directed at the scope of patent claims (i.e. how much inventive activity is covered by a patent) to address concerns over stifling research [31]. Although this suggestion might help us address concerns such as the access of scientists to patented research tools (e.g. DNA primers and microarrays) [32], further research is needed to address the broader set of issues raised by the possible monopoly power effects of patents, particularly on developing nations. Gold and Caulfield have recently argued that certain ethical concerns, such as the obligation to share the benefits of commercial biotechnology research with those countries from which biological samples were taken, can be addressed through the use of an *ordre public* or morality clause found in the patent legislation of many countries [33]. This clause permits countries to withhold patents in certain circumstances. However, this solution is limited to those patent systems with an *ordre public* clause and does not provide a solution to the broader spectrum of intellectual property rights.

A transdisciplinary and integrated approach

Although there has been a growing understanding of the disparate factors involved in evaluating the effect of biotechnology intellectual property rights, there is a need to consolidate and rationalize this knowledge in a proactive manner. For ethicists, scientists, economists, business people and lawyers to adapt intellectual property regimes to the challenges posed by modern biotechnology, an integrated transdisciplinary method to conduct research in this area needs to be developed. Such a method would avoid the errors described earlier by providing alternative formulations of policy regimes for protecting biotechnological innovation in a manner that accounts for the multitude of social, ethical and market concerns that influence the dynamics of biotechnological research, development and commercialization. To accomplish this, we suggest the creation of concrete models of intellectual property systems informed by different balances of these various concerns. On the one hand, these models will provide researchers with theoretical frameworks that can be applied to data to analyze alternative intellectual property regimes. On the other hand, these models will help researchers evaluate the social and ethical implications of these regimes. The products of both types of research will help policy makers determine the impact of alternative regimes under scenarios relevant to biotechnology and to countries that differ in their abundance of biotechnology resources, cultural and ethical practices, and development of their biotechnology industries.

In creating these models, we should not restrict ourselves to focusing on the regulatory mechanisms that protect intellectual property itself but should return to the long-accepted view that intellectual property regimes be designed to maximize the social benefits of innovation accruing to society. New models must turn inertia-laden intellectual property regimes

away from intellectual property itself towards the issue of distributive justice that underlies calls for broader social access to new intellectual property. For example, harmonization of intellectual property rights at stronger levels is only one of multiple policy alternatives that produce an optimal social welfare level globally [23]. Furthermore, models need to explicitly account for income and wealth redistribution mechanisms for balancing the economic costs and benefits of intellectual property rights across countries, firms and consumers. Only when such redistribution concerns are made explicit in models will it be possible to design policies with incentives that are compatible with developed and developing countries.

These models will have an important proactive role in public policy and academic research. First, they can facilitate public policy debate nationally and internationally on the selection of alternative policy arrangements. Second, the models can serve as starting points for the formulation of countries' (most particularly, developing nations) negotiating positions on international conventions. These include TRIPs made as part of the WTO agreements and agreements made under the auspices of the World Intellectual Property Organization. For example, parties to the WTO are currently reviewing the provisions of the TRIPs agreement that deal with patenting plants and animals, leading certain developing nations to call for a re-opening of the agreement. Third, the models can serve as multidisciplinary research tools for those conducting health policy, economics, law, philosophy and/or political science research around the world.

Conclusion

Methodologically, we have to treat intellectual property as a transdisciplinary issue, not as a protected silo of legal and regulatory interest. We need to challenge the presumption that regulatory regimes demand uniformity in intellectual property legislation. Greater diversity in intellectual property regulation would better address the different and often highly specialized contexts in which the social benefits of intellectual property might be maximized. Context-specificity might require different kinds of legal protocols as are appropriate to the technology and domain of application. Our models will provide the methodological underpinnings necessary to sort out the issues and to provide a starting point for informed future research and negotiation.

Essentially, what is called for is a reorientation in our thinking so that the social benefits of intellectual property might be proactively wrestled out of the hands of social systems that, by their very nature, are reactive and conservative. Biotechnology has already challenged the way we think about ourselves and our environment. It is time that it also challenged our assumptions and complacency about intellectual property law.

Acknowledgements

We acknowledge the assistance of Wendy Adams of the Faculty of Law at the University of Western Ontario, and Amy J. Glass of the Dept of Economics at Texas A&M University, for their comments and suggestions.

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Toxicogenomics and toxic torts

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One of the first practical applications of toxicogenomics will probably be in the context of toxic tort personal injury litigation. Gene expression changes that 'fingerprint' exposure to particular classes of toxic substances can potentially be used to demonstrate exposure, prove causation and support novel damage claims in lawsuits brought by citizens injured by toxic exposures. Although the potential use of toxicogenomic data in toxic tort litigation is immense, there is a danger of premature use of such data before they have been adequately validated and characterized.

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Toxicogenomics is the study of the response of the genome to toxic agent exposure; it has been described as 'a tool of unprecedented power' in toxicology [1]. The term 'toxicogenomics' in its broadest meaning encompasses profiling of gene expression, protein composition (proteomics) and the metabolic constituents (metabonomics) of a cell. A key toxicogenomic technique is to profile (using a DNA microarray or 'gene chip') the

cell-wide changes in gene expression following exposure to toxins. This approach creates the potential to provide a molecular 'fingerprint' of exposure or toxicological response to specific classes of toxic substances [1–3].

Gene expression changes measured by DNA microarrays can provide a more sensitive and characteristic marker of toxicity than typical toxicological endpoints such as morphological changes, carcinogenicity and reproductive toxicity [4]. Moreover, altered gene expression can occur immediately following exposure, whereas the clinical manifestation of toxicity might take days, months or even years to develop. Initial 'proof-of-principle' experiments have successfully identified the category or toxicological mechanism of toxic chemicals on the basis of their gene expression profiles [3,5,6]. The potential promise of this technology is enormous. For example, DNA microarrays could be used to identify or confirm the category of toxic substances to which an individual was exposed, based on gene expression profiling.

Notwithstanding the tremendous potential of gene expression profiling, many obstacles and uncertainties remain to be resolved before toxicogenomic data should be used outside the research context for practical, regulatory or legal applications [7,8]. The toxicological significance of gene expression changes must be validated, including