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Intellectual Property Issues in Biotechnology: Health and Industry

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1. Introduction

If a true “modern bioeconomy”² is to emerge in the years ahead, intellectual property will no doubt play a critical role. Intellectual property rights – the manner in which they are recognised, traded and managed, nationally as well as globally – will influence the form such a bioeconomy takes, where it will flourish and flounder, and to whom the principal benefits will flow. The general aim of this paper is to canvass those issues. In summarising the available evidence about intellectual property’s impact upon incentives and access, and applying that body of evidence to the health and industrial biotechnology sectors, we may formulate a rough forecast of our bioeconomic future.

Cognisant, however, that intellectual property increasingly constitutes the terrain upon which disputes over North-South inequalities are waged, our paper also attempts to place its analysis within current international discourse, as evidenced by the WIPO Development Agenda and the WHO’s Intergovernmental Working Group on Public Health, Innovation and Intellectual Property. Throughout our analysis we endeavour to take the present “development divide”³ into account, recognising that the emergence of a modern bioeconomy portends, in the eyes of some, a new dimension of wealth and health inequity along a “biotechnology divide”,⁴ or else risks being perceived as a mechanism that helps perpetuate the status quo.⁵ While it is clearly premature to determine the truth behind any such allegation – the evidence of social welfare impacts of increased intellectual property protections in developing countries in the “post-TRIPs” era is, thus far, unclear⁶ – it would be a mistake to ignore it, as it shapes how different countries and regions understand and discuss intellectual property. In any event, to the extent that one is concerned with the impact of the bioeconomy on (especially developing) countries, one cannot ignore the importance of distributive justice in one’s analysis. The promise of a bioeconomy ought, therefore, to be connected to something greater than economic growth in and of itself.⁷ Indeed, developing countries have been encouraged to revamp or fundamentally alter their intellectual property systems in line with systems of the West on the strength of biotechnology’s promise to deliver nothing short of emancipation. We therefore offer our survey of intellectual property (IP) issues in the context of the current development divide and attendant distributive justice concerns.

In terms of structure, the paper is organised along a temporal dimension. Section 1 canvasses the “state of the art”, utilising the available empirical evidence (from the past, albeit as recent as possible) to probe two intersecting relations: the role IP plays in terms of incentivising biotechnological innovation, and how IP facilitates versus circumscribes access to biotechnological research inputs and outputs. Our analysis of each relation, moreover, reflects the above normative agenda: we highlight ways in which the status quo fails to remedy the development divide while also suggesting potential solutions to address industrial and public health issues in developing country contexts – in essence, performing a global cost-benefit analysis

² For the purposes of this Chapter, we use the term “bioeconomy” in a relatively narrow sense – that is, it is not meant to encompass industrial sectors based on the use of any and all kinds of living materials. That would include *traditional* industries such as forestry, fishing, food processing, and select textiles. Rather, we use the term to capture more *modern* biotechnologies (e.g. technologies based on genetic or cell/tissue engineering), and we focus specifically upon biotechnologies with *health* and *industrial* fields of application. Precise definitions of these terms are offered in the Appendix to this paper.

³ Margaret Chon, “Intellectual Property and the Development Divide” (2006) 27:6 *Cardozo Law Review* 2813 [hereinafter Chon, “Development Divide”].

⁴ E. Richard Gold *et al.*, “The Unexamined Assumptions of Intellectual Property: Adopting an Evaluative Approach to Patenting Biotechnological Innovation” (2004) 18 *Public Affairs Quarterly* 299 [hereinafter Gold *et al.*, “Unexamined Assumptions”].

⁵ Some have argued that the very notion of a bioeconomy and the institutions engaged in exploring the prospect thereof have only reproduced dominant economic ideologies – serving, in other words, as a legitimating programme for wealth and power imbalances extant between the West and the rest. See, e.g., Kean Birch, “The Neoliberal Underpinnings of the Bioeconomy: The Ideological Discourses and Practices of Economic Competitiveness” (2006) 2:3 *Genomics, Society and Policy* 1.

⁶ See for e.g., Carsten Fink & Keith E. Maskus eds., *Intellectual Property and Development: Lessons from Recent Economic Research* (Washington, DC: World Bank, 2005) [hereinafter Fink & Maskus, *Intellectual Property and Development*].

⁷ See Chon, “Development Divide”, *supra* note 3, citing, *inter alia*, Amartya Sen, *Development as Freedom* (New York, NY: Random House, Inc., 1999).

throughout. The first section concludes by foregrounding the risk of continuing to analyse IP issues from within an “innovation versus access” paradigm. Section 2 is best characterised as focusing on the present. We explore several different IP regimes, whether or how they are likely to change or are already changing in response to globalising forces and international institutions, and in turn ponder how those (shifting) regimes could shape the evolution of a bioeconomy for a particular country, region, or perhaps even globally. The second section also considers whether changes in the field of biotechnology itself raise new or pressing IP challenges. Two cases are considered. The first speaks to the increasingly globalised nature of scientific research, by examining the patentability of stem cell technologies around the globe and delving into a host of other IP issues raised by one large-scale cross-border research initiative, the “Cancer Stem Cell Consortium” proposed between Canada and the State of California. The second case study zeroes in on one emerging area of biotechnology, synthetic biology, and evaluates whether it represents a “perfect storm” of IP problems as some commentators allege.⁸ Section 3 concludes the paper with a set of general remarks and cautious predictions about the future, the onset of a viable modern bioeconomy, and the place of IP in terms of advancing distributive justice concerns within each.

A final introductory word about scope: our review of the evidence and analysis of diverse IP regimes is necessarily overarching in nature and subject to certain limitations, including space. We are also working with certain definitions of “health” and “industrial” biotechnology and, insofar as possible, attempting to limit our inquiry with those definitions in mind.⁹ However, as explained next, the available evidence is far from complete, which requires us to stray outside these parameters on occasion. Further, given the general scarcity of evidence, we presume (unless there are particular reasons for resisting this) that what applies in one area applies in others. This is particularly true with regard to industrial biotechnology, which has been very lightly treated in comparison with the more widely studied health biotechnology. While there are obvious differences between health and industrial biotechnology – in terms of both industrial structure and policy implications – we have drawn on existing knowledge of the former to inform our analysis of the latter. Finally, while the analysis does contemplate multiple forms of IP protection (copyright; trade secrets; know-how), it is heavily skewed towards patent rights as they are the dominant, if not preferred, mode of IP protection in the biotechnology realm, not to mention the most studied and controversial.

2. State of the Art

2.1 Evidentiary Limitations

The assumption that intellectual property rights generally, and patent rights in particular, are crucial if not absolutely necessary to foster innovation is deeply engrained in governmental policy making and judicial reasoning in many developed countries.¹⁰ Nevertheless, even in the pharmaceutical and biotechnology sectors where the case for intellectual property appears strongest owing to high R&D costs, lengthy time to market, etc., there remains only a “modest body of evidence” to support this thinking.¹¹ Early empirical

⁸ Arti Rai & James Boyle, “Synthetic Biology: Caught between Property Rights, the Public Domain, and the Commons” (2007) 5:3 PLoS Biology 389 [hereinafter Rai & Boyle, “Synthetic Biology”].

⁹ Definitions of these categories are provided in the Appendix.

¹⁰ Gold *et al.*, “Unexamined Assumptions” *supra* note 4.

¹¹ E. Richard Gold *et al.*, “Needed: models of biotechnology intellectual property” (2002) 20:8 TRENDS in Biotechnology 327, citing A.J. Glass & K. Saggi, “Licensing versus Direct Investment: Implications for Economic Growth” (2002) 56 J. Int. Econ. 131; N. Gallini & S. Scotchmer, “Intellectual property: when is it the best incentive system” In *Innovation Policy and the Economy*, vol. 2, Jaffe *et al.* eds. (MIT Press: 2001) at 51; and, Keith E. Maskus, *Intellectual Property Rights in the Global Economy*, Institute for International Economics, Washington DC (2001).

studies of individual countries performed in the 1960s found that patents positively influenced levels of innovation by 15-25%.¹² But as Gold *et al.* explain in detail:

More recent work has...cast doubt on this conclusion. The international economics literature considers cross-country differences in patent systems and the implications of these differences for economic behavior. The link between patents and innovation in the multi-country (open economy) is less clear.

Even within a closed economy, patents on initial innovations may deter later discoveries that build on patented innovations. There are also structural reasons to believe that one can never know, in fact, whether patents actually encourage or discourage innovation. First, [...] while patent law takes a “one-size-fits-all” approach to innovation, the markets for different products and knowledge assets differ significantly from one another. Second, the empirical study of the effects of patents on innovation suffers from the lack of control. Given that innovation is driven by many factors (including access to capital, access to skilled managers, first mover advantage, curiosity, *etc.*), cross-jurisdictional comparisons are difficult. Since countries rarely radically change their patent systems without changing fundamental aspects of their economies, single jurisdiction controls are usually lacking. Several studies that examine changes within a single jurisdiction – the semi-conductor industry in the US between the 1970s and 1980s and the strengthening of the Japanese patent system in the 1980s – indicate that patents either reduced innovation or had no effect. Third, [...] industry rarely relies solely on a single patent to secure its inventions. Normally, firms use a combination of patents, trade secrets, and even trademarks to protect their innovations. In addition, firms also use other mechanisms such as complementary asset management (by forming alliances) and innovation lead-time to gain advantage over competitors.

All of these intellectual property management mechanisms make it difficult, if not impossible, to isolate the effect of patents on innovation.¹³

Yet many countries consider patents “to encourage the right kind of innovation” and have “not only unconditionally [accepted] the assumption that the patent system is economically efficient, but also institutionalize[d] this assumption by relying to an ever-greater degree on patent protection as a policy tool.”¹⁴ The effects of this policy shift are readily observable (although factors other than policy change are also at work, including, notably, the maturation of the biotechnology sector itself).¹⁵ The number of patent applications filed and associated activities (*e.g.* licensing agreements entered into; start-up companies formed) have increased exponentially over the last two to three decades.¹⁶ The number of technology transfer offices – the entities largely responsible for executing these activities – at academic research institutions has also grown dramatically during the same period.¹⁷

¹² Gold *et al.*, “Unexamined Assumptions”, *supra* note 4 at 303-04, citing M. Schankerman, “How Valuable Is Patent Protection? Estimates By Technology Field” (1998) 29:77 *RAND J. of Economics* 77; M. Schankerman & A. Pakes, “Estimates of the Value of Patent Rights in European Countries During the Post-1950 Period” (1986) 96 *The Economic Journal* 1052; E. Mansfield, M. Schwartz & S. Wagner, “Imitation Costs and Patents: An Empirical Study” (1981) 91 *The Economic Journal* 907.

¹³ Gold *et al.*, “Unexamined Assumptions”, *supra* note 4.

¹⁴ Gold *et al.*, “Unexamined Assumptions”, *supra* note 4 at 307.

¹⁵ D.C. Mowery, R.R. Nelson, B.N. Sampat, & A.A. Ziedonis, “The Growth of Patenting and Licensing by U.S. Universities: An Assessment of the Effects of Bayh-Dole Act of 1980” (2001) 30 *Research Policy* 99.

¹⁶ *Ibid.*

¹⁷ For example, although less than a handful of U.S. universities had created organizations like WARF to manage patent portfolios in the early twentieth century, only 27 TTOs existed before 1980. During the “boom” years of 1983 to 1999, however, 122 offices were created in the U.S. See Association of University Technology Managers, *AUTM U.S. Licensing Survey: FY 2005, Survey Summary*, at 17 (2007), online: <[http://www.autm.net/events/File/US_LS_05Final\(1\).pdf](http://www.autm.net/events/File/US_LS_05Final(1).pdf)> (visited Apr. 11, 2007). The first three TTOs in Canada were established during the 1970s at McGill University, L’Ecole Polytechnique, and Cape Breton University.

While a host of concerns have been levied against this state of affairs, alleging that the practice as well as the integrity of the scientific research is under unprecedented threat (by virtue of patent blocking, hold-up, royalty stacking, or so-called “anticommons” issues, and the inevitable skewing of research agendas),¹⁸ to date the evidence has generally not borne them out.¹⁹ Recently, new evidence of a modest anticommons effect has surfaced but clearly more empirical research is necessary.²⁰ Still, biotechnology research, its many sub-disciplines and offshoots, is not grinding to a halt. And this is notwithstanding infamous examples such as Myriad Genetics Inc.’s alleged attempt to assert its patent rights against health care providers in Europe, Canada and elsewhere performing diagnostic tests for genetic alleles correlated with breast cancer. Rather, members of the research community have adopted “working solutions” to circumvent additional costs of patent rights, operated on the assumption that a research exemption will immunise them from liability in the event of an infringement action, or chosen to remain ignorant of any patent rights implicated by their line of research inquiry.²¹

In this regard too, however, the evidence is deficient or inconclusive. As explained in greater detail below when considering the relation between IP and access to research inputs and outputs, some level of concern exists that these working solutions may mask subtler research shaping effects tied to who can participate in the research process and what types of research they are apt to engage in. In one field of biotechnology, diagnostic testing, there is a reasonably strong empirical basis to believe that there is a *bona fide* problem. How far this extends within health biotechnology remains unknown. Overall one can conclude that, while patent rights may not be impeding research and development in general, they are, by direct or indirect means (including through miscommunication), impeding health care delivery.²² As biotechnology progresses further and further away from a single mutation, single function model towards a more complex analysis of multiple genes, their functions, and complicating environmental factors, some suggest that anticommons-type problems are more likely to ensue.²³ Given our limited state of knowledge, one cannot make similar statements in respect of industrial biotechnology.

Thus, broadly speaking, the evidence is inconclusive in terms of how important or detrimental IP rights can be to progress in health and industrial biotechnology. And as a result, stakeholders on all sides of the debate have become selective in what evidence they choose to pay attention to or invoke, the increasing polarisation and contributing to the present impasse over what, if anything, should be done. However, it is critical to recognise how non-stated assumptions about what counts as a positive versus negative effect of patents contribute to this impasse. Commentators’ conclusion as to whether an anticommons exists, for instance, often turns upon whether or not they foresee certain things (*e.g.* the ability to negotiate a material transfer agreement) as being linked directly to patent rights.²⁴ In our view, it is better to adopt a

Eleven “key” Canadian universities followed suit during the 1980s. See Donald Fisher & Janet Atkinson-Grosjean, “Brokers on the Boundary: Academic-industry Liaison in Canadian Universities” (2002) 44 *Higher Education* 449.

¹⁸ Various terms are used but there are essentially two types of problems, each of which is explained in subsection 1.3.1 below.

¹⁹ T. Caulfield, R. Cooke-Deegan, S. Kieff & J. Walsh, “Evidence and Anecdotes: An Analysis of Human Gene Patenting Controversies” (2006) 24:9 *Nature Biotechnology* 1091 [hereinafter Caulfield *et al.*, “Evidence and anecdotes”].

²⁰ Moreover, as Gold *et al.* explain in response to Caulfield *et al.*, “Evidence and anecdotes”, *ibid.*, policy makers may not have the luxury of waiting as they “must make their decisions here and now based on the evidence that does exist and the best hypotheses available. The health care system cannot wait, for example, for the true dimensions of the anticommons problem to be clear before addressing pressing political and social issues...” See E. Richard Gold *et al.*, “Gene Patents – More Evidence Needed, But Policymakers Must Act” (2007) 25:4 *Nature Biotechnology* 388 [hereinafter Gold *et al.*, “Gene patents”].

²¹ For a summary of these findings see Caulfield *et al.*, “Evidence and anecdotes”, *supra* note 19.

²² See Gold *et al.*, “Gene patents”, *supra* note 20.

²³ John H. Barton, “Emerging Issues in Genomic Diagnostics” (2006) 24 *Nature Biotechnology* 939 [hereinafter Barton, “Emerging issues”]; and, National Research Council, *Reaping the Benefits of Genomic and Proteomic Research* (National Academies Press, Washington D.C.: 2006) [hereinafter NRC, *Reaping the Benefits*].

²⁴ For an in-depth discussion of this example in particular, see Section 1.3.1 below.

consequentialist perspective when identifying the positive and negative effects of patent rights. From this perspective, patents are justified to the extent that the direct and indirect consequences of their existence increase wealth, health, and industrial practices more than they harm these. True, they may have positive or negative effects on other walks of life, but those will be too hard to identify let alone measure. What is important to note, rather, is that effects (positive and negative) are not those that arise from a reading of applicable patent legislation, but rather from how real people actually react and deal with IP. Therefore, if IP rights are so confusing that people stay away from some research or if there is a miscommunication that leads people to not conduct certain work, that negative effect is, from a consequentialist perspective, accurately attributable to IP. Indeed, in hindsight, Myriad Genetics' main mistake appears to have been in failing to effectively communicate its business plans; it claims never to have intended to exercise its patent rights against health care providers. But because of how its actions were perceived, this instance is rightly characterized as a patent problem in our view. Conversely, if a patent law prohibits certain behaviour that in practice is nevertheless widespread, then this is not a negative effect of patents. This explains, we suggest, the findings of Walsh *et al.*²⁵ that the fact that the United States possesses no research exception does not impede research, as researchers simply *act* as if such an exception existed. In short, an anticommons or blocking situation that may not have to do with patent law *per se* remains patent law's problem if researchers or other potential users act as if patent law prevents them from doing something. This does not mean that the solution to the problem is necessarily a change to patent legislation, but it nevertheless counts as a cost of the patent system writ large.

In addition to limitations due to a general lack of evidence, this conceptual distinction is very seldom acknowledged in the literature. As we turn to examine IP rights as incentives to innovate, and as barriers or drivers of access, these limitations should thus be kept in mind and will resurface. Evidence regarding biotechnology-related IP issues in the developing country context, positive or negative, carefully defined or otherwise, is, moreover, almost entirely lacking.²⁶

2.2 Incentives to Innovate

2.2.1 Nature of the innovation

The classic and, as yet, still dominant rationale for granting IP rights is to incentivise creativity and innovation.²⁷ However, while economists have long been able to show that *some* incentive to encourage innovation is needed,²⁸ it remains contentious whether IP rights versus other rewards such as prizes and

²⁵ J.P. Walsh, A. Arora & W.M. Cohen, "Science and the Law. Working Through the Patent Problem" (2003) 299 *Science* 1021 [hereinafter Walsh, Arora & Cohen, "Working Through the Patent Problem"]; and, J.P. Walsh, C. Cho & W.M. Cohen, "Science and Law. View from the Bench: Patents and Material Transfers" (2005) 309 *Science* 2002 [hereinafter Walsh, Cho & Cohen, "Patents and Material Transfers"].

²⁶ Keith Maskus, for instance, concludes that there is a lack of overall evidence with respect to developing countries, which are, by no means, all alike. The most positive impact seems to be in FDI [foreign direct investment – the investment of a firm directly into the economy of another country, often through a subsidiary] but it is unclear how this balances against access. See, for *e.g.*, Fink & Maskus, *Intellectual Property and Development*, *supra* note 6.

²⁷ See for example Mark A. Lemley, "Ex Ante versus Ex Post Justifications for Intellectual Property" (2004) 71:1 *University of Chicago L. Rev.* 129 [hereinafter Lemley, "Ex Ante versus Ex Post"]. We note that other justifications for granting patent rights, such as their diffusion function, turn out to be unconvincing. The evidence to date is that patents are a poor source of information. See, for example, A. Arundel & E. Steinmueller, "The use of patent databases by European small and medium-sized enterprises" (1998) 10 *Technology Analysis and Strategic Management* 157; James Bessen, "Patents and the diffusion of technical information" (2005) 86 *Economics Letters* 121.

²⁸ K. Arrow, "Economic Welfare and the Allocation of Resources for Invention", in Universities-National Bureau of Economic Research Conference. Series, *The Rate and Direction of Economic Activities: Economic and Social Factors* (Princeton, Princeton University Press: 1962).

government grants offer the best alternative.²⁹ Innovation will, moreover, not cease to occur without IP rights, and not simply because of non-economic motives to invent or governmental subsidies.³⁰ The evidence to date paints a much more nuanced picture where the relative importance of IP rights (patents especially) is contingent upon the nature of the innovation process in each particular industry or sector. Dan Burk and Mark Lemley explain:

[I]nnovation differs by industry in a variety of ways. Each distinct technology displays an idiosyncratic profile of technical and economic determinants for research, development, and return on investment. Given this, there is no *a priori* reason to believe that a single type of legal incentive will work best for every industry. Indeed, there is every reason to believe that achieving optimal innovation in different industries will require greater or lesser measures of legal incentive, and in some cases perhaps even no legal incentive at all.³¹

The strongest support for the incentivising effects of patents across all industries emanates from the pharmaceutical industry. Major cross-sectoral studies conducted by both Levin *et al.* and Cohen *et al.* in the 1980s and 1990s, respectively, found that R&D managers in pharmaceutical companies attributed significantly more importance to patent rights relative to their counterparts in other sectors.³² Earlier studies by Mansfield as well as Taylor and Silberston reported similar findings, and these findings appear to hold across jurisdictions.³³ Returning to Burk and Lemley's point, the underlying reason why such importance is attributed to IP stems from the nature of innovation in the pharmaceutical industry: the costs associated with developing (new) drugs are relatively high whereas the costs of imitating them through reverse engineering are relatively low.³⁴ Few pharmaceutical compounds survive the length of the entire clinical trial process. The logic is thus that patents – as a means to recoup R&D costs associated with all of the failures as well as the few that succeed – are needed to induce a company to take on those risks.

Early studies of health-related biotechnological products reported significantly lower attrition rates and clinical development times.³⁵ More recent studies with larger sample sizes contradict these findings, however, and suggest that these R&D and regulatory “costs” may be very similar to the pharmaceutical

²⁹ See Nancy Gallini and Suzanne Scotchmer, “Intellectual Property: When Is It the Best Incentive System?”, in 2 *Innovation Policy and the Economy* 51, Adam B. Jaffe *et al.*, eds., 2001; Brian D. Wright, *The Economics of Invention Incentives: Patents, Prizes, and Research Contracts*, (1983) 73 *An. Econ. Review* 691.

³⁰ See Lemley, “Ex Ante versus Ex Post”, *supra* note 27 at 130, citing Michael Abramowicz, “Perfecting Patent Prizes” (2003) 56 *Vand. L. Rev.* 115; Steven Shavell and Tanguy van Ypersele, “Rewards versus Intellectual Property Rights” (2001) *J. L. & Econ.* 525 at 537-540; and, Yochai Benkler, “Coase’s Penguin, or, Linux and the Nature of the Firm” (2002) 112 *Yale L.J.* 369.

³¹ Dan L. Burk & Mark A. Lemley, “Policy Levers in Patent Law”, *Social Science Research Network Electronic Paper Collection*, online: <<http://ssrn.com/abstract=431360>> [hereinafter Burk & Lemley, “Policy Levers”].

³² Richard D. Levin *et al.*, “Appropriating the Returns from Industrial Research and Development” (1987) *Brookings Papers on Economic Activity* 783; W. Cohen *et al.*, “Appropriability Conditions and Why Firms Patent and Why They Do Not in the American Manufacturing Sector” Working Paper (Pittsburgh: Carnegie-Mellon University 1997).

³³ C.T. Taylor and Z. A. Silberston, *The Economic Impact of the Patent System* (Cambridge, UK: Cambridge University Press, 1973); Edwin Mansfield, “Patents and Innovation: An Empirical Study” (1986) 32 *Management Science* 175. In Europe, Arundel and Kabla determined that only firms operating within four industrial sectors – pharmaceuticals and chemicals chief among them – were more likely than not (*i.e.* in greater than 50% of cases) to file a patent application in respect of a particular innovation. Analogously, a study conducted in Switzerland found that patents were regarded as an effective means of appropriation by R&D managers in only a few industries, most notably again, pharmaceuticals. See, respectively, Anthony Arundel & Isabella Kabla, “What Percentage of Innovations are Patented? Empirical Estimates for European Firms” (1998) 27 *Research Policy* 127; Najib Harabi, “Appropriability of Technical Innovations: An Empirical Analysis” (1995) 24 *Research Policy* 981.

³⁴ See *e.g.* Henry Grabowski, “Patents, Innovation and Access to New Pharmaceuticals” (2002) 5:4 *Journal of International Economic Law* 849.

³⁵ Henry Grabowski, “Patents and New Product Development in the Pharmaceutical and Biotechnology Industries” (Working Paper No. 02-25, Duke University, Department of Economics, online: <<http://econpapers.repec.org/paper/dukdukeec/02-25.htm>> (visited Dec. 10, 2007) [hereinafter Grabowski, “New Product Development”], discussing Brigitta Bienz-Tadmor *et al.*, “Biopharmaceuticals and Conventional Drugs Clinical Success Rates” (1992) 10 *BioTechnology* 521; and, M.M. Struck, “Biopharmaceuticals R&D Success Rates and Development Times” (1994) 12 *BioTechnology* 674.

sector.³⁶ That biotech companies spend far more of their total budgets on patent prosecution compared with other types of technology companies supports the same inference.³⁷ Increasing patent protection, moreover, “gives a substantial boost to R&D in drugs and biotechnology, but much less additional innovation in other fields such as electronics and semiconductors.”³⁸ Again, the evidence concerning industrial biotechnology is simply lacking. However, it is unlikely that this sector places the same reliance on patents as either the pharmaceutical or biopharmaceutical sectors. Regulatory requirements that are less burdensome in both time and cost and lessened liability concerns would suggest that the industrial biotechnology sector would resemble other science-based but non-health-related industries where there is only a moderate level of reliance on patents. However, this is simply informed speculation: an empirical study is required to determine whether the anticipated pattern emerges.

Even in the pharmaceutical and biopharmaceutical sectors, some argue that these findings merely show that “some mechanism is necessary to promote innovation in this sector, and those firms that dominate under the current system are dependent upon the tools that brought them to dominance.”³⁹ In other words, new business models that are less predicated on securing patent rights and/or exercising the legal monopolies they confer primarily for financial gain purposes could alter the present equation. This argument is usually invoked in support of a shift towards a more equitable use of patent rights – to increase, for instance, generic drug production in low- and middle-income countries, or in support of research on “neglected diseases” – in the service of public health goals. We canvass these proposals below. However, for the time being, one could argue that advances in health biotechnology are already challenging the “blockbuster”-type business model popularised by pharmaceutical companies. To begin with, the market for many health biotechnology products is generally far smaller than for drugs. And while it is conceivable that certain platform technologies such as stem cells could lead to a vast array of clinical applications, the lag in time and uncertainties involved in translation have rendered consistent private venture capital financing difficult to sustain, causing a number of firms – even those holding key IP rights in the field – to alter their course.⁴⁰ To compensate, massive new injections of public funding have been devoted to stem cell research in some jurisdictions.⁴¹ Thus, while IP is certainly still being sought in connection with these initiatives, it is clearly not sufficient in and of itself to see the entire R&D process through to its conclusion.

Further, health biotechnologies have a distinct market advantage over traditional pharmaceuticals. Whereas the regulatory burden imposed on generic pharmaceutical manufacturers is relatively light compared to the original manufacturer, the same is not true of generic biologics. This is because pharmaceuticals are often simple molecules. A generic manufacturer of those molecules must simply demonstrate that it is able to produce the same molecule as the original manufacturer. A biologic is a complex (sometimes living) material that cannot be easily copied. A generic manufacturer can rarely simply recreate the same biologic. Instead, it will produce a similar one. As there is no guarantee that two similar biologics will act in the same way, the generic manufacturer must run a full set of clinical trials to prove the safety of the biologic. This increased regulatory burden both slows down and increases the cost of generic competition for the original biologic. Thus, even without patent rights, first mover advantage is strong.

³⁶ Grabowski, “New Product Development”, *ibid.* See also E. Richard Gold, “Biomedical Patents and Ethics: A Canadian Solution” (2000) 45 McGill Law Journal 413.

³⁷ Burk & Lemley, “Policy Levers”, *supra* note 31.

³⁸ Burk & Lemley, “Policy Levers”, *supra* note 31 at 22.

³⁹ Amy Kapczynski, Samantha Chaifetz, Zachary Katz, & Yochai Benkler, “Addressing Global Health Inequities” Berkeley Tech. L. J. [hereinafter Kapczynski *et al.*, “Global Health”].

⁴⁰ See V. Brower, “Human ES Cells: Can You Build a Business around Them?” (1999) 17 Nature Biotechnology 139; E. Marshall, “The Business of Stem Cells” (2000) 287 Science 1419; G. Vogel, “Stem Cells Lose Market Luster” (2003) 299 Science 1830; and, L.B. Giebel, “Stem Cells – A Hard Sell to Investors” (2005) 23 Nature Biotechnology 798.

⁴¹ E.g. S. Herrera, “Leaders and Laggards in the Stem Cell Enterprise” (2005) 23 Nature Biotechnology 775.

Perhaps, then, a variant of the incentive theory of IP rights first articulated by Edmund Kitch as the “prospect theory” of patent rights,⁴² but framed more recently by others as “commercialisation theory,”⁴³ offers added justification. This theory essentially holds that IP rights are necessary to efficiently coordinate actors and resources for the purpose of developing a given (health, industrial or other) technology into a marketable product. As Lemley convincingly argues, however, the notion that the initial inventor (or her/his/their assignee) is better positioned to control and coordinate subsequent research and technology development relative to a competitive marketplace simply does not hold, empirically or even theoretically, across industrial sectors.⁴⁴ Rather, “[p]rospect theory is needed [or adds explanatory value to the classic public goods story] when control over subsequent development is a necessary part of the incentive to produce the pioneering invention in the first place, as is arguably true with pharmaceuticals.”⁴⁵ But justifying IP rights as a mechanism to increase commercialisation without regard to the nature of innovation in a particular industry and attention to relevant market factors would seem incorrect or at least vastly incomplete.

The relative importance of IP rights as incentives in the context of a modern bioeconomy will, then, ultimately turn upon the nature of the biotechnology in question – whether it is health or industrial related, whether it is a broadly enabling or a downstream application – the business model to be employed, and other non-IP factors (*e.g.* costs of the regulatory process; whether possess first-mover advantage).

2.2.2 Transplanting IP to developing countries

Even if we are willing to accept that IP rights (especially patents) provide a necessary incentive for biotechnology companies to engage in the R&D process, it is unmistakably clear that they are insufficient incentives to address the particular health and industrial needs of the world’s poor.⁴⁶ To be precise, IP rights, as incentives, fail in two key respects. First, they fail to provide sufficient incentive to develop products that are particular to many developing countries. Between 1975 and 1996, for example, merely 1% of new drugs were designed to treat so-called “tropical diseases”.⁴⁷ Second, IP rights fail to incentivise the optimisation of existing products and devices for delivery and use in developing country settings.⁴⁸ In the health care field, this latter shortcoming, without detracting from the importance of developing treatments for tropical and other “neglected diseases”, is clearly the more pressing issue. “It is”, as Kevin Outterson exclaims, “the poor themselves who are neglected, rather than just their diseases”.⁴⁹ Ninety per

⁴² Edmund W. Kitch, “The Nature and Function of the Patent System” (1977) 20 J. L. & Econ. 265

⁴³ See, *inter alia*, F. Scott Kieff, “Property Rights and Property Rules for Commercializing Inventions” (2001) 85 Minn. L. Rev. 697.

⁴⁴ Lemley, “Ex Ante versus Ex Post”, *supra* note 27 at 140-41.

⁴⁵ *Ibid.*

⁴⁶ This is most obvious in the health care field although the same logic applies, in principle, to industrial biotechnology. In the health care field, strong evidence exists that worldwide health R&D expenditures focus disproportionately on the needs of the developed world and insufficiently on adapted medicines to developing countries or to addressing those health needs that only exist (except at the margins) to developing countries. See United Nations Dev. Programme, *Incentives to Reduce the 10/90 Gap* (2002).

⁴⁷ O. Trouiller and P.L. Olliaro, “Drug development output from 1975 to 1996: What Proportion for Tropical Diseases?” (1999) 3 Int. J. Infect. Dis. 61. See also Jean O. Lanjouw, “Intellectual Property, and the Availability of Pharmaceuticals in Poor Countries” (Center for Global Development Working Paper No. 5, April 2002), Social Science Research Network, online: <<http://ssrn.com/abstract=999982>>.

⁴⁸ Medecins Sans Frontieres & Drugs for Neglected Diseases Working Group, *Fatal Imbalance – The Crisis in Research and Development for Drugs for Neglected Diseases* (2002); Patrice Trouiller *et al.*, “Drug Development for Neglected Diseases: A Deficient Market and a Public-Health Policy Failure” (2002) 359 Lancet 2188; Warren Kaplan and Richard Laing, World Health Organization, *Priority Medicines for Europe and the World* (2004): <<http://mednet3.who.int/prioritymeds/report/index.htm>>;

⁴⁹ Kevin Outterson, “Access to Global Disease Innovation” (Submission to World Health Organization Inter-governmental working group, November 15, 2006), online: <http://www.who.int/phi/public_hearings/first/15Nov06KevinOutterson.pdf>.

cent of the disease burden in least developed countries is exactly the same (albeit with varying proportions) as in developed countries.⁵⁰ But there is simply very little to zero market incentive for IP rights holders to adapt existing therapies – developing, for example, fixed-dose combinations of HIV/AIDS antiretrovirals or formulations suitable for children – for use by afflicted populations in the developing world. Again, while there is a lack of empirical study, there is no reason to believe that same phenomenon – given the different levels of infrastructure such as a steady electricity supply, clean water and different education and skill levels – does not exist in the industrial biotechnology sector.

What is more, there is reason to believe that exceptional cases, in which an actor is committed to adapting products in relation to developing country needs, are more likely to fail. Again, drawing on evidence in the biopharmaceutical sector, while increased transaction costs associated with the proliferation of patent rights may not stop commercially valuable research, they can significantly complicate and preclude research at academic and non-profit institutions working to produce products for the developing world.⁵¹ “Indeed, several of the concrete examples we have of patent thickets that have caused lengthy delays, or of broad and exclusively licensed research tool patents that have obstructed research initiatives, relate to products intended for developing countries.”⁵²

In an effort to address or mitigate these shortcomings in the health sector, proposals for complementary incentive mechanisms such as direct government grants to the private sector, “advance market commitments” and “prize funds” have been made. A few pilot studies are under way, but there are presently no empirical data as to whether these mechanisms provide sufficient or even significant added incentives to encourage researchers and firms to engage in R&D projects intended to address the health problems of poorer peoples. And even where such mechanisms do guarantee net profits, they still may not be sufficient to encourage larger firms, or at least larger firms in the Western world, because of the “opportunity costs” associated with foregoing other areas of R&D with Western markets.⁵³ Unfortunately, not only does there exist less (or no) evidence about the effect of these alternative mechanisms on industrial biotechnology in developing countries, but there has been little effort to even adapt these alternatives to the needs of the industrial sector.

2.3 Access Quagmires

Questions surrounding IP and incentives inevitably dovetail with questions of access. Diminutions of patent rights, one argument goes, will lead private actors to rely instead on trade secret protection, denying the public the knowledge and information conveyed in the body of the patent itself. Another common view is that any reduction in the incentives that patents provide will reduce the number of new products from the R&D pipeline. In the following subsection we put these large claims to the side as they are not subject to empirical verification; rather, we more rigorously investigate how IP rights – again focusing

⁵⁰ The common set of illnesses include cancer, heart disease, HIV/AIDS, and pulmonary diseases; see, for *e.g.*, E. Richard Gold, Tina Piper, Jean-Frederic Morin, L. Karen Durell, Julia Carbone & Elisa Henry, “Preliminary Legal Review of Proposed Medicines Patent Pool”, study commissioned by the World Health Organization, July 26, 2007 (manuscript on file with author) [hereinafter Gold *et al.*, “Proposed Medicines Patent Pool”].

⁵¹ Arti K. Rai, “Proprietary Rights and Collective Action: The Case of Biotechnology Research with Low Commercial Value”, in *International Public Goods and Transfer of Technology Under a Globalized Intellectual Property Regime*, 288, Keith E. Maskus & J.H. Reichman eds., 2005 [hereinafter Rai, “Collective Action”]. See also John P. Walsh *et al.*, “Research Tool Patenting and Licensing and Biomedical Innovation, in *Patents in the Knowledge-Based Economy* 285 at 304, Wesley M. Cohen and Stephen A. Merrill eds. (Washington, DC: National Academies Press, 2003).

⁵² Kapczynski *et al.*, “Global Health”, *supra* note 39.

⁵³ For example, while funds sufficient to guarantee a sizeable profit were offered to a number of large pharmaceutical companies to produce meningococcal conjugate vaccine for use in African countries, none of those firms was willing to accept them because of the opportunity costs of diverting resources away from other more profitable areas of R&D. A group of firms in Asia were, however, willing to co-operate. See L. Jodar *et al.*, “Meningococcal Conjugate Vaccine for Africa: A Model for Development of New Vaccines for the Poorest Countries” (2003) 361 *Lancet* 1902.

primarily on patent rights – as well as contractual agreements entered into in respect of them (“licensing agreements”) or biological materials to which they may attach (“material transfer agreements”) impact the research process, its inputs and outputs. The body of evidence we examine emanates predominantly from the US setting, which we cautiously assume is roughly representative of the situation in other developed nations. In developing countries, the situation may be entirely different. In that context, access to the Internet⁵⁴ is a more immediate concern than access to particular biotechnology inventions, in the sense that knowledge of developments in the field (whether disclosed in publications, online databases, or patent applications) is, by definition, a prerequisite to gaining access to inventions thought to be of use (and any potential barriers that might be encountered at that later stage). Our analysis focuses upon those later stages, but we consider this prior access problem in the subsequent subsection.

2.3.1 Access to research inputs and outputs

Research inputs and outputs can be characterised as falling within three broad, non-mutually exclusive groups: knowledge or data, research materials, and products. Note the contingency of these terms: one entity’s starting material (or input) may be another entity’s end product (or output) if, for example, the latter’s business model consists of selling research tools such as a cell line or plasmid. Access to knowledge, moreover, transcends the upstream/downstream R&D spectrum. Still, these categories are useful to keep in mind as the IP-related access issues (and the extent to which commentators are inclined to frame them as such) vary depending on whether knowledge, materials or products are the objects under consideration.

Infrastructure issues (*e.g.* access to the Internet) aside, difficulty in gaining access to research findings and data appears to be a problem in the field of genetics. A national survey of genetics researchers in the United States (which sampled 1 240 geneticists from among the 100 highest-funded universities) determined that approximately half of the researchers polled were unable to obtain information or materials from another academic researcher, 21% of whom accordingly opted to discontinue their planned line of research inquiry.⁵⁵ While these findings are not directly attributable to the existence of patent rights or patent applications, agreements with industrial sponsors or preserving confidentiality for filing patent applications was the cause in roughly 20% of the cases. The most commonly cited reason for refusing to share data was the “effort required”; however, as others have pointed out, this category “probably also includes costs associated with difficulties in concluding complex negotiations over [material transfer agreements]”.⁵⁶ In other words, this first type of access issue may have more to do with the increasing commercialisation of academic research generally and the accompanying behavioural changes in which the exponential growth of IP rights witnessed in the last quarter-century or so only plays a part.⁵⁷

⁵⁴ As Peter Yu explains:

To date, developed countries account for more than 80 percent of the world market for information technology, while Internet penetration is very limited in sub-Saharan Africa, the Middle East, Latin America, and South Asia. There are 510.5 computers per 1 000 people in the United States, but only 3.2 per 1 000 people in South Asia and 8.4 per 1 000 people in sub-Saharan Africa. Of the estimated 332 million people who use the Internet, less than 1 percent lives in Africa. [footnotes omitted]

See Peter K. Yu, “Introduction to Symposium, Bridging the Digital Divide: Equality in the Information Age” (2002) 20 *Cardozo Arts & Ent. L.J.* 1 at 4.

⁵⁵ Eric G. Campbell *et al.*, “Data Withholding in Academic Genetics: Evidence from a National Survey” (2002) 287 *JAMA* 473. See also D. Blumenthal *et al.*, “Data withholding in genetics and other life sciences: prevalences and predictors” (2006) 81:2 *Acad. Med.* 137.

⁵⁶ Rai, “Collective Action”, *supra* note 51 at 294.

⁵⁷ For a discussion of these broader contextual changes see generally Jennifer Washburn, *University, Inc.: The Corporate Corruption of American Higher Education* (New York: Basic Books, 2005). Arguably, though, IP rights are the principal reason why, if not the means through which these changes are occurring.

When a biotechnological invention is actually patented, two main types of access problems can arise. The first is often referred to as a “blocking” or “hold-up.” Individual patent-holders simply refuse to license necessary inventions to researchers or health care providers (perhaps because the invention is already exclusively licensed to someone else) or require license fees that are prohibitively expensive for the would-be user. Myriad Genetics’ purported use of its BRCA1/2 patents, issued first in the United States and then in Europe and Canada, has become the archetypal case of a blocking problem in the genetics context.⁵⁸ While this instance of patent blocking may have been more appearance than reality as no negotiations took place and Myriad claims it would have been flexible, the case has exemplified the type of concern that researchers and policy makers have with patents. We have been unable to uncover any similar problem in the industrial biotechnology area. This does not mean that they do not exist but may merely reflect the fact that, given its sensitivity, health issues are better tracked and analysed.

The second type of access problem has been variously termed “royalty stacking” or, more generally, the “tragedy of the anticommons.”⁵⁹ In this situation, the number of licences that must be negotiated before research can move forward – or before diagnostic tests, vaccines, or treatments can be provided – is so high that the sum costs of securing all necessary licences is prohibitive. In their now-famous 1998 article, Michael Heller and Rebecca Eisenberg suggested that the sheer proliferation of patent rights, particularly those relating to DNA sequences, could substantially increase “transaction costs”, potentially engendering a tragedy of the anticommons capable of imperilling progress in any number of biotechnology research avenues. An anticommons can, in theory, result in any technological field where a proliferation of patent rights has occurred. In the area of biofuels, for example, one source claims there has been a “patent boom” during the last six years, in the US as well as internationally, with increases of more than 150% in 2006 and 2007.⁶⁰

However, there is also evidence that the blocking and/or anticommons concerns may be exaggerated.⁶¹ In 2003, John Walsh, Ahish Arora, and Wesley Cohen presented data from the United States indicating that barriers to access imposed by patents are often avoided by adopting “working solutions” such as going offshore, inventing around the patent, licensing, using public databases and research tools, or simply using the invention without obtaining permission, *i.e.* infringing the patent.⁶² A larger survey published in 2005 along with equivalent studies in other jurisdictions yielded similar findings.⁶³

Some note that the Walsh studies are not entirely persuasive and argue that the costs of working around patents may actually limit who is able to participate in the research process and what kinds of research objectives are apt to be pursued.⁶⁴ Other data, moreover, contradict the Walsh findings. A member survey

⁵⁸ Myriad controlled patents on the BRCA1 and BRCA2 genes as well as a test it had developed for identifying them. The company retained the exclusive right to perform the test, which it threatened to enforce against Canadian provinces that began performing the test themselves rather than shipping all samples to Myriad’s labs in Utah for testing, making the test three times more expensive than many other genetic tests and introducing other unusual conditions. Ontario continued performing the test despite being threatened with legal action: see Laura Eggertson, “Ontario defies U.S. firm’s genetic patent, continues cancer screening” (2002) 166:4 CMAJ 494.

⁵⁹ Michael A. Heller & Rebecca S. Eisenberg, “Can Patents Deter Innovation? The Anticommons in Biomedical Research” (1998) 280 Science 698 [hereinafter Heller & Eisenberg, “The Anticommons”]

⁶⁰ Ronald Kamis & Mandar Joshi, “Biofuel Patents Are Booming” (January 2008), online: <<http://www.bakerstreamingvid.com/publications/Biofuel%20Report.pdf>>. Note, however, that these figures include not only issued patents but patent applications as well (at least a portion of which will presumably not be granted).

⁶¹ Caulfield *et al.*, “Evidence and anecdotes”, *supra* note 19.

⁶² Walsh, Arora & Cohen, “Working Through the Patent Problem”, *supra* note 25.

⁶³ Walsh, Cho & Cohen, “Patents and Material Transfers”, *supra* note 25; Straus *et al.*, “Empirical Survey on Genetic Inventions and Patent Law”, Address at the OECD Expert Workshop on Genetic Inventions, Intellectual Property Rights and Licensing Practices (2002); and, D. Nicol & J. Nielsen, “Patents and Medical Biotechnology: An Empirical Analysis of Issues Facing the Australian Industry” (Centre for Law and Genetics, Occasional Paper No. 6, 2003).

⁶⁴ To begin with, the questions posed by Walsh *et al.* to survey participants raise certain methodological concerns: see Arti K. Rai & Rebecca S. Eisenberg, “Bayh-Dole Reform and the Progress of Biomedicine” (2003) 66 L. & Cont. Probs. 289 [hereinafter Rai

conducted by the American Association for the Advancement of Science in 2005 found that 40% of respondents reported difficulties in obtaining access to patented technologies, and over half of these said their research was delayed or changed course as a result.⁶⁵ Another study examined a pool of 169 “patent-paper pairs” – each pair being tied to a single piece of scientific research or particular scientific achievement – to test what anticommons theory would predict; namely, that “[r]elative to the expected citation pattern for publications with a given quality level...the citation rate to a scientific publication should fall after formal IP rights associated with that publication are granted.”⁶⁶ The authors found what they deemed to be a “modest” anticommons effect: “the citation rate after the patent grant declined by between 9 and 17%”, with the decline becoming “more pronounced with the number of years elapsed since the date of the patent grant, and is particularly salient for articles authored by researchers with public sector affiliations”.⁶⁷

Both the 2003 and 2005 Walsh studies do, however, document increasing difficulties with respect to sharing tangible research materials and tools that are strictly speaking not caused by IP rights, but rather the terms, conditions, and associated negotiating process of concluding material transfer agreements (MTAs) to govern materials exchange.⁶⁸ Even so, MTAs typically accord to the material providers reach-through rights to IP developed by the recipient. To the extent that bargaining breakdown is tied to those terms, then, access is properly characterised as an IP issue.⁶⁹ More fundamentally, it is highly artificial to separate these two forms – IP and physical property – of property protection. They are instead better understood as interacting with and reinforcing one another: MTAs, as a general rule, attach confidentiality obligations and use restrictions, in large part, for the purpose of safeguarding the ability of material providers (and/or their corresponding sponsors) to file subsequent patent applications.

As noted earlier, the available evidence does clearly show a *bona fide* problem with access to gene-based diagnostic tests, for research and especially clinical purposes. One early and small-scale study found that 30% of clinical laboratories reported not developing or abandoning testing for a gene associated with haemochromatosis once the patent issued.⁷⁰ Another investigation of over 100 laboratories found that 25% of respondents discontinued clinical testing because of a patent or licence; although the BRCA1/2 test was the most commonly identified, eleven other genetic tests ceased to be offered because of the existence of

& Eisenberg, “Bayh-Dole Reform”]; and Paul A. David, “The Economic Logic of ‘Open Science’ and the Balance between Private Property Rights and the Public Domain in Scientific Data and Information: A Primer” (Stanford Inst. for Econ. Pol’y Research, Discussion Paper No. 02-30, 2003). It may also be inaccurate to suggest either that these working solutions necessarily lessen transaction costs, or that they do not carry potentially significant costs of their own. Indeed, if licensing is categorised as a working solution, all of the concerns raised by Heller and Eisenberg and others remain intact. Moreover, working solutions “such as building up a defensive patent portfolio so as to improve one’s bargaining position” may simply be unavailable to small non-profit organisations, which “carry a disproportionate burden in relation to public interest research and development”: see Janet Hope, *Open Source Biotechnology* (Jul. 27, 2005) (unpublished Ph.D. thesis, Australia National University), <<http://rsss.anu.edu.au/~janeth/OpenSourceBiotechnology27July2005.pdf>>.

⁶⁵ S. Hansen, A. Brewster & J. Asher, “Intellectual Property in the AAAS Scientific Community: A Descriptive Analysis of the Results of a Pilot Survey on the Effects of Patenting on Science” (2005).

⁶⁶ Scott Stern & Fiona Murray, “Do Formal Intellectual Property Rights Hinder the Free Flow of Scientific Knowledge? An Empirical Test of the Anti-Commons Hypothesis” (2005) NBER Working Paper No. W11465.

⁶⁷ *Ibid.*

⁶⁸ But see Victor Rodriguez *et al.*, “Do Material Transfer Agreements Affect the Choice of Research Agendas? The Case of Biotechnology in Belgium” (2007) 71:2 *Scientometrics* 239 (determining that unable to “conclude that agreements signed by industry and government affect research agenda setting in academia”); and Victor Rodriguez *et al.*, “Material Transfer Agreements and Collaborative Publication Activity: The Case of a Biotechnology Network” (2007) 16:2 *Research Evaluation* 123 (finding that “material transfer agreements might not have interfered in such a way to limit co-publication activity of research organizations in the network” under study).

⁶⁹ This we are not likely to ever know.

⁷⁰ Jon F. Merz *et al.*, “Industry opposes genomic legislation” (2002) 20:7 *Nature Biotechnology* 657.

patent rights.⁷¹ In terms of research use, 53% of respondents halted development of a new clinical test due to a patent or license.⁷² Some instances of health care service providers continuing to conduct testing have been reported, but numerous other providers, fearing expensive litigation, have stopped testing outright.⁷³ This is once again illustrative of our point that it does not matter whether these difficulties are a problem with patent rights *per se* or of the way they are perceived – either can impact access. Just as it is appropriate to take into account perceptions of patents as being important to a firm’s ability to attract investment, it is equally legitimate to consider researcher perceptions that patents prevent access. As there is no reason to expect that scientists’ knowledge of the patent system is any deeper in the industrial biotechnology field, one would expect similar results to exist there.

Despite the fact that the evidence on the anticommons problem is mixed overall, a 2006 Committee organised by the US National Research Council highlighted several “reasons to be concerned about the future:”

First, the lack of substantial evidence for a patent thicket or a patent blocking problem clearly is linked to a general lack of awareness or concern among academic investigators about existing intellectual property. That could change dramatically and possibly even abruptly in two circumstances. Institutions, aware that they enjoy no protection from legal liability, may become more concerned about their potential patent infringement liability and take more active steps to raise researchers’ awareness or even to try to regulate their behavior. The latter could be both burdensome on research *and* largely ineffective because of researchers’ autonomy and their ignorance or at best uncertainty about what intellectual property applies in what circumstances. Alternatively, patent holders, equally aware that universities are not shielded from liability by a research exception, could take more active steps to assert their patents against them. This may not lead to more patent suits against universities – indeed, established companies are usually reluctant to pursue litigation against research universities – but it could involve demands for licensing fees, grant-back rights, and other terms that are burdensome to research. Certainly, some holders of gene-based diagnostic patents are currently active in asserting their intellectual property rights. Even if neither of these scenarios materializes, researchers and institutions that unknowingly and with impunity infringe on others’ intellectual property could later encounter difficulties in commercializing their inventions.

Finally, as scientists increasingly use the high-throughput tools of genomics and proteomics to study the properties of many genes or proteins simultaneously, the burden on the investigator to obtain rights to the intellectual property covering these genes or proteins could become insupportable, depending on how broad the scope of claims is and how patent holders respond to potential infringers. The large number of issued and pending patents relating to gene-expression profiling and protein-protein interactions contributes to this concern.⁷⁴

The final quoted paragraph’s point is important. As science moves away from the “one mutation/one function model to analysis of much more complicated relations among many genes and gene functions”, patents on genetic inventions could create more access problems,⁷⁵ just as producers of micro-array/chip

⁷¹ Mildred K. Cho *et al.*, “Effects of Patents and Licenses on the Provision of Clinical Genetic Testing Services” (2003) 5:1 J. Mol. Diag. 3.

⁷² *Ibid.*

⁷³ NRC, *Reaping the Benefits*, *supra* note 23 at 68 citing Cho *et al.*, *ibid.*, and Michelle R. Henry, Mildred K. Cho, Meredith A. Weaver & John F. Merz, *DNA Patenting and Licensing*, 297 Science 1279 (2002).

⁷⁴ NRC, *Reaping the Benefits*, *supra* note 23 at 134 [emphasis in original].

⁷⁵ Barton, “Emerging issues”, *supra* note 23, citing NRC, *Reaping the Benefits*, *supra* note 22.

devices may face complications in assembling all of the relevant patent rights.⁷⁶ This concern remains speculative for now.

As various biotechnologies mature and approach clinical use, there is a risk that the costs of these access obstacles earlier up the R&D chain will be transferred to the health care consumer in the form of higher prices. Even in the absence of these upstream obstacles, charging higher prices for want of competition is precisely what the legal monopoly afforded by patents gives the rights holder the power to do. Were this pricing not available, many manufacturers claim, the pipeline of new products would run dry.

Despite commonalities in the risks and costs involved, some biotechnologies give rise to other risk profiles due to the politics surrounding them. For instance, the California Institute for Regenerative Medicine (CIRM), bolstered by the massive amount of public funding at its disposal, has recently purported to address, *ab initio*, upstream access obstacles while also exerting downstream pricing controls through the enactment of IP regulations applicable to funding recipients.⁷⁷ These regulations attempt to answer many of the questions raised above, requiring grantees to share data and materials in a timely fashion, license technologies non-exclusively insofar as practicable, and generally allow research use by academic institutions while also ensuring that certain protections are in place to make any resulting stem cell-based therapies affordable to a wider segment of the population. Whether these and other provisions of the regulations will prove efficacious in practice, undermine the efficiency of stem cell research commercialisation, or extend far enough, is quite debatable.⁷⁸ It is noteworthy that numerous proposals to enforce some form of pricing control in the pharmaceutical context have failed repeatedly in the United States, however. Perhaps large-scale, state-sponsored biotechnology projects could help legitimise such a practice or establish a new norm.

In summary, the explosion of IP rights and commercialisation activities over the last two to three decades has undoubtedly added costs upstream – how much, we do not know. However, these changes also appear to have encouraged more firms and venture capitalists to invest and partner more in upstream research, which, given the dynamics of technology transfer, is a necessary step in making end products available. There is thus not a solid empirical basis upon which to definitively conclude whether the status quo is good or bad in terms of overall social welfare in respect of health and industrial biotechnology, at least in the developed world context. We do know with relative certainty, though, that the current regime is not conducive to producing health-related biotechnologies for the world's poor, and we can speculate that the same holds for industrial biotechnology. And any view that points to regulatory capacity and delivery system issues to suggest that patent rights are not a crucial part of the access problem simply misses the

⁷⁶ Barton, "Emerging issues", *supra* note 23.

⁷⁷ These regulations can be viewed at California Institute for Regenerative Medicine, Regulations, online: <<http://www.cirm.ca.gov/reg/default.asp>> (visited Nov. 30, 2007). The regulations that are applicable to "non-profit" funding recipients have been formally enacted whereas those applicable to "for-profit" entities are currently still pending.

⁷⁸ There are significant reasons to doubt that any of CIRM's provisions relating to pricing will work in practice. To begin with, the "plans" to enable the uninsured to access therapies simply have to be "consistent with industry standards", and industry does not have a history of making therapies, even ones developed primarily through public funding, cheaply available. For example, the National Cancer Institute provided USD 44.6 million to develop the cancer drug Avastin, yet Genentech (a California-based company) set the price at USD 100 000 a year. Second, the California Discount Prescription Drug Program is a brand new measure, which some suggest is apt to face legal challenge. Third, and most importantly, in California many therapies are not purchased with public funds, and many Californians are not eligible for the discount programme; thus these protections simply do not come into play in many cases. Thus, CIRM's pricing provisions arguably fall "far short of ensuring that all Californians will have affordable access to the therapies, drugs and cures that their tax dollars fund". See California Stem Cell Report, Affordable Access to Stem Cell Cures Hits Hard Sledding, (visited Jan. 7, 2007), online: <<http://californiastemcellreport.blogspot.com/2006/12/affordable-access-to-stem-cell-cures.html>>. See also David E. Winickoff, "Governing Stem Cell Research in California and the USA: Towards a Social Infrastructure" (2006) 24:9 TRENDS in Biotechnology 390.

point. Rather, patents are inevitably part of the decision-making landscape; they structure the industry and the opportunities to enter the market. Therefore, their existence and distribution is a relevant factor in understanding innovation systems (as opposed to patent systems narrowly conceived) and whether or how they do or do not meet the various needs of different populations.

We turn to examine potential mechanisms to address the various access issues in the next subsection.

2.3.2 Potential remedial mechanisms

Evolving best practices for patenting and licensing biotechnological inventions

The BRCA1/2 story and the anticommons hypothesis have proven to have considerable rhetorical force, kick-starting policy-making exercises in several countries.⁷⁹ These exercises were not restricted to either genetic testing or to health biotechnology. For example, much of the impetus for patent reform in the United States came about as a result of health access concerns. Nevertheless, the bulk of policy making focused on health biotechnology and, even more specifically, on gene patents.

In the United States, even prior to the Myriad controversy and publication of the anticommons piece, the National Institutes of Health (NIH) was sufficiently concerned about the *possibility* that research was being stalled by a lack of access to patented “research tools” to establish a working group on the topic.⁸⁰ The working group’s 1998 report concluded that “many scientists and institutions involved in biomedical research are frustrated by growing difficulties and delays in negotiating the terms of access to research tools”.

The NIH issued a set of principles and guidelines for the sharing of biomedical research tools the following year, in which it stated that recipients of its funds “are expected to ensure that unique research resources [...] are made available to the scientific research community”.⁸¹ To achieve this aim, the *Research Tool Guidelines* state that research tools need not always be patented, and that, if patented, exclusive licences should be avoided, except when an exclusive licence is deemed necessary to ensure further development of the tool, in which case the institution should seek to limit the exclusive license to the particular commercial field of use and retain the rights to use and distribute the tool for use in other research. The *Research Tool Guidelines* were followed in 2005 by the NIH *Best Practices for the Licensing of Genomic Inventions*,⁸² which were motivated by similar concerns about access to genetic inventions (which may or may not also be research tools). These *Best Practices* include many recommendations similar to those for research tools, including that institutions only seek patent protection on genomic inventions generated using federal funds where it considers that “significant further research and development is required by the private sector to bring the invention to practical and commercial application”, and that, where possible, non-exclusive licences should be pursued as a best practice. Where exclusive licences are deemed necessary, the NIH recommends limiting those licenses by requiring expeditious development of the technology as a condition of the licence and including limitations by field-of-use, specific indication, and geographical territory, and reservation of a right to use the invention in the institution’s research as well in that of other non-profit

⁷⁹ Caulfield *et al.*, “Evidence and anecdotes”, *supra* note 19.

⁸⁰ It defined research tools as “the full range of resources that scientists use in the laboratory”, including “cell lines, monoclonal antibodies, reagents, animal models, growth factors, combinatorial chemistry libraries, drugs and drug targets, clones and cloning tools (such as PCR), methods, laboratory equipment and machines, databases and computer software”. See National Institutes of Health, Working Group on Research Tools, *Report of the National Institutes of Health (NIH) Working Group on Research Tools* (1998), online: <<http://www.nih.gov/news/researchtools/>>.

⁸¹ Department of Health and Human Services, National Institutes of Health, Principles and Guidelines for Recipients of NIH Research Grants and Contracts on Obtaining and Disseminating Biomedical Research Resources: Final Notice, 64 Fed. Reg. 72090 (Dec. 23, 1999) [hereinafter *NIH Research Tool Guidelines*].

⁸² National Institutes of Health, *Best Practices for the Licensing of Genomic Inventions* (2005), <http://ott.od.nih.gov/pdfs/70FR18413.pdf> [hereinafter *NIH Best Practices*].

institutions. Although the *Best Practises* stresses that they are not binding, the document attracted some negative attention from the academic technology transfer community when first issued.⁸³ Nevertheless, a recent report on genetic patenting by the U.S. National Research Council suggested that if the guidelines are not sufficiently followed they should be made a condition of funding.⁸⁴

At an international level, the OECD *Guidelines for the Licensing of Genetic Inventions*⁸⁵ were issued in 2006, again motivated by concerns among member countries with “how genetic inventions have been licensed and exploited, particularly for diagnostic genetic services in the human health care field.” While they do not address the question of whether to seek patent protection for genetic inventions (which is addressed in both the NIH *Research Tool Guidelines* and *Best Practices*), the thrust of the *Guidelines* with respect to licensing decisions is similar to the two NIH guidance documents. They suggest that “foundational genetic inventions” should generally be non-exclusively licensed and that all genetic inventions should be licensed “broadly” and with the goal of increasing rather than decreasing access. Also like the NIH *Best Practises*, the OECD *Guidelines* make reference to a number of terms and conditions (e.g. milestones; field-of-use limitations) that might be included in any licence agreement with a view to maximising utilisation.

Whereas the NIH *Best Practices* are recommendations from the NIH to the institutions it funds, the OECD *Guidelines* are intended “to assist OECD and non-OECD governments in the development of governmental policies and in their efforts to encourage appropriate behaviour in the licensing and transferring of genetic inventions”.⁸⁶ However, despite the broad commonalities between the NIH and OECD documents (reflecting a reasonable degree of consensus about what best practices should be), and the fact that the OECD *Guidelines* have generally been well received by member countries such as Canada⁸⁷ and Japan, there is no evidence to date of formalised implementation. To some extent, this reflects the fact that the NIH *Best Practices* and, presumably, the OECD *Guidelines* mirror existing best practices in the academic technology transfer field. Indeed, there is evidence of this in the U.S., but only from a sampling of highly experienced university TTOs.⁸⁸ Practices at less established TTOs, which more commonly have unrealistic expectations about revenue generation, may differ considerably. As more and more academic institutions in developed and developing countries place an emphasis on formalized technology transfer as opposed to standard knowledge transfer, it will be critical to ensure that awareness of the principles and practices outlined in the two NIH policies and OECD *Guidelines* are disseminated broadly while at the same time taking into account particular challenges of the context in which each institution operates.

Indeed, the OECD *Guidelines* were not crafted to deal specifically with issues of access disadvantaging the developing world. Other models, most notably “equitable access” (EA) licensing and “neglected disease” (ND) licensing put forth by individuals involved with the Universities Allied for Essential Medicines (UAEM) organisation, do attempt to address those challenges head-on.⁸⁹ By including specific clauses in licensing agreements with private sector companies, university technology transfer offices can help to

⁸³ D. Malakoff, “NIH Roils Academe With Advice On Licensing DNA Patents” (2004) 303 Science 1757.

⁸⁴ NRC, *Reaping the Benefits*, *supra* note 23.

⁸⁵ OECD, *Guidelines for the Licensing of Genetic Inventions* (2006), online: <<http://www.oecd.org/dataoecd/39/38/36198812.pdf>> (visited Dec. 7, 2007) [hereinafter OECD *Guidelines*].

⁸⁶ *Ibid.*

⁸⁷ In the same year, the Canadian Biotechnology Advisory Committee issued its report *Human Genetic Materials, Intellectual Property and the Health Sector*, in which it supported the OECD *Guidelines*, suggesting that they serve as a basis for crafting rules to determine whether an “abuse of rights” has taken place. Canadian Biotechnology Advisory Committee, *Human Genetic Materials, Intellectual Property and the Health Sector* (2006), online: <<http://cbac-cccb.ca/epic/internet/incbac-cccb.nsf/en/ah00578e.html?>> (visited Nov. 22, 2007).

⁸⁸ Lori Pressman *et al.*, “The Licensing of DNA Patents by US Academic Institutions: An Empirical Survey” (2006) 24:1 Nature Biotechnology 31 [hereinafter Pressman *et al.*, “The licensing of DNA patents”].

⁸⁹ Kapczynski *et al.*, *supra* note 39.

secure freedom for those companies to operate as third parties to sell generic medicines in low- and middle-income countries (EA licensing) or to engage neglected disease research (ND licensing). However, while support in principle for the use of such clauses appears to be growing, both within the academic technology transfer community⁹⁰ and those purporting to place pressure upon it,⁹¹ their use is far from standard practice.

These various guidelines are of application not only in developed but in developing countries. In fact, the preamble of the OECD *Guidelines* specifically notes the benefit that developing countries can derive from following them. What is important to note, however, is that technology transfer and licensing practices are generally far less developed in lower-income countries than in high-income countries (although there is a considerable variation even among the latter countries). This has two implications.

First, it is not enough to suggest that developing countries simply implement the guidelines without more. Developing country research institutions and industry need to better understand the process of technology transfer and what it can (better diffusion and the building of a platform for knowledge sharing) and cannot (significant revenues) offer. Specifically, they need to understand that one cannot simply transplant a technology transfer from one country – such as the United States – to another.⁹²

Second, developing countries have an opportunity to design technology transfer systems that avoid some of the problems faced by technology transfer in developed countries. Specifically, they can investigate the possibility of constructing their technology transfer offices not on the basis of institutional affiliation but area of expertise, and of allowing competition between offices so that they better serve inventors. Further, these offices can adopt practices at the very beginning that incorporate the various guidelines described above.

None of this will happen, however, without significant training in technology transfer and knowledge management. Most courses offered to date only describe the mechanics of intellectual property and do not provide the critical perspective of the benefits, costs and limits of intellectual property rights necessary to design and implement a technology transfer system that will actually meet the goals of developing countries. One of us (Gold), together with partners in Kenya, offered a course in Eastern Africa in the summer of 2007 that aimed at exactly this. As a direct outcome of the course, the students – made up primarily of senior researchers in universities and public research institutes – are now involved with developing their institutions' IP policies and in one case is creating a technology transfer office. More such courses are needed, however, if developing countries are to derive the benefits of current learning about technology transfer.

Co-operative strategies: Using the public domain, patent pooling, and open source

Another potential means to ensure that patent rights do not impede research or decrease affordability of downstream products is to dedicate patentable information or technologies to the public domain. In the biotechnology context, publicly funded researchers engaged in the Human Genome Project did precisely that, spurred by the threat of parallel efforts to accomplish the feat in the private sector. A few years later, participants in the “SNP Consortium” adopted the same tactic. However, the set of circumstances that gave rise to these two colossal efforts indeed was unique (in terms of scientific competition as well as

⁹⁰ The University of British Columbia's technology transfer office has, for instance, recently released a “global access strategy”. See Universities Allied for Essential Medicines, “UBC Releases Global Access Strategy Draft”, online: <<http://www.essentialmedicine.org/ubc-releases-global-access-strategy-draft/>> (visited Nov. 30, 2007).

⁹¹ See, e.g., Universities Allied for Essential Medicines, “Philadelphia Consensus Statement: Toward Increasing Access to Medicines”, online: <<http://consensus.essentialmedicine.org/>> (visited Nov. 30, 2007).

⁹² Sara Boettiger & Allan B. Bennett, “The Bayh-Dole Act: Implications for Developing Countries” (2006) 46 *IDEA The Intellectual Property Law Review* 259.

politically), and would therefore seem difficult to reproduce or rely on in the future. Of course, individual researchers and their parent institutions are, to some extent, free to dedicate their inventions to the public domain on a case-by-case basis. But, putting the costs of patent prosecution to the side, a number of incentives now exist (both pecuniary and non-pecuniary) for researchers and institutions to attempt to patent inventions whenever practicable.

Partially in recognition of this growing tendency and the fact that far more patent rights exist (especially in academe) than in the past, many have identified the creation of “patent pools” as an alternative to a public domain approach for all areas of biotechnology. Some have put patent pools forward as a potential mechanism to circumvent licensing costs by bringing together all of the necessary parties (in terms of the patent rights as well as technological skills and resources they possess) to achieve a particular objective. Yet not a single example of a functioning patent pool in the area of biotechnology currently exists.⁹³ A proposal has been put forward to UNITAID, the international body that seeks to purchase medicines for HIV/AIDS and other diseases for developing countries, to construct a patent pool for essential medicines. One of the authors of the present report was commissioned to review the feasibility of the pool and concluded that, if narrowly constructed, such a pool was not only legally but practically feasible.⁹⁴ Roughly four years removed from the public health crisis over SARS, the pool of academic institutions and researchers that was ostensibly established in connection with the sequencing of the SARS virus has yet to deliver any vaccine.⁹⁵ The heterogeneity of interests or competitive tendencies of those involved appears to be a major part of the problem.

Perhaps for this reason, others have looked to the “open source” software movement for inspiration – at least on the surface, its normative agenda of facilitating information exchange appears simple and clear.⁹⁶ And despite material differences between the software and biotechnology contexts,⁹⁷ diverse biotech research initiatives, each broadly subscribing to open source principles, are under way in the aftermath of the Human Genome Project. Noteworthy examples include the “Tropical Disease Initiative”,⁹⁸ the “Biological Innovation for Open Society” (BIOS) project,⁹⁹ the “Ensembl Genome Browser,”¹⁰⁰ and the “HapMap” project.¹⁰¹

⁹³ Rai & Boyle, “Synthetic Biology”, *supra* note 8.

⁹⁴ Gold *et al.*, “Proposed Medicines Patent Pool”, *supra* note 50.

⁹⁵ Birgit Verbeure *et al.*, “Patent pools and diagnostic testing” (2006) 24 TRENDS in Biotechnology 115 at 117-18.

⁹⁶ There appears to be a growing literature hypothesising that biotechnology could learn a great deal from open source: see, *e.g.*, D. Burk, “Open Source Genomics” (2002) 8 B.U. J. Sci. & Tech. L. 254.

⁹⁷ For example, some worry that standardised licences are harder to develop with respect to biological materials, and what constitutes the “source code” or qualifies as an improvement may be more difficult to discern with biotechnologies compared to computer software. Moreover, whereas copyright vests in the author automatically upon completing a work, significant fees must be spent to obtain and maintain patents over scientific inventions. Thus the notion of free licensing, even when properly understood, may seem less than attractive. Finally, the question of whether open source biotechnology could be tantamount to “patent misuse” has been raised. See J. Hope, “Open Source Biotechnology: A New Way to Manage Scientific Intellectual Property” (2005) 18:1 GeneWatch Magazine; R. Feldman, “The Open Source Biotechnology Movement: Is It Patent Misuse?” (2004) 6 Minn. J.L. Sci. & Tech. 117.

⁹⁸ The Tropical Disease Initiative, online: <<http://www.tropicaldisease.org>> (visited Nov. 30, 2007).

⁹⁹ Biological Innovation for Open Society, online: <<http://www.bios.net/daisy/bios/home.html>> (visited Nov. 30, 2007).

¹⁰⁰ The “Ensemble Genome Browser” is a joint venture between the European Bioinformatics Institute and the Wellcome Trust Sanger Institute, which utilises open source software to create free, annotated maps of eukaryotic (predominantly mammalian) genomes. Ensembl seeks to release data into the public domain immediately and “imposes no restrictions on access to, or use of, the data provided and the software used to analyze and present it.” Meanwhile, several spin-off projects using Ensembl technology to analyse other types of genomes have developed. Online: <<http://www.ensembl.org/index.html>> (visited Nov. 30, 2007).

¹⁰¹ The International HapMap Project, online: <<http://hapmap.org>> (visited Nov. 30, 2007). This project, which began in 2002, is perhaps the most productive open source project to date. It has brought together scientists and funding agencies from Japan, the United Kingdom, Canada, China, Nigeria, and the United States. All of the data generated are made freely available provided those who access them do not attempt to restrict the access of others. International HapMap Consortium, “A Haplotype Map of the Human Genome” (2005) 437 Nature 1299. National Institutes of Health Human Genome Research Institute, “International

Despite varying degrees of progress and success, each of these biotech projects – loosely grouped under the banner of “open source” – has been successful in attracting significant sources of funding from public as well as private donors. In principle, these initiatives demonstrate that the licensing criteria and R&D methodology that are characteristic of the open source model can be applied in the biotech context to serve a combination of social goals and technological objectives. Nevertheless, they are all fairly narrow in scope and none provides a general model applicable to biotechnology in general. A great amount of work therefore still needs to be undertaken to develop a general and financially stable method to apply open source in a general biotechnology context. Until such a method is devised, open source initiatives should remain narrow and targeted, and governmental support for open source in the biotech realm is likely best spent on the same.

Paying patent rents for developing country population

Rather than, or in addition to, attempting to address unwanted patent-imposed costs through licensing practices or by creating patent pools or open source initiatives to facilitate upstream access to research inputs and potentially defray future product costs, some suggest simply “buying out” patent rights in order to make essential medicines or devices available to countries that could not otherwise afford them.

One compelling case relates to the human papillomavirus (HPV), which is known to be a significant factor in causing cervical cancer – a global, not neglected, disease.¹⁰² Approximately 260 000 women die each year in the world from cervical cancer. But whereas extensive screening and treatment programmes have dramatically improved health outcomes in wealthy countries, the remainder of the world’s population suffers 93% of the global mortality burden from cervical cancer. Still, “the deaths of less than 17 000 women per year in wealthy countries offered sufficient financial rewards to prompt both Merck and GlaxoSmithKline (GSK) to spend hundreds of millions of dollars to bring HPV vaccines to market.” These vaccines are *believed*¹⁰³ to be capable of preventing up to 70% of cervical cancer cases; however, at the cost of roughly USD 360 per person, they will be utterly unaffordable to the vast majority of women in the world who could benefit from them. In fact, to be “priced proportionately to per capita health expenditures, the average price should average no more than \$3 outside of high-income countries and no more than \$1.35 in low-income countries.”¹⁰⁴

Previous efforts to negotiate voluntary differential pricing arrangements for HIV/AIDS antiretrovirals have “proven cumbersome and not up to the task of global health needs.” Therefore, on the strength of the (debatable) assumption that the HPV vaccines are an effective way of lowering the incidence of cervical cancer, Kevin Outterson has instead called upon the patent holders to license their rights for generic HPV vaccine production for the developing world, at a price of USD 30 million to each company per year during the life of the patents – a figure that roughly reflects lost “patent rents” (*i.e.* the difference between

HapMap Consortium Expands Mapping Effort”, February 2005, online: <<http://www.genome.gov/17015412>> (accessed: 26 November 2007). The International HapMap Project, “The Responsible Use and Publication of HapMap Data”, online: <http://www.hapmap.org/guidelines_hapmap_data.html.en> (accessed: 26 November 2007). The project also does not preclude any of the participants from patenting units of genetic variation (“single nucleotide polymorphisms” or “haplotypes”) for which “specific utility” is found provided that the patent is not used to deny others access to that data: see the International HapMap Project, “Data Release Policy”, online: <<http://www.hapmap.org/datareleasepolicy.html.en>> (visited: Nov. 26, 2007).

¹⁰² Kevin Outterson, “Putting Patients First: An Open Access Generic Licensing Proposal for HPV Vaccines in Developing Countries”, under review, on file with the author [hereinafter Outterson, “Putting Patients First”].

¹⁰³ We are careful to note that there has been heavy criticism of inoculation programmes in Canada and elsewhere. Given the extremely low risk, the fact that the vaccines only apply to a few of the virus species and the cost of intervention, some members of the medical community have heavily criticised the programme.

¹⁰⁴ Outterson, “Putting Patients First”, *supra* note 102.

the marginal cost of producing a particular medicine or vaccine and its market price).¹⁰⁵ Outterson explains that under this proposal:

Nothing would change in high-income countries. Merck and GSK could sell their HPV vaccines normally in more than 90% of their revenue markets. But for the remainder of the world, where more than 93% of the cervical cancer deaths occur, they would sell the remaining intellectual property rights to a global institution which would permit open access generic production for developing countries. [...] If needed, the scope of the license could be calibrated to account for relatively richer middle-income countries such as Brazil, India and China. This adjustment would reduce the cost of the license and allow the companies to retain these growing markets while permitting generic access in the rest of the world. Any such adjustments should acknowledge local conditions, however; India is home to one fifth of the world's cervical cancer burden and lacks effective national screening programmes.

In addition to its fiscal feasibility,¹⁰⁶ equitable considerations also militate in favour of this particular proposal: both Merck and GSK conducted clinical trials with women from a broad range of countries, including low- and middle-income countries.¹⁰⁷ On the other hand, vaccines are notoriously difficult to manufacture relative to drugs; the manufacturing process is often contingent upon access to tacit knowledge or know-how as opposed to a patented technology, thus rendering the notion of a “generic vaccine producer” somewhat fictitious.¹⁰⁸ A similar problem exists with hard-to-reproduce inputs into industrial biotechnology. Bioreactors and other biological materials may not be easily reproduced and thus face the same problem as vaccines or biologics. More fundamentally, the problem with this and other like-minded patent buy-out proposals is that they offer nothing in terms of providing an alternative incentive to address health concerns without the wealth to drive market-oriented innovation systems.¹⁰⁹ This is not to say that patent buy-outs are not perfectly worthy of pursuit, especially where the necessary funds can be secured. But their “stop-gap” nature fails to provide any substantive guidance as to how IP rights can aid in structuring a modern bioeconomy in order to more readily address distributional concerns along the developmental divide.

2.4 Analysing Costs and Benefits: Beyond the Innovation/Access Paradigm?

Weaved throughout the above discussion of incentives to innovate and access issues was a rough assessment of the costs and benefits of IP rights in the biotechnology realm, particularly in terms of how those rights serve the interests of developed versus developing country populations. The challenge in the policy-making arena, whether concerned with addressing health needs, industrial growth, or both, is universally framed as one of balancing innovation and access. However, in our view, this binary lens has

¹⁰⁵ Kevin Outterson, “Patent Buy-outs for Global Disease Innovations for Low- and Medium-Income Countries” (2006) 32 Am. J. L. & Med. 159.

¹⁰⁶ Interestingly, the Bill and Melinda Gates Foundation recently funded a USD 27.8 million initiative to determine how the HPV vaccines should be deployed in the developing world. See Outterson, “Putting Patients First”, *supra* note 102.

¹⁰⁷ Outterson, “Putting Patients First”, *supra* note 102.

¹⁰⁸ Admittedly Outterson does not necessarily envision such a thing – his proposal would simply allow any “legitimate manufacturer” to produce the vaccines, provided they are willing to do so for a price which would be equivalent to a generic price. See Outterson, “Putting Patients First”, *supra* note 102.

¹⁰⁹ Outterson acknowledges this and, in fact, points to it as a reason why his proposal is practicable. See Outterson, “Putting Patients First”, *supra* note 102.

exceeded its utility. While access concerns have succeeded in increasing public consciousness of IP issues, it appears also to have inspired irresponsible rhetoric surrounding legitimate patents rights. Conversely, perceiving themselves to be under constant attack, many non-state actors have become more stalwart in their support for instituting even stronger IP protection. There is thus a critical need to reframe IP issues in a way that legitimises questions of wealth distribution and benefit-sharing, not to mention sustainability, without being interpreted as suggestive of weakening standards of IP protection. We will return to this conceptual move in Section 3 after surveying how the landscape of biotechnology-related IP issues is shifting in response to, or in conjunction with, politico-legal and scientific events presently in the process of unfolding.

3. Contextual Contingencies

In this second main section of the paper we seek to evaluate how different IP systems that are presently in flux, as well as changes that are afoot in the field of biotechnology itself, could shape a modern bioeconomy.

3.1 Globalising Forces

3.1.1 The role of institutions: Patent offices, WIPO, WTO, and WHO

Prior to surveying a select group of IP systems that may prove particularly relevant to any future bioeconomy, it is important to briefly take stock of two phenomena occurring at the institutional level. These phenomena have the potential to shape the application and interpretation of IP laws (and possibly emerging bioeconomies) in markedly different ways.

The first phenomenon has recently been identified by Peter Drahos.¹¹⁰ In his view, we have witnessed increasing convergence in systems of patent administration among the “trilaterals” (*i.e.* the patent offices of the United States, Europe and Japan) since the early 1980s. By providing a “steady drip drip of technical assistance” to patent offices in developing countries over a period of years, the trilaterals have fostered a significant amount of “technocratic trust”. This, in turn, tends to align developing world patent offices with the interests pursued by their developed world counterparts. Drahos explains:

An example of this leadership based on technocratic trust came from fieldwork in Vietnam, where over the years the E.P.O. has been active. When examiners in the Vietnamese patent office come to consider say a patent application in the pharmaceutical field they begin by looking at how the E.P.O. has decided the application and what it has said in its search report. They do not confine themselves to the E.P.O [...] They may also look at the way in which the U.S. P.T.O. and J.P.O. have treated the application. The decision tree [they follow] is the product of years of technical assistance, which includes training visits to beautiful Munich with its designed gardens and wonderful restaurants. It is the story of quiet and steady cultural integration in which examiners from patent offices of the periphery journey to the patent kingdoms of the west to be instructed in systems of apparent technological superiority to their own, systems that continue to influence them once they return home. ?

The result, Drahos posits, is a “circle of decision-making in which the E.P.O. [or J.P.O. or U.S. P.T.O.] trains developing country examiners to make decisions in their own countries that predominantly benefit foreign companies”, in other words, transferring economic rents to foreign patent owners.

¹¹⁰ Peter Drahos, “‘Trust Me’: Patent Offices in Developing Countries”, Social Science Research Network, online: <http://papers.ssrn.com/sol3/papers.cfm?abstract_id=1028676> (visited Nov. 30, 2007).

As we note below, a considerable degree of substantive variation still exists in how patent laws are applied and interpreted in the United States, Europe and Japan. However, Drahos is correct in stating that developing countries should pay far more attention to the operation of their national patent offices, if only to reconcile their evolving practices with other national objectives being pursued by other parts of government and by the country on the international stage.¹¹¹

This dovetails with the second phenomenon of note: increasingly, countries, particularly developing ones, seek out new international fora in which to draw attention to IP issues and express their dissatisfaction with the current regime. As Laurence Helfer has explained, since 2001:

[I]nternational intellectual property lawmaking has broken out of the confined institutional spaces of WIPO and the WTO and permeated deeply into international regimes concerning biodiversity, plant genetic resources, public health, and human rights. In that same period, the TRIPs Agreement has come under increasing challenge, especially but by no means exclusively from developing countries and NGOs. [...] [T]he recent expansion of intellectual property lawmaking into new international venues is the result of regime shifting by state and nonstate actors who are dissatisfied with many of the intellectual property treaty bargains negotiated by WTO members and are actively seeking ways to revise or supplement them.¹¹²

According to Helfer, this ongoing process of “regime shifting” should be understood as playing a constructive role. Working outside or at the margins of jurisdictional boundaries is, in itself, important because of the power imbalances that reside inside those spaces.¹¹³ The WHO’s Intergovernmental Working Group on “Public Health, Innovation, and Intellectual Property” is, for example, in the midst of developing a *Global Strategy and Plan of Action* in order to give effect to recommendations made by a WHO Commission in 2005.¹¹⁴ If brought into being and successfully implemented – neither of which is obvious¹¹⁵ – several of the elements contained in this *Global Strategy and Plan of Action* could help to address IP-related incentive and access issues canvassed in Section 1 above. At the same time, some institutions with formal jurisdiction over IP issues have given signals that they may be prepared to go

¹¹¹ Indeed, as Drahos points out, one effect of the technical assistance being provided to developing country patent offices is that they have become stronger players in national policy networks, and they may be particularly predisposed to take positions that are at odds with other objectives such as improving access to medicines. Drahos explains in depth:

As players in national policy networks developing country patent offices have the following features. First, by virtue of the long-running technical assistance programs they are integrated into one or more of the Trilateral Offices. Second, they receive resources from these offices, often on a long-term basis and they have the capacity to generate income from the grant of patents. This means that in comparison to other national bureaucracies in developing countries they are often better resourced. Third, the fee income they generate comes largely from a foreign clientele, especially multinational companies with global patenting strategies. Fourth, because of the technological and jurisprudential complexity of patent work the operation of patent offices remains opaque to other policy areas of the developing country’s civil service. Developing country patent offices are thus unusual players in national policy networks because they are disposed to be pro-patent, are integrated into international patent policy networks from which they draw resources and serve a clientele that is predominantly foreign. From the perspective of innovation policy, patent offices as actors in policy networks are likely to close off or circumscribe policy initiatives that question the role of patents in innovation. Technical assistance that builds the capacity of patent offices to be players in policy networks is essentially building a capability that is pro-patent in disposition. This, in short, is technical assistance that tilts the policy playing field in a particular direction.

¹¹² Laurence R. Helfer, “Regime Shifting: The TRIPs Agreement and New Dynamics of International Intellectual Property Lawmaking” (2004) 29 *Yale J. of International L.* 1 at 81-82 [hereinafter Helfer, “Regime Shifting”].

¹¹³ *Ibid.*

¹¹⁴ World Health Organization, Commission on Intellectual Property Rights, Innovation and Public Health (Geneva, Switzerland: World Health Organization, 2005), online: <<http://www.who.int/intellectualproperty/report/en/index.html>> (visited Dec. 9, 2007).

¹¹⁵ See for *e.g.*, Intellectual Property Watch, “WHO IP and Health Group Ends Meeting with Substantive Progress” (Nov. 10, 2007), online: <<http://www.ip-watch.org/weblog/index.php?p=820>> (visited Dec. 10, 2007).

beyond a narrow IP mandate. WIPO's membership has, for instance, signalled a commitment to build issues of particular concern to developing countries into its mandate by adopting a "Development Agenda".¹¹⁶ While difficulties surrounding WIPO's Secretary General may undermine these efforts in the short term, the Development Agenda exemplifies the shift to a broader understanding of the role of IP systems in developing countries.

While reasons exist to doubt that these initiatives will ever translate directly into changed practices, the manner in which they are treated and the disputes they engender will inevitably shape how IP is perceived, politicised, governed, and utilised by nation-states. This will, in turn, have implications for any future bioeconomy. (Indeed, we use the example of Brazil in the next subsection to illustrate this very point.)

3.1.2 A survey of IP heterogeneity: OECD countries, India, China and Brazil

The *Patent Cooperation Treaty* of 1970 substantially streamlined the process for parties wishing to obtain patent rights in multiple countries by creating a uniform procedure for filing patent applications internationally. In 1994, TRIPs established a set of minimum standards of IP protection that signatory states are expected to implement and comply with in order to avoid trade sanctions from other WTO member states. Because of these and other instruments designed to achieve similar ends (*e.g.* regional patent cooperation treaties; bilateral free trade agreements), it is often suggested that there is increasing harmonisation, both procedural and substantive (the latter to a lesser extent), across nations.

However, a considerable degree of substantive variation in patent laws remains among both developed and developing countries. These substantive differences are especially visible or apt to arise in the biotechnology realm. In terms of developed countries, most if not all apply the same three principal criteria in determining patentability – novelty, inventiveness (or non-obviousness), and industrial application (or utility). However, in addition to country-specific variations in how these principal criteria are interpreted by the judiciary, many European country patent laws also include a list of exclusions from patentable subject matter that are *not* present under US law. Specifically, the European Parliament's *Directive 98/44/EC on the legal protection of biotechnological inventions* excepts from patent eligibility, *inter alia*, the "human body, at the various stages of its formation and development, and the simple discovery of one of its elements" – although notably not these elements once taken out of the body – and "uses of embryos for industrial purposes".¹¹⁷ The European Patent Office has invoked these provisions in denying a number of patent applications in the field of stem cell research, a decision upheld on appeal.¹¹⁸

These exclusions from patentable subject matter are premised upon an "*ordre public*" or "morality" exception found in the European Patent Convention, and incorporated into several Member Country patent laws. Contrary to some forecasts, we have yet to witness noticeable declines in an either industrial or health-related biotechnology in response to even the most restrictive laws. This is probably explained by the fact, set out near the outset of this paper, that IP is only one of many factors that influence the rate and type of biotechnological innovation (and thus a successful bioeconomy). That the US federal government has been far from supportive of stem cell research has likely, for instance, had more impact on innovation in that field than the fact that patent rights over stem cells are more readily available in the United States compared to many European jurisdictions.

¹¹⁶ For a discussion of the significance of this, see Chon, "Development Divide", *supra* note 3.

¹¹⁷ EC, *Directive 98/44 of the European Parliament and of the Council of 6 July 1998 on the Legal Protection of Biotechnological Inventions*, O.J. Legislation (1998) No L213 at 13, articles 5(1) and 6(2)(c), respectively. See also article 5(2).

¹¹⁸ For a detailed discussion of this jurisprudence, see Matthew Herder, "Proliferating Patent Problems with Human Embryonic Stem Cell Research?" (2006) 3 *Journal of Bioethical Inquiry* 69 [hereinafter Herder, "Proliferating Patent Problems"].

Attitudinal differences between jurisdictions are, in other words, potentially critical. There are far more biotechnology companies in the United States than there are in Japan. One reason for this may be the difference in attitudes toward bankruptcy in both countries. In Japan, bankruptcy is generally perceived as a personal stain whereas in the United States it is part of doing business.¹¹⁹ Given that starting a biotechnology company is risky – that is, it presents a high risk of bankruptcy – Japanese entrepreneurs are less likely than their US counterparts to do so. This leads, in turn, to a difference in market structures that affect policy choices. The United States, with a higher proportion of biotechnology companies compared to pharmaceutical companies, worries less about the potential of biotechnology companies to block access to research tools than does Japan, where the proportion is substantially less. As a result, the Japanese government is currently trying to find mechanisms to create “clearing houses” over tool patents through voluntary means.¹²⁰

Our first general point is, then, that given the degree of substantive variation that exists among what may be characterised as the more established patent systems corresponding to the primary markets – *i.e.* the United States, Europe and Japan – both in terms of patent law particulars as well as other factors capable of significantly influencing innovation systems, it does not necessarily follow that increasing substantive harmonisation is possible, let alone desirable, for any future bioeconomy. On the other hand, the general trajectory of major developing country patent systems (or innovation systems more broadly and the politics surrounding them) is relevant as they will influence the overall character of any future bioeconomy. We focus on three countries of special interest: India, China, and Brazil.

In the decades following its abolition of patents on pharmaceutical products (as opposed to processes), India has maintained what is arguably the world’s strongest generic drug manufacturing industry. In 2005, however, the country significantly altered its patent regime in order to meet its obligations under TRIPs. The provision allowing only methods or processes of manufacture (as opposed to products) for certain classes of inventions to be patented was deleted, creating product patent protection in all fields of technology.¹²¹ But at least one key substantive difference has already emerged. Section 3(d) of the 2005 *Patents (Amendment) Act* excludes from patentable subject matter mere “new form[s] of a known substance which does not result in the enhancement of the known efficacy of that substance or the mere discovery of any new property or new use for a known substance or of the mere use of a known process, machine or apparatus unless such known process results in a new product or employs at least one new reactant”. This provision is essentially intended to guard against a phenomenon known as “evergreening” – a problem thought by some to plague other patent systems – wherein patent holders seek to extend their monopoly over a particular product by filing additional patents in respect of variants of what essentially amounts to the same invention. Employing the concept of “efficacy” to demarcate between legitimate new products and processes versus evergreening is, however, an exercise foreign to all patent law systems save now in India. Given that evergreening is a potential problem for all patent systems, India’s experience with section 3(d) is worth following.

The pharmaceutical industry, probably realising the potential of other countries to follow India’s lead, has vigorously opposed the provision. Thus, when the Indian Patent Office rejected a patent application by Novartis in respect of the beta-crystal form of a known cancer drug, imatinib (marketed as Gleevec in the United States) on the basis of section 3(d), a legal challenge ensued.¹²² On 6 August 2007, though, the Chennai High Court dismissed Novartis’s suit, upholding the Patent Office’s rejection of the patent claim

¹¹⁹ Bankruptcy is also seen as a personal stain in continental Europe. This has implications for risk taking and start-ups that, in our opinion, far outweigh patent law.

¹²⁰ Personal discussions with Japanese Patent Office, October 2007.

¹²¹ *The Patents (Amendment) Act*, 2005 No. 15 of 2005.

¹²² ICTSD, Bridges Weekly Trade News Digest, vo. 11, no. 29, Sept. 5, 2007, “Novartis Patent Challenge Dismissed in India”, online: <<http://www.ictsd.org/weekly/07-09-05/story3.htm>>.

under section 3(d), and deferring any assessment of the section's (in)consistency with respect to TRIPs to the WTO. Some reported that Novartis promptly announced that R&D funding that had been earmarked for India would instead be diverted to China while a Novartis spokesperson denied such a decision. Even if the claim is true, some have suggested that it was prompted not by the Court's ruling with respect to section 3(d), but rather "other business conditions...such as the low cost of clinical trials and researchers".¹²³ Moreover, since the enactment of the amendments in 2005, at least a dozen large international pharmaceutical companies have invested heavily in the country according to Indian press reports. Whether section 3(d) could stymie investment in research and thus slow or prevent a bioeconomy in India is thus far from supported by the evidence.

Although its patent laws are not without their own peculiarities – including a broad set of exclusions from patentable subject matter that precludes, for example, patenting many human and some animal genetic engineering techniques and resulting products¹²⁴ – China is of interest primarily because of the country's sheer economic power and potential to become a strong player in the bioeconomy. Like many other countries, there has been a dramatic increase in patent activity in China in recent years; over a ten-year span, the number of patents issued has more than doubled and the number of patent applications filed has increased fourfold.¹²⁵ Further, according to Japanese Patent Office statistics, China has the lead in the number of nanobiotechnology patents in the world. However, Salter, Cooper and Dickins contend that, "when compared with other countries, China has made very few applications to the EPO, the U.S. Patent and Trademark Office (USPTO) and the Japanese Patent Office (JPO), and clearly will not be able to develop its global R&D until it seriously improves its position in this area."¹²⁶ We are less persuaded that a change in patenting strategy will have such a significant impact. The reason for this is that it ignores culture, particularly the country's deeply rooted (even prior to communism) communitarian as opposed to individualistic values as well as its history as a fertile setting for imitation. If China is to benefit from the bioeconomy, it may, ironically, be better off exploiting its cultural differences by building a model on a less rather than a more proprietary basis. What such models will look like and their eventual success are currently unknown. But what is more certain is that the export of developed world IP traditions to a country for which such traditions are completely alien have a low chance of success. For this reason, we are sceptical that China's recent decision to alter its laws in an effort to mimic the *Bayh-Dole Act* of the US, permitting publicly funded scientists at Chinese research institutions to patent their inventions and spin them off into start-up companies, will result in a biotech boon for the country.¹²⁷

Brazil's patent legislation, the *Industrial Property Law*, possesses its own set of idiosyncrasies as well. Of particular note to biotechnology, parts of natural living beings and biological materials found in nature "even if isolated therefrom, including the genome or germoplasm" are not patentable.¹²⁸ Under the US, European, and the Japanese systems, isolation or purification is sufficient to overcome the bar on patenting naturally existing phenomena. Brazil's increasing presence on the world stage – as the developing country

¹²³ *Ibid.*

¹²⁴ Article 5 of the *Modified Patent Law* excludes "inventions-creations", which are contrary to the laws of the State, contrary to social morality, or detrimental to public interest" from patentable subject matter. The Patent Examination Guidelines specify that Article 5 is to be interpreted so as to exclude the following from patentability: "the process for cloning humans or cloned humans; the process for changing the inherent identity of the human reproductive system; the exploitation of human embryos for industrial or commercial purposes; the process for changing animals' inherent identity that may result in animal suffering but has no substantial benefit to human or animal medical treatment, and the animal obtained thereby; invention that may result in personal injury, property damage or environmental pollution, or the characteristics or device of which involve nationally important political events, people's feeling or religious beliefs."

¹²⁵ Brian Slater, Melinda Cooper & Amanda Dickins, "China and the global stem cell bioeconomy: an emerging political strategy?" (2006) 1:5 *Regenerative Medicine* 671 at 678 [hereinafter Slater, Cooper & Dickins, "China"].

¹²⁶ *Ibid.*, citing O. Doring, "Chinese Researchers Promote Biomedical Regulations: What Are the Motives of the Biopolitical Dawn in China and Where Are They Heading?" (2004) 14:1 *Kennedy Inst. Ethics. J.* 39.

¹²⁷ "China amends patent-rights law to boost innovation" (2008) 451 *Nature* 121.

¹²⁸ *Industrial Property Law*, 14/05/1996, No. 9.279, article 10(IX).

most actively attempting to legitimise, if not promote, the use of flexibilities under TRIPs to address public health priorities – is, however, of greater interest here.

Brazil was one of a group of fourteen developing countries, which, during the Uruguay round of trade negotiations, pushed strongly for language that was eventually embodied in Articles 7 and 8 of TRIPs. These articles stress development objectives, for instance, by providing member states with the ability to “adopt measures necessary to protect public health and nutrition, and to promote the public interest in sectors of vital importance to their socio-economic and technological development”.¹²⁹ Subsequently, these references to development were successfully invoked during the “Doha development round” of negotiations to bolster the use of compulsory licensing under Article 31 by developing countries that possess a local generic manufacturing capacity, while also allowing the “most desperate countries to override patents on expensive antiretroviral drugs and order cheaper copies from generic manufacturers in other countries”.¹³⁰ Negotiations over the implementation of these concessions are, however, ongoing. Brazil, in concert with a spate of other developing countries, continues to agitate for reform. Most recently, Brazil spearheaded a push to include a list of principles related to the protection of a “right to public health” within the text of the *Global Strategy and Plan of Action* currently being formulated by the WHO’s Intergovernmental Working Group on Public Health, Innovation & Intellectual Property.

Without expressing an opinion as to the merits of the principles introduced by Brazil, we raise the possibility that this move could derail the entire WHO process or at least divert attention from other specific elements of the strategy that, if acted upon, could immediately help developing countries strengthen their capacity to innovate and better manage IP in line with public health priorities. While it is true that IP rights have often been exercised in a manner fundamentally inconsistent with health concerns, particularly in developing countries, this need not be the case. In other words, by failing to conceive of IP as a tool rather than an end, Brazil’s stance of juxtaposing IP rights with public health priorities carries the risk of exacerbating the current development divide. And this could prove particularly damaging if that view is endorsed by developing countries around the globe.

3.2 New Scientific Frontiers, New IP Challenges, Familiar Distribution of Wealth and Health Benefits?

In the two subsections that follow, we provide two concrete illustrations of the theme implicit in much of the foregoing: that the role and effect of IP rights is subject to a complex mix of factors, including distributive justice claims, making it impracticable to develop clear and overarching policies relating to their proper deployment. The two examples we discuss represent biotechnologies thought to hold tremendous potential for health and industry, and the bioeconomy more generally. The first centres around stem cell technologies – with a specific health care focus – whereas the second focuses on synthetic biology, a technology that finds application in both the industrial and health care settings.

¹²⁹ *Legal Instruments-Results of the Uruguay Round*, Agreement on Trade-Related Aspects of Intellectual Property Rights, 15 April 1994, Marrakesh Agreement Establishing the World Trade Organization, Annex IC, 33 I.L.M. 81, 1994, article 8.

¹³⁰ Chon highlights that the fact that these provisions are hortatory rather than mandatory is a serious limiting factor. See Chon, “Development Divide”, *supra* note 3 at 2834-2835ff.

3.2.1 Cross-border science: Patenting stem cell technologies around the world and the Canada-California Cancer Stem Cell Consortium

Nation-states the globe over including Japan, the United Kingdom, Australia, Israel, Canada, China, South Korea, India, and Singapore (not to mention individual US states) are presently racing to take the lead in stem cell science, attempting to secure first mover advantage in the “global stem cell bioeconomy”.¹³¹ The patentability of stem cells, especially those derived from embryonic material, and related technologies varies considerably across many of these jurisdictions, as does the tendency of local scientists and research institutions to file patent applications with the US, European, and Japanese patent offices corresponding to the major markets. Some suggest these factors could dramatically impact incentives to invest in the stem cell field for that region. Salter, Cooper, and Dickins, for instance, speculate that China, in addition to increasing stem cell research funding, must institute stronger IP protection and encourage greater foreign patent filings if it is to realise its ambitions for the field.¹³² Interestingly, though, in Europe, where the patentability of embryonic stem cell inventions has been shrouded in uncertainty for some time,¹³³ the numbers of patent applications and grants have grown steadily recently.¹³⁴

In terms of access concerns, a few seminal patents controlled by the Wisconsin Alumni Research Foundation (WARF) have received a great deal of attention. Many alleged that these patents (and the manner in which WARF was licensing them) threatened to undermine progress in the field. With the validity of these rights suspended temporarily, if not permanently, some observers nevertheless suggest that the field may be particularly susceptible to patent blocking and patent thicket problems owing to the proliferation of stem cell patents globally since the late 1990s.¹³⁵ The new patent filings by WARF over pluripotent stem cells derived from adult rather than embryonic cells may only exacerbate this situation.¹³⁶ Observers advocate a clearinghouse mechanism to avoid these potential pitfalls.¹³⁷

A host of other IP issues connected to the process of commercialising stem cell technologies – and the emerging cross-border research initiatives arranged for that purpose – are equally pressing, especially when questions of benefit-sharing among each government’s respective citizenry are considered. More generally, cross-border research and development projects are an increasingly common phenomenon. Co-ordinating such research and commercialisation efforts, in which IP can at times play a decisive role, will thus become integral to a vibrant bioeconomy. One response to the complexity of these issues is the proposed Canada-California “Cancer Stem Cell Consortium” (CSCC), a cross-border research project funded by the California Institute for Regenerative Medicine (CIRM) and Canadian government funding agencies.

While officially consummated by governments on each side of the US/Canadian border,¹³⁸ CSCC is still far from operational. However, once the money – USD 250 million from each party – begins to flow, and research commences, three important IP-related co-ordination issues will need to be addressed.

First, research involving multiple institutions raises issues of joint IP ownership. In the absence of some form of agreed IP protocol among participating institutions, the cross-border nature of the researcher greatly complicates the identification of control over IP rights. According to some officials, even the intra-

¹³¹ This phrase is taken from Salter, Cooper & Dickins, “China”, *supra* note 125.

¹³² Salter, Cooper & Dickins, “China”, *supra* note 125 at 681.

¹³³ See for *e.g.*, Herder, “Proliferating Patent Problems”, *supra* note 118.

¹³⁴ Although many have been assigned to US entities, indicating that investment in Europe still may not be strong. Karl Bergman & Gregory D. Graff, “The Global Stem Cell Patent Landscape: Implications for Efficient Technology Transfer and Development” (2007) 25:4 *Nature Biotechnology* 419 at 420-21 [hereinafter Bergman & Graff, “stem cell patent landscape”].

¹³⁵ *Ibid.*

¹³⁶ Online: <<http://www.madison.com/tct/mad/topstories/257875>> (visited 26 November 2007).

¹³⁷ Bergman & Graff, “stem cell patent landscape”, *supra* note 134.

¹³⁸ See Governor Schwarzenegger Highlights California-Canada Partnership on Life-saving Stem Cell Research, online: <<http://gov.ca.gov/index.php?/print-version/press-release/6481/>> (visited Nov. 30, 2007).

institutional agreements among campuses of the University of California system are unclear. Adding foreign partners – here Canada – promises to aggravate the situation. Since many Canadian technology transfer offices have far less experience with cross-border IP issues relative to their California counterparts, the Canadian partners may be placed at a considerable disadvantage.

The CSCC funding model envisages that moneys will flow directly from funding agencies (in Canada, California, or both) to specific research projects. This gives rise to a second difficulty: each funding body likely has its own funding policy and requirements relating to IP developed with its funds.¹³⁹ Technology transfer officials will thus have to wade through and monitor compliance with the details of each of these different, potentially conflicting policies unless a standardised IP protocol (which complies with both jurisdictions' applicable laws) is developed.

In addition, the co-mingling of funds from Canadian research funding organisations with those from California – in particular, those from CIRM – raises a series of other issues which we group together as a third potential IP co-ordination stumbling block. To date, CIRM has introduced (and since passed the first of) two sets of IP regulations governing non-profit and for-profit organisations, respectively. Each of these regulations sets out a number of requirements in relation to the use of funds generally, dissemination/publication of research results, sharing of research materials, patenting and licensing inventions developed with CIRM funds, plans to ensure that any resulting stem cell-based therapies are accessible/affordable to Californians, and royalties/share of revenues to be returned to the State under a number of different scenarios.¹⁴⁰

These requirements could prove problematic in the context of the CSCC for a number of reasons. Consider, in particular, the provisions intended to provide a return of financial benefits to the State of California.¹⁴¹ Any research grouping under the CSCC that accepts funding from CIRM would be required to return 25% of revenues earned from licensing agreements in respect of any patented inventions developed with CIRM funds.¹⁴² Putting aside legitimate questions about whether such a payback obligation is likely to result in significant returns,¹⁴³ the optics of Canadian tax dollars (in the form of government grants) flowing directly into the coffers of the State of California is likely to attract criticism. Should Canadian funding agencies therefore institutionalise a similar payback obligation into their respective funding agreements? How would doing so impact the commercialisation process? Technology transfer managers may strongly resist such requirements as they significantly limit their flexibility in developing an appropriate technology transfer strategy for resulting research. One open question is whether their resistance may be strong enough to refuse to accept the research funds. This would not be unprecedented – it has occurred with respect to money received from foundations – but never with this amount of money at stake.

¹³⁹ For example, recipients of Genome Canada funding are required to establish “commercialisation committees,” comprised of researchers, technology transfer officials, and representatives of the funding body, to deliberate and decide how to proceed at each turn in the commercialisation process.

¹⁴⁰ For a detailed analysis of these provisions and payback obligations more generally, see Matthew Herder, “Asking for Money Back – Chilling Commercialization or Recouping Public Trust in the Context of Stem Cell Research” *Columbia Science & Technology L. Rev.* (forthcoming 2008).

¹⁴¹ There may be an issue of extraterritoriality here, which could prevent these provisions from applying to Canadian institutions.

¹⁴² There are a number of important caveats to this payback requirement. First, net revenues from a licence or licences of a CIRM-funded patented invention must exceed USD 500 000 in the aggregate before the obligation to repay 25% is triggered. Second, *net* revenues do not include the inventor's share and the direct costs incurred in the generation and protection of the patents from which the revenues are received. And third, in the (likely) event that multiple sources of funding are used to support the research leading to net revenues in excess of the USD 500 000 threshold, the return to the State of California will be proportionate to the CIRM financial support for the research that resulted in the invention.

¹⁴³ Contrary to what the study commissioned by the “Yes on [Proposition] 71” campaign predicted, others have noted that CIRM's USD 3 billion in funding is likely to produce only marginal direct financial returns. See, e.g., Richard J. Gilbert, “California's Stem Cell Initiative: Converting the Legal and Policy Challenges” (2006) 21 *Berkeley Tech. L.J.* 1107.

While likely not determinative of overall outcomes, the foregoing IP-related co-ordination issues will nevertheless help shape the distributional impact of any emergent stem cell bioeconomy. If IP ownership is shared, for example, it could spark new investment in each region (although California's storied history as a technological pioneer should work in its favour). On the other hand, while CIRM's IP regulations do attempt to improve the accessibility of any resulting stem cell-based therapies for California health care consumers, it is not clear whether those provisions or any analogous measures adopted by Canadian research funding institutions in connection with the CSCC will work to facilitate uptake in the context of Canada's publicly funded health care system. As large-scale cross-border research initiatives increasingly become a trend in the modern bioeconomy, tackling these co-ordination IP issues upfront will become critical in order to anticipate various distributional consequences. As explained next, the synthetic biology community is attempting to put a similar insight into practice.

3.2.2 Synthetic biology as a “perfect storm” of IP issues?

Synthetic biology, which incorporates elements of engineering, computer software programming and biology lies at the interface of both industrial and health application within biotechnology, promising to deliver everything from biofuels to new medical substances and devices.¹⁴⁴ If achieved, synthetic biology's aim of standardising biological parts could radically reduce the costs of developing all manner of biotechnological products, whether health or industrial. It could, by the same token, decrease the need for tacit knowledge during the R&D process, in turn reducing the know-how advantage possessed predominantly by US firms at the present time, and fostering stronger competition outside the United States¹⁴⁵ However, whether this vision of standardisation is realistic remains heavily debated in scientific circles.

Meanwhile, IP represents a potentially serious complicating factor given that the interests of the existing biotech sector (which typically places tremendous emphasis on IP rights) may be at odds with the “synbio” research community (which may, as explained above, reduce the relative importance of those rights by undercutting know-how advantage, or, as explained below, attempt to pre-empt the proliferation of patent rights by dedicating technologies to the public domain).¹⁴⁶ Synthetic biology, by arising at this specific moment, may also be particularly vulnerable to being slowed by proprietary problems. Indeed, Arti Rai and James Boyle warn that “[t]here is reason to fear that tendencies in the way that U.S. [intellectual property] law has handled software on the one hand and biotechnology on the other could come together in a ‘perfect storm’ that would impede the potential of the technology”¹⁴⁷ for both the health and industrial sectors.

Unlike foundational technologies in software (which developed prior to either copyright or patent protection being available for that subject matter) and biotechnology (which have for the most part either not been patented or made widely available), synthetic biology is rising just as norms have significantly altered in favour of patenting (both in scope and in number) and commercialisation. Rai and Boyle predict that the consequences of this could be negative: “Considerable historical evidence, including evidence from virtually every important industry of the 20th century, suggests that broad patents on foundational research can slow growth in the industry.”¹⁴⁸ Moreover, many of the access issues canvassed above –

¹⁴⁴ For an in depth summary of synthetic biology, see James Newcomb, Robert Carlson & Steven Aldrich, *Genome Synthesis and Design Futures: Implications for the U.S. Economy* (Bio Economic Research Associates, 2007) [hereinafter Bio-Era Report].

¹⁴⁵ *Ibid.* at 34.

¹⁴⁶ *Ibid.* at 49-50.

¹⁴⁷ Rai & Boyle, “Synthetic Biology”, *supra* note 8.

¹⁴⁸ Rai & Boyle, “Synthetic Biology”, *supra* note 8 at 390, citing R.P. Merges & R.R. Nelson, “On the Complex Economics of Patent Scope” (1990) 90 Columbia L. Rev. 839.

patent thickets, hold-up, and reach-through claims – are likely not only to arise in the synthetic biology context, but to be worse because of increased patenting behaviour.

A group of researchers at the Massachusetts Institute of Technology participating in the Registry for Standard Biological Parts (which works as a catalogue of existing biological components and also offers assembly services) have coalesced in support of the idea of establishing a synthetic biology “commons” dubbed the “BioBricks Foundation.” Rai and Boyle survey a variety of hurdles to which this idea gives rise while also highlighting tools or models that could be used to overcome them. For example, whether strings of DNA and other elements or products of synthetic biology are copyrightable and thus amenable to being manipulated into an open source “copyleft” type of scheme is not yet clear. If this option were available, it would provide a low-cost mechanism to create a commons based on copyright – which is free to obtain and thus easy and low cost to use – rather than on patents – which are expensive to obtain and maintain. If copyright is not available, then attempting to engineer a patent-based commons in the vein of the “Biological Innovation for an Open Society” (BIOS) is a possible alternative. This option nevertheless not only leaves open issues of antitrust and patent misuse but incentives to participate, particularly given the costs of patent prosecution and maintenance. Seeking non-assertion agreements from synthetic biology IP rights holders (the bulk of whom are within academia), adapting a “clickwrap” licence similar to the one used in connection with the HapMap project, or lobbying for some form of *sui generis* protection (with limitations), are also alternatives worthy of consideration. In the end, Rai and Boyle temper any optimism for a copyleft, open source-like approach, concluding that the ground-up approach taken by researchers is, while imperfect, a wise move for the time being:

Intellectual property rights are relatively unimportant as incentives in the production of copyleft software. But synthetic biology might be different. Though the uses of synthetic biology are by no means limited to biomedicine, at the end of some biological chains of innovation will lie the expensive development and commercialization of a drug. While taking a drug all the way through clinical trials...may not cost as much as drug companies claim, it does cost hundreds of millions of dollars. Whether patent rights are the best incentive mechanism for purposes of eliciting pharmaceutical R&D is not a question we can address here. Suffice it to say our current system of financing pharmaceutical innovation relies heavily on these rights.

[...]

In the meantime, the decision, already implemented, of the MIT Registry of Standard Biological Parts to place its parts into the public domain certainly provides important protection against the threats of patents clogging innovation in the synthetic biology space. Placing parts into the public domain not only makes the parts unpatentable, but it undermines the possibility of patents on trivial improvements. In the end a public domain strategy comparable to that employed by the public Human Genome Project may not be ideal, but it is certainly a good start.¹⁴⁹

While industrial applications of synthetic biology may not be as costly, a similar logic would apply to that sector as well.

Given the structure and, perhaps more importantly, the cultural belief in patents – untainted by the lack of empirical foundation – as a prime means of providing an incentive to develop new products from synthetic biology – patents may simply be unavoidable. Nevertheless, the reins must be pulled in on the proliferation of patent rights at too early a stage. Indeed, writing elsewhere with Rebecca Eisenberg, Rai has suggested that a formal gatekeeping mechanism to preclude or weed out patents on foundational,

¹⁴⁹ Rai & Boyle, “Synthetic Biology”, *supra* note 8 at 392.

broadly enabling platform technologies thought to hold significant social value (citing WARF's patented stem cell inventions as a case in point), should be created.¹⁵⁰ What the synthetic biology case study shows is that communities can, at times, engineer and implement creative and practical strategies of their own making, although it is still unclear how effective this particular strategy will be.¹⁵¹

Without resolving the myriad potential IP issues raised by synthetic biology, preserving a space for flexible action as opposed to encouraging a uniform approach to IP (*i.e.* seek strong IP protection to the greatest extent possible) will, in our opinion, prove important as the modern bioeconomy takes root. As stated earlier, the evidence linking increased IP protection with the facilitation of a vibrant a modern bioeconomy is simply lacking both in the developed and especially in the developing country context. Rather, as history has demonstrated again and again, heterogeneity of IP systems and approaches to IP rights better advances technological development than does a one-size-fits-all approach.¹⁵²

4. Looking Ahead

The central conclusion that one should draw from the foregoing analysis is that our knowledge of the actual role that intellectual property rights play in driving innovation, impeding innovation, and disseminating innovation is poor and unlikely, in the short term at least, to get better. There are several reasons for this.

First is the lack of accepted metrics by which to measure the success or failure of an intellectual property system. We tend to measure relatively simple things like number of patents issued, licensing revenues, opinion relating to the importance of intellectual property rights, number of technology transfer offices, and so on. These metrics do not, however, measure the actual impact of intellectual property on innovation but, instead, behaviours that may or may not contribute to more and better quality innovation. Greater patent numbers may, for example, simply reflect a higher patenting rate, leading not only to waste (by patenting objects that should not be patented) but to an increased probability of an anticommons effect. Opinion evidence often simply measures belief or faith in the intellectual property rather than concrete effect. Further, not being empirically driven, these opinions may fade or change over time. None of these metrics actually measure what we care about: increased innovation and dissemination of that innovation that actually and markedly increases well-being. The problem is that defining, let alone measuring, factors beyond these simple ones is difficult.

Second, there continues to be relatively little empirical evidence on intellectual property systems even using the above (inadequate) metrics. Some fields, such as industrial biotechnology, are almost completely ignored. Other technologies are subject to such a variety of factors that it is impossible to disaggregate the effect of intellectual property on innovation. Lack of patent protection of embryonic stem cells in Europe has not, as discussed earlier, seemingly affected levels of research in Europe while the existence of patents in the United States has not increased innovation. Patents and other intellectual property not only act in concert with many other factors, but cannot even be isolated at a theoretical level. For example patents, which are premised on risk taking, are linked to attitudes toward bankruptcy. The effect of a patent on innovation is therefore modified by these attitudes. Similarly, patents have differential effects depending on a country's level of development. Intellectual property is simply so embedded in the culture and

¹⁵⁰ Rai & Eisenberg, "Bayh-Dole Reform", *supra* note 64.

¹⁵¹ In fact, many of the "parts" placed into the public domain by MIT researchers may be encompassed by pending patent applications.

¹⁵² I. Inkster, "Patents as Indicators of Technological Change and Innovation – An Historical Analysis of the Patent Data 1830-1914", in *The Role of Intellectual Property Rights in Biotechnology Innovation*, D. Castle ed. (Cheltenham, U.K.: Edward Elgar, forthcoming 2008).

economy in which it operates, that general conclusions about the costs and benefits it brings about are meaningless.

Third, we have yet to define what counts as a cost or benefit of innovation let alone of the patent system. This is part of the general problem we noted in Section 1.4, that we lack a conceptual framework beyond the outdated access-incentive paradigm. Patents have a wide-ranging effect that cannot be captured through traditional economic measures. For example, while transaction costs involved in identifying patent holders and negotiating licence agreements with them is a cost attributable to the patent system, should we include other costs? Should we include, for example, any negative distributional consequences among the costs of the patent system? Similarly, do we include the social cost of encouraging researchers to focus on applied rather than on public health research, when we know that the latter have historically proved to be more effective in increasing health? Is encouraging nanobiotechnological innovation a cost or a benefit when we have little knowledge about the environmental and health effects of materials at a nano scale? Until we agree on a meaning of cost and of benefit that captures more than narrowly conceived economic measures of wealth and profit, can we hope to paint a realistic picture of the effect of intellectual property on innovation systems?

Given that for over a decade, intangible assets (including intellectual property) are of greater value to industry than are tangible assets such as factories and inventory, we cannot afford the luxury of the ambiguous conclusion reached by Fritz Machlup in 1958:

If we did not have a patent system, it would be irresponsible, on the basis of our present knowledge of its economic consequences, to recommend instituting one. But since we have had a patent system for a long time, it would be irresponsible, on the basis of our present knowledge, to recommend abolishing it.¹⁵³

While the patent system itself is not, and realistically ought not to be, put into question, our continued ignorance of how the system works cannot be an excuse not to pursue change at the margins, particularly in the intersection of law and practice.¹⁵⁴ We therefore must attempt to anticipate trends and develop policy even while waiting for empirical evidence to finally fill the gaps.

In an attempt to anticipate trends in respect of intellectual property and health and industrial biotechnology, it is useful to distinguish between developments in three areas: 1) in intellectual property law itself, 2) in the practice surrounding the use of intellectual property, and 3) in health and industrial biotechnology. Let us briefly look at each.

To begin with, it does not follow that greater substantive harmonisation of intellectual property laws would best serve the interests of any future bioeconomy. While the trend in both developed and developing countries during the late 1990s and early 2000s was to increase patentable subject matter, patent scope, and ease of obtaining patent rights, there are strong signs that this trend has reversed. Not only have developing countries introduced limitations (as in India on evergreening), but developed country courts both are making it harder to obtain patent rights and are curtailing the scope of rights granted. The Supreme Court of the United States recently stated that it was appropriate that, as science advances, patents over inventions be harder to obtain:

We build and create by bringing to the tangible and palpable reality around us new works based on instinct, simple logic, ordinary inferences, extraordinary ideas, and sometimes even genius. These

¹⁵³ Fritz Machlup, *An Economic Review of the Patent System*, Washington, DC: US Government Printing Office, 1958 at 80.

¹⁵⁴ Gold *et al.*, “Gene patents”, *supra* note 23.

advances, once part of our shared knowledge, define a new threshold from which innovation starts once more. And as progress beginning from higher levels of achievement is expected in the normal course, the results of ordinary innovation are not the subject of exclusive rights under the patent laws.¹⁵⁵

Other senior courts such as the House of Lords have espoused similar reasoning of late.¹⁵⁶ Moreover, although patent law is in theory technology-neutral – that is, it is formulated not only for biotechnology but all fields of endeavour¹⁵⁷ – courts have begun the exercise of addressing the concerns (anticommons, blocking patents, *etc.*) that are peculiar to, or at least thought to be more pronounced in, the biotechnological realm (especially health-related biotechnology) discussed earlier. One can only expect this trend to continue for the next 5-10 years.

Major changes are also in store in the areas of practice. Industry and governments have begun to recognise the limitations of traditional approaches to deploying intellectual property on innovation. Industry is trying to move away from fairly simplistic management strategies such as hoarding intellectual property or suing every possible infringer, to strategies that better reflect the interactive nature of innovation and the need to share. In doing so, industry is trying to develop metrics that better reflect the real value of intellectual property not only to the firm but to society.¹⁵⁸ Universities are also attempting to measure their performance in diffusing technology by identifying indicators that measure the impact that university research has on the community as a whole rather than on licence revenues that the university receives. At the international level, international organisations and industry have recently recognised that current intellectual property practices may not always lead to the greatest social benefit. Documents such as the Noordwijk Medicines Agenda, the WIPO Development Agenda and recent work by the Intergovernmental Working Group on Public Health, Innovation and Intellectual Property at the WHO all point to the need to create and disseminate new models for the licensing and sharing of intellectual property. It is too early to describe the features of these models, but they will likely involve greater reliance on bundling intellectual property (for example, through pools, clearinghouses and public-private partnerships), selecting not to enforce patent rights, developing consortia and other measures that build on the exchange of knowledge rather than on hoarding it.

While predictions of the future of health and industrial biotechnology are bound to be wrong, we can anticipate increased interest in patenting at earlier and earlier stages in the research process. Biotechnology began this trend when research institutions decided to patent upstream discoveries such as research tools and genes. Stem cell technology, synthetic genomics and nanobiotechnology are pushing this trend further – the latter two within industrial biotechnology, which, as previously noted, has so far escaped notice. While WARF has agreed not to pursue its patent rights against university researchers using its new stem cell discovery, it remains an open question whether the changes we expect in practice will offset any increased patenting activity.

Given the above, we anticipate growing attention to be paid to new business models that rely less on strong proprietary methods of managing intellectual property and more on collaboration. Policy development should therefore focus on incentives that governments could put into place to assist this process. Beyond such traditional instruments as direct funding of research, income tax credits and purchasing power,

¹⁵⁵ KSR Int'l Co. v Teleflex Inc., 127 S. Ct. 1727 (2007).

¹⁵⁶ Synthon BV v. Smithkline Beecham plc [2005] UKHL 59.

¹⁵⁷ For an in-depth discussion of how patent law doctrine has been interpreted and applied in varying ways depending upon the field of technology, see generally Burk & Lemley, "Policy Levers", *supra* note 31.

¹⁵⁸ Karen L. Durell & E. Richard Gold, "Looking Beyond the Firm: Intellectual Asset Management and Biotechnology", in *The Role of Intellectual Property Rights in Biotechnology Innovation*, D. Castle ed. (Cheltenham, U.K.: Edward Elgar, forthcoming 2008). See also Patrick H. Sullivan, *Value Driven Intellectual Capital: How to Convert Intangible Corporate Assets Into Market Value* (John Wiley and Sons, 2000).

governments in developed and developing countries will need to identify incentives to induce industry and universities to co-operate both within and between countries.

Finally, when and if a modern bioeconomy emerges, intellectual property will, in our view, be crucial to any strategy intended to address distributive justice concerns. Maintaining flexibilities in implementing intellectual property regimes is unlikely to prove enough, however, as developing countries often do not exercise them. We touched on some of these reasons earlier, such as the effect of the trilaterals influencing developing world patent office practice. But developing countries have also largely failed in formulating internal intellectual property policies that take into account their local needs. They do this, paradoxically, at the same time that they call for greater flexibilities and recognition of their needs at the international level. Brazil is emblematic of this. At international negotiations touching on intellectual property, Brazil is among the most vehement proponents of placing health above commerce. Nationally, however, not only has Brazil not taken advantage of many of the existing flexibilities, but it seems to be removing some of the flexibilities it has exercised, judging by two bills recently introduced into its Congress.¹⁵⁹ Just as OECD countries and the pharmaceutical industry are beginning to entertain discussions about how to better align intellectual property with development, developing countries must also ensure to reconcile local practice and policy with calls for reform on the international stage.

¹⁵⁹ Bill no. 2729/2003 aims to increase criminal sanctions applicable to the non-authorized use of patented technologies despite the fact that international agreements and developed countries do not impose criminal sanctions for patent infringement, while Bill no. 4961/2005 would extend patent protection to substances extracted from natural biological resources.

Appendix

Below, we reproduce the definitions formulated by the OECD with respect to the terms “modern bioeconomy”, as well as the “industrial” and “health” fields of application or “scenarios”.

Basic definitions

The OECD provides both a single definition and a list-based definition of biotechnology. The single definition defines biotechnology as “*the application of science and technology to living organisms, as well as parts, products and models thereof, to alter living or non-living materials for the production of knowledge, goods and services*”. This definition is too broad to be useful for the scenarios and will include traditional biotechnologies such as fermentation of food products (beer, cheese, soy sauce, etc.) and conventional plant breeding. Its main function is to provide an opening to include new developments in modern biotechnology that are not included in the OECD’s list-based definition (see Box 1).

The scenarios for the bioeconomy project should exclude traditional biotechnology. The focus is on **modern** biotechnologies, including both basic and applied research relevant to the categories in Box 1. Core modern biotechnologies involve the use of **genetic information at the molecular level** (using gene sequencing data), the ability to manipulate genetic codes with **recombinant technology**, and **synthetic biology** to directly build proteins and other valuable organic compounds. Modern biotechnology also includes **allied technologies** such as new drug delivery systems (*i.e.* pegylation for large molecule therapeutics), medical devices such as tissue engineering and some diagnostics, bioinformatics, and nanobiotechnology.

The OECD list-based definition of biotechnology also includes two types of biotechnologies that are not based on genetic information: cell and tissue culture and engineering, and process biotechnology techniques. These are included because they are intermediary between traditional biotechnology and modern biotechnology based on genetic information or recombinant technology, and because they are important for specific application fields.

Box 1. OECD list-based definition of biotechnology techniques

- 1. DNA/RNA:** Genomics, pharmacogenomics, gene probes, genetic engineering, DNA/RNA sequencing/synthesis/amplification, gene expression profiling, and use of antisense technology.
- 2. Proteins and other molecules:** Sequencing/synthesis/engineering of proteins and peptides (including large molecule hormones); improved delivery methods for large molecule drugs; proteomics, protein isolation and purification, signalling, identification of cell receptors.
- 3. Cell and tissue culture and engineering:** Cell/tissue culture, tissue engineering (including tissue scaffolds and biomedical engineering), cellular fusion, vaccine/immune stimulants, embryo manipulation.
- 4. Process biotechnology techniques:** Fermentation using bioreactors, bioprocessing, bioleaching, biopulping, biobleaching, biodesulphurisation, bioremediation, biofiltration and phytoremediation.
- 5. Gene and RNA vectors:** Gene therapy, viral vectors.
- 6. Bioinformatics:** Construction of databases on genomes, protein sequences; modelling complex biological processes, including systems biology.

7. Nanobiotechnology: Applies the tools and processes of nano/microfabrication to build devices for studying biosystems and applications in drug delivery, diagnostics etc.

Health scenario

Include the following biotechnologies for both human and animal applications:

- a) Products produced using the technologies listed in items 1-3 and 5-7 inclusive of the OECD list-based definition (Box 1), or the use of these technologies in research for health applications.
- b) Large molecule recombinant therapeutics, including monoclonal antibodies (MABs), recombinant vaccines, enzymes, and hormones.
- c) Diagnostic tests (including DNA testing) for genetic conditions and molecular diagnostics for infections, cancer screening, other diseases, and tissue rejection; protein testing using micro-arrays and immunoassays of blood, etc.
- d) Molecular imaging (using peptides to bind to receptors) to identify diseases or tumours.
- e) Products produced using stem cells, or research into stem cells.
- f) Small molecule therapeutics developed through a significant contribution of biotechnology. Examples include using DNA-based molecular methods to identify new active molecules produced by micro-organisms, using comparative genomics to identify new drug targets (as with comparing metabolic pathways between hosts and parasites), or using other genetic information to identify drug targets.
- g) **Neutraceuticals** (food products with health benefits) produced using biotechnology.
- h) Application of pharmacogenomics, based on knowledge of a patient's genetic status, to develop personalised medicine.
- i) New methods of producing tissues or organs, including xenotransplantation, tissue engineering to construct *in vitro* organs and tissues, and new tissues produced through stem cells.
- j) Bioprospecting to identify novel therapeutic compounds and/or the gene sequences that produce them.

The following should **be excluded** from the health scenario:

- a) Neutraceuticals or functional foods that are not based on modern biotechnology, such as food products with added nutrients that are produced through chemical synthesis or extraction from plants. These types of food products have been available for decades.
- b) Small molecule therapeutics (the majority of most new drugs) that are not based on genetic knowledge, either in their development or in the identification of targets.
- c) Biologics, or therapeutics extracted from plants or animals (for instance insulin produced by pigs or horses, estrogen extracted from yams, etc), except when a modern biotechnology technique, such as genetic modification, is used to produce therapeutics from plants or animals (biopharming).

Grey areas:

It is not clear if some technologies should be counted as part of the bioeconomy or not. An example is using micro-organisms to produce chiral versions of small molecule drugs, such as fluoxetine (Prozac), that can also be synthesised.

Industrial-environmental scenario

Include the following biotechnologies for industrial processing, biofuels, bioremediation, and biosensors:

- a) Industrial-environmental products and processes using the technologies listed in items 1, 2, 4, 6 and 7 of the OECD list-based definition (Box 1), or the use of these technologies in research with industrial-environmental applications.
- b) Advanced fermentation and bio-reactors to produce chemicals.
- c) Chemical production processes in which one or more chemical production steps have been replaced by bioconversion or biocatalysis.
- d) Biopolymers, including bioplastics produced from starch.
- e) Enzyme production and application to textiles and animal feed.
- f) Production of biodiesel, bioethanol and biogas.
- g) Use of micro-organisms to desulphur fossil fuels, use in oil recovery, etc.
- h) Bio-leaching in mining to extract high value minerals such as copper, zinc and cobalt.
- i) Biopulping, de-inking, biobleaching and other applications of enzymes or micro-organisms to the production of pulp and paper.
- j) Bioremediation using micro-organisms or enzymes to clean contaminated soil, water and air.
- k) Bio-sensors that measure organic products through sensors using enzyme, antibodies, DNA, or micro-organisms.
- l) Bioprospecting to identify novel compounds with industrial applications and/or the gene sequences that produce them.

The following should be **excluded** from the industry-environmental scenario:

- a) Wastewater sewage treatment, unless using modified micro-organisms or other advanced biotechnologies.