Appropriate Governance of the Life Sciences - 2

The Case for Smart Regulation

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This policy brief is one of a series describing Innogen's research on strategic innovation issues in life sciences, the governance and regulation of innovation and the resulting innovation trajectories determining which products are developed and which companies take the lead in developing them.

A smarter approach to regulation could change the climate for innovation

To say that regulation has an important impact on the kinds of product that are developed by an industry sector is a statement of the obvious – regulation is designed to ensure that products are safe, effective and of high quality. However, the impacts of regulation are also more far-reaching, determining overall company strategies, which types of company succeed, and ultimately the structure and dynamism of the sector as a whole.

For example, comparing the lightly regulated information and communication technology (ICT) sector with the heavily regulated life sciences, the former sees a much greater degree and rapidity of change in products and capabilities arising from technological innovation and small start-up companies are able to build up rapidly to become major players on the basis of innovations that effectively challenge the status quo.

Innovation in the life sciences, on the other hand, is dominated by a relatively small group of multinational companies. Regulation now forms an insurmountable barrier to entry for any start-up company with an innovative idea that might challenge the status quo (Note 1).

While it would be inappropriate to suggest a lowering of safety standards in life sciences, the development of a smarter approach to regulation could go a long way to change the climate for innovation (Note 2).

IMPACT OF REGULATION ON THE STRUCTURE OF THE PHARMACEUTICAL INDUSTRY

Thus, regulatory decisions can have a formative influence on the structure and dynamism of an entire industry sector. This is particularly true of pharmaceuticals where the lengthy and demanding nature of the regulatory system has been a major contributor to the overall shape of the sector, including the so far unchallengeable supremacy of the multinational companies. The high costs and long delays entailed in taking a new product through the regulatory system ensure that only large multinational companies (MNCs) have the resources to operate throughout the whole innovation cycle. This barrier to entry for small companies has shaped the structure of the sector, leaving MNCs in their currently dominant position and insulating them from challenges from smaller innovative companies with a high growth potential. Small companies either rely on MNCs to take their products through to market, or alternatively they need to make themselves attractive acquisition targets, in both cases tailoring their innovation strategies to match those of the MNCs.

Because of their influence on this balance of power between MNCs and other companies in the health care sector, regulatory agencies have a particularly important role in shaping the sectors of the future, through major structural reforms of the regulatory system or through more targeted approaches to particular technologies.

REGULATORY STYLES IN AGRO-BIOTECHNOLOGY

We studied the effectiveness of regulatory initiatives in achieving their aims in agro-biotechnology and also their impact on firms' innovation strategies. The important dimensions were: (i) whether a regulation was *enabling* (providing encouragement or inducements to

undertake a desired course of action) or *constraining* (creating disincentives to undertaking undesirable actions)*;* and (ii) the extent to which it *discriminated* among products on a basis appropriate to the overall policy aim.

Enabling and discriminating regulation

The US Food Quality Protection Act (FQPA) 1996 created a 'fast track' approach to regulation for pesticides that could demonstrate a better health or environmental safety profile than products currently on the market. This discrimination enabled companies with such societally desirable products to gain an advantage over others and rapidly changed the behaviour of some companies in the agro-biotechnology sector.

According to managers we interviewed, the large number of candidates with these desirable properties already in the queue for registration was making it difficult to register other pesticides in a reasonable time scale. They saw the FQPA as *enabling* them to compete more effectively to get certain products through to the market place faster, by *discriminating* in favour of better products. This clearly was not enabling for companies that did not have such products in their pipelines, although it would probably stimulate them to move their R&D in this direction in the longer run.

Constraining and indiscriminate regulation

The European Drinking Water Directive (80/778/EEC), at the time of our research, set a low limit on the permitted level of contamination of drinking water by pesticides but did not discriminate among pesticides on the basis of their environmental or human toxicity hazards. This prompted companies to reject from their R&D pipelines any chemicals likely to appear in drinking water, e.g. because of mobility in soils. In our categorisation, this legislation thus failed to *discriminate* across pesticides with up to 1000-fold difference in toxicity by focusing only on the less appropriate characteristic of mobility in soils. It also acted as a *constraint*, imposing penalties rather than creating an incentive as in the FQPA.

Strobilurin fungicides demonstrate the effect-iveness of enabling and dis-criminating regulation

Comparing the European Drinking Water Directive and the US FQPA

Managers in Zeneca Agrochemicals (prior to the merger with Novartis to form Syngenta) described how these two regulatory instruments had affected their R&D for the strobilurin fungicides. These were developed from research on natural products found in mushrooms and were widely regarded as very safe from both human health and environmental points of view. Zeneca's strobilurin fungicide was the first product to be registered under the FQPA fast track system as a relatively safer product. However, this class of chemicals narrowly escaped being rejected from Zeneca's development pipeline because of their mobility in soils and hence the risk of falling foul of the EC Drinking Water Directive.

It is important to note the distinction that the enabling/constraining dimension relates to the perceptions of industry managers, whereas the degree of discrimination relates to the physical, chemical or biological properties of the products, as defined by regulators.

APPLICATIONS IN HEALTH CARE – PHARMACOGENETICS

In pharmaceuticals, some initiatives have discriminated among particular products with the intention of enabling or encouraging innovation in particular directions, for example the US FDA Fast Track and the Orphan Drugs Act. However the more usual pattern is one of gradual accretion of regulatory constraints on the development of new drugs and hence reinforcement of current innovation models and industry structures.

One particular set of regulatory challenges arises from pharmacogenetics, the development of drugs targeted to sub-groups of patients with specific favourable genetic pre-dispositions. This is currently the subject of both regulatory and technological innovation and the outcome could be an opening up of new innovative opportunities for smaller companies, rather than favouring larger multinationals. For example, to support innovation in these areas, a regulatory agency could usefully learn from our evaluation of agrochemical regulation and focus on the extent to which a regulatory approach is able to discriminate between different types of product and the appropriateness of this discrimination.

REGULATING INNOVATIVE TECHNOLOGY – GM CROPS AND STEM CELLS

Scientific discoveries in biotechnology are leading to new, path-breaking products, such as stem cell-based therapies or GM crops, for which there is an expectation that regulation is necessary, but no clear regulatory precedent (Note 1). The usual policy response in such

cases is to look for a pre-existing regulatory framework into which the new type of product can be fitted. An alternative option is to design a new path-breaking regulatory framework tailored to the specific properties of the new technology.

Based on our research covering both innovation and governance in life sciences, we considered whether there might be a relationship between the emergence of a path-breaking innovation and the need for an equally path-breaking regulatory system – could one say that path-breaking innovation requires path-breaking regulation? The most notable application of this approach has been the European regulatory system for GM crops (Note 3), which is not widely regarded as a paragon among governance initiatives and is unlikely to spawn imitators in other areas.

Path-breaking or path-dependent regulation for life science innovations?

However, there is a more subtle relationship between the development of a path-breaking innovation and the need for a correspondingly novel regulatory approach. As we pointed out in the first policy brief in this series (Note 1), innovative technology may be path-breaking for one company or sector and path-dependent for another. For example, it was not inevitable that GM crops would be developed only by the agrochemical industry, for which they were indeed path-breaking. In the 1980s and early 1990s it looked equally likely that they could be developed by food and/or seed companies, for which they would have been mainly path-dependent.

A complex set of interactions among policy makers at European, US and international levels, and also among the agro-biotechnology, food production and distribution, and seed industry sectors, contributed to the regulatory framing of GM crops in the USA and EU. It might have been useful at that time to have a decision rule that guided policy makers to adopt the regulatory system that applies to the industry sector for which the new technology is path dependent (in this case the seeds sector), rather than that for which it is path-breaking (in this case the agro-biotechnology sector). This could have made a significant difference to the extent and direction of innovation in GM crops today.

Can this retrospective analysis be applied to innovative developments arising from stem cell science such as tissue-based therapies for which regulatory systems are currently being framed by the FDA and EMEA? One parallel with GM crops is the existence of a dominant industry sector for which the technology would be path-breaking (pharmaceutical multinationals) and another for which it would be path-dependent (smaller tissue engineering based companies). Comparison with the GM crops context would suggest that if regulations for stem cell-based therapies can be framed so as to be path-dependent for smaller tissue engineering-based companies, we will see faster and more innovative development of novel stem cell based therapies. On the other hand, if the regulations relate more closely to the sector for which the technology would be path-breaking (pharmaceuticals), we are likely to see longer delays in the development of these therapies, fewer innovative treatments and few or no small companies working independently on tissue-based therapies.

A SMARTER APPROACH TO REGULATION IN LIFE SCIENCES

Regulatory systems can, by a series of incremental changes over a long period, become increasingly dysfunctional and out of step with innovation in the technologies they regulate. Also, as a regulatory system builds up in this way it becomes increasingly complex and a change or addition to one set of regulations can have unpredicted implications, for example for new products in development or for companies outside the expected range of the regulations. However, the de-novo development of path-breaking regulation for path-breaking technology is also fraught with difficulties and may equally discourage, rather than encouraging innovation.

As a starting point for further discussions and developments in this area, we draw the following general lessons for the better governance of innovative technology.

The potential shape of smarter regulation

1. Regulatory initiatives can have major, rapid and positive influences on innovation processes and we need to use such insights to design or re-design the regulatory systems of the future.
2. Regulations appropriate to one policy area often have unexpected negative impacts when applied in other areas, particularly when regulators are not aware of potentially useful but vulnerable new products and processes under development.
3. A regulatory policy that *enables* positive change in industry strategies and *discriminates* among products on the basis of societally relevant criteria, is likely to be more effective and efficient than one which is *indiscriminate* and attempts to *constrain*

undesirable behaviour.

4. The *enabling* criterion will affect the speed with which a particular regulatory policy is able to exert its influence, while the extent and appropriateness of its *discrimination* among products or processes will determine its effectiveness in guiding product development in particular directions.
5. The development of path-breaking regulation for path-breaking technology should only be undertaken as a last resort
6. In considering which regulatory precedent is most appropriate for innovative technology, a useful ground rule would be to consider first the regulatory system in operation for the industry sector for which the innovation is path-dependent, rather than one for which it is path-breaking.

NOTES

Note 1. Joyce Tait, 2007. Innogen Policy Brief, *Multinational Company Innovation Strategies*, Appropriate Governance of the Life Sciences – 1

Note 2. This paper is based on a series of research projects involving interviews with regulators and senior industry managers carried out by Joyce Tait, Joanna Chataway and David Wield, beginning in the 1980s, and more recently involving Christopher Paul Milne, Tufts Centre for Drug Development, Boston. The most recent publications are:

Milne, C-P, Tait, J., Cabanilla, L., Wegner, J. (2007) Evolution along the Government-Governance Continuum: impacts of regulation on medicines innovation. (Manuscript in preparation.)

Tait, J. (2007) Systemic Interactions in Life Science Innovation. Technology Analysis and Strategic Management, 19(3), 257-277, May 2007.

Tait, J. and Chataway, C. (2007) The Governance of Corporations, technological change and risk: Examining industrial perspectives on the development of genetically modified crops. Environment and Planning – C: Government and Policy, 25, 21-37.

Tait, J., Chataway, J. and Wield, D. (2006) Governance, Policy and Industry Strategies: Agro-biotechnology and Pharmaceuticals. In eds. M. Mazzucato and G. Dosi, Knowledge Accumulation and Industry Evolution. Cambridge University Press, pp 378-401.

Chataway, J., Tait, J. and Wield, D. (2006) The governance of agro- and pharmaceutical biotechnology innovation: public policy and industrial strategy. Technology Analysis and Strategic Management, 18(2), 1-17.

Tait, J., Chataway, J. and Wield, D. (2001) Policy Influences on Technology for Agriculture: Chemicals, Biotechnology and Seeds - Final Report. Policy Influences on Technology for Agriculture (PITA): Report to the European Commission Targeted Socio-Economic Research Programme (TSER), Project no. SOE1/CT97/1068. Available at: http://www.technology.open.ac.uk/cts/pita/ and http://www.supra.ed.ac.uk/NewWeb/Reports.htm

Note 3. Joyce Tait, 2007. Innogen Policy Brief, *Risk Governance of Genetically Modified Crops.* Appropriate Governance of the Life Sciences – 3

Social science research in the ESRC Genomics Network (EGN) interprets the field of genomics broadly, including plant, animal and health related innovations in life sciences. The Network ranges across five of the UK's leading universities, and involves over a hundred researchers, administrative and support staff, and international visiting research fellows. It is one of the largest social science investments in the ESRC's current portfolio, and is becoming the largest concentration of social scientific research on life sciences in the world.

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