Institution: The University of Edinburgh

Unit of Assessment: 23 Sociology

4: Impacts on Life-Science Innovation and its Governance

1. Summary of the impact

Our research on life-science innovation, its regulation and governance has led to three systematic frameworks with which we conduct 'action research' with decision-makers in government and companies: TARGET, which supports regional R&D policy-making; AGIT, which focuses on improving policy and the regulation of life-science innovation; and ALSIS, which allows decision-makers in companies systematically to work through the decisions they will need to make in innovation processes. Users of all three frameworks in both government and companies testify to the way in which they have led to improved decision-making. Our lead researcher, Tait, has applied insights from AGIT in high-level policy roles in areas such as synthetic biology and cell-based therapies, and others involved testify to the impact of her interventions. Other evidence of impact includes companies finding this research valuable enough to partner with us in it.

2. Underpinning research

Life-science innovation covers, for example, stem-cell therapies, new approaches to drug development and new agricultural biotechnologies. It is an area of huge importance and promise, eg in stem-cell therapies for heart failure and crippling degenerative diseases. Yet, as our research and that of others has shown, the potential therapeutic, environmental and economic benefits of life-science innovation have often been slow to appear. The causes, we have found, are multiple, and include: the intrinsic complexity and unpredictability of the innovation processes involved; shortfalls in venture-capital funding and the availability of staff with the required skills; over-ambitious policy goals (eg to develop a biotech industry in a region with no strengths in that field); poor handling of public/stakeholder engagement; and inappropriate regulation. In respect to regulation, for example, 'allogenic' stem-cell therapies, in which a patient is treated with human cells derived from a single carefully selected donor, clearly require regulation, but currently in both the US and Europe they are regulated mainly under the same regime as new drugs. Some aspects of that regime – for example, the requirement for early stage trials on animals and the difficulty of deriving data relevant to human efficacy and safety from such trials – are ill-designed for these therapies. Moreover, the protracted, extensive procedures demanded by the drug-regulatory regime are too expensive for small and medium-sized stem-cell enterprises, while the culture of the big pharmaceuticals companies may not mesh well with the demands of this new field.

In our view, achieving progress in these difficult areas requires action research in which academics such as our team (Tait, University of Edinburgh [UoE] since 1998; Rosiello, UoE since 2003; Mittra, UoE since 2003; and Mastroeni, UoE since 2009) collaborate directly with policy-makers in government and companies, rather than simply studying innovation processes as external observers. We have developed three systematic frameworks for conducting this action research. All of them involve structured sets of questions to elicit from policy-makers the features of the situation they face and to help them reflect on that situation in a way that is informed by the results of our previous research, for example with actors in similar situations.

2.1 Targeted R&D Policy (TARGET) is designed to support policy-makers in Europe's regions and smaller countries, who face increasing pressure to be selective in their funding of R&D rather than spread funds too thinly (this is the European Commission's 'Smart Specialisation' approach), but with little existing effective guidance or resources to help them do this wisely. TARGET is a systematic methodology for mapping a) the strengths and weaknesses of the existing innovation system in a given region/country and sector (so far, we have concentrated on biotechnology), and b) the stages of the innovation process that key developments within that sector have reached. TARGET then helps policy-makers identify both the strategic and the tactical decisions that need to be taken to give those innovation processes a realistic chance of successfully coming to fruition.

TARGET was developed and tested by applying it in retrospective case studies of the development of biotechnology in five regions/small countries, which have had varying degrees of success in biotech (Israel, North Carolina, the Øresund 'region' of Denmark/Sweden, Scotland and Singapore) and then applied 'in real time' in collaboration with policy makers in Galicia, Lithuania and Slovenia, and in France's Direction générale de la compétitivité (Rosiello et al*.,* 2011a, b).

2.2 Adaptive Governance of Innovative Technology (AGIT) is based on extensive longitudinal research on innovation in a number of areas of the life sciences (pharmaceuticals, agro-biotechnology, biofuels, human stem-cell therapies). This research has eg revealed the crucial role of decisions taken in early stages of product development (eg the decision referred to above to subject allogenic stem-cell therapies to the full drug-testing regime) that then have unforeseen outcomes (see, eg, Mittra and Tait, 2012; Mittra, Tait and Wield, 2011). For example, AGIT:
i) helps policy-makers identify the potential enabling and/or constraining roles of their decisions;
ii) encourages policy-makers to retain the scope for future modification of policies and regulations as more is learned about the benefits and risks of a technology, product or process;
iii) encourages them to consider new, more critical approaches to stakeholder engagement.

2.3 Analysis of Life-Science Innovation Systems (ALSIS), implemented using Banxia's Decision Explorer software, is a method that allows managers in companies systematically to work through the decisions that will need to be made as they move innovations towards practical use. It allows them to examine a variety of scenarios (for example, in which demand for the product in question suddenly rises or falls, or regulatory/production difficulties emerge). In particular, ALSIS is informed by the results of our detailed AGIT research on regulation and its likely medium-term changes (it can be hard even for experienced industry personnel to keep abreast of changing, dauntingly complex regulatory frameworks and practices). ALSIS was developed and tested in action research with early stage companies involved in developing regenerative medicine products based on human embryonic stem-cell lines (Mastroeni et al., 2012).

3. References to the research

1. Mastroeni, M., Mittra, J. & Tait, J. (2012) *Methodology for the Analysis of Life Science Innovation Systems (ALSIS).* Innogen Centre Report to Technology Strategy Board. Available via http://www.research.ed.ac.uk/portal/files/8470021/REALISE_Case_Study_Report_Innogen.pdf.
2. Mastroeni, M., Tait, J., & Rosiello, A. (2013) Regional Innovation Policies in a Globally Connected Environment. *Science and Public Policy*, 40, pp. 8-16, DOI: 10.1093/scipol/scs115.
3. Milne, C.P. & Tait, J. (2009) Evolution along the Government-Governance Continuum: FDA's Orphan Products and Fast Track Programs as Exemplars of 'What Works' for Innovation and Regulation. *Food and Drug Law Journal,* 64(4), pp. 733-753, PDF available on request from HEI.
4. Mittra, J. & Tait, J. (2012) Analysing Stratified Medicine Business Models and Value Systems: Innovation-Regulation Interactions. *New Biotechnology*, 29(6), pp. 709-719, DOI: 10.1016/j.nbt.2012.03.003.
5. Mittra, J., Tait, J. & Wield, D. (2011) From Maturity to Value-Added Innovation: Lessons from the Pharmaceutical and Agro-Biotechnology Industries, *Trends in Biotechnology,* 29(3), pp.105-109, 10.1016/j.tibtech.2010.11.004.
6. Rosiello, A. et al. (2011a) *TARGET Policy Report: Promoting the Biotechnology Sector*. http://jiis.org/.upload/TARGET%20Policy%20Report.pdf
7. Rosiello, A., Avnimelech, G. & Teubal, M. (2011b) Towards a Systemic and Evolutionary Framework for Venture Capital Policy. *Journal of Evolutionary Economics*, 21(1), pp.167-189, DOI: 10.1007/s00191-010-0189-x.

Main underpinning research grants

1. 2002-13: Tait, J., (PI), et al., *Innogen: Centre for Social and Economic Research on Innovation in Genomics, Phases 1 & 2*. ESRC, £7.2M (Refs. RES-145-28-1004; RES-145-25-0008).
2. 2010-11: Tait, J. (PI) et al., Technology Strategy Board & ESRC, *A Therapy Realization Pathway Tool (REALISE)*, £154,000.
3. 2009-11: Rosiello, A. (PI), EU FP7 *Target Project*; Grant Agreement 34522 –Total €839,950; funding to Edinburgh University, €165,000.

4. Details of the impact

Our team has engaged closely with life-science practitioners and decision-makers in both government and firms, via: 51 talks by Tait to audiences with strong industry/government representation; 33 workshops with industry/government participants; the advisory committees listed in section 4.2; and a series of publications in outlets read by practitioners, such as *Science* (29 April 2011) and *Nature Biotechnology* (26 [2008]: 500-501): both available via www.wiki.ed.ac.uk/display/REF2014REF3B/UoA+23. Above all, though, impact has been achieved via the action research involved in TARGET, AGIT and ALSIS.

4.1 Impact of TARGET (corroboration sources: see section 5.1)
Our action research implementing TARGET in real time involved us directly in policy-making processes. For example, when employing it in Lithuania, it became clear to us that a major barrier to effective biotechnology policy making was a 'turf war' between two ministries. We therefore recommended the creation of an independent steering committee, which was then established and helped overcome barriers to communication. [Text removed] of the Lithuanian National Research Council comments 'The evidence of positive impact of your work is the development in the policy making … in the …science centers program which is in progress now' (email, 20 April 2012).

More generally, policy-makers who have used TARGET report that they have found it very helpful in determining the best policies to implement, according to the local context and capabilities. Eg:

> 'Your expertise … has been particularly useful to us as we develop and test … "smart specialization" [see section 2.1] as framework for innovation policy making' ([text removed], Organisation for Economic Cooperation and Development [OECD], email, 7 May 2012).
> 'Your input and recommendations … were a valuable contribution to the development and refinement of the Lower Austrian Smart Specialisation Strategy' ([text removed], Ecoplus, Business Agency for Lower Austria Ltd, email, 7 May 2013).

4.2 Impact of AGIT (corroboration sources: see section 5.2)

Tait is employing the results of AGIT in advising government policy-makers on how to improve regulation so that it moves beyond simply the rejection of unsafe or ineffective products to becoming more supportive of beneficial innovation. Tait is currently a member of the Emerging Science and Bioethics Advisory Committee (ESBAC) and the Synthetic Biology Leadership Council (SBLC) where she has been given leading roles in sub-committees to advise, based on the ALSIS and AGIT approaches, on governance-related aspects of their remits.

On SBLC she has on several occasions submitted advice, on request, direct to its Co-Chair David Willetts MP, and Willetts has arranged to visit Innogen to discuss how its ideas could be applied to the 'eight great technologies' in which he hopes the UK can be a world leader. Testimony to Tait's role includes:

> 'Professor Tait's … clear views on how innovative governance can be applied to a variety of regulatory situations are of great value to ESBAC. Synthetic biology, cell based therapies and stratified medicine all represent emerging scientific areas where a commonality of approach to regulation will be advantageous.' ([text removed], email, 11 April 2013);
> '…discussion of regulatory issues with you has been invaluable … to clarify our position with regard to ongoing strategy. … shaping our response to European legislation on the regulation of ATMPs [Advanced Therapy Medicinal Products], …and [enabling] us to improve the impact we … make on behalf of the patients and families with genetic diseases' ([text removed], Genetic Alliance, UK, email, 2 May 2013);
> '… the valuable input you have already made [to] … the SBLC. [including] … your summary of the issues arising from the Convention on Biological Diversity (CBD), which … had a clear impact on our prioritisation of issues [and] is now leading to valuable ongoing discussions and follow-up actions with key stakeholders. Your direct involvement and extensive experience is also playing an important role in shaping plans for a regulatory and governance sub-group that will facilitate the way we engage with stakeholders.' ([text removed], SBLC, email, 9 May 2013)

Tait has also, for example, advised the Technology Strategy Board (an independent advisory body that reports to the Department for Business, Innovation and Skills) on the creation of its Responsible Innovation Framework (RIF):

> 'Your input to the early thinking and framing of the RIF, the subsequent execution of the Framework … and your role as an assessor has contributed significantly to the current position we now have. … The impact of your help and support in helping shape the policy and the process has been invaluable' ([text removed], Technology Strategy Board, email, 11 March 2013).

Companies using AGIT report that it helps their staff understand the complexities of regulation in this sphere. Thus [text removed] of the large Swiss seeds, agrochemical and biotechnology company Syngenta comments:

> 'Innogen's Adaptive Governance of Innovative Technology framework has helped me to

understand the stages in the development of regulation of new technology and how science ought to influence each stage.' (email, 13 Sept 2013)

Further evidence of the usefulness of AGIT to Syngenta is that it is now funding research by our team applying AGIT and our team's perspectives on stakeholder engagement with a view to improving the regulation of agricultural biotechnologies; this is the first time Syngenta has funded research into the governance of new technology.

4.3 Impact of ALSIS (corroboration sources: see section 5.3)

The companies using ALSIS similarly report that it has enabled them to make better-informed decisions on product and process development in light of the emerging regulatory system and its impact on business decision-making. For example, [text removed] of Roslin Cells Ltd, comments:

'Your analysis methodology and the specific tools used to undertake the value chain analysis was extremely effective … As a direct impact … we have extended our product offering and improved the analysis which we use to assess the viability of new opportunities.' (letter, 12 Sept 2013)

Other evidence of the practical usefulness to companies of ALSIS and our other methodologies is that substantial numbers of companies are now prepared to invest staff time and effort in joint research with our team. Five multinational companies (including eg GlaxoSmithKline) and nine smaller companies are now involved as partners with us in joint projects with funding from the Research Councils and Scottish Funding Council. Two executives explain why they have chosen to partner with our team:

'GSK [GlaxoSmithKline] have identified [the Edinburgh team] … as a world-leading group who have demonstrated, strong credentials for leading large investments.' ([text removed], GlaxoSmithKline, letter, 17 Dec 2012)

'The [Innogen] team is a world-leading group who … have the inherent skills and experience necessary to support innovation processes, [and] to contribute to the successful governance of synthetic biology.' ([text removed], Selex ES, letter, 19 Dec 2012)

Note re testimony: [text removed] were participants in the action research (using TARGET, AGIT and ALSIS, respectively). [Text removed] are now partners with us in joint projects. [Text removed] recruited Rosiello's expertise to advise OECD on Smart Specialisation. [Text removed] are reporters on the impact.

5. Sources to corroborate the impact

PDFs of all emails and letters available at www.wiki.ed.ac.uk/display/REF2014REF3B/UoA+23.

5.1 Impact of TARGET: emails from staff members of Lithuanian National Research Council, 20 April 2012; OECD, 7 May 2012; and Ecoplus, Business Agency for Lower Austria Ltd, 7 May 2013.
5.2 Impact of AGIT: emails from: [text removed], 11 April 2013; [text removed], 2 May 2013; [text removed], Synthetic Biology Leadership Council, 9 May 2013; [text removed], Technology Strategy Board, 11 March 2013; Syngenta, 13 Sept 2013.
Research Collaboration Agreement between Syngenta and University of Edinburgh, 23 April 2013.
5.3 Impact of ALSIS: letters from: [text removed] of Roslin Cells Ltd, 12 Sept 2013, and staff members of GlaxoSmithKline, 17 Dec 2012, and Selex ES, 19 Dec 2012.
5.4 Individual users/beneficiaries who could be contacted to corroborate claims
The usefulness of this research as a basis for large-scale industry/academia collaborations can be corroborated by: Biocatalysis and Synthetic Chemistry Manager, GlaxoSmithKline R&D; and Head of Business Innovation, Selex ES.
Syngenta Fellow, Syngenta AG: can corroborate the usefulness of Innogen's Adaptive Governance of Innovative Technology framework.
Director, Genetic Alliance UK: can attest to the usefulness of the research of Tait et al. in supporting his work advising patients suffering from genetic diseases and their families.
Project Manager, Clusters, EcoPlus, Lower Austria: can corroborate usefulness of TARGET for Smart Specialisation strategy.