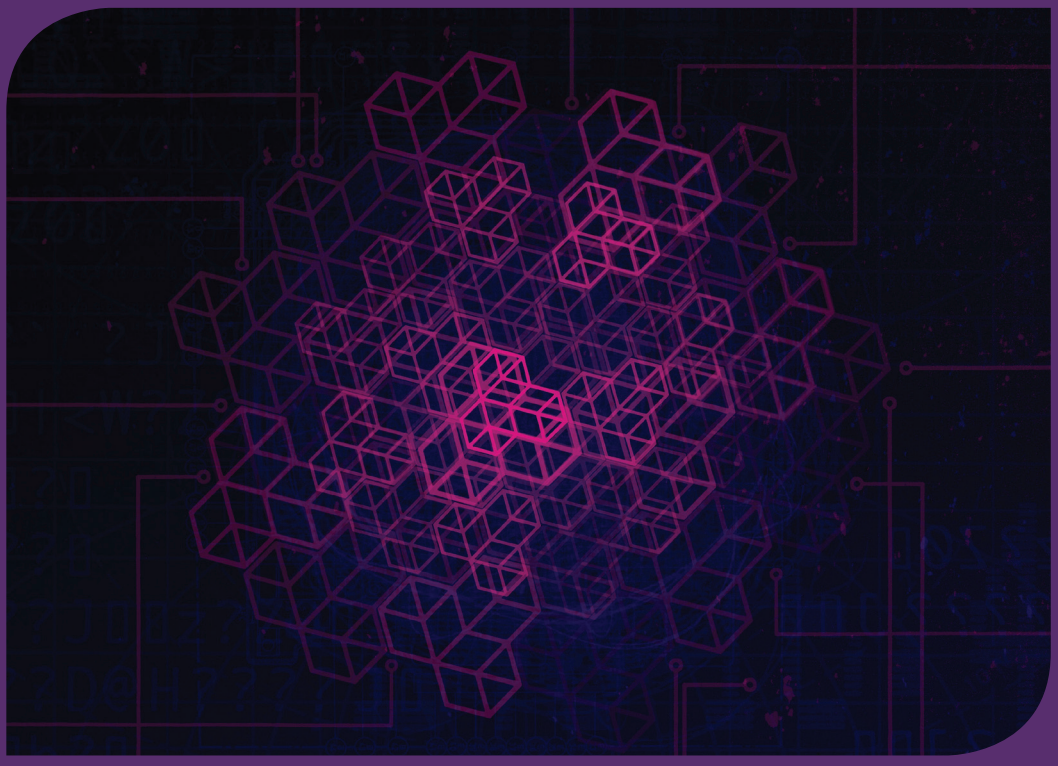
SHAPING THE FUTURE OF OPEN INNOVATION:

A practical guide for life sciences organisations

September 2014



kinapse casmi wellcome trust

Authors: R Pigott, R Barker, T Kaan, M Roberts

Significant contributors: N Davie, M Morys, G Outteridge

Contents

1. Executive summary

Open innovation, which we define as the process of innovating with others for shared risk and reward to produce mutual benefits, has evolved significantly over the last two decades. 'Open access' or 'open source' are important phenomena, but this report focuses on how open collaborations in life sciences are developing. This trend is driven by the declining productivity of the pharmaceutical industry, the emergence of technologies that all players need to be successful, the recognition of the wastefulness of duplicated programmes and – most importantly – the search for innovative yet affordable therapies for untreated, complex, life-limiting diseases.

Partnerships between a wide range of life sciences organisations are becoming ever more numerous, cross-disciplinary and open (in terms of data and knowledge sharing), and are reaching further down the value chain. The purpose of this report is to explore and evaluate these trends and suggest what the future might hold.

Four open innovation goals are being pursued – creating products, developing tools and models, building information databases, and accessing the skills and support of the 'crowd' in problem solving. Using a combination of literature analysis, surveys and structured interviews with more than 40 organisations, and multi-stakeholder workshops – and having been guided by a senior group of open innovation practitioners – we have identified the following four actions as being of key importance to successful collaboration:

1. Aligning objectives: Organisations engage in open innovation for a number of scientific, economic and altruistic reasons. The most important factor in avoiding failure when entering a partnership is ensuring that the objectives of the partners are truly aligned.

2. Managing intellectual property (IP): While divergent attitudes to IP and its importance in innovation can hold back open innovation, in practice there are mechanisms, like 'protected commons' and patent pools, that can enable partners to balance the need for openness on research results with the ultimate need for a clear IP position on products requiring major investment. The key is for partners to anticipate and discuss their respective IP needs in advance and incorporate the right design into their partnership agreement. A wide range of potential solutions are available.

3. Bridging cultures: Inherent cultural differences between groups can be a barrier to open innovation. Academics are motivated by publications and can misunderstand the commercial relevance of a project; industry participants can be reluctant to share know-how and can suffer from the 'not invented here' syndrome; health providers can be difficult to engage and often aren't incentivised to innovate. Research charities and patient organisations are becoming more active in the search for new treatments and are increasingly holding other participants to account.

As open innovation becomes more accepted, all these groups are learning to work together more effectively and to recognise one another's expertise, constraints and motivations – both as organisations and as individuals. We found that university technology transfer offices are more often cited as barriers than as facilitators. Likewise, although health services such as the NHS are being encouraged to innovate, and there are a few successful academic–industry–health service projects, their incentives and cultures still hold back partnerships. We need further change on both fronts if open innovation is to flourish.

Of all the tools available, partners spending real time together focused on shared scientific and clinical goals is the most powerful, and this is obviously easiest to do when they are located close together.

4. Structuring for success: Professional management is as important in collaborations as in any other enterprise, but needs to be genuinely joint and goal-oriented. Specific techniques and metrics of success vary depending on the structure, objectives, R&D stage and maturity of a partnership. There need to be clearly defined roles, strong leadership and agreed milestones in order for a collaboration to run smoothly. Tough-minded joint go/no-go decisions are critical to avoid 'consortium fatigue'. Having a neutral convener can help create a trusted environment and facilitate productive partner relationships, but there is no substitute for regular in-person review meetings, focused initially on leading indicators of success but increasingly on the ultimate outputs. Most of the initiatives we reviewed gave themselves high marks for success to date, but many would acknowledge it is too early to assess overall outcomes.

Emerging models: The last few years have seen the rapid development of crowdsourcing, and to some extent crowdfunding, in life sciences. We found a great deal of early promise and excitement, including among established companies, as well as a plethora of models. Skilled set-up, thoughtful marketing and the judicious use of financial rewards are all important, but it was acknowledged, even by those directly involved, that we still understand little about the motivations of those contributing (whether ideas or money). Further research on this topic could greatly increase the impact of these developments.

Looking beyond the sector, we see initiatives to create IP exchanges and auctions, patent pools and clearinghouses, and these are beginning to make an impact in life sciences. More facile databases and artificial intelligence are likely to accelerate this trend, so that less and less knowledge is hidden from the rest of the field.

Tool kit: We have created a tool kit (Appendix 1) to answer two questions for practitioners: should we take an open innovation path to address our problem, and, if so, how should we structure the collaboration? We hope that our step-by-step approach to confront the key questions at the outset will improve the chances of future open initiatives succeeding.

Future ecosystem: We are moving towards a more open world, which organisations must engage in in order to survive. The traditional linear, in-house R&D model is being abandoned and is being replaced by a dynamic network of partnerships. The boundary of what is being conducted in an 'open' fashion is being pushed towards later stages in the development pipeline, and there is also a greater focus on open source and open access approaches to knowledge sharing. Open innovation is beginning to have a major impact on both discovery and development; we predict that this will extend to the critical third step of securing beneficial patient outcomes. The outline of the radically different, and very intriguing, life sciences 'ecosystem' of the future is beginning to appear.

2. Introduction

"I would really hate people to think that open innovation is a theoretical exercise – it's about getting things to market in a cost-effective way. It's about translating research better."

Dr Martino Picardo, CEO, Stevenage BioScience Catalyst

Henry Chesbrough first coined the term 'open innovation' to mean "a paradigm that firms can and should use external ideas as well as internal ideas, and internal and external paths to market, as the firms look to advance their technology. The business model utilizes both external and internal ideas to create value, while defining internal mechanisms to claim some portion of that value."[1] Since then, a huge variety of definitions for open innovation have been suggested.

For the purposes of this report, we have described open innovation as:

"The process of innovating with others for shared risk and reward to produce mutual benefits for each organisation, creating new products, processes or ideas that could not otherwise have been achieved alone, or enabling them to be achieved more quickly, cheaply or efficiently."

An open innovation partnership involves sharing ideas, data, tools or intellectual property (IP) with other organisations, often in a very transparent manner. Crucially, mechanisms need to be put in place to allow the value created from the collaboration to be captured by each contributor in some way. Open innovation can involve partnerships between organisations of the same type (e.g. multiple pharmaceutical companies) or several of different types (e.g. academics and healthcare providers) and can sometimes involve the public (some crowdsourcing and crowdfunding models). The results of open innovation partnerships can be, but don't necessarily need to be, 'open access' or 'open source', as defined below.

Box 1. Definitions

Open innovation
The process of innovating with others for shared risk and reward to produce mutual benefits for each organisation, creating new products, processes or ideas that could not otherwise have been achieved alone, or enabling them to be achieved more quickly, cheaply or efficiently.

Open access
Open access literature is digital, online, free of charge, and free of most copyright and licensing restrictions[2]. It removes the pricing and permission barriers imposed by subscription journals and allows free availability and unrestricted use of content.

Open source
In open source, knowledge is made freely available to the wider community, not just the partners in collaboration[3]. The open source model originated in the software industry, in which source code was freely distributed and computer enthusiasts added features and made improvements, which they were then required to share with the wider community[4]. In the context of life sciences, knowledge is shared widely among scientists and sometimes the public, so that they can work together on medical innovation projects, such as developing a new drug for a neglected disease.

Box 1. Definitions of open innovation, open access and open source

Previous reviews have focused on how open partnerships have evolved and on the current models of collaboration in life sciences. We will be examining in some detail four key areas – objectives, IP, culture, and practical considerations – to assess the barriers and opportunities presented by open innovation, in order to guide organisations through the steps towards engaging in an open partnership. Although our project examined life sciences broadly, the majority of examples and insights relate primarily to biopharmaceuticals.

2.1 On a path to open innovation in life sciences

In the 1990s more than 90 per cent of life sciences research companies in the USA were collaborating with academia, and there were nearly 1500 alliances between pharmaceutical and biotechnology companies[5]. However, these collaborations were mostly within a linear, transactional model: each player knew their role and was largely confined to it, and most of the 'handoffs' were quite 'arms-length'. Academia received funding from research charities (governmental and non-profit organisations) to conduct research and publish new targets; industry (either in the form of small and medium enterprises (SMEs) or major pharmaceuticals) turned them into patented candidate drugs for development; and the successful products were promoted for use in health systems, which were passive recipients of what the industry chose to develop and launch (

Figure 1).

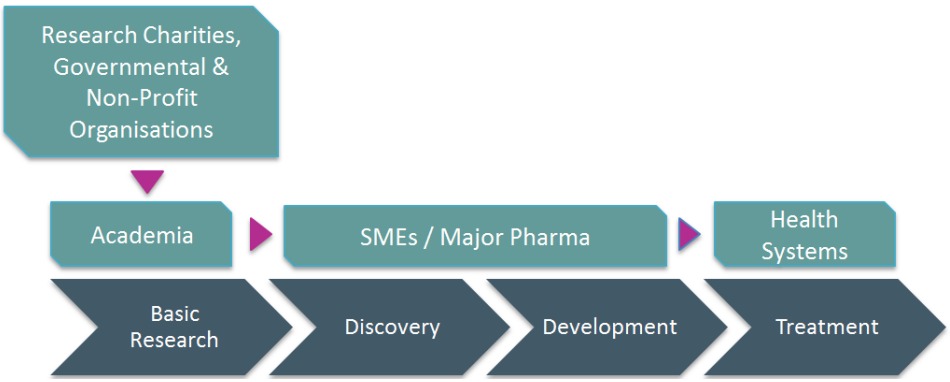


Figure 1. Traditional linear innovation approach

This historical partnership system was largely 'closed': discoveries were patented at an early stage and there was limited organisational interchange. In fact, companies prided themselves on being or becoming 'FIPCOs' – fully integrated pharmaceutical companies – this being seen as the key goal by life sciences investors. This system generated a global pharmaceuticals market worth US$300 billion a year that, until recently, was expected to enjoy double-digit growth[6]. With the 10 largest pharmaceuticals controlling over one-third of the market, the innovation system underpinning it was not seriously questioned until relatively recently.

This largely 'closed' system is inefficient in several ways. As one of our interviewees, Professor Chas Bountra (Chief Scientist of the Structural Genomics Consortium), commented: "One prospective new protein target would be having its structure determined by 20 different groups simultaneously – a huge waste of resources." More subtly, the failure to integrate payer and patient views into the drug discovery process at an early stage has led to costly, late-stage failures when developers are not reimbursed appropriately for drugs or patients fail to adhere to their medications. This model has clearly failed to deliver, as overall system productivity has fallen exponentially[7].

Over the last 20 years the life sciences industry has increased its level of 'openness'. Industry–academic partnerships that were once quite restricted in scope and based on individual relationships between researchers have gradually become more systematic and are now established across multidisciplinary areas (Figure 2)[8]. This began in non-economic spaces such as neglected diseases (e.g. the Medicines for Malaria Venture) but the phenomenon is now spreading to economic markets. Some consortia cover multiple therapy areas and comprise a wide range of expertise and capabilities (e.g. the Centre for Drug Research and Development). Joint steering mechanisms, such as those exemplified in Pfizer's partnerships with 20 academic collaborators, emphasise the importance of collaborative rather than transactional relationships. More recently there has been a push to share data for a reduced cost or even free of charge in the spirit of open access, and towards engagement of a much wider group of collaborators through crowdsourcing and crowdfunding.

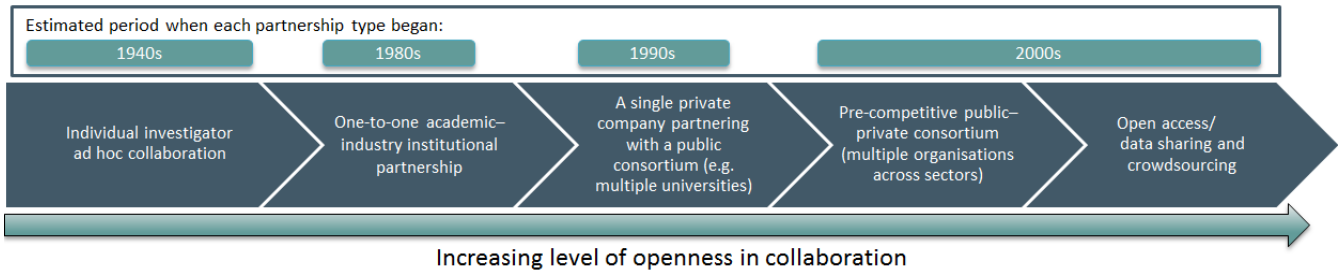


Figure 2. Progress of open innovation in a life sciences partnership

Pharma and biotech companies have been increasingly active in open innovation alongside other pioneering industries, such as the software, electronics and telecommunications industries[9]. A study by the Organisation for Economic Co-operation and Development (OECD)[10], for example, showed that in 2003 pharma and biotech companies filed over 13 per cent of the European Patent Office's (EPO) applications with multiple applicants, compared to the chemical industry, which filed only around 8 per cent of such applications.

2.2 Driving forces shaping open innovation

"The advantage is that the diversity is a real plus – if you did it in your own lab you're stuck with the thinking of people there, and the degree of innovation allowed is perhaps minimal."

Dr Piero Olliaro, Team Leader of Intervention and Implementation Research, TDR, WHO

There are many motivations for engaging in open innovation (Figure 3), including:

- resolving shared challenges within the medical innovation process (e.g. in nanomedicine, via the French BioAlliance consortium)
- economic or time benefits (e.g. partners pooling investments in protein structure determination in the Structural Genomics Consortium)
- common needs for widely accepted tools or standards (such as the biomarker discovery efforts at the Critical Path Institute or in the Innovative Medicines Initiative (IMI)* programmes)
- a general sense that collaboration is required to address challenges of broad societal and/or global significance (as in the Medicines for Malaria Venture).

* We have not examined IMI in any detail in this report because we are conducting a separate project to understand and optimise its impact and it is yet to be reported.

Beyond the benefits to individual participants there are also systemic benefits to the ecosystem. Open innovation can cut the cost of failure by avoiding duplication and reducing attrition, promoting cross-sector collaborations and technological convergence, encouraging idea generation in a shared risk environment, and providing a mechanism to share best practices and data more widely.

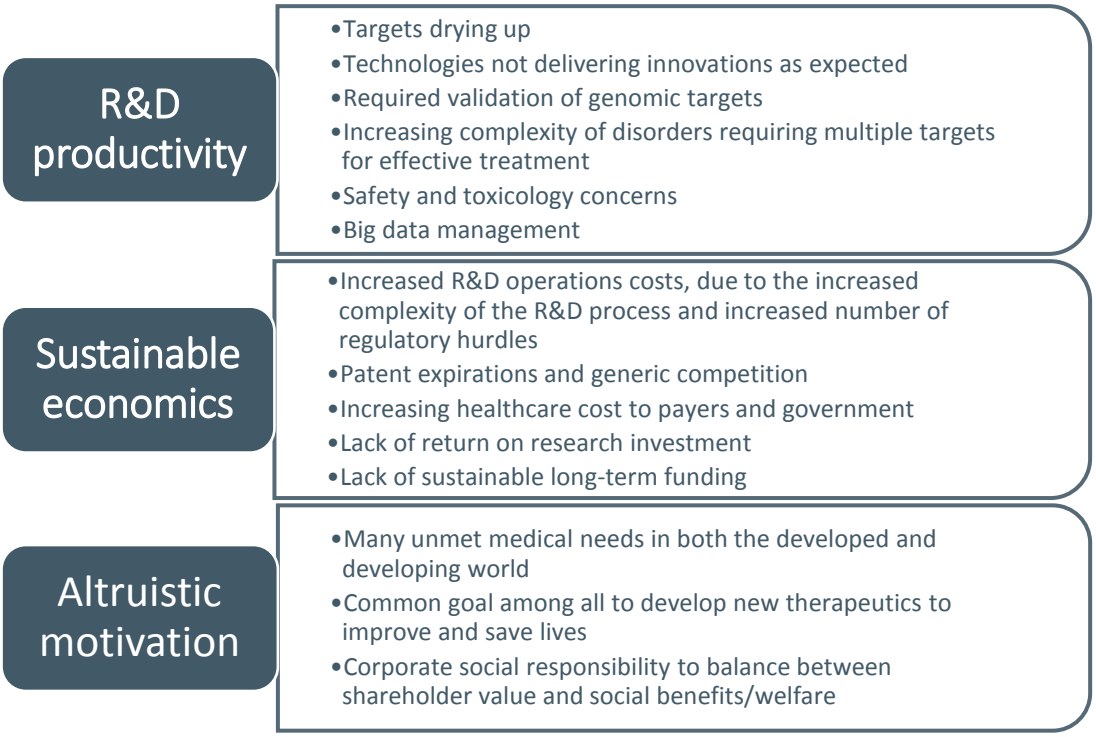


Figure 3. Key driving factors behind open innovation in life sciences

In this report we discuss the barriers to and facilitators of open innovation and examine emerging models. In-depth analysis of a number of case studies has given us insight into four key dimensions of open innovation, namely objectives, IP, culture and practical considerations. Evaluation of these real-world examples has fed into our open innovation tool kit, a practical guide for organisations who are considering engaging in open innovation partnerships.

"No single group can solve all the problems in this space. We need to work together in partnership."

Dr Gustavo Stolovitzky, Director, DREAM Project

3. Methodology

3.1 Literature review

Articles relating to life sciences open innovation were accessed and reviewed via Google and academic databases including PubMed, Academic Search Complete and Business Source Complete. Search terms used included “life sciences open innovation”, “pre-competitive”, “academic–industry partnerships”, “IP management”, “public–private partnerships”, “crowdsourcing”, “academic drug discovery centres”, “open access”, “open source” and “patent pool”. Relevant articles were reviewed and analysed to extract key ideas and issues on life science open innovation.

3.2 Advisory group

An advisory group was formed of experts in the field of open innovation, consisting of members from industry, academia, government, funders, charities and policy groups (Table 1). The group included active scientists, policy experts, trade bodies and economists. An advisory group meeting was held at the Wellcome Trust at the start of the project to help steer the direction of research and highlight key themes to pursue. A draft version of this report was also shared with the expert panel, and their comments were integrated into the final publication.

Professor Chas Bountra	Chief Scientist, Structural Genomics Consortium
Dr Thomas Daniel	President of Global Research and Early Development, Celgene
Dr Aled Edwards	CEO, Structural Genomics Consortium
Dr Stephen Friend	President, Co-founder and Director, Sage Bionetworks
Dr Richard Horton	Editor-in-Chief, *Lancet*
Dr Jackie Hunter	Chief Executive, Biotechnology and Biological Sciences Research Council (BBSRC)
Sir Robin Jacob	Professor of Intellectual Property Law, University College London; former Lord Justice of Appeal
Dr Hannah Kettler	Economist and Senior Program Officer, Bill & Melinda Gates Foundation
Harpal Kumar	CEO, Cancer Research UK
Sara Osborne	Head of Policy, Cancer Research UK
Dr Zahid Latif	Head of Healthcare, Technology Strategy Board (TSB)
Dr Louise Leong	Director of R&D Policy, Association of the British Pharmaceutical Industry (ABPI)
Professor Mariana Mazzucato	RM Phillips Chair in the Economics of Innovation, University of Sussex Science and Technology Policy Research Unit (SPRU)
Dr Mary Moran	Executive Director, Policy Cures
Nicola Perrin	Head of Policy, Wellcome Trust
Dr Martino Picardo	CEO, Stevenage BioScience Catalyst
Professor Adrian Towse	Director, Office of Health Economics

Table 1. Open innovation project advisory group

3.3 Survey

A survey (Appendix 2) was circulated to a number of individuals involved in open innovation partnerships identified in the literature review. The survey aimed to provide an initial insight into the rationale for entering a partnership, the metrics used to measure progress, and how successful the collaborators believed their collaborations had been. This provided a small sample of data, which were followed up in all but one case with an in-depth interview.

3.4 Interviews

Structured interviews were conducted with 26 key individuals from the open innovation case studies identified (using the interview framework in Appendix 3). The interviews aimed to gather information and the participants' perspectives on the following factors:

- objectives
- intellectual property
- practicalities
- human factors
- metrics
- evaluation.

Each interview lasted between 30 minutes and 1 hour, was recorded with permission of the participant and later transcribed. A full list of participants can be found in Appendix 4. Quotes taken directly from these interviews have been used throughout this report and have been attributed to the interviewees (with their permission).

3.5 Analysis

NVivo 10 software was used to analyse the results of the survey and interviews. NVivo is a tool for organising, evaluating and interpreting semi-structured data. The results of the survey and the interview transcripts were uploaded onto the program, coded accordingly and analysed for trends and common themes.

3.6 Workshop

Our initial work identified that health systems do not engage in partnerships as much as academia and industry. In association with the Academy of Medical Sciences, we held a workshop on 'Open Innovation and the NHS'. This workshop explored the key issues and opportunities surrounding collaboration with the UK NHS (as an example of a health system), with a focus on open innovation models. Delegates from the NHS, academia, industry, government and funding bodies participated in the workshop.

In particular, participants discussed current relevant examples of open innovation in the UK and whether there is scope for health systems such as the NHS to collaborate in new ways with academia and industry. Specific challenges for open innovation were identified, such as incentives, cultural barriers and issues surrounding intellectual property (IP). Opportunities that such collaborations provide were highlighted, with this including a discussion about the success metrics for open innovation collaborations.

Outcomes consisted of a number of best practice guidelines for open innovation collaborations with the NHS and a full report[11], which is available on the Academy's website.

3.7 Tool kit

Informed by the literature, workshops and the analysis of qualitative data, we have produced a practical tool kit (Appendix 1) containing guidelines for organisations that are considering engaging in open innovation. The tool kit consists of a step-by-step guide to assist potential partners in deciding whether an open innovation approach is appropriate for their objectives, and, if so, which partners, structures, agreements and metrics they should use.

4. Objectives

4.1 The classic description of open partnerships

Life sciences open innovation partnerships are commonly classified by their organisational structures, for example as academic drug discovery centres, academic–industry alliances or public–private pre-competitive consortia, or as being crowdsourced.

Figure 4 provides a 'descriptive taxonomy' that can be used to categorise these collaborations in terms of number of partners, R&D stages involved and the 'openness' of knowledge sharing.

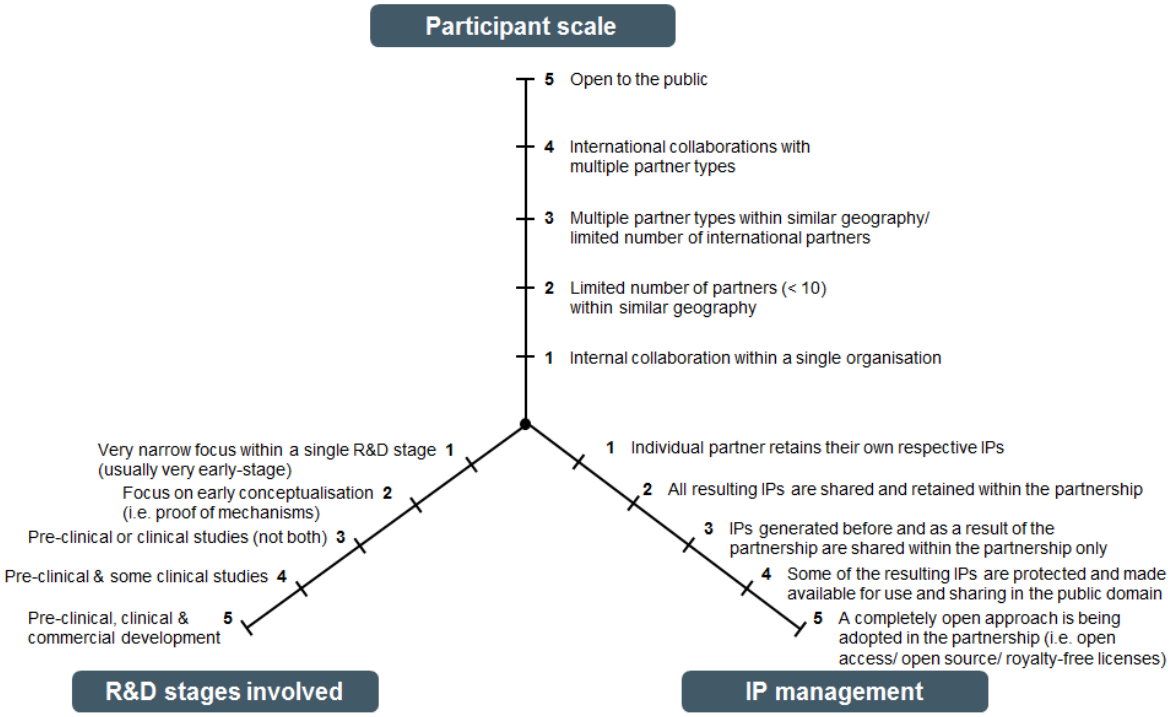


Figure 4. A descriptive taxonomy of open innovation partnerships

4.2 A new taxonomy based on objectives

However, the above traditional 'descriptive' classification, based on partnership structure or types of partners, fails to correlate with the actual work and objectives of the partnerships. We propose a different taxonomy based on common objectives (input motives merged with output measures) as a more holistic and accurate reflection of the field.

From an examination of more than 40 open innovation partnerships in life sciences, four broad categories of prime objectives emerged (case examples are grouped against these objectives in Figure 5).

1. *Development and commercialisation of new drugs*

These partnerships have the common objective of producing new drugs. They can be further broken down depending on whether they are (a) focused on a single disease/therapy type only or (b) cover multiple diseases/therapy types. Where the interests are focused on a specific disease/therapy type, the collaborations often cover multiple R&D stages from early research through to commercial

development, whereas collaborations that cover multiple diseases/therapy types tend to be more focused on a specific R&D stage, such as compound screening or basic pre-clinical research.

Typical goals in this category include developing products for given disease areas and bridging the gap between early scientific discovery and translation into new therapies. The objectives of the Edinburgh BioQuarter, for example, are very clearly to accelerate the development of new treatments for human and animal diseases and to work with researchers, industry and investors to create new drugs, diagnostic tools and medical devices.

2. Tools, standards and models development

The creation of common tools (such as biomarkers), common standards (such as nanoparticle characterisation) or common models (such as cell-based toxicology screening) are a second, very vibrant focus of open innovation. All types of common assets have the potential to stimulate progress in these 'enabling technologies' and so accelerate progress towards therapies. The creation of a common lexicon and convergence on a common tool or standard are vital elements in such initiatives.

Typical goals in this category include the discovery/development and qualification of biomarkers or protein structures. Genomics is a growing area for open innovation: the goal of the CLARITY Challenge, run by the Boston Children's Hospital, was to identify the best methods and practices for the analysis, interpretation and reporting of individuals' DNA sequence data, to provide the most meaningful results to clinicians, patients and families.

3. Information databases

These partnerships create and maintain databases to share information in support of processes such as drug development. They effectively pool knowledge (as in the case of known toxicology profiles) that enables all participants to move more reliably towards their own research targets. Some information databases are being developed and shared among a limited group of collaborators within a partnership, whereas others share the consolidated data from collaborators openly via public access.

Typical goals in this category include collecting data, providing a mechanism for knowledge sharing and improving the accessibility of data. For example, the objectives of ChemSpider, a chemical structure database coordinated by the Royal Society of Chemistry, are:

- to bring together compound data on the web
- to improve the quality of public chemistry data sources
- to provide a publishing platform for the addition and preservation of data
- to make these data accessible and reusable
- to integrate with publications.

4. Networking platforms

These partnerships do not seek to develop and commercialise new products; rather they aim to provide the critical networking platforms needed for collaborators to share and 'crowdsource' knowledge and funding. Some of these are also open to the public for contribution. They very effectively leverage the dispersed skills in areas like medicinal chemistry.

Goals for this category tend to be in terms of utilisation of the platforms and the outcomes achieved as a result: Experiment aims to enable research and provide a platform where science can be shared openly, and an open source project run by the World Health Organization (WHO) and the University

of Sydney aimed to find a more effective method of synthesis for the drug Praziquantel, which it succeeded in doing.

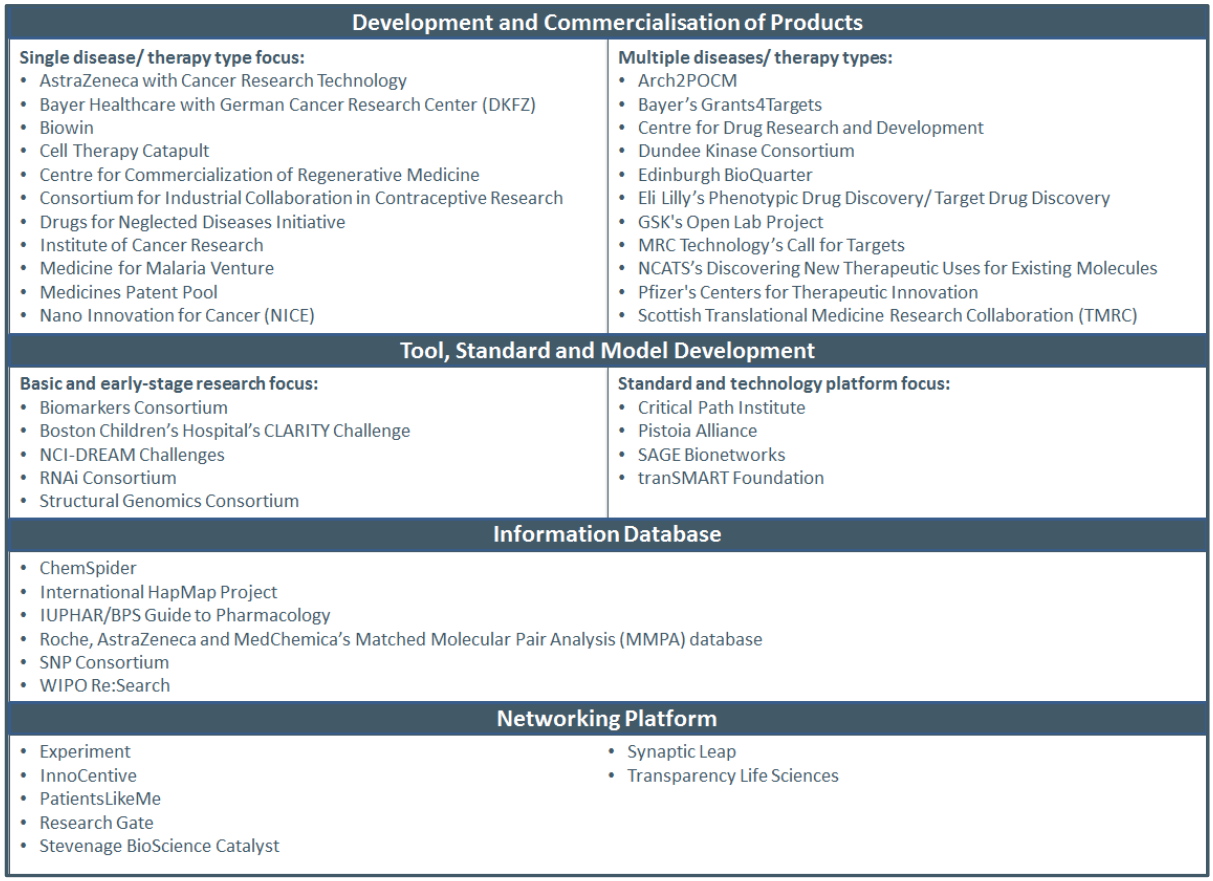


Figure 5. Classification of life sciences open innovation partnership examples by common objectives

All the above structures have the potential to play their part in addressing the R&D productivity issues outlined earlier in this report. Different structures, processes, collaborators and metrics are required to tackle distinct problems. All, therefore, have a role to play in the ecosystem of the future.

4.3 The importance of aligning objectives

By far the most compelling point that came through in the interviews was the importance of ensuring that the objectives of each partner are truly aligned. This is, of course, not an exclusive feature of open innovation; the UK National Audit Office states that priorities and desired outcomes must be realistic and understood in order to initiate successful projects, but this becomes steadily more critical as the number and diversity of partners increases[12]. In short, if there is not enough common ground in terms of objectives, shared risks and desired benefits, then open innovation should not be pursued.

5. Intellectual property (IP)

"Let's start with the blunt answer. There are no IP-related issues in open innovation that cannot be resolved."

Dr Martino Picardo, CEO, Stevenage BioScience Catalyst

The rapid growth of partnering over the past decade has led to more ambitious, open attitudes that are transforming conventional methods for creating and managing IP assets. Novel collaborative structures have given rise to hybridised IP mechanisms that incentivise collaboration itself, bridge differences and enable achievement of collective objectives (see section 8.3 for specific examples). These IP policies continue to evolve, seeking to balance the maximisation of commercial value with the maximisation of benefit to public health.

IP is typically viewed as a significant barrier to open innovation. We found that it is not, or need not be. Different stakeholders bring varying historical cultures and approaches to IP asset management: public–private collaboration in competitive drug development still bears the stigma of a perceived 'publish versus patent' culture clash. The benefits of open innovation therefore remain greatly untapped within many areas of biomedical research. However, there are now several examples of IP strategies and models that have been successfully implemented that challenge these preconceptions, which we examine here.

"Being aware of what issues might come up for different stakeholders in terms of IP, and being able to work around these in a constructive way so that the asset can be shared, is very important."

Jennifer Dent, President of BIO Ventures for Global Health, WIPO Re:Search

5.1 Using IP to align objectives

IP policy is the gateway that controls access to and the use of scientific knowledge. There is a spectrum of IP 'openness' between the two poles of open public domain and closed private systems. A range of collaborative models exist that seek to preserve commercial value while carving out public benefits from research for humanitarian uses. Being too 'open' may choke the commercial rewards that drive competitive research and private investment and can lead to a 'free rider' problem[13]. Being too 'closed' is increasingly unsustainable.

In a particular scenario, the IP policy should be based on the objectives of the open collaboration. The policy for open access research may take the form of an open access disclaimer or notification term on a website or database. A drug discovery programme with potential commercial value, on the other hand, will often contractually agree a protected commons approach.

Universally, IP strategy was viewed by the participants in this research as a critical factor, to be clearly agreed at the outset – including in instances where IP "was not an issue" – so no IP could be claimed or exploited for value. Even those upholding 'open science' values conceded that, in practice, some protection of commercial interests is often a necessary compromise if commercial partners' skills are to be engaged in a collaboration.

Perhaps most insightful was the qualitative finding that among those engaged with open innovation at both ends of the spectrum, IP itself was not viewed as a barrier to collaboration, and many viewed it as a critical means for facilitating it.

Box 2. Case study: patent landscaping for vaccines

The World Health Organization (WHO) is proposing the development of an open patent pool to improve vaccine development for neglected diseases. Vaccines require several interrelated component processes for manufacture. Difficulty in navigating the escalating number of overlapping patent claims and their stacked fees and royalties for vaccine development has become increasingly untenable and has stifled innovation.

Historically, many vaccines have been developed in public institutes: few patents were filed and those that were tended to be by private industry for improved methods of manufacture. Consequently, 50–80 per cent of vaccine patent ownership was consolidated within the large private sector. The landscape has now drastically changed. Vaccine patenting has skyrocketed – there are currently an estimated 10 000 patents and patent applications relating to only 25–50 possible therapeutic targets, such as TB, malaria and HIV. Current analysis now shows that the vast majority of vaccine patent ownership is spread across universities and small and medium enterprises that have received funding from public bodies[14].

This fragmented patent proliferation appears to have "increased technical uncertainty", causing manufacturers to be unsure which patents are required for vaccine development. Patent holders demanding upfront licensing fees leads to further complications. In particular, technology transfer for universities operates under a traditional model of licensing each patent ad hoc for upfront high-value fees and royalty schemes; often £1 million in fees and £1 million per year per patent. It therefore becomes commercially impractical for industry to license each patent, creating what was described in one of our interviews as a "patent thicket".

Martin Friede's proposed solution is a type of informal patent pool: "Where research that was funded by public money resulted in IP, the patents should be made accessible for R&D without cash up front, with a guarantee of negotiable access once a product has been developed and is going to be put on the market."[15] If the vaccine fails then developers do not lose licensing fees, but if the vaccine succeeds in going to market then royalty payments flow to the patent holder (see 'Easy Access IP Licensing' and 'Patent Clearing Houses' in section 8.3).

The concept is similar to UNITAID's Medicines for Patent Pool and the Pool for Open Innovation, which pool drug patents to treat neglected tropical diseases, but this pool would be focused on vaccines and public sector patents rather than industry-owned ones. Some potential measures of success would be the number of ideas in the patent pool that are being used by the 10 major vaccine manufacturers in their development and the number of current clinical trials of products containing these ideas.

Box 2. Case study of the WHO-proposed vaccine patent pool for neglected diseases, featuring quotes from Martin Friede, Team Leader, Technology Transfer Initiative, WHO

The question then remains: to what degree and at what stage should 'open' biomedical research be restricted to protect commercial value and spur better innovation via commercial competition? A prescriptive approach or blanket policy was not viewed as desirable by interviewees, and the consensus was that IP strategies should be flexible and adapted to the interests and objectives of each partner.

"A one-fits-all solution is unlikely to be found. We are exploring different approaches from open source and data sharing which might be adapted to different phases of R&D and beyond. Currently there are examples of sharing of information within a restricted number of partners… Whether this works we can't say at this stage but it's a concept worth exploring."

Piero Olliaro, Team Leader of Intervention and Implementation Research, TDR, WHO

Many academics have advocated that in life sciences collective management of IP resources through a 'protected commons' is preferable to working in the public domain[16]. The commons approach generally seeks to retain open access for early research while protecting potential commercial value by placing limits on who can access common resources. How it is defined and restricted among a specific community of researchers is decided by the collaborators.

Through contractual agreement, collaborators can achieve 'IP comfort' regarding their ability to control the potential loss of IP assets that might provide a competitive edge[17]. The key is for collaborators to define and agree in writing how to balance any competing ownership interests and then translate this into a flexible IP management strategy. The principles of contract law are then in operation to govern any resulting ownership and enforcement issues, obligations and limitations.

"IP doesn't have to be a barrier but an enabler of what you're trying to achieve. Think about what the different groups are trying to accomplish and then have a discussion about IP and how it can enable that to happen."

Dr Mike Strange, Head of Operations, Tres Cantos Medicines Development Campus, GlaxoSmithKline

These contracts do not need to be onerous and costly. We found that the sophistication of the agreed IP policy can vary radically depending on three factors: (1) commercial value (whether potential, perceived or existing); (2) the R&D stage within the commercialisation life cycle; and (3) the degree of academic collaboration involved. The higher the commercial value, the less 'open' the partnership (with the significant exception of early-stage research at medical frontiers such as regenerative medicine, where common scientific challenges are faced). The degree of academic collaboration can affect the IP policy, with overvaluation of IP, frustration with university technology transfer offices (TTOs), and the academic desire to publish and share methodology able to influence the agreement.

Box 3. Case study: the Biomarkers Consortium

The Biomarkers Consortium (BC) is a precompetitive consortium established in 2006 as a multi-sector, multi-institution, large-scale effort to qualify biomarkers up to the stage of regulatory approval. It then makes its findings available via open access. It seeks to qualify biomarkers that have utility across a therapeutic area, disease area or class of drugs.

In general, its IP policy comprises the following basic guidelines:

1. the end result of a project is generally not a product (although it may qualify markers that can themselves result in a product [diagnostic] or facilitate development of products [such as a drug or device])
2. any pre-existing (background) IP must be made available to the consortium to ensure no IP rights will encumber the availability of the end result
3. care must be taken to balance commercial benefit with broad public health benefit, consistent with the mission of government partners.

The BC faced the question of how to balance commercial and public health needs with respect to IP generated during the conduct of the I-SPY 2 breast cancer clinical trial, since biomarkers discovered as a result of the trial could be developed directly into companion diagnostics for one of the drugs tested. The challenge was to find a way to enable a company that provided a drug for the trial to access the biomarker IP with some control over regulatory submission and marketing of the resulting diagnostic, while not blocking companies developing other similar drugs from effective use of the same biomarker.

The solution was to have the Foundation for the National Institutes of Health (FNIH) act as an independent third party broker of the biomarker IP from the trial. FNIH received an exclusive licence for the IP generated from the trial, with the right to sublicense. It could then offer to license the IP with limited exclusivity to a company that provided a drug to the trial (i.e. with the IP's use limited to the specific drug contributed) and license non-exclusively to others, effectively striking a practical balance between an appropriate commercialisation of assets and the preservation of public health benefit.

Box 3. Case study of the Biomarkers Consortium

Box 4. Case study: the Lankenau Institute for Medical Research's Chemical Genomics Center (LCGC)

One way to maximise drug development from combined academic and company resources is to use a double-blind technique. This allows academic researchers to directly access industry proprietary tools and libraries for compound discovery. Simpson and Reichman discuss a detailed example of this, the Double-Blinded Drug Discovery initiative founded by LCGC[18].

LCGC acts as a third party 'key holder' for sets of compounds that pharmaceutical companies make available to academic researchers, who can conduct screening of the compounds while being blinded to their structures. If researchers identify active targets, then investigators can request container key codes from LCGC so that their company may then decode the target structures. The university receives milestone payments for active targets identified when screening, and if those structures are unencumbered (not subject to internal investigation programmes at the company or the IP is not otherwise restricted) then the university is permitted to publish the compounds.

Box 4. Case study of LCGC's Double-Blinded Drug Discovery initiative

Box 5. Case study: Discovering New Therapeutic Uses for Existing Molecules, a National Center for Advancing Translational Sciences (NCATS) initiative

NCATS, part of the US National Institutes of Health (NIH), launched a commercial drug-repurposing programme. Funders dedicated US$20 million to the pilot scheme, which placed 58 abandoned drugs contributed by eight pharmaceutical companies into the hands of academics to find new therapeutic uses. Although repositioning old drugs for new treatments was the stated purpose, the scheme's primary objective was to explore new ways to get academic investigators to engage with pharmaceutical companies, using crowdsourcing of expertise from across the wider research community. In the pilot a three-way relationship between NIH, pharmaceutical companies and academic investigators was established. The three parties have very different cultures; challenges were identified but, ultimately, none of these was insurmountable.

NIH, particularly NCATS, worked with the pharmaceutical companies to advertise the compounds within the research community. NCATS conducted peer reviews of the academic proposals received, and successful proposals were funded by NIH. The companies provided the drugs and cleared any pre-clinical requirements. Investigators of approved proposals signed confidentiality agreements with their related companies and entered into bilateral exchange-of-knowledge discussions to determine if their projects should proceed. Projects considered worthwhile then entered a bilateral protected commons using model collaborative agreements specifically designed for the purpose.

The initiative deemed the pilot a success and highlighted the advantage of using this novel approach to tap into the diversity of ideas that academics have for any given compound. Feedback from the pilot indicated that the most valuable lesson was the need for communication to negotiate and align objectives.

Box 5. Case study of Discovering New Therapeutic Uses for Existing Molecules, an NCATS initiative

Templates and tool kits for managing IP in open innovation partnerships have been developed to provide guidance and reduce transaction costs. The Lambert tool kit published by the UK's Intellectual Property Office[19] exists for industry–academic IP collaboration. However, very few people currently use this as a starting point for negotiations; it tends to be offered as a 'compromise proposal'[20]. The majority of those who employ the Lambert agreements do find them useful though. NIH's translational initiative NCATS worked with pharmaceutical industry representatives to develop template public–private collaboration agreements, which have been advertised and made publically available[21]. Adapting such model collaboration agreements allows partners bespoke control over risk management.

Ultimately, it is not IP itself but differing cultural attitudes toward IP valuation and management that are most often cited as obstacles. The conclusion of our review is that heterogeneity of actors and agendas and their competing IP interests can be overcome if common objectives are compelling enough. Creative yet clear study design and contract provisions provide an array of tools to protect confidential business information and commercial value.

"The thing everyone has commonality around is the science, and I think everyone is working for the same goal, which is to develop new therapeutics. Having that is tremendously helpful, and if we do come across a barrier, everyone is eager to come to a solution because we're all working towards the same objectives. If we weren't then there might be a problem!"

Christine Colvis, Program Director, Discovering New Therapeutic Uses for Existing Molecules, NCATS

6. Cultural factors

6.1 Cultural barriers

Different stakeholders in a collaboration will have inherently different cultures, reflecting divergent motivations, incentives and personalities. These have practical consequences: multinational companies, biotech SMEs (small and medium enterprises) and academia work to different timescales and have different procedures, constraints and levels of flexibility. Whereas an academic's main priority might be their publications, a pharmaceutical company will be more interested in target validation and portfolio advancement, and this can cause tensions if objectives are not fully aligned. Individuals have roles and aspirations within their own institutions, so the potential outcomes of a collaboration need to offer sufficient potential benefits to incentivise not only the institution but also the people working on the project.

Academia

> **"I have been astonished by some of the university [technology transfer offices] in terms of their vast over-perception of the value of some patents that have been invented by the researchers."**
>
> *Dr Martin Friede, Team Leader, Technology Transfer Initiative, WHO*

One of the most important difficulties to navigate is the over-perception of the value of an academic discovery: that it may lead to a commercial product but is typically many uncertain and costly steps away from it. A significant barrier that industrial partners described when liaising with academia, particularly in Europe, were university technology transfer offices (TTOs). Many of these lack the expertise to determine the value of patents from research and have insufficient commercial knowledge to understand what the real hurdles are in bringing a product to market and how to structure deals appropriately in life sciences. Several interviewees held the strong view that having a TTO involved is bad for business and indeed that most universities fail to make a return from them once incoming royalties are offset by their administrative costs. There is also a view that encouraging universities to be so strongly focused on intellectual property (IP) often actually impedes the emergence of new science. When a TTO is slow and bureaucratic this adds to tensions.

Despite the addition of the 'impact' assessment to the Research Excellence Framework (REF) in the UK, the opinion of some interviewees was that current university and national systems of recognition and reward in the UK still need to better recognise translational research. Traditional funding sources are not always geared towards supporting translational research, and the publication of resulting material is often deemed less attractive by high-impact journals[22].

Another issue cited was that academia can sometimes see partnerships as simply a funding source to replace a traditional funding grant, when in fact open innovation is about joint participation from all stakeholders. Academics can sometimes misunderstand the potential commercial benefits of a project where companies are engaging for philanthropic reasons, which can cause difficulties. Perhaps surprisingly, another issue raised was that it can be tricky to get people in academia to share their data back after industry partners have released information to them, despite their work being publically funded.

"Individuals that can move out of the traditional academic role and understand that we are living in a very different environment and [that] these types of partnership opportunities require a different way of thinking…will [be] led to a very successful and very exciting opportunity that is currently not afforded by traditional funding mechanisms."

Dr Anthony Coyle, Vice President and CSO, Centers for Therapeutic Innovation, Pfizer

Industry

From the academic point of view, working with industry can create its own set of difficulties. In pharmaceutical companies there is a focus on teams, metrics, deliverables and the budget, whereas in academia it's very much about the individual's research reputation. Researchers from industry also state that they need to find a balance between working in areas that are of high value to their company and those of academic interest. In the face of continually changing priorities, management teams and budgets, this can be a challenge. Sometimes industry partners can try to control 'open' projects in the same way as they do their in-house programmes. At the same time, academic researchers dislike the feeling of being constrained and tend to focus on their own success criteria, losing sight of the commercial interests of industry partners.

Interviewees from pharma companies, as well as from other stakeholder groups, felt that industry has to overcome inherent cultural norms to work effectively in open partnerships. The 'not invented here' syndrome has led to the flatlining of certain pharmaceutical giants, whereas others have learnt that they need to partner in order to survive. Sometimes companies can worry about losing competitiveness and don't want to disclose their strategies or be open and flexible with their IP, which can lead to a feeling of mistrust within a collaboration. However, industry researchers are not as protective of their information as some academics.

"The interesting thing is that the pharmaceutical companies had no problem buying into the idea of open sharing because in pharma, you're used to the idea that nothing you do belongs to you personally. You sign a confidentiality agreement that [says that] everything you think belongs to the company, whereas for academics their data is much more personal."

Dr Timothy Wells, Chief Scientific Officer, Medicines for Malaria Venture

The non-engagement of senior management was also highlighted as a barrier by industry researchers; convincing them that partnering is a good idea can be a difficult and lengthy process. Without buy-in from the top level, open innovation cannot proceed.

Health providers

Case study interviews and a workshop focused on open innovation and the UK NHS revealed that, while academics are aware of the requirement to bring in research funding and so are set up with the management and financial structures to enable them to do so, it is much more difficult for health system staff, whose primary role is treating patients, to free up time. The NHS is fragmented, and competition exists between separate providers, which can pose an additional barrier to collaboration and the dissemination of ideas throughout the system. Furthermore, potential partners expressed confusion over who their initial point of contact in the NHS was.

Partners found that convincing health providers such as the NHS to accept open innovation as a benefit is also challenging when targets are focused on the immediate pressures of delivering care, improving waiting times and freeing up bed spaces. Generally, at a Health Board level it's difficult to

convince people of the benefits of innovating from within, and bringing other ideas into the NHS is also difficult.

> **"The NHS is critical for success but is overly bureaucratic."**
>
> *Dr Anne Mandy, Senior Research Fellow, University of Brighton*

Workshop delegates emphasised that the NHS culture does not encourage or incentivise innovation and that there is a perception that innovation comes from elsewhere. At an NHS Trust level regulators such as Monitor do not require evidence of innovation and performance targets do not recognise research and invention. There is distrust of 'disruptive innovators' and no reward for mavericks[23]. Engrained trust issues exist relating to the use of patient data, and health providers can feel like 'junior partners' in collaborations, particularly when they are being exploited simply as a means of accessing patients.

The balance between risk and benefit of innovation and collaboration needs to be addressed, recognising the risk associated with not engaging in a partnership that could potentially benefit patients.

Box 6. Case study: Creative Advances for Fibrosis Therapies

At our joint 'Open Innovation and the NHS' workshop with the Academy of Medical Sciences[24], Dr Richard Marshall (Senior Clinical Lead in Respiratory R&D, GlaxoSmithKline) described the need for novel therapeutics to target fibrosis, which is a common cause of mortality and morbidity in chronic inflammatory and metabolic diseases. In response to this need CRAFT (Creative Advances for Fibrosis Therapies) was formed, which involves (predominantly) UK universities and the Royal Brompton & Harefield NHS Foundation Trust. These partners investigated the biology of fibrosis and fed into the GlaxoSmithKline (GSK) Fibrosis Drug Performance Unit (DPU), by looking for established biomarker and surrogate outcome data as early markers of drug success for future trials.

Dr Marshall described how collaboration with the NHS had enabled the largest ever observational study of idiopathic pulmonary fibrosis (IPF) patients, with recruitment of 500 patients in two years, a participation rate unrivalled globally. A further success from the fibrosis network was in the development of positron emission tomography (PET) studies in IPF, in which academics from the network discovered a new application of imaging and were able to publish the novel finding. GSK took on this technique and performed a reproducibility study, validating the academics' findings and establishing the technique as an effective means of tracking disease progression.

Dr Marshall observed that the key to the success of this network was the production of "mutually beneficial science", as well as having motivated clinicians and patients willing to engage with research into a disease with a high unmet medical need. He also stressed the importance of geographical proximity to the success of the collaboration, which allowed movement of people between centres: all of the collaborating institutions except one are UK-based.

Box 6. Case study of an open partnership between GSK, academia and the NHS

Funders

Some participants felt that research funders need to be more flexible when it comes to investing in radical open innovation models that disrupt the system and challenge current ways of working. The culture within major funding organisations emphasises certainty that they are already working on the most important things, and resulting inflexibility in budgets and processes can lead to a lack of funding for the most innovative emerging models or for interdisciplinary ventures.

6.2 Breaking barriers

Taking together this research, we have found that, despite inherent cultural differences between partners, there is a general consensus that organisations are learning to work together much better: barriers are being broken down and there is an increased appetite to engage in open innovation. The size of barriers also depends on the stage of research: there tend to be fewer 'culture clashes' at early stages compared to projects in the commercial space.

"Working with partners outside your organisation can result in them asking questions you hadn't thought of asking yourself. That sets for a very dynamic, fast-moving innovation environment."

"There's much more appetite to do things together, not pretending that we know all the answers and bringing people together."

Dr Mike Strange, Head of Operations, Tres Cantos Medicines Development Campus, GSK

Working with people from different organisations has also shown to bring partners unforeseen benefits, such as the questioning of engrained ways of working and possibly improving them. As different partners engage in more and more open innovation initiatives, it becomes easier to work together and there is increasing appreciation of one another's values, constraints and methodologies.

In summary, as long as there is commonality in the science and everyone is working towards the same goal, cultural differences can be overcome.

Box 7. 'Open Innovation and the NHS' – challenges to overcome

- Models of successful open innovation between industry, academia and the NHS do exist. These are characterised by trust and openness between partners, shared risk and reward, and the delivery of mutually beneficial outputs. Identification and effective utilisation of unique strengths within partner organisations is key.

- When collaborative partnerships are established on these principles, they can deliver outputs faster, better and cheaper than single-sector working and can tackle clinical problems that defy the resources and skills of any one group working alone.

- Cultural differences between the three constituents may lead to mutual suspicion and misunderstanding and confound the development of productive working partnerships. Education, communication and freedom of movement of individuals between industry, academic and clinical work places are required to break down these barriers.

- The size and complexity of the NHS may act as a barrier to collaboration and the dissemination of novel ideas throughout the healthcare community. Potential collaborators can struggle to identify a relevant and accountable individual within NHS organisations to make contact with regarding research partnerships.

- Different understandings of what constitutes success and variable outcome measures between sectors can make it difficult to align goals. New metrics are required to measure the wider benefits of collaborative innovation for patient benefit.

- There is a failure to incentivise and reward innovation in the NHS. Action should be taken to embed the 'innovation for better outcomes' imperative within NHS incentive schemes.

- Existing NHS structures – Academic Health Science Networks (AHSNs) in particular – are currently poorly utilised, as they need time to embed themselves and build local relationships to fully realise their potential.

- Delegates were keen that cultures with the three sectors of industry, academia and the NHS were not caricatured. The diversity of skills and attitudes in each sector was recognised.

Box 7. The main outcomes from a joint workshop with the Academy of Medical Sciences called 'Open Innovation and the NHS'

7. Practical considerations

As in any initiative, effective organisational management and project governance are important for establishing clear guideposts to set up, track progress and demonstrate success throughout the lifespan of an open innovation partnership. Well-defined objectives, responsibilities, governance structures, risk- and benefit-sharing strategies, milestones, and metrics of success are some of the key items that should be agreed upon in advance. One of the challenges is that it can take a long time to develop a project, achieve sign-off, and exchange the financial and legal agreements, sometimes as a result of misalignment of different organisations' budget cycles and project management timelines. Open and regular discussions are necessary to address these issues on an ongoing basis to avoid any misunderstandings that could build up over time and risk derailing the collaboration.

7.1 Choosing a partner

As open innovation partnerships seek to capitalise on and maximise the complementary expertise and resources within the life sciences ecosystem, various types of participants can contribute to them (Figure 6). The more that collaborations effectively leverage complementary capabilities, the more successful they are likely to be.

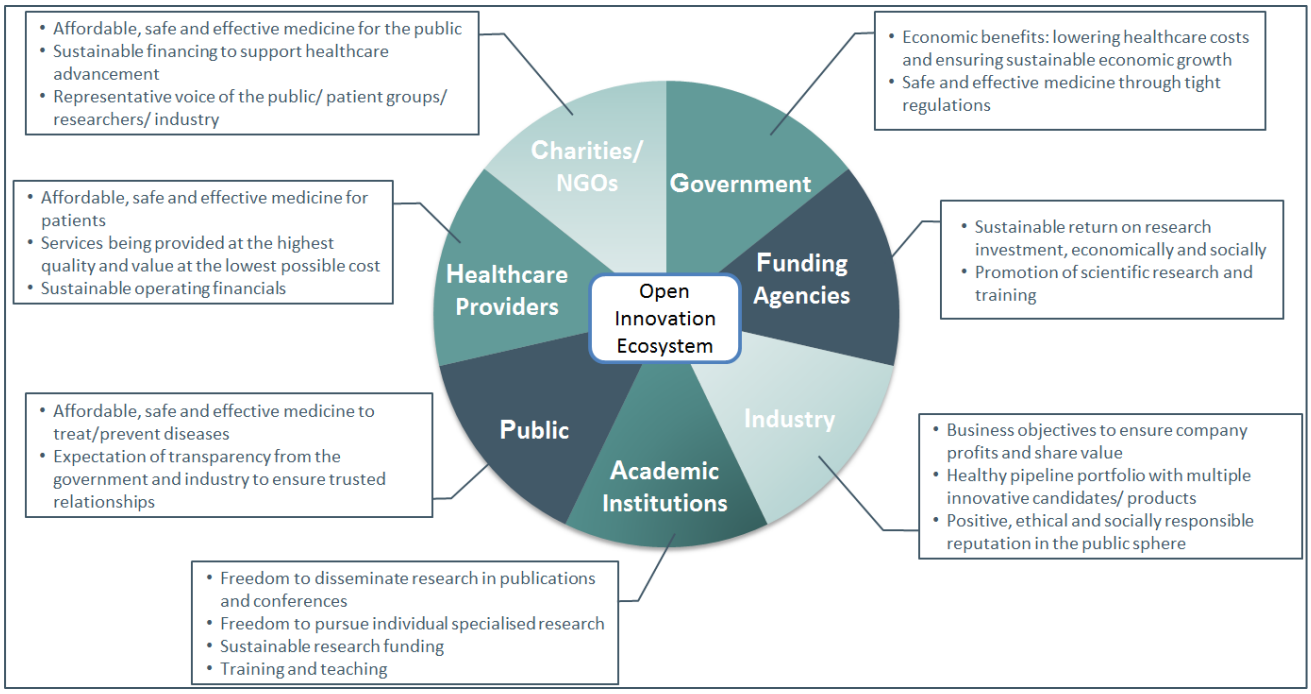


Figure 6. Ecosystem of life sciences open innovation partners and their respective interests

Interviewees reported that selecting a partner often has more to do with choosing the right individuals within an institution rather than the institution itself; without champions who embrace goals as their own and drive the initiative forward, a project will invariably fail. If these champions leave the organisation during the project, this can represent a significant risk to the success of the venture. Equity and equality in a partnership is key, so systems need to be developed that ensure that all partners have equal input into project decisions. Pragmatic aspects must also be taken into account: for example, major international collaborations spread costs further but also increase logistical burdens, so the benefit–risk ratio of partnering with distant or overseas organisations needs to be carefully assessed.

As discussed in the 'objectives' section of the report, the key to a successful open collaboration is ensuring that the goals of each partner are substantially aligned and that the benefits of taking part significantly outweigh the risks for each institution.

7.2 How to manage open partnerships

Analysis of the case study interviews has shown that open innovation project management practices differ depending on the structure of the initiative (public–private partnerships are obviously managed very differently from crowdsourcing projects, for example) and sometimes vary according to objectives, though there are also a number of common strategies employed across all models. Best practice recommendations have been formulated as a result of our stakeholder discussions.

> **"I think it is key to have some people in charge to get the consortium working efficiently. In terms of the partners, we have established a contact list and we have asked them to identify in their own organisation one person who is in charge of the operations and another in charge of the financials."**
>
> *Aude Michel, Head of Corporate Business Development (BioAlliance Pharma), Nano Innovation for Cancer (NICE)*

First of all, it is paramount that each partner organisation has a clear point of contact to ease communications between groups. Individuals within each organisation need to clearly understand their responsibilities in the context of the partnership and who they are supposed to report to. Most importantly, project management guidelines need to be set at the beginning and should be simple, clear and sufficiently granular.

Collaborations aiming to develop and commercialise new medicines tend to employ industry-like project management strategies, using the same tools and processes and placing heavy emphasis on milestone achievement and go/no-go decision gates. Crowdsourcing models also have a particular set of project management principles. When data or a challenge is released, the often vast numbers of suggestions that are submitted need to be reviewed and tested by an expert group, which is no minor undertaking.

Often the most efficient way of managing open innovation partnerships is if a neutral convener is involved. These organisations have an independent standpoint and can create a trusted environment for partners to discuss potentially confidential information. Furthermore, they often speed up the process of producing and signing contracts by facilitating the process. The National Institutes of Health (NIH), for example, has created a set of template collaborative research agreements, which they guide prospective partners through[25]. Neutral partners can also provide personnel to manage specific relationships and steer partners through projects.

> **"One of the learning curves is that you've got to let it breathe. You cannot micromanage."**
>
> *Dr Martino Picardo, CEO, Stevenage BioScience Catalyst*

When health systems such as the NHS are involved, it is important that another partner or the neutral convener plays a major role in managing the project and removes some of the administrative burden, thus enabling the health service representatives to use their limited time working on the project most effectively. Industry and academia generally have expertise in managing budgets and research facilities in-house, so are more able to play an active role in this area.

7.3 Project selection

In some cases, processes for project selection are required in open partnerships. At this point it is important for partners to co-develop proposals and ensure that each party understands what benefits to expect from project outcomes. One case study recommended a triage model for larger collaborations (Figure 7), whereby partners jointly produce an initial non-confidential proposal and, if this is approved by the relevant committee, they co-author a full, confidential proposal for submission.

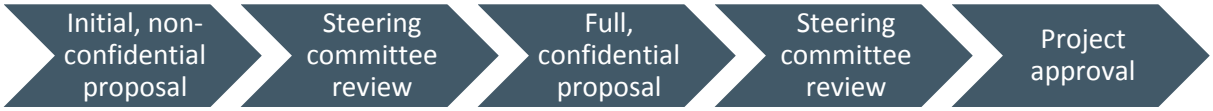


Figure 7. Triage model of project selection

7.4 Joint decision making

Most partnerships have at least one steering committee or executive board that makes the final decisions on project selection, monitors progress and decides whether a project needs to be terminated. To be successful, these boards need to contain representatives from all the partner organisations as well as independent bodies. Regular physical meetings (1–2 times a year) and virtual communication (monthly) are required to ensure partners remain on the same page. The decision-making process should be built into the contract at the beginning so all partners understand the procedures and are clear on how they will have the chance to contribute.

7.5 Knowledge sharing

"There were a few project groups that we weren't in touch with that frequently and those projects seemed to struggle much more."

Christine Colvis, Program Director, Discovering New Therapeutic Uses for Existing Molecules

All interviewees agreed that the most important aspect of running partnerships is regular and open communication. With good communication comes a greater understanding of one another's constraints, timelines and budgets, and this invariably improves partner relationships.

Despite the increased logistical difficulty of bringing together project teams from different organisations, it is imperative that partners meet face to face as much as possible to maintain momentum. In the interim virtual communication in the form of video or conference calling should be scheduled regularly.

A virtual sharing network can also be a useful tool to allow multiple organisations to access the documents they need with ease, though it requires extra investment to build and administer the platform.

7.6 Milestones

The key to ensuring milestone delivery is setting out a clearly defined roadmap detailing the key junctures at the very start of the project, which all partners understand and buy into. Progress should be reported to the relevant board at regular intervals throughout the project. An example cited was the traffic light system, in which the status of a project is rated as red, amber or green depending on the extent to which it is achieving its objectives.

"The fact that we had face-to-face meetings every six months was a really good device. People committed in advance and then they and their team would work really hard leading up to the meeting to make sure that they had achieved their milestones so that they wouldn't be letting the rest of the project down. It sounds pretty informal, but it actually worked remarkably effectively."

Professor Peter Donnelly, Director of the Wellcome Trust Centre for Human Genetics (University of Oxford), International HapMap Project

Milestones can change, particularly during early discovery, so partners recognised the importance of building flexibility into their plans. If there is significant deviation from the proposal in terms of budget or milestones then the project should be brought back to the board for approval.

In some cases milestone payments are clearly linked to deliverables. This works best in models such as public–private partnerships, but has also been transferred to crowdsourcing, where prizes are sometimes offered to contributors who solve particular challenges.

Box 8. Case study: Stevenage BioScience Catalyst

A joint venture between GlaxoSmithKline (GSK) and the Wellcome Trust, Stevenage BioScience Catalyst (SBC) is the UK's first biomedical open innovation campus. SBC consists of an incubator and an accelerator facility with associated business support services on the same site (behind the security gates of GSK).

SBC was launched as one of several open innovation "experiments" by GSK in response to the relatively poor quality and quantity of sustainable, viable biotechnology companies in the UK. The hypothesis was that if an incubator was built next to one of the biggest pharma companies in the world and an environment that facilitates engagement was created, then it would lead to more robust, viable business opportunities in the life sciences sector. This model had support from both the Wellcome Trust (keen on translational research through early academic–industrial engagement) and the government (through the Technology Strategy Board and the Department of Business Innovation and Skills) to support local and regional economic development.

The ethos of the organisation is to create a "safe haven" for early-stage companies to do business. In addition to standard business incubation support services, this involves the "beer and pizza social network side of things" as well as the physical "bumper car" model of creating enough opportunities for people to encounter one another. Using a combination of tools, such as science seminars and networking in the facilities, SBC creates different technical and scientific business opportunities that enable people to engage and interact.

Having launched in February 2012, SBC has now hit 80–90 per cent occupancy and has plans for the addition of two more buildings, indicating that the stakeholders have deemed the venture an initial success.

Box 8. Case study of Stevenage BioScience Catalyst (SBC), featuring quotes from Dr Martino Picardo, CEO of SBC

7.7 Geography

Clearly the geographical location of partners has a big impact on the straightforwardness of running a partnership. Co-located partners emphasised the importance of working side by side and regularly

interacting, which fosters the notion that partners are a team. Secondments can have a similar effect. Some collaborators felt that positioning partners or potential partners together in the same building creates vibrancy and stimulates collaboration in a way that doesn't happen when organisations are working separately, and that it helps to break down barriers surrounding culture and confidentiality.

Some respondents were of the opinion that working with other organisations in the same country can be more productive than working in international partnerships, because cultural and language differences can sometimes be a barrier (in EU consortia, for example). Furthermore, working in different time zones can make communicating effectively and meeting regularly a challenge.

"That's what is nice about Belgium – it's very easy to see one another and we try to have face-to-face meetings as much as possible. Moreover, the BioWin projects often involve a limited number of partners. What can make some projects complex is geography, but also the number of partners. We are part of an [Innovative Medicines Initiative] project with 22 different partners, and although this creates a unique opportunity, there is associated complexity for the management of such projects."

Dr Philippe Denoel, External R&D and Innovation (GSK), BioWin Consortium

On the other hand, the advantage of crowdsourcing is the diversity of responses, which you wouldn't get if you only looked for ideas in one place. However, it was universally recognised that incorporating ideas from a large number of stakeholders from across the globe can be operationally challenging and requires a lot of work.

7.8 Metrics

"I have to say we're not very good at tracking milestones. I think others could learn from what we're doing if we put more attention into tracking and annotating what worked well and what didn't."

Dr Stephen Friend, President, Sage Bionetworks

The results of our research revealed that some open innovation ventures are better at collecting and tracking metrics than others and that reporting on open innovation partnerships has sometimes been story-driven. We believe that it is vital to collect impact data and scientifically analyse partnerships in order to measure success. Both quantitative and qualitative metrics are required, though the latter are more difficult to qualify.

To define the metrics for success, partners need to:

- outline what success looks like at an early stage ('leading indicators')
- define ultimate quantitative and qualitative outcome/impact measures
- collect baseline data on both
- understand that the criteria will vary at different stages of partnership development and the R&D pipeline.

Collaborations with different objectives clearly need to use different metrics to measure progress. A collaboration that has the ultimate aim of developing a new medicine needs metrics based around portfolio advancement, whereas a partnership focused on tool creation needs to measure the

viability of new models. Furthermore, the structure of the partnership can inform which metrics are necessary to measure its success; a crowdsourcing platform needs to monitor usage levels and quality of user input, which doesn't necessarily apply to other open innovation models.

The R&D stage that the partnership is centred on also informs the success criteria. Those at earlier stages might focus on the extent of target validation for example, while those at later R&D stages might directly measure the number of new medicines developed. Finally, the evolutionary stage of the partnership impacts which metrics should be used to measure success at a given point. New partnerships will need to use input metrics (e.g. initial investment, employee skills of partners, 'openness' of IP), whereas collaborations that have been in existence for a substantial amount of time can begin to measure the outcomes. Depending on the particular objectives, structure and age of the partnership, metrics should be cherry-picked to produce a tailor-made list of progress measurements.

There are a number of qualitative measures of progress, which are less easily articulated in the form of metrics but are still extremely important in gauging success. These are primarily linked to the human factors involved in non-traditional partnering models and can include: improvements in ease of working together, community building and connectivity; the positive impact on ways of working as a result of external collaborations; and acceptance and embracement of open innovation within an organisation. These qualitative factors must be taken into account alongside quantitative metrics when analysing the achievements of open collaborations.

When asked to rate how successful their partnership had been on a scale of 1 to 10, with 1 being completely unsuccessful and 10 being completely successful, partners tended to rate their collaborations quite highly (average 8/10). Interestingly, when asked to rate how successful they thought the collaboration had been from their partners' point of view, the average score was slightly lower, at 7.7/10. In general, feedback was very positive on the topic of whether collaborations had achieved their objectives, though it was acknowledged that some were far too young to have realised them yet, that objectives can continually change (particularly in early-stage research), and that some collaborations will never achieve their objectives because they are too broad and ambitious (but that they will further knowledge in the field).

"We have been able to effectively partner with academia, to access exciting new areas of science, to attract leaders in the scientific community to join us and identify some really interesting candidate molecules that would not have been identified if we were working in isolation."

Dr Anthony Coyle, Vice President and CSO, Centers for Therapeutic Innovation, Pfizer

8. Emerging models

8.1 Crowdsourcing

> **"This is one of the ways of the future – tapping into the wisdom of the crowds to solve problems that are hard and can't be done alone."**
>
> *Dr Gustavo Stolovitzky, Director, DREAM Project*

Crowdsourcing and challenge-based competitions can accelerate some types of research by allowing a global community to input the results of their own experiences and expertise, which could take single groups years to acquire alone, probably duplicating previously failed experiments in the process. Many crowdsourcing platforms directly use the structures of existing software engineering programmes such as GitHub, which allow users to download information and come back with solutions. This method exposes people to fields that they perhaps haven't worked in before, bringing new insights to complex biomedical problems and fostering innovative, non-traditional scientific communities.

Several capabilities were listed as requirements to run a successful crowdsourcing platform. Firstly, and perhaps most obviously, a sophisticated website is needed to present the data in a clear way and allow users to input effectively, which requires expertise in IT systems. There also needs to be a central understanding of the science behind the problems the community is being asked to solve. Sometimes this can mean partnering with experts in the field before challenges or questions are even released. Skill is needed to curate the data, ensure it is available in a usable form, and subsequently analyse, sequence and normalise it. There is also an art in building and organising the community, ensuring people with the right expertise participate by interacting with them in a productive way.

Crowdsourcing coordinators emphasised that challenges must be sufficiently clear and specific and must build on prior knowledge to ensure that the responses yielded are fruitful. Directors of crowdsourcing platforms need to ask themselves: What are the key questions in a given area? What data are currently available? How can we curate the data? How can we provide the data to people to solve the challenge? Organising the responses is a significant undertaking, and how the submissions are evaluated is very important. Not only that, a balance needs to be struck between releasing enough data for contributors to complete the challenge and overloading them with information.

So what about the intellectual property (IP)? A lot of crowdsourcing platforms have completely open (IP) models where the operators don't expect to own any of the resulting knowledge or potential products. If a compound has resulted from the work, the key question is how to commercialise it. Who is going to fund its subsequent development, and what are the IP implications of this? Some groups are trialling more sustainable models for their platforms, such as integrating subscription tiers for pharmaceutical companies who wish to access the data.

> **"Companies are schizophrenic about the IP. They are intrigued by the power of group efforts to de-risk and simultaneously they feel that there's sort of a *prisoner's dilemma* where they're saying: 'If our company gives money and gives the data…is it fair that it is going to be used by everyone?'**
>
> *Dr Stephen Friend, President, Sage Bionetworks*

The question of how to best promote open source to potential contributors is an important one. At the moment we don't fully understand the reasons why people do and do not participate in crowdsourcing projects, though motivations could include philanthropy, career building, publications or public relations benefits. Further research into this could help us understand how to use the crowd to its highest potential. Prizes were suggested as one method of incentivising people to participate, and it will be increasingly important for life sciences crowdsourcing platforms to adopt such motivators as competitors arise. Via its BRIDGE project Sage Bionetworks has looked at how best to engage citizens in open source science. The tool connects patients with scientific communities and allows them to help define research questions, as well as giving them the option to share their health data.

"I always resisted prizes in the past – I didn't want money to muddy the water in that it changes people's motivations. But I have to admit that there is the possibility that if you have enough money involved and if you design the prize right, which is quite complicated, then a lot more people might get involved – hundreds or thousands more people."

Associate Professor Matthew Todd, University of Sydney, Founder of the Open Source Malaria Consortium

Box 9. Case study: Transparency Life Sciences – an open approach to drug development

Transparency Life Sciences (TLS) is the world's first pharmaceutical company completely based on open innovation. TLS approaches the value-creation process of drug discovery from a different angle by generating ideas and designing experiments, in this case clinical trials, via broad involvement of all stakeholders – patients, physicians, regulators, statisticians and others. Another key element of TLS's approach is its dramatic reduction of the number of patient site visits (and the cost of trials), which it achieves by relying on data obtained using telemonitoring and other new "remote" technologies. In short, TLS is aiming to completely revolutionise the way clinical trials are designed, executed and analysed in areas of unmet medical need. This is a new way of tackling the serious issues that pharma is facing today by collating ideas from other industries and sections of society.

The potential product portfolio consists of hundreds of "distressed" clinical-stage compounds that have the potential to be rescued or repositioned, drawn from a number of sources, such as big pharma and universities. Clinical trials are executed in a "patient-centric" way, in which, wherever possible, they are brought to patients' homes by means of digital devices. Value is generated for TLS by in-licensing the IP that covers a molecule and also by entering into co-development deals and forming joint ventures for commercialisation.

What is needed to successfully run such a platform? Clearly expertise in drug development is fundamental, as are the IT systems necessary to build the crowdsourcing platforms. Central to the model is the culture of "content not context" – a primary focus on managing projects.

TLS is a start-up and, due to the lengthy nature of drug development, only time will tell whether the business model is viable and more successful than the current legacy model. However, the community has begun to accept the route as a possible way forward and is beginning to collaborate.

Box 9. Case study of Transparency Life Sciences (TLS), featuring quotes from Tomasz Sablinski, Founder and CEO, TLS

Box 10. Crowdsourcing considerations

Crowdsourcing comes with its own specific set of considerations. Firstly, not all problems will be solved with a single challenge. Sometimes results come in that don't answer the question sufficiently, so the challenge needs to be tweaked in the same way as you would adapt an experiment in a lab.

Secondly, open source platforms don't run themselves – they need to be led in a productive way. At the centre of an open source project you typically require a funded kernel of activity. Somebody needs to be driving it, generating and releasing data, engaging the community, and clearly defining questions. Investments need to be made in setting up a mechanism whereby discussion is encouraged and proposed solutions are tested, so there is a cost in terms of people and money. When it comes to outlining the questions or challenges, these need to be very specific, robust and focused in areas where contributors can see areas of synergy.

Promoting open source to the 'crowd' is another important factor. It isn't just a case of posting a question and hoping people will engage. Organisers need to publicise their platform through relevant specialist networks, target individuals and groups; likewise they need to educate scientists and citizens on how to take part and on the mechanisms for answering questions. Monetary prizes are another way of encouraging the masses to engage, but they are not the only incentive for people to contribute.

Funders need to pay more attention to this way of working, perhaps by including sections in proposals where they ask researchers to define how they're going to attract more people to work on the data that they produce. Finally, funders can reinforce accountability for the sharing of data produced by publically funded research, to reduce duplication and maximise the output of grant money.

Box 10. Recommendations for crowdsourcing ventures

8.2 Crowdfunding

"Crowdfunding is definitely new for science, but crowdfunding principles in general are not entirely new. What we've tried to do is take the best lessons from product crowdfunding, like Kickstarter, but also social microfinance. That said, it's definitely still evolving for us. Even how we work today will probably change in 6 to 12 months."

Denny Luan, Co-founder, Experiment

Crowdfunding is when an entrepreneur raises external financing from a large audience (the 'crowd') – each of whom provides a very small amount of investment – instead of soliciting a small group of sophisticated investors[26]. In the context of life sciences, crowdfunding offers a new avenue to researchers and businesses for financing ideas that would otherwise go unfunded. In a climate where venture capital funding for early-stage life sciences is difficult to come by (though recent analysis suggests that the situation is improving[27]), entrepreneurs are looking to the growing number of crowdfunding tools to raise capital for their medical inventions. Crowdfunding is also a useful tool for researchers looking to get preliminary data or validate their ideas so that they can potentially apply for a larger grant. There are two models: donation-based, in which the crowd simply contributes money to their chosen project; and equity-based, in which investors buy a monetary stake in the company.

The benefits of crowdfunding span beyond financial gains: raising the company or research profile, becoming part of a like-minded, evolving community and receiving expert feedback are just some of the other advantages of listing a project on a crowdfunding platform. It can also provide access to new corporate clients by attracting potential partners who are interested in using the innovation in their own business[28].

The emergence of life sciences crowdfunding has also brought controversy. Research isn't peer-reviewed in the same way as when grant funding is awarded, so well-meaning members of the public could be donating to or investing in 'bad science'. The question has therefore been raised of "whether crowdfunding in Silicon Valley, which tends to be more impressed with technology and marketing than peer-reviewed data, is compatible with medical research."[29] Crowdfunding can also raise IP concerns, as releasing ideas into the public domain before they have been protected could lead to others imitating them with 'me too' projects. In the equity-funding model it could prove complicated to answer to such a large number of stakeholders, and crowdfunding currently comes hand-in-hand with a vast amount of paperwork that puts administrative pressure on small firms.

Despite these issues, it can't be denied that funding in life sciences has dwindled and that crowdfunding is one clear route towards mitigating that. Furthermore, there are solutions to some of the concerns raised. VentureHealth, an online crowdfunding platform for life science companies, uses a 'carried-interest' model, which means that it only receives a return on investment if its portfolio companies do so[30]. Therefore, the company is motivated to support only the most promising opportunities on its platform. More regulation is likely to be put in place to ensure that abuse of funds does not occur, and the new Financial Conduct Authority rules in the UK are likely to be adapted to encompass crowdfunding[31].

8.3 Intellectual property

> **"If you put more information out, you get more back."**
>
> *Dr Malcolm Skingle, Director of Academic Liaison, GlaxoSmithKline*

Many organisations that accrue IP rights accumulate a substantial proportion of unused, 'dusty' IP, which they will not exploit. These patents may be licensed to realise any latent value or be exchanged for assets that are better suited to its pursuits.

According to the OECD, key barriers to licensing unused IP are: the difficulty for patent holders to identify potential licensees and partners; the complexity and cost of licensing contracts; the IP having low commercial value; and the IP consisting of technology that is not ready for utilisation or marketing.[*] To overcome these issues, a number of novel licensing schemes such as IP market exchanges, IP auctions and 'Easy Access IP' licences have emerged. These models reduce transaction costs by using simple standard contracts or by centralising a market that makes it easier for owners and IP seekers to match.

Easy Access IP

Small and medium enterprises characteristically do not engage widely with academia due to their having small IP portfolios and a lack of funding. This model facilitates their engagement by making IP

[*] The OECD conducted a voluntary survey of patent applicants (2007–2008) which revealed that most patent holders have underutilised IP portfolios that they are willing to license, but that they often fail in doing so because they cannot find a market. OECD. Collaborative Mechanisms for Intellectual Property Management in the Life Sciences. 2011. **oecd.org/sti/biotech/48665248.pdf** [accessed 30 July 2014]

that is owned by academics available to companies for no upfront fee in return for royalties, using a one-page standard legal agreement. This form of licensing is particularly attractive for IP in the early stages of research, which requires further validation of translational potential by companies. The UK House of Commons Select Committee on Science and Technology has recommended that a formal assessment of Easy Access IP be conducted to determine if it is facilitating IP transfer and wealth creation[32].

IP auctions

IP auctions are another emerging model that aims to improve the valuation and sale of unexploited IP. For example, Penn State University launched an auction of 70 exclusive licences held by the College of Engineering (the first known university IP auction[33]) in an attempt to attract companies and move IP off the proverbial shelf. Auctions are a new form of IP trading that offer a potential way to overcome the limitations of current ad hoc licensing strategies, but they only succeed if they are able to reach potential buyers.

Patent databases and IP marketplace exchange listings

Many collaborative efforts have addressed the 'open' sharing of research materials and data but have neglected to address the need for better transparency in IP licensing practices[34]. Because the recording of changes to the ownership of patents is not mandatory in many cases, public patent records may not reflect the identity of current ownership, which creates obstacles when navigating patents for collaboration and innovation.

Academics have suggested that a universal registry of non-confidential patents for biomedical inventions, specifically for stem cell technologies, should exist, in much the same way as a land registry[35]. When ownership changes hands the IP transfer would be registered, thereby providing long-awaited clarity to patent licensing practices.

Extending participation beyond the public sphere to engage other actors, such as pharmaceutical or biotechnology companies, in registering portfolios and listing any non-core, unused or low-value IP assets for exchange with academia could further stimulate and speed up innovation as well as offer new sources of revenue.

Box 11. Case study: BioInnovit

BioInnovit is an online global life sciences exchange network, created especially for public research to assist in innovation marketing, innovation commercialisation, and patent licensing. The platform's central feature is the LSX MART, an online 'stock market-like' platform for swaps of IP assets, in which shares of future revenues can be offered in exchange for funding. The platform includes an interface to calculate the new patent value (NPV) of IP assets and an interface to post IP assets for sale, respond to bids from potential buyers and exchange IP documentation for due diligence. Buyers are companies and investors in the field, such as venture capital and private equity operators.

Box 11. Case study of BioInnovit

Pooling and patent clearinghouses

As biomedical innovation becomes increasingly complex, the current system of individually negotiated IP licences becomes unfit for purpose. Patent pooling and clearinghouses offer a mechanism by which complementary IP technologies can be voluntarily registered and managed.

Patent pools work well in philanthropic scenarios, such as the search for treatments for diseases with unmet clinical needs or the establishment of better standards in areas where 'patent thickets' have been created. For example, GlaxoSmithKline donated patents relating to neglected tropical diseases into a patent pool for R&D that would provide treatments in lower- and middle-income countries royalty-free. The initiative grew into the Wipo Re:Search initiative in 2011.

Patent pools are generally limited to non-profit areas in the field of open innovation because they are associated with highly regulated legal standards. Clearinghouses offer a more informal alternative as they allow companies to choose from a 'menu' of related IP. This means that they can 'bundle' processes together in order to create a platform technology more easily.

Academics have called for a clearinghouse model for stem cell and human genomic technologies, similar to the PIPRA model for agricultural biotechnology. Such mechanisms centralise related patents, making it easier to source and negotiate licensing 'bundles' for innovation. They allow for a central governance mechanism, tracking of industry standards and useful annotation of banked patents.

Box 12. Learning from non-life sciences examples: IP listings, crowdsourcing and challenges

IP listings or registries

IP databases, such as the iBridge Network, centralise a registry of IP assets from member universities, making them more readily available to a worldwide research community. In the iBridge Network direct interaction with the inventor(s) by those interested in using the IP for their own R&D is encouraged, which further opens dialogue and increases the opportunity for cross-fertilisation of knowledge and ideas associated with the original invention. The iBridge Network features an online searchable database that makes it easier to identify partners for collaboration and increases the efficiency of technology transfer through straightforward, flexible licensing of associated IP rights.

IP listings or databases exist ad hoc in certain fields of life sciences, but often lack the maintenance, supervision, visibility or broad participation to be impactful resources. Some very good examples exist as parts of other IP collaborative mechanisms, such as patent pools (e.g. the Medicines Patent Pool), clearinghouses and entities that manage and coordinate the licensing of various member portfolios.

Targeted crowdsourcing

Online crowdsourcing can be enhanced by 'targeted crowdsourcing' through semantic software and market intelligence to increase participation and ensure access to the most appropriate talents. Approaches like Presans' can be utilised to attract the attention of experts without registering them on any portal and to embed real-time feedback throughout the crowdsourcing process. This highly targeted approach could be useful for crowdsourcing expertise in specialist life sciences subjects.

Challenges

Well-established open innovation platforms such as OpenIDEO have paved the way for similar models in life sciences. OpenIDEO hosts challenges submitted by individuals and companies for discussion in the online community, and challenges are accepted for discussion only if they are for social good. Lessons from these paradigms could be transferred in order to provide additional tools for collaborations, to enhance the challenge process and increase community interaction. Furthermore, rewards could be shared within the community rather than being given to a limited number of winners only.

Box 12. Emerging open innovation models in non-life sciences

9. Conclusion

9.1 The route to a successful open innovation partnership

> **"The next generation will start from saying: 'Why wouldn't you use open innovation?'"**
>
> *Dr Martino Picardo, CEO, Stevenage BioScience Catalyst*

There is no one-size-fits-all model for succeeding at open innovation. Partners need to be open-minded about one another's cultures, capabilities and constraints, which will allow sufficient room to tailor a partnership model that takes these factors into account. One of the most important requirements is that the partners have a common understanding of the definition of open innovation as it applies in their case, and what it really means to work together openly.

Following these 15 key principles will establish the right environment for open innovation:

1. Clearly define the opportunities and potential benefits and risks (including conflicts of interest) for each partner.
2. Ensure objectives are aligned at the outset.
3. Don't be opportunistic about engaging in open innovation. Only commit if it fits with strategic priorities and if the goals are truly harmonised.
4. Think through what the outputs will be and how value will be distributed.
5. Appreciate and make the most of one another's areas of expertise and commit quality resources.
6. Continuously communicate to maintain openness and transparency throughout the project.
7. Set clear IP ownership policies and strategies establishing who will own any resulting IP rights and agree on what can be made public.
8. Be clear about what the commercial benefit is and how and by whom it will be captured.
9. Be clear about what will happen at the end of the project.
10. Have a neutral convener if this will facilitate decision making.
11. Invest in building the right team to manage projects and relationships effectively.
12. Clearly define the roles of each partner and understand that there are expectations for every side to contribute.
13. Have a robust review process to keep the project on track and make go/no-go decisions.
14. Maintain a level of flexibility in budgeting and ways of working and have the ability to evolve.
15. Don't try to tell partners what to do – work together!

Three essential ingredients from this list warrant further discussion:

a. Definition of 'open': Whether it is open access, open science, open source, open research or open innovation, each party should probe both internally and each collaborator to establish what everyone understands 'open' to mean in the context of the project. Partners must then ensure that a mutually agreed and clear understanding exists and that this is expressed in writing before proceeding.

b. Objectives: Each party must unambiguously agree the objectives of the collaboration in writing, including any specific milestone targets to be achieved during the lifespan of the collaboration and what the ultimate outcomes should be. If the objectives are not clearly

aligned then partners should consider whether a collaboration is really the most appropriate way to achieve their goals.

c. **IP ownership**: Who owns and who is responsible for any IP rights entered into the collaboration? Who owns any IP or know-how arising as a result of the collaboration? Even in the most straightforward model where no IP will be claimed and all results are released to the public domain, the IP policy should be expressly and clearly agreed between the parties at the outset.

9.2 The new life sciences ecosystem

> **"The network and the ecosystem are as important as individual opportunities."**
>
> *Dr Michael May, CEO, Centre for Commercialization of Regenerative Medicine (CCRM)*

The challenges facing life sciences organisations are resulting in fundamental changes in how the 'innovation system' operates. In fact, we can distinguish three distinct systems: for discovery, for development, and for the achievement and analysis of outcomes. So far we have seen open innovation initiatives in only the first two of these. The following schematic tries to capture some of the players and interrelationships involved and the centrality of the patient in the system, who should be involved in all three stages:

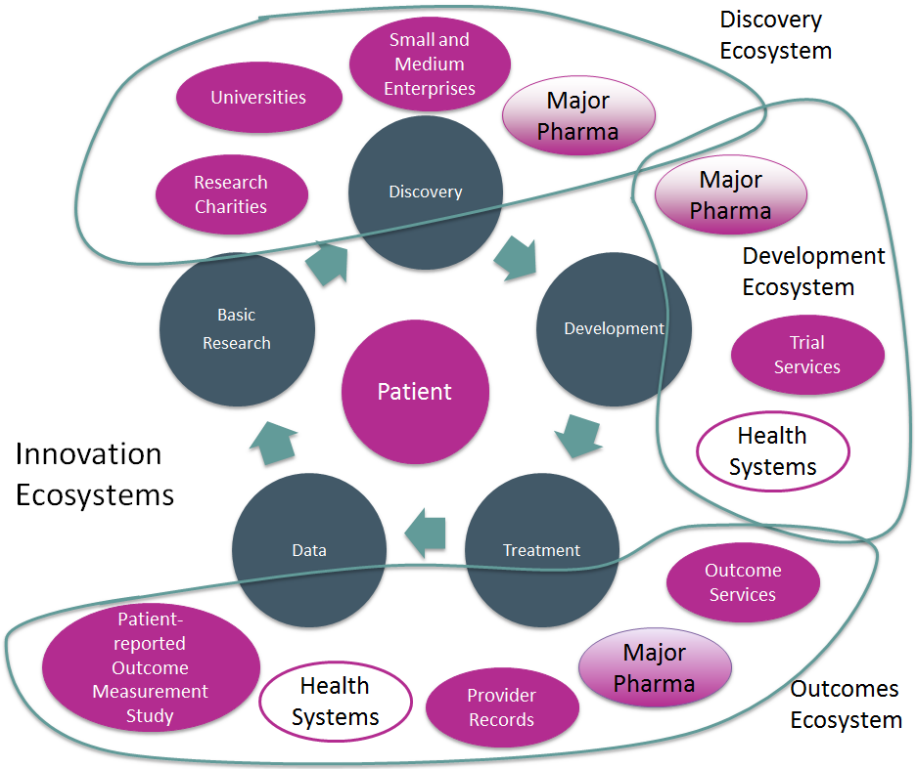


Figure 8. The emerging 'innovation system' in life sciences

There are multiple potential roles at different stages for particular players, such as major pharmaceutical companies, who could be active in the discovery and development of their products and in securing positive outcomes from their use. Likewise, health systems do not need to be passive recipients of the products: they can take an active role and partner or even co-invest in the

development of new products. There are also increasing numbers of relationships and feedback loops in this emerging system, which is best thought of as a cycle rather than a linear chain of events.

Partnerships of many kinds are possible. Pre-competitive discovery consortia can involve universities, research charities and companies of various sizes. Major companies are also partnering with one another and with health systems to work in development in areas involving high risk and cost, such as dementia. Collaborations are likely to span across sectors too – as Professor Brian D Smith predicts in his book, "pharma are just as likely to partner with retailers, healthcare providers, information technology companies and consumer goods companies" as they are other life science organisations[36].

As yet, there are limited numbers of partnerships in the 'outcome' stage, in which patients need to be more actively and scientifically managed to ensure that innovation has the desired impact. However, we can expect this to occur in the future, as health systems will increasingly seek to reward innovators according to the outcomes they achieve rather than for merely supplying products. Commercial companies may not have the necessary skills or be able to secure the access to patients they need to achieve successful outcomes, so independent services could emerge to optimise the outcomes from treatments on behalf of innovators and health systems.

Open partnerships are increasingly pushing the boundaries of data sharing towards the later stages of drug development. For example, Arch2POCM is focused on how to get academic and industry efforts to take targets through to compounds and all the way through to clinical trials while keeping the data accessible to others, sharing data all the way to proof of concept (Phase IIb). The Institute of Cancer Research has begun to do this with a breast cancer drug, holding back from partnering with industry to allow the data to stay open.

The ecosystem is also moving towards a more open source and open access environment, where research outputs are shared rather than remaining in a single entity or behind a subscription-only firewall. Greater emphasis needs to be put on releasing data that are in a useable form to stimulate interaction with as many users as possible. Currently, most online scientific journals are an electronic version of the written publication; the innovation lies in making those publications more machine-readable so that researchers can begin to extract information and apply artificial intelligence to link them together. The transaction costs of doing so also need to be reduced.

What does this new ecosystem imply for competition and symbiosis among or between the various 'species'? We can expect, and are already seeing, less head-to-head competition between major companies in domains in which shared efforts increase the overall likelihood of success, such as target validation or biomarker identification. There may also be a changed dynamic between small and medium enterprises and majors, as – while the latter become even more dependent on the former's discovery efforts – we have an increasing number of examples of 'big biotech' companies that have broken through to the large scale at the expense of established majors. So both symbiosis and competition for limited market resources are evident.

In summary, we are moving towards a more open world, which organisations must engage in to survive. The linear system where each player's position was clearly defined has evolved into a dynamic ecosystem of non-traditional partnerships in which data, expertise and knowledge are shared. The roles of industry, academia, health providers, research funders and charities in innovation are increasingly overlapping. As social and economic pressures make the healthcare landscape more demanding for all, open innovation represents a major tool for the creation of a more productive and sustainable ecosystem.

Appendix 1

Tool kit

Based on the insights from this research, we have produced an open innovation tool kit to guide organisations that are considering engaging in open innovation. The tool kit aims to help parties decide whether open innovation is appropriate for achieving their objectives, which partners they should be working with and the structures, intellectual property (IP) agreements and metrics that should be put in place.

Part 1 of the tool kit assists organisations in deciding whether to engage in open innovation or whether it would be more efficient and effective to work towards achieving their objectives in-house. These questions should be answered by each partner individually.

Part 2 should be completed by all partners together, with answers being informed by the insights from each section of this report. It focuses on the important logistical, operational and cultural factors involved in establishing an open innovation partnership. The act of completing this framework will surface most of the key issues partners need to resolve together in order to move forward.

Box 13. Template collaborative agreements

There are a number of templates for constructing collaborative agreements that we recommend partners use:

1. **Association of the British Pharmaceutical Industry (ABPI) Joint Working template**[37]

This is a seven-step flow chart that maps the journey of a Joint Working project from the idea-generation stage to the development of a Joint Working agreement.

Compiled by ABPI members, the Department of Health and the NHS Confederation, it aims to simplify the initiation of Joint Working projects. The tool kit is targeted at NHS and industry partners, and it is recommended that users refer to the ABPI's *Code of Practice for the Pharmaceutical Industry*[38] and the Department of Health's *Best Practice Guidance on Joint Working*[39] when using it.

2. **National Institute for Health Research (NIHR) model Industry Collaborative Research Agreement**[40]

The model Industry Collaborative Research Agreement (mICRA) is designed to support clinical research collaborations involving the pharmaceutical and biotechnology industries, academia and NHS organisations across the UK. It includes a decision tree to inform users whether a study is collaborative and whether the mICRA is applicable.

3. **Lambert Tool kit**[41]

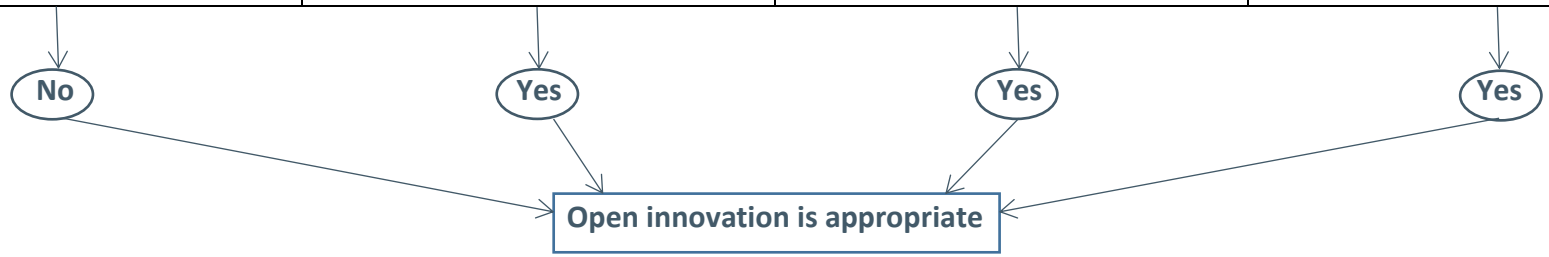
The Lambert tool kit, published by the Intellectual Property Office (IPO), provides model licensing agreements to aid university–business research collaboration. It facilitates discussions about who will own what IP generated in collaborative research, and can be used as a 'solid foundation' for negotiation but not for 'off-the-shelf' agreements. A recent IPO review concluded that the tool kit needs to be updated to reflect modern legal practice and the more flexible needs of collaborative research where both sides undertake research[42].

Box 13. Template collaboration agreements from the ABPI, NIHR and IPO

Open innovation tool kit

Part 1 – Is open innovation appropriate?

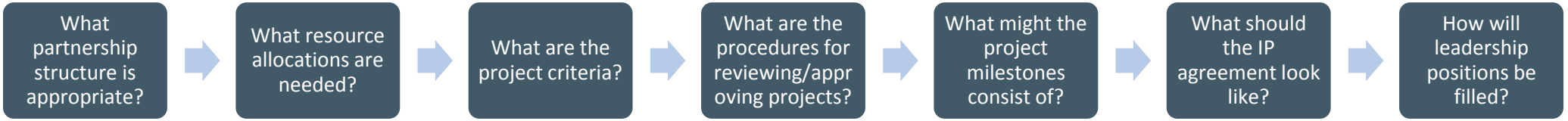
Goals	Capabilities	Culture	Finance and Logistics
Considerations			
- What are the specific goals of the project? - What are the specific outputs and ultimate outcomes? - How are my initial goals affected by partner involvement?	- What capabilities/skills are we missing? - Are there partners with these capabilities and with potentially aligned goals? - What is the quality of the potential partners? E.g. citation score of academics - Do they have previous successful experience of collaborations?	- Can we work with these partners? (Have I met those who will be involved? Is there an existing relationship? Do we have experience of working with organisations with different cultures?) - What is the 'partnering climate' of the other organisation(s)?	- What is the potential benefit–risk ratio of working with partners? - What resources are required on both sides? - Does the project represent value for all concerned, including patients?
Questions			
Can the goals be achieved by working alone?	Are there partners with complementary capabilities and aligned interests?	Can we see the cultures of the potential partners integrating effectively?	In principle, can we construct a balanced and effective partnership (in terms of structure, resources and shared risk–benefit)?



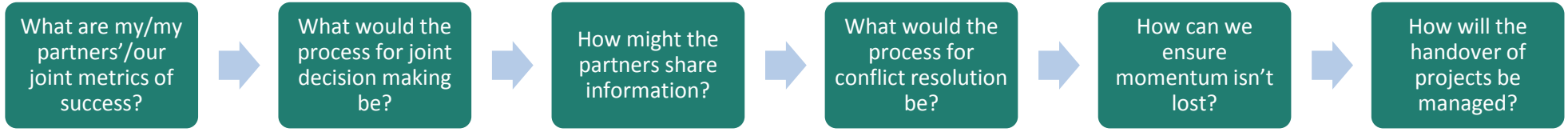
Open innovation tool kit

Part 2 – What should the partnership look like?

1. Set-up → What will the structure of the collaboration be?



2. Operations → How will the partnership work?



3. Evaluation → How will we measure and demonstrate success?

To what extent have we achieved our metrics of success?

Joint agreement templates:

ABPI Joint Working template

NIHR Collaborative Agreement templates

Lambert tool kit

Appendix 2

Thank you for agreeing to take part in this study. Please complete the following questionnaire in as much detail as possible.

Page 1: General information

1. What is the name of the partnership and which partners are involved?

2. Which partner do you represent and what is your position title?

Page 2: The partnership

3. Why did you choose to collaborate – what did you hope to gain?

4. Why did you select the specific partners involved?

5. Did you encounter any issues with the IP agreement?

Yes/No (If yes, please explain what the challenges were.)

Page 3: Success measures

6. In your opinion, how successful is (or was) the partnership overall?

Please rate the overall 'success' of your partnership on a scale of 1–10.

Completely unsuccessful Completely successful

1 2 3 4 5 6 7 8 9 10

Please explain your 'success' score:

7. How much do you think you have benefited from this project?

Didn't benefit at all Benefited extremely

1 2 3 4 5 6 7 8 9 10

Please explain your score, including details of what you have gained from the collaboration:

8. How much do you think your partner(s) have benefited from this project?

Didn't benefit at all Benefited extremely

1 2 3 4 5 6 7 8 9 10

Please explain your score, including details of what your partner(s) have gained from the collaboration:

Page 4: Metrics of success

The following questions are about the metrics your partnership uses to measure progress.

Do you have any formal or informal metrics to measure progress in the following areas?

Please tick those that apply and indicate how often they are reported and whether the results are published.

Metric	**Used?**	**Reported?**					**Published?**
		Weekly	**Monthly**	**Quarterly**	**Yearly**	**Ad hoc**	
9. Finance and resources							
Benefit-to-cost ratio of participating							
Efficiency of expenditure on alliance vs in-house expenditure							
Additional funding raised							
R&D spend by each partner							
Cost per structure developed							
Return on investment							
Number of commercialised products							
Commercial value of products							
Overall increase in profit for both/all partners							
10. R&D							
Continuity of R&D (continuity of engagement in R&D							

activities)							
No. of molecules deposited in databases							
Establishment of new technologies							
Impact of projects on development pipeline							
Achievement of decision points along value chain (e.g. validated target, identified lead)							
Time to market of product(s)							
Countries where product(s) are available							
Attrition rate							
No. of products in clinical development							
11. Networks and knowledge sharing							
Committed IP							
Patents filed/pending							
Intensity of interaction between partners (e.g. joint labs?)							
Robustness of data-sharing mechanisms							
Ratio of e-sharing : teleconference : face-to-face							
Joint publications							
Citation score for joint publications							
No. of projects continued after partnership funding							
No. and size of new partnerships/spin-offs							
12. Milestones, objectives and operations							
Formal agreement of objectives							
Achievement of objectives							

% milestone achievement							
Extent of delays in milestone achievement							
Extent to which objectives have changed since outset							
Lead time for initiation of activities							
Project review frequency							
Quality of project reviews							
'Organisational drag' imposed by consortium rules and operations							
13. Human capital							
Diversity of partners							
Quality of partners							
Partner motivation							
Employee skill level							
Staff training offered by partnership							
Number of completed PhDs/postdocs							
Recruitment level							

Page 5: Future collaborations

14. Would you repeat the collaboration if the opportunity arose? If yes, would you do anything differently?

15. Would you be happy to take part in a short face-to-face or telephone interview to tell us more about the partnership at a later date?

Yes/No

Thank you again for taking part. If you have any further questions, please contact the Project Coordinator, Rosie Pigott (rosie.pigott@casmi.org.uk).

Appendix 3

Thank you for agreeing to take part in this interview for our research project on open innovation (OI) in life sciences for the Wellcome Trust. We are defining OI as a partnership between different organisations that aims to achieve something that couldn't otherwise have happened.

As you know, we are investigating a broad range of OI partnerships in order to create a practical tool kit for organisations that are considering engaging in OI.

The results of this interview will of course be anonymised, and participants will not be named in the report or any of the resulting work. The interview will be recorded as a reference guide for our researchers.

We will be discussing the objectives of your partnership, its structure and intellectual property (IP) agreements, practicalities, human factors and the metrics that you use.

If you're ready, I will begin recording now**.**

1. Objectives

The following questions are about the objectives of the partnership:

a. To begin with, could you tell me a little bit about the partnership – a brief overview.
b. What skills/experience did your organisation bring to the problem?
c. What was the rationale for creating a partnership?
d. Why did you choose to collaborate with these specific partners? For example, did they have particular resources or skills that could complement those of your own organisation?
e. Here is a list of your objectives taken from your website. Do you agree that these are the goals of the partnership?
f. To what extent do you feel that you have achieved your agreed objectives?

2. IP structure

These questions are about the IP model used by the partnership:

a. Broadly, what is the IP agreement?
b. Who do you envision will own the IP rights to the end product?
c. Did you encounter any issues with the IP agreement? If so, how were these resolved?
d. Would you make any alterations to the IP agreement if you were to repeat this collaboration?

3. Practicalities

The following questions are about operational practicalities:

a. What is your project management structure? (I.e. how does the leadership from the different organisations work together?)
b. How do you make decisions as a partnership?
c. What, if any, is your process for conflict resolution?
d. Which mechanisms do you use to ensure that milestones are achieved?
e. Which mechanisms of knowledge sharing do you use (e.g. secondments, consortium meetings, electronic portals)?

f. How successfully do you think these structures and processes work? Can you give an example of when they have worked successfully and when they have not worked so well?
g. Where are you geographically located in relation to your partners? Do you think that this has any influence on how effectively you are able to work together?

4. Human factors

These questions consider the important human factors involved in working with partner organisations:

a. How easy was it to work in partnership? (For example, did the personalities involved interact well? Were there issues with communication or the sharing of information?)
b. Do you think your organisation has been fully engaged in the project?
c. Did you encounter any internal resistance to working in partnership? If so, how did you deal with that?
d. Do you feel that your partner(s) has/have been fully engaged in the project?
e. Has the motivation and engagement changed over the course of the project? If so, what factors do you think caused partners to lose motivation? Or, if not, what factors kept the partners engaged?
f. How similar did you find the cultures of the partner organisations? How successfully do you think the cultures have been able to integrate for the purposes of this project?

5. Metrics

The following questions are about the metrics that your partnership uses to measure progress:

a. What are the key metrics you use to measure the success of your partnership?
b. How successful do you think the partnership has been from your point of view?
c. How successful do you think the partnership has been from your partners' points of view?
d. What are the 'stakes' involved in this project? If the partnership is not successful, what does each partner stand to lose?

6. Evaluation

Finally, we will speak briefly about the value you feel has been added from taking an open approach and whether anything could have been done differently.

a. What are the main lessons you have learnt from taking part in this partnership?
b. Would you repeat the collaboration if the opportunity arose?
c. If yes, would you do anything differently? If no, why not?

That concludes the interview. Thank you again for taking part. Do you have any questions or anything you would like to add?

Please feel free to contact me or any member of the team if you have any further questions or comments at a later date.

Appendix 4

Interviewee	Title	Organisation
Dr Anthony Coyle	Vice President and Chief Scientific Officer	Pfizer's Centers for Therapeutic Innovation
Dr Mike Strange	Head of Operations	Tres Cantos Medicines Development Campus, GlaxoSmithKline (GSK)
Dr Philippe Denoel	External R&D and Innovation (GSK)	BioWin
Dr Michael May	President and CEO	Centre for Commercialization of Regenerative Medicine
Dr Timothy Wells	Chief Scientific Officer	Medicine for Malaria Venture
Aude Michel	Head of Corporate Business Development (BioAlliance Pharma)	Nano Innovation for Cancer (NICE)
David Wholley	Director	Biomarkers Consortium
Professor Chas Bountra	Chief Scientist	Structural Genomics Consortium
Dr Wen Hwa Lee	Strategic Alliances Manager	Structural Genomics Consortium
Dr Stephen Friend	President, Co-founder and Director	SAGE Bionetworks
Professor Peter Donnelly	Director of the Wellcome Trust Centre for Human Genetics (University of Oxford)	International HapMap Project
Christine Colvis	Program Director	Discovering New Therapeutic Uses for Existing Molecules
Dr Catherine Brownstein	Instructor in Pediatrics (Boston Children's Hospital)	CLARITY Challenge
Dr Julio Saez-Rodriguez	Group Leader at the European Bioinformatics Institute (EMBL-EBI)	DREAM Challenges
Richard Kidd	Manager of Informatics (Royal Society of Chemistry Publishing)	ChemSpider
Jennifer Dent	President of BIO Ventures for Global Health	WIPO Re:Search
Denny Luan	Co-founder	Experiment
Dr Tomasz Sablinski	Founder	Transparency Life Sciences
Robert Terry	Manager of Knowledge Management	World Health Organization, TDR
Dr Martin Friede	Team Leader of the Technology Transfer Initiative	World Health Organization
Dr Piero Olliaro	Team Leader of Intervention and Implementation Research	World Health Organization, TDR
Associate Professor Matthew Todd	Founder of the Open Source Malaria Consortium	University of Sydney

Dr Francis Moussy	Leader of Diagnostics and other Health Technologies	World Health Organization
Dr Malcolm Skingle	Director of Academic Liaison	GSK
Dr Martino Picardo	CEO	Stevenage BioScience Catalyst
Dr Simon Best	Chair of the Commercialisation Programme	Edinburgh BioQuarter
Susan McKee	Business Development Executive	Edinburgh BioQuarter

References

[1] Chesbrough, HW (2003). Open Innovation: the new imperative for creating and profiting from technology. *Harvard Business School Press.*

[2] Suber, P (2012). Open Access. *MIT Press*.

[3] Hunter, J (2010). Is the pharmaceutical industry open for innovation? *Drug Discovery World* Fall: 9–14.

[4] Munos, B (2006). Can open-source R&D reinvigorate drug research? *Nature Reviews Drug Discovery* 5: 723–9.

[5] Niedergassel, B and Leker J (2009). Open innovation: chances and challenges for the pharmaceutical industry. *Future Medicinal Chemistry* 1(7): 1197–1200.

[6] WHO. Pharmaceutical Industry. *WHO programme description* http://www.who.int/trade/glossary/story073/en/

[7] Scannell, JW, Blanckley, A, Boldon, H and Warrington, B (2012). Diagnosing the decline in pharmaceutical R&D efficiency. *Nature Reviews Drug Discovery* 11: 191–200.

[8] Kleyn, D and Kitney, R (2007). Partnership and innovation in the life sciences. *International Journal of Innovation Management* 11(2): 323–47.

[9] Gassmann, O, Enkel, E, Chesbrough, H (2010). The Future of Open Innovation. *Blackwell Publishing Ltd.*

[10] Backer, KD (2008). Open Innovation In A Global Perspective: What do existing data tell us? *OECD publication.*

[11] Academy of Medical Sciences (2014). Open Innovation in the NHS: A forum workshop. *Academy of Medical Sciences publication.*

[12] National Audit Office (2011). NAO Guide: Initiating successful projects. *National Audit Office publication.*

[13] Levin, RC (1986). A new look at the patent system. *American Economic Review* 76(2): 199–202; Nelson, RR (1982). The role of knowledge in R&D efficiency. *Quarterly Journal of Economics* 97: 467–8; Eisenberg, RS and Nelson, RR (2002). Public vs proprietary science: a fruitful tension? *Daedalus* 131: 89–91.

[14] WIPO Patent Landscape Reports Project (2011). Patent Landscape Report on Vaccines for Selected Infectious Diseases. *WIPO publication.*

[15] Friede, M (2014). The need for a new business model for developing vaccines against poverty-related diseases. *Unpublished.*

[16] Chander, A and Sunder, M (2004). The romance of the public domain. *California Law Review* 92: 1337; Winickoff, DE, Saha, K, Graff, GD (2009). Opening stem cell research and development: a policy proposal for the management of data, intellectual property, and ethics. *Yale Journal of Health Policy, Law, and Ethics* 9(1): 95.

[17] Hunter, J (2010). Is the pharmaceutical industry open for innovation? *Drug Discovery World* Fall: 9–14.

[18] Simpson, PB, Reichman, M (2013). Opening the lead generation toolbox. *Nature Reviews Drug Discovery* 13: 3–4.

[19] Intellectual Property Office. Lambert tool kit. http://www.ipo.gov.uk/lambert

[20] Intellectual Property Office (2013). Collaborative Research Between Business and Universities: The Lambert toolkit 8 years on. *Intellectual Property Office publication.*

[21] National Institute for Health Research (2011). Model Industry Collaborative Research Agreement (mICRA). *National Institute for Health Research publication.*

[22] Academy of Medical Sciences (2014). Open Innovation in the NHS: A forum workshop. *Academy of Medical Sciences publication.*

[23] Ibid.

[24] Ibid.

[25] Discovering New Therapeutic Uses for Existing Molecules (2012). Template Agreements. *NCATS publication.*

[26] Belleflamme P, Lambert, T, Schwienbacher, A (2014). Crowdfunding: tapping the right crowd. *Journal of Business Venturing* 29(5): 585–609.

[27] Kramer, B and Patrick, M (2013). Trends in Terms of Venture Financings in Silicon Valley: Fourth quarter 2013. *Fenwick & West LLP publication.*

[28] Hughes, V (2012). Strapped for funding, medical researchers pitch to the crowd. *Nature Medicine* 18: 1307.

[29] Hayden, E (2014). Crowd-funded HIV vaccine project sparks debate. *Nature News (10 February).*

[30] Grant, R (2013). VentureHealth's crowdfunding portal gets blood flowing into ailing life sciences sector. *VB News.*

[31] Parums, D (2014). 'Crowdfunding' and its supporting role in life science and healthcare projects. *Life Sciences Connect (Thompson Reuters publication).*

[32] House of Commons Science and Technology Committee (2013). Bridging the Valley of Death: Improving the commercialisation of research: Government response to the Committee's Eighth Report of Session 2012–13. *House of Commons publication.*

[33] Penn State University to auction patent licenses. *Penn State News (5 March 2014).*

[34] Graff, KB (2007). Collaboative IP Management for Stem Cell Research and Development. *Public Intellectual Property Resource for Agriculture publication.*

[35] Ibid.

[36] Smith, BD (2011). The Future of Pharma: Evolutionary threats and opportunities. *Gower Publishing Ltd.*

[37] ABPI (2012). Joint Working: A quick start reference guide for NHS and pharmaceutical industry partners. *ABPI publication.*

[38] ABPI (2014). The Code of Practice for the Pharmaceutical Industry. *ABPI publication.*

[39] Department of Health (2008). Best Practice Guidance on Joint Working Between the NHS and Pharmaceutical Industry and Other Relevant Commercial Organisations. *Department of Health publication.*

[40] National Institute for Health Research. Model Industry Collaborative Research Agreement (mICRA). *National Institute for Health Research publication.*

[41] Intellectual Property Office (2005). Lambert tool kit. *Intellectual Property Office publication.*

[42] Intellectual Property Office (2013). Collaborative Research Between Business and Universities: The Lambert toolkit 8 years on. *Intellectual Property Office publication.*

CASMI
School of Life and Medical Sciences
University College London
Gower Street
London WC1E 6BT, UK
E info@casmi.org.uk
casmi.org.uk

CASMI
Room 4403, Level 4
John Radcliffe Hospital
Headington
Oxford OX3 9DU, UK
E info@casmi.org.uk
casmi.org.uk

Kinapse
Tuition House
27–37 St George's Road
London SW19 4EU, UK
T +44 (0)20 8946 7600
F +44 (0)20 8946 5991
E info@kinapse.com
www.kinapse.com

Wellcome Trust
Gibbs Building
215 Euston Road
London NW1 2BE, UK
T +44 (0)20 7611 8888
F +44 (0)20 7611 8545
E contact@wellcome.ac.uk
wellcome.ac.uk

Cover image: Alex Williamson, Wellcome Images