Collaborative Health R&D Primer

Collaborative Health R&D Primer

This is a simple primer on collaborative health R&D.

Want background? Read...

- the ***introduction***, and illustrative ***scenarios***.
- the report ***"Open Source for Neglected Diseases: Magic Bullet or Mirage?"***.

Interested in implementations? See...

- our ***interviews of collaborative R&D leaders.***
- the examples in each Tactic or Tool, and the ***question index***

Motivated to support? Consider...

- ***opportunities*** to fund, study, and improve collaborative health R&D.

Collaborative Health R&D Primer

This is a simple primer on collaborative health R&D.

Want background? Read...

- the ***introduction***, and illustrative ***scenarios***.
- the report ***"Open Source for Neglected Diseases: Magic Bullet or Mirage?"***.

Interested in implementations? See...

- our ***interviews of collaborative R&D leaders.***
- the examples in each Tactic or Tool, and the ***question index***

Motivated to support? Consider...

- ***opportunities*** to fund, study, and improve collaborative health R&D.

About This Primer

Background

The goal of this site is to explain collaborative approaches for health R&D simply. We try to bring clarity to what open source, open innovation, open collaboration, open access, etc mean in the context of health R&D.

The site aims to be a resource for funders, researchers, policy-makers, and others who have an interest in collaborative health R&D, particularly for global health. More specifically, we aim to:

- Specify terminology for important tools and tactics in an intuitive and useful way (see Taxonomy notes below).
- Create a follow-up to our 2011 report ***"Open Source: Magic Bullet or Mirage"***.
- Suggest questions to consider before using a tool.
- Be as simple, self-contained, interesting, and timeless as possible.
- Be relevant, keeping in mind ***advice on circulating good ideas***.

Our thanks go to the many collaborators, colleagues, and ***interviewees*** who have generously shared their time and wisdom, including Hima Batavia, Alph Bingham, Barry Bunin, Rob Carlson, Leslie Chan, Aled Edwards, the Global Health Technologies Coalition, Ben Good, Bernard Munos, Michael Nielsen, Jean-Pierre Paccaud, Ahmed Shelbaya, Melissa Stevens, Matt Todd, Mark Tovey, Zakir Thomas, and others. The site header graphic is used from Wikimedia Commons under a ***Creative Commons Attribution-Share Alike 3.0 license***.

Background health R&D resources:

- ***Getting Started: a medical research and development primer***
- ***Global Health Primer***

This site was created by ***Hassan Masum***, with support and advice from Aarthi Rao and others at ***Results for Development***. Collaborative health R&D is a huge and rapidly changing field, and a note of humility is in order. This primer is simple, not

comprehensive; a starting point, not definitive. We hope to have conveyed the essence of several important approaches, along with relevant questions, references, and opportunities. As the ***list of opportunities*** makes clear, there is much to be done.

Taxonomy and terminology notes

Open collaboration vs controlled collaboration

Open has been widely used to describe collaborative tools and practices: open source, open innovation, open access, etc. We use *open collaboration* in a relatively strong sense, to denote open collaboration where the R&D process does not a priori constrain who can participate, and the R&D outputs are open for all to use.

For the alternative, we use *controlled collaboration* - a term chosen to be both descriptive and neutral. "Controlled" can have both positive connotations (e.g. risk management) and negative ones (e.g. top-down processes). It also describes the idea of collaboration where there are constraints on who can contribute and benefit.

Other terms considered for this dimension of the collaborative tools taxonomy include:

- Open vs Closed
- Open vs Moderated
- Open vs Regulated
- Unrestricted vs Restricted
- Universal vs Selective
- Unlimited vs Limited
- Unconstrained vs Constrained
- Public vs Private
- Nonexclusive vs Exclusive

(Note that *controlled collaboration* in the sense used in this site, is actually not dissimilar to open innovation as used in the business and innovation literature. "Open innovation" often does not mean what one might think: innovation whose results are open for others to use, as in open source. Rather, "open innovation" in the sense popularized by Henry Chesbrough and others often means opening up specific parts of the R&D process to inputs and / or collaboration with entities outside of the usual organizational boundaries - but with no necessity for the resulting R&D innovation to be open or shared. This demonstrates the value of clear and descriptive terms.)

[Open | Controlled] [Tactics | Tools] as shorthand

This site uses *open tactics* as shorthand for tactics for *open collaboration*. Similarly, *controlled tools* is shorthand for tools for *controlled collaboration*, and so forth.

Other taxonomies of collaborative health R&D methods

Below are three taxonomies (aside from the one in this site) that may be of interest to the reader.

1. In Figure 1 of ***Open source for neglected diseases: magic bullet or mirage***?, Masum and Harris offer a diagram of initiatives drawing from open source approaches. The y axis goes from more closed to more open. The x axis goes from earlier to later stage: discovery, preclinical, clinical, and filing.

2. In a slide deck, AltshulerGray suggests ***8 models of precompetitive collaboration***. These are derived from a 4x4 matrix. The y axis goes in 4 steps from (open participation, open output) to (restricted participation, restricted output). The x axis goes from building enabling platforms to conducting research, with the 4 steps being develop standards / tools; generate / aggregate data; create new knowledge; develop a product.
3. In ***Harnessing crowds: mapping the genome of collective intelligence***, Malone, Laubacher, and Dellarocas distinguish collective intelligence systems with two pairs of key questions: i) Who is performing the task? Why are they doing it? ii) What is being accomplished? How is it being done? They suggest that the set of answers to these questions can be viewed as forming a "genome" of a particular collective intelligence system. Analyzing the genomes of all such systems may help in understanding conditions where particular systems work well, and opportunities for creating new systems. As they say, "One of the important lessons learned in this work is that there are many ways to classify examples of collective intelligence.... Other frameworks that emphasize different factors could be useful for different purposes."

There is ample scope for further analysis. For example, collaborative health R&D methods could be analyzed by factors like scale of overall investment and expertise required; public versus private benefit; and skill and time requirements from collaborators. The ***list of opportunities*** suggests some applications of this type of analysis, such as roadmapping what needs to be done in the field.

Introduction

Collaborative Health R&D Primer

Introduction

> "Is open source for neglected diseases a magic bullet or a mirage? We believe the correct answer is neither."
>
> - Hassan Masum and Rachelle Harris in ***Open Source for Neglected Diseases: Magic Bullet or Mirage?***

The challenge

The traditional "business model" for creating new health technologies and therapies ***is in trouble***.

Pressure to control prices is increasing, and yet the creation of many new therapies has become more costly. It can take over a decade to get a new treatment onto the market, with clinical trials being expensive and time-consuming. Commentators have argued that these massive expenditures have yielded disappointingly few significant new therapies.

There is also limited R&D focus on diseases whose sufferers are poor or few in number. Neglected tropical diseases constitute a large fraction of the world's disease burden - yet they receive only ***a small fraction of global R&D spending***. Similarly, thousands of rare diseases collectively affect many people and pose a massive R&D challenge. The scientific complexity of many diseases (and of human biology itself) impedes prevention and cure.

To achieve more from health R&D investments, we need new approaches that connect diverse innovators, improve analytical capabilities, and provide relevant expertise where it is needed. We need to reduce duplication of effort and ignorance of disease biology.

Collaborative health R&D

These challenges may benefit from *collaborative health R&D*, which we define as *technology-enabled collaboration across organizational boundaries to solve R&D challenges*.

Early evidence - such as the examples on this site - suggests that collaborative tools and approaches can help to deliver new health solutions with greater speed and less cost. By sharing knowledge and insights, innovators can advance their work (***an opportunity Bernard Munos discusses***).

This site aims to clarify approaches to collaborative health R&D, and opportunities for better applying these approaches. Many approaches have been tried. Examples include crowdsourcing (***Innocentive***), Wikis (***Gene Wiki***), drug development databases (***TDR Targets***), open source platforms (***OSDD***: Open Source Drug Discovery), prizes (***X-Prize***), games (***FoldIt***), and novel licensing schemes inspired by open-source software (***BIOS***).

These approaches all share the basic idea of technology-enabled collaboration across organizational boundaries. However, they vary in their goals and methods, and in how "open" they are.

Commentators have ***noted the potential of collaborative approaches*** for spurring biomedical innovation. While such approaches may seem to depart from familiar market-driven models which rely on competition, this site mentions many examples where ***precompetitive collaboration*** and new business models can enable co-operation and sharing even for profit-oriented entities - especially since much biomedical R&D is financed with public or charitable funding. For neglected diseases R&D in particular, the ***WHO has rated collaborative R&D as a promising area***.

Why collaborate?

People and organizations rarely collaborate for purely altruistic reasons. Effective collaborations allow participants to "do well by doing good". Health R&D is no exception.

Personal incentives for collaborative R&D are diverse. Aside from financial gain, incentives include reputation development, solving an interesting problem that is too hard to do individually, and working with a great team. (Similar incentives ***have been studied*** in areas like ***open source*** software.)

Organizational incentives are shaped by competitive considerations. Collaboration can make R&D more effective and efficient, for example via ***platforms like Collaborative Drug Discovery***. It can manifest in ***precompetitive collaboration*** that benefits all parties, such as jointly creating new tools or ***patent pools***.

Effective collaboration can help in competing for public admiration or grant funding, ***as Matt Todd recounts***. And it can enable innovative business models - for example, creating a virtual organization with a lower cost structure and greater ability to tap external innovation. Altruism can help motivate collaboration, but it is usually not the main reason.

Tools and tactics

Collaborative R&D approaches can be divided into two basic categories: *tools* and *tactics.* ***Tools for collaborative R&D*** are platforms that enable effective collaboration. They include databases, collaborative platforms, and Wikis. They structure data and knowledge, and provide an architecture of interaction.

Along with tools, ***tactics for collaborative R&D*** are also necessary. These tactics include open access, humanitarian licensing, and precompetitive collaboration. They structure agreements and obligations, and provide laws and templates that let tools work well.

Controlled and open

There is another way to subdivide collaborative R&D approaches: *controlled* and *open*. In *controlled collaboration*, there are controls and constraints on who can contribute and benefit. However, collaboration still takes place within these constraints.

In *open collaboration*, the R&D process is open for all who are sufficiently qualified and willing to participate. The R&D outputs are open for all to use. (For more on this terminology, see the ***notes***.)

Combining *tools vs tactics* with *controlled collaboration vs open collaboration* gives a matrix which helps categorize approaches to collaborative R&D:

	Controlled Collaboration	Open Collaboration
Tools	***Controlled Tools*** (e.g. secure collaboration platforms)	***Open Tools*** (e.g. Wikis and open source software)
Tactics	***Controlled Tactics*** *(e.g. Intellectual Property toolkit)*	***Open Tactics*** (e.g. open access and licenses)

You can focus on:

- ***Tools for collaborative R&D*** (like Wikis, databases, and secure platforms).
- ***Tactics for collaborative R&D*** (like humanitarian licensing, open access, and precompetitive collaboration).

You can also browse guided by ***questions to consider***

Questions to consider

- **For which challenge(s) that you are facing might collaborative R&D approaches help? How?**
- Are collaborative tools or collaborative tactics more relevant to you?
- Is collaborative R&D necessary in your context? Why or why not?

Further reading

- Ekins S, Hupcey MAZ, Williams AJ (Editors). ***Collaborative Computational Technologies for Biomedical Research.*** Wiley, 2011.
- ***Insider Views of Collaborative R&D for Health*** interview series. Results for Development, 2012.
- Masum H, Harris R. ***Open Source for Neglected Diseases: Magic Bullet or Mirage?*** Results for Development, 2011.
- Munos B, Chin W. ***How to Revive Breakthrough Innovation in the Pharmaceutical Industry.*** *Science Translational Medicine* 3(89): 89cm16, 29 June 2011.
- Nielsen M. ***Reinventing Discovery.*** Princeton University Press, 2011.
- Paul SM , Mytelka DS , Dunwiddie CT , Persinger CC , Munos BH , Lindborg SR, Schacht AL. ***How to improve R&D productivity: the pharmaceutical industry's grand challenge.*** *Nature Reviews Drug Discovery* 9(3): 203-214, 2010.
- World Health Organization. *Research and Development to Meet Health Needs in Developing Countries: Strengthening Global Financing and Coordination.* Report of the CEWG (Consultative Expert Working Group on Research and Development: Financing and Coordination.) World Health Organization, 2012.

Practical Applications

How can collaborative R&D be applied to solve problems or add value? These scenarios illustrate how collaborative approaches are relevant to common health R&D challenges.

Unleashing unforeseen innovation

R&D is not a linear process. ***Breakthroughs often come from unexpected quarters***. Tapping this sort of "open innovation" may be difficult for cultural or organizational reasons, such as when health R&D groups focus all their energies on a specific condition. How can innovators be brought out of the woodwork?

Drug development databases can make it easier to repurpose compounds developed for one indication, and apply them for a different indication. ***Crowdsourcing*** can find and motivate cross-disciplinary innovators worldwide, through mechanisms such as innovation platforms and prizes. Successful ***Wikis*** can allow mass collaboration on collating and interpreting research outputs.

Increasing the impact of publicly-funded R&D

Universities and government labs do much of the basic R&D on which health advances depend. In the U.S. and many other countries, this R&D is often commercialized through start-ups and out-licensing. How can publicly-funded institutions achieve impact through commercial success while also meeting humanitarian objectives and ***keeping knowledge open***?

Open and humanitarian licenses can ensure that licensees "do well by doing good" â€“ joining other ***intellectual property*** options of technology transfer offices. ***Valuing openness*** can suggest metrics which measure the public benefit of keeping knowledge open, and provide incentives to academics to contribute to open initiatives. ***Open acccess*** has experienced tremendous growth in academia since 2000; there are now guides and free open access platforms that can be copied and adapted.

Addressing the high cost of drug development

New drugs take much time and money to create. This translates into expensive healthcare, untreatable conditions, and poor health outcomes. Commentaries have suggested that drug development costs are too high and unsustainable. ***How can this be reversed?***

Platforms for controlled collaboration can allow organizations to co-operate across geographical, organizational, and informational boundaries. ***Open source tools*** can be as good as expensive commercial tools for some R&D applications, if organizations have the capability to find and adapt them. ***Precompetitive collaboration*** lets competitors jointly invest to make R&D cheaper and more effective for all.

Advancing innovation in middle-income countries

Since the 1990's, there has been a dramatic expansion in the biotechnology and health R&D ***capabilities of innovative middle-income countries such as India, China, and Brazil. Yet the road to producing world-class and / or affordable***

results is long and hard. How can the capabilities of these new health R&D innovators be amplified and utilized, especially when funds are limited?

Open access dramatically improves researchers' access to knowledge, as do ***science and drug development databases***. ***Open initiative*** platforms can leverage talent in the form of educated youth, diasporans, and international collaborators. A practical understanding of appropriate ***intellectual property strategies*** can help fund innovation. ***Sharing what works*** can reduce risk and cost when doing R&D in resource-limited settings, and bring the benefits of "reverse innovation" to the rest of the world.

Question Index

Opportunities

To adopt

Are there features you could adopt from innovative precompetitive collaborations?

For which barriers that you are currently working on might precompetitive collaboration produce rapid collective advances?

For which challenge(s) that you are facing might collaborative R&D approaches help? How?

Have you considered using open tactics for some or all of your collaboration?

Have you explored the available and relevant open source tools? Have you compared them to proprietary alternatives?

Have you scanned existing health R&D lessons? Do they suggest issues you share with other parties that could be tackled together?

If you are exploring a new treatment, could citizen trials complement clinical trials?

What existing metrics for open contributions are of most value to you? How could you increase your performance on these metrics?

To create

Are there opportunities for creating open access resources in your area? Might this help your reputation or demonstrate thought leadership?

Are you sharing your successes in an interesting and insightful way?

Can you seed a new market through investing in estimating its public and private benefits?

Have you considered contributing to or creating a "health commons"?

Is there an opportunity to become a leader in a specific open source application that is core to your business?

What are the opportunities for using citizen trials for neglected diseases?

What clauses could you include or negotiate in your licenses that would cost you little or nothing, but have large public benefit?

What metrics for open contributions can you adapt or create?

To collaborate

Can you do more data sharing? How?

Can you share licensing experiences and knowhow with your peers?

Do you have data or tools that you can contribute to databases, such as for a disease or target area which your organization will not pursue?

Is there opportunity for structural change in how you and your organizational peers collaborate?

What existing precompetitive collaborations might you join?

What information and research outputs can you make open access?

What open access resources do you benefit from? How can you give back?

Risks

Business

Are you facing risks with respect to your handling of IP issues? Could collaborative IP approaches mitigate these risks?

Can you accept the risks, resource requirements, and loss of control of an open source approach?

Do you have sufficient resources? A long-term commitment?

Do you understand the collaborative activities of your competitors?

Do you understand the legal, business, and other implications of using open tools?

If considering a new online method for sharing lessons, have you clarified the method's value and ongoing resource requirements?

What guarantees do you have from the tool maker? What evidence is there of the tool's quality and likely longevity?

Will crowdsourcing really save you time and money?

Will the tactic be practical in your situation?

Sociocultural

Do you have realistic expectations of the initial interest your new Wiki will receive? What is your plan to grow this interest?

Do you understand when and why open initiative platforms work well? When and why they fail?

Has the tactic worked well previously? If so, do you understand where and why it worked? If not, do you have good reasons to believe it will work this time?

If considering sharing your trial data, are you familiar with others' experiences, privacy implications, and benefits to others and yourself? How trustworthy is the platform by which you would share data?

Is collaboration necessary? If so, are your collaboration partners committed?

Is it easy and secure to collaborate with other parties using the tool?

Will adopting open tactics deter potential participants in your initiative, who believe they need greater exclusivity to pay for their R&D?

Why would people contribute to your Wiki?

Technical

Are you ready to take the risk of being an early adopter? Have you seen the tool in action, and spoken with trusted users and implementors?

Do you have a group of enthusiastic initial users? If not, can you leverage users from an existing initiative or organization?

Do you have an experienced open source veteran as an advisor or core team member?

Does the tool allow your data and research outputs to be exported? To be made public later, if you so choose?

Have you tested the platform extensively? Has this testing been done by diverse users from your organization?

If considering a game, are you prepared to create an intensely enjoyable activity that requires little background knowledge and contributes to R&D activities?

What are your security requirements? What assurances do you have that the platform meets these requirements?

What will you do if the platform is hacked? Goes bankrupt?

Considerations

Knowledge

Are collaborative tools or collaborative tactics more relevant to you?

Are you familiar with at least one Wiki success? At least one failure?

Are you familiar with humanitarian and open source licensing approaches?

Do you understand how and why the tactic enables controlled collaboration?

Do you understand how and why the tactic fosters open collaboration?

If considering starting a new open initiative platform, have you thoroughly explored existing ones?

What other organizations are using or funding the platform?

Who are the people behind the platform?

Personal context

Are you learning from and sharing your interesting failures? What would motivate you to share more failures?

Are you prepared to "give back" to the open tool development community?

Do you have the right conditions for the tactic to apply?

Do you understand exactly how the collaborative tool will help your health R&D?

Have you stripped down your R&D question or challenge to the essential core which cannot be solved in-house? Is this core amenable to crowdsourcing?

How do IP issues help or hinder your collaborative efforts?

How much are open contributions currently worth to your organization?

How much are others using your open access outputs? Which outputs are most used?

How will you measure success? Share your experience?

Is collaborative R&D necessary in your context? Why or why not?

What specific parts of your project would most benefit from an open source approach? Why?

Resources

Are you familiar with IP best practice resources like the IP Handbook?

Are you familiar with both the social and technical workings of Wikipedia? Is there a way to leverage the Wikipedia software, experience base, or user community?

Are you familiar with existing crowdsourcing platforms? Can you use one of these, instead of creating a new one?

Are you familiar with relevant science and drug development databases, including their scope and policies and the relevant scientific background?

Are you familiar with tools for controlled collaboration in your area of interest? Have you compared the open and non-open alternatives?

Do you have the right conditions and sufficient resources to use the tactic?

If considering a challenge community like Innocentive, are you prepared to offer sufficient prize funds and tailor your challenge to the community's capabilities?

If managing or funding clinical trials, what are the bottlenecks and costs in your process? How might collaborative approaches help?

Tactics

Tools for collaborative R&D are only effective if used well. This requires good tactics for collaborative R&D - tactics or policies that enable and structure collaborative R&D.

Tactics for collaborative R&D could be rules about what must be made public, as with open access. They could enable sharing of best practices, or increase transparency and effectiveness of regulatory systems. They could be Intellectual Property tactics that let investors into health R&D get a return on their investment, while encouraging or mandating humanitarian use.

Both open and controlled tactics can enable collaborative R&D. Open tactics focus on collaborative processes that are in principle open to all. In contrast, controlled tactics focus on collaborative processes with selected partners and constraints.

You can focus on:

- ***Controlled Tactics*** that enable collaborations with selected partners and constraints.

- ***Open Tactics*** that enable open collaborations.

Questions to consider

- **Has the tactic worked well previously? If so, do you understand where and why it worked? If not, do you have good reasons to believe it will work this time?**
- Will the tactic be practical in your situation?
- How will you measure success? Share your experience?

Controlled Tactics

Tactics and policies for controlled collaboration must balance two competing objectives. On one hand, the benefits of collaboration are desired - each party has some capability or resource that the other will benefit from. On the other hand, control is desired over the collaborative process and its outputs - each party wants to ensure a return on its investment.

Managing intellectual property is a basic part of the controlled collaboration rulekit. This includes defining rights and obligations that collaborating parties have to each other. It also includes navigating rights that third parties and the public have with respect to the controlled collaboration's R&D.

Precompetitive collaboration can encourage controlled collaboration in innovative ways. Sometimes competitors can selectively co-operate in ways that benefit them all. Examples include co-operating on common technical or safety standards, co-investing in removing common barriers, or jointly advocating for mutually-beneficial policy change. The complexity and costs of health R&D have motivated precompetitive collaborations such as new drug development models.

You can focus on:

- ***Managing IP (Intellectual Property)*** to structure controlled collaborations, and understand the innovation landscape.
- ***Precompetitive collaboration*** when competitors selectively cooperate on projects of mutual benefit.

Questions to consider

- **Do you have the right conditions and sufficient resources to use the tactic?**
- Do you understand how and why the tactic enables controlled collaboration?
- Have you considered using open tactics for some or all of your collaboration?

Managing IP

> "Pragmatic IP management is building bridges between the world's islands, be they economic, institutional, or geographic."
> - Anatole Krattiger in ***The IP Handbook***

Intellectual property (IP) refers to the rights given to the inventor or developer of an idea. In its classical form, copyright protects authors from plagiarism, and patents protect inventors from copying without compensation.

Effective IP management is central to many controlled collaborations. What must each party share? Where are the boundaries of the collaboration? Who will benefit from the collaborative outputs?

Beyond the contractual dimensions of IP, the collection of rights and obligations in the health field forms an "IP landscape" for R&D. Navigating this landscape can be a precondition for establishing effective controlled collaborations such as ***patent pools***. ***Open and humanitarian licenses*** are applications of IP that help promote affordability and build a commons in the health IP landscape.

In health R&D, those who fund expensive R&D and clinical trials may naturally seek to recoup costs through IP-enabled market exclusivity. The resulting higher pricing can be in tension with affordability. (Collaborative approaches like ***precompetitive collaboration***, ***crowdsourcing***, ***trials innovation***, and ***controlled platforms*** may reduce R&D expenses and hence pricing pressures.) There is also debate about how to balance private profits with ***"the commons"*** - the public intellectual wealth that enables follow-on innovation and use of discoveries.

Examples

The IP Handbook "…offers up-to-date information and strategies for utilizing the power of both intellectual property and the public domain." It decreases IP management information gaps for R&D organizations, especially smaller organizations. As a comprehensive open access resource which includes case studies and targeted advice, the IP Handbook democratizes knowledge of the IP system.

Cambia's ***Patent Lens*** is an open access and free full-text patent informatics resource, which made searching biotech patents easier. A newer project is the ***Initiative for Open Innovation***, which aims to "create, test, validate and support new modes of collaborative problem solving" in the life sciences, with a focus on navigating complex IP landscapes. Patent Lens and the the Initiative for Open Innovation are examples of "innovation cartography tools", which help to clarify patents and their uses.

Standardized IP agreements can reduce fixed costs of structuring collaborations. The ***Lambert Toolkit*** provides model agreements for universities and companies that wish to undertake collaborative research projects. ***Consent to Research*** aims to provide standardized "Portable Legal Consent" for people to donate data about themselves and their health to scientists, spurring ***innovation in clinical trials***.

Questions to consider

- **Are you familiar with IP best practice resources like the *IP Handbook?***
  The IP Handbook focuses on the IP aspects of developing new health and agricultural solutions. Separate site guides and chapter summaries are available for policymakers, senior administrators, tech transfer managers, and research scientists. Case studies include global perspectives from government agencies, non-profits, for-profits, and universities.

- How do IP issues help or hinder your collaborative efforts?
- Are you facing risks with respect to your handling of IP issues? Could collaborative IP approaches mitigate these risks?
- Have you considered contributing to or creating a "health commons"?

Further reading

- International Expert Group on Biotechnology, Innovation and Intellectual Property. ***Toward a New Era of Intellectual Property: from confrontation to negotiation***. Montreal, Canada; September 2008.
- Van Overwalle G (Ed.). ***Gene patents and collaborative licensing models: patent pools, clearinghouses, open source models and liability regimes***. Cambridge University Press, Cambridge, UK; 2009.

- World Health Organization (WHO) Commission on Intellectual Property Rights, Innovation and *Public Health. Public health, innovation and intellectual property rights: report of the commission on intellectual property rights, innovation and public health*. WHO Press, Geneva, 2006.

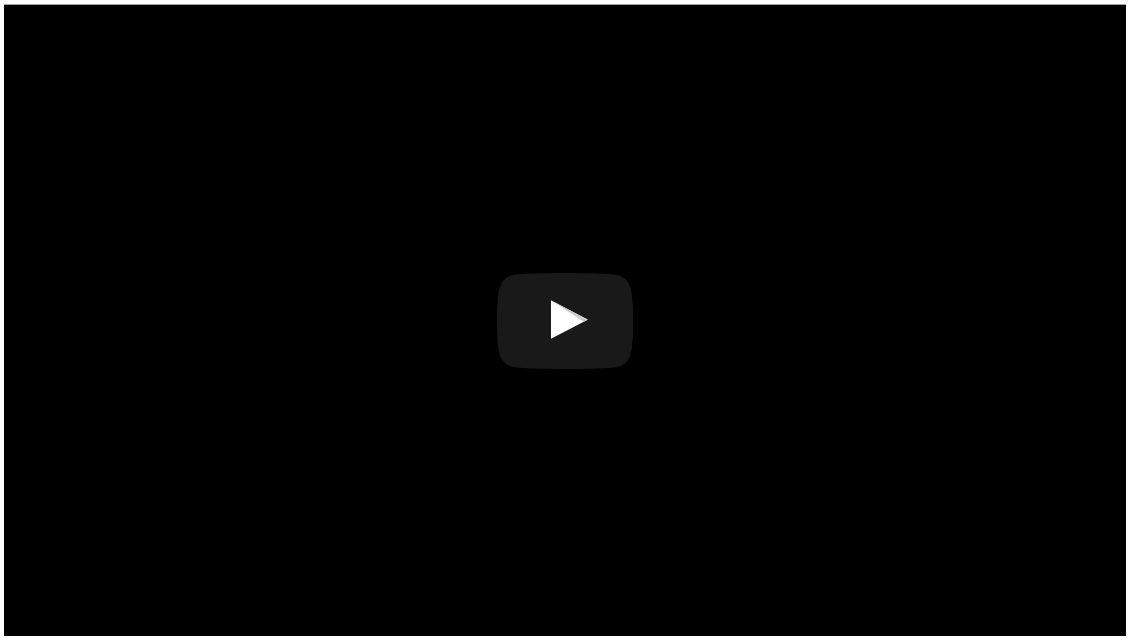
Precompetitive collaboration

> "Precompetitive collaboration is not a new concept. It's happening, and it delivers results. So the real question is how can we make that happen on a larger scale?"
>
> - Stephen Eck in ***Establishing Precompetitive Collaborations to Stimulate Genomics-Driven Product Development***

Sometimes competitors can selectively co-operate in ways that benefit them all. For example, they can set common standards or co-invest in improving shared tools.

This often occurs as *precompetitive collaboration* – collaboration on projects of mutual benefit between entities (like companies) which may produce competing goods or services later in the R&D process.

Precompetitive collaboration improves the prospects of all collaborators relative to common challenges they face. It can also benefit the public by reducing duplication of effort, increasing the effectiveness of R&D investments, and establishing common standards and resources. (All parties can benefit from public initiatives like ***NIH NCATS*** that catalyze solutions to shared challenges.)



- Courtesy of ***1DegreeBio***

The complexity and costs of health R&D have motivated many ***models for precompetitive collaboration***. Examples include consortiums (the ***Biomarkers Consortium***), alliances to improve tools and standards (the ***Pistoia Alliance***), and proposed new drug development models (Arch2POCM, discussed below).

In contrast to ***open initiative platforms***, precompetitive collaborations often limit the partners involved. They assume that each party has specific interests and assets. (Sometimes precompetitive collaborations make use of open tactics and tools, but within an overall controlled collaboration.)

A core challenge of precompetitive collaboration is balancing each party's interests and assets with the advantages possible from collaboration.

Examples

Arch2POCM is creating "...an open access patent-free drug discovery and development Public Private Partnership (PPP) designed to kick-start pharmaceutical productivity and biomedical research innovation." Its key objective is to develop and test compounds against novel protein targets to take projects to Phase II clinical trials, and make this data widely available. The pharmaceutical industry would be able to use the research as a base to create new proprietary molecules. "[It] is envisioned that Arch2POCM will seed independently funded crowdsourced experimental medicine studies in both academic labs and pharmaceutical companies." (***Aled Edwards explains the rationale behind Arch2POCM***.)

PDPs (Product Development Partnerships) for global health partner extensively with non-profit, government, philanthropic, and for-profit partners, and often use precompetitive collaboration. For example, they use a ***variety of licensing strategies*** to meet the needs of collaborators while promoting global access. This is illustrated in the ***IP policy of DNDi*** (Drugs for Neglected Diseases initiative).

ANDI (the African Network for Drugs and Diagnostics Innovation) is a new health innovation network. Its mission: "To promote and sustain African-led health product innovation to address African public health needs through efficient use of local knowledge, assembly of research networks, and building of capacity to support economic development." ***It is envisioned*** that ANDI will boost intracontinental collaboration between scattered African health R&D hubs, increase local ownership of research and its outputs, and channel increased capacity for ***science-based health innovation in sub-Saharan Africa***.

Questions to consider

- For which barriers that you are currently working on might precompetitive collaboration produce rapid collective advances? The Institute of Medicine report ***Precompetitive Collaborations to Stimulate Genomics-Driven Product Development*** suggests many such opportunities. Examples include enabling sharing of stored biospecimens and data derived from them; sharing materials and personnel, not just information; establishing governance structures and neutral convenors; and building "...a robust national infrastructure to conduct and disseminate the data from clinical trials".
- What existing precompetitive collaborations might you join?
- Do you understand the collaborative activities of your competitors?
- Is there opportunity for structural change in how you and your organizational peers collaborate?
- Are there features you could adopt from innovative precompetitive collaborations?

Further reading

- IOM (Institute of Medicine). ***Establishing Precompetitive Collaborations to Stimulate Genomics-Driven Product Development: Workshop Summary***. *Washington, DC: The National Academies Press, 2011.*
- National Research Council. ***Toward Precision Medicine: Building a Knowledge Network for Biomedical Research and a New Taxonomy of Disease***. Washington, DC: The National Academies Press, 2011.

- Topol E. ***The Creative Destruction of Medicine: How the Digital Revolution Will Create Better Health Care***. Basic Books, 2012.
- Vicens Q, Bourne PE. ***Ten Simple Rules for a Successful Collaboration***. *PLOS Comput Biol.* 2007 March; 3(3): e44.

Open Tactics

Open tactics are tactics or policies that structure or incentivize open collaborations.

Open tactics can specify a "minimal set of agreements" which collaborating parties must agree to. Open access is a good example: parties agree to make specified research data or outputs public, so that others can benefit from and build on them.

Open tactics can entail pre-competitive collaboration to overcome common challenges. Sharing what works can help all parties to benefit from each others' experience. It can reduce risks for all parties, in getting their R&D outputs developed appropriately and delivered at scale.

You can focus on:

- ***Licensing (open and humanitarian)*** which encourages licensees to act in ways that give long-term public health benefit, and creates a commons of knowledge and capability over time.
- ***Open access*** to data, publications, and other information, thus reducing barriers to accessing and building on knowledge.
- ***Sharing what works*** to draw attention to good solutions, and scale them up faster.
- ***Valuing openness*** to motivate investment in collaborative approaches and give credit for individual contributions.

Questions to consider

- **Do you understand how and why the tactic fosters open collaboration?**
- Will adopting open tactics deter potential participants in your initiative, who believe they need greater exclusivity to pay for their R&D?
- Do you have the right conditions for the tactic to apply?

Licenses (open and humanitarian)

> "[O]pen licenses have been part of the creation of entire ecosystems of co-creation that would otherwise have been impossible."
>
> - John Wilbanks in ***Openness as Infrastructure***

Certain licenses can encourage open collaboration. They can make resources required to do R&D more readily available, and even enforce certain kinds of openness.

Open source software licenses are the rules behind ***open source tools***. There are many ***types of open source licenses***, which differ significantly in the rights and responsibilities of licensees. Typically, such licenses have a "viral" quality. Users must be allowed to examine and modify the software. In return, they may only be able to distribute such modified software under the same license terms as the original software. (Proprietary platforms can access open source components.)

Creative Commons (CC) licenses have gained significant usage over the last decade. CC licenses have "some rights reserved". For example, one CC license allows material to be used and modified as long as the original author is acknowledged. Another CC license allows verbatim redistribution only.

These two examples demonstrate the use of licenses to enforce desired positive behavior. Those who accept such licenses also accept pre-specified obligations. The licensor believes that these obligations will encourage or mandate the licensee to act in ways that give long-term public health benefit.

Over time, open licenses can create a commons of knowledge and capability. For example, each piece of open source health software is forever open for others to use, learn from, build on, and adapt for local contexts. This reduces risks of vendor lock-in and barriers to knowledge access, and creates a common pool of knowledge.

Examples

Humanitarian (or global access) licensing strategies are contractual stipulations that facilitate the use of health R&D where it is most needed. They can stimulate funding for collaborative R&D, while ensuring that the product of the collaborative R&D will have the desired health impact. They have been ***used by some universities*** and foundations, and ***specific contractual provisions analyzed***.

BIOS was a licensing scheme proposed by Cambia. It attempted to popularize open source licenses for biotechnology projects, similar to existing open source licenses for software. "Those who join a BiOS "concordance" agree not to assert IP rights against each others's use of the technology to do research, or to develop products either for profit or for public good." The project has faced challenges, such as motivating usage of the licenses, and uptake has been low to date. Understanding BiOS details and experiences may be helpful in designing future health R&D open licenses.

The ***Science Commons Biological Materials Transfer Project (MTA)*** "…develops and deploys standard, modular contracts to lower the costs of transferring physical biological materials such as DNA, cell lines, model animals, antibodies and more...and allows for the emergence of a transaction system along the lines of Amazon or eBay by using the licensing as a discovery mechanism for materials." The ultimate goal is to make health R&D collaboration easier, by making it easier to share biological research materials while maintaining appropriate rights.

Questions to consider

- **Are you familiar with humanitarian and open source licensing approaches?*Specific clauses can reserve rights*** for humanitarian and research use - for example, ensuring that scientists can make use of a health product for research focused on neglected diseases. ***Field of use provisions*** can allow a split between for-profit and non-profit markets - for example, allowing one partner to sell in rich countries, and another in poor countries at a lesser or no cost.

- What clauses could you include or negotiate in your licenses that would cost you little or nothing, but have large public benefit?
- Can you share licensing experiences and knowhow with your peers?

Further reading

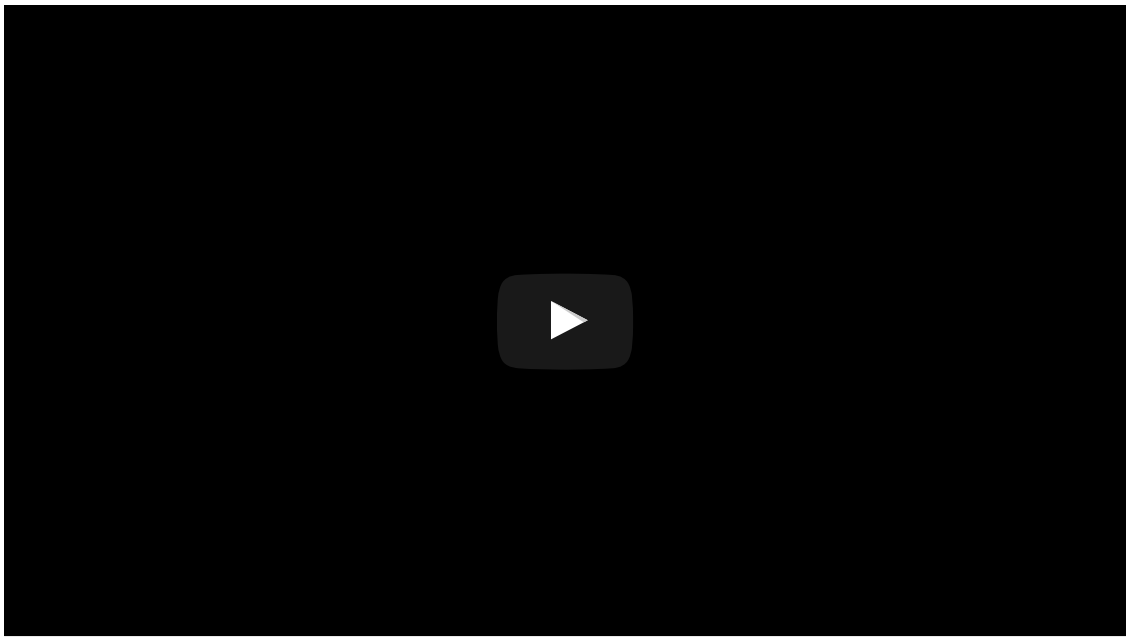
- Brewster, AL, Chapman AR, Hansen SA. ***Facilitating Humanitarian Access to Pharmaceutical and Agricultural Innovation***. *Innovation Strategy Today* 1(3):203-216. 2005.

- Chen CE, Gilliland CT, Purcell J, Kishore SP. ***The Silent Epidemic of Exclusive University Licensing Policies on Compounds for Neglected Diseases and Beyond***. *PLoS Negl Trop Dis* 4(3): e570. 2010.
- National Research Council. ***Designing the Microbial Research Commons: Proceedings of an International Workshop***. Washington, DC: The National Academies Press, 2011.
- Williams AJ, Wilbanks J, Ekins S. ***Why Open Drug Discovery Needs Four Simple Rules for Licensing Data and Models***. *PLOS Computational Biology* 8(9): e1002706. 2012.

Open Access

> "With open access, researchers can read and build on the findings of others without restriction."
> - PLOS (Public Library of Science) in ***Open Access | PLOS***

Open access means free and open access to data and information. It is one of the most basic aspects of open collaboration – one that has seen tremendous expansion over the last decade.



- Courtesy of ***Ignite Sydney***

There are two key types of open access in health R&D: open access to publications, and open access to data. For publications, the argument for open access is twofold. First, health R&D and public health will ***benefit from reduced barriers to accessing knowledge***. Second, ***taxpayers are entitled to access research they have paid for***.

Open access to data includes access to many types of R&D outputs. Most obviously, it includes data sets accompanying research articles. It can also include access to biomedical data which an organization has decided not to pursue, or negative results from research or clinical trials.

Practical barriers to open access to data include researchers and organizations resisting "giving data away". However, many clinically relevant data sets have been ***released into open databases***, and this is being increasingly encouraged by policies of funding agencies. ***Open source tools*** can ***facilitate data access***.

Examples

Thousands of open access journals have been started over the last decade. The ***Public Library of Science (PLoS) family of journals*** is one of the best known in the biomedical field. Many tools and ***guides are available*** for ***starting an open access journal***.

Many health R&D funders have open access and / or open data principles. Examples include the ***Bill and Melinda Gates Foundation data access rules***, the ***Wellcome Trust open access policy, and the NIH public access policy***.

There have been calls for ***institutional data sharing cultures***. Major funders have jointly stated support for ***data sharing more generally***. Opportunities exist to make data sharing easier and more widespread. For example, epidemiological data increases in value with sample size, and sharing this data between new treatment developers, health agencies, and health providers could have many benefits.

Questions to consider

- **What information and research outputs can you make open access?**

  Looking at ***case studies of open access implementation*** may help. BioMed Central briefly explains ***how three universities implemented central funding*** for open access, to enable open access to be paid for at an institutional instead of individual level. Many ***case studies of open access journals*** have been written.

- How much are others using your open access outputs? Which outputs are most used?
- What open access resources do you benefit from? How can you give back?
- Are there opportunities for creating open access resources in your area? Might this help your reputation or demonstrate thought leadership?

Further reading

- Dyke SOM, Hubbard TJP. ***Developing and implementing an institute-wide data sharing policy***. *Genome Medicine*, 3:60. 2011.
- Piwowar HA, Becich MJ, Bilofsky H, Crowley RS, on behalf of the caBIG Data Sharing and Intellectual Capital Workspace. ***Towards a Data Sharing Culture: Recommendations for Leadership from Academic Health Centers***. *PLoS Medicine* 5(9): e183. 2008.
- Suber P. ***Open Access***. MIT Press, 2012.

Sharing What Works

> "[P]ast challenges have been surmounted and serve as object lessons: Even in countries with few financial resources and limited health infrastructure, sensible and systematic efforts to improve health have worked."
>
> - Nancy Birdsall in ***Millions Saved: Proven Success in Global Health***

Those who do not learn from history are doomed to repeat it - in biomedical applications as elsewhere.

Sharing what has worked can draw attention to good solutions, and scale them up faster. ***Sharing what has not worked*** can help others to avoid making the same mistakes.

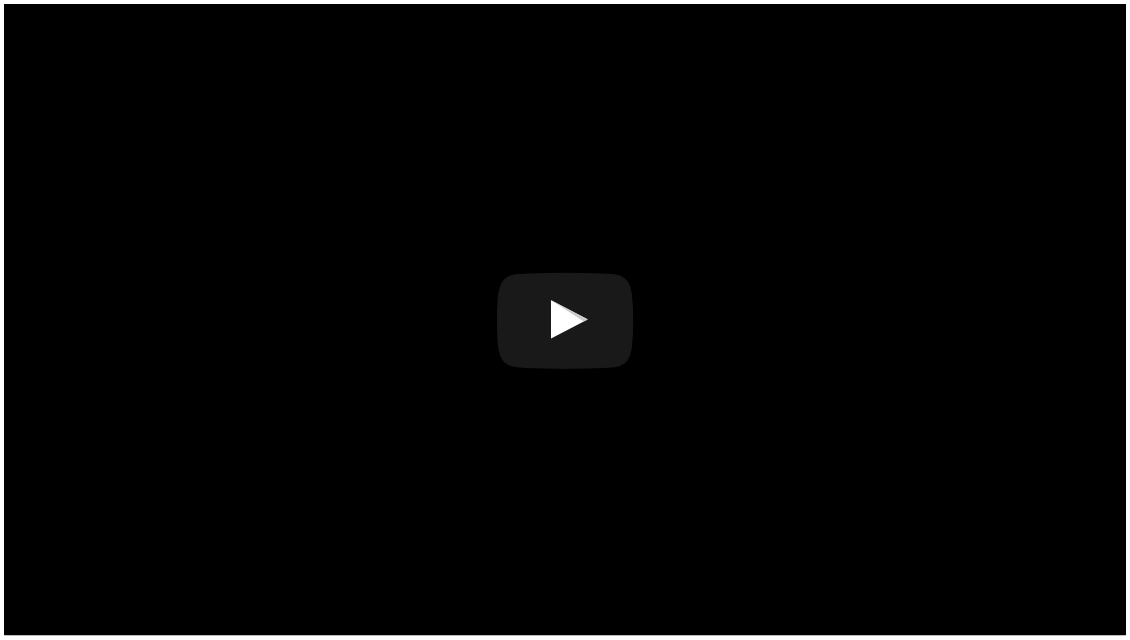
Lessons shared online through blogs, videos, and social media can be "findable" and engaging. Formal case studies and evaluations may provide deeper knowledge to a smaller audience. ***Citizen engagement*** can give feedback on what seems to work. Any or all of these methods may be mandated by funders, for reasons similar to mandating open access.

Over time, sharing lessons can clarify common challenges, which can then be collaboratively tackled. For example, ***regulatory issues*** are faced by many health product developers in later stages of the R&D cycle. Understanding the regulatory landscape worldwide, collaborating for positive changes in this landscape, and ***innovating new approaches to clinical trials*** and regulatory issues can benefit all parties.

Examples

Case studies can capture past experiences to inform future endeavors. The ***IP Handbook health case studies*** focus on IP management and collaborations. The ***Alliance for Case Studies for Global Health*** has published a collection of case studies focusing on global health collaborations. ***Millions Saved: Proven Success in Global Health*** explores 20 cases of successful large-scale projects to improve health in developing countries.

Online hubs where global health lessons are shared include ***The Gates Notes*** and ***Global Health Hub***. The ***Center for Health Market Innovations*** maps out over one thousand "...programs working to improve health and financial protection for the poor".



- This video is the courtesy of R4D's Center for Health Market Innovations (CHMI). It features Managing Director, Gina Lagomarsino, at the World Health Congress 2011 discussing the role of CHMI in organizing information about private healthcare innovations.

Questions to consider

- **Are you sharing your successes in an interesting and insightful way?**

  The above examples of case studies suggest what can be achieved given time to write up cases in detail. Many successful health R&D and nonprofit groups have online hubs that can act as models, such as the ***Gates Foundation***, ***Results for Development***, and ***DNDi***. Integrate ongoing feedback from your target audience. Design your outputs to be readable, credible, and findable.

- Are you learning from and sharing your interesting failures? What would motivate you to share more failures?
- If considering a new online method for sharing lessons, have you clarified the method's value and ongoing resource requirements?
- Have you scanned existing health R&D lessons? Do they suggest issues you share with other parties that could be tackled together?

Further reading

- Bingham A, Ekins S. ***Competitive Collaboration in the Pharmaceutical and Biotechnology Industry***. *Drug Discovery Today*, 14: 1079-1081, 2009.
- Levine R. ***Case Studies in Global Health: Millions Saved***. Jones & Bartlett, 2007.
- Patton MQ. ***Developmental Evaluation: Applying Complexity Concepts to Enhance Innovation and Use***. Guilford Press, 2010.
- Social Research Unit at Dartington, UK; Bill and Melinda Gates Foundation. ***Achieving Lasting Impact at Scale: Behavior Change and the Spread of Family Health Innovations in Low-Income Countries*** (Synthesis and Summary Report). 2011.

Valuing Openness

> "[I]ncentive building can be applied to any type of scientific knowledge: preprints, data, computer code, science wikis, collaboration markets, you name it. In each case the overall pattern is the same: citation leads to measurement leads to reward leads to people who are motivated to contribute."
>
> - Michael Nielsen in ***Reinventing Discovery***

How much is open collaboration worth?

There are many potential cost and time savings from collaborative R&D. For example, it could be possible to reduce duplication of effort due to ignorance of work going on elsewhere. To put fewer drugs into costly trials that others already have reason to believe won't work. To collaboratively speed up regulatory processes, and to fill knowledge gaps in systems biology. Where these savings can be demonstrated, open collaboration can spread.

The value of the "commons" created from collaboration and open R&D outputs is hard to measure, just as the value of public libraries might have been unclear before they were established. How much would be saved by not having compounds of interest locked up in proprietary databases, not experiencing financial and complexity barriers with the IP system, and not missing R&D advances through lack of collaboration?

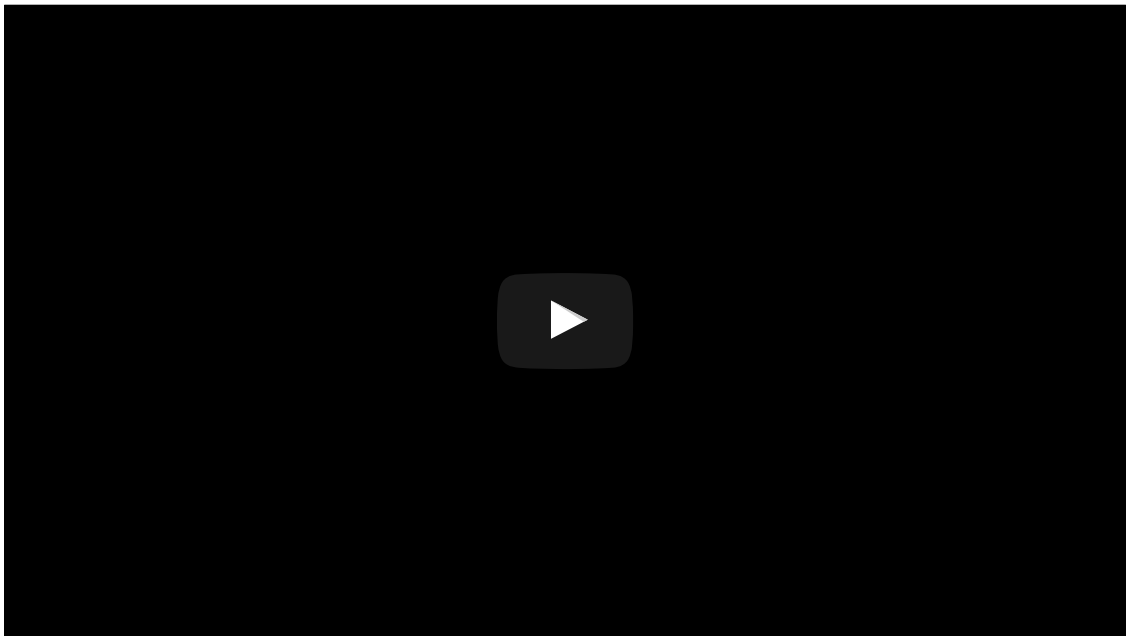
Reasonable estimates could motivate investment in collaborative approaches. Such estimates might build on ways of ***measuring return on investment in health research***.

Can credit be assigned for individual contributions to open collaborations? While many experiments are being tried online (such as ***altmetrics*** and ***WikiTrust***) impact will come from systems recognized across a field. If credit was measured in a reliable and agreed-upon way, more substantive contributions might be motivated.

For example, academics would likely contribute more to open collaborations if they got credit for doing so, as they currently do for publishing journal articles. Companies could likewise benefit from being able to publicize the "public value" they are generating. (***Matt Todd relates relevant experiences***.)

Examples

The Arch2POCM ***organizational model*** is ***investigating potential savings and innovation acceleration*** from precompetitive collaboration. Bernard Munos has ***written several articles*** with related themes, and observed some ***metrics for open innovation***.



- Courtesy of ***River Valley Technologies***

There have been estimates of the ***impact of open source software***. Similar methodology might be used to estimate the potential impact of open approaches and tools in health R&D.

BVGH has ***published several estimates*** of the market potential for neglected disease cures. Such estimates can motivate collaborations for neglected disease research. Similarly, the IFC has published ***The Business of Health in Africa***. There is an opportunity for expanded estimates which add indirect public and health benefits to direct financial revenues.

Questions to consider

- **What metrics for open contributions can you adapt or create?**

  For example, it might be possible to track usage of an open source platform, technology, or data set. Cumulative uses could be recorded and analyzed. (***Mendeley*** and similar systems do similar functions for research publication metrics.) Once usage metrics have been established, it might be possible to estimate the value of usage, better reward open contributions, and even estimate instances when researchers were stymied by cost or lack of access.

- What existing metrics for open contributions are of most value to you? How could you increase your performance on these metrics?
- How much are open contributions currently worth to your organization?
- Can you seed a new market through investing in estimating its public and private benefits?

Further reading

- Canadian Academy of Health Sciences. ***Making an Impact: a preferred framework and indicators to measure returns on investment in health research***. Report of the Panel on the Return on Investments in Health Research, January 2009.
- Grootendorst P, Hollis A, Levine DK, Pogge T, Edwards AM. ***New approaches to rewarding pharmaceutical innovation***. *CMAJ* 183(6): 681-685. April 5, 2011.
- Nielsen M. ***Reinventing Discovery***. Princeton University Press, 2011.

Tools

Collaborative tools are accelerating health solution development. They come in many types, such as databases, platforms, and software applications.

Some tools focus on *open collaboration*. In principle, anyone can take part in or benefit from open collaborative activities. (In practice, even the most open Wiki or database limits what people can do, to stop unproductive or malicious activities.) ***Open source*** is a type of open collaboration - but open collaboration is a broader concept than open source.

Other tools focus on controlled collaboration. In controlled collaboration, activities are limited to a selected group. (A controlled collaboration such as a drug-development project may ultimately help people worldwide – but the collaboration itself is controlled.)

In both cases, tools for collaborative R&D (like databases, collaborative platforms, and Wikis) should be seen as complementary to ***tactics for collaborative R&D*** (like open access, intellectual property, and organizational models). Tools structure data and knowledge, and provide an architecture for online collaboration. Tactics structure interactions and obligations, and provide the laws and templates that let collaboration work well over the long run.

You can focus on:

- ***Controlled Tools*** that enable collaborations with selected partners and constraints.
- ***Open Tools*** that enable open collaborations.

Questions to consider

- **Are you ready to take the risk of being an early adopter? Have you seen the tool in action, and spoken with trusted users and implementors?**
- Do you understand exactly how the collaborative tool will help your health R&D?
- Is collaboration necessary? If so, are your collaboration partners committed?

Controlled Tools

Controlled tools are software or platforms that enable controlled collaboration for health R&D. They are complementary to ***open tools*** (i.e. tools for open collaboration).

Organizations using controlled tools want to benefit from collaborative technologies. At the same time, they wish to maintain control over their data and research outputs.

You can focus on:

- ***Controlled platforms*** which allow one to collaborate with other drug discovery groups through a secure web-based interface, and control how and with whom information is shared.
- ***Crowdsourcing*** contributions from a broad range of participants, who may come from outside typical organizational and disciplinary boundaries.
- ***Trials innovation*** such as where individuals do trials for personal benefit, and the results of many individuals' trials are combined via collaborative platforms to better understand clinical implications.

Questions to consider

- **Is it easy and secure to collaborate with other parties using the tool?**
- Does the tool allow your data and research outputs to be exported? To be made public later, if you so choose?
- What guarantees do you have from the tool maker? What evidence is there of the tool's quality and likely longevity?

Controlled Platforms

> "The more that you give people the power of having data secure, and partitioning, and knowing that for commercial interest they can protect it - the more they are actually able and willing to collaborate."
>
> - Barry Bunin in ***Insider Views of Collaborative R&D for Health***

Platforms for controlled health R&D collaboration let geographically and organizationally distributed users collaborate on diverse R&D tasks. Requirements for such platforms have been ***explored in detail***.

Platforms which support controlled collaboration must allow each user to control what happens to the data they put into the system, and which partners are invited as collaborators. (This is in contrast to ***open initiative platforms***.)

Platforms for controlled collaboration can be thought of as virtual spaces with several features. They are secure and confidential. They have collaboration and project management functionality. They allow easy data access and manipulation.

Examples

Collaborative Drug Discovery is a cloud-based platform that allows users to "...analyze [data] with sophisticated data mining and presentation tools specialized for drug discovery research...share data securely with one or more groups...[and] view and mine openly available data."

HEOS is a "...secure, web-based platform for drug discovery collaborations." It allows users to "consolidate and manage complex information (chemistry, biology, ADME, PK, etc.); provide decision tools to scientists and management; provide a collaboration platform for geographically- dispersed partners."

Questions to consider

- **What are your security requirements? What assurances do you have that the platform meets these requirements?**

  Controlled collaboration is normally done by parties that wish to retain benefits from their collaboration. This can only be done if the collaboration environment is secure. The first step is to clarify your specific security requirements, such as audit capabilities and fine-grained permissions. The platform can then be investigated to see if it claims to meet these requirements. Consider verifying these claims via a technically-sophisticated trusted advisor.

- Have you tested the platform extensively? Has this testing been done by diverse users from your organization?
- What other organizations are using or funding the platform?
- Who are the people behind the platform?
- What will you do if the platform is hacked? Goes bankrupt?

Further reading

- Bost F, Jacobs RT, Kowalczyk P. ***Informatics for neglected diseases collaborations***. *Current Opinion in Drug Discovery & Development* 13(3):286-296 (2010).
- Ekins S, Hupcey MAZ, Williams AJ (Editors). ***Collaborative Computational Technologies for Biomedical Research***. Wiley, 2011.

Crowdsourcing

> "[N]eglected diseases have exactly the right kind of architecture of problems and needs that effectively demand open innovation."
>
> -Alpheus Bingham in ***Insider Views of Collaborative R&D for Health***

Crowdsourcing can be thought of as a particular type of mass collaboration. It starts by structuring a problem so that many people can make partial or candidate contributions.

Next, such partial or candidate contributions are invited from a large group of people (the "crowd"). These contributions are evaluated - in isolation, or in combination.

If the contributed solution(s) solve the problem, then the process halts, and the contributor(s) are rewarded. If the contributed solution(s) are insufficient, further solutions are sought.

There are several key elements to the process. Many people are making contributions. These contributors are drawn from a pool that typically crosses disciplinary boundaries. Contributors self-select the problems they wish to tackle.

The problem itself is often structured to encourage contributions from non-specialists. This can be done by stripping away non-essential elements, or by breaking down a complex problem into simpler sub-problems.

Examples

Three examples illustrate three types of crowdsourcing.

Innocentive (spun out of pharmaceutical giant Eli Lilly in 2005) is an example of a "challenge platform". It acts as a matchmaker between those who want problems solved, and those who like to solve problems. Each posted challenge

specifies conditions, including rewards to solvers. Challenges for global health have been posted, such as ***increasing the affordability of polio vaccine in lower-income countries***. The U.S. Department of Health and Human Services suggests ***guidance for challenges and competitions***.

Prizes for global health have been proposed to spur innovation. They clearly specify conditions that would-be solvers must meet in order to claim the prize. Prizes should be designed to be "not too easy and not too hard". They should not be used when there is only a single organization that could realistically solve the problem, nor when the solution requires simply scaling up a known approach.

Foldit has made a game out of protein structure prediction and design. Protein structure is an important component of disease research. Foldit has led to several ***scientific results and publications***, and was followed up by the RNA-folding game ***EteRNA***. (***Ben Good*** and ***Alpheus Bingham*** suggest the promise of scientific games.)

These three examples illustrate a spectrum of crowdsourcing approaches. Note that large prizes require more time and resources from solvers than the typically smaller challenge in a platform like Innocentive. On the other hand, games require less time and resources from solvers – but they typically engage many more solvers than challenge platforms or prize competitions.

Questions to consider

- **Will crowdsourcing really save you time and money?**

  It can take substantial effort to create a mass collaborative game, and substantial funds to set up a prize. Many times this may not be worthwhile. For example, the team at Freebase (a website that aggregates general knowledge) concluded that it was ***more effective to pay people wages*** for tasks they had been trying to crowdsource. There are many ***cases and documents on crowdsourcing and open innovation*** from a variety of industries. ***Guidebooks*** have also been written (though not specific to life sciences).

- Have you stripped down your R&D question or challenge to the essential core which cannot be solved in-house? Is this core amenable to crowdsourcing?
- Are you familiar with existing crowdsourcing platforms? Can you use one of these, instead of creating a new one?
- If ***considering a game***, are you prepared to create an intensely enjoyable activity that requires little background knowledge and contributes to R&D activities?
- If considering a challenge community like Innocentive, are you prepared to offer sufficient prize funds and tailor your challenge to the community's capabilities?

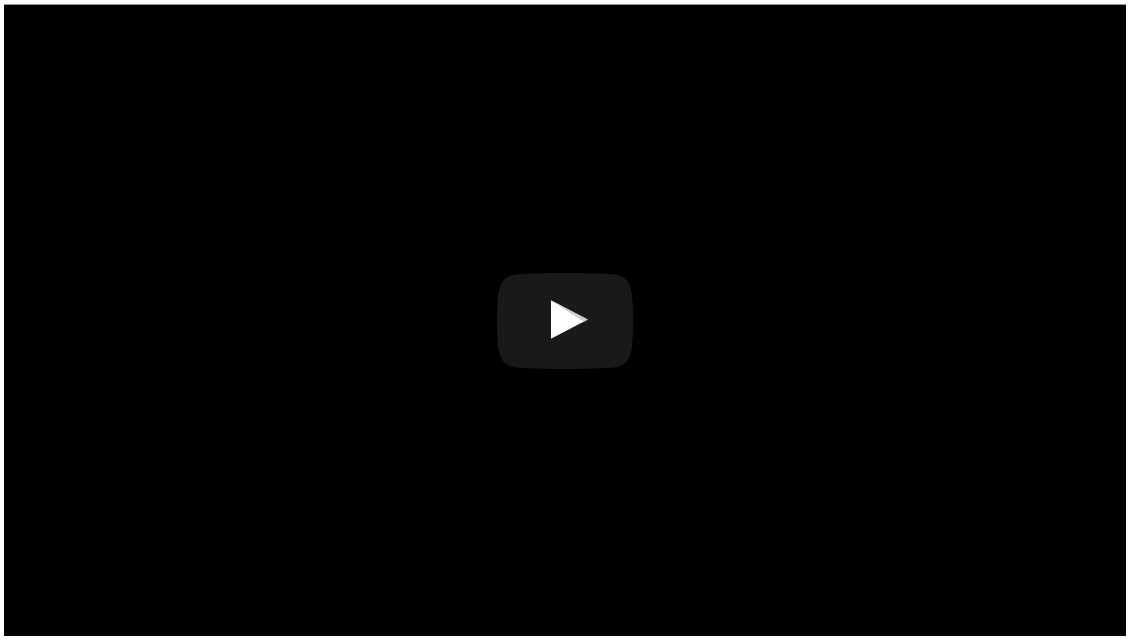
Further reading

- Bingham A, Spradlin D. ***The Open Innovation Marketplace***. FT Press, 2011.
- Good BM, Su AI. ***Games with a scientific purpose***. *Genome Biology* 12:135, 2011.
- Sloane P (Editor). ***A Guide to Open Innovation and Crowdsourcing***. Kogan Page, 2011.

Trials Innovation

> "[I]t's a tragedy that we use so little data in health. Facebook would never change its advertising algorithms with a sample size as small as a phase III clinical trial."
>
> - John Wilbanks in ***Consent to Research***

Clinical trials are critical to determining the safety and efficacy of new treatments. However, they are expensive and time-consuming.



- Courtesy of ***TED***

One emerging approach to this challenge is patient-led quantified "citizen trials" of new treatments and lifestyle changes. Each individual does a trial for personal benefit. The results of many individual trials are then combined to better understand clinical implications, using collaborative platforms for data sharing and analysis.

Citizen trials have scientific weaknesses compared to clinical trials, such as selection bias and self-reporting errors. They also raise concerns of safety, such as whether patient health will be adequately monitored. On the other hand, when practical they may be cheaper and faster complements to traditional trials, and draw from large numbers of participants. Citizen trials are largely motivated and funded by patients themselves, and so the incremental cost to network and learn from them is low.

Trials innovation poses privacy issues concerning control of personal health data. One approach is to take a middle way between complete privacy and complete public release. For example, platforms supporting citizen trials may anonymize personal details, while keeping relevant individual and statistical data available to support R&D. Consent can be "attached" to one's clinical trial data to pre-authorize secondary uses.

Collaborative platforms may help in the design and analysis of clinical trials. They may also host clinical trial data sets that are made publicly available for follow-on research. Open-source platforms may economically and effectively manage clinical trial data and processes. With effective handling of scientific and privacy issues, collaborative approaches are beginning to make the clinical trials process more efficient and effective.

Examples

PatientsLikeMe is a health data-sharing platform that helps patients share experiences and manage their own conditions. It also provides anonymized patient data to researchers. A matchmaking function links users with clinical trials appropriate to their conditions, location, and physical status. A cohort of users conducted ***a patient-led observational study on the effect of***

lithium on ALS. The results agreed with subsequent randomized trials, and suggested potential for accelerating clinical discovery and evaluation.

Quantified Self defines itself as "a place for people interested in self-tracking to gather, share knowledge and experiences, and discover resources." Enthusiasts combine informatics, sensors, and experimentation to analyze what affects their health and productivity. Communities have sprung up in cities worldwide, and are exploring how personal health trials could be collaboratively networked and analyzed.

The ***Consent to Research*** project helps people donate data about themselves and their health to data-driven scientists. Consent is attached to the data that is donated, and travels with the data ("Portable Legal Consent"). This makes it easier to reuse clinical trial data for secondary uses not foreseen by the original study developers. The system is voluntary. It allows patients to specify that they wish their data to be shared broadly to advance medical progress, while respecting privacy constraints.

Transparency Life Sciences aims to apply collaborative intelligence "as a way to design, execute, and analyze clinical studies". ***OpenClinica*** is a web-based clinical data capture and management platform built on ***open source*** and open standards. It has reported partnerships with institutions such as DNDi, Oxford University, and Brazil's Butantan Institute. The ***Clinical Trial Comparator Arm Partnership (CTCAP)*** is encouraging "...corporations to contribute existing data from non-commercially-sensitive placebo and comparator clinical trial arms". The data would be curated and hosted in a publicly available repository, and support the development of better computational models of disease.

Questions to consider

- **If you are exploring a new treatment, could citizen trials complement clinical trials?**

  While clinical trials remain the gold standard for showing effectiveness, they may in some cases be complemented by citizen trials. Points to consider include: are there sufficient people who are undertaking citizen trials in your treatment area? Have safety and liability issues been thoroughly explored? Could citizen trials provide early data that informs the design or focus of clinical trials?

- If considering sharing your trial data, are you familiar with others' experiences, privacy implications, and benefits to others and yourself? How trustworthy is the platform by which you would share data?
- If managing or funding clinical trials, what are the bottlenecks and costs in your process? How might collaborative approaches help?
- What are the opportunities for using citizen trials for neglected diseases?

Further reading

- Kotz J. ***Bringing patient data into the open***. *SciBX* 5(25), June 21 2012.
- National Research Council. ***Toward Precision Medicine: Building a Knowledge Network for Biomedical Research and a New Taxonomy of Disease***. Washington, DC: The National Academies Press, 2011.
- National Research Council. ***Transforming Clinical Research in the United States: Challenges and Opportunities: Workshop Summary***. Washington, DC: The National Academies Press, 2010.
- Wicks P, Vaughan TE, Massagli MP, Heywood J. ***Accelerated clinical discovery using self-reported patient data collected online and a patient-matching algorithm***. *Nature Biotechnology* 29: 411—414, 2011.

Open Tools

Open tools - or tools for open collaboration - are software or platforms that enable open collaboration for health R&D. They are complementary to ***controlled tools*** (i.e. tools for controlled collaboration).

Open tools are used by organizations that are comfortable with sharing most or all of their collaborative process and outputs with the world at large.

You can focus on:

- ***Databases*** which collect scientific, disease, or drug development information, and share it openly.
- ***Open initiative platforms*** like OSDD (Open Source Drug Discovery).
- ***Open source software*** created collaboratively, and openly available for use or modification.
- ***Wikis*** which let anyone edit and contribute content, and result in a useful biomedical resource.

Questions to consider

- **Do you understand the legal, business, and other implications of using open tools?**
- Are you familiar with tools for controlled collaboration in your area of interest? Have you compared the open and non-open alternatives?
- Are you prepared to "give back" to the open tool development community?

Databases

> "What society wants is for all this information to be out there, free of charge, no patents, no restrictions."
> - Aled Edwards in ***Structural Genomics Consortium FAQ***

Scientific databases for health R&D publish information such as genomics and proteomics data. This information underpins all health R&D activities, and is often a focus of ***precompetitive collaboration*** (as ***Aled Edwards discusses in the SGC and Arch2POCM initiatives***).

Because the information is fundamental to follow-on R&D, and is often publicly funded, it is often publicly available. (However, publicly available data may or may not be public domain - it can have patent or other restrictions on usage. The ***history of genomics data illustrates*** this interplay between the public domain and intellectual property.)

Scientific databases often accept data from many sources. They are used by a wide user community, and may be collaboratively operated. Analytical and visualization tools are often included to help make sense of the data.

Drug development databases make available data that focuses on information and cures for specific diseases. The hope is that many users will apply the published data to develop drugs or other cures. (Tracking such usage can help assess the ***value of open data***.)

Examples

TDR Targets "...seeks to exploit the availability of diverse datasets to facilitate the identification and prioritization of drugs and drug targets in neglected disease pathogens. Th[e] database functions both as a website where researchers can look for information on targets of interest, and as a tool for prioritization of targets in whole genomes."

ChEMBL-NTD (and the related ***Malaria Data site***) is "...a repository for Open Access primary screening and medicinal chemistry data directed at neglected diseases - endemic tropical diseases of the developing regions of the Africa, Asia, and the Americas." ***WIPO Re:Search*** is "...a searchable, public database of available intellectual property assets and resources" for neglected diseases.

The ***Protein Data Bank*** "...is the single worldwide repository of information about the 3D structures of large biological molecules, including proteins and nucleic acids ... Understanding the shape of a molecule helps to understand how it works. This knowledge can be used to help deduce a structure's role in human health and disease, and in drug development."

EuPathDB "...is a portal for accessing genomic-scale datasets associated with the eukaryotic pathogens." ***EnsemblProtists*** and ***EnsemblBacteria*** are "...genome databases for important species of protists and bacteria." Other entry points into the universe of biomedical databases include ***Entrez cross-database search*** and the ***PSI|Nature Structural Biology Knowledgebase Search Engine***.

Questions to consider

- **Can you do more data sharing? How?**

  Data sharing can be a challenge due to resource constraints. This may be mitigated through collaborative tools that ease the process. Funders may be able to provide technical assistance or better tools across a set of grantees. Peers can suggest how they handled similar data sharing challenges, and collaborate in approaching funders or database developers to make data sharing easier. Other challenges in data sharing include getting ***credit for open contributions***, and understanding relevant ***intellectual property considerations***.

- Are you familiar with relevant science and drug development databases, including their scope and policies and the relevant scientific background?
- Do you have data or tools that you can contribute to databases, such as for a disease or target area which your organization will not pursue?

Further reading

- Crowther GJ, Shanmugam D, Carmona SJ, Doyle MA, Hertz-Fowler C, et al. (2010) ***Identification of Attractive Drug Targets in Neglected-Disease Pathogens Using an In Silico Approach***. *PLoS Negl Trop Dis* 4(8): e804. doi:10.1371/journal.pntd.0000804
- Galperin MY, Fernandez-Suarez XM. ***The 2012 Nucleic Acids Research Database Issue and the online Molecular Biology Database Collection***. *Nucleic Acids Res*. 2012 Jan;40(Database issue):D1-8. Epub 2011 Dec 5.

Open Initiative Platforms

> "In an open innovation model or an open source model, you need to motivate people. You need to excite them to work with you and to work towards a common goal."
>
> - Zakir Thomas in ***Insider Views of Collaborative R&D for Health***

Open initiative platforms are online health R&D collaborations which allow anyone to apply to help the initiative. Most or all of the work is made public.

Like ***Wikis***, open initiatives hope to leverage smaller contributions from a large number of people. These initiatives wither if there is a lack of contributor critical mass.

Unlike Wikis, open initiative platforms structure lab-based activities. They also include a more sophisticated toolset (***like platforms for controlled collaboration***). Platform capabilities and governance are essential to success.

From the point of view of a contributor, joining an open initiative platform can allow small productive contributions to an existing initiative, without the responsibility of starting a new initiative.

Examples

India's ***OSDD*** (Open Source Drug Discovery) project uses a collaborative online platform to better understand diseases and collectively discover new therapies. It initially focused on tuberculosis (TB) research, followed more recently by a malaria research initiative. The platform includes data and project management capabilities, which collectively structure tasks so people can work on small pieces and collectively contribute to a larger goal. With thousands of contributors, an active community, significant government funding, and high-profile scientific leaders, it has garnered attention globally. ***Accomplishments*** include an annotated map of the TB genome. It remains to be seen whether OSDD can succeed in producing new drugs.

Synapse "...is an innovation space that brings together scientific data, tools, and disease models into a Commons that enables true collaborative research. The platform consists of a web portal, web services, and integrations with data analysis tool and is organized around novel 'Analysis Communities' that any scientist can create or join."

The Tropical Disease Initiative modeled itself on open source approaches ***as early as 2004*** and ***produced a set of potential drug targets*** from pathogen genomes that have been released under a Creative Commons license for further work. Thus far, participation in TDI appears to be modest. As ***TDI itself notes***, "… major stumbling block for open source drug discovery has been the absence of a critical mass of preexisting work that volunteers can build on incrementally."

Questions to consider

- **If considering starting a new open initiative platform, have you thoroughly explored existing ones?**

  Creating a successful online platform is difficult in general. For open initiatives in health R&D, this difficulty is compounded by the difficulty of the collaborative task and the diversity of the participants. You should be familiar with a range of open initiative platforms that have been implemented to date - for health R&D, and for collaborative tasks more generally. Which ones impress you? Why? Have you spoken with their founders and lead users? What was their history, and which of their features can you adapt?

- Do you have sufficient resources? A long-term commitment?
- Do you understand when and why open initiative platforms work well? When and why they fail?
- Do you have a group of enthusiastic initial users? If not, can you leverage users from an existing initiative or organization?

Further reading

- Derry JM, Mangravite LM, Suver C, Furia MD, Henderson D, Schildwachter X, Bot B, Izant J, Sieberts SK, Kellen MR, Friend SH. ***Developing predictive molecular maps of human disease through community-based modeling***. Nature Genetics 2012 Jan 27;44(2):127-30.

- Ekins S, Hupcey MAZ, Williams AJ (Editors). ***Collaborative Computational Technologies for Biomedical Research***. Wiley, 2011.
- Orti L, Carbajo RJ, Pieper U, Eswar N, Maurer SM, et al. ***A Kernel for Open Source Drug Discovery in Tropical Diseases***. *PLoS Negl Trop Dis* 3(4): e418, 2009.

Open Source

> "By gaining a deeper and more realistic understanding of the potential and challenges of open source for neglected-disease R&D, the approach could evolve and become important for creating a healthier world."
> - Hassan Masum and Rachelle Harris in ***Open Source for Neglected Diseases: Magic Bullet or Mirage?***

Open source originally described freely redistributable software whose internal workings are publicly available. More recently, open source has been used to describe other goods which are redistributable and inspectable, such as open source hardware or biological components.

The ***Open Source Initiative*** describes open source as "a development method for software that harnesses the power of distributed peer review and transparency of process". Many ***open source licenses*** have a "viral" quality, requiring that modified versions of the original program be distributable under the same license terms as the original.

Proprietary platforms can access open source components. ***Various forms of open source*** have been adopted by commercial, nonprofit, and government enterprises to form the basis for new business models.

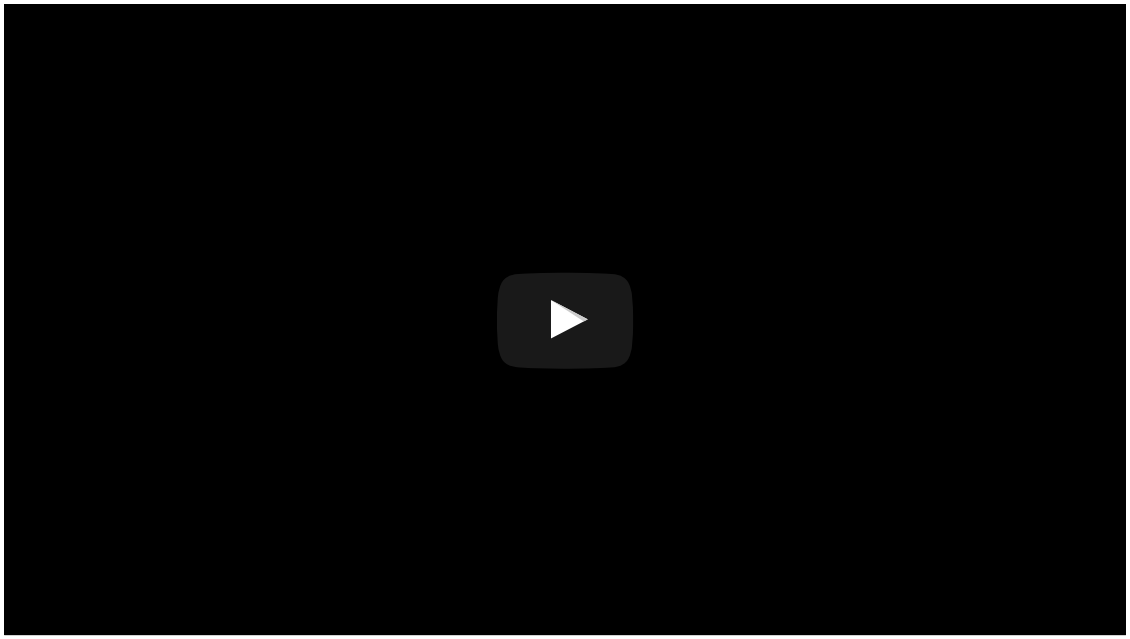
However, there are challenges in applying open source to neglected diseases. Lab equipment and clinical trials are expensive, and these costs must be recouped. Safety and regulatory issues in health R&D increase time, risk, and cost. A lab may not have a culture of online and open collaboration. The R&D time frame and risk is arguably larger for a typical drug as compared to a typical software project.

These challenges notwithstanding, there are areas such as the examples below where open source approaches seems to have potential for neglected diseases research and broader health R&D. There have also been experiments in translating ***open source approaches to medical devices***, and to biomedical R&D ***open initiative platforms***.

(The term "open source" is informally used in a generic sense, to indicate R&D with some aspects of the process or results being open. But open source as described above is a more precise concept, with specific requirements such as availability of source code or blueprints and rights to modify and reuse. Open innovation is similarly used imprecisely, as ***discussed in the taxonomy notes***.)

Examples

Open source tools in chemistry and ***bioinformatics*** have been successful, and could be better supported. For example, there are opportunities to develop open source analysis tools in ***open databases***. Another area of opportunity is open source clinical trials software, such as ***OpenClinica***.



- Courtesy of ***TED***

Guides have been created on ***open source software for university technology managers*** and other groups. There may be an opportunity for such a how-to guide focused on open source for health R&D.

The ***BioBricks Foundation*** aims to create "freely available standardized biological parts" - synthetic biology modules that can be composed and recombined, like software modules are today. These could be useful in ***biomedical applications of synthetic biology***, which are gaining increased ***funding interest for global health applications***.

Questions to consider

- **Have you explored the available and relevant open source tools? Have you compared them to proprietary alternatives?**

  For example, greater use and development has been advocated of open source computational models for molecular properties such as ADME (absorption, distribution, metabolism, and elimination) and toxicity. ***According to Sean Ekins of CDD***, "Free technologies on the web for this kind of thing are just as good as commercial software costing big companies millions of dollars in license fees. Therefore, they can do the same modeling at zero cost. If this is the case here, there may be other places they can cut costs using free tools that the companies have not explored aggressively..."

- Do you have an experienced open source veteran as an advisor or core team member?
- Can you accept the risks, resource requirements, and loss of control of an open source approach?
- What specific parts of your project would most benefit from an open source approach? Why?
- Is there an opportunity to become a leader in a specific open source application that is core to your business?

Further reading

- Marti-Renom MA (Editor). ***Open Source Drug Discovery***. Chapman and Hall/CRC, 2012.
- Masum H, Harris R. ***Open Source for Neglected Diseases: Magic Bullet or Mirage?*** Results for Development, 2011.
- Munos B. ***Can Open-Source Drug R&D Repower Pharmaceutical Innovation?*** *Clinical Pharmacology & Therapeutics 87*: 534-536, May 2010.

- Reynolds CJ, Wyatt JC. ***Open Source, Open Standards, and Health Care Information Systems***. *J Med Internet Res.* 2011 Jan-Mar; 13(1): e24.

Wikis

> "The knowledge about a particular gene's function is typically dispersed throughout hundreds or even thousands of distinct journal articles that may or may not be open access. By aggregating that distributed knowledge into coherent narratives that are freely accessible, easily discoverable, and supported with links to supporting literature, the Gene Wiki serves to better connect both researchers and interested lay people with knowledge about human genes."
>
> - Ben Good in ***Insider Views of Collaborative R&D for Health***

Wikis are special web sites that allow users to easily edit and add to their content. For a basic explanation, watch ***Wikis in Plain English***. For a familiar large-scale example, read ***about Wikipedia***.

Wikis are easy to use for novice users. They also hold the promise of tapping many contributors, each of whom incrementally improves content. Technically, a basic Wiki is easy to set up.

However, the majority of Wikis (including ***biological Wikis***) fail to reach their potential. A key reason is that Wiki administrators have unrealistic expectations of how many people will contribute. People are busy. They will often not take time to edit a Wiki, especially if the Wiki looks like no one else has contributed yet.

A more subtle reason is that successful Wikis have a good deal of governance behind the scenes. Wikipedia, for example, has ***sophisticated editorial oversight***, as well as thousands of committed contributors.

Example

GeneWiki is the best-known example of a successful Wiki for collaborative health R&D. It "...is dedicated to the goal of applying community intelligence to the annotation of gene and protein function." ***GeneWiki aims*** "to provide a well written and informative Wikipedia article for every notable human gene" and "to invite participation by interested lay editors, students, professionals, and academics from around the world".

One key to ***GeneWiki's success*** has been its leveraging of the Wikipedia platform. GeneWiki is closely linked to the overall Wikipedia project, though it has a distinct contributor and editorial community. Arguments have been made to ***leverage Wikipedia for global public health*** more broadly.

Questions to consider

- **Are you familiar with at least one Wiki success? At least one failure?**

  Wikis have been implemented in a wide variety of contexts. Sometimes they succeed. Often they fail to reach expectations. Understanding why, and learning suggested best practices, will maximize your chances of success. One starting point is the ***IBM guide to using wikis for public managers***.

- Do you have realistic expectations of the initial interest your new Wiki will receive? What is your plan to grow this interest?
- Why would people contribute to your Wiki?

- Are you familiar with both the social and technical workings of Wikipedia? Is there a way to leverage the Wikipedia software, experience base, or user community?

Further reading

- Good BM, Clarke EL, de Alfaro L, Su AI. ***The Gene Wiki in 2011: community intelligence applied to human gene annotation***. *Nucleic Acids Res.* 2012 Jan;40(Database issue):D1255-61. Epub 2011 Nov 10.
- Heilman JM, Kemmann E, Bonert M, Chatterjee A, Ragar B, Beards GM, Iberri DJ, Harvey M, Thomas B, Stomp W, Martone MF, Lodge DJ, Vondracek A, de Wolff JF, Liber C, Grover SC, Vickers TJ, MeskÃ³ B, Laurent MR. ***Wikipedia: a key tool for global public health promotion***. *J Med Internet Res.* 2011 Jan-Mar; 13(1): e14.
- Mergel I. ***Using Wikis in Government: a guide for public managers***. IBM Center for The Business of Government, 2011.

What Are The Opportunities?

What are the opportunities to scale up and improve collaborative health R&D? We invite you to browse the list below. (Some of the top opportunities are highlighted.)

There are opportunities big and small for many types of contributors, including funders, scientists, tool-builders, and policy-makers.

Contents

Funders

Why would you fund more open or collaborative health R&D? To maximize your funding impact. By funding open science, you can create platforms and data which will be used. By funding collaborative tools, you can boost R&D productivity.

Fund supporting projects

As a health R&D funder, adopt open collaboration policies and expand data sharing requirements for grantees. Fund the needed supporting infrastructure, including dedicated collaboration managers. (Examples: ***Leslie Chan interview***, ***Matt Todd interview***.)

Invest in better tools that move the whole field ahead, such as computational models and open clinical trial and epidemiology databases.

Co-invest in scaling up high-profile open collaboration projects, like India's ***Open Source Drug Discovery***.

Catalyze training and mentorship to address management challenges specific to open collaboration projects (such as motivating volunteers, co-ordinating them to work toward a common goal, and leading large groups of people in the open). (Example: ***Zakir Thomas interview***.)

Start a small and agile secretariat which curates collaborative health R&D resources and tactics, grows them over time, provides innovators with industry-experienced consulting, and actively seeks and promotes potential collaborations.

Start a specific funding initiative similar to the ***Grand Challenges Explorations*** grants (e.g. $50,000 and access to mentorship, with a possibility of larger follow-ups) to prototype a range of innovative approaches.

Start and support collaborative health R&D initiatives in developing countries - ***as Bernard Munos says***, "...They have the patients and the motivation, are change-friendly, and have no legacy to restrict their creativity."

Invest in and advocate for a simpler patent landscape that focuses rewards on significant innovation, and balances short-term private gain with longer-term public gain.

Fund a long-term program specifically for scientific games which involve both specialists and citizens. (Example: ***Ben Good interview***.)

Build communities

Start a demand-driven website to focus discussion currently occurring in many disparate forums, and to seed connections among experts and enthusiasts. (Example from development field: NextBillion.) Incorporate a group blog on collaborative health R&D, where the contributors are respected and insightful insiders in the community.

Develop a common forum (perhaps piggybacking on existing meetings) where policy makers, academic researchers, industry, and NGO representatives can meet regularly to discuss the potential and shortfall of collaborative health R&D models. (Example: ***Sage Bionetworks Commons Congress***.)

Iteratively develop collaborative approaches that are supported by diverse stakeholders with traditionally conflicting interests. (Example: ***Arch2POCM***.)

Create an events calendar which aggregates collaborative health R&D conference, workshop, and meeting events by time, place, and focus. (Example platform: ***Lanyrd***.)

Develop online communities that can filter crowdsourced proposals for health R&D solutions. (Example: Alph Bingham interview.)

Establish roadmaps and platforms

> Establish buy-in and joint commitments of high-profile leaders and institutions for initiatives tackling a well-defined set of collaborative R&D challenges. (Example: ***Grand Challenges in Global Health***.)

With a community of informed stakeholders, periodically roadmap and prioritize options for large-scale, long-term investments to improve collaborative health R&D - including converging on a few tested initiatives worthy of substantial support. (Example from semiconductor R&D: ***ITRS***.)

Develop a large-scale cross-disease platform initiative that enables sharing of data and pooling of interests for scientific and other communities; it might include metrics, collaborative access to and development of analytical tools, data sets, needs assessments, shared experiences, and so forth. (Example: ***Synapse***.)

Map realistic incentives to do controlled and open collaboration, from the points of view of pharmaceutical companies, PDPs, research consortia, individual scientists, and other groups.

Use a combination of expert advisors and automated algorithms to monitor new technologies from non-health fields for ones which might become disruptive health innovations. Complement this with "what-if" scenarios that describe desired attributes and use cases of health solutions which do not yet exist. (Example: ***Bernard Munos interview***.)

Scientists and product developers

Why would you start or support more open and collaborative health R&D? To increase your R&D productivity. Open science and collaborative tools are research accelerators.

Build tools

> Start an online Q&A site specialized to collaborative and / or global health R&D. (Example: ***Stack Exchange***.)

Build a tool that visually clarifies when and where specific IP provisions might benefit the international development and health R&D agenda, such as mandating that key enabling technologies be open source or enjoy patent exemptions. (Example: ***Gapminder***.)

Create a system for customizing and recommending collaborative licenses for users, drawing from approaches such as humanitarian licensing schemes, Cambia's BIOS license, the ***Consent to Research*** project, and Science Commons. Include a toolkit of "march-in rights" and similar humanitarian licensing clauses, which ensure that downstream partners (e.g. technology licensees) create products that are affordable and have health impact.

Develop a framework allowing isolated biobank specimens to be pooled, easily searched, and shared precompetitively and securely. (Example: ***Establishing Precompetitive Collaborations to Stimulate Genomics-Driven Drug Development***.)

Develop and test a "fair reward principle" that distributes rewards for massive collaboration on lab-based work or clinical trials, so that parties contractually agree in advance to share future rewards by some fair division process.

Find ways to estimate the financial, social, or knowledge impact of a future successful open source model for neglected-disease research - to make a clear articulation of business and societal benefits.

Devise better ways of dividing complex health R&D problems into manageable subproblems in order to enable the kind of mass-collaborative approach that has worked in many online systems.

Develop low-maintenance systems that bring people up to speed quickly on open health projects and complementary tactics that encourage people to comment, contribute, question, and criticize openly - thus speeding the accretion of collective wisdom and minimizing information bottlenecks within projects. (Example: ***Matt Todd interview***.)

Start initiatives

With engagement from industry, science, and funding stakeholders, advance a new networked initiative for precompetitive collaboration to create new treatments. Incorporate realistic incentives for diverse parties to collaborate, including pharmaceutical companies, PDPs, research consortia, and individual scientists - and design this collaboration to result in new treatments developed with less time and cost. (Example: ***Arch2POCM***).

Make in-house software tools available for controlled or open collaborations - for example, by requiring that users publicly acknowledge the tool creators, and contribute back their experiences and any tool improvements.

Support fine-grained population-wide epidemiological data sharing between new treatment developers and health providers, which could have a broad range of benefits.

Use open-source synthetic biology as a test case to explore collaborative approaches to health R&D and risk management.

Engage long-term with large lead users implementing collaborative R&D, to learn from their process and suggest approaches to adopt.

Aggregate funding opportunities for collaborative health R&D, including past funding and granting agency profiles, to create a one-stop shop for project implementors seeking funding - including health R&D challenges from innovation platforms like ***Innocentive*** and prize competitions like ***X-Prize***.

Negotiate an experimental site or country license for a controlled collaborative health R&D platform such as ***Collaborative Drug Discovery***, overcoming both financial and cultural barriers. Evaluate what the license achieves.

Create an end-to-end R&D pipeline that is transparent, community owned and operated, capable of supporting dozens of initiatives, and funded with pledges by individuals or groups on a project-by-project basis.

Do "macro-economic" evaluation

Estimate benefit of collaborative health R&D for avoidance of research and clinical trial duplication and reduction of risk and cost, working with initiatives like ***CTCAP*** (Clinical Trial Comparator Arm Partnership). (Example: ***Arch2POCM Business Model***.)

Estimate the public and private value of protecting the commons on which health R&D depends, and the impact of policy alternatives for governing this commons.

Evaluate the impact over the last few years of the release of neglected-disease drug information by pharmaceutical companies such as GSK, and the opportunities for increasing this impact.

Combine information about market sizes and purchasing power with scientific feasibility, to understand where shared development of new products could yield revenues (using collaborative, open science platforms that can pool intellectual property and human resources).

Policy makers and researchers

Why would you spend resources on evaluating open and collaborative health R&D? To clarify what works. Good data and analysis will help good approaches to spread, and highlight policy opportunities.

Do case studies

Provide a detailed profiling platform of collaborative initiatives for health R&D, summarizing which initiatives are active, what types of collaborators they are seeking, and what they and previous projects have achieved. Include a matchmaking service with scientists, funders, and citizens who are seeking to contribute to a collaborative initiative. (Example: ***CHMI***.)

Write a collection of credible success stories, to help convince those on the fence to consider collaborative R&D approaches. (Example: ***Case Studies for Global Health***.)

Do in-depth case studies of selected collaborative initiatives for health R&D, looking for generalizable lessons. (Example: ***Cambia and OSDD***.)

Start a site like ***Admitting Failure*** to collect failures in implementing collaborations - both in health and in allied R&D fields.

Collect specific ways in which lack of health R&D collaboration is increasing cost, time, or risk (and make this collection easy to search and understand).

Estimate the value of tools like the ***IP Handbook*** and ***Patent Lens*** which aim to make the IP process itself more accessible, and devise additional high-value tools specifically to assist collaborative health initiatives.

Where applicable, do direct comparisons of collaborative models to identify when and why each is best.

Implement metrics

Build a widely-used information utility that measures one's achievement as part of a collaboration, thus providing more incentives to participate. Incorporate metrics which recognize collaboration, engagement, and impact, and which provide professional value for contributions to collaborative initiatives - for example, to allow aggregating one's contributions into a cumulative "score" for use with granting agencies and promotion committees, similar to how publication metrics are used today. (Examples: ***Leslie Chan interview***, discussion of new open science metrics in ***Reinventing Discovery***.)

Implement "value tracking", by which all use of an open platform, technology, or data set would automatically be recorded, and subsequently be valued; implement complementary tracking of instances in which researchers were stymied by cost or lack of access.

Evaluate collaborative initiatives for health R&D, incorporating metrics developed specifically for the area.

Track the number of new drugs developed largely by open source methods that reach clinical trial stage, and the number that are actually delivered to populations.

Clarify use cases

With strong engagement from end users, draw together research and practice to develop an accessible, periodically-updated, and practical "collaborative health R&D toolkit" suggesting where and how to apply particular collaborative approaches.

Do further research and testing to define the key determinants of where collaborative approaches tend to work (or fail) in health R&D.

Develop a list of business models for sustainably providing health R&D resources which are free to some or all parties - for example, the "pay once and use forever" model of PLOS, or implementing tiered pricing with basic free services subsidized by more advanced paying services. (Example: C Anderson's list from his book ***Free: the future of a radical price***.)

Build on search engine methods to develop a "collaborative health R&D activity index - for example, by analyzing link, key phrase, and citation patterns in websites, scientific material, press releases, speech transcripts, articles, discussion forums, and so forth - and analyze this index by geography, organization, time, unusual flows of interest, and correlated search terms and categories.

We invite you to suggest additional opportunities, and to share your experience implementing any of these opportunities. Please contact us at policyassessment [@] resultsfordevelopment.org (with subject "Collaborative Health R&D").

Global Health R&D Policy Assessment Center is a project of Results for Development, with funding from the Bill & Melinda Gates Foundation.