TOOL BOXES FOR ADVANCING THE RESPONSIBLE DEVELOPMENT OF SYNTHETIC BIOLOGY

The following pages describe the proposals co-designed by the participants in the Industrial Dialogue workshops on synthetic biology in Manchester and Budapest. They offer examples of how these principles may be translated into practical approaches for companies and societal actors.

The IDs produced a number of proposals, which, to varying extent, put RRI principles into practice. The insight that responsible innovation depends on an ecosystem of diverse and interacting players has the consequence that tools for responsible innovation in industry are not confined to a discrete action taken within a specific company. Rather, it is in multi-stakeholder constellations that a company can cooperate with a societal actor and a regulator to address a genuine societal concern. Because of this multi-stakeholder nature of RRI, participants proposed complex toolboxes, rather than individual tools.

The Manchester and Budapest IDs worked-up six toolboxes (comprising multiple tool elements) in detail, with three further tool 'elements' described below as providing interesting additional insights and suggestions, which could be contenders for incorporation into the final toolbox designed for implementation in the synthetic biology pilot from the elements listed below

The Manchester ID produced three Tool-box Prototypes:

1/ An Accreditation Process

2/ A Repository of Learning Case Studies

3/ A Multi-stakeholder cross-disciplinary Peer Review Process

The Budapest ID produced three primary Tool-box Prototypes

4/ A Synbio Cross-stakeholder Oversight Group,

5/ A Researcher Incentive System Incorporating a Repository of Short 'signalling' (pre peer-review) Articles

6/ A Multi-disciplinary Education and Public Engagement Web-platform

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The Industrial Dialogue workshops produced a number of proposals, which, to varying extent, put RRI principles into practice. The insight that responsible innovation depends on an ecosystem of diverse and interacting players has the consequence that tools for responsible innovation in industry are not confined to a discrete action taken within a specific company. Rather, it is in multi-stakeholder constellations that a company can cooperate with a hospital and a regulator to address a genuine societal concern. Because of this multi-stakeholder nature of RRI, participants proposed complex toolboxes, rather than individual tools. The following describes the proposals emerged in Manchester and Budapest.

The Tool-boxes are briefly described below:

2.1 An Accreditation Process

The toolbox in brief

The aim of the Accreditation toolbox is to make expectation clearer and to show who is achieving it. Why should we set a standard? To build trust, reputation, getting good services to market, building a value chain, fostering engagement, creating additional benefits and opportunities for a technology.

How does it work?

- It can take the form of a website badge that says 'accredited by'.
- What power has this accreditation? Necessary to have out-facing public recognition of the tool, it should be more like a 'fair trade' sign – a body that has some recognition.
- We should think about the following: what do we want to accredit, who decides that a process/idea is appropriate, what access and review/decision process is involved.
- We are talking about accreditation against a guidance, rather than a standard type of a product.
- It can be a loop: set a standard – submission – review. It is a loop because 'submission' version is not forever, later you update a standard and report against the previous

version. It's a dynamic process.

- This accreditation allows people to see what people (industry experts, academia) are doing. It makes things more transparent.
- There should be a pool of assessors.
- What is the level of authority of accreditation body is?
- The review should consist of 2 steps – peer review and final review.
- The standard should be synthetic biology specific. Who is going to set it? Could be SBLC, NGOs, government groups, cross-governmental organisations. It should be a body with an international view. But does this list represent everybody? Moreover, there may be constraints from the legal perspective, legal people may say that these processes are not feasible.
- Should accreditation be done for a company or a project? It should be a company level because companies do many projects per year.
- What should be considered – RRI as a process, RRI as a product, various case studies.
- Cost: when should organisations pay and for what (for a review or a submission)?
- There should be a core of actual reviewers, but the discussion should be open. Why are we seeking for open feedback? Public perception of a technology? Is it a corporate governance? Peer review will be an opportunity for public discourse.
- Also, we cannot let everybody give equal opinions, there should be different levels of accessibility of this tool. If people sign up to comment they have to read guidelines, general etiquette.
- What is the funding model for the whole accreditation scheme? Central funding or we charge companies? Mix of public/private funds. Independent governance from the funding source.
- Reviews are at national level.

Key requirements and open issues:

- What is the selling point?
- Company or research group? Business?
- What are the benefits of accreditation?

2.2 A Repository of Learning Case Studies

The toolbox in brief

The toolbox is a collection of *learning* case studies.

How does it work?

- Need to be 'learning case studies' showing experiences, not presented as success/failure, nor 'good practice'
- Need equal attention to what didn't work with explanations of what didn't work, where the struggles were and why.
- Open Repository: collect together what already exists: transparency
- Different case studies for different purposes/audiences, eg organisation based (such as a single company); new product based (such as a new way of producing a flavouring), or societal 'challenge' based (such as clean water)
- Case studies for industry can show industry how to do RRI, for example Stage-gate process, more detailed.
- Time-frames, benefits of taking the long-term view V short-termism.
- Short vignettes, for example for schools or teaching materials, or key-messages.
- Encourage not-so-successful examples as teaching materials, ask people to share experiences of challenges encountered.
- Prototype, which explored what we would want to achieve for case-studies – how would case studies be used by RRI relevant groups and facets of spiders webs.
- Envisaged as a repository of simple accessible studies there to promote RRI, to whole variety of audiences (may need to tip the communication format to different audiences, for example industry needs will be very different to school needs)
- Show proactive and anticipative approaches to challenges of what went/could go wrong, including different scenarios, such as 'foresight' methods.
- Need for repository and long/short term management. This would involve a cost of upkeep.
- Need independent mechanism to keep the process honest and a mechanism for moderations/feedback. Use guiding principles of openness, transparency and trust.

- Spiders web shows that is goes in different directions, but is all connected
- Cases need to be succinct, and accessible, and written to a common template format, with examples of success stories (and disappointments), purposes, promotion of dialogue about learning from mistakes, access from different audiences.
- Recognise that RRI carries in context, whether local or regional, or sector specific.
- Have resources that are online, and that can be delivered through workshops
- Tool was generated quickly, after initially "painful" exchange between multidisciplinary groups of tool developers.
- Can be incorporated into the Accreditation Tool/Process at 1/ above

Key requirements and open issues

- Need to be clear: Case studies of what? Not just ivory tower.
- Who will have oversight/ownership of the repository?
- Who will be responsible for monitoring/maintaining and keeping up to date

2.3 A Multi-Stakeholder Cross-disciplinary Peer Review Process

The toolbox in brief

The peer review process aims to cover research and funding, and it aims to involve business and industry.

How does it work?

- In research, the process would involve discussion in funding application (plans) and again reviewed after process to understand retrospectively what happened.
- In business, would also need to discuss plans for RRI in plans, and then retrospectively how the process went.
- This would need feedback to be built into the tool, so as to continually generate and update best practice understanding for the peer review process
- Can be incorporated into the Accreditation Process.

Key requirements and open issues

- Needs RRI guidelines to assess/do peer review side
- Needs training is to enable peer reviewers from different disciplines and perspectives to input,
- This cross-disciplinary sensitivity and balanced cross-disciplinary expertise doesn't currently exist.

2.4. Synthetic Biology RRI Cross-stakeholder Working Group

The toolbox in brief

The Synthetic Biology RRI Cross-stakeholder Working Group aims to create resources and incentives for RRI and Synthetic Biology. It has been developed in the Budapest Industrial Dialogue. It is proposed to be a source for voluntary self-regulation, a think tank and a point of reference.

It addresses the following challenges identified during the IDs:

- Framework conditions: need for clear definitions (what is RRI); need for clear regulatory framework for balancing risks versus benefits; needs bodies of oversight (for example ethics councils); need for an award system that values transparency and openness; and last but not least need for a reputational system for companies based on process (how you do the work) and products (what is the outcome -do we want this product).
- Regulations and guidelines: need for well-defined boundaries between legislation and regulation/guidelines. Need for clarity for when moving beyond current regulations, which is highly relevant in the case of new technologies such as synthetic biology.
- Governance models: more inclusive and participative innovation and governance processes, more collaboration between industry and research, more coordination between the stakeholders, regular meeting between stakeholders as well as a platform for information sharing among stakeholders, use the opportunities offered by www.
- Communication: need for open and fair communication between all stakeholders, need for shared language/common understanding
- Incentives to develop capacities: need for having chances to meet, need for resources and time to have stakeholder dialogue, need for new roles – for example intermediaries for helping industry and scientists to address RRI. Need for financial and logistical means and funding.

How does it work?

The Synthetic Biology RRI Cross-stakeholder Working Group is a roundtable formed by four categories of stakeholder and named as a Working Group on Synthetic Biology and RRI. The four participating stakeholder groups are: societal actors, industry, academy and regulators. The industry representative could be from a major biotech association (for example EuropeBio) but representatives of smaller SMEs or start-ups should be also included. The regulators could be from for example EMA, EFSA, EEA or ECDC also might be an option. The WG should use already existing European bodies, expert groups, or organizations, like the EGE, SCENHIR, etc.
The WG (approximately 12-16 persons) receive its mandate and some money from the EC, Brussels and it is formed in a way to avoid redundancies and misuses of expert and financial resources. The decisions made by this WG will impact on synthetic biology community and industrial participants. The WG would have a yearly meeting, and quarterly teleconferences. The WG is leaded by a chair and would employ a half time working secretary.

The function of the WG would be to mandate an ad hoc committee to define what RRI is, and what we understand as RRI in Synbio. Than to write a code of Ethics for RRI and Synbio, to collect Best Practices, participate to building up a web page, to issue the certification of excellence, (the way to be decided would be similar to an audit system, the WG prepare the framework for this) and offering an RRI award for Synbio. Dissemination would happen via webpage set up by the WG and also through connection to global participants in synbio conferences, or other synbio events.

Key requirements and open issues:

- Need for a mandate from the EC for setting up this WG
- willingness and interest of the expert bodies to participate
- well defined and competitive criteria for selecting the WG members
- Defining how the representatives from the academia and civil society will be selected and by whom? How long will be their mandate?

2.5 A Researcher Incentive System Incorporating an Online Repository of Short (pre-peer reviewed) Articles (named UMBILICOM)

The toolbox in brief

UMBILICOM is an online platform that aims to bridge the information gap between science and innovation, to foster transparency of research activities, to educate the public on science issues and the scientists on regulatory/contextual issues. On this platform public opinion can be monitored and fed-back to researchers. The different needs of public/academic researchers and industry researchers might create the need for a two gateways platform, with different levels of openness.

It addresses several of the challenges identified during the Industrial Dialogues:

- Framework Conditions: necessary to update the evaluation system for scientist and researchers to include RRI related activities too (educating public, open science, public engagement in science);
- Governance model: fosters collaboration between academic research and industry research, makes more transparent the innovation process
- Accessibility: open access for the public research on synthetic biology;
- Education: general public can get information, enter into discussion (thus learn) and provide opinion on synthetic biology research proposals from the earliest stage of research
- Communication: UMBILOCOM offers a platform for synthetic biology researchers to communicate their research proposals so these can be debated with the larger community (peers, but interested persons from the general public)
- Building trust: through being open about the ongoing research plans, and providing space for continuous feed-back from the community the public's trust in the researchers/scientists can be increased.

How does it work?

The original idea behind the toolbox was a researcher's incentive system though which researchers could be incentivized towards publishing and discussing very quickly/early with scientific peers and general public the various aspects of their yet immature research results or ideas. The incentive would be acknowledging this activity in the course of researchers'

evaluation, by considering additional factors than the generally used impact factors. One such additional factor could take into account how the researchers communicate their research with the general public.

- The technical solution proposed is on online Phased Release Platform that protects IP where research can publish and discuss their research ideas and results at a very early stage.
- The framework condition is putting in place an evaluation system that takes into account the proposed new impact factor

UMBILICOM has been developed initially with a focus on public/academic researchers. On this platform early/immature research results or ideas can be presented and opened up very rapidly for early discussion with peers and general public to assess if it is a good idea to follow or not. The platform would enable continuous updating during the research process, and it would include a function where the ethical implications can be discussed with peers and members of the general public. Negative results, doubts, uncertainties should also be included, as a valuable source from which much can be learned. Public opinion can be monitored and feed-backed to researchers, though rating functions (counters, scores). Several metrics, indicators where proposed for evaluation of researchers' activity on the platform. The platform would be open for both peers and general public.

The different needs of academic/public researchers and industry researchers/companies, as well as the difference between the rewards systems they follow was acknowledge by the designers of the toolbox. Industry researchers might have different needs from university researchers, for example secrecy, IP rights and in general the protection of ideas might be more important for them, or they are more interested in business to business connections than with very overarching, open connections with the general public, so a more closed platform would be welcomed.

Acknowledging this difference the idea of two separate platforms/or two gateways – one for public research and one for industry research - was formulated. A company or industry researchers might be interested in the information shared on the public platform. The companies could have even the role in sustaining the platform, and creating a space where IP issues are handled properly. Starting points for an industry platform could be existing platforms for mandatory registration of certain types of research that already exist due to safety concerns, but maybe not to start with this during the piloting.

Key requirements and open issues

- personal and financial resources for setting up and operating the platform
- need for spreading the information about the platform to all potentially interested stakeholders
- a company or more who would undertake the responsibility of maintaining the platform
- reward systems that would acknowledge this effort both in public and industry research

The open question related to this toolbox is how to deal with research that is publicly and privately funded, respectively. What could be an incentive for a company to join such a system? The designers of this toolbox could not find a final answer, but a possible solution was proposed, namely to create two separate platforms/or two gateways to meet the needs of both industry researchers and university researchers.

2.6 A Multi-disciplinary Education and Public Engagement Web-platform bringing together issues on Ethics/Legislation/Science.

The toolbox in brief

The Synbio Info Website toolbox is an educational website, focusing on three major issues: ethics, legisltaion and scince. It is aimed to be used for lay people and lay experts too. It is a web based platform for a variety of stakeholders and activities, with the main aim of creating a public forum for Synbio RRI, focusing on topics and dilemmas. It addresses the following to challenges identified during IDs:

(1) Education: need for education on synthetic biology and RRI – both for the public and for the researchers. More initiatives are needed to create a shared language and to consolidate dissemination. Opportunity for educating people about positive effect of synthetic biology might have on their everyday life.

(2) Communication - Misleading/inadequate communication and information generate fear and undermine trust. The website would offer reliable information on synthetic biology, and related doubts, hopes, concerns.

How does it work?

It is a webpage that would offer simple guidance that serves different needs. The website is structured according to these needs (science, ethics, regulation). The 3 sections or dimensions are developed according to these needs.

- The science dimension focuses on the following main topics: What is synthetic biology? Case studies. List of examples, groups in synthetic biology research. Case studies. E-learning & test your knowledge.
- The Ethics dimension of the webpage focuses on the history of science, code of ethics, ethical issues that might emerge in synthetic biology research and innovation, and include an 'ask the expert' section, plus a FAQ, and sustainability.
- The legislation dimension of the webpage would be an interactive flowchart to understand if a given activity would go under the synthetic biology legislation, EU legislation and guidance documents, and also national rules of conduct etc.

Key requirements and open issues

- the need for personal and financial resources to set up and run the webpage
- the need for maintaining the webpage and quality check of the information

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SELECTION OF THE TOOL FOR PILOTING IN COMPANIES

3.1 Selection criteria

During the second year of SMART-map, a single tool was selected for piloting, from the proposals which emerged during the Industrial Dialogues, one per field (Precision Medicine, Synthetic Biology, 3D Printing in Biomedicine). The toolboxes co-designed by the participants and described above, often contain a higher level of complexity than we can achieve during the timeframe of the pilots. Therefore, the project team analysed both the six toolboxes and the ideas that were put forward during the fast prototyping sessions in order to compile a list of pilotable proposals. The aim was to identify a list of tools that could be piloted *within* a company. Tools in this list had to pass three criteria, lest they were excluded. These criteria are:

1. Does the tool address a technical question (e.g. the development of a standard for data interoperability)? If yes, exclude.
2. Does the tool contain activities performed within a company? If yes, include.
3. Can the tool be piloted within the budget and timeframe of the project? If yes, include.

3.2 Portfolio of Tools – Selecting from the Synthetic Biology suite of six proposed tools.

Description	Criterion: Only addresses a Technical Question? If Yes: exclude	Criterion: Activities that can be performed within a company or relevant to industry application? If Yes: include	Criterion: Can the tool be piloted (or part-piloted as a learning experiment) within the budget and timeframe of the project? If Yes: Include	Criterion: Do existing initiatives meet the same needs?

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1/ An Accreditation Process	N	Y needs both a small group of 'mini' ecosystem actors and pilot companies/organisations to work together	Y It would take time for a small group of 'mini' ecosystem or Task Group to draw up Terms of Reference, simple guidelines, and criteria for evaluation/award for companies to then respond to.	Not for Synthetic biology, Can learn from other Accreditation Processes
2/ A Repository of Learning Case Studies	N	Y	Partially, ie can begin collecting cases for example from the Accreditation process/SMART-Map pilot implementation cases	Partially EG IGEM cases
3/ A Multi-Stakeholder Cross-disciplinary Peer Review Process	N	Y (needs both a small group of ecosystem actors and pilot companies/organisations willing to have their work/RRI case study as contender for	Partially, with a small number of cases, no more than 3 review-cases would be feasible.	Learn from previous experiences for example UK Research Councils and Innovate UK

		review to work together)		
4/ A Synthetic Biology RRI Cross-stakeholder Working Group	N	Y Dependent on the willing participation of businesses on the group	Partially, it would take time to mobilise such a high-level expert group from scratch, agree terms of reference etc.	In UK it exists already in the form of SBLC, though civil society is not well represented on the Council. Various similar initiatives exist at European Level for example Synenergene
5/ A Researcher Incentive System Incorporating an Online Repository of Short (pre-peer reviewed) Articles (named UMBILICOM)	N	Partially More focussed on academic research than industry, but industry may find the Toolbox useful (for example combined with one of the other tools?)	Partially Would take a lot of time and resources to set up before the outputs could be made available and therefore useful for businesses	Probably not a sufficient instrument to address the problem of structural researcher incentivises working contrary to RRI principles
6/ A Multi-disciplinary Education and Public Engagement	N	Partially More focussed on Academia and general publics	Partially Would take a lot of time to set up, gather content	Some existing examples for example Synenergene,

Web-platform bringing together issues on Ethics/Legislation/ Science.		than industry. Industry may express interest as users	articles, before companies could start to use it	Matter for all Individual EU project sites and Synthetic Biology Centres sites in UK

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