

Synthetic Biology Regulators' Meeting. Public statement, 3 October 2008

At the end of September 2008, representatives of the Biotechnology and Biological Sciences Research Council (BBSRC), Engineering and Physical Sciences Research Council (EPSRC), Medical Research Council (MRC) and members of respective panels that advise BBSRC and EPSRC on ethical and other societal issues met to discuss the emerging science of synthetic biology with regulators and members of the UK Government's advisory committees that advise on the regulation of relevant research. Also participating in discussion were scientific researchers, and officials from Government Departments, the Arts and Humanities Research Council, the Economic and Social Research Council, and learned societies[†].

The meeting was convened by BBSRC on behalf of Research Councils UK (RCUK). It is part of an RCUK programme of activities to help scientists, research funders, and policymakers to identify, anticipate and address any societal issues that might arise from synthetic biology, and to enable UK R&D to seize the applications and benefits offered by the science. The meeting was chaired by Professor Alan Thorpe, RCUK champion for Science in Society.

Participants considered a range of hypothetical scenarios of future research developments and applications, as well as some broader generic questions. These included topics such as: risk assessment for minimal cells with no natural equivalent; approaches to entirely 'synthetic organisms'; regulatory responsibilities for different types of application; and UK and international approaches.

The discussion clarified the processes and capacity of the existing EU and UK regulatory frameworks, and the responsibility on applicants/researchers to provide the detailed information required by the regulatory bodies, on which case-by-case assessments of risk are made, and risk management procedures identified. It was recognised that there are inherently uncertainties surrounding some currently hypothetical applications for which there is no precedence or existing evidence base. It was considered essential that the current interactive processes for obtaining detailed information from applicants should be used to obtain data on which decisions could be made, and that the regulators should ensure that such evidence is provided.

Speaking at the end of the meeting, Professor Thorpe said:

"The Research Councils are committed to public engagement around the research that they fund. This meeting has provided valuable insights into how regulatory matters will be addressed, and about how the advisory committees are engaging with potential new developments. Regulation, transparency and ethical and other social issues such as those identified in a recent BBSRC-commissioned study by Balmer and Martin of the University of Nottingham*, are likely to feature significantly in wider public dialogue, along with the potential medical and other technological benefits. The Councils are working together, and with other bodies, on forthcoming public engagement around the potential products and processes of synthetic biology and their social context."

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Summary of main points from discussions at the meeting of 30 September 2008 (to be read in conjunction with earlier statement: above)

Introduction:

- BBSRC convened the meeting on behalf of Research Councils. Its principal aim was to help practising scientists, research funders, policymakers, regulators and advisers to consider the adequacy of the UK's regulatory framework for products that might arise from synthetic biology - including, for example, the design and production of life-like entities for potential application in sectors such as medicine, energy and electronics. (Participants list *).
- The meeting was chaired by Professor Alan Thorpe, who outlined the meeting's objectives, and invited participants to introduce themselves. Dr Brian Johnson presented a short resume of current scientific activities, including, for instance, 'bio-bricks' approaches to the synthesis of molecules and organelles, and the top-down production of minimal cells and bottom-up production of cell-like vesicles. To stimulate discussion, he invited participants to consider several hypothetical scenarios of possible developments in synthetic biology and some more generic questions about how such research might be regulated. Discussion was widened to include comments and questions from the observers. Professor Thorpe led the concluding discussions and invited comments on related topics and public engagement on synthetic biology.

Main points:

- The participants deemed all the issues raised to be reasonable and illustrative of possible scenarios. However, some regarded questions about access to biotechnologies and licensing of cell components such as oligonucleotides as inappropriate for the focus of the meeting, *viz.* current UK procedures and international agreements.
- The overriding message from advisory committee members was that none of the questions and hypothetical scenarios suggested a paradigm shift that would necessitate amending the UK's regulatory framework. However, some issues may require particular attention within the framework (see below).
- In discussion, advisory committee members explained that UK regulatory processes and procedures are evidence-based and conducted on a case-by-case basis that takes account of whether recombinant DNA techniques have been employed in generating new products, as well as the properties of the product. In each case, emphasis is on identifying, characterising and managing risk. The onus is on the applicant to convince regulators and their advisory bodies that the product will not cause harm to human health or the environment in the context of the proposed use. Applicants are responsible for providing data and evidence to support this risk assessment and can obtain guidance, which is updated as and when necessary.

- The meeting considered the adequacy of this process to enable decision making in areas where there is currently no precedent or evidence base. It recognised that there is inevitable uncertainty about the extent to which applicants should be able to supply adequate data, until this is 'tested' by real applications. The onus would remain on applicants to satisfy the advisory committees.
- Regulators and advisory Committee members reported that developments in synthetic biology are being kept under review. Certain products, such as minimal cells, for which there are no natural comparators, may present new challenges in characterising risk. However, the point was made that developing 'novel' organisms would require applicants to generate new and specific information and data, which regulatory bodies would closely interrogate, and would help to inform risk assessment. For example, a risk assessment decision could be made on the lines that there is too much uncertainty to allow research/production outside a certain level of containment.
- Consideration was given to whether totally synthetic organisms could be made in such a way as to fall outside the regulations for GMOs that are concerned with 'altered' organisms; and if so how this should most appropriately be addressed. There was also discussion of whether new risk assessment procedures might be needed for potential food products in which synthetic organisms were introduced into gut flora. Evidence/data to inform the risk assessment of these organisms will need to be compiled during their development in the laboratory, which is likely, in the first instance, to be subject to appropriate containment and rigorous scrutiny.
- In line with current practice, when dealing with applications for deliberate release, advisory committees and regulators would be able not only to request whatever information was needed for assessing hazard and risk, but also to specify the highest levels of 'containment' until sufficient data were provided (see above). Applicants might be required, for instance, to start making products using less potentially hazardous routes. There are precedents for this approach, such as work on strains of 'flu virus.
- There was agreement on the importance of ensuring that unnecessary regulation does not 'strangle at birth' the potential benefits of synthetic biology products; and that regulatory procedures should be realistic and proportionate, not burdensome.
- In discussion, participants recognised the importance of transparency in the UK regulatory framework, including public meetings, and of holistic approaches. It will be important to recognise that requirements will be different for different stages of production, for example for use in initial production and clinical trials. Approaches might benefit from consideration of issues in earlier technologies e.g. xenotransplants. Similarly, some potential clinical uses, e.g. of therapeutic microbes, might have environmental impacts that differ from current 'deliberate release' applications. Cross-membership of some advisory committees, for example those considering respectively 'contained use' and 'deliberate release', is current practice and helps to provide operational consistency. A precautionary approach may be appropriate initially in cross-disciplinary areas, such as protein

'gates' in electronic chips, where there is a regulatory framework but may be relatively little information.

- Research applications go through local ethics committees and research council ethical review processes in addition to their review through regulatory committee reviews. A view was expressed that constitution of these committees should be considered to ensure their capacity to manage this risk. Consideration of Ethical Legal Societal Issues (ELSI) is also an important part of the new synthetic biology networks.
- Reviewers also have a role in alerting funders to potentially dangerous techniques and the possibilities for misuse.
- Committee members considered that virtually all envisaged synthetic biology applications would fall within the GMM contained use regulations/EC Directive 2001/18/EC on the deliberate release of GMOs into the environment. The functional definition, 'ability to replicate' is used, and it was considered that this would be helpful in dealing with potential ambiguities regarding terms such as 'life' or living organisms'. One committee member said that a European Union (EU) working group is challenging the definitions in the EU's GM legislation with new techniques used to develop novel organisms (including synthetic organisms).
- Products produced outside the EU would need to conform to EU Directives and domestic regulations if used in Europe.

Broader issues and next steps:

- Participants recognised that public engagement and dialogue are very important, and that public perceptions of synthetic biology are likely to be based around several issues, not solely the safety considerations which form the basis of the advisory committees' work.
- It is important that regulators and advisers take account of public perceptions and concerns, and do not rely not solely on information from applicants. However, this must be balanced with a free flow of scientific knowledge and evidence.
- Although not a specific focus of this meeting, it was considered that concerns about deliberate misuse of synthetic biology were not qualitatively different from those posed by other biotechnologies.
- As well as the regulatory framework, processes paralleling the 'non-proliferation' approach of other sectors might be appropriate. The role of peer review in self-regulation was also considered, as was the need for discussion around Intellectual Property, which lay outside the remit of this meeting.

Ends.

* **List of participants and affiliations:**

Name	Institution	Representing
Alan Thorpe (Chair)	Chief Executive, NERC	NERC and RC Science in Society
Brian Johnson (Chair for scenarios discussion)	Independent consultant	BBSRC Bioscience for Society Strategy Panel
Louise Ball	DEFRA	ACRE secretariat
Keith Lindsey	Durham University	ACRE member
Chris Pollock	Independent consultant	ACRE member
Michael Paton	Health and Safety Executive	SACGM secretariat
Penny Hirsch	Rothamsted Research	SACGM member
Patrick Harrison	Home Office	Home Office
Paul Brantom	Independent consultant	ACNFP member
Derek Burke	Independent consultant	BBSRC Bioscience for Society Strategy Panel
Martin Taylor	The Royal Society	EPSRC Societal Issues Panel
Onora O'Neill	British Academy	EPSRC Societal Issues Panel
Amanda Collis	BBSRC	BBSRC science
Tony Peatfield	MRC	MRC science
Dek Woolfson	University of Bristol	BBSRC research
Alistair Elfick	University of Edinburgh	EPSRC research
Emma Frow	University of Edinburgh	ESRC research
Jake Gilmore	AHRC	AHRC
Monica Winstanley	BBSRC	BBSRC
Sharon Fortune	BBSRC	BBSRC
Richard Dyer	Bioscience Federation	Bioscience Federation
Androulla Gilliland	DEFRA	ACRE secretariat
Stephen Axford	DIUS	DIUS
Peter Ferris	EPSRC	EPSRC
Joanne Coleman	EPSRC	EPSRC
Melanie Knetsch	ESRC	ESRC
Kenton Thompson	GO-Science, DIUS	GO-Science, DIUS
David Cope	POST	POST
Matthew Harvey	The Royal Society	The Royal Society
Alan Walker	The Royal Academy of Engineering	The Royal Academy of Engineering

ACRE - Advisory Committee on Releases to the Environment

SACGM - Scientific Advisory Committee on Genetically Modified Organisms

ACNFP - Advisory Committee on Novel Foods and Processes