This response was submitted to the consultation held by the Nuffield Council on Bioethics on Emerging biotechnologies between April 2011 and June 2011. The views expressed are solely those of the respondent(s) and not those of the Council.

EMERGING BIOTECHNOLOGIES

Biotechnology builds on tools, resources and knowledge gained from nature and it is perhaps the fact that useful products originate from life, rather than say binary data or an inanimate metal, that contribute to controversy over their use. The domestication of plants and animals during the Neolithic revolution is perhaps the earliest example of biotechnology. Modern agricultural processes and technologies make use of current knowledge and understanding of plants and animals.

An emerging biotechnology uses the very latest scientific discoveries for further research and development, making use of previously unknown properties or processes. At the John Innes Centre our focus is on the environmental and societal benefits that such new discoveries can offer. Moreover, a deep understanding of plants and microbes can help improve our understanding of how other organisms function, including humans.

Emerging biotechnologies at JIC

Emerging biotechnologies relevant to JIC research include: synthetic biology, plant- and microbial-made pharmaceuticals, new therapeutic technologies, nanotechnology and the latest developments in genetic engineering such as zinc finger nucleases. These technologies help researchers build their understanding of basic plant and microbial science to underpin targeted trait improvement and to use their understanding of plants and microbes to benefit agriculture, the environment, human health and well-being.

Public engagement

Such a deep understanding of plants and microbes is required for some of the biotechnologies emerging today that even scientists in slightly different fields need to have them explained by a specialist. It is little wonder then that they can seem fantastically futuristic and unfathomable to the rest of society.

The two terms ‘dread’ and ‘unknown’ have emerged from research as the two main dimensions people use when judging whether something is risky or not[1]. Due to their complexity, many biotechnologies would fall into the “unknown” category. They can be hard to understand or appreciate, putting them at a disadvantage in terms of how they are perceived.

With this in mind, an important role of public engagement is not only to give greater insights into the technologies themselves, but also to proactively

identify consumer concerns and to highlight tangible benefits of biotechnologies for consumers. Environmental and societal benefits might include improved nutrition, new medicines, new ways to deliver medicines and more sustainable crops.

Public engagement should also be employed to ensure transparency in the development of regulatory frameworks for emerging biotechnologies.

Cultural and historical context

The most controversial biotechnology employed at JIC has been genetic engineering. The use of genetic engineering in research does not necessarily lead to the development of a transgenic organism for use in agriculture. Biotechnology has been used to gain a better understanding of gene function and with this knowledge it has already been possible to speed up breeding programmes through marker-assisted breeding, addressing problems in many areas of agricultural production.

The routine use of genetic engineering in microbial research at JIC has produced new antibiotics and other natural products.

Ongoing research opens new possibilities for raising and stabilizing yields, improving resistance to pests, diseases and abiotic stresses such as drought and cold, for enhancing the nutritional content of foods and for further drug discovery and delivery.

Organisations such as the Soil Association, when the prospect of genetic engineering first emerged, may have been able to see the benefits it could confer in terms of reducing the environmental impact of agriculture. Crops can be developed which need less pesticides, less fertiliser and less water and that generate less pollution.

However, the technology became seen as largely the preserve of multinational companies seeking less lofty goals. By their commercial nature the companies have to be focused on generating profit and on protecting intellectual property.

In the early years, the term ‘genetic engineering’ became almost a totemic symbol for fears about the corporate control of agriculture and it is still sometimes hard to divorce the many potential benefits of this particular biotechnology from these wider concerns.

First generation GM crops were seen to benefit commercial farmers, seed producers and agrochemical companies while consumers would take the risk of consuming foods that were perceived to carry some safety risk.

At JIC we share the sustainability goals of the environmental movement and still hope genetic engineering can be adopted by it, for example becoming a useful tool in organic agriculture by producing more reliable yields with less inputs.

Plant-made pharmaceuticals (PMPs)

Micro-organisms have been used for decades as living factories, for example antibiotics are derived from the soil bacterium *Streptomyces*. The use of plants to produce pharmaceutical and industrial proteins is likely to be the next major commercial development in biotechnology[2].

Plants offer a number of benefits over conventional mammalian or bacterial cell culture systems including lower start-up costs, increased flexibility over scale and storage and the potential to produce high volumes at relatively low cost. Crops such as tobacco, maize, potato, rice and safflower have been genetically altered to yield therapeutic proteins that are then processed, regulated and could be sold as pharmaceuticals. A number of products are now in late phase clinical trials.

Another approach to producing biopharmaceuticals in plants is to use a 'transient expression system', where a plant is used purely as a host and where its genome is not altered. This technology could be employed where a vaccine is needed quickly, as with a rapidly spreading epidemic like bird flu.

The use of PMPs challenges two very different established regulatory frameworks, one concerning GM plants and the other covering the development of biotechnology-derived drugs. It is necessary to determine how the differences between PMP crops and GM food/feed crops will translate into risk assessment, confinement and monitoring requirements.

A general challenge facing emerging regulatory frameworks in the USA, Canada and the EU is clarification of the overlaps between different regulatory bodies, in particular between the USDA and FDA in the USA, between the CFIA and Health Canada in Canada and between EFSA and EMEA in the EU. A roadmap for applicants clearly setting out the remits of these bodies and their responsibilities would be helpful[3].

On a more global level, it is important to highlight a concern that countries with weaker biosafety infrastructures could pose a risk to this emerging technology if containment is breached. This is of particular importance if developers conduct field trials and production in these countries. Strategies to avoid such problems will therefore have to be developed at the international level, for example through the Cartagena Protocol on Biosafety, the OECD and the Codex Alimentarius.

A proactive stance from regulators is needed. At the same time a strong pipeline of PMP products would facilitate regulatory development. Research and innovation policy might need to explore possible ways to support 'ice-breaker' products.

It is important that regulatory frameworks are developed in an open and transparent manner, involving a broad range of stakeholders. This is

particularly the case in Europe and might help to diminish the distrust that has clouded discussions about first-generation GM crops.

A JIC example of “red biotechnology”

The benefits of “red biotechnology” are clear. This term covers the application of biotechnology in medicine to produce human therapeutics to prevent or cure disease. An example under research by JIC scientists is worth highlighting as the terms nanotechnology and synthetic biology can also be applied to it.

JIC scientists have successfully engineered virus particles to be devoid of their RNA to produce nano-sized vectors for drugs that can be delivered to particular tissues. Targeting particular tissues has the potential to reduce side effects by leaving healthy cells intact. Scientists are working with the cowpea mosaic virus (CPMV) as it is small enough to be able to move in the bloodstream, is not toxic and is able to enter cells. It can also be produced in large quantities by infecting plants.

Current research is focusing on delivering the anticancer drugs to cancerous cells. Scientists will investigate the best way of loading the particles with the anti-cancer drug and their ability to deliver the drug to cancer cells. The ultimate aim will be the development of a generic targeted drug delivery system. In collaboration with an industrial partner the scientists have filed a patent on the use of plant virus particles for delivery of drugs and other biological reagents.

Regulation

Current regulations for GM technology are robust and should remain so to maintain public confidence. One useful addition to the regulatory system would be more formal consideration of benefits. As stated in a recent paper:

“The Cartagena Protocol on Biosafety has resulted in the precautionary principle being embedded in much current and new legislation. The inclusion of a benefit component would cause no inherent conflict with the CPB, but requires a change in mindset amongst the regulators.”[4]

From open source model to patent thickets – review needed

‘Open source biotechnology’ has been the subject of debate and has been recommended as one way to avoid ‘patent thickets’ at the other end of the spectrum.

In some cases, patents covering the basic tools for genetically engineering plants can constrain the application of biotechnology to crop improvement.

JIC would support a review of the current regulatory framework to assess whether it is fit for purpose and to help establish the right balance between protecting commercial interests and expediting progress and collaboration on

research for public good. This could come under the remit of a parliamentary scientific inquiry.

JIC scientists have initiated the development of a pre-breeding programme, which was awarded funding in February 2011. This provides a model of how the results of biotechnology research can benefit government and commercial goals alike.

All the information generated in the programme will be stored in a central database, and seed stored centrally in the UK, both being freely available to both academics and breeders. The new germplasm generated in this project will be exploited by breeders for crossing with their elite lines to develop new varieties for use by farmers. It is the first pre-breeding programme of its kind in the UK in over 20 years.[5]

Summary of recommendations

- Continued public engagement to proactively identify consumer concerns, to highlight benefits of biotechnologies and to provide insights into how they work and how they might be applied in practice
- Roadmap of current regulatory frameworks for applicants
- International standardisation of biosafety infrastructures
- Proactive, transparent stance from regulators
- Ice-breaker products
- Inclusion of benefit component to risk analysis for genetic engineering
- Review of route to commercialisation to reduce ‘patent thickets’ and to ensure regulations are fit for purpose

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