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The Case for Reforming the EU Regulatory System for GMOs.

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Background. The first iteration of the EU Directive that controls the deliberate release of GMOs into the environment was adopted in 1990, and the first commercial planting of GM crops occurred in 1996 in the USA (or 1998 in the EU). Since then, the global cultivated area has risen to exceed 170 M ha and the majority of global production of soya and cotton is via GM varieties [1]. Over this period, cultivation within the EU has been restricted to ca 0.1M ha. Although the main barrier to release of GM food crops for cultivation in the EU lies at the political level, the UK Advisory Committee on Releases to the Environment (ACRE) has recently raised concerns both about the regulatory approach adopted by the EU and the implementation of the current ~~current processes for carrying out~~ Environmental Risk assessment~~s~~ (ERA) process ~~and about their future fitness for purpose~~ (ACRE http://www.*wp1-3). This article summarises these concerns and suggests a way forward.

Addressing current challenges. These include the lack of precision with which the concept of adverse effects (harm) is used within ERA and the challenges of developing a proportionate approach to unanticipated effects

Adverse Effects. There is no consensus within the EU as to what constitutes an adverse environmental effect~~. This has led to increasing data requirements and to inappropriate recommendations for risk management options. The~~, and this leads to difficulties a~~s~~re illustrated by GM herbicide tolerant crops. These systems allow farmers to practice efficient weed control to enhance crop productivity, potentially at the expense of biodiversity that depends upon weeds at the base of the food chain. This negative impact could be compensated for by

Comment [RSH1]: Actually the example we give, with GMHT crops, is about absence of defined risk management because harm has not been defined. This more general statement is more relevant to GMIR crops.

setting aside field margins or other areas for farmland biodiversity, but in the absence of clear guidelines on what does or does not constitute harm, appropriate compensatory measures cannot be usefully defined. Defining harm would also facilitate a more structured approach to ERA [2], thus reducing the inclusion of extraneous information and improving the value of the ERA in decision-making.

~~Monitoring and d~~Dealing with the unexpected. In addition to assessing the risks associated with the intended changes made to a GM crop, ERA must also address the possibility that any identified unintended changes could cause harm. In the absence of a plausible link between a characteristic of a GM crop (and its use) and such harm, there is the potential for open-ended evidence-gathering that does not add value to the risk assessment. It is not ~~possible~~ practical to test for ~~ERA to identify~~ unintended effects in advance by testing every characteristic of a GM crop and its use under every conceivable scenario. It is important therefore, that the EU adopts a proportionate approach that makes optimal use of existing evidence. There is a significant 'weight of evidence' available from the cultivation of GM crops outside of the EU as well as from existing information requirements. Where this evidence indicates changes to a GM crop, ~~or its use ,are identified and potentially~~ that can be linked to adverse effects, the ERA should follow a structured ~~and proportionate~~ process to characterise the risk to the environment. Where identified but unintended changes cannot be plausibly linked to adverse effects, further data should not be required.

Comment [RSH2]: I think its important in this section to distinguish between identified unintended changes and 'unknown unknowns'

Comment [RSH3]: I think this conclusion is required for clarity

Finally, some countries, including those in the EU, require post-market monitoring to detect any unanticipated adverse effects from the commercial growing of GM crops. In this context, ~~Where~~In terms of unintended effects, ~~cannot be defined nor linked to a GMO,~~ ACRE supports the use of effective questionnaires -to detect significant changes aimed at users of the product but is doubtful of the value of large-scale environmental monitoring to attribute causality to the cultivation of GM crops (http://www.defra.gov.uk/acre/files/pmem-final-report.pdf; ACRE http://* WP2).

Emerging Challenges For Process-based Regulation. The current EU Directive lists techniques that can lead to the generation of GMOs and those which are deemed not to. However, these lists are not exhaustive, which leads to confusion ~~in interpretation of the regulations~~ as to whether the legislation applies to novel organisms developed by techniques that were not envisaged when the legislation was adopted in 1990. This approach to regulating organisms based on how they were produced (so-called "process-based") ~~was adopted in 1990 and at this time, many of the techniques being used and developed today were not envisaged. Consequently, it is not clear whether the organisms produced by them are captured by the GMO legislation. This~~ results in regulatory uncertainty – a major block to innovation and to effective ERA. Adoption of a process-based regulatory system ~~dditionally, basing a regulatory system on how organisms are produced has resulted in~~ also results in organisms with the same phenotype being dealt with differently (e.g. ~~phenotypically identical~~ herbicide-tolerant plants produced by transgenesis or traditional mutagenesis). This disparity may ~~increase~~ become more evident depending on whether regulators consider organisms produced by a suite of

Comment [RSH4]: And |I think this paragraph is needed.

Comment [RSH5]: Comment from Louise about this section:

' ACRE has already been criticised for not understanding how the legislation works so it's important to get this right.

The original draft talks about a process-based approach then, at the end talks about whether the product occurs naturally without connecting the 2.. I've moved the text from the end to the front to make it clear that the definition has 2 parts and there are problems with both parts i.e. process –based bit only categorically deals with transgenics and the genotype element is nonsensical given what we now know about genomes.

I amended the text so that it wasn't so confusing and added the 'genotype' element in the last section.'

Comment [RSH6]: Comment from Louise: 'Why? Once captured we could carry out an effective ERA'.

new techniques as GMOs. ~~Regulation of process-based approaches is both open to interpretation and difficult to future-proof. P~~For example, plants developed using chemical or radiation mutagenesis are exempt from existing EU regulation. However, the same trait in the same organism caused by the same sequence alteration but using a different mutagenic process (such as zinc finger nucleases, TALENS or oligonucleotides) may be covered, depending on the interpretation of the EU Commission and member-state regulators. Furthermore, ~~T~~their views are likely to differ as reflected in ~~It is likely that the conclusions will reflect those set out in~~ the EU Commission's working group report on New Technologies [3]. Other emerging technologies involve~~clude~~ GM techniques ~~that are captured by the definition of a GMO during the~~ as part of the breeding process but ~~that~~ result in ~~an~~ organisms that do~~es~~ not contain any inserted or recombinant DNA (e.g. reverse breeding). As the process requires the use of a GM intermediate, some may argue that the resultant organism is captured by the ~~directive~~ GMO legislation whereas others may ~~consider~~not. ~~that it is not because the product could have occurred naturally.~~

Comment [m7]: This concept hasn't been introduced.

We conclude that a process-based approach to regulation is difficult to interpret and to future-proof and this will become more apparent as the technology and its application advances.~~problematic now, and likely to become more so in the future~~. ~~This is also consistent with current views of genome organisation that do not align with the EU definition of a GMO ("***an organism…in which the genetic material has been altered in a way that does not occur naturally by mating and/or natural recombination.***") When this was written, genomes were considered to be relatively uniform and stable and the definition was intended to~~

~~capture the range of artificially induced alterations to an organism's genetic material. Now that the extent of natural genetic and epigenetic variation is more fully understood, identifying alterations that do not occur naturally is much more challenging. Within an individual and between individuals of the same species, the genetic material can exist in naturally altered forms whilst the phenotype remains unchanged, through the effects of genetic redundancy between multigene family members [4,5] Equally, a single nucleotide change can result in a significant phenotype change (ACRE http://www.wp3*).~~

Comment [m8]: Confuses the story line

Options for Change. A major reason for regulating organisms based on how they were developed is to address the concern that the technologies may cause unintended alterations to the organisms' genetic material that could not have occurred naturally or through conventional breeding. Since the GMO legislation was adopted in 1990 we have learned a great deal from genomic studies. We now understand that this notion that genomes are relatively uniform and stable entities is incorrect. Within an individual and between individuals of the same species, the genetic material can exist in naturally altered forms whilst the phenotype remains unchanged, through the effects of genetic redundancy between multigene family members [4,5] Equally, a single nucleotide change can result in a significant phenotype change (ACRE http://www.wp3*). We have also gained significant evidence from the widespread use of GMOs. From this we conclude that~~We propose that~~ there is little scientific justification for a regulatory system that is triggered by the process by which new organisms are developed (i.e. recombinant DNA technology) rather than by their novelty or potential for harm (i.e. their phenotype).

Additionally, we suggest that a regulatory system that takes account of potential benefits and includes potential compensatory measures (thus encouraging a more explicit cost-benefit approach) would better align with other regulatory frameworks and result in greater potential benefits for the environment and human health than the existing system. This approach would also improve the efficiency of the process to ensure appropriate ~~risk~~ assessment without stifling innovation.~~technological~~ . It ~~and~~ would obviate the pressure to develop ~~need for~~ technological approaches ~~that are developed purely to deliver material~~ that ~~lie~~s outside current regulations (ACRE http://www.wp2*). Shifting to a phenotype-based system would ~~also~~ permit resolution of the wider issues discussed above and promote proportionate and effective ~~ERA~~ assessments backed by appropriate post-market ~~surveillance~~ monitoring (ACRE http://www.wp3*). Further details of such a system are given in (ACRE http://www.wp1*)

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