Rationalizing governance of genetically modified products in developing countries

To the Editor: Ever-more powerful genetic technologies, such as genome-editing endonucleases and marker-assisted breeding, continue to facilitate the development of genetically modified (GM) crops engineered with complex traits, such as, nutritional quality, climatic resilience and stacked disease-tolerance mechanisms. But in many developing countries, the uptake of these GM products is being jeopardized by the sluggish pace and inadequacy of regulatory oversight. This is a serious concern because developing countries stand to benefit most from the adoption of new varieties of staple GM crops, such as vitamin-enhanced rice and bananas or disease-resistant maize and cassava. Despite the availability of the formal risk analysis framework—which provides all the critical components of risk assessment, risk management and risk communication important for structured regulatory decision making on such products—we believe that policymakers do not always understand the underlying factors behind a risk analysis well enough to facilitate implementation of robust and realistic biosafety practices. Here, we argue for a rethink of the way in which capacity development and training is implemented in developing countries for biosafety programs assessing bioengineered products in developing countries.

As a group of international experts in biotechnology and biosafety, we have engaged in dialogs sponsored by bodies such as the United Nations' (UN) Food and Agriculture Organization (Rome)[1], and have recently drawn up a series of observations and guidelines in an effort to promote constructive debate aimed at resolving this important impasse that is hindering the uptake of improved crops in many parts of the world[2]. We assert that improved crop-breeding methods are needed to feed the growing world population and to address many of the socioeconomic, environmental and other challenges facing developing countries[3]. In light of recorded benefits of GM crops, and the exciting prospects for recently emerging technologies, it is clear that they could play major roles in advancing some of the UN's key sustainable development goals[4], especially goals 2 (end hunger, achieve food security, improve nutrition and promote sustainable agriculture) and 13 (take urgent action to combat climate change and its impact by the year 2030).

In many parts of the world, the perceived risks of GM organisms (GMOs), however slight and poorly quantified, have tended to have a greater impact on framing the structure of their regulatory systems than the overwhelming evidence of these products' substantial benefits. This situation has been exacerbated by public advocacy groups promoting often unbalanced or uncorroborated stories to stigmatize the use of GMOs in agriculture. As a result, the regulatory governance of GMOs continues to be a major hurdle to their development and acceptance, especially in developing countries.

Current risk analysis and regulatory systems in many developed countries—in many cases supported by international organizations and agencies—have tended to undermine the rational application of GM crops in developing countries. At the heart of the problem is a lack of agreement as to whether and how both scientific and non-scientific evidence can and should be integrated into regulatory decision-making for GM crops. The risk analysis framework embodied in the International Plant Protection Convention, the Codex Alimentarius (Codex) and the World Trade Organization (WTO; Geneva) is based solidly on science. In contrast, the precautionary principle embedded in the UN Cartagena Protocol on Biosafety balances scientific evidence with economic, social and environmental norms. The application of the precautionary principle to GM regulation has been at the heart of the controversy between the United States and European Union (EU; Brussels) for almost two decades now, and this dispute has now spread to affect many developing countries as well. The main problem is that decisions in Europe are often made on political grounds, rather than on a scientific basis. These decisions then influence the way GM policy is formulated and implemented by national governments in many developing countries[5]. Indeed, the level of concern in much of South America is sufficiently strong that last August, the agriculture ministers from five major crop-producing countries signed a joint declaration that urged the EU (as well as China) to stop delaying GMO import authorizations[6].

In countries such as Brazil and India, public research and development of locally important GM crops is impeded by an overly stringent application of the precautionary principle. In India, for example, GM mustard, eggplant and chickpea have been entangled in one legal challenge after another and have faced very onerous regulatory measures over the past decade. Rather than creating greater confidence among consumers and farmers, this has contributed to widespread mistrust that continues to metastasize. One result is that risk-assessment decisions for new GM products in India have been repeatedly delayed. This pattern is repeated in many other developing countries that struggle to develop and deploy local GM products (**Box 1**).

The inclusion of socioeconomic considerations in the Cartagena Protocol conflicts with the science-based approach enforced by the WTO. In particular, the *ad hoc* approach to taking into account socioeconomics, that is neither structured nor evidence-based, has contributed to a 'go-slow approach' in developing functional biosafety policy and limiting crop development in many developing countries for the benefit of the population especially countries in Africa. There has been limited progress in defining how socioeconomics should be used in the Cartagena Protocol. Lack of clear definitions and interpretations of socioeconomic considerations and difficulties in measuring unpredictable factors in *ex ante* studies continue to

Box 1 Mauritius as a case study

Mauritius acceded to the Cartagena Protocol in 2002 and in response to its obligations, a GMO Act was passed in 2004. This act, however, is widely recognized within the country as being unfit for purpose and has never been fully implemented. As a result, local researchers developing improved GM sugarcane varieties have been forced to terminate their work owing to the lack of a regulatory framework.

The country received support from UNEP-GEF from 2007 to 2011 to implement a "workable and transparent" national biosafety framework[14]. The UNEP-GEF support focused on the development of regulations and technical guidelines, training, the establishment of facilities for GMO detection, and public awareness. However, the basic problems associated with the GMO Act were never addressed. These include the following:

- The lack of clear policy objectives toward the development of biotech in the country.
- The lack of any provision for an office to administer the Act.
- The fact that all derivatives or products of GMOs are legislated the same as living organisms, despite the fact that processed products can often not be identified as containing GM material.
- The fact that all GMOs and their derivatives or products are required to be comprehensively labeled (including specifying the traits and characteristics of the product), yet there is no threshold specified for adventitious presence.
- The fact that no GMO permit can be issued, unless the particulars of the permit holder have been specified in regulations.
- The unclear definition of a 'user,' which includes consumers, because all users are required to hold a GMO permit.
- The strongly political make-up of the National Biosafety Committee, which is supposed to examine all applications for GMO permits.
- A requirement for the National Biosafety Committee to take account of social and economic effects, without any consideration as to how this might be done.
- A strong focus on contraventions, prohibition orders, suspension or revocation of permits, and stop orders, all of which generate a negative view of the technology.

Only recently has discussion started about the need to revise the GMO Act, which would require a new legislative process. This is driven in part by the desire of the Minister of Agro-Industry and Food Security to establish a new Biotechnology Institute to take biotech forward in the country and by the desire of local scientists to be able to use all technologies at their disposal. On the negative side, there are substantial consumer concerns that GM food is unknowingly being imported, yet the GMO detection laboratory is still not functioning and the labeling requirements in the GMO Act are, in any case, impractical.

The net result is that 15 years after acceding to the Cartagena Protocol, Mauritius still has no functional GMO legislation. The country is highly food insecure, relying on imports for around 75% of its food requirements, while researchers who see the potential for new agricultural biotechnologies to stimulate its agricultural productivity are becoming increasingly frustrated with the lack of progress.

bring into question the relevance of socioeconomics in GMO regulation.

One possible way forward would be to include assessment of socioeconomic considerations only when there is clear evidence of the socioeconomic changes that would result from the introduction of the GMO. This, of course, requires developing countries to have the capacity to identify and properly assess relevant socioeconomic issues. The issue of labeling illustrates the challenge. There is considerable disagreement between the Cartagena Protocol, Codex and WTO on the need for labeling to differentiate the export and import trade and to signal provenance to the consumer. Labeling in developing countries is complicated by high illiteracy rates, challenges of regulating roadside foods and limited access to data[7]. China offers an example where unclear labeling (partially enforced labeling) requirements for GMOs have generated heated debate that became so confusing that it largely excluded key stakeholders, such as farmers and consumer groups, from the decision-making process. Although this issue remains highly contentious and insufficiently addressed at the national level in most developing countries, extensive trade patterns make consensus at the international level both necessary but difficult. The knock-on effect is seen among developing countries (including Kenya, Egypt and Bangladesh), which have struggled to set effective rules for GMO labeling, at times practically blocking access to important supplies of foodstuffs[8].

One preferred strategy is to build regulatory and scientific capacity. Limited technical capacity for food safety assessment remains a huge problem in Africa. This is a problem as many African countries are conducting laboratory or confined field trials of GM food crops, often without the required expertise to perform food safety risk assessments. But efforts so far have been mixed. The UN Environment Programme–Global Environment Facility (UNEP-GEF) capacity building program under the Cartagena Protocol, for example, has encouraged a strict interpretation of the precautionary approach in many African countries, leading to limited adoption of GMOs. This is compounded by one-off workshop training initiatives by international organizations that fail to deliver the kind of capacity required to develop functional biosafety systems. Our opinion is that short-term training will not have much impact where there is limited scientific capacity and insufficient knowledge in risk analysis. Programs, such as the UNEP-GEF capacity-building program, need to take into consideration the reality on the ground before embarking on further training[9]. A rethink of capacity development and investment in training could pave the way for better implementation of biosafety programs. It is often overlooked that much of the required capacity and skills can already be found in existing environmental management agencies, food safety agencies and agricultural organizations, such as phytosanitary inspection services and agricultural research institutes. This would suggest that tailored, hands-on capacity development initiatives are needed to hone existing skills.

Taken together, poor (or no) decision making under conditions of inherent uncertainty at the national level, lack of agreement at the international level and weak regulatory capacity continue to undermine effective deployment of GMOs. Although this is a problem for the effective use of GMOs, the greater concern is that this regulatory challenge could extend to the new genome-editing techniques. It is entirely possible that genome-editing approaches may fall under the same regulatory constraints as GMOs, despite obvious distinctions between them, not the least of which is the impossibility of distinguishing between the effects of some types of genome editing and naturally occurring DNA polymorphisms. Indeed, there is a lively debate as to whether or not genome-editing techniques should be classified within the scope of GMO regulation. Some

non-governmental organizations are already asserting that genome-editing techniques are essentially genetic modification, whereas other agencies take the opposing view[10].

Recent reports by the US National Academies of Sciences, Engineering, and Medicine (Washington, DC) and the UK House of Commons Science and Technology Committee (London) both present evidence to support the position that GMO risks are no different from traditional plant breeding[11,12]. But so far, this evidence is not influencing the debate. Both reports conclude that the EU regulatory regime that supports the precautionary principle is only used as a political tool to discourage the adoption of GMOs. Lack of genuine interest among EU policymakers in promoting agricultural biotech for food security in developing countries reinforces their opposition against GMOs[13].

One political development that may shift the debate about GMOs is the UK Brexit vote in 2016. Given the UK's historical role in developing and supporting new plant technologies, the movement of the British market outside of the EU's regulatory framework could have far-reaching consequences. It could interject a more rational discussion about the future regulation of GMOs in Europe, and particularly the status of new crop varieties that result from genome-editing technologies.

We posit that the continued implementation of the Cartagena Protocol is more likely to lead to barriers than solutions. Risk-assessment models in developing countries would be better focused on local agricultural and environmental practices, rather than being based on a Western model. This could conceivably encourage regional harmonization of risk assessment and put fewer burdens on individual countries. Ultimately, this may facilitate less expensive and, quick and safe evaluation of local GM crops.

Ultimately, we call for a more structured and evidence-based approach to the regulation of GMOs that, while taking into account the values or traditions that shape the interests, perceptions and concerns of different stakeholders, is not held hostage to political expediency. A rigorous and transparent methodology that captures the concerns of both pro- and anti-GM groups and considers both science-based and non-science based evidence (as opposed to opinions) could be a way forward. This could help chart a more useful direction for assessment and regulation of the new genome-editing techniques so that we avoid the disjointed and suboptimal deployment of GMOs.

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1. Food and Agriculture Organization of the United Nations. International Symposium on the role of agricultural biotechnologies in sustainable food systems and nutrition (Rome) http://www.fao.org/3/a-bc547e.pdf (2016).
2. Adenle, A.A. *et al.* (eds.) *Genetically Modified Organisms in Developing Countries. Risk Analysis and Governance* (Cambridge University Press, 2017).
3. Food and Agriculture Organization of the United Nations. *FAO Statistical Yearbook* Part 4, 312-352 (FAO, Rome 2012). http://www.fao.org/docrep/015/i2490e/i2490e04d.pdf (2012).
4. United Nations. Sustainable Development Goals. http://www.un.org/sustainabledevelopment/sustainable-development-goals/ (2016).
5. Andrzejczak, K. in *Economic Integrations Competition and Cooperation* (eds. Kandzija, V. & Kumar A.) 777–796 (CEMAFI International, 2016).
6. ISAAA. *Crop Biotech Update* http://www.isaaa.org/kc/cropbiotechupdate/article/default.asp?ID=15748 (2017).
7. Adenle, A.A. *et al. Food Policy* **43**, 159–166 (2013).
8. Ramessar, K., Capell, T., Twyman, R.M., Quemada, H. & Christou, P. *Nat. Biotechnol.* **26**, 975–978 (2008).
9. Johnston, S. *et al. Internationally Funded Training in Biotechnology and Biosafety: Is it Bridging the Biotech Divide?* (Yokohama: United Nations University-Institute of Advanced Studies, 2008).
10. Abbott, A. *Nature* **528**, 319–320 (2015).
11. National Academies of Sciences, Engineering, and Medicine. *Genetically Engineered Crops: Experiences and Prospects* (Washington, DC: The National Academies Press, 2016).
12. United Kingdom House of Commons, Science and Technology Committee. *Advanced Genetic Techniques for Crop Improvement: Regulation, Risk and Precaution.* Fifth Report of Session 2014–15 http://www.publications.parliament.uk/pa/cm201415/cmselect/cmsctech/328/328.pdf (2015).
13. Atanassov, A. *et al. Nat. Biotechnol.* **28**, 551–552 (2010).
14. Brandolini, G.V. *Terminal Evaluation Report: Support for Implementation of the National Biosafety Framework for Mauritius* (GFL-2328–2716–4952). Prepared for the United Nations Environment Programme (UNEP), Nairobi, Kenya (UNEP, Paris, 2014).

An alternative proposal to the destruction of abandoned human embryos

To the Editor: Since the world's first *in vitro* fertilization (IVF) birth in 1978, over 6 million healthy offspring have been born through IVF—an accomplishment that was celebrated with the award of a Nobel Prize in 2010 (ref. 1). Despite IVF's widespread adoption, the use of human embryos in biomedical research remains controversial, and investigators working in this area face many challenges obtaining samples. Although special protections and considerations are rightly afforded to human embryos by clinical and scientific societies in reproductive medicine, here we identify guidelines that may limit embryo availability and we propose changes to address embryo donation for research purposes. Specifically, we suggest that the prohibition against using 'abandoned' embryos for research purposes warrants reevaluation.

The American Society for Reproductive Medicine (ASRM; Birmingham, AL), its sister organization, the Society for Assisted Reproductive Technology (SART)[2–4] and the American College of Obstetricians and Gynecologists (ACOG; Washington, DC)[5] have all issued statements addressing the availability of cryopreserved embryos for human research, disposition of abandoned embryos, embryo donation for human embryonic stem cell research and embryo research in general.

When IVF cycles produce more embryos than are transferred, professional guidelines instruct patients to be given full disposition over excessive embryos and mandate documentation of patient choice in a very detailed informed consent document. The options offered by virtually all US IVF centers are identical and include (i) cryopreservation