GM mosquitoes in Burkina Faso:

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A briefing for the Parties to the Cartagena Protocol on Biosafety

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GeneWatch UK

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Third World Network

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Genetically modified (GM) *Anopheles gambiae* mosquitoes were exported from Perugia in Italy to Burkina Faso in November 2016. The GM mosquitoes were developed at Imperial College, London (Windbichler et. al., 2008; Klein et al., 2012), and were sent, via Italy, to "contained use" facilities in Bobo-Dioulasso, for use in experiments by a research consortium called Target Malaria.[1] Target Malaria states that the exporters received a permit from the National Biosafety Agency (under the Ministry of Higher Education, Scientific Research and Innovation, MESRSI) to import the GM "sterile male" strain of mosquitoes to an insectary in Burkina Faso. At the insectary, GM female mosquitoes from this "sterile male" strain have been mated with male *Anopheles coluzzii* mosquitoes born to pregnant females originally sourced from a village in the Kou valley (Hayes, et al., 2018).

The Institut de Recherche en Sciences de la Santé (IRSS) in Burkina Faso is a member of Target Malaria and runs the insectary. In 2018, it made an application to release between 2,000 and 10,000 of these GM *An. coluzzii* mosquitoes into the environment in 2018; in the village of Bana, west of Bobo-Dioulasso, in the Kou valley (Swetlitz, 2017). This village is one of three villages – Bana, Souroukoudingan and Pala – that Target Malaria and the IRSS have studied since 2012, and Souroukoudingan has also been identified as a possible alternative site for the field release. The application to make open releases of GM mosquitoes was reportedly approved by the National Biosafety Agency (Agence Nationale de Biosécurité, ANB) in Burkina Faso in September 2018, and, as a result, the first open releases of GM mosquitoes in Africa are planned to be made over the coming year (O'Mahony, 2018; Target Malaria, n.d.).

This briefing updates earlier work by the African Centre for Biodiversity, Third World Network and GeneWatch UK (ACB, 2018). It covers concerns regarding the lack of informed consent to the proposed experiments and evidence of poor compliance with regulatory requirements, including the Cartagena Protocol on Biosafety.

1. Lack of fully informed consent

The World Medical Association's Declaration of Helsinki outlines the internationally agreed ethical principles for medical research involving human subjects (World Medical Association, 2018). It includes the requirement that "Medical research involving human subjects may only be conducted if the importance of the objective outweighs the risks and burdens to the research subjects".

The proposal to release up to 10,000 GM mosquitoes over the coming year is a training exercise for the researchers; Target Malaria says that the mosquitoes will not be used for malaria control. This is because repeated large releases would be needed to seek to suppress the wild population of mosquitoes, which, even if successful, would be prohibitively expensive (Target Malaria, 2015). Therefore, the proposed releases in 2018 are not intended or expected to provide any direct benefit to the local population in terms of malaria control. This is not an early stage trial of the GM mosquitoes intended to be tested later for their impact on malaria, but a proposed release of an entirely different GM mosquito. Thus, there is no justification for making the releases. Conducting experiments with no potential benefit may be regarded as a waste of time and money and is unethical when the organisation proposing the releases accepts that there are risks, such as the incidental release of some biting female GM mosquitoes during the experiments (discussed further below).

The Declaration of Helsinki (World Medical Association, 2018) also states that:

> *26. In medical research involving human subjects capable of giving informed consent, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks*

1. http://targetmalaria.org/

of the study and the discomfort it may entail, post-study provisions and any other relevant aspects of the study...

Thus, people must be fully informed about the potential risks of the study for their consent to meet ethical requirements. This cannot be the case until a comprehensive risk assessment has been published to the necessary standards and opened for public consultation. This is discussed further below.

Concern about the process of informed consent is exacerbated by evidence that Target Malaria is paying compensation of 400 CFA francs (approximately 70 US cents) per hour of capture for people to collect biting female mosquitoes from their own bodies. Volunteers are required to sit for six hours in a room at night, with the lower part of their leg exposed up to the knee, so that the mosquitos land on it, and to collect these mosquitoes with a suction tube (Target Malaria Burkina Faso & IRSS, n.d.). The use of a financial incentive to individuals to expose themselves to biting female mosquitoes, and potentially to malaria, is ethically extremely questionable.

2. Poor compliance with regulatory requirements, including the Cartagena Protocol

2.1 Lack of transparency

Public information that the proposed open release of GM mosquitoes has been approved has come entirely from Target Malaria. The website of the regulator, the ANB, states only that an authorisation has been granted for laboratory experiments on genetically modified mosquitoes.[2] No information about the application for release is publically available. The reported approval for open release is also not currently available, although previous approvals for experimental releases of GM sorghum and cowpeas are provided on the ANB website.[3] In addition, no information has been placed on the Biosafety Clearing House, although again the previous approvals for experimental releases of GM sorghum and cowpeas are available there.[4] The Cartagena Protocol, to which Burkina Faso is a Party, requires that a Party's final decision regarding the importation or release of living modified organisms is made available to the Biosafety Clearing House (paragraph 3(d) of Article 20).

There is no published environmental risk assessment (ERA), other than that published by Target Malaria itself (discussed further below) and there has been no public consultation, apart from "public engagement" activities conducted by Target Malaria (the organisation proposing the releases). This is despite the fact that the Cartagena Protocol requires Parties to make available summaries of the risk assessments generated by its regulatory process to the Biosafety Clearing House (paragraph 3(c) of Article 20), as well as to consult the pubic in the decision-making process (paragraph 2 of Article 23).

It also remains unclear when the proposed open release of GM mosquitoes would take place, as there appear to be ongoing problems with breeding sufficient numbers of GM mosquitoes in the laboratory. Since the male GM mosquitoes are sterile, the GM females must be mated with wild males in the laboratory to produce each new generation. According to an "ecological risk assessment" for the proposed open release, published by Target Malaria (Hayes, et al., 2018:14), the organisation initially planned to conduct the controlled field release in July 2018. By this time, the wild type colony was expected to have been raised under contained laboratory conditions for 62 generations and backcrossed into the GM line 29 times. The field release, however, is contingent on the insectary generating a sufficiently large population of male GM

2. http://www.anb.gov.bf/ogm-autorise.shtml
3. http://www.anb.gov.bf/decision/ad.shtml
4. https://bch.cbd.int/database/results?searchid=719850

mosquitoes, as well as the receipt of regulatory approval. Problems with breeding the GM male mosquitoes in sufficient numbers may, therefore, have occurred and future problems could lead to further delays.

2.2 Lack of a transboundary notification

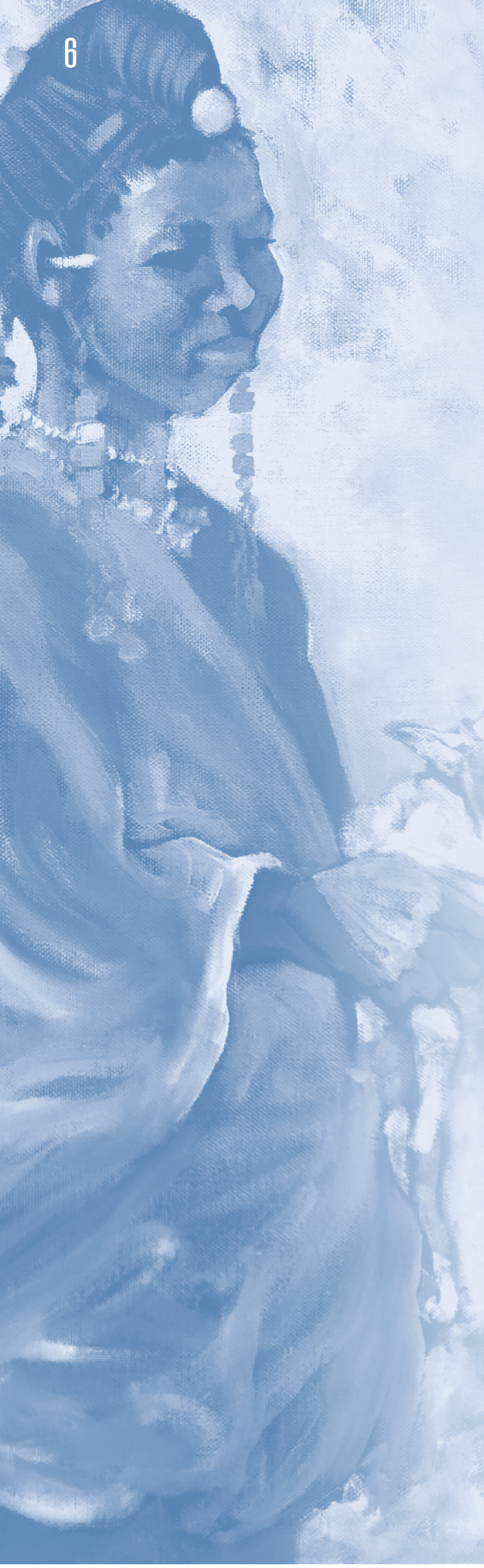
Under European Union (EU) law, the exporter should provide prior notification, including a publicly available environmental risk assessment that meets European standards before exporting GM insect eggs for open release to foreign countries. This legal requirement arises because GM insect eggs are live genetically modified organisms (living modified organisms or LMOs) covered by the Cartagena Protocol on Biosafety (CPB) to the Convention on Biological Diversity, to which the UK, Italy and Burkina Faso are all Parties. The relevant legal requirements for export are implemented in the EU through the European Regulation (EC) 1946/2003 on transboundary movement of genetically modified organisms. This Regulation requires that the ERA provided by the exporter meets the EU standards on risk assessment contained in EU Directive 2001/18/EC (European Parliament & Council of the European Union, 2003).

Regulation (EC) 1946/2003 is important because it requires the exporter to provide a comprehensive, publicly available risk assessment that meets EU standards, for GMOs intended for release into the environment.

Target Malaria argues that it is not required to make a transboundary notification that includes such a risk assessment for the proposed release of male-sterile GM mosquitoes in Burkina Faso, because the GM mosquitoes were exported for an initial period of contained use (for which a notification is not required under EU law) before release. However, this interpretation would make a nonsense of the Cartagena Protocol and the legal requirements that follow from it, because GMOs exported for contained use could subsequently be released into the environment without meeting the requisite risk assessment standards.

The same argument to avoid a transboundary notification according to EU law was made previously by the UK-based GM insect company Oxitec when it exported GM mosquito eggs to Malaysia for mating with a local strain before open release in 2010. (Nonetheless, the Malaysian Biosafety Act 2007 does require prior notification for contained use involving LMOs, accompanied by an emergency response plan and specific measures to be taken.) However, subsequently, a transboundary notification was made for Oxitec's exports to Malaysia, according to the UK minister responsible for oversight of the legislation.[5] No further releases of Oxitec's GM mosquitoes in Malaysia were conducted.

5. HL Deb, 2 November 2011, c264W. https://www.theyworkforyou.com/wrans/?id=2011-11-02a.264.3&s=oxitec#g264.5



The legal requirement to provide a transboundary notification is a minimum requirement towards ensuring adequate protection of biological diversity and human health. Avoidance of transboundary notifications has previously been a major issue with the commercial GM insect company Oxitec (GeneWatch UK, 2014). However, Target Malaria has claimed to be holding itself to higher standards. It is therefore unacceptable that no transboundary notification has been made by the exporter in this case. This also has major implications for risk assessment standards, discussed further below.

In addition to the requirement that the ERA meets EU standards, it must be produced by the exporter, not by a local partner (such as IRSS) in the importing country. This is important because it puts the onus on the developer of the GM mosquitoes (i.e. Imperial College, London, or one of its partners in the Target Malaria consortium) to ensure the ERA's accuracy and completeness, rather than shifting the responsibility to an institution in the importing country. If a transboundary notification is made, the exporter is responsible for its content, and can more readily be held liable if the information supplied in the accompanying ERA is incorrect.

2.3 Limitations of the published environmental risk assessment

The US Foundation for the National Institutes of Health (FNIH) has commissioned and published an "ecological risk assessment" for the proposed open release from the Commonwealth Scientific and Industrial Research Organisation (CSIRO) in Australia (Hayes, et al., 2018). In its introduction to this report, Target Malaria states that the CSIRO risk assessment methodology is consistent with recent recommendations from the US National Academy of Science, Engineering, and Medicine for gene drive applications. The use of these recommendations as the basis of the assessment is highly questionable because:

(i) The proposed release does not involve the use of "gene drive";
(ii) The use of EU standards is required for the export of GM insects for open release from the EU (as detailed above);
(iii) Burkina Faso has yet to adopt national guidance on how to conduct a risk assessment for GM mosquitoes but might be expected to pay due regard to international experience.

Burkina Faso has adopted a law and regulations covering genetically modified organisms (GMOs).[6] The law requires a risk assessment to be conducted before any open release of GMOs. However, there is no specific guidance on how to conduct such a risk assessment for GM mosquitoes.

6. https://bch.cbd.int/database/results?searchid=689144

Nevertheless, in addition to the EU Guidance discussed below, other guidance does exist. In particular, under the Cartagena Protocol, the Ad Hoc Technical Expert Group (AHTEG) on Risk Assessment and Risk Management has produced guidance on the risk assessment of genetically modified mosquitoes.[7] In addition, relevant academic papers that discuss the risk assessment of GM insects, including GM mosquitoes, include Reeves et al. (2012) and David et al. (2013). Had it developed specific guidance, Burkina Faso would likely have drawn at least on the AHTEG guidance and possibly also EU guidance, discussed further below.

To meet European standards for GMOs that are not plants, a list of issues that must be covered in the risk assessment is included in Annex II, D.1 of the relevant EU Directive 2001/18/EC. Guidance published by the European Food Safety Authority (EFSA) outlines the issues and evidence that should be covered by the ERA (EFSA, 2013). Pages 73 to 107 of the EFSA guidance provide details on the specific areas of risk of GM insects.

The CSIRO risk assessment acknowledges some risks as a result of the proposed experiments. For example, it states (Hayes, et al., 2018: 2) that Target Malaria have stipulated that their female separation protocols will limit the incidental release of female GM mosquitoes to no more than 5 for every 1,000 male GM mosquitoes released. Nevertheless, since GM female mosquitoes can bite humans and spread disease, the release of biting females still poses some risk to local people. All CSIRO's subsequent analysis assumes that Target Malaria's condition will be met, without providing any demonstration of it. For comparison, the commercial company Oxitec has breached its own sorting protocol and released large numbers of biting female GM mosquitoes in experiments in the Cayman Islands (GeneWatch UK, 2018). Therefore, it is not clear how the avoidance of a similar problem during the proposed experiments in Burkina Faso will be guaranteed.

The CSIRO risk assessment (Hayes, et al., 2018: 59) also notes that analysis of Mark Release Recapture experiments conducted by Target Malaria to date indicates that recapture rates are low (0.3% to 1.7%) and that male mosquito dispersal distance varies from about 40m to 550m.This indicates that monitoring is likely to be inadequate to determine whether GM mosquitoes spread outside the release site, another important aspect of the risk assessment.

Other risk endpoints have been omitted from the CSIRO report. For example, both the EFSA and AHTEG Guidance highlight the importance of assessing the impact of proposed GM mosquito releases on competitor species, especially other species of mosquitoes that may transmit disease. Target Malaria is now involved in a new ecological study, which will reportedly consider this question in the context of future proposed releases (Zhang, 2018). However, none of this data is available in the context of the current application.

Both the EFSA and AHTEG Guidance also require an assessment of the impacts on other 'non-target' species, such as predators. The CSIRO risk assessment considers the plausibility of effects on non-target organisms following the field release in light of the predicted survival of GM male and female mosquitoes: stating that this risk is low (Hayes, et al., 2018: Section 5). However, it does not attempt to assess the impacts on non-target species, for example, by conducting feeding trials. In contrast, an application by Oxitec to release GM olive flies in the EU was rejected because of insufficient data from feeding trials of the GM flies to non-target organisms (Butler, 2014)[8] further highlighting that the CSIRO risk assessment does not meet EU standards.

7. Biosafety Clearing House. Guidance on Risk Assessment of Living Modified Organisms: Risk Assessment of Living Modified Mosquitoes. http://bch.cbd.int/onlineconferences/guidancedoc_ra_mosquitoes.shtml (English) or available as pdf in English: http://www.cbd.int/doc/meetings/bs/mop-06/official/mop-06-13-add1-en.pdf and Spanish: http://www.cbd.int/doc/meetings/bs/mop-06/official/mop-06-13-add1-es.pdf
8. Ecologistas celebran negativa liberar moscas modificadas geneticamente [In Spanish]. La Vangardia.7th August 2015. http://www.lavanguardia.com/vida/20150807/54435701348/ecologistas-celebran-negativa-liberar-moscas-modificadas-geneticamente.html

The CSIRO report notes (Hayes, et al., 2018: 22) that "A key challenge to probabilistic risk assessment for a novel technology is the lack of empirical information on its safety and reliability". Its conclusions are therefore largely based on "expert elicitation" of parameters for which no, or limited, measurements exist (as described in Section 2.3, and discussed in Section 6.2), combined with a series of (somewhat complex and contradictory) assumptions about when to update these expert opinions using laboratory or field measurements. A more detailed report of the elicitation process highlights significant uncertainties and some major disagreements amongst experts (Hayes, et al., 2015).

In contrast to CSIRO's "expert elicitation" approach, the EFSA Guidance emphasises the role of "stakeholder elicitation", aiming to lead to consistency among stakeholders in both the understanding of uncertainty and the use of terms, and warns that predictive bias can be caused by limited, subjective expert judgements. As a general principle, the EU also requires the use of a step-by-step approach, whereby scientifically reliable evidence based on qualitative, and, whenever possible, quantitative analyses, is combined with an explicit uncertainty analysis in order to support the final conclusions of the ERA. This implies the need for a lot more experimental data to underpin the ERA (for example, from laboratory and caged experiments and environmental surveys).

The conclusions of the CSIRO report highlight a particular problem with the difficulties in assessing whether the GM construct will increase the vectorial capacity of female GM mosquitoes to transmit malaria or other diseases (o'nyong'nyong virus and lymphatic filariasis). This is a particular area of concern, where considerably more data and in-depth understanding should be required before releasing GM mosquitoes into the environment.

In addition, many citations in the CSIRO report reference unpublished data from Target Malaria (for example, on local mosquito population surveys and on key characteristics of the insectary mosquitoes), which have not been exposed to independent scrutiny. The statement that there "appears to be" no plausible mechanism for toxicity to humans, for example, relies on unpublished data from Target Malaria, which is claimed to demonstrate that the I-PpoI protein has no toxic or allergic properties and is not present in mosquito saliva or carcasses (Hayes, et al., 2018: 20). The report also states (Hayes, et al., 2018: 21) that Target Malaria has investigated whether the GM construct is mobile or mutates between generations: but again it relies entirely on unpublished data. Figure 4.7 (Hayes, et al., 2018: 63) also indicates some survival (although not to adulthood) of offspring of the GM mosquitoes when male GM mosquitoes were mated with female G3 strain mosquitoes: again, this data has not been published (Hayes, et al., 2018: 62). Numerous other examples of reliance on unpublished data occur in the report. Without publication of all this data, CSIRO's so-called independent risk assessment cannot be properly subjected to independent scrutiny.

In addition, the summary of the CSIRO report states (Hayes, et al., 2018: 2): "The report is not a complete evaluation of all potential risks. Some potential risks, such as the risks to social endpoints identified in Burkina Faso's legislation, are not addressed in this analysis". This begs the question of where these missing social risks have been evaluated and how the public will be informed about any such assessment.

2.4 Lack of consultation on the ERA or on national guidance for an ERA

According to the CSIRO report (Hayes, et al., 2018: 3), in November 2016, the CSIRO asked Target Malaria's stakeholder engagement team to collate the local community's concerns about the field release to help identify risk assessment endpoints. However, following this initial stage, there is no evidence of public or regulatory input or scrutiny of the report. In addition, there is no public information regarding whether the ANB has adopted the CSIRO report, developed its own ERA, or subjected the CSIRO report to detailed scrutiny: in other words, information about the ERA which underpins the reported approval of the open release experiment is entirely missing. This lack of transparency

has been compounded by the lack of national guidance on what should be included in an ERA for GM mosquitoes. Best practice would have been to develop such guidance first, and to publish it for public consultation, rather than allowing the developer of the GM mosquitoes to decide what should be in the ERA. An ERA should then have been published by the regulator, including aspects omitted from the CSIRO report which are required under Burkina Faso's legislation (such as social aspects). Further, there has been no public consultation on the ERA, which should have taken place prior to any decision to approve the proposed releases. The Cartagena Protocol, in its Article 23.2, obliges Parties to consult the public in the decision-making process regarding LMOs.

The lack of a comprehensive, published ERA, which has been subject to a full public consultation, undermines the reported approval of these experiments. In addition, it makes it impossible to implement requirements for fully informed consent, because local people cannot be fully informed about the risks before making a decision on whether to accept them.

3. Conclusions

Since the benefits of the proposed trial do not outweigh the risks, the proposed open release of GM mosquitoes in Burkina Faso should not be undertaken.

Further, under EU law, the exporter should provide a transboundary notification, including a publicly available environmental risk assessment that meets EU standards before exporting GM insect eggs for open release to foreign countries. This is a minimum requirement to provide adequate protection of the biological diversity and human health.

Transparency, public consultation (including on the environmental risk assessment) and fully informed consent (which requires participants in trials to be informed about the risks) are important issues, which must be fully addressed before any open release of GM mosquitoes into the environment is considered in the future. Specific guidance on the environmental risk assessment of GM mosquitoes also needs to be adopted in Burkina Faso, with adequate public consultation and debate, before open releases of GM mosquitoes are contemplated there.

These issues will become of even more importance for larger-scale releases of GM insects (should they be proposed in the future), where the environments of other Parties may also be exposed to risks. Failure to address these issues now will add to concerns that other strains of GM insects, potentially including those with gene drive, will be released in future without adequate controls to protect biological diversity and human health.

About the organisations publishing this briefing

On 7 April 2015 the African Centre for Biosafety officially changed its name to the **African Centre for Biodiversity (ACB)**. This name change was agreed by consultation within the ACB to reflect the expanded scope of our work over the past few years. All ACB publications prior to this date will remain under our old name of African Centre for Biosafety and should continue to be referenced as such. We remain committed to dismantling inequalities in the food and agriculture systems in Africa and our belief in people's right to healthy and culturally appropriate food, produced through ecologically sound and sustainable methods, and their right to define their own food and agricultural systems.

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GeneWatch UK is a not-for-profit group that monitors developments in genetic technologies from a public interest, human rights, environmental protection and animal welfare perspective. GeneWatch believes people should have a voice in whether or how these technologies are used and campaigns for safeguards for people, animals and the environment.

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