

Conflicts of interest at the European Food Safety Authority erode public confidence

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In September 2012 Professor Gilles-Eric Séralini, a researcher at the University of Caen in France, published his team's findings that a Monsanto genetically-modified (GM) maize and Roundup herbicide caused increased rates of organ damage, tumours and mortality in rats fed over a 2-year period.¹ The study was significant because it followed the rats over a long-term period, with the first tumours only appearing after 4–7 months. In contrast, the safety studies carried out by GM seed companies in support of EU authorisations typically last for a maximum of 90 days.^{2–4} In other words, these studies are incapable of seeing long-term effects such as those found in Séralini's study.

Europe's food safety agency, the European Food Safety Authority (EFSA), dismissed Séralini's study on the grounds of 'inadequate design, analysis and reporting'.^{5–6} However, far from laying to rest public concerns about GM foods, EFSA's review of the study¹ sparked renewed accusations of conflicts of interest of the type that have plagued the agency since its founding in 2002. EFSA's critics questioned the objectivity of its review because the agency's original opinion that the GM maize was safe⁷ had led to its EU authorisation. So, in dismissing Séralini's study, EFSA was in effect defending its own decision. Also, EFSA has argued against the need for mandatory animal feeding trials on GM foods, adding that if they are carried out, 90 days is sufficient to see any effects.^{8–9} Member of the European Parliament Corinne Lepage said that, if EFSA had accepted that Séralini's findings had any validity, this would have been equivalent to 'cutting the branch on which the agency has sat for years'.⁷

EFSA was accused by scientific organisations and individual scientists of applying double standards to studies on GM foods. They said that EFSA rejected Séralini's findings yet accepted less rigorously

designed studies from industry as proof of safety of GM foods.^{10–12} In comparison with the industry studies,^{2–4} Séralini's study:¹

- ▶ measured more parameters more often and over a longer period;
- ▶ tested more doses, allowing dose-response to be meaningfully analysed;
- ▶ analysed all animals for blood and urine chemistry instead of selecting 10 from each group of 20, a practice that enables bias;
- ▶ distinguished between effects caused by the GM maize, Roundup alone, and a combination of the two;
- ▶ excluded the additional 'reference' control diets included in industry tests. These 'reference' diets introduce variables from irrelevant factors, such as different growing conditions, that can mask toxicological differences arising from the genetic modification of the crop. This practice is contrary to an EU Directive which stipulates that the purpose of the risk assessment is to identify differences in the GM crop arising from the genetic modification.¹³

EFSA's review of the study did not address this contentious issue of double standards.^{5–6}

EFSA LINKS WITH INDUSTRY-FUNDED GROUPS

The Séralini affair was the latest in a long series of controversies over EFSA's closeness to industry. An earlier dispute involved the long-standing relationship of the chair of EFSA's management board, Diána Bánáti, with the industry-funded International Life Sciences Institute (ILSI).¹⁴ ILSI arranges forums in which industry scientists collaborate with publicly-funded scientists from government regulatory bodies to design risk assessment methodologies for chemicals, pesticides and GM foods.^{15–16} ILSI is funded by the same agribusiness, food and biotechnology companies¹⁷ whose products EFSA assesses for safety.

In October 2010 Members of the European Parliament and civil society groups called for Bánáti's resignation from the EFSA management board on

which she had served since 2008. Bánáti had joined ILSI's European board of directors in April 2010 but did not publicly report the conflict of interest before her re-election to the EFSA board later that year. In response to criticism, Bánáti resigned from the ILSI board but controversially kept her job as EFSA chair. Then, in May 2012, in a type of conflict of interest known as the 'revolving door', Bánáti had to resign from EFSA when she rejoined ILSI as executive director.^{14–18}

CONFLICTS OF INTEREST IN GENETICALLY-MODIFIED ORGANISM RISK ASSESSORS

EFSA experts involved in assessing the risks of GM foods have attracted criticism for their closeness to industry. In 2010, 12 out of 21 experts on the genetically-modified organism (GMO) Panel that issued a scientific opinion that was key to the approval of a GM potato had conflicts of interest as defined by the Organisation for Economic Cooperation and Development (OECD).¹⁹

In 2011 the European Ombudsman ruled in favour of a complaint about Suzy Renckens, scientific coordinator of EFSA's GMO Panel since EFSA was established in 2002. Renckens left EFSA in 2008 and went straight into a lobbying job with the biotechnology company Syngenta without any restrictions being imposed by the agency. The Ombudsman ruled that EFSA 'failed to observe the relevant procedural rules and to carry out a sufficiently thorough assessment of the potential conflict of interest'.^{20–22}

Conflicts of interest in members of EFSA's management board and expert panels were among the issues that prompted the European Parliament to postpone approving the agency's 2010 expenditures.^{23–24}

In 2012 the European Court of Auditors issued its report on the conflicts of interest policies at four European agencies, EFSA among them. The Court concluded that, while EFSA's policies were among the most advanced, none of the agencies 'adequately' managed conflicts of interest.²⁵

EFSA REWRITES CONFLICTS OF INTEREST POLICY

In 2011, under pressure from the European Parliament,²⁶ EFSA rewrote its 'independence policy'.²⁷ While the new rules contain improvements, some conflicts of interest are still allowed.²⁸ In 2012 EFSA renewed eight expert panels, giving an opportunity to see how its new policy worked in practice. Improvements were noted. Some experts with conflicts

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of interest, notably with ILSI, are no longer on the panels. Some who remain have given up their ILSI involvement, though others have not. Other conflicts of interest, such as receiving research funding from industry, are still evident.²⁸

Conflicts of interest on EFSA's management board are permitted by a loophole in EFSA's founding regulation, which states that four members 'shall have their background in organisations representing consumers and other interests in the food chain'.²⁹ 'Other interests' are interpreted by EFSA and EU authorities as including industry interests. However, the presence of industry figures on EFSA's management board is unacceptable. EFSA does not have the power to change the founding regulation, which is the responsibility of the EU institutions.

CONFLICTS OF INTEREST INFLUENCE GMO POLICY

Conflicts of interest are particularly serious when they leave a permanent mark on how technologies and products are regulated. In such cases, even if an expert with a conflict of interest is removed, their work remains behind them. In 2012 the term of office of GMO Panel chair Harry Kuiper expired. Kuiper had occupied this position since 2003, during which time he was involved in the risk assessment of every GM food submitted to EFSA since the agency was set up. Throughout his term of office he retained links with ILSI. Though Kuiper is gone, the risk assessment standards that he helped develop remain—a situation that has given rise to another complaint to the Ombudsman.³⁰

Even the design of EFSA's GMO risk assessment standards was influenced by an ILSI task force headed by a Monsanto employee. They are based on the concept of comparative assessment, a rewording of the controversial concept of 'substantial equivalence'. Substantial equivalence assumes that GM crops are equivalent to non-GM crops and do not require rigorous safety assessment.¹⁵

Currently, in the EU, substantial equivalence must be measured, but the analysis is confined to known basic components of the GM food such as protein and fats. Unexpected changes such as novel toxins or allergens are likely to be missed. Though currently, whatever the outcome of the analysis, a full risk assessment is required, a new Regulation³¹ adopted in February 2012 via the EU Commission's opaque comitology process still makes the weak comparative assessment the basis and guiding principle of the risk assessment.³²

EFSA must bear responsibility for the inadequacy of the comparative assessment because it has never defined the degree of similarity that a GM crop must have to a non-GM crop to qualify as equivalent. Also, when differences are found in the GM crop, EFSA often dismisses them as being within the normal range of variation and/or as not biologically relevant. Yet EFSA has not properly defined these concepts. It allows industry to define the normal range of variation based on an ILSI database of historical crop varieties grown in differing conditions.^{15 33} An EFSA opinion allows industry to define biological relevance on a case-by-case basis.³⁴

These tactics mask or dismiss differences in the GM crop arising from the genetic modification process—even though identifying such differences is the purpose of the risk assessment as defined in an EU Directive.¹³ The risk is that substantial equivalence may be assumed even though there are unexpected toxins or allergens in the GM crop. Unexpected toxins could sometimes be exposed by rigorous animal feeding trials, but these have hitherto not been mandatory. EFSA's opinion arguing that feeding trials are not always necessary contained large amounts of text lifted from an ILSI report.¹⁵

EFSA's flawed assumptions of the substantial equivalence of GM foods were thrust into the spotlight by Séralini's 2012 study.¹ Earlier, Monsanto had carried out a 90-day feeding trial with the same maize in support of its application for regulatory authorisation. Differences were found in the GM-fed rats,² but EFSA concluded that they were 'of no biological significance'³⁵ and the EU authorised the maize in 2004.

Séralini's team obtained Monsanto's raw data and re-analysed it. They found signs of liver and kidney toxicity in the GM-fed rats.³⁶ They conducted their 2012 study as a direct follow-up to Monsanto's study to see what happened to the signs of toxicity when the study period was extended to 2 years and found that they escalated into serious organ damage.¹ The findings showed that EFSA's view that the differences in the GM-fed rats were not biologically significant was incorrect. The study highlighted serious shortcomings in EFSA's risk assessment of GM foods, as was noted by Members of the European Parliament, who called for reform.³⁷

EFSA PROMOTES INDUSTRY CONCEPT TO ASSESS CHEMICALS RISK

In the area of chemicals, as with GM foods, EFSA's closeness to industry has resulted in risk assessment methodologies of

questionable scientific rigour. In its review of conflicts of interest at EFSA, the Court of Auditors criticised EFSA's handling of the concept of the threshold of toxicological concern (referring to it as an anonymous 'concept').²⁵ This concept has been promoted for years by industry groups such as ILSI^{38 39} to assess the risk of chemicals on which little or no toxicological testing has been done. Chemical industry consultancy Cantox defines the threshold of toxicological concern as a level of human intake or exposure considered to pose 'negligible risk, despite the absence of chemical-specific toxicity data'.⁴⁰

A less reassuring explanation for why industry favours the concept emerged from interviews with proponents. By waiving detailed toxicological testing, the threshold of toxicological concern enables substances to be fast-tracked through the risk assessment, cutting time to market approval from as much as 4 years to as little as a few months. The concept also allows inadequately tested chemicals to remain on the market if expected exposures are below a level deemed safe on the basis of an assessment that depends heavily on assumptions.⁴¹

In 2012, EFSA's scientific committee published an opinion recommending the use of the threshold of toxicological concern in the risk assessment of chemicals in food.⁴² The opinion stated that an exposure level of 0.15 µg per person per day is acceptable for genotoxic substances (substances that damage DNA, possibly giving rise to cancer and birth defects).⁴² EFSA's opinion contradicted its own previous opinion which stated that it is current practice to assume that there is no safe level of exposure for genotoxic substances.⁴³ It also undermined the pesticide Regulation, which forbids approval of genotoxins.⁴⁴

The impartiality of the 2012 opinion is in doubt, since 10 of the 13 members of the EFSA working group on the threshold of toxicological concern had a publishing history favouring its use or had previously advocated its use. Eight had formal links with ILSI.⁴⁵

EFSA UNDERMINES PESTICIDES LAW

A public health protection democratically established in an EU pesticides Regulation of 2009 was undermined by EFSA. The Regulation made clear that pesticides must no longer be assessed only on the basis of industry tests. It stipulated that studies from the 'scientific peer-reviewed open literature' had to be included in the dossier that industry submits to regulators in support of pesticide authorisations.⁴⁴

The Regulation marked a breakthrough. For the first time the large body of evidence on pesticide risks in the peer-reviewed literature would inform risk assessments. This would almost certainly result in restrictions or bans on some pesticides.

However, EFSA effectively extracted the Regulation's teeth. The agency issued a guidance document to help industry evaluate the reliability of studies from the peer-reviewed literature for possible inclusion in the dossier.⁴⁶ EFSA gives as its first and main criterion of reliability the Klimisch classification, derived from a paper by employees of the chemical company BASF. Klimisch *et al* state that only tests performed according to Good Laboratory Practice (GLP) rules, the type of tests that industry performs to support regulatory authorisations, are reliable without qualification. Studies from the open literature, which generally do not use GLP, are categorised as unreliable by Klimisch *et al*.⁴⁷

Thus EFSA gave industry an excuse to exclude almost any peer-reviewed study from its dossier. It steered pesticide risk assessment in the opposite direction to that intended by the Regulation.

INDUSTRY TESTS ITS OWN PRODUCTS FOR SAFETY

A factor that compromises the independence of the regulatory process is that industry tests its own products for safety. This system lies outside EFSA's control as it is laid down in EU law. Yet it encourages bias. Reviews of the scientific literature on products such as tobacco,^{48 49} the plastics chemical bisphenol A,^{50 51} pharmaceuticals^{52 53} and GM crops^{54 55} confirm that industry-linked or industry-sponsored studies are more likely to conclude that the product is safe, whereas independent studies are more likely to find risk.

FIVE DEMANDS FOR REFORM

In November 2012, civil society and farmer groups gathered outside EFSA's headquarters in Parma, Italy, to protest the 'industry capture' of the agency and present demands for reform in five areas, listed below. The first is not within EFSA's power, but requires EU-wide action.

End reliance on industry-funded research

EU laws should be rewritten to end reliance on industry-funded research. A fee should be levied on industry to pay for testing, but a barrier must be placed between industry and the scientists who do the testing. This could be

accomplished by tasking a publicly-funded body with using the industry fund to commission independent scientists to carry out tests. Some of the industry money should fund public interest research into risks, which is lacking in the area of GM crops.

Prevent conflicts of interest

EFSA's conflicts of interest policy must be tightened to remove loopholes. Its founding regulation must be rewritten to exclude people with links to industry. EFSA experts, who currently work on a voluntary basis, should be paid.

Sanctions for experts and staff who breach public trust through conflicts of interest should be defined in European law. The laws of some member states include sanctions such as temporary bans on holding public office and the withholding of salary.⁵⁶

EFSA, like other organisations, is unable to police itself on conflicts of interest. An independent body should oversee EU agencies.

Establish a code of scientific practice

The reasoning behind EFSA's opinions on certain substances should be clarified by establishing a code of scientific practice for risk assessments. This would set out in a clear and transparent way how EFSA experts search for and evaluate scientific evidence, increasing the transparency and replicability of EFSA's decision-making and enhancing public confidence. It is not acceptable to exclude studies from the peer-reviewed literature because they do not adhere to GLP rules.

The code could draw on methodologies from evidence-based medicine for reviewing large bodies of data of different types and translating them into decisions, such as the Navigation Guide⁵⁷ and the Cochrane Collaboration.⁵⁸

Improve transparency and accountability

EFSA must make accessible all data and information on which it bases risk assessments. EFSA's opinions should be independently peer-reviewed.

Ensure wider participation in decision-making

Risk assessment should take into consideration social, economic and ethical factors. While those aspects are outside EFSA's remit, EFSA should broaden the expertise on its expert panels to include, for example, embryologists, endocrinologists, neurodevelopment experts, ecologists and soil biologists.

CONCLUSION

While EFSA has made progress on addressing conflicts of interest, it has much to do to improve the rigour of its scientific decision-making and to gain public trust.

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