Joint input of Testbiotech and Friends of the Earth Europe input on food derived from genetically engineered animals

during consultation about "EFSA Panels on GMO and AHAW; 2011. Draft for public consultation - Scientific Opinion on the Draft Guidance on the risk assessment of food and feed from genetically modified animals including animal health and welfare aspects."

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1. On the introduction:
EFSA´s general approach to genetically engineered animals is biased and based on a flawed approach. It looks like some of the experts who were consulted, who are known to be proponents of genetic engineering in livestock, have had a substantial impact on this draft. As a consequence, the draft Guidance does not address the real complexity of assessing the impact of animal genetic engineering for food, nor does it ask the relevant questions required for a proper risk assessment.

Genetic engineering in livestock is largely driven by private interests. The goals behind this push are massively influenced by economic interests such as higher production for meat and milk, and the introduction new intellectual property (IP) protected technologies into animal breeding.

EFSA's draft Guidance does not take into account a number of considerations that are highly relevant in this context. Firstly, any decision on the introduction of genetically engineered animals products and technologies into the European food supply must be guided by European animal welfare legislation. Secondly, European consumers, who largely reject genetic engineering and cloning of animals for the purpose of food production, will be impacted by the introduction of these products. Thirdly, European farmers and food producers will also be impacted by new dependencies and major uncertainties concerning the acceptance and safety of their products. All of these considerations must be part of any risk analysis of food and feed from genetically engineered animals.

Interestingly, the EU took a different approach in assessing the cloning of animals for food production. Instead of starting with a Guidance for risk assessment, a survey was delivered that also includes basic aspects of animal welfare and potential suffering of animals (EFSA 2008a).

Importantly, cloning is widely used during the production of genetically engineered animals. Therefore, it is important that aspects discussed by EFSA (2008a), such as health risks and risks for animal health, are included in the assessment of food derived from genetically engineered animals.

Apart from cloning, genetic engineering of animals implies further relevant aspects regarding animal welfare. For an overview, please see, for example, van Reenen (2009) who was one of the first experts to genetically engineer cattle in order to produce additional substances in their milk. He explains: “Therefore, as pointed out by several authors (...), genetic modification per se may place an animal at risk because of an alteration of an existing delicate balance that has been established through many generations of selection, and that represents a wide range of optimized gene combinations that may be difficult to manipulate without causing unexpected deleterious effects on the phenotype. The available evidence, for example on growth hormone and cytokine transgenes, clearly supports this suggestion.”

He concludes that animal welfare aspects should have a high priority if transgenesis in animals is going to be assessed. “As discussed in previous sections of this paper, there are convincing arguments to support the idea that treatments imposed in the context of farm animal transgenesis are by no means biologically neutral in their effects on animal health and welfare. On the contrary, several treatments seem to directly threaten the pre- and postnatal survival of transgenic farm animals, and there is every reason to assume that overt pathogenicity and lethality merely represent the very extremes of a wide range of possible detrimental effects of experimental manipulations and phenotypic changes related to transgenesis on animal health and welfare.”

In this context, it must be noted that targeted gene insertion in larger species is still very difficult. Culturing embryonic stem cells (which is a major tool for selecting the cells for production of transgenic animals) is so far possible in small animals but not in larger species, so there will be unintended effects in most cases.

Thus, these aspects cannot be separated from risk assessment and overall risk analysis of genetically engineered animals. An integrated approach needs to be developed that includes these aspects from the beginning. Even if EFSA only wants to deal with certain aspects within this process, it has to be pointed out what exactly will be needed by the risk manager before any conclusions are drawn.

2. On the general principles (page 8 ff)

In general, the potential market authorisation of products derived from genetically engineered animals has to be seen as a new issue that involves many scientific and ethical issues that are outside the purview of the risk assessments as performed by EFSA on plants and microorganisms. Even so, EFSA is more or less trying to transfer risk assessment as performed on genetically engineered plants (which is a matter of controversial debate) to animals. This approach is basically wrong from both a scientific and ethical perspective.

Scientifically, EFSA fails to address the relevant differences in risk assessment between products derived from plants and those derived from animals. Since this fundamental element is missing, the whole structure and content of the Guidance is not consistent and not suited to target the most relevant questions. Some of the differences between plants and animals that are relevant for risk assessment are listed below:

(1) Genetic regulation in plants and animals is different in decisive elements. The number of DNA-elements involved in epigenetic mechanism and genomic regulation is higher in most mammals/vertebrates than in plants. In consequence, the impact of genetic engineering on epigenetic regulation and genetic stability, on gene expression and its interaction with the environment need to be analysed in greater detail. For example, it is known that culturing

mammalian cells as well as the process of cloning (which is used in most cases to produce genetically engineered animals) impacts both cell regulation and animal health. Furthermore, physiological and even mental stress can impact gene regulation and gene expression in many ways during the life time of an animal. On the other hand, sufficiently evaluated methods to continuously investigate and monitor the genomic and metabolic status of animals under various conditions (such as birth, illness, transport, periods of high production, specific housing conditions, particular feeding regimes) are not available. These methods should be seen a major prerequisite to assess the risks in products derived from genetically engineered animals. In conclusion, the risk assessment of food and feed derived from animals needs to develop specific tools and criteria that are different from those currently used in plants.

(2) Genetic diversity in most animal species used for breeding is much higher than that which can be expected from plant varieties whose genomes are largely homogeneous. Thus, generational effects and the effects of interbreeding will have a much higher impact on genetic stability, including gene expression, epigenetic regulation and other unintended side effects. Even in conventional animal breeding, multigenerational studies are necessary before new animals are introduced into populations for large scale breeding. Detailed Guidance concerning species and particular breeds will be needed to assess relevant effects in genetically engineered animals.

(3) Unlike plants where the time for harvesting can be fixed to a particular period of vegetation, this not the case with products derived from animals. For example, meat and milk can be derived from animals at different stages of an animal's life, in various physiological conditions, and very different environments. Each of these conditions can impact composition, quality of the products, and the level of risk to the animal and the potential consumer of products derived from the genetically engineered animal. Thus, the quality and the risks of the products are quite dynamic. Detailed Guidance would be required under which conditions these products should be assessed.

(4) Animals cannot be seen as separate biological units. The biological system of animals is closely interconnected with the biological status of the microorganisms living in their gut and skin. Changes in composition of flora of related microorganisms can substantially influence the quality and the risks (such as transmissible diseases) of relevant products. Therefore, risk assessments of animals must take into account the interaction between the animals, their environment, and the flora of microorganisms and their dynamics being impacted by specific genetic conditions or feeding regimes.

(5) In contrast to risk assessment in plants, components of toxicological relevance can only be expected in some cases. Much more relevant are, for example, contagious, transmissible diseases that can show highly unexpected patterns - as known from BSE. Additionally, hormone active substances and compounds of immunological relevance must be taken into account. Detailed and adequate tools on how to assess these risks have first to be developed and not be deduced, for example, from feeding trials as performed with plants. For example, the long term impact of nutritional effects on human health cannot be investigated by feeding studies using poultry or rabbits over a period of 42 days.

In conclusion, the proposed comparative risk assessment is derived from current GMO panel practice and does not meet the specific requirements of assessing risks from products derived from genetically engineered animals. It already starts with the fact that decisive data are missing: Since nothing like a standard composition analysis is available, no sufficient conclusions can be drawn if differences in compositional analysis are observed. This problem was already discussed in risk assessment of products from cloned animals. In assessing the data as presented by FDA (2008) and

EFSA (2008a), the Center for Food Safety (cited by EFSA 2008b) rightly addresses some open questions:
“The significant differences in cloned milk composition revealed by these studies raise serious concerns about whether milk from clones is safe for human consumption. Without more data, and standards for which ‘normal variations’ in protein and fatty acid compositions of meat and milk are safe, any conclusions regarding the safety of food products derived from clones and their progeny are premature.”

In its draft, EFSA is aware of this problem and proposes, “to develop consensus documents on the composition of food and feed derived from different animal species”. However, even if these consensus documents were available and were used in a similar way to what the GMO panel does in its risk assessment of genetically engineered plants (i.e. referring to OECD documents and a database set up by International Life Sciences Institute, ILSI), this would not be a solution. These data have to be considered as “historical data” unrelated to the actual animals or trials. Thus, this kind of comparison inevitably contains major uncertainties and cannot be a substitute for comprehensive risk assessment.

3. On recommendations (page 42)
In general, what is needed is a restart of this whole process, a simple review of parts of the current draft will not suffice. We recommend this draft Guidance be withdrawn. As explained, the draft documents fail to address the decisive questions, and take a wrong approach to risk assessment.

If a new process is started, it should start with a consultation with relevant stakeholders without undue influence from private interests that stand to profit from the introduction of genetically engineered animals into the European food supply. From the outset, this process must integrate consumer and farm sector interests as well as animal welfare protection.

References:
EFSA (2008a): Scientific Opinion of the Scientific Committee on a request from the European Commission on Food Safety, Animal Health and Welfare and Environmental Impact of Animals derived from Cloning by Somatic Cell Nucleus Transfer (SCNT) and their Offspring and Products Obtained from those Animals. The EFSA Journal (2008) 767, 1-49

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