AMFEP
142, Avenue Jules Bordet
Brussels 1140
Belgium
Email : amfep@kellencompany.com
TEL : +32 2761 16 35

To: NBTConsultSubmissions@foodstandards.gov.au
CC: submissions@foodstandards.gov.au

18 April 2018

Re. NBT consultation Paper

Dear Madam, dear Sir,

AMFEP, the association of Manufacturers and Formulators of Enzyme Products, very much appreciates the opportunity to provide input to the public consultation on "Food derived using new breeding techniques – review". This is a very timely theme, with important repercussions on innovation and on addressing global socio-economic challenges related to food production.

Although the focus of the review is on the application of "New Breeding Techniques" to plants and animals, we would like to emphasize the importance of these techniques also for microorganisms, be it as production organisms for food or feed ingredients, as processing aids, or as dairy cultures or probiotics. The question how certain applications of genetic engineering will be classified will also have regulatory implications on products produced with microorganisms. Since "New Breeding Techniques" is not a term used in the context of microorganisms, we will use in our input below the more generic term "genome editing".

The New Breeding and/or genome editing techniques have strongly challenged the binary and (largely) mutually exclusive GMO vs. non-GMO, process-centric regulatory approach, and have highlighted that the reality is far more gradual and overlapping. The same genetic changes can be obtained with different techniques. However, in the context of the current regulatory framework, and depending on the technique actually used, largely different regulatory burdens would apply, and the product may or may not be suitable for certain markets (e.g., organic). In addition, if it is no longer possible to determine with which technique a certain genetic change was introduced (classical mutagenesis, natural evolution, or genome editing), control and enforcement will be a formidable challenge.

Some of the questions in this public consultation are again process-centric, i.e. directed at the question of which applications of genome editing can and should be exempted from the GMO regulatory scheme. Similar to the initial GMO vs. non-GMO approach, such a process-centric approach to genome editing is highly questionable. Some techniques of genome editing can be used to introduce single base pair substitutions, but can also be used to insert entire heterologous genes. In addition, genome editing can be done rapidly and in a multi-parallel fashion, thereby abolishing the distinction between the different processes. For instance, by a series of single base pair substitutions (which may all be exempted from a "GMO definition"), an entire heterologous gene may be created. Arbitrary rules would need to be

established to judge which applications of genome editing would be exempted from the GMO regulatory framework, which would add to confusion and uncertainty (and, as we know from the GMO discussion, to public reservation).

For all these reasons, we call for a fundamental shift from a primarily process-centric to a primarily product-centric approval system, where the regulatory burden and implications are determined by the final product or final production organism, independently of the method used to obtain it.

With this in mind, our feedback on the questions raised are the following:

Questions 3.1.1: Do you agree, as a general principle, that food derived from organisms containing new pieces of DNA should be captured for pre-market safety assessment and approval? Should there be any exceptions to this general principle?
We do not think that it is sensible, proportionate and effective to have a pre-market safety assessment and approval by authorities for all (micro-) organisms containing new pieces of DNA. What needs to be considered a new piece of DNA? A single base change, a change of e.g. 5 nucleotides, or introduction of an entire functional gene? We call for a product-centric and risk-based approach where the regulatory process and burden is proportionate to the (extent of) changes in the product or production organism, and the associated risks. This may translate into a system where some products or production organisms are not subject of regulatory assessment (e.g., substances substantially equivalent to what could be isolated from nature or could be caused by classical mutagenesis, do not lead to GMMs requiring regulatory assessment), while others may be subject to a clearly defined notification process (allowing timely introduction of innovations in the market; e.g. products or production organisms with a single or a few base substitutions in metabolic genes), and still others need to undergo a full pre-market safety assessment and approval process (e.g., products or production organisms with extensive genetic modifications, or with impacts of potential safety concern on sequences or side products).
Please note that it is a sine qua non for every producer to only introduce and place safe products on the market, independently of the regulatory process to be followed.

Questions 3.1.2: Should food from null segregant organisms be excluded from pre-assessment and approval? If yes, should that exclusion be conditional on specific criteria and what should those criteria be? If no, what are your specific safety concerns for food derived from null segregants?
As outlined above, we call for a product-centric regulatory approval scheme, where the final product determines the regulatory status and burden, not the process how a certain product or production organism has been obtained. Therefore, if a genetic modification is only used transiently, but is no longer present in the final product or production organism (as is the case for null segregants), <u>and</u> if it can be shown that, indeed, the genetic modification is no longer present (e.g., by genome sequencing or by more targeted genetic techniques), the transient use should <u>not</u> determine the regulatory status and burden.

Questions 3.1.3: Are foods from genome edited organisms likely to be the same in terms of risk to foods derived using chemical or radiation mutagenesis? If no, how are they different? If yes, would this apply to all derived food products or are there likely to be some foods that carry a greater risk and therefore warrant pre-market safety assessment and approval?
There is no straightforward answer to the questions raised here. Genome editing can be more subtle than chemical or radiation mutagenesis. For instance, with its high precision, genome editing can be used to introduce a single base substitution. On the other hand, for chemical or radiation mutagenesis, next to the beneficial mutation screened for, there may be a number of background mutations, with

unknown impacts on the metabolism of the organism. The screening after chemical or radiation mutagenesis is often based on phenotype, therefore the genotypic changes are not assessed and phenotypic changes not selected for can also be missed. Still, genome editing can also be used to introduce more extensive genetic changes (e.g., introduction of one or multiple heterologous genes) which would not be possible with reasonable effort by applying classical mutagenesis techniques alone. In all cases, the risk is dependent on the changes made, not on the process used. Both conventional and new techniques can be used to make changes with no risks attached as well as changes with potential risks attached. Therefore, basing the regulation only on the process is not actually predictive of the possible risks.

Questions 3.2: Are you aware of other techniques not currently addressed by this paper which have the potential to be used in the future for the development of food products? Should food derived from other techniques, such as DNA methylation, be subject to pre-market safety assessment and approval?

As there will always be technological developments that we may anticipate or not, a process-centric approach will inherently risk becoming outdated as soon as some non-anticipated technological developments happen. Again, a product-centric approach is far less prone of becoming outdated with technological developments, and focusses on aspects of a product or production organism that truly matter. Therefore, a change towards a product-centric regulation would be highly advantageous, as then the issues of outdated regulations due to the appearance of a new technique would not happen.

Questions 3.3: Do you think a process-based definition is appropriate as a trigger for pre-market approval in the case of NBTs? If no, what other approaches could be used? If yes, how could a process-based approach be applied to NBTs? Are there any aspects of the current definitions that should be retained or remain applicable?

With the New Breeding Techniques it is possible to create products which are completely indistinguishable from products which have been created via the more conventional techniques. Identical end products with different processes would then be differently regulated, even though there is no clear risk difference. If the regulation is process-centric, there will always be uses which are on the edge of two different regulations, and there will always be unclarity, pushing for the solution which has the lesser regulatory burden. The aim of the regulations should be to protect against possible risks, therefore this can best be done by regulating the end-product and the possible risks it contains, independent of the method used to create it. In conclusion, a process-centric regulation is not appropriate and a product-centric regulation would be more suitable to cover NBTs and other possible future techniques.

Questions 3.4: Are there other issues not mentioned in this paper, that FSANZ should also consider, either as part of this Review or any subsequent Proposal to amend the Code?

Rather than raising additional issues, we would find it important to define the policy objectives that should be achieved with an possible revision/amendment of the Code. The consequences of a simplistic, binary (GMO vs. non-GMO), process-centric perspective are well known in the meantime, and trying to fit new technologies into 'corset' will not resolve the fundamental issues associated with this approach. Therefore:

- *Are NBTs/genome editing (and modern biotechnology in general) seen as a promising and important means towards a more sustainable future, and an indispensable tool to address some of the socio-economic challenges in the provision of sufficient, healthy food globally?*
- *Should the aim be to create a regulatory environment for NBTs/genome editing that encourages innovation in this field?*

- *Should the aim be to secure engagement of and endorsement by the public by focusing the discussion primarily on the benefits of the products, rather than on the technological processes how they have been produced?*

If so, now (i.e., with the advent of the genome editing technologies) would be the time for a fundamental shift from a primarily process-centric to a primarily product-centric regulatory framework. We hope for the required courage and vision to make this change happen.

Many thanks in advance for your consideration of these remarks

Kind regards,

Patrick Fox
AMFEP Secretary General