Commentary

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Recent Advances and Future in Livestock for Animal Feeing

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Description

Methods and approaches that can be used in food and nutrition research are changing at a faster pace than ever. With regards to methods and approaches used to study the safety of foods and food ingredients, these have been reviewed in Part I and include the development of thresholds of toxicological concern (TTC), read-across and grouping strategies, adverse outcome pathways (AOPs) and associated in vitro assays to determine perturbations to key events in AOPs. Members of the International Life Sciences Institute (ILSI) Europe have formed an expert group to review possibilities, opportunities and challenges for the potential use of non-animal testing strategies in nutrition research, which can ultimately be used in support of regulatory submissions for pre-market authorisation. In this article, non-animal methods or approaches refer to the 3Rs concept (Replacement, Reduction and Refinement), meaning the use of animal-free methods when and where possible, but any opportunity to reduce or refine would also be appropriate.

This article is part of a series evaluating the current legislative requirements in Europe in the field of food safety and nutrition research in light of the use of animal testing and opportunities for transformation or a paradigm-shift. Furthermore, it informs about approaches and methods to contribute to this transformation, following the principles of the 3Rs that were developed over 50 years ago. In section II, EU legislation pertaining to nutrition research and assessment are generally discussed with regards to animal and non-animal testing requirements. Section III discusses legislation of specific food groups, and section IV reviews regulations dealing with health claims on foods. Section V informs about approaches and methods with the potential to contribute to a shift to non-animal testing strategies in nutrition research and assessment, focussing on organoid cultures, organ-on-a-chip systems, and gastrointestinal tract simulators. In so doing, the article provides a framework for non-animal testing strategies for nutrition assessment to meet testing demands now and in the future.

European Food Safety Authority

EU food legislation aims to serve two main aims: firstly, to reach the highest level of consumer protection from both unsafe substances and from being misled; and secondly, to ensure the effective functioning of the internal European market. In 2002, Regulation (EC) No 178/2002 (European Commission, 2002a) entered into force that lays down the general principles and requirements of food law (known as the General Food Law (GFL)). This framework regulation also establishes the European Food Safety Authority (EFSA).

The number of experimental animals used for scientific research is mostly composed of rodents (more than 95%) and it is expected to reduce as more and more alternative, non-animal testing methods or reduction and refinement methods as part of the 3Rs concept are being employed. In fact, all testing carried out in Europe shall comply with the requirements laid down in Directive 2010/63/EU (European Commission, 2010) on the protection of animals used for scientific purposes, which requires to replace, reduce, and refine the use of experimental animals. This Directive is based on Article 13 of the Treaty on the Functioning of the European Union (TFEU) that requires both the Union and individual Member States to 'pay full regard to' protection and welfare of animals. Compliance with this 3Rs principle is a legal obligation in the EU for research activities as well as regulatory testing using live animals since the Directive 2010/63/EU came into force in 2013. This Directive is a horizontal piece of legislation and applies to testing conducted under sector legislation like the specific regulations dealing with food safety aspects: food additives or supplements, novel foods, genetically modified organisms (GMO) foods or food susceptible of nutritional and/or health claims. As Article 13 of the Directive outlines, replacement approaches to an existing animal method must be used if "another method or testing strategy for obtaining the result sought, not entailing the use of a live animal, is recognised under the legislation of the Union." Concerning reduction or refinement of animal procedures, the Directive demands to select the method that "uses the minimum number of animals; involves animals with the lowest capacity to experience pain, suffering, distress or lasting harm and causes the least pain, suffering, distress or lasting harm and is most likely to provide satisfactory results".

Mechanism of Selenium

It is postulated that most of the antioxidant effects of Se are likely exerted by its presence in the form of catalytically active residues, SeMet, in reactive oxygen species (ROS)-detoxifying selenoenzymes. Se-containing proteins (selenoproteins), including glutathione peroxidase (GPx) (Chang et al., 2020; Sharma et al., 2021), TrxR, and selenoprotein P (SeP), are primarily implicated in maintaining redox homeostasis and

reversing cell apoptosis induced by oxidative stress-related factors, suggesting that selenoproteins may protect against oxidant-induced toxicity in cells. The expression of selenoproteins is strictly controlled by the Se translation process, which is highly dependent on the full utilization of Se.

In addition to being present at the catalytic site of enzymes, Se compounds are implicated in direct redox reactions, with presumably higher rate constants for reactions with multiple oxidants than its sulfur analog due to the nucleophilic properties of ionized selenol and the ease of oxidation of Sec and SeMe. Notably, accumulating evidence has emerged regarding the effects of a super physiological Se dose on generating oxygen radicals by inducing oxidation and cross-linking of protein thiol groups essential for cell survival. These contradictory roles pose new challenges to the development and application of Se in livestock production.