EMPIR Call 2015 – Health, SI, Normative and Research Potential

Selected Research Topic number: **SRT-h05**
Version: 1.0

Title: Metrological infrastructure for emerging food contaminants by innovative analytical tools

Abstract

Mycotoxins occur in a wide variety of food and feed commodities, and are of major public health concern because they are the most hazardous of all food and feed contaminants in terms of chronic toxicity.

About 25 % of the world's food crops are contaminated with mycotoxins posing a severe health risk to humans. While priority mycotoxins are already regulated by maximum levels and controlled by official methods, there also exist modified “masked” forms of these mycotoxins which are not regulated in this manner. Therefore there is a need to provide the metrological infrastructure to enable traceable and comparable measurements of these modified mycotoxins in food.

Keywords

Food safety; traceable analytical methods; matrix reference materials; toxic food contaminants; modified mycotoxins; masked mycotoxins

Background to the Metrological Challenges

In the past decade, it has become clear that in mycotoxin-contaminated commodities, many structurally related compounds coexist with their free mycotoxins, defined as modified mycotoxins.

Modified (often called “masked”) mycotoxins are found in plants resulting from plant defence reactions after fungal infection or are produced by the fungus itself. Modified mycotoxins are metabolites of the parent mycotoxin, e.g. by conjugation with endogenous hydrophilic (polar) molecules. Modified mycotoxins may remain undetected by analytical methods, potentially causing underestimation of mycotoxin exposure. As modified toxins represent an emerging issue, it is not surprising that toxicological data are scarce, but several studies highlight the potential threat to consumer safety from these substances. Despite demonstration of the natural occurrence of modified mycotoxins, there are no directives, regulations or recommendations in food and feed taking these modified derivatives into account. One of the major reasons is the lack of a metrological infrastructure. Certified reference materials (CRM) and traceable calibration standards are largely or wholly commercially unavailable.

During the last decade liquid chromatography coupled to tandem mass spectrometry (LC-MS/MS) became the method of choice for mycotoxin analysis due to its high sensitivity, selectivity and capability for multi-analyte measurement. However, sensitivity shifts of the MS/MS-system and matrix (suppression) effects require the use of internal standards to obtain accurate results. For that purpose isotopic labelled standards are preferred which are commercially available for all EU regulated mycotoxins. In contrast, isotopic labelled standards are urgently needed for toxins currently under discussion for EU regulations and addressed by CEN mandate M/520 as well as for emerging enniatins and modified mycotoxins to ensure accurate LC-MS/MS quantification. To close this gap ^{13}C-, ^{2}H- and/or ^{15}N-isotopic labelled internal standards have to be developed and implemented in analytical methods.

Objectives

The JRP shall focus on an integrated approach for the development of metrological capacity and the metrology research necessary to support standardisation in this area. The overall objective is to establish a sustainable metrological infrastructure enabling reliable quantification of emerging food contaminants, in particular modified mycotoxins.

EURAMET MSU, Hampton Road, Teddington, Middlesex, TW11 0LW, UK
Phone: +44 20 8943 6666 Email: msu@npl.co.uk
msu.euramet.org

The EMPIR initiative is co-funded by the European Union's Horizon 2020 research and innovation programme and the EMPIR Participating States

The specific objectives are:

1. To develop and to characterise traceable calibration standards of native and isotopic labelled mycotoxins. Native conjugates (glucosides, sulphates, acetates) of priority *Fusarium* mycotoxins to be prepared by chemical and/or biochemical synthesis. Isotopic labelled standards (^{13}C, ^{2}H and ^{15}N) of these modified mycotoxins and other groups of mycotoxins relevant for upcoming regulations) to be prepared
2. To develop and to characterise SI traceable matrix reference materials (RM) for mycotoxins with very low uncertainty values. Authentic food products to be produced and screened for modified mycotoxins, identification of co-occurrences and possible correlations of (modified) mycotoxins identified. Candidate RMs to be selected and prepared based on their natural mycotoxin contents - success criteria for RM suitability to be proven homogeneity assessed by ANOVA and sufficient stability tested by an isochronous scheme. At least 6 different matrix RMs to be prepared and characterised for subsequent validation studies.
3. To develop and to validate analytical methods for purity determination of modified mycotoxins and investigate harmonisation in case of already existing standard methods. The focus to be on efficient, solvent saving extraction and clean-up methods and sensitive (multi-analyte) measurement methods, implementation of the developed isotopic labelled standards to improve measurement accuracy (trueness and precision). Final method validations to be performed by both an intra-laboratory study and external studies by inter-laboratory comparison.
4. To transfer and to disseminate project results which significantly improve metrology in support of food safety and health protection, i.e. the achieved knowledge and developed technologies (traceable standards, innovative measurement methods and reliable reference materials for emerging mycotoxins). Furthermore, a food sample survey will be performed to extend the data base for the assessment of modified mycotoxins.
5. To work closely with the European and International Standards Developing Organisations, and the users of the Standards they develop, to ensure that the outputs of the project are aligned with their needs, communicated quickly to those developing the standards, and in a form that can be incorporated into Standards at the earliest opportunity.

These objectives will require large-scale approaches that are beyond the capabilities of single National Metrology Institutes and Designated Institutes, and it is expected that multidisciplinary teams will be required. To enhance the impact of the research, the involvement of the appropriate user community such as medical practitioners, medical (academic) hospitals and industry is strongly recommended, both prior to and during methodology development.

Proposers should establish the current state of the art, and explain how their proposed project goes beyond this.

EURAMET expects the average EU Contribution for the selected JRPs in this TP to be 1.8 M€, and has defined an upper limit of 2.1 M€ for this project.

EURAMET also expects the EU Contribution to the external funded partners to not exceed 35 % of the total EU Contribution to the project. Any deviation from this must be justified.

Any industrial partners that will receive significant benefit from the results of the proposed project are expected to be unfunded partners.

Potential Impact

Proposals must demonstrate adequate and appropriate participation/links to the “end user” community, describing how the project partners will engage with relevant communities during the project to facilitate knowledge transfer and accelerate the uptake of project outputs. Evidence of support from the “end user” community (e.g. letters of support) is also encouraged.

You should detail how your JRP results are going to:

- Address the SRT objectives and deliver solutions to the documented needs,
- Feed into the development of urgent documentary standards through appropriate standards bodies,
- Transfer knowledge to the health and food sectors.

You should detail other impacts of your proposed JRP as specified in the document “Guide 4: Writing a Joint Research Project”

You should also detail how your approach to realising the objectives will further the aim of EMPIR to develop a coherent approach at the European level in the field of metrology and include the best available contributions from across the metrology community. Specifically the opportunities for:

- improvement of the efficiency of use of available resources to better meet metrological needs and to assure the traceability of national standards
- the metrology capacity of EURAMET Member States whose metrology programmes are at an early stage of development to be increased
- organisations other than NMIs and DIs to be involved in the work

Time-scale

The project should be of up to 3 years duration.