

The role of organic chemical metrology in food safety for South Africa

Speaker / Author: Maria Fernandes-Whaley

National Metrology Institute of South Africa (NMISA)
P/ Bag x34, Lynnwood Ridge, Pretoria, 0040, South Africa
e-mail: mfwwhaley@nmisa.org
Phone: 012 841 2105 Fax: 086 509 5996

Abstract

Food safety refers to the assurance that food will not cause harm to the consumer when prepared and/ or eaten according to its intended use (Codex). Part of this assurance is established through legislation setting maximum tolerable limits for natural or man-made chemical contaminants/ residues present in food. The accurate measurement of these contaminants is important not only for the consumer but also for the producer. Incorrect measurements will have serious financial implications for the food industry.

Measurement accuracy or “trueness” may be established through the use of certified reference materials or through traceable reference measurements. The organic laboratory at the NMISA is available to assist South African analytical laboratories in obtaining traceability to the SI units and ensuring global measurement equivalence through the provision of these services which demonstrate “trueness”.

With the recent spate of melamine contamination in animal feed and foodstuffs, the SA Department of Health has introduced new regulations concerning the maximum tolerable levels for melamine in food. Given the urgent need for reliable measurements, the NMISA is working on the development of a reference measurement service for melamine in milk. This will be followed with similar work on melamine in animal feed.

In the past year the NMISA organic laboratory has investigated the measurement infrastructure for mycotoxin analysis in SA. Mycotoxins are toxic secondary metabolites released by fungi growing on various agricultural commodities, e.g., maize, wheat, nuts, wine and coffee beans. These toxins exhibit toxic, carcinogenic and estrogenic properties that are harmful to human health.

This presentation will focus on the survey results in terms of laboratory needs including accuracy, traceability and staff competency. It will also elaborate on the process that the NMISA is following in order to provide a reference measurement service and to produce a fully characterized maize reference material for mycotoxins.

1. Introduction

Agricultural commodities, whether domestically produced, imported or exported, need to be tested locally by competent analytical laboratories on which the responsibility rests to ensure food safety prior to human/ animal consumption.

Local analytical laboratories that are deemed competent are usually those that have obtained accreditation through the South African National Accreditation System (SANAS). To obtain accreditation the laboratory has to demonstrate fully validated analytical procedures. Part of the validation process involves the use of a certified matrix reference material to verify the accuracy of the measurement result obtained using the analytical procedure. An additional requirement for demonstrating competence is through participation in proficiency testing schemes for the target analytes in specific matrices [1].

The Metrology in Chemistry (MiC) division at the NMISA was established to assist analytical laboratories in obtaining traceability to the SI units to ensure global measurement equivalence through services such as higher order reference measurements and through the provision of certified reference materials (CRMs) [2].

Traceability by definition is a “property of a measurement result whereby it can be related to a reference through a documented unbroken chain of calibrations, each contributing to the measurement uncertainty” [3]. This tracing back of all measurements to a common reference ensures that all measurement results are comparable and their equivalence may be determined. Figure 1 depicts a flow diagram of the NMISA organic laboratory’s approach to providing traceability to analytical laboratories in South Africa.

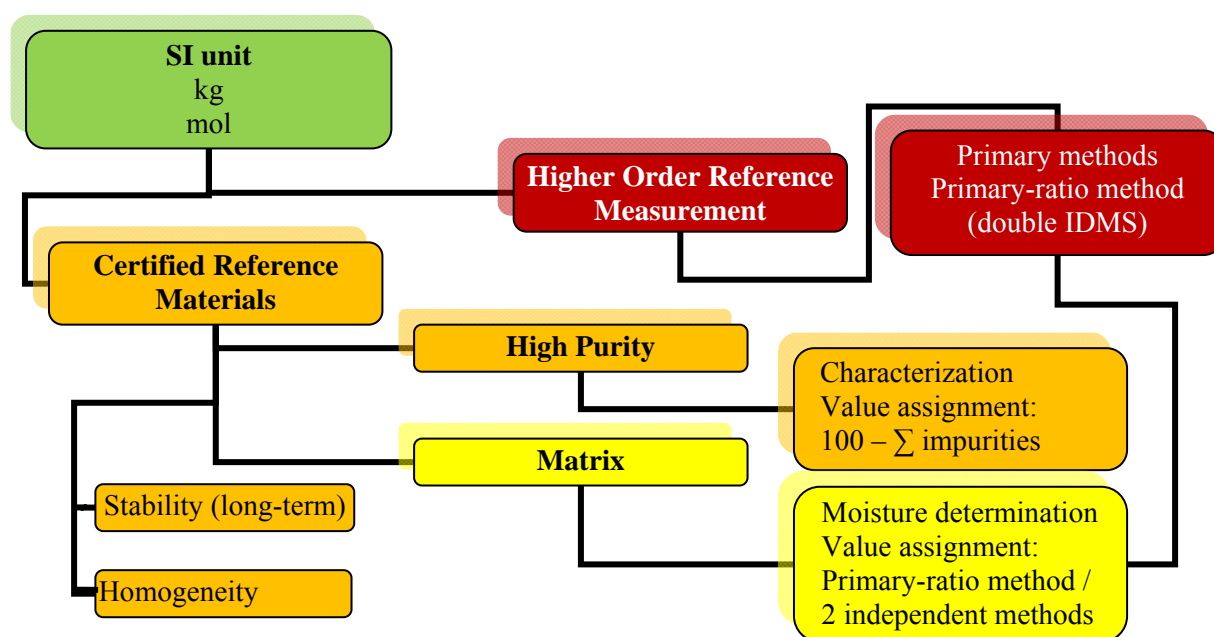


Figure 1 NMISA organic laboratory approach towards provision of traceability to analytical laboratories

For certification purposes, primary methods and primary-ratio methods are often used for value assignment as they immediately provide traceability to an SI unit without requiring calibration (such as secondary methods). Double isotope dilution mass spectrometry, a primary-ratio method typically used in the organic laboratory, is expensive but yields accurate measurement results traceable to the SI with small uncertainties [4].

Other NMIs have different approaches to value assignment, for reference measurements or towards the production of CRMs. The various options are also described in guide ISO Guide 34 concerning the production of reference materials [5]. For example, NIST in the U.S.A, the oldest established NMI, often uses 2 to 3 independent methods (from sample extraction to

analytical technique) to obtain a measurement result, if these results agree within a certain range, the mean of these results then becomes the assigned value and the uncertainties for each result are combined to assign the associated measurement uncertainty. Typically, LGC in the U.K., and NMIA in Australia, apply double isotope dilution MS for all reference measurements and materials. The Institute for Reference Measurements and Materials (IRMM) in Belgium select competent (ISO 17025 accredited) laboratories and then these laboratories perform the measurements. Usually 15 laboratories are selected, so that a good estimate is achieved, the submitted results are then assessed, outliers removed, etc. The mean of the accepted values together with their combined measurement uncertainties are then used to assign the value to the CRM. Information concerning how the CRM was prepared and value assigned may be obtained from the certificate of analysis or certification report [6].

South African legislation, particularly with respect to food safety, serves as a guideline to the NMISA indicating which analytes are important for accurate quantitation in specific matrices. This year the SA Department of Health rapidly introduced legislation establishing minimum acceptable levels for melamine in food. This meant that several laboratories had to develop methods (as no official methods existed at the time) for the extraction and analysis of melamine from primarily milk, milk products and animal feed [7, 8]. There are also several established regulations for mycotoxins in food and animal feed conveying the need for reliable measurement results [9].

The need for reference materials was recognised when incorrect recovery results were obtained through experiments involving spiking of a known amount of analyte into a blank matrix. A disadvantage of spiking is that it is not a true representation of the naturally incurred analyte and its *in-situ*-produced analogues. For example, initial measurements of melamine were underestimated as it was only later discovered that melamine, when hydrolysed, forms cyanuric acid. Melamine, through hydrogen bonding, forms a tightly bound complex with cyanuric acid in the matrix. Extraction conditions used at the time were not sufficient to break this complex and the amount of melamine present was underestimated [7].

In this paper the NMISA organic laboratory's approach to providing traceability to analytical laboratories will be discussed. In brief, the NMISA is currently focusing on establishing reference methods for analytes of national importance with regard to food safety. With additional human and capital resources the next step is to start producing high purity calibration solutions and matrix reference materials. The reference materials, over the short-term, may be used for proficiency testing and progress into a certified matrix reference material.

2. NMISA Organic Laboratory Measurement capability for food safety

The organic laboratory is in the process of demonstrating its ability to perform measurements on several organic substances relating to food safety. Whenever possible, the NMISA organic laboratory benchmarks its capability through participation in international comparisons with other NMI's. These comparisons are organized by the Consultative Committee for amount of substance (CCQM) [10].

According to the Food Safety Initiative of the Consumer Goods Council of South Africa [11], the substances of concern with regard to food safety can be divided into the following categories:

1. Pesticide residues
2. Veterinary drug residues
3. Mycotoxins
4. Migration from materials and articles in contact with food
5. Processing contaminants
6. Industrial and environmental chemicals

Elaboration on each of these categories will indicate that the organic laboratory has already demonstrated or is in the process of demonstrating competence in a number of these categories, see table 1 below.

Table 1 Summary of the Food Safety Initiative (FSI) priority categories and the current measurement capability of the NMISA organic laboratory.

<i>FSI category</i>	<i>Current NMISA benchmarked measurements</i>	<i>Current NMISA projects</i>
Pesticide residues	Pesticides in solution by GC-MSD CCQM P31c-1	Persistent Organic Pollutants project: Chlorinated pesticides, PCBs, dioxins and furans (various matrices) by GCxGC-ID-TOFMS.
Veterinary drug residues	The extraction of chloramphenicol in milk and analysis by LC/MS/MS CCQM P90	Preparation for the extraction of chloramphenicol in pork muscle tissue and analysis by LC/MS/MS (CCQM P122)
Mycotoxins		Mycotoxin project: Ochratoxin-A in wine; Mycotoxins in maize (LC/FLD and LC/MS/MS)
Processing contaminants		Melamine project: The extraction of melamine and related analogues in milk by LC/MS/MS Methoxypyrazines in wine by SPME GC-TOFMS
Industrial and environmental chemicals	PAHs in mussel tissue (marine) & soil by GC-MSD and GC-TOFMS. CCQM P31a-1	Persistent Organic Pollutants project: PAHs in soil & sediment by GCxGC-TOFMS. Brominated flame retardants in plastic, GC-TOFMS.

3. The NMISA mycotoxin project (2008-2011)

Mycotoxins are toxic secondary metabolites released by fungi growing on various agricultural commodities, e.g., maize, wheat, nuts and coffee beans [12]. These toxins exhibit toxic, carcinogenic and estrogenic properties that are harmful to human health. Table 2 summarizes the most common harmful mycotoxins occurring in various foodstuffs and their effect on human and animal health [12, 13].

Table 2 Summary of harmful mycotoxins in various foodstuffs [12, 13]

<i>Mycotoxin</i>	<i>Producing organism</i>	<i>Foodstuffs</i>	<i>Toxicity impact</i>
Aflatoxins (B1, B2, G1, G2 and M1)	<i>Aspergillus flavus</i> <i>Aspergillus parasiticus</i>	Grains (maize) Groundnuts Nuts Dried fruit Milk Spices Cereals Infant formula	Liver disease in animals Carcinogenic Mutagenic Human carcinogen (Aflatoxin B1)
Deoxynivalenol (Vomitoxin, DON)	<i>Fusarium graminearum</i> <i>Fusarium culmorum</i>	Wheat Maize Oats Cereals Bread Pasta	Vomiting syndrome (vomiting upon intake) Immunosuppressant
Fumonisin (FB1, FB2 and FB3)	<i>Fusarium moniliforme</i> <i>Fusarium proliferatum</i>	Maize Maize-based foods: Meal Oil Beer	Oesophageal cancer Liver disease Leukoencephalomalacia in horses
Ochratoxin A	<i>Aspergillus ochraceous</i> <i>Penicillium verrucosum</i>	Cereals Dried vine fruit Roasted coffee beans Soluble coffee Wine Grape juice	Kidney toxin Animal carcinogen Causative agent in human Balkan Endemic Nephropathy
Patulin	Several fungi belonging to genera <i>Aspergillus</i> and <i>Penicillium</i>	Fruit juices Apple derived spirit/fermented drinks Cereals	Suspect carcinogen Antibiotic properties
Zearalenone	<i>Fusarium graminearum</i>	Wheat Maize Oats Cereals Bread	Endocrine disrupting compound – estrogenic effects

The risks posed by mycotoxins have prompted the introduction of several international regulations. The European Commission regulation (EC) No 1881/ 2006 sets maximum levels for certain contaminants in foodstuffs [14]. The regulation, stating a maximum level of 200 µg/ kg fumonisins (sum of B1 and B2) in processed maize-based dried foods and dry baby foods for infants and young children, was effective from 1 October 2007 [14]. The same maximum level was set for deoxynivalenol in processed cereal-based dried foods and dry baby foods for infants and young children, i.e., foods originating from wheat/ oats/ maize [14].

Contamination of the commodity can occur prior to harvesting or during post-harvest storage. Fungal growth is an extremely common problem in regions where traditional storage methods are used, e.g., in the former Transkei and parts of Africa where hot and humid conditions prevail. Most mycotoxins are chemically stable and tend to survive storage and processing even at elevated temperatures [12, 13].

Viljoen [15] investigated the prevalence of mycotoxins in grain and grain products in South Africa. Deoxynivalenol occurs regularly in domestic wheat [15], while fumonisin B group mycotoxins occur most frequently in domestic maize. Aflatoxins are nearly absent in SA maize [15]. The most abundant toxin in maize is fumonisin B1, which has been classified as possibly carcinogenic to humans by the World Health Organization [15]. The Medical Research Council PROMEC unit in Cape Town performs investigations focused on the identification of the toxins and carcinogens produced by *Fusarium* species [16]. Their aim is to determine cancer incidence and investigate the control and prevention of fungal infections in rural communities [16].

Currently, there are no certified matrix reference materials or established PT schemes for mycotoxins being produced or organized in Africa. The NMISA will be the first NMI in Africa to provide this service, initially for South Africa, and in due course for the entire continent.

The mycotoxin project was a feasibility study undertaken in two parts. The first part was to establish the existing mycotoxin analytical infrastructure in SA, and what role the NMISA could play in providing traceability to these laboratories. This was achieved by sending out a survey to all laboratories involved in mycotoxin analyses.

The second part was to evaluate extraction and analysis techniques for the determination of Ochratoxin-A in wine (South Africa's most important agricultural product) and for selected mycotoxins in maize (South African staple diet).

Since the discovery of mycotoxins in the early 1960's, several analytical techniques have been established to monitor toxin levels in various foodstuffs. Figure 2 shows the combination of extraction and analytical techniques currently being applied in SA laboratories as established through the NMISA mycotoxin survey.

These techniques range from simple tests which are cheap and do not require skilled operators (TLC, ELISA, ROSA strips and fluorometry), to modern and expensive techniques requiring highly skilled operators (HPLC, GC and LC-MS/MS). The difference between the two extremes lies in the certainty with which each toxin can be identified and quantified. Such certainty often prevents the unnecessary rejection/ destruction of an entire consignment

for export/ import. Although it should not be necessary to use the latest analytical instrumentation, the measurement result needs to be accurate within a specified uncertainty.

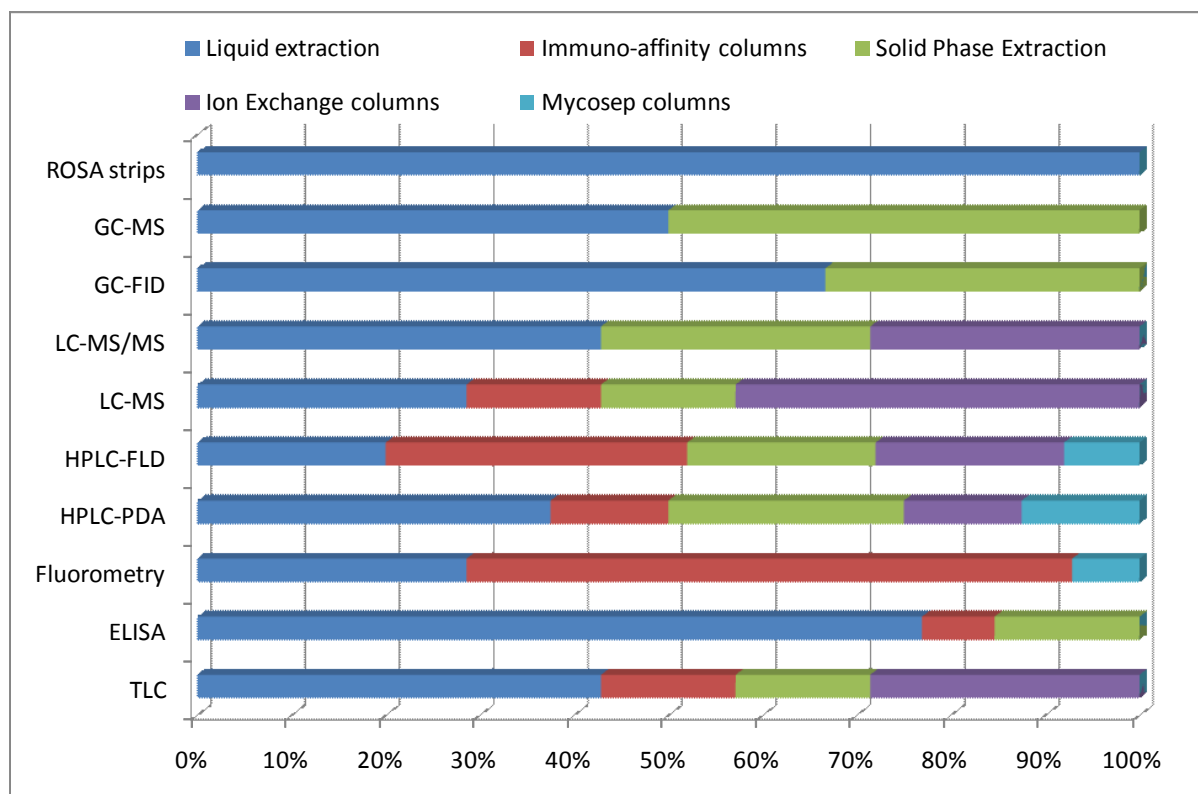


Figure 2 Current extraction and analytical techniques applied in SA laboratories for mycotoxin analysis

General problems experienced by SA laboratories involved in mycotoxin analysis include the following:

3.1. Lack of competent technicians

Most laboratories are struggling to find competent technicians, and once trained, they struggle to retain their staff. Students leaving tertiary academic institutions do not have the minimum skills required to work in a laboratory. There appears to be a need for basic literacy and numeracy skills training in the country. This is not a new problem; the issue is the theme of this year's T&M conference and has already been raised at earlier T&M conferences [18, 19].

3.2. Reliable calibration standards

There was one reported incident where the concentration provided by the supplier was incorrect and led to an incorrect result in the laboratory's PT scheme participation. It was also a time-consuming exercise to trace back to the source of the error.

Some laboratories are using their own isolated and purified toxins, or preparing calibration solutions from purchased solid toxins. Apart from being a hazardous process, assigning the concentration value using UV absorption may be incorrect

when the inappropriate solvent is used, the instrument is not functioning correctly or when the analyst is not competent.

3.3. Lack of appropriate/ applicable (C)RMs

In the case of one specific laboratory, there are no other laboratories in South Africa performing the same type of measurement for mycotoxins in animal muscle/ tissue. Often there are no (C)RMs available for specific analytes in specific matrices, they must occasionally send samples overseas for reference measurements at great expense. Alternatively, the laboratory must resort to blind spiking of a “blank” matrix. In these cases the spike at times behaves differently to the naturally incurred material particularly during extraction procedures, where the analyte is naturally bound to the matrix content, e.g., lipids or proteins.

Certain laboratories were concerned that toxin types and levels in PT samples are often not applicable to the South African toxin types and levels in their respective matrices.

Reference materials that are currently available are typically a single mycotoxin (excluding the aflatoxins) per matrix. The ideal situation would be to have several mycotoxins characterized in a single matrix.

3.4. Access to information

A few laboratories do not have access to information, e.g., information on representative sampling procedures, suppliers of analytical reagents and reference materials, estimation of uncertainty training courses, particularly on other laboratories involved in mycotoxin analysis to which they may refer potential clients.

3.5. Finances

Laboratories have to compromise on the analytical techniques used for mycotoxin measurements as farmers and processors cannot afford the cost of analysis but still require an accurate measurement result.

Clients prefer to use accredited laboratories but do not wish to pay for the cost of analysis which is typically higher than those from non-accredited labs.

Laboratories cannot afford to obtain and maintain accreditation.

Laboratories can no longer afford to regularly participate in international PT schemes. This is a requirement for proving the continued competency of the analyst. A major limitation in Africa is the lack of resources and funding which would allow laboratories to provide better quality measurements [17]. Generally, exporting agricultural commodities to Europe or America requires a certificate of analysis from an accredited laboratory, indicating that the commodity falls below the regulated maximum levels of contamination [17].

Sample sizes from PT schemes are not large enough to be used as control samples at a later stage.

A definitive conclusion of the mycotoxin survey conducted in 2008-2009 was that laboratories, being diverse in purpose and funding, require some confirmation that their measurement result is correct despite the “low cost” of extraction and analysis techniques applied. It was also established that maize is one of the commodities analysed frequently in SA.

It was recommended that the NMISA organic laboratory assist the measurement community by providing a maize reference material that certifies the entire mycotoxin content, and not only those currently regulated by the Department of Health. In addition, the NMISA organic laboratory should assist the measurement community by providing a proficiency testing scheme for maize to all identified interested laboratories. However, these services are reliant on sufficient funding from the government, through the Department of Trade and Industry.

The NMISA is in the process of developing a reference method for the extraction and analysis of 11 mycotoxins in maize by LC-MS/MS. However, only 6 of these will be quantified by isotope dilution mass spectrometry due to limited funding and isotope availability. The work still required for this measurement involves the optimization of extraction conditions for all the mycotoxins present in the maize, optimizing the cleanup procedure and ensuring complete isotope equilibration.

4. The NMISA Melamine project (2009-2012)

Melamine is a nitrogen-based compound used in industrial and commercial plastics that can cause kidney failure and ultimately death when consumed at certain levels. It has been found in infant formula and other milk products as a result of the producing animal consuming feed that has been deliberately contaminated with melamine to artificially raise the protein content. The protein content of animal feed is directly proportional to its monetary value [7].

Several deaths due to renal failure were reported. In 2007, several pets died from eating food contaminated with “gluten 60” from China. In 2008, milk and milk products from China were deliberately contaminated with melamine causing the death of infants, mostly in Asia. Melamine is used as a masking agent for addition of water to milk. In SA milk was contaminated due to animal feed contamination with maize gluten [8].

New South African draft regulations stipulate melamine levels within foodstuffs at 1 mg/ kg for infants (< 36 months) and 2.5 mg/ kg for all other foodstuffs. Contravention of the proposed levels is a criminal offence. These levels have been confirmed by the World Health Organisation (WHO) as adequate to ensure sufficient protection of the health of consumers (December 2008). The draft regulations are also available on the webpage of the Directorate at: http://www.doh.gov.za/departement/dir_foodcontr-f.html [9].

Melamine testing has therefore become a necessity for any manufacturer or importer of foodstuffs in South Africa.

Several laboratories in SA now measure melamine using a variety of analytical techniques. It is imperative that the NMISA be competent in the extraction and analysis of melamine from milk in order to provide a measurement result that ensures traceability to the kilogram. The

value assignment of melamine in milk may then be offered as a reference measurement or reference material to laboratories seeking the reassurance that their analytical method validation (regardless of technique) is accurate.

Sample preparation will involve the extraction and cleanup of milk on solid phase-ion exchange extraction (SPE) cartridges followed by concentration and reconstitution. The components in the extract may be separated by Ultra Performance Liquid Chromatography (UPLC) using HILIC column technology and analyzed by positive electrospray ionization tandem mass spectrometry (ESI-MS/MS). The method itself is not novel; however it will provide traceability to the kilogram and the application of isotope dilution will guarantee a smaller measurement uncertainty than those obtained by commercial laboratories. The use of isotope dilution mass spectrometry must also be investigated. Melamine isotopes are available from Cambridge Isotope Laboratories (CIL). Another option would be to investigate a second alternative extraction and analysis technique that may be used to confirm the melamine concentration determined using the UPLC-ESI-MS/MS method. Derivatization of melamine and its related analogues followed by GC-MS analysis has been applied and will also be established if required.

The final output expected from this project is a fully validated extraction and analysis method for melamine in milk, using UPLC isotope dilution-ESI-MS/MS. The measurement result will include a complete uncertainty budget based on method validation data. The accuracy of our method may then be tested through participation in a FAPAS PT scheme or bilateral comparisons with the relevant NMIs.

5. Certified reference materials

5.1 High purity CRMs for calibration purposes

NMISA is currently benchmarking itself through international comparisons with other NMIs for the value assignment of high purity organic substances. Our successful participation in a suite of purity comparisons will demonstrate the NMISA's competency in value assignment that would allow us to start preparing our own high purity CRMs for calibration purposes.

A major finding with international mycotoxin PT schemes is that much of the variation arising between analytical laboratory results could be attributed to the source of the calibration standards used. Therefore most NMIs are now producing the high purity CRM together with the matrix CRM for analyses. For example, the Institute for Reference Materials and Measurements (IRMM) is supplying high purity deoxynivalenol (DON) CRM together with their DON in maize matrix CRM [21].

It was also a finding in the NMISA mycotoxin survey that reliable calibration standards are needed.

5.2 Purity assignments

A purity assessment involves two stages namely 1) identifying and 2) quantifying the components. These steps usually comprise of a suite of techniques and instruments, e.g., gas chromatography (GC), high performance liquid chromatography (HPLC), thin layer chromatography (TLC), nuclear magnetic resonance (NMR), titrimetry, differential scanning calorimetry (DSC), mass spectrometry (MS), thermal gravimetric analysis (TGA), Karl Fischer titrimetry, infra-red (IR) and ultraviolet (UV) spectroscopy [22].

Any material is a mixture that essentially consists of the primary or major component in the presence of impurity components [22]. The first stage in a purity assessment is the confirmation of the identity (qualification) of each of these components [22]. This requires the use of MS, IR, UV and/ or NMR [22]. At the NMISA, MS and UV are currently being applied.

The amount of substance, once qualified, can be quantified by one of two methodologies: 1) quantify the major analyte (the assay approach), or 2) subtract the sum of all impurities from 100 % [22]. The route taken is usually determined by the type of impurities identified and the analytical instrumentation available. Currently, the internationally accepted route is the latter.

Assays generally require a primary direct method of measurement, particularly when there is no CRM available for the measurand. This approach has to demonstrate specificity, i.e., ensure that only the major analyte is being measured.

When a secondary method is used for assay, excellent repeatability and accuracy are essential in order to achieve small uncertainties in the final measurement [22]. This is not readily achieved as the major component requires a large dilution before it is suitable for instrumental analysis. This dilution factor causes a large variation in the final result.

A generally accepted method of quantification of the major component is the process of quantification of all impurity components present and subtraction thereof from the original sample. However, missing an impurity could lead to errors in the final measurement result [22]. Hence the necessity exists for several measurement techniques, in order to fully quantify all impurities.

5.3 CCQM comparisons

The Organic Laboratory has participated in two international comparisons for purity assessment, namely CCQM P20.e: theophylline (1, 3-dimethylxanthine), and CCQM K55a: 17 β -estradiol. Theophylline is a widely used anti-asthmatic medication routinely tested by clinical and diagnostic laboratories. β -Estradiol is an estrogen typically used to regulate female hormone levels. No pure substance CRM is currently available for either theophylline or β -estradiol [24, 25].

The key comparison suite, K55, consists of the value assignment of four high purity substances where K55a was for β -estradiol, K55b will be for Aldrin (pesticide) and this will be followed by K55c (oxytetracycline, a veterinary drug) and K55d (fumonisin/ mycotoxin) although the latter two are yet to be confirmed. The idea behind the comparison suite is to value assign a range of analytes which cover non-polar to polar, lipophilic to hydrophilic, small to large molecule size, few to several isomers, those that are only “GC-analyzable” to those only “LC-analyzable” and a combination of the two.

For both comparison studies in which the NMISA participated, high performance liquid chromatography with diode array detection was used to quantify the individual components of the drug materials. Trace level impurities could be measured in the presence of excess major component with a %RSD of less than 0.5%.

In both comparisons, quantification of the organic impurities was readily achieved. For the theophylline comparison the sample was spiked with known impurities for which calibration standards were obtained. For the estradiol comparison the impurities had to be identified first. Fractions of the individual impurity HPLC peaks were collected, concentrated and analyzed by GC-TOFMS and LC-MS/MS. Some standards were commercially available, while others could not be purchased due to financial and time constraints. Peak area percentage was used to estimate the total organic impurity fraction using a wavelength of 220 nm.

In both cases the largest individual impurity was water. Incorrect determination here dramatically effects the final value assignment. In the theophylline comparison it was reported that the water determination by gravimetric loss on drying resulted in an overestimation of the NMISA result [26]. In the estradiol comparison, the laboratory had obtained a Karl Fischer Coulometric titrator, which allowed accurate quantification of the trace levels of moisture present in the sample. The NMISA final measurement result therefore estradiol compared well with other established NMIs.

5.4. Matrix CRMs for bias/ “trueness” determination

It was recommended that the NMISA organic laboratory assist the measurement community by providing a maize reference material that certifies the entire mycotoxin content, and not just those currently regulated by the Department of Health. This is a long-term project.

These materials require extensive homogeneity and stability testing to ensure a representative sample. Matrix CRMs are indispensable in the method validation process for establishing the accuracy of a measurement technique. Well characterized naturally incurred analytes within a matrix are always in demand as they are a better representation of the real sample than spiked matrices. Spiked analytes are not always “absorbed” into the matrix, particularly solids, and are often more easily extracted than the incurred analyte.

However, due to the labour intensiveness of producing such a material, not many are commercially available.

In South Africa most laboratories are evaluating their methods through participation in PT schemes such as FAPAS (Food Analysis Proficiency Assessment Scheme) [23], or through the use of reference materials (RM) from FAPAS and sample preparation/instrument suppliers. A RM, as opposed to a CRM, offers no traceability or uncertainty of measurement, but RM's are useful in quality control for assessing continued performance in the lab.

6. Conclusion

This paper presented some of the NMISA mycotoxin survey results in terms of laboratory needs including accuracy, traceability and staff competency. It elaborated on the process that the NMISA organic laboratory is following in order to provide a reference measurement service for melamine in milk and mycotoxins in maize. The reference measurement for maize serves as a stepping stone towards characterizing and certifying a maize reference material for mycotoxins. The NMISA participation in international purity assignment comparisons for benchmarking value assignment capability was also described towards the production of high purity CRMs for calibration purposes to be used in conjunction with matrix CRMs.

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