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CECALAIT'S NEWSLETTER

ANALYTICAL QUALITY CONTROL
THE COMPLEMENTARITY OF THE TOOLS

Summary of the talk by Mr. TROSSAT (CECALAIT) at CECALAIT's AGM 2006

Analysis laboratories adopt quality assurance systems in order to respond at best to requirements concerning the reliability of their results. The participation in proficiency tests and the use of standard reference materials are key elements among the various tools permitting to demonstrate and/or to control the accuracy and the traceability of the analysis methods applied by the laboratories. However, the use of only one tool is insufficient to ensure a satisfactory follow-up of the results accuracy. It is therefore necessary to establish a typical control program.

THE QUALITY ASSURANCE TOOLS

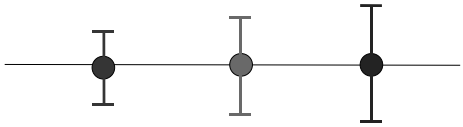
Laboratories have three principal quality assurance tools at their disposal:

- **Proficiency tests (PT)**: The frequency of these tests must be monthly to quarterly according to the matrix. Many samples, covering the measurement range of the method, are sent "in blind" to the participating laboratory. For each sample, a consensual assigned value is calculated from the results of all the participating laboratories (after selection according to the method applied and elimination of outliers). This tool permits to detect systematic or random deviations, level effects…
  Control of the homogeneity and stability permits to ensure the quality of the results for participating laboratories.

- **External standard reference materials (ESRM or SRM)**: Generally, the frequency of use of these samples is weekly to monthly. The samples are commonly mono-level (method control) or pluri-level (calibration). They are sent to user laboratories with a reference value obtained from results of an interlaboratory test realised with expert laboratories.
  A control of homogeneity and stability is performed on each batch of samples.

- **Internal standard reference materials (ISRM, pilot, temoin…)**: These samples must be used daily to weekly. The reference value (or target) is attributed by the user (by test, by comparison with external reference materials, by standard addition…). As with the external reference materials, the samples are generally mono-level (method control) or pluri-level (calibration).
  A control of homogeneity and stability must be performed on each batch of samples.

These tools differ at many levels:
- Their aim (objectives) is different,
- The uncertainties on the assigned values are different, so, the maximal tolerated errors vary according the tool.



PT ESRM ISRM

The use of proficiency tests or standard reference materials only is insufficient to ensure the test quality. Indeed, these tools used individually are photographs of the laboratory's accuracy at an instant T. Therefore, they do not permit to ensure a satisfactory traceability of the determinations' accuracy over the period.
The solution would be to equal the complete analytical traceability film over a given period. It is then necessary to build a program of the analytical quality control operations (with control of traceability).

A TYPICAL QUALITY CONTROL PROGRAM

A typical control program corresponds to a combination of the various tools available to ensure the traceability of accuracy over time. In practice, this program must define the use of ESRM and ISRM tools between two proficiency tests.
To imagine this program, it is necessary to:
- clearly define the quality objectives by method. These objectives must be based on the laboratory's needs, the client's expectations, the method's robustness and the economical aspect of the measurand ;
- list the available internal and external tools.

This program will then be built associating different tools and considering the uncertainty (linked with the maximum tolerated error), the desired reactivity, the feed back in case of anomaly and the impact on the laboratory work.

INTERPRETATION OF THE RESULTS

When the program is applied, it is indispensable to analyse and interpret the results obtained with the various tools, in order to set up adapted curative and corrective actions.

➢ **Proficiency tests:** The laboratory may evaluate its results in relation to the assigned values and compare

the statistical parameters (mean and deviation of standard deviation) calculated from results of all the samples, to the fixed limits.
In the case of limit overshooting, the causes of the deviations must be found in order to set up corrective action.

➢ External and internal reference materials:
Firstly, the maximal tolerated errors (or tolerance) must be defined by analytical methods. They could be calculated, either according to ISO 5725-6 standard (critical deviation), or fixed a priori by the laboratory.
The laboratory could also fix operating and data interpretation modes (setting up of a control chart of individual results with the use of the cumulated or "floating" mean).

The follow-up of the quality control program then permits the rapid implementation of technical corrective actions and an immediate feed-back on the previous results. According to the case, this program will be modified by an intensification of the controls or by a validation of new arrangements with external reference materials.

CONCLUSION

The setting up of a structured analytical quality control program by method is indispensable, to respond at best to the laboratories' needs and clients' expectations.
Thanks to its necessary potential for evolution, according to the performances obtained, it will be an effective tool to ensure the quality of a laboratory's analytical results.

FOR A GLOBAL APPROACH OF VALIDATION

Summary of the talk by Mr.FEINBERG (INRA Paris) at CECALAIT's AGM 2006

Within the context of the ISO 17025:2005 standard requirements, laboratories have to validate their alternative methods and estimate their uncertainties of measurement. To combine these two requirements, a global procedure, the exactitude profile method, constitutes a new approach. This procedure, composed of several stages described below, will constitute the body of the NF V 03-110 standard revision.

The life cycle of a method includes various stages:

- The selection, the conception and the development,
- The validation (intra and/or inter-laboratories),
- The uncertainty estimation,
- Routine use and performance control.

With the setting up of quality assurance systems in laboratories, the analysis method validation and the uncertainty estimation, required in the ISO 17025:2005 standard, are now important objectives. To verify if a method is adapted to its objectives, laboratories have to respond to the requirements described in the following articles:
- 5.4.5.1. Validation is the confirmation by examination and provision of objective evidence that the particular requirements for a specified intended use are fulfilled, and
- 5.4.5.2. The laboratory shall validate non-standardised methods, laboratory designed / developed methods, standardised methods used outside of their intended range and amplification or modification of standardised methods to confirm that the methods are fit for their intended use.

The validation strategy, which consists in verifying that the method gives a result that is different from the target, is inappropriate. Indeed, it leads to failures due to the fact that the less accurate methods are easier to validate.
The validation therefore orientates itself towards a different approach:
- The definition of an acceptability limit, representing the "intended use" of the method.
- The definition of the non-acceptable results probability:
  → To know the percentage of future non-acceptable measurements,
  → To define an interval, in which a known proportion of future measures will be, and to verify if it is within the acceptability zone.

The exactitude profile

The exactitude profile, constituting the body of the NF V 03-110 standard, permits to respond to these questions.
This new intra-laboratory validation approach is spread over several stages:
- The collection of calibration data,
- The collection of validation data,
- The prediction of concentrations found,
- The calculation of tolerance intervals,
- The building of the exactitude profile.

- **The collection of calibration data**

The objective of this stage is to establish the instrumental response function. The experimental plan contains measurements on samples at different levels and on several series of measurements (the series can represent the day, the operator or the instrument).
This stage is necessary only within the context of a method which does not directly give the concentrations of the analyte sought for.

- **The collection of validation data**

This stage is used to verify the performances of the method when using the applied operating procedure.
Several series of measurements on samples at different concentration levels are necessary to obtain the data required for this verification. The reference values assigned to different samples can be obtained in many ways: standard additions, reference method, reconstituted matrix or raw solutions, isotopic dilution…

- **The prediction of concentration**

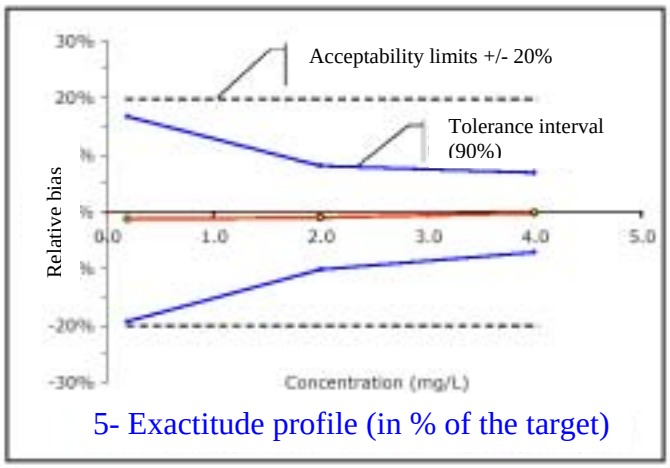
The first stage consists in the building and the choice of calibration models using the calibration data. Various mathematical models can be used to calculate the method response function, but regression using the least squares method is the most accessible.
The second stage is the determination, by reverse prediction, of concentrations found in the validation samples (application of the reverse function to the response function determined during phase 1 of this stage).

- **The calculation of tolerance intervals**

The statistical calculations are realised on concentration data found by reverse prediction. Then, the repeatability variance, the inter-series variance and the intermediary fidelity variance are calculated for each level, according to the principles described in the ISO 5725 standard.
Afterwards, a tolerance interval β can be deduced by level, in which a proportion β (generally 90%) of the future results of the method to be validated are expected to be found.

- **The building of the exactitude profile**

The exactitude profile is defined as a combination, represented in graphical form, of one or many tolerance intervals calculated at different levels and of an acceptability interval. It permits a global vision of the adequacy of the method's performances to the required specifications in the application field.



5- Exactitude profile (in % of the target)

The principle of the exactitude profile method is a global approach combining accuracy and reliability of the validated method. The decision concerning the validity of the tested method is realised directly on the graphical illustration. It also presents many other advantages such as:

- **The possibility of using numerous calibration models to calculate an instrumental response function,**
- **Its adaptation to large application fields, and**
- **The capacity to use a correction factor.**

However, the fixing of acceptability limits is a prerequisite to this method. With this approach, it is supposed that the data has a normal distribution, which constitutes an eventual disadvantage. But, in many situations, as for microbiological counts, this hypothesis is false. Nevertheless, a simple transformation of data into log permits to turn this limit around, as it has been demonstrated in several examples.

FORTHCOMING EVENTS

Classified in chronological order

MILK AND DAIRY PRODUCTS		
21-25 May 2007 Munich, Germany	IDF / ISO analytical week	http://www.fil-idf.org
SHEEP AND GOATS MILK		
18-20 April 2007 Alghero, Sardinia, Italy	5th International symposium on the challenge to sheep and goats milk sectors	http://sheepgoatsmilk.fil-idf-pr.com

STANDARDS, DRAFT STANDARDS

Classification in alphabetic order by theme

ISO published standards

CASEINS AND CASEINATES		
CASEINS / CASEINATES MOISTURE CONTENT	ISO 5550:2006 (IDF 78) October 2006	CASEINS AND CASEINATES Determination of moisture content (reference method)
CHEESE AND PROCESSED CHEESE PRODUCTS		
CHEESE / PROCESSED CHEESE PRODUCTS CHLORIDE CONTENT	ISO 5943:2006 (IDF 88) October 2006	CHEESE AND PROCESSED CHEESE PRODUCTS Determination of chloride content – Potentiometric titration method
MILK		
MILK / SOMATIC CELLS	ISO 13366-2:2006 October 2006	MILK Enumeration of somatic cells Part 2: Guidance on the operation of fluoro-opto-electronic counters
MILK AND MILK PRODUCTS		
MILK / MILK PRODUCTS / LEAD CONTENT	ISO/TS 6733:2006 (IDF 133) November 2006	MILK AND MILK PRODUCTS Determination of lead content – Graphite furnace atomic absorption spectrometric method
MILK / MILK PRODUCTS / MILK-CLOTTING	ISO 23058:2006 (IDF 199) September 2006	MILK AND MILK PRODUCTS Ovine and caprine rennets – Determination of total milk-clotting activity
MILK / MILK PRODUCTS / ANTIMICROBIAL RESIDUES	ISO/TS 26844:2006 November 2006	MILK AND MILK PRODUCTS Determination of antimicrobial residues – Tube diffusion test
MILK PRODUCTS		
MILK PRODUCTS / NEAR INFRARED	ISO 21543:2006 (IDF 201) September 2006	MILK PRODUCTS Guidelines for the application of near infrared spectrometry
PROCESSED CHEESE		
PROCESSED CHEESE / EMULSIFYING AGENTS / ACIDIFIERS	ISO 12082:2006 November 2006	PROCESSED CHEESE AND PROCESSED CHEESE PRODUCTS Calculation of the content of added citrate emulsifying agents and acidifiers/pH-controlling agents, expressed as citric acid
QUALITY		
QUALITY /	ISO 17025/Cor1:2006 August 2006	General requirements for the competence of testing and calibration laboratories Technical corrigendum

NEW EU STANDARDS AND REGULATIONS

Classification is established in alphabetical order of the first keyword

CONTAMINANTS / FOODSTUFFS

O.J.E.U. L 364, 20th December 2006 – Commission Regulation (EC) No 1881/2006 of 19 December 2006 setting maximum levels for certain contaminants in foodstuffs
http://eur-lex.europa.eu/LexUriServ/site/en/oj/2006/l_364/l_36420061220en00050024.pdf

DIOXINS / PCB

O.J.E.U. L 322, 22nd November 2006 – Commission Recommendation of 16 November 2006 on the monitoring of background levels of dioxins, dioxin-like PCBs and non-dioxin-like PCBs in foodstuffs
http://eur-lex.europa.eu/LexUriServ/site/en/oj/2006/l_322/l_32220061122en00240031.pdf

O.J.E.U. L 366, 21st December 2006 – Recommendation of the EFTA Surveillance Authority No 144/06/COL of 11 May 2006 on the reduction of the presence of dioxins, furans and PCBs in feedingstuffs and foodstuffs
http://eur-lex.europa.eu/LexUriServ/site/en/oj/2006/l_366/l_36620061221en00930095.pdf

FOOD ADDITIVES / PURITY CRITERIA

O.J.E.U. L 346, 9th December 2006 – Commission Directive 2006/129/EC of 8 December amending and correcting Directive 96/77/EC laying down specific purity criteria on food additives other than colours and sweeteners
http://eur-lex.europa.eu/LexUriServ/site/en/oj/2006/l_346/l_34620061209en00150025.pdf

FOOD INGREDIENT

O.J.E.U. L 296, 26th October 2006 – Commission Decision of 23 October 2006 authorising the placing on the market of lycopene from *Blakeslea trispora* as a novel food ingredient under Regulation (EC) No 258/97 of the European Parliament and of the Council
http://eur-lex.europa.eu/LexUriServ/site/en/oj/2006/l_296/l_29620061026en00130016.pdf

FOOD HYGIENE

O.J.E.U. L 320, 18th November 2006 – Commission Regulation (EC) No 1662/2006 of 6 November 2006 amending Regulation (EC) No 853/2004 of the European Parliament and of the Council laying down specific hygiene rules for food of animal origin
http://eur-lex.europa.eu/LexUriServ/site/en/oj/2006/l_320/l_32020061118en00010010.pdf

O.J.E.U. L 320, 18th November 2006 – Commission Regulation (EC) No 1663/2006 of 6 November 2006 amending Regulation (EC) No 854/2004 of the European Parliament and of the Council laying down specific rules for the organisation of official controls on products of animal origin intended for human consumption
http://eur-lex.europa.eu/LexUriServ/site/en/oj/2006/l_320/l_32020061118en00110012.pdf

O.J.E.U. L 320, 18th November 2006 – Commission Regulation (EC) No 1664/2006 of 6 November 2006 amending Regulation (EC) No 2074/2005 as regards implementing measures for certain products of animal origin intended for human consumption and repealing certain implementing measures
http://eur-lex.europa.eu/LexUriServ/site/en/oj/2006/l_320/l_32020061118en00130045.pdf

O.J.E.U. L 320, 18th November 2006 – Commission Decision 2006/765/EC of 6 November 2006 repealing certain implementing acts concerning food hygiene and health conditions for the production and placing on the market of certain products of animal origin intended for human consumption
http://eur-lex.europa.eu/LexUriServ/site/en/oj/2006/l_320/l_32020061118en00500052.pdf

INFANT FOOD

O.J.E.U. L 299, 28th October 2006 – Commission Regulation (EC) No 1609/2006 of 27 October 2006 authorising the placing on the market of infant formulae based on hydrolysates of whey protein derived from cows' milk protein for a two-year period
http://eur-lex.europa.eu/LexUriServ/site/en/oj/2006/l_299/l_29920061028en00090010.pdf

O.J.E.U. L 339, 6th December 2006 – Commission Directive 2006/125/EC of 5 December 2006 on processed cereal-based foods and baby foods for infants and young children
http://eur-lex.europa.eu/LexUriServ/site/en/oj/2006/l_339/l_33920061206en00160035.pdf

MICROBIOLOGICAL CRITERIA

O.J.E.U. L 278, 10th October 2006 – Corrigendum to Commission Regulation (EC) No 2073/2005 of 15 November 2005 on microbiological criteria for foodstuffs
http://eur-lex.europa.eu/LexUriServ/site/en/oj/2006/l_278/l_27820061010en00320032.pdf

PESTICIDES / RESIDUE LEVELS

O.J.E.U. L 263, 23rd September 2006 – Commission Directive 2006/59/EC of 28 June 2006 amending Annexes to Council Directives 76/895/EEC, 86/362/EEC, 86/363/EEC and 90/642/EEC as regards maximum residue levels for carbaryl, deltamethrin, endosulfan, fenithrothion, methidathion and oxamyl
http://eur-lex.europa.eu/LexUriServ/site/en/oj/2006/l_175/l_17520060629en00610076.pdf

SWEETENERS / CRITERIA OF PURITY

O.J.E.U. L 346, 9th December 2006 – Commission Directive 2006/128/EC of 8 December 2006 amending and correcting Directive 95/31/EC laying down specific criteria of purity concerning sweeteners for use in foodstuffs
http://eur-lex.europa.eu/LexUriServ/site/en/oj/2006/l_346/l_34620061209en00060014.pdf

VETERINARY MEDICINAL PRODUCTS / RESIDUE / FOODSTUFFS

O.J.E.U. L 271, 30th September 2006 - Commission Regulation (EC) No 1451/2006 of 29 September 2006 amending Annexes I and II to Council Regulation (EEC) No 2377/90 laying down a Community procedure for the establishment of maximum residue limits of veterinary medicinal products in foodstuffs of animal origin, as regards fluazuron, sodium nitrite and peforelin
http://eur-lex.europa.eu/LexUriServ/site/en/oj/2006/l_271/l_27120060930en00370039.pdf

O.J.E.U. L 325, 24th November 2006 - Commission Regulation (EC) No 1729/2006 of 23 November 2006 amending Annexes I and III to Council Regulation (EEC) No 2377/90 laying down a Community procedure for the establishment of maximum residue limits of veterinary medicinal products in foodstuffs of animal origin, as regards firocoxib and triclabendazole
http://eur-lex.europa.eu/LexUriServ/site/en/oj/2006/l_325/l_32520061124en00060008.pdf

O.J.E.U. L 343, 8th December 2006 - Commission Regulation (EC) No 1805/2006 of 7 December 2006 amending Annex I to Council Regulation (EEC) No 2377/90 laying down a Community procedure for the establishment of maximum residue limits of veterinary medicinal products in foodstuffs of animal origin, as regards thiamphenicol, fenvalerate and meloxicam
http://eur-lex.europa.eu/LexUriServ/site/en/oj/2006/l_343/l_34320061208en00660068.pdf

O.J.E.U. L 354, 14th December 2006 - Commission Regulation (EC) No 1831/2006 of 13 December 2006 amending Annex I to Council Regulation (EEC) No 2377/90 laying down a Community procedure for the establishment of maximum residue limits of veterinary medicinal products in foodstuffs of animal origin, as regards Doramectin
http://eur-lex.europa.eu/LexUriServ/site/en/oj/2006/l_354/l_35420061214en00050007.pdf

IN THE PRESS – ON THE WEB

Classification in alphabetical order of keywords

STANDARDS / CODEX

Publication of 4 new Codex standards:

► *CODEX STAN 250-2006* : Codex standard for a blend of evaporated skimmed milk and vegetable fat
http://www.codexalimentarius.net/download/standards/10608/CXS_250e.pdf

► *CODEX STAN 251-2006* : Codex standard for a blend of skimmed milk and vegetable fat in powdered form
http://www.codexalimentarius.net/download/standards/10612/CXS_251e.pdf

► *CODEX STAN 252-2006* : Codex standard for a blend of sweetened condensed skimmed milk and vegetable fat
http://www.codexalimentarius.net/download/standards/10616/CXS_252e.pdf

► *CODEX STAN 253-2006* : Codex standard for dairy fat spreads
http://www.codexalimentarius.net/download/standards/10620/CXS_253e.pdf

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