Validation in an academic environment: achieving quality in analytical data

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EURACHEM WS 2016 – May 9th 2016

PRESENTATION OUTLINE

- Introduction
- Method validation in academia
- QMS in the Laboratory of Food Analysis
- Accreditation in research: an added value?
- Take-home-message

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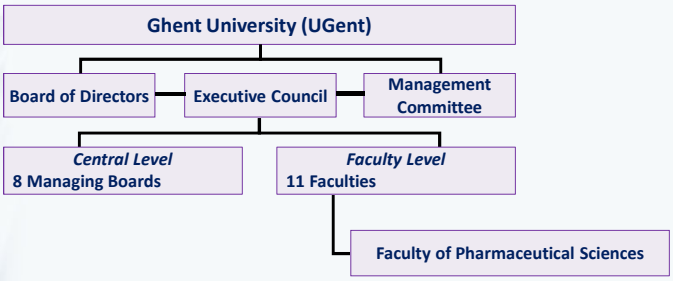
INTRODUCTION



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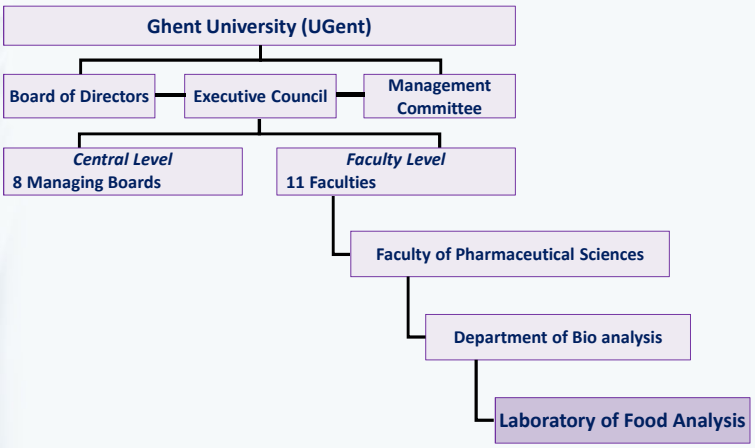

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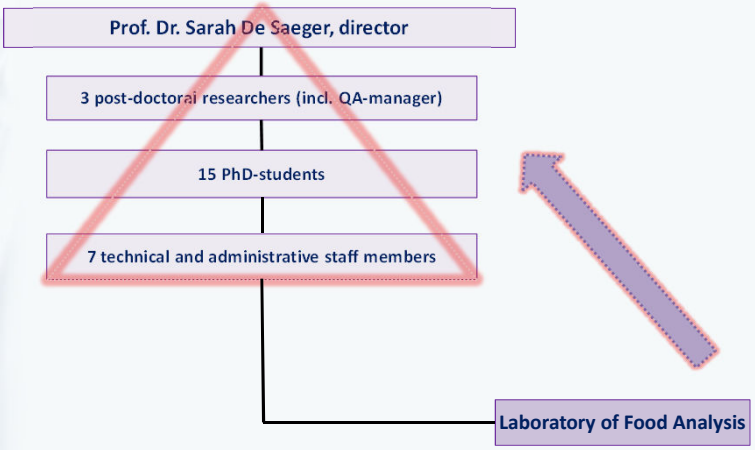
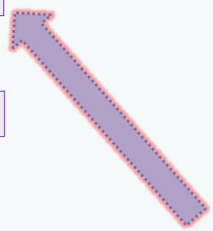


INTRODUCTION

SERVICE WORK – ROUTINE ANALYSIS

EDUCATION: BA & MA

RESEARCH



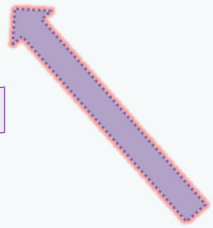
Laboratory of Food Analysis

INTRODUCTION

SERVICE WORK – ROUTINE ANALYSIS

- Accreditation according EN ISO/IEC 17025 (BELAC)
- ° 1996
- Residues and contaminants
- Scope LC-MS/MS analysis:
  - multi-mycotoxins in feed (ANAL-18)
  - multi-ergot alkaloids in food/feed (ANAL-19)
  - multi-modified mycotoxins in food/feed (ANAL-20)

RESEARCH



Laboratory of Food Analysis

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- QMS in the Laboratory of Food Analysis
- Accreditation in research: an added value?
- Take-home-message

METHOD VALIDATION IN ACADEMIA

Quote: 'are research students/postdocs sufficiently aware of method validation principles?'

Pharmaceutical Sciences

- 2nd BACHELOR: Instrumental analytical chemistry
principles of statistical analysis (method evaluation / method validation) and monitoring (internal quality control) of analytical results

- 3rd BACHELOR: Bio analytical practicum
comparison of method validation parameters screening and confirmatory tests for residues and contaminants in food and feed

- 1st MASTER: Medicine's analysis and quality
method validation and internal quality control in the pharmaceutical industry

- PhD
Specialist courses Doctoral Schools on statistics and method validation

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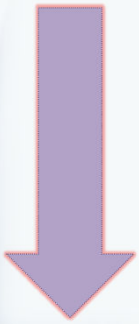
- Introduction
- Method validation in academia
- **QMS in the Laboratory of Food Analysis**
- Research in accreditation
- Quotes and take-home-message

QMS IN THE LABORATORY OF FOOD ANALYSIS

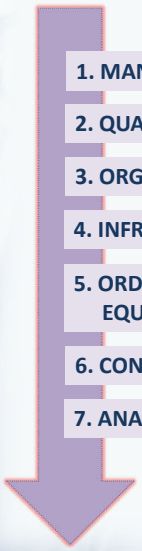
Quote: 'Do academic labs have the same depth and structure of validation study as in a commercial lab?'

Quote: 'How to convince the academic environment about the necessity to be part of quality control (validation, use of CRM, proficiency tests)?'

Quote: 'Do university institutions have implemented a QMS?'



QMS IN THE LABORATORY OF FOOD ANALYSIS



1. MANAGEMENT DECLARATION AND STATUTE OF LAB
2. QUALITY MANAGEMENT
3. ORGANISATION AND STAFF
4. INFRASTRUCTURE
5. ORDERING AND MANAGEMENT OF REAGENTS, APPLIANCES, EQUIPMENT AND YEARLY-CONTROLLED MATERIALS
6. CONTROLS
7. ANALYSES

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QMS IN THE LABORATORY OF FOOD ANALYSIS

2. QUALITY MANAGEMENT

Quality manual

- To guarantee quality of performed analyses

Standard operating procedures (SOP's)

- ADMIN, CONTROL, QUAL, CLEAN and ANAL
- Work sheets, registers and templates
- Revision every 3 years

Complaints (KWALI-01)

- Internal and external

Audits and meetings (ADMIN-36)

- Internal audit (4x/year)
- External audit (BELAC)
- Management review meeting and general meeting
- OA-meeting

QMS IN THE LABORATORY OF FOOD ANALYSIS

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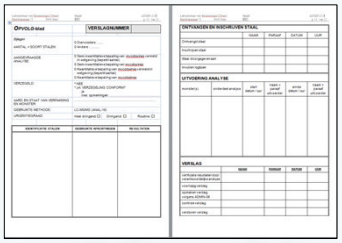
Complaints (KWALI-01)
- Internal and external

Audits and meetings (ADMIN-36)
- Internal audit (4x/year)
- External audit (BELAC)
- Management review meeting and general meeting (1x/year)
- QA-meeting (2x/year)

QMS IN THE LABORATORY OF FOOD ANALYSIS: an example

Sample management

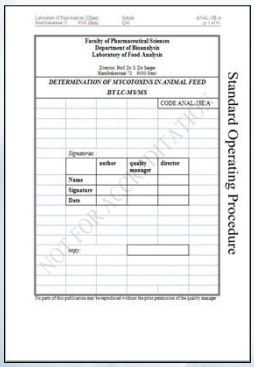
SOP
ADMIN-25: Sample registration
ADMIN-18: Storage of samples before (and after) analysis
CONTR-07: Control temperature of fridge and freezer


QMS IN THE LABORATORY OF FOOD ANALYSIS: an example

Sample management → **Sample analysis**

SOP KWALI-06: Method validation


Faculty of Pharmaceutical Sciences
Department of Bioanalysis
Laboratory of Food Analysis

DETERMINATION OF MYCOTOXINS IN ANIMAL FEED
BY LC-MS/MS

CODE ANAL.: [illegible]

	author	quality manager	director
Name			
Signature			
Date			

Standard Operating Procedure

- for **newly developed** methods
- **description** of validation parameters, **implementation (protocol)** and performance **criteria**
- ***In-house*** validation

- Linearity (range), LOD, LOQ, CCα, CCβ, trueness, apparent recovery, repeatability, intra-laboratory reproducibility, selectivity/specificity, false + and -, measurement uncertainty

- Criteria **Commission Decision 2002/657/EC** (guidelines for the validation of analytical methods used in the residue monitoring plan)

QMS IN THE LABORATORY OF FOOD ANALYSIS: an example

Sample management → **Sample analysis**

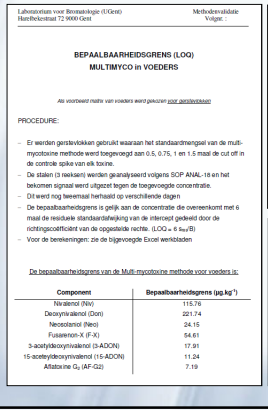
SOP KWALI-06: Method validation

		Qualitative method		Quantitative method	
		Screening	Confirmation	Screening	Confirmation
Limit of detection (LOD) or CCα		+	+	+	+
Limit of quantification (LOQ) or CCβ		-	-	+	+
Accuracy	Trueness	-	-	-	+
Accuracy	Precision: Repeatability + intralaboratory reproducibility	-	-	+	+
Selectivity/specificity		+	+	+	+
False Positive/Negative		+	-	+	-
Measurement uncertainty		+	+	+	+
Linearity/Range		-	-	+	+

QMS IN THE LABORATORY OF FOOD ANALYSIS: an example

Sample management → **Sample analysis**

SOP KWALI-06: Method validation



Laboratorium voor Bromatologie (UGent) — Methodevalidatie
Harelbekestraat 72 9000 Gent — Volgnr. :

BEPAALBAARHEIDSGRENS (LOQ)
MULTIMYCO in VOEDERS

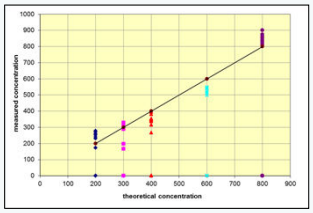
Als voorbeeld matrix van voeders werd gekozen voor gerstvlokken

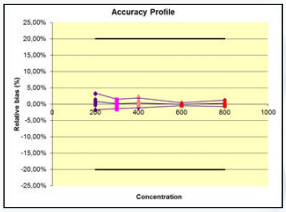
PROCEDURE:

- Er werden gerstvlokken gebruikt waaraan het standaardmengsel van de multi-mycotoxine methode werd toegevoegd aan 0.5, 0.75, 1 en 1.5 maal de cut off in de controle spike van elk toxine.
- De stalen (3 reeksen) werden geanalyseerd volgens SOP ANAL-18 en het bekomen signaal werd uitgezet tegen de toegevoegde concentratie.
- Dit werd nog tweemaal herhaald op verschillende dagen
- De bepaalbaarheidsgrens is gelijk aan de concentratie die overeenkomt met 6 maal de residuele standaardafwijking van de intercept gedeeld door de richtingscoëfficiënt van de opgestelde rechte. (LOQ = 6 $s_{y/x}$/B)
- Voor de berekeningen: zie de bijgevoegde Excel werkbladen

De bepaalbaarheidsgrens van de Multi-mycotoxine methode voor voeders is:

Component	Bepaalbaarheidsgrens (µg.kg^{-1})
Nivalenol (Niv)	115.76
Deoxynivalenol (Don)	221.74
Neosolaniol (Neo)	24.15
Fusarenon-X (F-X)	54.61
3-acetyldeoxynivalenol (3-ADON)	17.91
15-acetyldeoxynivalenol (15-ADON)	11.24
Aflatoxine G_2 (AF-G2)	7.19





Measurement uncertainty

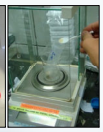
μ	200,00	300,00	400,00	600,00	800,00
$s^2(w)$	971,6617	239,2229	347,4733	325,0302	867,1245
$s^2(b)$	359,3813	2908,6590	941,4397	0,0000	0,0000
γ (= $s^2(r)/s^2(R)$)	0,7300	0,0760	0,2696	1,0000	1,0000
	0,7300	0,0760	0,2696	1,0000	1,0000
bias uncertainty u(β)	13,0697	27,3331	16,258	5,20	8,50
u(δ)^2	170,8171	747,1000	264,3160	27,0858	72,2604
variance β toler.interv	1501,8601	3894,9818	1553,2291	352,1160	939,3848
comp. uncertainty u(Y	38,754	62,410	39,411	18,765	30,649
expand. uncertainty U	77,508	124,820	78,82	37,53	61,30
rel. exp. uncertainty U	38,75%	41,607%	19,706%	6,255%	7,662%

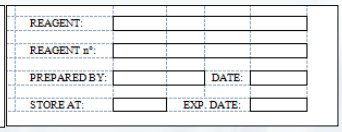
QMS IN THE LABORATORY OF FOOD ANALYSIS: an example

Sample management → **Sample analysis**

SOP

ADMIN-32: Management of reference materials and standards
ADMIN-02: Placing orders and management of reagents and appliances
CONTR-18: Control dispenser
CONTR-05: Control electronic balances
CLEAN-12: Cleaning moulinettes
CONTR-01: Calibration water bath





QMS IN THE LABORATORY OF FOOD ANALYSIS: an example

Sample management → **Sample analysis** → **LC-MS/MS analysis**

SOP

CLEAN-11: Maintenance of LC-MS Quattro Micro

CLEAN-13: Maintenance of LC-MS Quattro Premier XE

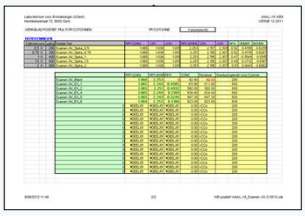
-> via a QC-injection scheme

QMS IN THE LABORATORY OF FOOD ANALYSIS: an example

Sample management → **Sample analysis** → **LC-MS/MS analysis** → **Identification/ Quantification**

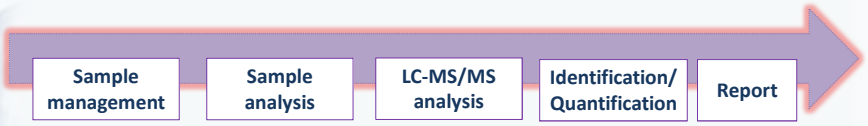
Identification and quantification

- 4 identification criteria (according to the **Decision 2002/657/EC**)

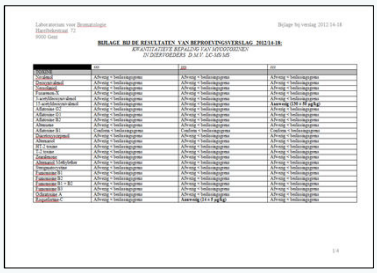


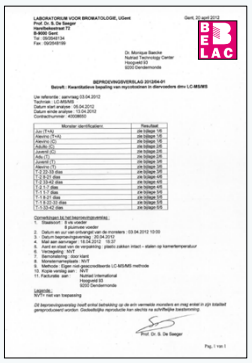
- Internal quality control (**1st line control**)
- Internal quality control (**2nd line control**, certified reference material)
- Independent external control (**3rd line control**, proficiency trials)

QMS IN THE LABORATORY OF FOOD ANALYSIS: an example



SOP ADMIN-08
Preparation of reports after analysis





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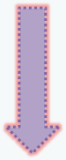
- QMS in the Laboratory of Food Analysis
- **Accreditation in research: an added value?**
- Take-home-message

ACCREDITATION IN RESEARCH: AN ADDED VALUE?

Quote: 'Is it possible to make good research/science without being interested in the quality of analytical data?'

Current state

- high-impact journals: prerequisite to acquire full-validation reports
- no single data-points
- competition ⇧
- to distinguish high-quality from low-quality results
- traceability of results
- problem follow-up: ° action points



EXTRAPOLATION QMS TO RESEARCH

ACCREDITATION IN RESEARCH: AN ADDED VALUE?

ADMIN-02 Ordering, bringing into use and stock management of reagents and appliances
ADMIN-03 Ordering and bringing into use of equipment
ADMIN-04 Management SOP's
ADMIN-05 Writing and changing staff records
ADMIN-06 Authorised signatures
ADMIN-08 Reporting results
ADMIN-09 Management personnel
ADMIN-11 Management register proficiency tests
ADMIN-12 Management monthly, sixmonthly and yearly controls
ADMIN-18 Sample treatment before and after analysis
ADMIN-20 Management documents in archive
ADMIN-21 Ordering and bringing into use of yearly to control materials
ADMIN-25 Sample registration
ADMIN-26 Reception of visitors
ADMIN-32 Management reference standards
ADMIN-33 Contact clients
ADMIN-34 IT-management
ADMIN-35 IT-users guide

ANAL Research methods

ACCREDITATION IN RESEARCH: AN ADDED VALUE?

CONTR-01	**Calibration warm water bath**
CONTR-02	**Calibration ovens**
CONTR-05	**Control electronic balances**
CONTR-06	**Calibration pH-meter**
CONTR-07	**Control temperature fridge and freezers**
CONTR-08	**Control thermometers**
CONTR-11	**Control and calibration pipettes**
CONTR-12	**Control temperature fridge and freezer**
CONTR-13	**Control electronic balances**
CONTR-16	**Control calibration masses**
CONTR-17	**Calibration and maintenance thermohygrograph**
CONTR-18	**Control dispensettes**
KWALI-01	**Complaints**
KWALI-02	Writing SOP's
KWALI-03	Changing SOP's
KWALI-04	**Training personnel**
KWALI-06	**Method validation**
KWALI-07	**Excel templates**
CLEAN-02	**Cleaning glass and plastic materials**
CLEAN-05	**Cleaning screw-caps and vials**
CLEAN-11	**Cleaning LC-MS Quattro Micro**
CLEAN-12	**Cleaning moulinettes**
CLEAN-13	**Maintenance LC-MS Quattro Premier XE**
CLEAN-14	**Maintenance Synapt/Xevo**

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TAKE-HOME-MESSAGE

Quote: 'What did method validation and QMS bring to universities?'

TAKE-HOME-MESSAGE

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= more WORK and COSTS

- Ensuring maintenance of quality management
- Life-long training staff
- Establish qualified and authorised personnel
  → flow personnel academia ↑
- Maintain and invest in qualified and calibrated equipment
- Perform necessary controls
- Simplifying administration to encourage staff: Sharepoint®

TAKE-HOME-MESSAGE

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= MORE RELIABLE RESULTS AND ACHIEVEMENT OF HIGH-QUALITY DATA!

- Benefits: project grants ↑, credibility to *e.g.* EFSA and publications ↑, impact factors ↑

DO YOU HAVE ANY QUESTIONS?