

# **Analytical methods for monitoring of biocides in the environment – are the data requirements sufficient?**

Angelika Steinborn, Lutz Alder

# Outline

- Introduction
- Evaluation of Residue Analytical Methods
  - Choice of matrices
  - Choice of analytes (residue definition)
  - Required validation data
- Confirmatory methods
- Multi-residue methods
- Summary and conclusion

# Why are biocides detected in milk?

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### Vorsicht bei bestimmten Spülmitteln für die Melktechnik!

[25.07.2012]

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Milcherzeuger sollten dringend ihr Spülmittel überprüfen!

Um unerwünschte Rückstände zu vermeiden und die Vermarktungsfähigkeit der Rohmilch nicht zu gefährden, sollten Milcherzeuger jetzt dringend die Desinfektions- und Reinigungsmittel für ihre Melk- und Kühltechnik überprüfen. Keinesfalls sollten länger Produkte mit quartären Ammoniumverbindungen (QAV) eingesetzt werden. Darauf weist der Deutsche Bauernverband hin.

Hintergrund: Bei einer Eigenkontrolle wurde bei frischen Kräutern eine Überschreitung der Höchstgrenze für QAV festgestellt. Die erhöhten Rückstände betrafen die Stoffe DDAC (Didecylidimethylammoniumchlorid) und BAC (Benzalkoniumchlorid), die insbesondere in Desinfektions- und Reinigungsmitteln vorkommen. Solche QAV-haltigen Reinigungsmittel werden auch für die Desinfektion von Melkanlagen und Melkgeräten verwendet. Selbst bei gründlichem Heiß-Wasser-Nachspülen ist nicht sichergestellt, dass die Melkanlagen frei von DDAC-Rückständen sind, so der DBV. Deshalb sollte dringend auf diese Produkte verzichtet werden!

Hier finden Sie eine Liste mit DLG-anerkannten Desinfektionsmitteln, in der die QAV-haltigen Mittel kenntlich gemacht sind. Der DBV empfiehlt, anhand dieser Liste zu überprüfen, ob das eingesetzte Reinigungsmittel QAV-haltig ist. Sollte dies der Fall sein, sollten Sie das Mittel absetzen und ein anderes QAV-freies Reinigungsmittel verwenden.

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[16.07.2012]

**EU hebt Grenzwert für DDAC an**



Nachdem in Pflanzenstärkungsmitteln überhöhte...

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[04.09.2012]

**GEA: Chlor als Alternative zu QAV's**

GEA Farm Technologies bietet einen Zirkulationsrei...

**top agrar**

[15.08.2012]

**Bleser verteidigt Brüsseler DDAC-Rückstandhöchstwert**

Für nicht berechtigt hält Staatssekretär Peter...

<http://www.topagraronline.com/news/Rind-Rindernews-Vorsicht-bei-bestimmten-Spuelmitteln-fuer-die-Melktechnik-896862.html>

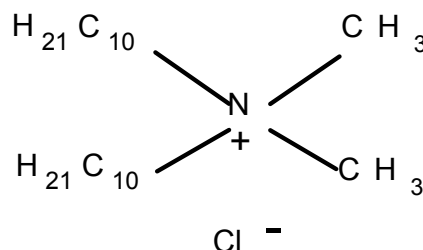
Angelika Steinborn, 2012-11-05, Berlin, Workshop Environmental Monitoring of Biocides

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# Introduction

## Example: Residues of DDAC in food

- Request to BfR for analytical methods for DDAC in food material



## Information from EU Assessment (draft CAR):

“The DDAC containing product ... is not intended for use in areas where food for human consumption is prepared, consumed or stored, or where the feedingstuff for livestock is prepared, consumed or stored...”



**Are the data requirements sufficient?**

## Rückstände von quartären Ammoniumverbindungen in Lebensmitteln

Das Bundesamt für Verbraucherschutz und Lebensmittelsicherheit (BfR) hat das Inverkehrbringen der Pflanzenstärkungsmittel „Vi-Care“ und „Wuxal Aminoplant“ untersagt. „Wuxal Aminoplant“ wurde auch als Zusatzstoff vermarktet. Grund dafür ist der Verdacht, dass infolge der Anwendung der genannten Produkte die gesetzlich festgelegten Rückstandshöchstgehalte von Didecyldimethylammoniumchlorid (DDAC) bzw. Benzalkoniumchlorid (BAC) in Höhe von 0,01 mg/kg überschritten werden können. Lebensmittel, welche die gesetzlich festgelegten Höchstgehalte überschreiten, sind nicht verkehrsfähig.

Bei DDAC und BAC handelt es sich um quartäre Ammoniumverbindungen, die außer im Pflanzenschutz auch in anderen Bereichen der Lebensmittelerzeugung eingesetzt werden, z.B. als Biozide (u. a. zur Desinfektion). Die gesetzlichen Rückstandshöchstgehalte für DDAC und BAC gelten unabhängig davon, ob diese Stoffe zu Pflanzenschutz-Zwecken oder als Biozide verwendet wurden.

## Woher können Rückstände von DDAC und BAC in Lebensmitteln stammen?

[http://www.bvl.bund.de/DE/04\\_Pflanzenschutzmittel/05\\_Fachmeldungen/2012/Rueckstaende\\_Ammonium.html](http://www.bvl.bund.de/DE/04_Pflanzenschutzmittel/05_Fachmeldungen/2012/Rueckstaende_Ammonium.html)

# Introduction

## General data requirements biocides

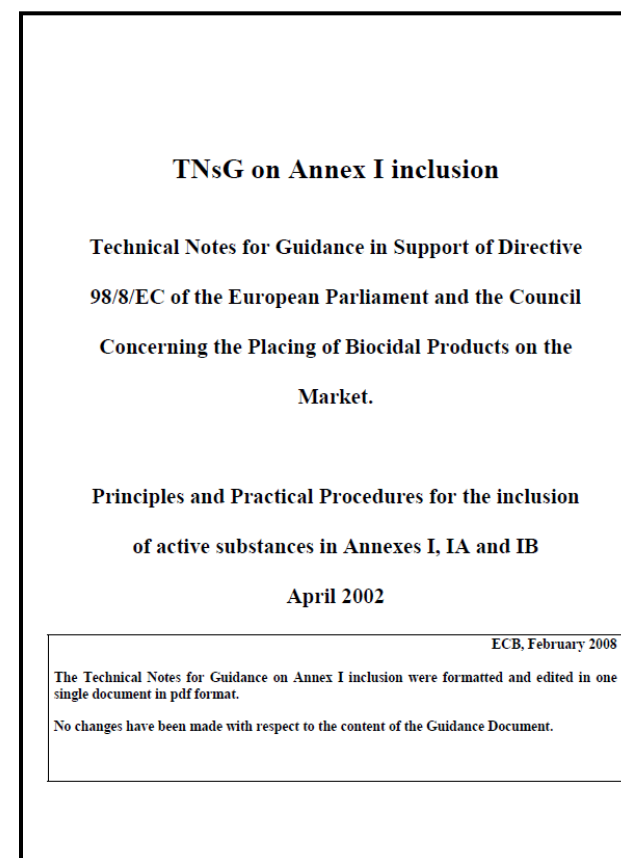
- ❑ Directive 98/8/EC of the European Parliament and of the Council of 16 February 1998
- ❑ Regulation (EU) No 528/2012 of the European Parliament and of the Council of 22 May 2012  
(shall apply from 01/09/2013)



## Detailed explanation of individual endpoints

- ❑ Technical Guidance Document (October 2000)

[http://ihcp.jrc.ec.europa.eu/our\\_activities/public-health/risk\\_assessment\\_of\\_Biocides/doc/TNsG/TNsG\\_DATA\\_REQUIREMENTS/TNsG-Data-Requirements.pdf](http://ihcp.jrc.ec.europa.eu/our_activities/public-health/risk_assessment_of_Biocides/doc/TNsG/TNsG_DATA_REQUIREMENTS/TNsG-Data-Requirements.pdf)



# Introduction

Analytical methods *in all relevant environmental media* including recovery rates and the limits of determination for the active substance, and *for residues thereof*, and *where relevant* in/on the following [Ann. IIA, IV.4.2.]:

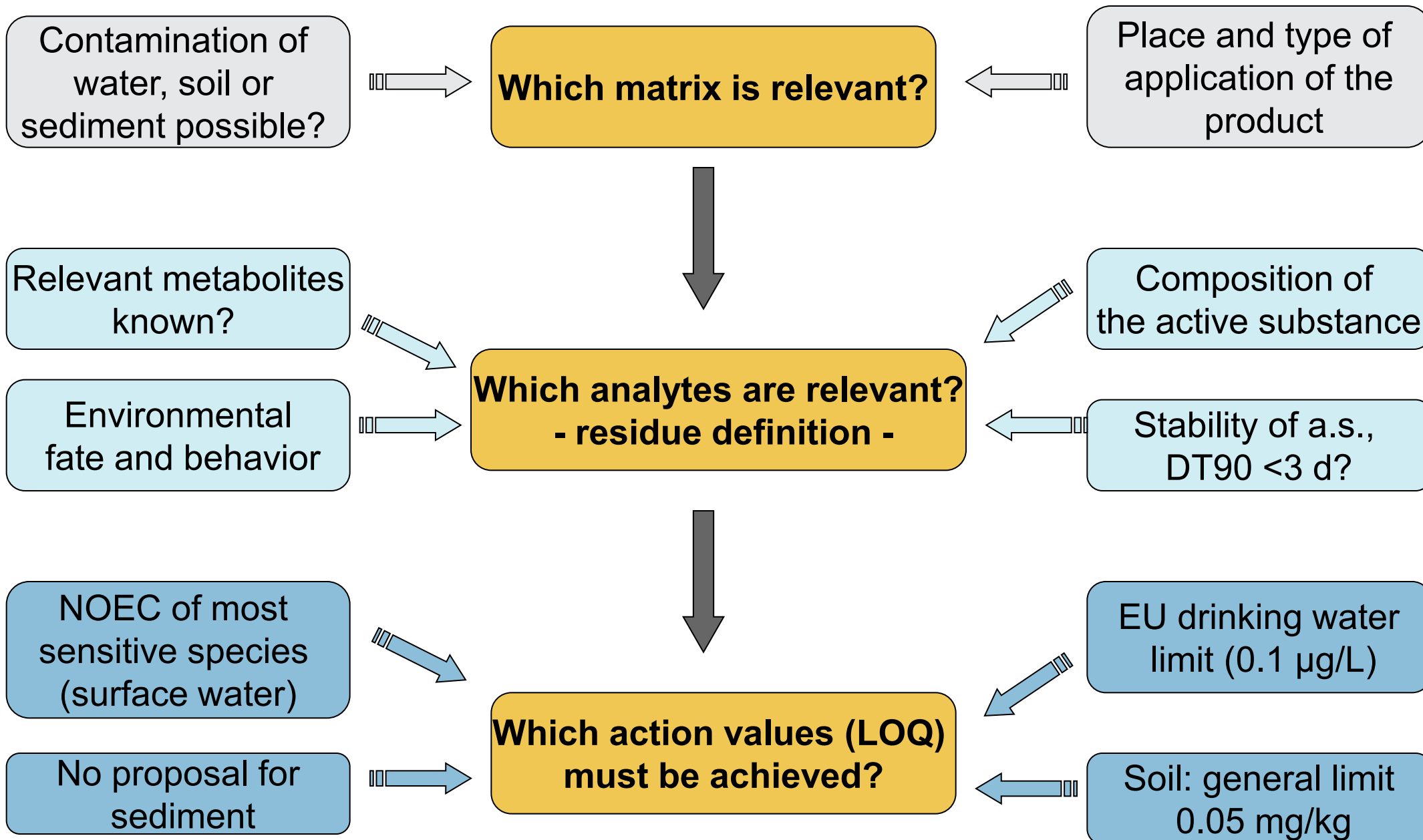
- (a) Soil
- (b) Air
- (c) Water
- (d) Animal and human body fluids and tissues



Which compounds belong to “residues thereof”?

Which environmental media are relevant?

# Evaluation of analytical methods for monitoring



a.s. = active substance

# Evaluation of analytical methods for monitoring

## Which matrices are considered relevant?

- ❑ Active substances approved for PT8 (wood preservatives)

Acceptable residue analytical methods available for:

Soil: 28 substances

Air: 20 substances

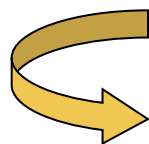
Drinking water: 25 substances

Surface water: 24 substances

Sediment: 5 substances out of 31 a.s. accepted for Annex I



- ❑ No common set of required methods.
- ❑ Waiver for non-submission, e.g. a.s. in ionic form (cyanide, boron salts) not in all cases available.
- ❑ In some cases data gaps should be filled at product authorization.
- ❑ No clear rules for additional matrices, e.g. marine sediment, sea water ...



**Discussion and harmonization necessary!**

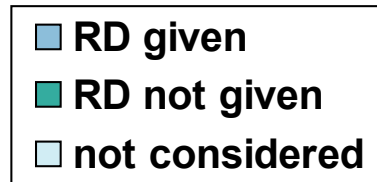
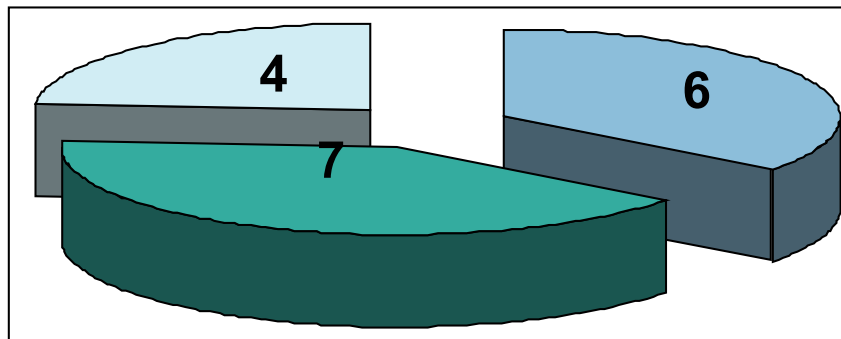


# Evaluation of analytical methods for monitoring

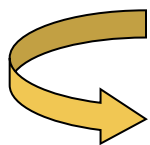
## Definition of relevant analytes (residue definition)

Product type 18: Insecticides, acaricides and products to control other arthropods

Inclusion in Annex I/IA decided: 17 active substances



Not considered:  
carbon dioxide, nitrogen, *bacillus thur.*,  
hydrogen cyanide



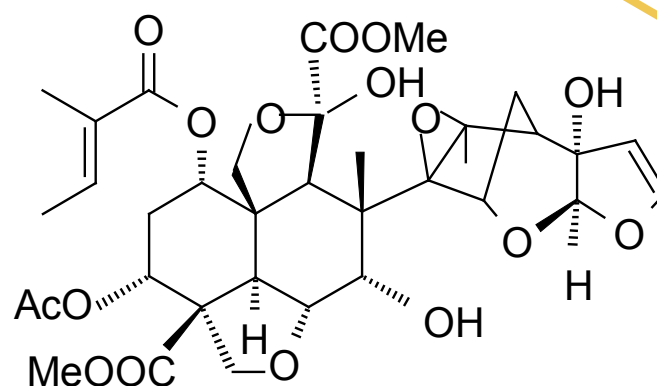
**In 30 % of relevant cases the residue definition (RD) was not discussed.**

# Evaluation of analytical methods for monitoring

## Why is a discussion of the residue definition necessary?

### ❑ 1st Example: **Margosa Extract**

Azadirachtin A is the main component of extracts isolated from seeds of the Neem tree (*Azadirachta indica*)



- ❑ Further components: Azadirachtin B, Aazadirachtin H, Nimbin, Salanin, Desacetyl-Nimbin, Desacetyl-Salanin, Fatty acids
- ❑ Composition of Neem extract strongly depends on the manufacturing process.

# Evaluation of analytical methods for monitoring

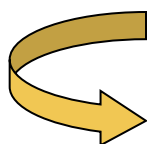
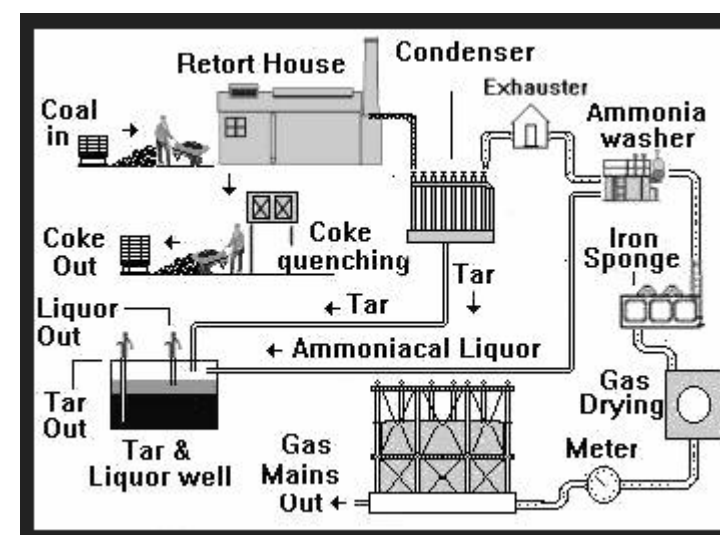
## Why is a discussion of the residue definition necessary?

### □ 2nd Example: **Creosote**

„Creosote is a **complex mixture** of **hundreds of** distinct compounds, ... The chemical composition is influenced by the origin of coal and also by the nature of the distillation process... .

**106 compounds** have been analysed for in the creosotes applied for.”

Source: Assessment Report, chapter 2.1.1, December 2010

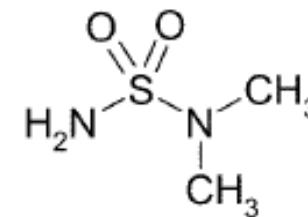


**Definition of one or more marker substances is necessary!**

# Evaluation of analytical methods for monitoring

## Why is a discussion of the residue definition necessary?

- 3rd example: **N,N-Dimethyl sulfamide (DMS)**



*Environ. Sci. Technol.* 2008, 42, 6340–6346

Other cases:

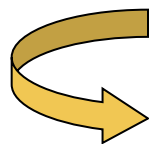
- Active substance is not stable in the environment (DT90 < 3d).
- Residues of toxic or ecotoxic by-products occur.

### ***N,N*-Dimethylsulfamide as Precursor for *N*-Nitrosodimethylamine (NDMA) Formation upon Ozonation and its Fate During Drinking Water Treatment**

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*Received December 6, 2007. Revised manuscript received February 3, 2008. Accepted February 21, 2008.*

the United States, the Assessment (OEHA) 3 ng/L NDMA in 20 by the federal environmental health based precautionary NDMA exposure v. The nitrosamine various areas, due drinking water resources (1). Moreover revealed that NDMA duct during water cording to more de that the NDMA quantity cannot be attributed tertiary amines with of importance, too. In this article, formation during c bank filtrates, and g




**Residue definition should include relevant metabolites, conversion products and degradation products.**

# Data requirements for analytical methods for monitoring

... are listed in:

## ❑ TECHNICAL GUIDANCE DOCUMENT (October 2000)

[http://ihcp.jrc.ec.europa.eu/our\\_activities/public-health/risk\\_assessment\\_of\\_Biocides/doc/TNsG/TNsG\\_DATA\\_REQUIREMENTS/TNsG-Data-Requirements.pdf](http://ihcp.jrc.ec.europa.eu/our_activities/public-health/risk_assessment_of_Biocides/doc/TNsG/TNsG_DATA_REQUIREMENTS/TNsG-Data-Requirements.pdf)



Details for  
Method  
Validation

## ❑ Additional guidance on: TNsG on Data Requirements, Part A, Chapter 2, Point 4 “Analytical Methods for Detection and Identification” and Part B, Chapter 2, Point 4 “Methods of Identification and Analysis” (May 2009)

[http://ihcp.jrc.ec.europa.eu/our\\_activities/public-health/risk\\_assessment\\_of\\_Biocides/doc/TNsG/TNsG\\_DATA\\_REQUIREMENTS/Addendum-TNsG-Data\\_Requirements\\_Analytical\\_Methods.pdf](http://ihcp.jrc.ec.europa.eu/our_activities/public-health/risk_assessment_of_Biocides/doc/TNsG/TNsG_DATA_REQUIREMENTS/Addendum-TNsG-Data_Requirements_Analytical_Methods.pdf)

## Which validation data are necessary?

**Selectivity:** Matrix interferences, blank value, confirmation

**Recovery:** 2 fortified concentration level, 5 samples per level

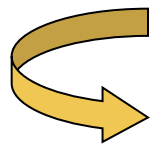
**Precision:** relative standard deviation of the recoveries per level

**Calibration:** Calibration line, raw data, equation of function

**LOQ:** Defined as lowest fortified level with acceptable recovery

**Chromatograms:** Blank samples, fortified samples at LOQ, standard chromatograms

**...and a clear documented description of the method and the validation!**

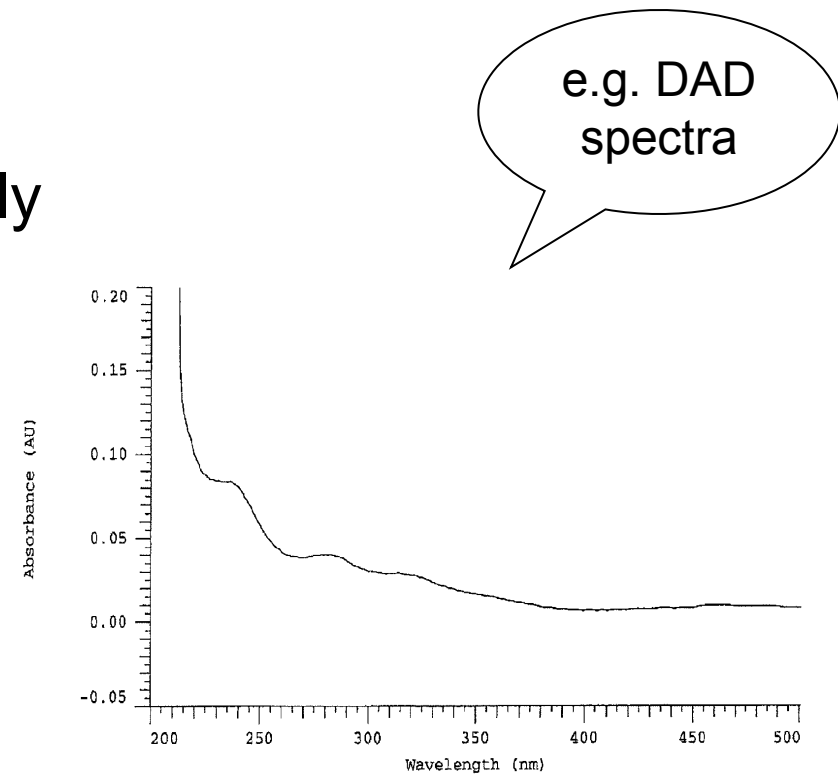


**General extent of validation comparable to the procedure for authorization of plant protection products (SANCO/825/00 rev. 8.1), but differences...**

# Frequent dissent: the type and extent of confirmation

## □ Requirement for Biocides

“... demonstration of selectivity, unless highly specific techniques are employed ...”



What is a “highly specific technique”?

What is meant by “demonstration”?

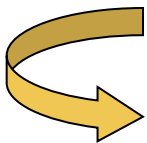
Which data are necessary to demonstrate “selectivity”?

# Frequent dissent: the type and extent of confirmation

## □ More explicit requirement for Pesticides:

“...confirmation, that the right analyte is detected **and** the signal is quantitatively correct ...”

- Includes qualitative and quantitative confirmation.
- Validation data (recovery, calibration, precision for at least  $\geq 3$  samples at LOQ) are required.
- acceptable techniques e.g. GC-MS & LC-MS  $\Leftrightarrow$  2 additional ions; MS/MS detection  $\Leftrightarrow$  2 additional transitions; GC  $\Leftrightarrow$  HPLC; GC-MS  $\Leftrightarrow$  GC-ECD; LC-MS  $\Leftrightarrow$  LC-UV...



**Update for biocides is necessary!**



# Multi-residue methods for biocides?

TNsG on Data Requirements: “In principle, residue methods proposed should be multi-residue methods, a standard multi-residue method should be assessed and reported...”

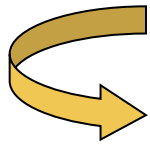
- ❑ DFG S19 and QuEChERS method for pesticides
- ❑ Applicability for soil, water(?)



- ❑ for drinking water samples: direct injection with LC-MS/MS separation and detection
- ❑ direct injection applicable e.g. for bendiocarb, cyproconazole, dichlorvos, fenoxacarb, imidacloprid, metofluthrin, pyriproxifen, tebuconazole, thiamethoxam, thiacloprid (regulated as pesticides + biocides)

## Summary and Conclusion (1)

- ❑ Clear rules to define the minimum scope of methods (which matrices?) are needed.
- ❑ PT based definitions are necessary identifying for which matrices residue analytical methods are indispensable.
- ❑ Generally acceptable waiving arguments should be discussed instead of numerous case-by-case decisions.
- ❑ The residue definition should be generally discussed by toxicological and ecotoxicological experts during the EU assessment and published in the Assessment Report.
- ❑ The requirements for the validation of analytical methods for biocides should be updated.
- ❑ Clarification about validation of confirmatory methods required!

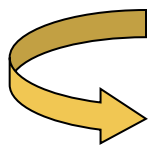


**Job for ECHA and Competent Authorities**

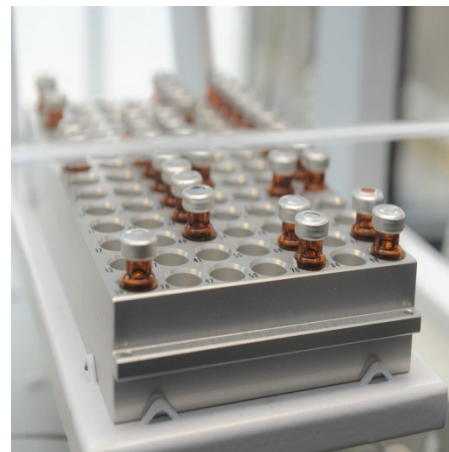


## Summary and Conclusion (2)

- ❑ Identification of high priority data gaps.
- ❑ Collection of data about validated multi-residue methods for environmental matrices.
- ❑ Testing of applicability of established multi-residue methods for biocides in environmental matrices.
- ❑ Development and validation of new multi-residue methods for selected matrices.



**Job for monitoring labs**





Risiken erkennen – Gesundheit schützen

**Thank you for your attention**

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# What's more up to date for pesticides?

- ❑ Analytical techniques no longer commonly available:
  - GC with packed columns
  - LC-LC column switching
  - electrochemical detectors for HPLC and ion pair chromatography
  
- ❑ Additional analytical techniques considered commonly available now:
  - GC-HRMS
  - GC-MS/MS
  - GC-MS<sup>n</sup>
  - LC-HRMS (+ LC-MS)

