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Intelligent Testing within REACH

Exploration of Annex XI to save animals and costs

Ineke Gubbels –van Hal
Regulatory Consultant & REACH Manager
Ciba Expert Services

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Contents

- REACH and animal testing
- Annex XI possibilities
- Implementation of ITS



REACH

- 30,000 phase-in substances
- Limited data available for HPVC
 - 14% base-set testing (~Annex VIII)
 - 65% less
 - 21% no data

Different for lower volumes?

REACH

Data generation

- High costs
- Numerous laboratory animals

REACH

Tonnage	Standard animal tests	Laboratory animals
> 1 tonne/year (Annex VII)	Local LymphNode Assay.	20-22
> 10 tonnes/year (Annex VIII)	Additional to Annex VII: skin and eye irritation, acute toxicity (all routes if appropriate), 28-day toxicity, reproduction screening, teratogenicity (1 species), toxicokinetic assessment, acute fish.	+ 270-1000
> 100 tonnes/year (Annex IX)*	Additional to Annex VII + VIII: 90-day study, developmental toxicity, long-term fish, aquatic bioaccumulation.	+ 1800-3600
>1000 tonnes/year (Annex X)*	Additional to Annex VII – IX: depending on the outcome of other studies chronic toxicity, two generation study, carcinogenicity, long-term birds.	+ 1700-3400

* At these levels testplans have to be submitted to the competent authorities

Annex XI

(Adaptation of the standard testing regime)

▶ intelligent testing

Annex XI

Use of existing data

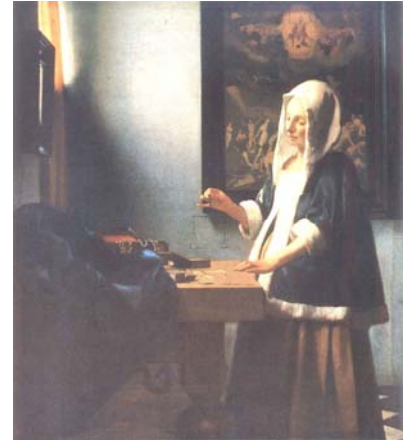
- Non-GLP data
 - physical-chemical
 - (eco)toxicological

- Historical human data

Annex XI

Weight of evidence

logPow:	model	21
	msds	>7
	handbook	WS 0.1 µg/L + miscible in organic solvents
LC50:	handbook	> 250 mg/L
	publication	> 2000 mg/L
	internal report	> 100 mg/L



Annex XI

(Q)SAR?

- ECOSAR
- TGD
- Commercial packages (DEREK/TOPKAT/MultiCase)
- New developments

Annex XI

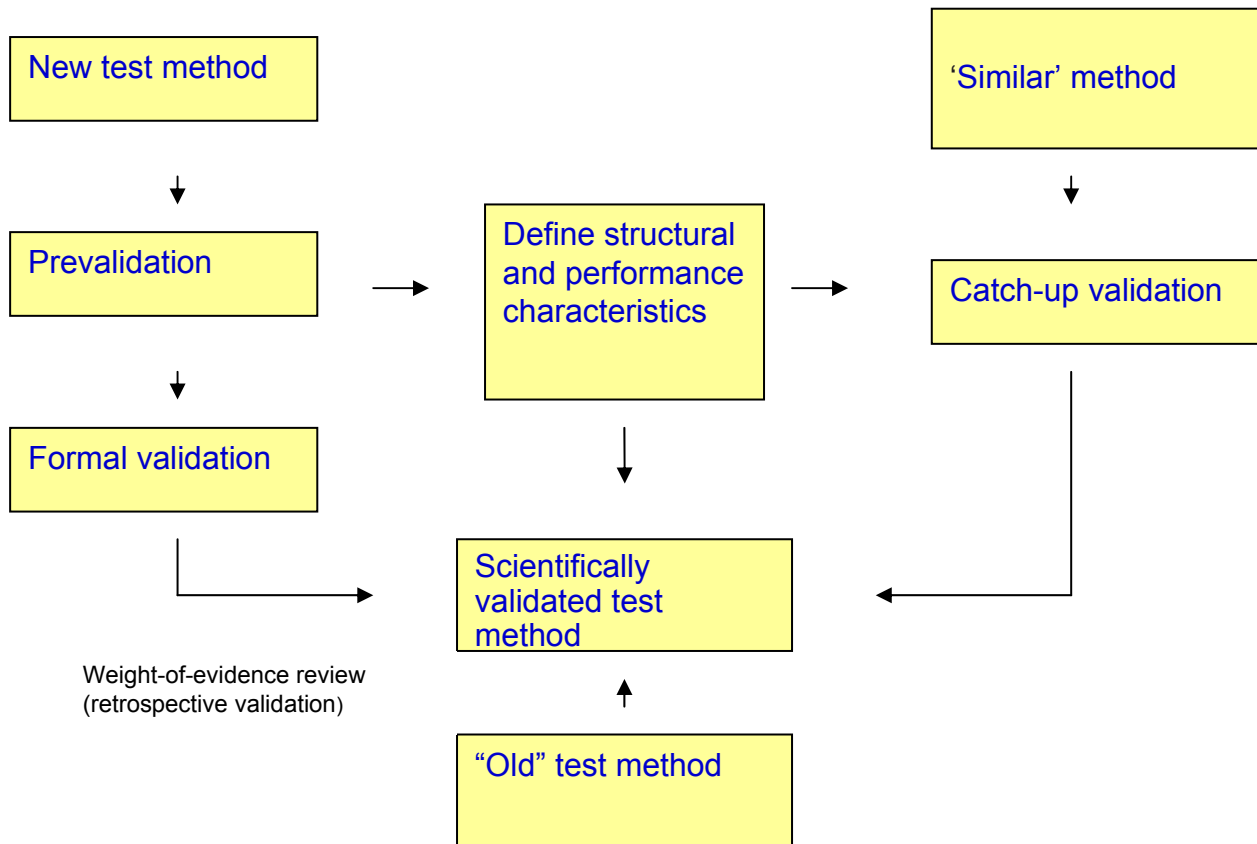
In vitro methods

validated: phototoxicity, skin corrosion

validation criteria: OECD, ECVAM

test batteries: reproduction toxicity

Annex XI

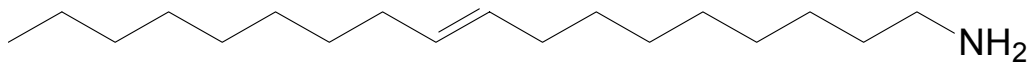
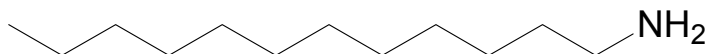
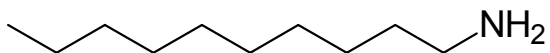
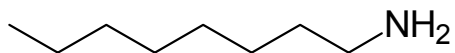


Annex XI

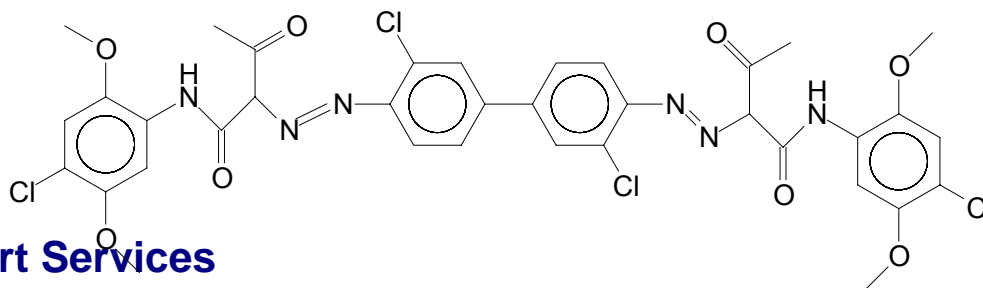
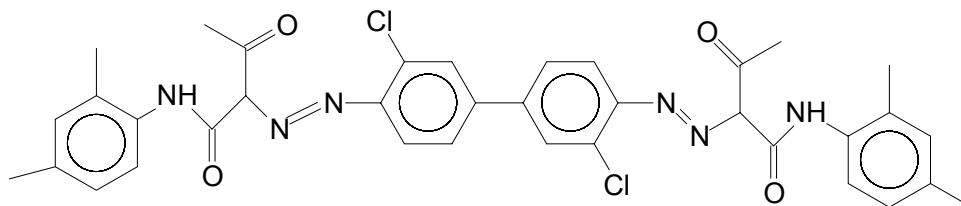
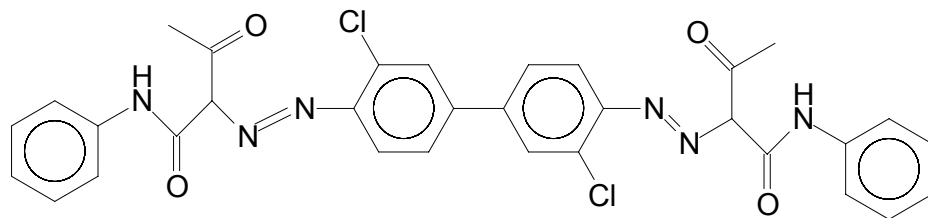
Read-across

- Common functional group
- Common precursor/breakdown product
- Constant pattern

Annex XI



Annex XI



Annex XI

Testing technically not possible

Exposure-driven testing

- Annex VIII 8.6 and 8.7
- Annex IX and X

Remarks

- Reliability of data
- Weight of evidence
- Replacement
 - Local effects
 - Systemic effects

Implementation

Time schedule	Expectations (?)
Short-term (1-2 years)	Existing data/weight-of-evidence/read-across/grouping
Mid-term (3-5 years)	<i>In vitro</i> tests local toxicity QSARs local toxicity
Long-term (5-10 years)	<i>In vitro</i> tests / QSARs Integrated approach for systemic toxicity

Implementation

Threats

- Conservatism
- Time pressure
- Price

Developments

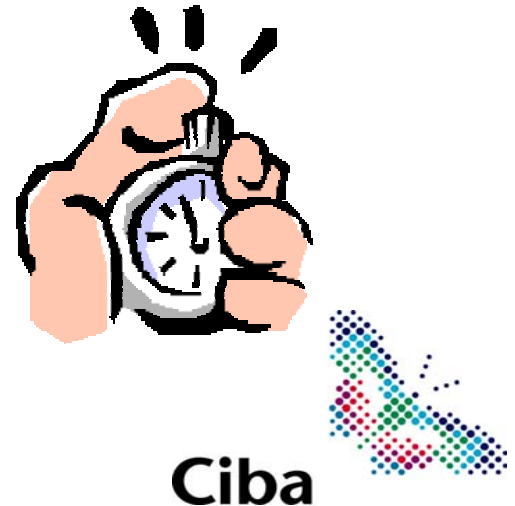
- *In vitro* tests
- (Q)SARs batteries
- > reduction/refinement
- Integrated testing strategies
- > replacement

Developments

Pragmatic approach

Annex XI +traditional methods

Time might be our greatest problem



Thank you for your attention

Questions?

ineke.gubbels@cibasc.com

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