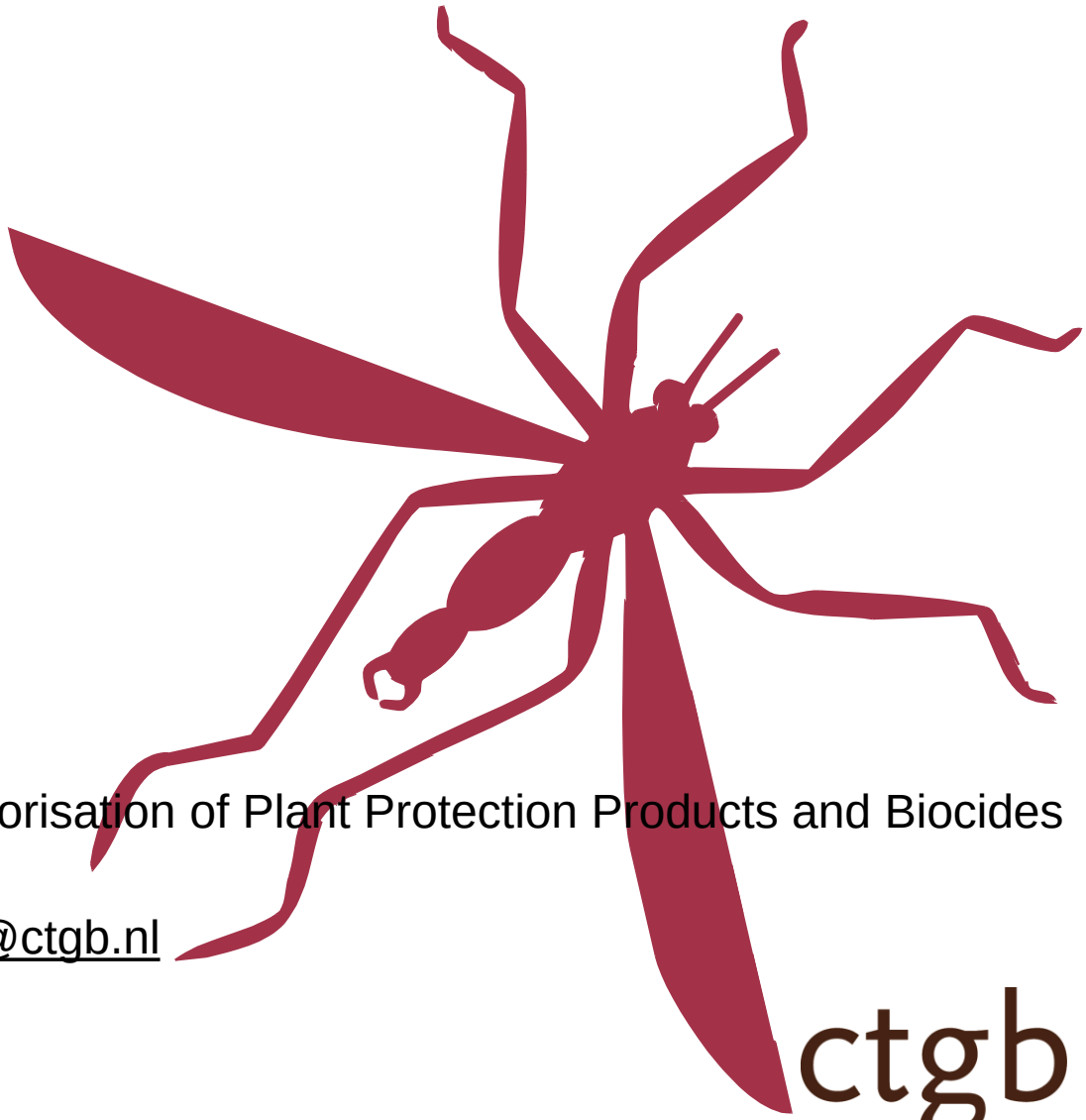
Residue evaluation other data requirements



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May 2012

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EU framework
Regulation (EC) 1107/2009

Data requirements active substances

- Commission Regulation (EU) No 544/2011
- Basic dossier
- “The information provided must be sufficient to permit an evaluation to be made as to the risk for man, associated with the handling and use of plant protection products containing the active substance, and the risk for man arising from residual traces remaining in food and water.”

- where relevant, set maximum residue levels, preharvest intervals to protect consumers and waiting periods, to protect workers handling the treated crops and products.

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EU framework
Regulation (EC) 1107/2009

Data requirements formulations

- Risk envelope
- All other crops, including their MRL and PHI
- National specific aspects (e.g. NL: leaching to ground water)

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Consumer exposure from the farm to the fork

consumer

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EU: Data requirements active substance

- Uptake and metabolism in appropriate plant group (leaf, root, fruit, grain, bean)
- Residue trials in crops (critical GAP)
- **Uptake, metabolism, distribution and excretion in livestock (laying hens, lactating goat, pigs)**
- **Livestock feeding studies**
- **Method for analysis of residue**
- **Succeeding crops**
- **Processing data**
- **Stability of stored samples**

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Livestock feed intake calculation

	% dry matter (dm)	chicken	Dairy cattle	Beef cattle	pig
Body weight		1.9	550	350	75
Daily maximum feed intake (dm)		120g	20 kg	15 kg	3 kg
Maximum		**% dm**	**% dm**	**% dm**	**% dm**
Group crop/ commodity					
I Green forage					
Grasses	20	-	100	100	-
Alfalfa/clover	20	-	40	40	15
Forage/rape	14	-	-	35	15
Kale/cabbage	14	5	35	35	15
Sugar beet leafs and	16	-	30	30	25
Silage (clover,	20	-	100	100	15
Fruit pomace	23	-	10	30	-
hay	85	-	100	100	15
II Grains					
Grains except Maize	86	70	40	80	80
Maize	89	70	30	30	40
Bran (Wheat and	89	15	20	20	20
III cereal straws	86	-	20	50	-
IV Pulses	86	30	20	20	40
V Root and Tubers					
potato, swede	15	20	30	60	60
Turnip	10	20	30	60	60
sugar/fodder beet	20	20	30	60	60
VI Oil seed/meal					
Soya bean, rape seed, peanut, sunflower seed, linseed	86	10	30	30	20

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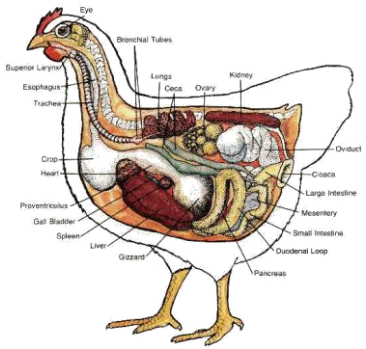
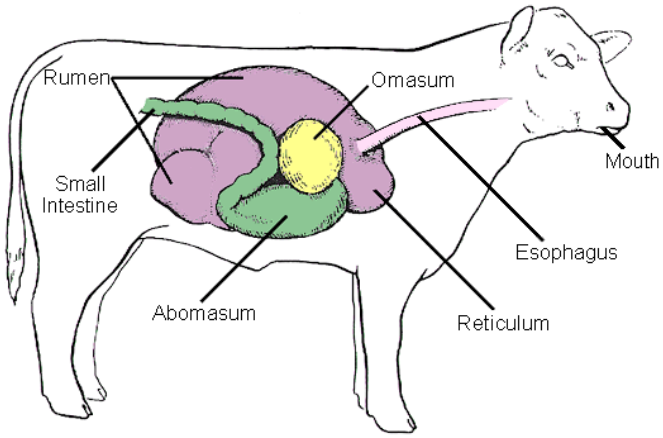
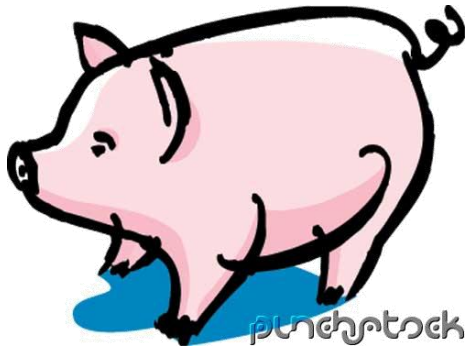
Metabolism in animals

- *If residue > 0,1 mg/kg dry feed*
- lactating ruminant, laying hen, pig







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Residue definition (animal)

Definition of residue is derived from metabolism studies in livestock

(using radio labelled substances at lab scale)

Why?	Compounds exposed to, to perform adequate risk assessment and enforcement
What?	Parent/metabolites
Where?	Edible animal parts

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Deriving animal MRLs: feeding studies




If residue > 0,1 mg/kg dry feed

28 days feeding trials => 'plateau'

	MRL for	
Milk	muscle	(fishery
Egg	kidney	products)
Fat	liver	

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Method of analysis

Method used in studies

- method should be fully described and fulfil criteria of SANCO/3029/99 (pre registration method)
- Untreated samples ‘spiked’ with analyte should be analysed together with the studied samples to check the method

Method for monitoring and enforcement

- method should be fully described and fulfil criteria of guidance document SANCO/825/00 (post registration method)
- Multi residue method: 300 actives in 1 analysis
  e.g. DFG S19
- T+ chemicals should be avoided

For existing substances, enforcement bodies have their own methods.

For new substances, applicant is responsible for submitting

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Method of analysis - characteristics

Extraction - organic solvent
- water phase, extracted with organic solvent
- organic solvent, clean up by chromatography (size, hydrophobicity)

Separation - GC, HPLC….

Detection - FID, UV, MS

Typical Limit of Quantitation (LOQ) with high-tech apparatus (HPLC-MS/MS) ~ 0.01 mg/kg

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Method of analysis – characteristics (2)

In general, pesticides are more or less fat soluble and less soluble in water

In general, metabolites (plant, animal) are more or less water soluble and less fat soluble.

It is difficult to develop a method in which both parent molecules and metabolites can be determined in one method.

For monitoring: keep residue definition as simple as possible (parent)

For risk assessment: keep residue definition as complete as necessary

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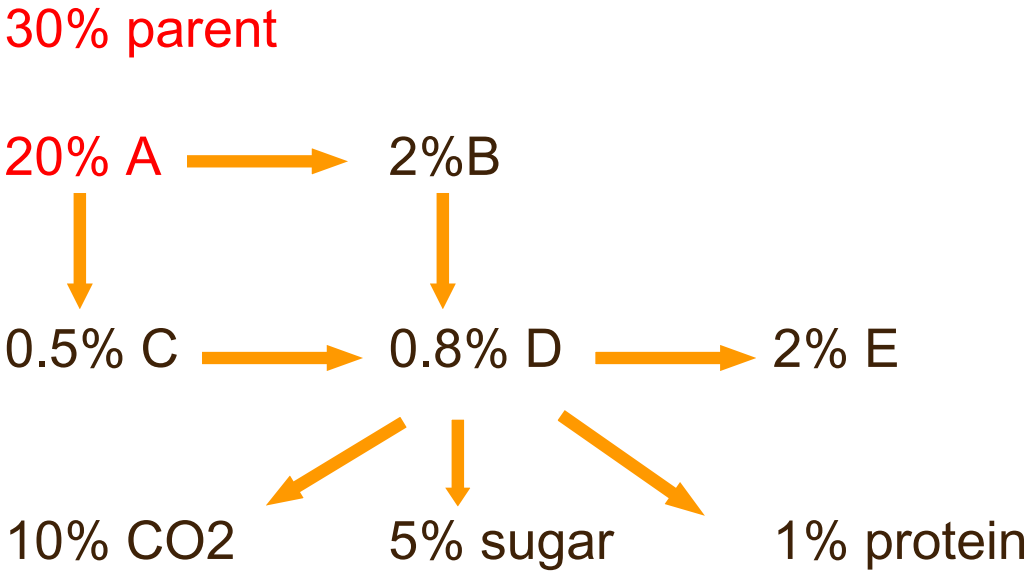
Example of residue definitions



- Residue definition for monitoring: parent
- Residue definition for risk assessment: parent + A
- Conversion factor (monitoring to risk assessment): 1.67

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Residues in Succeeding crops

When spraying a pesticide, x% is intercepted by the crop (fungicide, insecticide) or the weeds, but 100-x% reached the soil.

If this pesticide, or one or more of its soil metabolites is more or less persistent, residues might be present in soil in the next season and might be taken up by the succeeding crop.

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Succeeding crops (2)

General rule/trigger in EU: If more than 10% of the residue is present after 100d (DT90>100d), residues in succeeding crops should be investigated.

A succeeding crop often is a different crop, depending on the agricultural circumstances. Therefore, leafy vegetables, root crops, pulses or cereals should be investigated.

Residue definition might be different from foliar treated crops!

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Processing

Common processing

cooking, backing, pasteurisation

Hydrolysis study (heating) with ^{14}C-pesticide to investigate the fate of the residue during heating.

$\Rightarrow$ Residue definition after heating identical to raw crop?

Special processing

fermentation, composite products, barley mouting

Peeling

Concentration or dilution

drying, mixing, pressing juice

Example: orange juice: relevant in NL since e.g. children consume little whole fruit but might drink a large amount of orange juice.

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Storage stability

- Field trials will be performed in different seasons/years and samples will be stored frozen (up to 1y) and analysed at once
- The time samples have been stored residues might have been decomposed (due to instability)
- Therefore, samples spiked with known concentration of analyte should be stored for the same period under the same conditions to determine stability

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Test guidelines

- Residues: ‘Lundehn’, 1607/V/97
- US: EPA harmonized test guidelines
- OECD guidelines for residues (equivalent to both EU and US guidelines)

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Quality check

Studies should be performed according to:

- standard test protocol = guideline (EC/OECD=validated)
- GLP (Good Laboratory Practice for lab studies)
- GEP (Good Experimental Practice for field trials)
- Review of studies by experts of competent authorities (EU, MRL: member states + EFSA)

Public (peer reviewed) literature often does not fulfil standard requirements, but can give additional information

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References

- EU Regulation (EC) 1107/2009 http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2009:309:0001:0050:EN:PDF
- EU guidelines for the generation of residue data under (EC) 1107/2009 and (EC) 396/2005
  http://ec.europa.eu/food/plant/protection/pesticides/publications_en.htm
- EU Commission Regulation (EU) 544/2011 http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2011:155:0001:0066:EN:PDF
- Regulation (EC) No 440/2008 http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2008:142:0001:0739:EN:PDF
- US framework: http://www.gpo.gov/fdsys/pkg/FR-2007-10-26/pdf/E7-20826.pdf
- EPA guidelines: http://www.epa.gov/ocspp/pubs/frs/publications/Test_Guidelines/series870.htm
- OECD guidelines: http://www.oecd-ilibrary.org/environment/oecd-guidelines-for-the-testing-of-chemicals-section-4-health-effects_20745788

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