



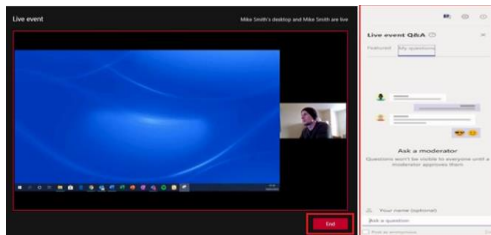
29 March 2021, 09:30-12:30/14:00-17:00
(Italian time)

First session: How to complete MSS composers for pesticides plant metabolism

Webinar guide for attendees

- This webinar **is being recorded**
- The webinar **is in English** and questions should be submitted in English through the platform (see hereunder).
- You are automatically connected to the audio broadcast. One-way audio (**listen only mode**).

Presentation window



Q&A box: For any questions related to the topic or unexpected IT issues





**RÉPUBLIQUE
FRANÇAISE**

*Liberté
Égalité
Fraternité*



WEBINAR: METAPATH

How to complete MSS composers for pesticides metabolism studies

1. Context



Evaluation of phytopharmaceutical active substances

Regulatory Requirement (Reg CE N° 1107/2009)

• Toxicology:

- Rat (ADME)

• Consumer Safety:

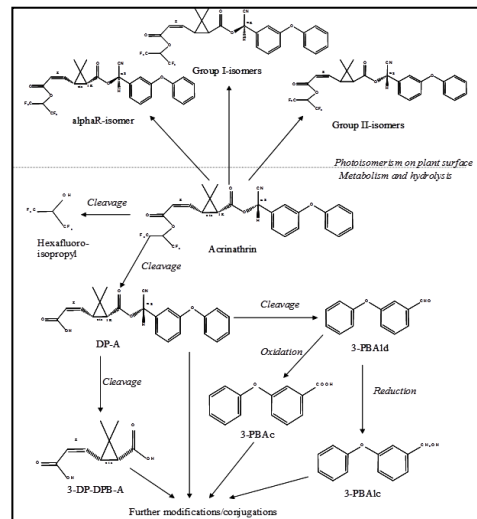
- Plants
- Livestock
- Processed commodities

• Environment:

- Soil
- Water

Metabolism Studies

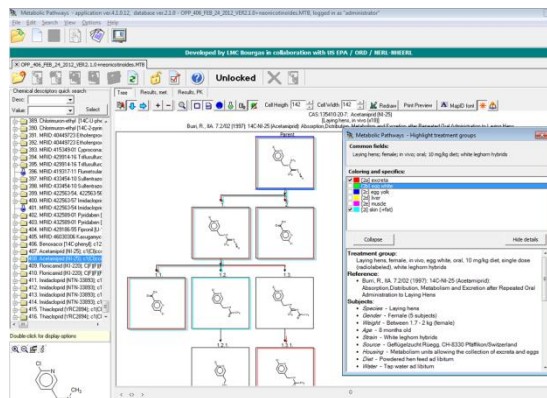
- Fate of radiolabeled active substances
- Identification of relevant metabolites
 - Toxicological properties
 - Distribution in different organs /compartments
- Residue Definition in food and environmental compartments



2. Metapath development

What is Metapath

- Database on pesticide metabolism
- Metabolic pathways
- Experimental conditions in the studies
- Chemical structure comparisons
- Search for common metabolites
- Metabolic profile comparisons



Metapath development

US-EPA 2005
Laboratory of
Mathematical
Chemistry, Bourgas,
Bulgaria:

**Database +Rat
MMS Composer**



MetaPath: An electronic knowledge base for collating, exchanging and analyzing case studies of xenobiotic metabolism

Richard C. Kolanczyk^{a,*}, Patricia Schmieder^a, William J. Jones^b, Ovanes G. Mekenyan^c, Atanas Chapkanov^c, Stanislav Temelkov^c, Stefan Kotov^c, Maria Velikova^c, Verginia Kamenska^c, Krasimir Vasilev^c, Gilman D. Veith^d

^a Mid-Continent Ecology Division, National Health and Environmental Effects Research Laboratory, Office of Research and Development, US EPA, 6201 Congdon Boulevard, Duluth, MN 55804, USA

^b Ecosystems Research Division, National Exposure Research Laboratory, Office of Research and Development, US EPA, 960 College Station Road, Athens, GA 30605, USA
^c Laboratory of Mathematical Chemistry, University "Prof. Asen Zlatarov", 1 Yakimov Street, Bourgas 8010, Bulgaria

^d International QSAR Foundation, 1501 W. Knife River Road, Two Harbors, MN 55616, USA

Metapath User group

•OECD Project Proposal: MetaPath, a Pesticide Metabolite Database with Data Evaluation Tools “Metapath User Group”

- USA, Canada, Australia, France,
 - Japan, Austria, Slovakia, UK,
 - EFSA, ECHA,
 - Industry
-
- Case Study PMRA : livestock Metabolism
 - Collaboration Anses –EPA (2012)
 - Project EFSA-ANSES-BfR (2019)



3. Inside Metapath



MSS Composer

Entry form for data to be entered in the base (rat livestock, plant and rotational crops)

- OECD harmonized Template
- Data Evaluation Report (DER) text format.
- XML File (Entry in the base)

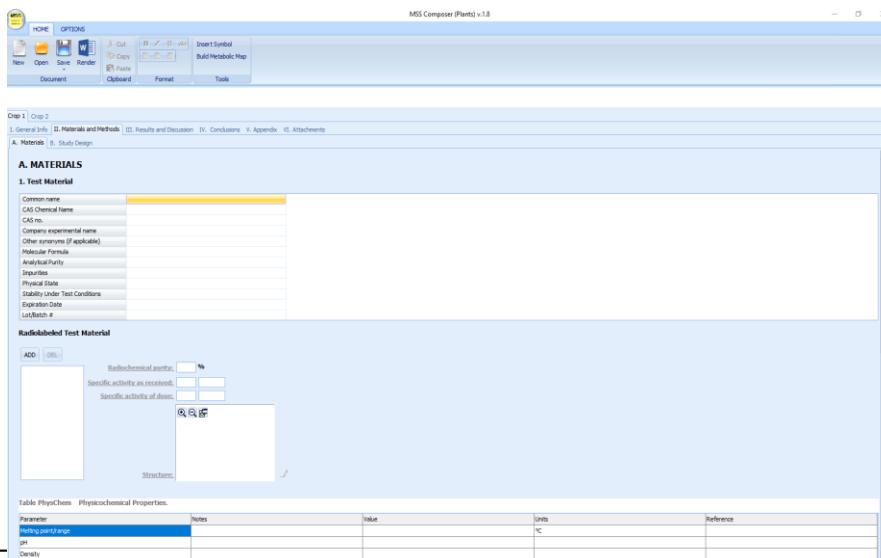


Table PhysChem Physicochemical Properties.

Parameter	Notes	Value	Units	Reference
Melting point			°C	
pH				
Density				

Metapath Database

- Metabolic profiles
- Tool for search and comparison

The screenshot displays the Metapath Database application interface. The main window shows a metabolic pathway for Acetaminophen (NI-25) starting from a parent compound and branching into various metabolites. The pathway is visualized with chemical structures and numbered nodes (1, 2, 3, 1.1, 1.2, 1.3, 2.1, 3.1). A search bar on the left lists various chemical descriptors, with Acetaminophen (NI-25) selected. A detailed information panel on the right provides the following data:

Metabolic Pathways - Highlight treatment groups

Common fields:
Laying hens; female; in vivo; oral; 10 mg/kg diet; white leghorn hybrids

Coloring and specifics:
 [2a] excreta
 [2c] egg yolk
 [2d] liver
 [2e] muscle
 [2j] skin (+fat)

Treatment group:
Laying hens, female, in vivo, egg white, oral, 10 mg/kg diet, single dose (radiolabeled), white leghorn hybrids

Reference:

- Burn, R., IIA 7.2/02 (1997): 14C-NI-25 (Acetaminophen): Absorption, Distribution, Metabolism and Excretion after Repeated Oral Administration to Laying Hens

Subjects:

- Species - Laying hens
- Gender - Female (5 subjects)
- Weight - Between 1.7- 2 kg (female)
- Age - 8 months old
- Strain - White leghorn hybrids
- Source - Geflügelzucht Ruegg, CH-8330 Pfäfers/Switzerland
- Housing - Metabolism units allowing the collection of excreta and eggs
- Diet - Powdered hen feed ad libitum
- Water - Tap water ad libitum

Metapath Database

Identification of common metabolites

Developed by LMC Bourgas in collaboration with US EPA / ORD / NERL-INHEERL

Chemical descriptors quick search

Desc: [] Value: []

Tree Results, met Results, PK

Unlocked

Sensitivity: 33.333%

Redraw Print Preview MapID font

CAS:135410-20-7: Acetamiprid (NI-25)
[Lactating goat, in vivo (x14)]

Buri, R., IIA, 7 2/01 (1997); 14C-NI-25 (acetamiprid): Absorption, Distribution, Metabolism and Excretion after Repeated Oral Administration to Lactating Goats

Parent

Chemical structure diagram showing the parent compound Acetamiprid (NI-25) and its metabolites. The parent structure is highlighted in a blue box. Metabolites are shown in a hierarchical tree structure, with some highlighted in red and others in green boxes. The diagram illustrates the metabolic pathways and the resulting metabolites.

CAS:136261-41-3: Imidacloprid (NTN-33893)
[Laying hens, in vivo (x8)]

Klein, O. and Brauner, A. (1992) [Methylen-14C]imidacloprid: Absorption, distribution, excretion and metabolism in laying hens

Parent

Chemical structure diagram showing the parent compound Imidacloprid (NTN-33893) and its metabolites. The parent structure is highlighted in a blue box. Metabolites are shown in a hierarchical tree structure, with some highlighted in red and others in green boxes. The diagram illustrates the metabolic pathways and the resulting metabolites.

Double-click for display options

DEPR/URSA

Conclusion

Identification of common metabolites

Chemical Structure

Similarity

Facilitate risk assessment

Residue definition

Aggregate RA

Improve hazard identification (QSAR complementarity)

Reduce animal testing and guideline study requirements

Mutualize between regulatory agencies

Streamline information flow between industry and regulators



Let's start

Monday 29 March

TIME	ITEM
09:30 – 09:45	Introduction & presentation of the project
09:45 – 10:00	Opening MSS
10:00 – 10:35	General Info tab
10:35 – 11:30	Materials
11:30 – 11:45	Coffee Break
11:45 – 12:30	Results tables part 1
12:30 – 14:00	Lunch Break
14:00 – 14:45	Results tables part 2
14:45 – 15:30	Appendix
15:30 – 15:45	Coffee break
15:45 – 16:15	Attachment / Render / Conclusion
16:15 – 17:00	Key points Q&A

Theory
Live session
Summary KP
QA

Let's start

Wednesday 31 March

TIME	ITEM
09:30 – 09:35	Introduction
09:35 – 10:30	Livestock composer
10:30 – 10:45	Coffee Break
10:45 – 11:30	Crop composer / rotational
11:30 – 12:00	Q&A session and conclusion

Theory
Live session
Summary KP
QA