Bundesamt für
Verbraucherschutz und
Lebensmittelsicherheit

Update on the German metabolite project

Implementing metabolites in routine analysis – findings and data evaluation

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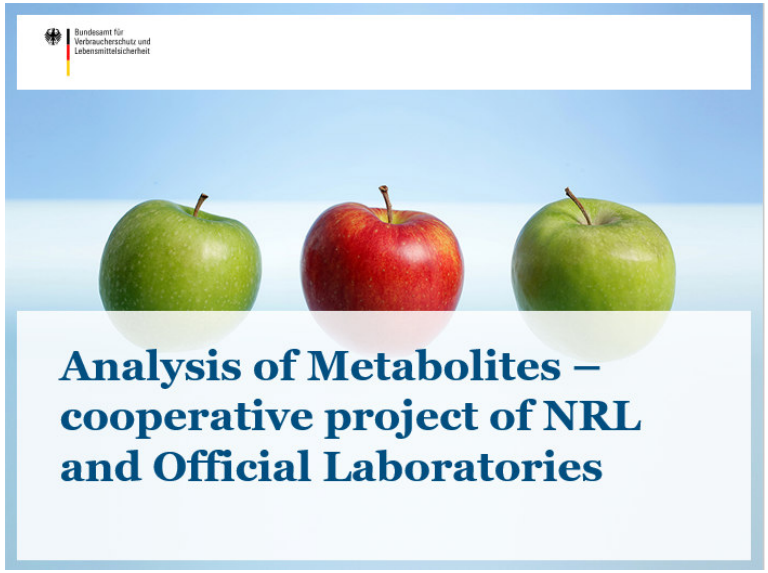
Update concerning project round 2019/2020

Project Round 2019/2020

➔ 13 out of 18 planned standards available to the labs

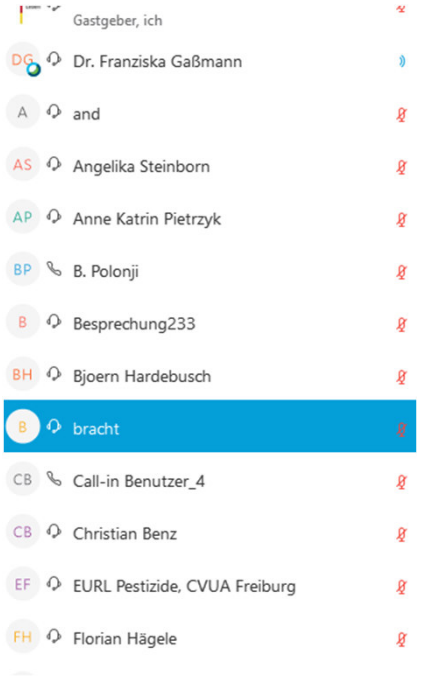
➔ 11 Labs took part and results of the method development available from 5 labs



Metabolite/ Analyte	Metabolite of	Reason	Mol. formula	CAS	Mol. Mass	Company
-	Pethoxamid	2018 authorisation	C16H22ClNO2	106700-29-2	295,8	HPC
Spiroxamincarbic acid	Spiroxamine	RD since 2016	C18H33NO4	156042-38-5	327,241	Bayer Pharma AG
M1	Iprodione	simplyfication of complex RD - non-authorised	C9H6Cl2N2O2	27387-87-7	245,06	LGC (Dr. Ehrenstorfer)
RP 30228	Iprodione	simplyfication of complex RD - non-authorised	C13H13Cl2N3O3	63637-89-8	330,17	LGC (Dr. Ehrenstorfer)
Halauxifen-methyl	-	new RD	C14H11Cl2FN2O3	943831-98-9	345,153	Dr. Ehrenstorfer (LGC)
RP 32490	Iprodione	simplyfication of complex RD - non-authorised	C10H7Cl2N3O3	79076-80-5	288,09	HPC
-	Mandestrobin	2015 authorisation	C19H23NO3	173662-97-0	313,39	Dr. Ehrenstorfer (LGC)
BTS 9608	Prochloraz	Working Document	C8H5Cl3O3	575-89-3	255,48	Dr. Ehrenstorfer (LGC)
BTS 9608	Prochloraz	Working Document	C8H5Cl3O3	575-89-3	255,48	Dr. Ehrenstorfer (LGC)
-	Mefentrifluconazole	2018 authorisation	C18H15ClF3N3O2	1417782-03-6	397,78	HPC
479M6	Metazachlor	wrong metabolite M16 needed!	C14H17N3O	75972-11-1	243,3	HPC
-	Oxathiapiprolin	2017 authorisation	C24H22F5N5O2S	1003318-67-9	539.52	HPC
CMBA	Sulcotrione	RD since 2017	C8H7ClO4S	53250-83-2	234,66	Santa Cruz
Desmethyl-Chlorpyrifos-methyl	Chlorpyrifos	RD since 2018	C6H5Cl3NO3PS	58997-13-0	308,51	HPC

Update concerning project development

Webmeeting in July 2020



- **20 participants**
- **Presentations from OfL and NRL to following topics:**
  - metabolite findings (2018-2019),
  - metabolites in drinking water,
  - analysis of biocides,
  - planning of the next project round 2020/2021

- **Include biocides (which may be analysed with multi residue methods) into the project – starting with pyrethroids**
- **Findings, data evaluation and data submission**

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Update concerning next project round 2020/2021

Project 2020/2021 – 11 Labs participating

NRL is currently preparing standards and solutions	
CGA 192155 (Fludioxonil)	6-Hydroxymethylpymetrozin
R014821 (Imazalil)	CGA371075 (Pymetrozin)
Pydiflumetofen	BH479-16 (Metazachlor)
Fenpyroximate-M3	Bicyclopyron
FK-772 (Imazalil)	SYN 503780 and SYN 545910 (Bicyclopyron)
CGA 107955 and CGA 67869 (Metalaxyl)	Allethrin; Azamethiphos; Cyphenothrin; Phenothrin; Transfluthrin
IN-MW977 and IN-MU210 (Proquinazide)	

Update concerning findings and data evaluation

To what end should the data be evaluated?

- **Is it possible to use the submitted data of the participating labs to identify relevant analytes and data gaps?**
- **Which metabolites are relevant and should be implemented from more labs? (e.g.: analysed for and found)**
- **Where are the data gaps and what shall we do about it? (e.g. no or very small number of analyses)**

Data evaluation – How?

- **Data of the national monitoring programm from 2018**
- **All Analytes from the projects (2012-2018) were included (137 table positions)**
- **50 main substances (including „sum“ entrys e.g. sulfoxaflore, sum of isomers) and 55 metabolites and 32 „real“ sums**

Wirkstoff	Wirkstoffgruppe	Metabolit/Summe	Anzahl der Untersuchungen	Untersuchungen ohne Rückstände (nicht bestimmbar)	Untersuchungen mit Rückständen	Untersuchungen mit Rückständen in %	Untersuchungen mit Rückständen über dem Höchstgehalt	Untersuchungen mit Rückständen über dem Höchstgehalt	Metabolit Projektjahr	Info	RD MRL Database!
Acetamiprid	Acetamiprid	Mu	15693	14875	818	5,21	17	8	-		
IM-2-1, N-desmethyl-acetamiprid, Metabolit von Acetamiprid	Acetamiprid	Meta	2733	2594	139	5,09	0	0	2012/2013	Acetampirid-N-desmethyl (M	
Acetamiprid, Summe aus Acetamiprid und IM-2-1-Metabolit, insgesamt berechnet als	Acetamiprid	Sum	232	222	10	4,31	0	0	-		
Acibenzolar-S-methyl,											

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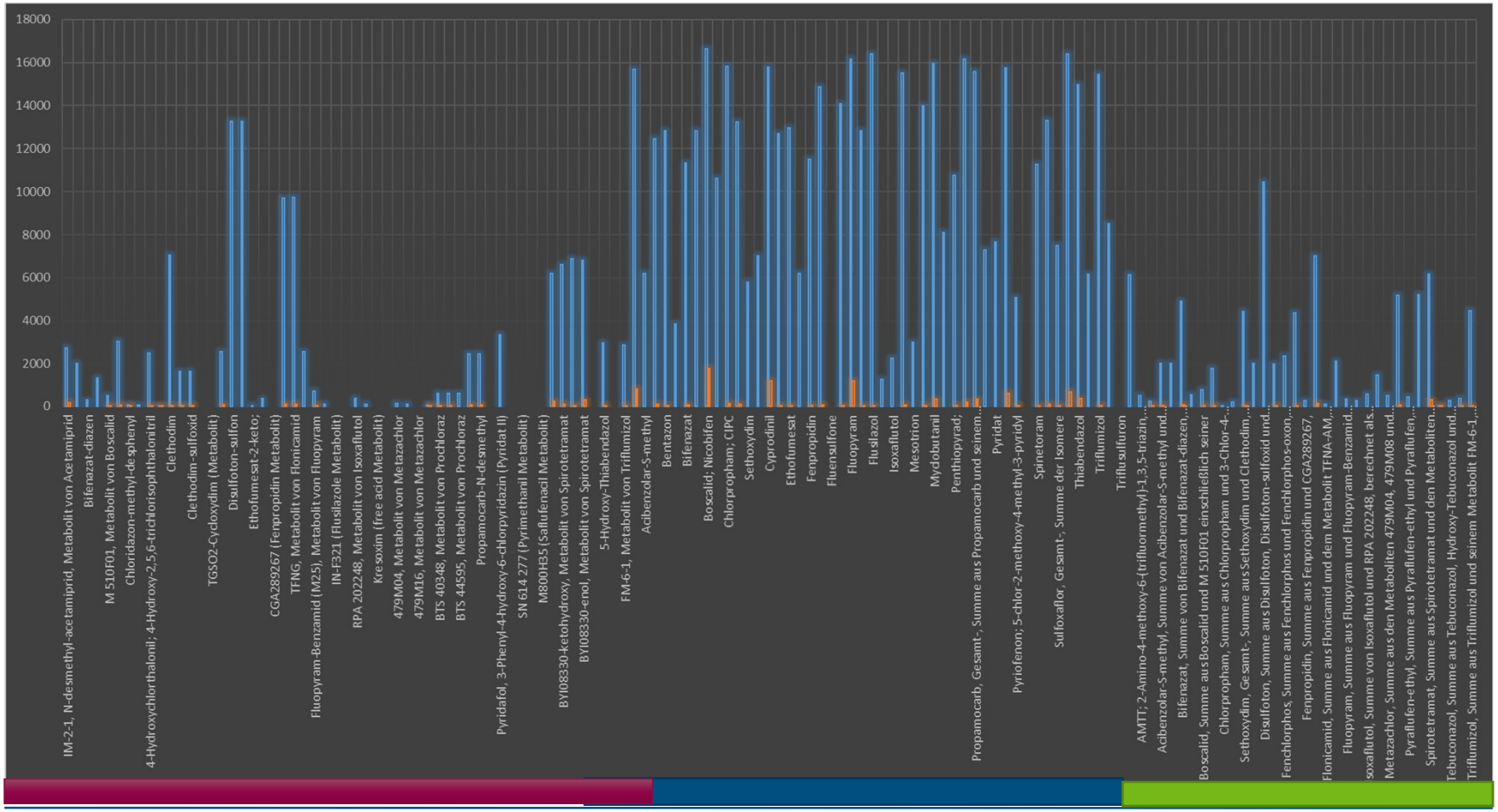
Identify relevant analytes

#Analyses (blue) and findings (orange)

Sorted metabolite (red), main substance (blue), sum (green)



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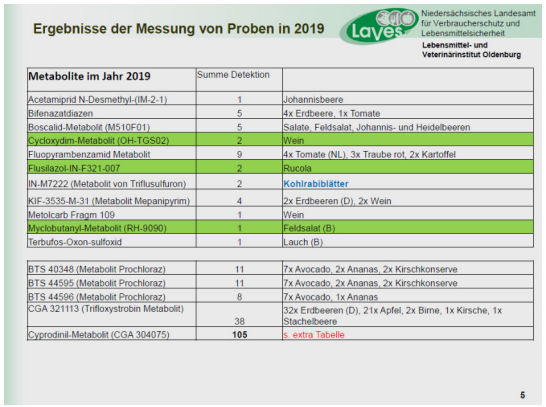
Findings from participating pesticide lab Oldenburg

- **Metabolite CGA 304075 (Cyprodinil) 105 findings (strawberries, other berries, cherries, apples, grapes – 18 different plant matrices)**
- **Metabolite CGA 321113 (Trifloxystrobin) 38 findings (strawberries)**
- **Metabolites of Prochloraz:**
  - BTS40348 and BTS44959 11 findings of each in avocado, ananas, cherries
  - BTS 44596 8 findings in avocado and ananas
- **Fluopyrambenzamide 9 findings (tomato, grapes, potatoes)**
- **Metabolite M510F01 (Boscalide) 5 findings (strawberries, tomato)**
- **Bifenazat-diazene 5 findings (salad, berries)**
- **Below 5 findings: Acetamipirid-N-desmethyl, Metabolite IN-M/222 (Triflusulfuron), Terbufos-oxon-sulfoxide**



Ergebnisse der Messung von Proben in 2019

Niedersächsisches Landesamt für Verbraucherschutz und Lebensmittelsicherheit
Lebensmittel- und Veterinärinstitut Oldenburg

Metabolite im Jahr 2019	Summe Detektion	
Acetamiprid N-Desmethyl-(IM-2-1)	1	Johannisbeere
Bifenazatdiazen	5	4x Erdbeere, 1x Tomate
Boscalid-Metabolit (M510F01)	5	Salate, Feldsalat, Johannis- und Heidelbeeren
Cycloxydim-Metabolit (OH-TGS02)	2	Wein
Fluopyrambenzamid Metabolit	9	4x Tomate (NL), 3x Traube rot, 2x Kartoffel
Flusilazol-IN-F321-007	2	Rucola
IN-M7222 (Metabolit von Triflusulfuron)	2	Kohlrabiblätter
KIF-3535-M-31 (Metabolit Mepanipyrim)	4	2x Erdbeeren (D), 2x Wein
Metolcarb Fragm 109	1	Wein
Myclobutanyl-Metabolit (RH-9090)	1	Feldsalat (B)
Terbufos-Oxon-sulfoxid	1	Lauch (B)
BTS 40348 (Metabolit Prochloraz)	11	7x Avocado, 2x Ananas, 2x Kirschkonserve
BTS 44595 (Metabolit Prochloraz)	11	7x Avocado, 2x Ananas, 2x Kirschkonserve
BTS 44596 (Metabolit Prochloraz)	8	7x Avocado, 1x Ananas
CGA 321113 (Trifloxystrobin Metabolit)	38	32x Erdbeeren (D), 21x Apfel, 2x Birne, 1x Kirsche, 1x Stachelbeere
Cyprodinil-Metabolit (CGA 304075)	105	s. extra Tabelle

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Results and slide from presentation of Iris Suckrau during webmeeting metabolite project

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Findings from participating pesticide lab Erlangen

- **Metabolite FM-6-1 (Triflumizole) 1 finding out of 3965**
- **Triflumizole 1 finding out of 7752 (0.086 mg/kg)**

- **Ethofumesat-2-keto 0 findings out of 3243**
- **Ethofumesat 6 findings out of 7751 (max. 0.296 mg/kg)**

- **Tritosulfuron 0 findings out of 7751**
- **AMTT 0 findings out of 3854**

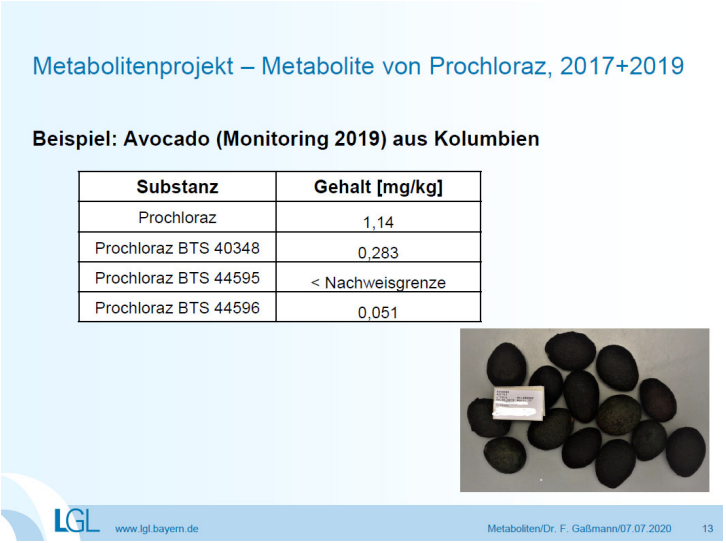
- **Chloridazon-desphenyl 0 findings out of 1780**
- **Chloridazon 2 findings out of 7756 (< 0.01 mg/kg)**

Results from presentation of Franziska Gaßmann during webmeeting metabolite project

Findings from participating pesticide lab Erlangen

products of animal origin

- **Prochloraz 0 findings out of 1587**
- **BTS 40348 0 findings out of 467**
- **BTS 44595 0 findings out of 467**
- **BTS 44596 0 findings out of 467**



plant products

- **Prochloraz 62 findings out of 7694 (max. 1.5 mg/kg)**
- **BTS 40348 39 findings out of 3950 (max 0.283 mg/kg)**
- **BTS 44595 10 findings out of 3950 (max. 0.016 mg/kg)**
- **BTS 44596 20 findings out of 3950 (max. 0.076 mg/kg)**
- **BTS 9608 0 findings out of 174**

Results and slide from presentation of Franziska Gaßmann during webmeeting metabolite project

Data gaps - no data submitted

Analyte/Metabolite	Group	Metabolite/Sum/ Main	Metabolit Projektjahr
OH-TGSO2-Cycloxydim (Metabolit)	Cycloxydim	Meta	2014/2015
TGSO2-Cycloxydim (Metabolit)	Cycloxydim	Meta	2014/2015
CGA289267 (Fenpropidin Metabolit)	Fenpropidin	Meta	2016/2017
IN-F321 (Flusilazole Metabolit)	Flusilazol	Meta	2014/2015
Halauxifen	Halauxifen-methyl	Meta	2016/2017
Kresoxim (free acid Metabolit)	Kresoxim-methyl	Meta	2014/2015
MNBA (Mesotrione Metabolit)	Mesotrion	Meta	2014/2015
Pyraflufen (free acid Metabolit)	Pyraflufen-ethyl	Meta	2016/2017
SN 614 276 (Pyrimethanil Metabolit)	Pyrimethanil	Meta	2016/2017
SN 614 277 (Pyrimethanil Metabolit)	Pyrimethanil	Meta	2016/2017
M800H11 (Saflufenacil Metabolit)	Saflufenacil	Meta	2016/2017
M800H35 (Saflufenacil Metabolit)	Saflufenacil	Meta	2016/2017
Saflufenacil	Saflufenacil	Main	-
Hydroxy-Tebuconazol	Tebuconazol	Meta	2017/2018
4-Chlorophenyl-methyl sulfone (Thiobencarb Metabolit)	Thiobencarb	Meta	2016/2017
Triflusulfuron	Triflusulfuron	Main	2017/2018

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Data gaps - very low number of analyses…

Analyte/Metabolite	Group	M/S/Main	A	w/oR	wR	wR%
5-Hydroxy-Clethodim-Sulfon	Clethodim	Meta	3	1	2	*
Ethofumesat-2-keto;	Ethofumesat	Meta	3	3	0	*
Chlorpropham, Summe aus Chlorpropham und 3-Chlor-4-hydroxyanilin-konjugate,	Chlorpropham	Sum	23	23	0	0
Spirotetramat, Summe aus Spirotetramat und Metabolit BYI08330-enol,	Spirotetramat t	Sum	23	0	23	100
Chloridazon-methyl-desphenyl	Chloridazon	Meta	38	31	7	18,42
RH9090, Metabolit von Myclobutanil, ausgedrückt als Myclobutanil	Myclobutanil	Meta	38	3	1	2,63
4'-Hydroxychlorpropham-O-sulfon-säure, Metabolit	Chlorpropham	Meta	39	39	0	0
Flonicamid, Summe aus Flonicamid und dem Metabolit TFNA-AM, ausgedrückt als	Flonicamid t	Sum	71	71	0	0
6-(2-Chlorphenoxy)-5-fluor-4-pyrimidinol, Metabolit von Fluoxastrobin	Fluoxastrobin	Meta	71	71	0	0
RPA 203328, Metabolit von Isoxaflutol	Isoxaflutol	Meta	71	71	0	0
479M08, Metabolit von Metazachlor	Metazachlor	Meta	78	78	0	0
479M04, Metabolit von Metazachlor	Metazachlor	Meta	117	117	0	0

A…# analyses; w/oR…without residue findings; w...with findings

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Data gaps - very low number of analyses…

Analyte/Metabolite	Group	M/S/Main	A	w/oR	wR	wR%
Chlorpropham, Summe aus Chlorpropham und 4'-Hydroxychlorpropham-O-sulfonsäure,	Chlorpropham	Sum	199	199	0	0
Acetamiprid, Summe aus Acetamiprid und IM-2-1-Metabolit, insgesamt berechnet als	Acetamiprid	Sum	232	222	10	4,31
Fenpropidin, Summe aus Fenpropidin und CGA289267,	Fenpropidin	Sum	264	264	0	0
Flusilazol, Summe aus Flusilazol und seinem Metaboliten IN-F7321, insgesamt	Flusilazol	Sum	264	264	0	0
Tebuconazol, Summe aus Tebuconazol, Hydroxy-Tebuconazol und deren Konjugate,	Tebuconazol	Sum	264	264	0	0
Bifenazat-diazen	Bifenazat	Meta	282	282	0	0
Fluopyram, Summe aus Fluopyram und Fluopyram-Benzamid (M25),	Fluopyram	Sum	335	335	0	0
Fenchlorphos-oxon	Fenchlorphos	Meta	348	348	0	0
RPA 202248, Metabolit von Isoxaflutol	Isoxaflutol	Meta	387	387	0	0
Thiabendazol, Summe aus Thiabendazol und 5-Hydroxythiabendazol,	Thiabendazol	Sum	397	390	7	1,76
Pyraflufen-ethyl, Summe aus Pyraflufen-ethyl und Pyraflufen, ausgedrückt als	Pyraflufen-ethyl	Sum	466	466	0	0
AMTT; 2-Amino-4-methoxy-6-(trifluormethyl)-1,3,5-triazin, Metabolit von	Tritosulfuron (ehemals!)	Mu	534	534	0	0
M 510F01, Metabolit von Boscalid	Boscalid	Meta	542	515	27	4,98

A…# analyses; w/oR…without residue findings; w...with findings

Conclusion 1

Is it possible to use the submitted data of the participating labs to identify relevant analytes and data gaps?

- not yet
- the extrapolation from the data is because of the low number of labs/matrices and the short time (only 2018) in our point of view unreliable

➔NRL tasks:

- enhance reliability

Conclusion 2

Where are the data gaps and what shall we do about it?

- **Labs have problems to implement analytes in routine analysis**
- **Not all participating labs submitt their data!**
  - Reason 1: not able to submitt the data via the portal
  - Reason 2: analyte not fully validated or shows problems during on-going validation

➔NRL tasks:

- **solve submitting problems with data evaluation panel**
- **spread positive results and enhance inter-lab communication**

Conclusion 3

Which metabolites are relevant and should be implemented from more labs?

- Those wich are possible to implement in the MRM for routine analysis and show some findings for example:
  - CGA 304075 (Cyprodinil)
  - Prochlorazmetabolites (BTS40348, BTS44959, BTS 44596)
  - Fluopyrambenzamide

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Thank you!

LLBB Frankfurt O.
Guido Warschewske

CVUA RRW
Jens Arne Andresen

CVUA Münster
Sabine Bracht
Eva Blanke

LAV Halle
Birgit Polonji

LALLF Rostock
Friederike Habedank

LGL Erlangen
Franziska Gaßmann

LLBB Berlin
Stefanie Ronczka

LUFA Speyer
Dieter Martens

LVI Oldenburg
Iris Suckrau

LUA Sachsen
Thomas Frenzel

Contact:

Nadja Buchner
NRL for pesticides
nrl-pestizide@bvl.bund.de

Extra: Data evaluation by NRL

- **Data from national Monitoring 2018 may be available to you via BVL-homepage:**

https://www.bvl.bund.de/DE/Arbeitsbereiche/01_Lebensmittel/01_Aufgaben/02_AmtlicheLebensmittelueberwachung/07_PSMRueckstaende/01_nb_psm_2018_tabellen/nbpsm_2018_tabellen_node.html

- **Data used from the table „overview about number of analyses, number of samples with residues, MRL exceedance and non-copliant samples“.**
- **In this evaluation (standing automatic evaluation) analytes or matrices with no reports are not visible.**
- **Relevant Codes were replaced by NRL and filled with 0 to evaluate which analytes are seldom analysed.**

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Analytes of the project up to 2018

4-HSA (Chlorpropham Metabolit)
4-Hydroxy-Chlorothalonil (Metabolit)
4-OH-Cyprodinil (Metabolit)
8-Hydroxy-Bentazone (Metabolit)
Acetampirid-N-desmethyl (Metabolit)
Ametoctradin
AMTT (Tritosulfuron Metabolit)
Benzovindiflupyr
BH 479-21 (Metazachlor Metabolit)
BH 479-4 (Metazachlor Metabolit)
BH 479-8 (Metazachlor Metabolit)
Bifenazate-diazene (Metabolit)
BTS 44596 (Prochloraz Metabolit)
BTS40348 (Prochloraz Metabolit)
BTS44595 (Prochloraz Metabolit)
CGA 210007 (Acibenzolar S-methyl Metabolit)
CGA 324041 (Acibenzolar S-methyl Metabolit)
CGA289267 (Fenpropidin Metabolit)
Clethodim-Sulfone (Metabolit)
Clethodim-Sulfoxide (Metabolit)
CPIA (Fenvalerat Metabolit)
Desmethylbixafen (Metabolit)
Desphenyl Chloridazon (Metabolit)
Disulfoton-Sulfone (Metabolit)
Disulfoton-Sulfoxide (Metabolit)
Ethofumesate-2-keto (Metabolit)
Fenchlorphos oxon (Metabolit)
Fluensulfone
Flufenacet oxalate (Metabolit)
Flufenacet sulfonic acid (Metabolit)
Fluopyram-benzamide (Metabolit)
FM-6-1 (Triflumizole Metabolit)
Halauxifen (Halauxifen-methyl Metabolit)
Hydroxy-Tebuconazole (Metabolit)
IN-F321 (Flusilazole Metabolit)
IN-M7222 (Triflusulfuron Metabolit)
Kresoxim (free acid Metabolit)
M 510F01 (Boscalid Metabolit)
M55 (Fluoxastrobin Metabolit)
M800H11 (Saflufenacil Metabolit)
M800H35 (Saflufenacil Metabolit)
N-desmethyl Propamocarb (Metabolit)
N-oxide Propamocarb (Metabolit)
MNBA(Mesotrione Metabolit)"
OH-TGSO2-Cycloxydim (Metabolit)
Open-ring-2-keto ethofumesate Lithium salt (Metabolit)
Penflufen
Penthiopyrad
Pyraflufen (free acid Metabolit)
Pyridafol
Pyriofenone
RH9090 (Myclobutanil Metabolit)
RPA 202248 (Isoxaflutol Metabolit)
RPA 203328 (Isoxaflutole Metabolit)
SN 614 276 (Pyrimethanil Metabolit)
SN 614 277 (Pyrimethanil Metabolit)
Spinetoram major
Spinetoram minor
Spirotetramat-cis-enol (Metabolit)
Spirotetramat-cis-keto-hydroxy (Metabolit)
Spirotetramat-enol-glucoside (Metabolit)
Spirotetramat-monohydroxy (Metabolit)
Sulfoxaflor
TFNA (Flonicamid Metabolit)
TFNA-AM (Flonicamid Metabolit)
TFNG (Flonicamid Metabolit)
TGSO2-Cycloxydim (Metabolit)

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Results available via FIS-VL