Risk Assessment of Pesticides in the European Union

Dr. José V. Tarazona
Head Pesticides Unit

efsa
European Food Safety Authority

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www.efsa.europa.eu

EU REGULATORY SYSTEM FOR PESTICIDES

EU assessment and approval decision of the active pesticide substance

Periodic Renewals

Submission
- Active substance

Risk Assessment
- Rapporteur MS
- **EFSA Peer-Review**

Art. 21 Request

Decision
- EU approval

MS assessment and pre-marketing authorisation of each formulation

Submission	Submission	Submission
Risk Assessment: • Member State • Zonal process	Risk Assessment: • Member State • Zonal process	Risk Assessment: • Member State • Zonal process
Decision	Decision	Decision

EU REGULATORY SYSTEM FOR PESTICIDES

EU assessment and setting of Maximum Residue Levels (MRL)

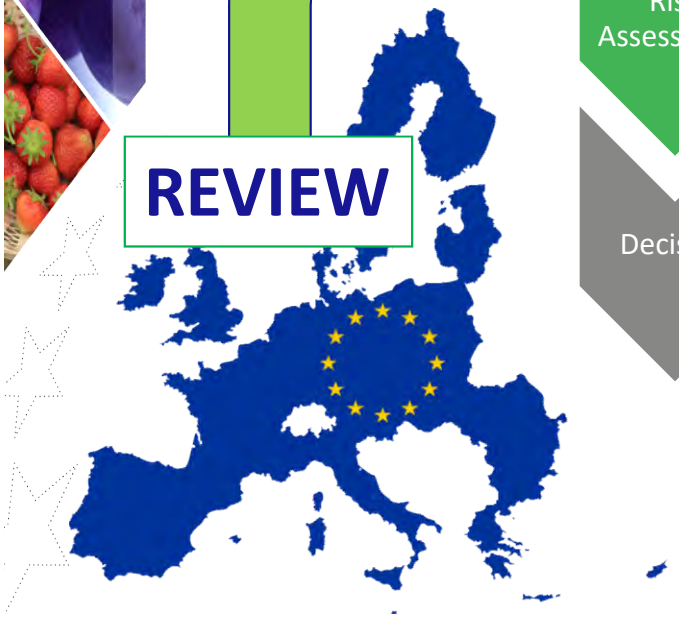
Submission
- Applicants

Risk Assessment
- **MS evaluation**
- **EFSA Assessment**

Art. 43 Request

Decision
- EC and MSs
- EU MRL

REVIEW



SCIENTIFIC RESOURCES

Overview

- Scientific Panel (independent external experts)
  - 21 Panel members
  - 5-10 working groups with additional experts
- Pesticides Unit staff
  - 50 scientist, 5.4 admin. staff
- Two MS expert networks
  - Ca 700 experts nominated by MSs

Pesticides Unit and Panel activities

Scientific Panel on Plant Protection Product and their Residues (PPR) & methodological development

- **Opinions**
- **Guidance documents**
- **Ad-hoc mandates**

Coordinates the Peer Review of active substances

Provides **Conclusions** and **Technical reports** for single active substances to support the EU decision-makers

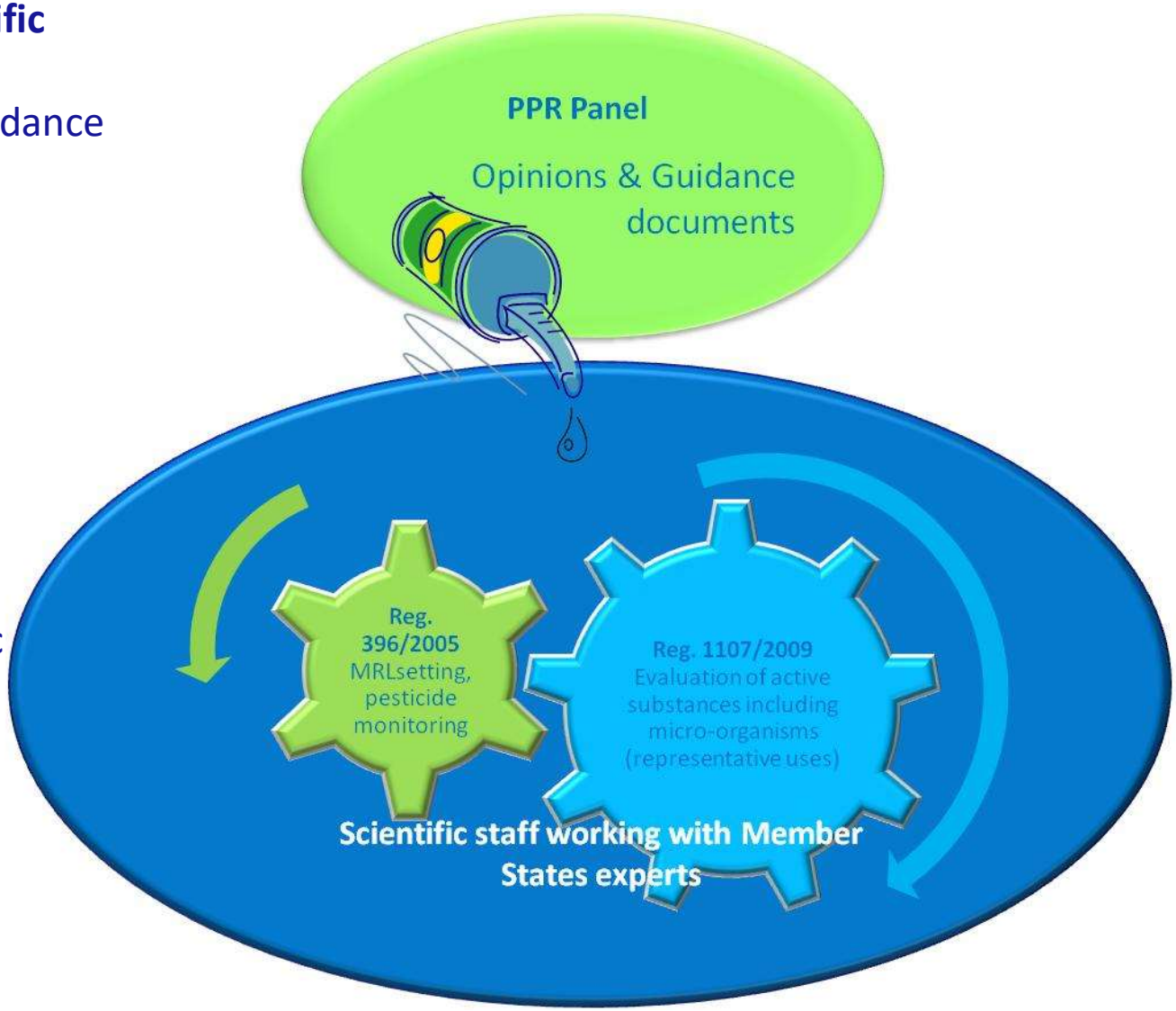
Pesticides Steering Network
Pesticides Monitoring Network

Maximum Residue Levels
&
Consumers risks

- **MRL Reasoned Opinions**
- **Annual reports: CODEX & residues monitoring**

Scientific consistency: PPR key role

General Scientific assessment:
Opinions & Guidance

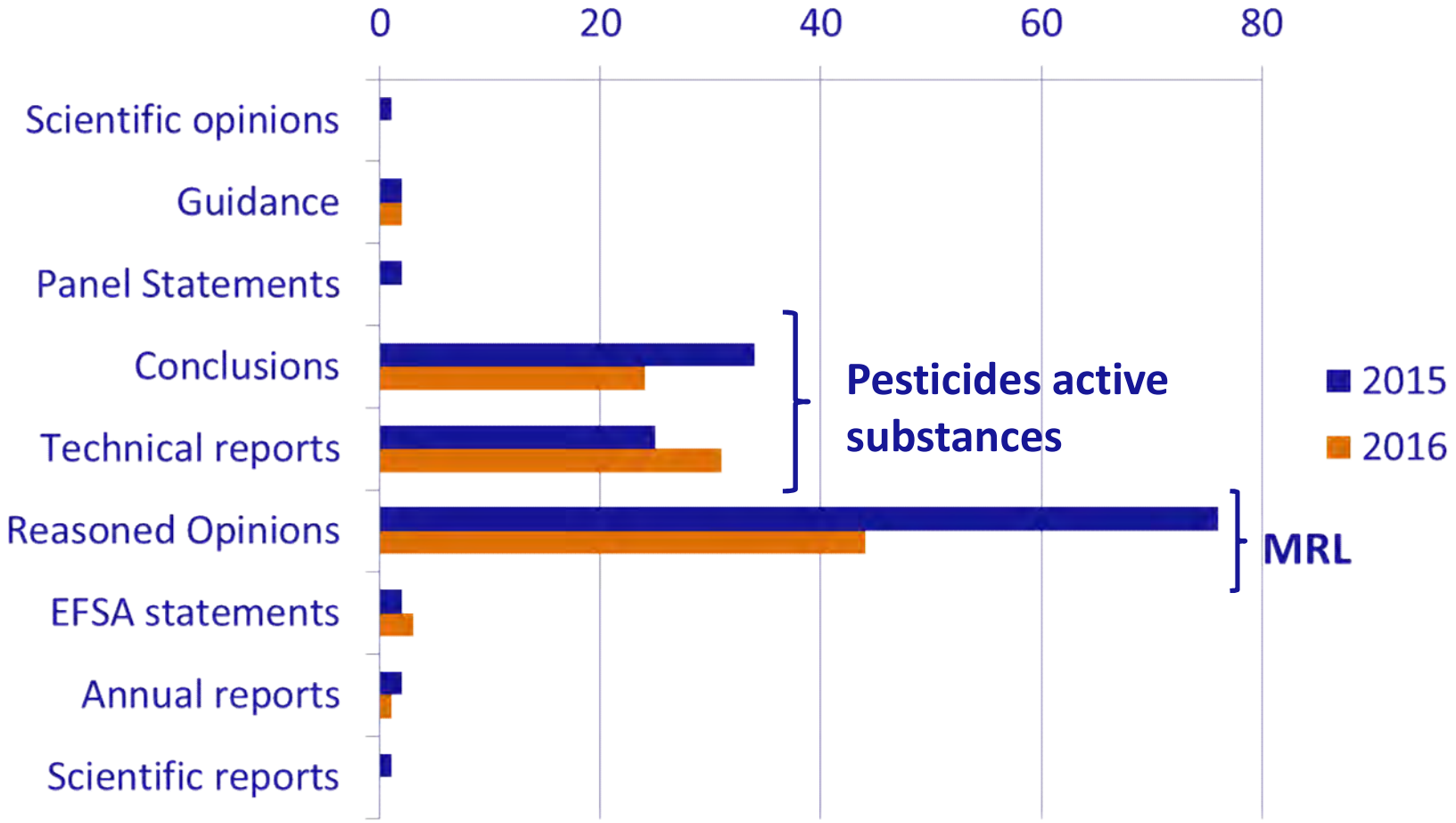


Dossier specific assessment:

Conclusions MRL Reasoned opinions

SCIENTIFIC OUTPUTS

Adopted in 2015 - 2016 (Jan-Aug)



Pesticides Unit and Panel activities

Methodological developments

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PPR Panel and methodological updates

Need identified
- PPR Panel
- Pesticides Steering Network

Preliminary work by EFSA
- Grants & procurements
- External report

Panel Scientific opinion
- Hearings
- Optional public consultation

Input from Risk Managers

Panel or EFSA guidance
- Hearings
- Networking
- Mandatory public consultation

Guidance ready for Risk Managers decision on enforcement

PPR Panel and methodological main activities

Toxicology and Human Health assessment

- Cumulative Assessment of Pesticides
- Use of epidemiological studies in pesticides risk assessment
- Residue definition for dietary risk assessment
- Dermal absorption
- Developmental neurotoxicity testing strategy

Environmental Fate

- Persistence in soil
- Environmental exposure including non-dietary bystanders and resident exposure

Ecotoxicology including

- Aquatic including sediment and modelling
- Terrestrial: vertebrates, bees and other arthropods, in-soil organisms, terrestrial plans

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Dermal absorption

Residue definition for dietary RA

Epidemiology

Cumulative assessment

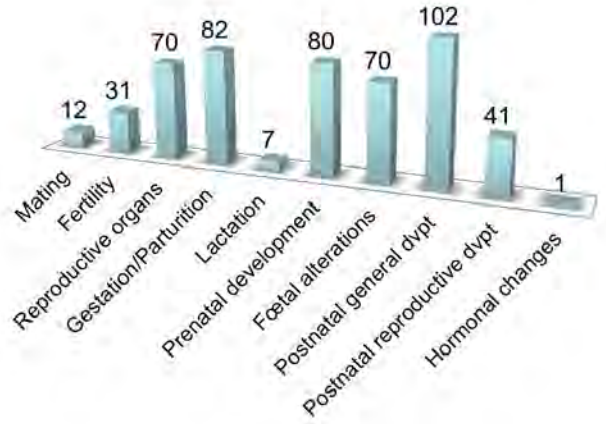
Developmental neurotoxicity

Methodological updates: Human health

Cumulative Assessment of Pesticides Link to summary of EFSA activities

- Data collection nervous system, liver, adrenal, eye, reproduction and development and thyroid system link

Effects on reproduction



- Implementation of the RA tool: MCRA made scalable for large cumulative assessment groups link
- Pilot project (Post marketing situation)
  - Acute effects on the nervous system
  - Chronic effects on the thyroid

Methodological updates: Human health

Use of epidemiological studies in pesticides risk assessment

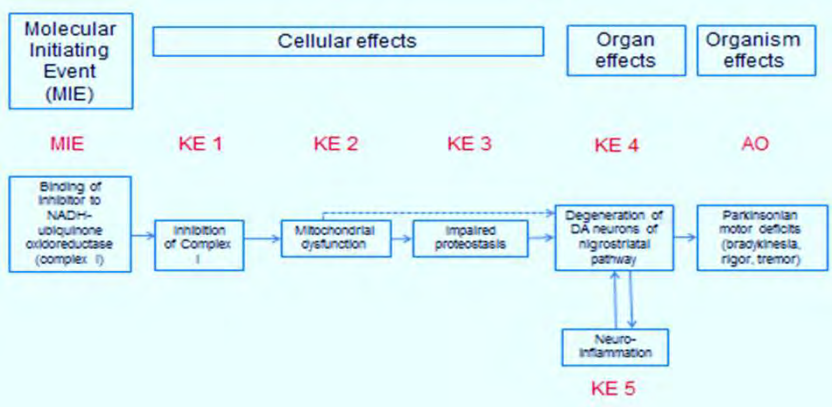
- Potential link of pesticides exposure with Parkinson's disease and childhood leukaemia.
  - Opinion based on Adverse Outcome Pathways (AOP) under public consultation
    - AOP1: Inhibition of the mitochondrial complex I of nigra-striatal neurons leads to parkinsonian motor deficits
    - AOP 2: Redox-cycling of a chemical initiated by electrons released by the mitochondrial respiratory chain leading to parkinsonian motor deficits
    - AOP 3: In utero DNA topoisomerase II poisons leading to infant leukaemia
    - AOP4: In utero induction of chromosomal rearrangements/translocations in haematopoietic stem/progenitor cells (HSPCs) followed by postnatal mutations and an aberrant immune response leads to childhood leukaemia
- Improving the use of epidemiological studies in pesticide risk assessments.

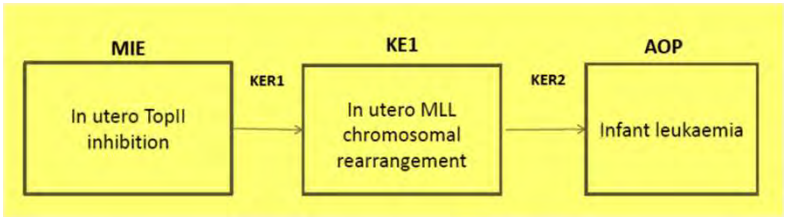
PROPOSED ADVERSE OUTCOME PATHWAYS

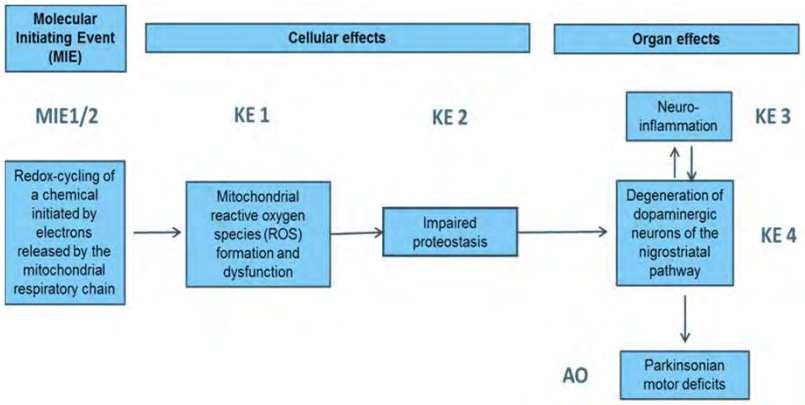
Parkinson's disease

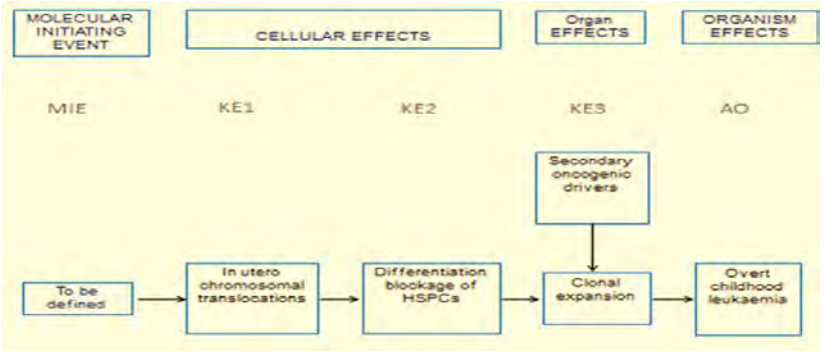
Childhood leukaemia

Molecular Initiating Event → Key events cascade → Adverse outcome









TIMELINE OVERVIEW

2014 2015 2016 2017 2018

Mandate [1] approved

Mandate [2] approved

Systematic review on Parkinson's disease/ child hood leukaemia

Stakeholder conference

Human biomonitoring data collection from occupational exposure to pesticides

Public consultation and publication of Scientific Opinion [1]

Public consultation and publication of Scientific Opinion [2]

Scientific conference organised by EFSA

Networking with MS within the Pesticide Steering Network

PPR Panel and methodological updates

Need identified
- PPR Panel
- Pesticides Steering Network

Preliminary work by EFSA
- Grants & procurements
- External report

Panel Scientific opinion
- Hearings
- Optional public consultation

Input from Risk Managers

Panel or EFSA guidance
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- Mandatory public consultation

Guidance ready for Risk Managers decision on enforcement

Persistency in soil

Terrestrial, sediment

Amphibians and reptiles

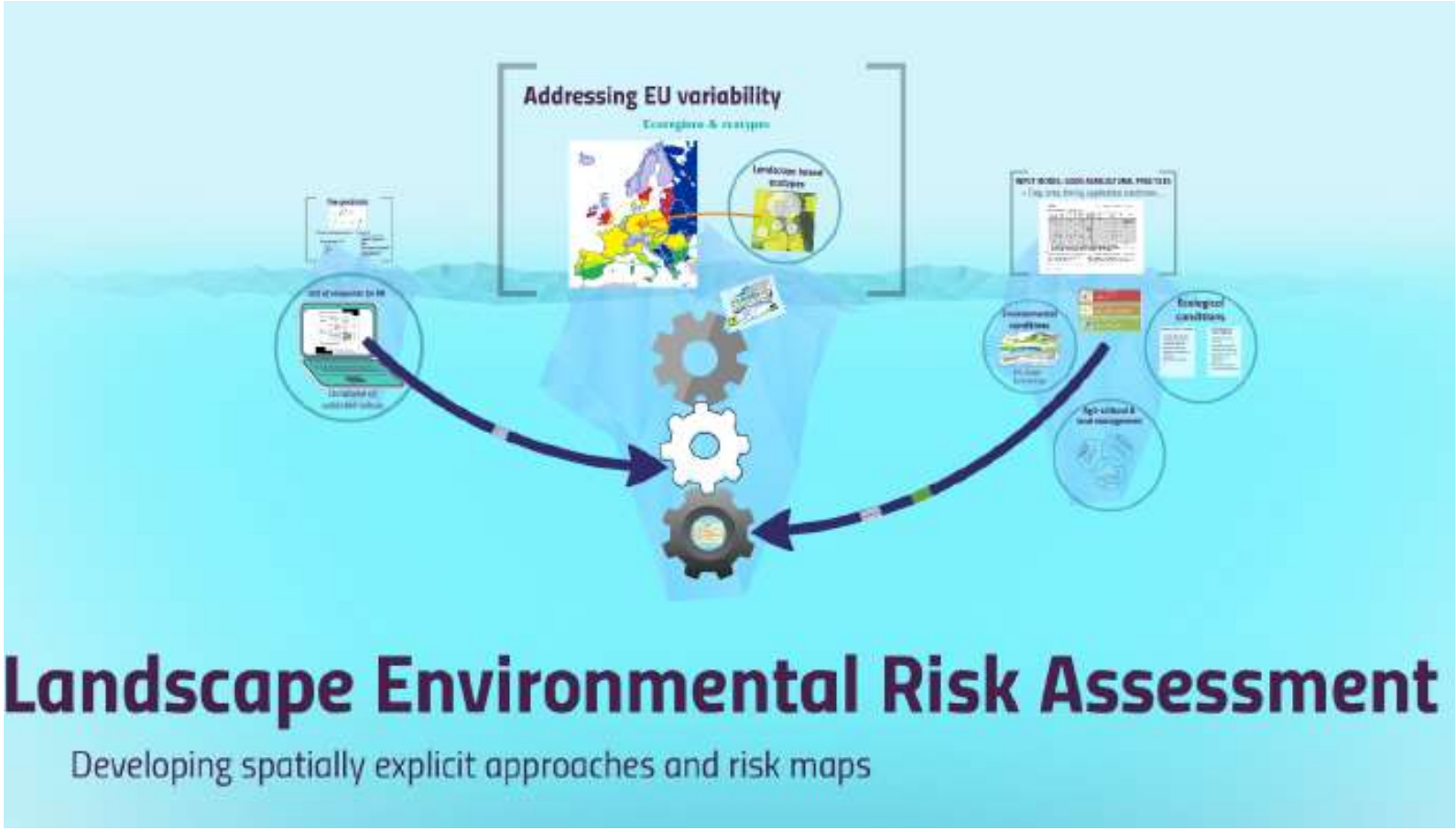
Ecological modelling

Bees

Landscape ERA

LANDSCAPE ENVIRONMENTAL ASSESSMENT

Spatial explicit risk maps addressing EU environmental variability



Pesticides Unit and Panel activities

Scientific Panel on Plant Protection Product and their Residues (PPR) & methodological development

- **Opinions**
- **Guidance documents**
- **Ad-hoc mandates**

Assessment of individual active substances

Coordinates the Peer Review of active substances

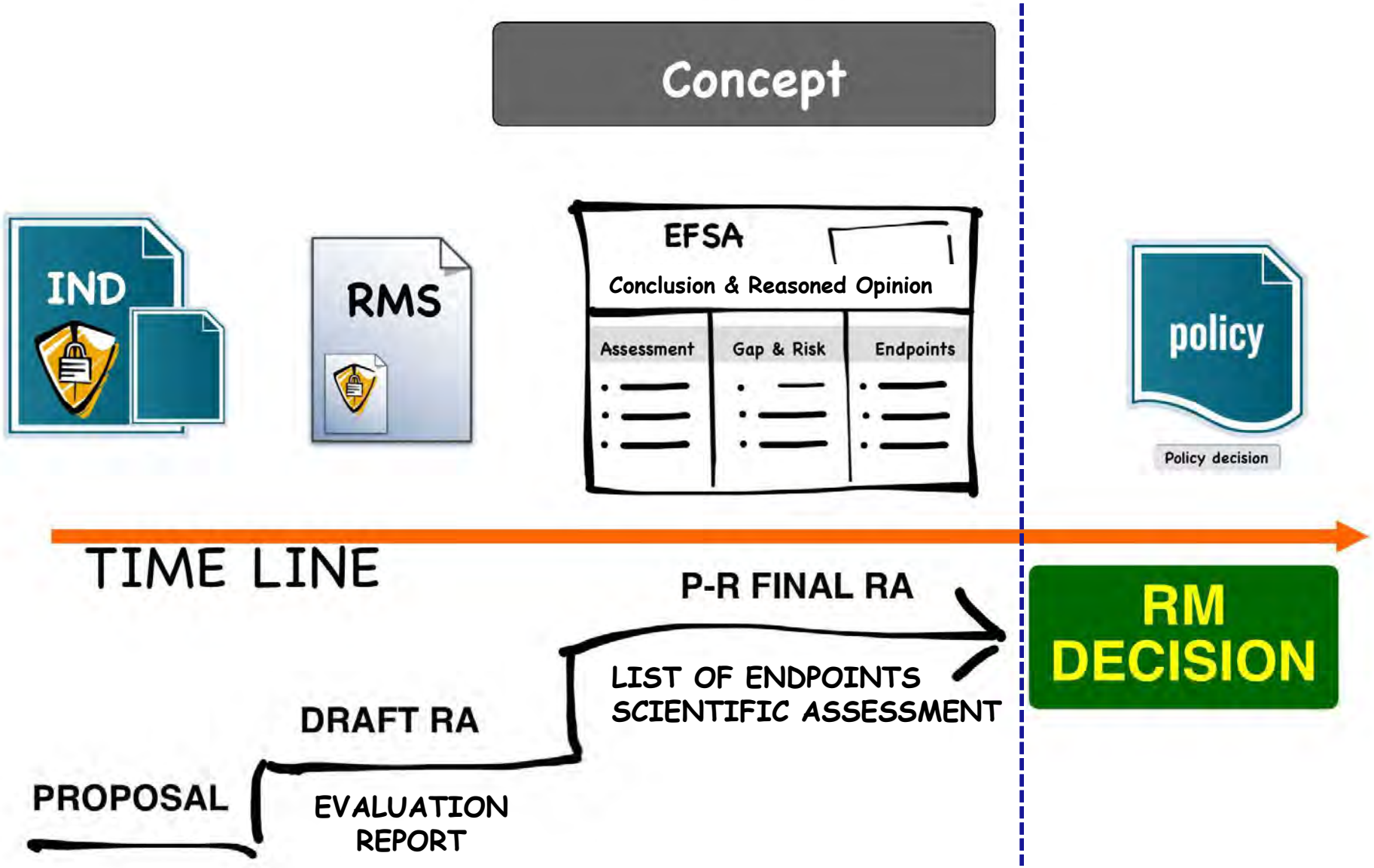
Provides **Conclusions** and **Technical reports** for single active substances to support the EU decision-makers

Pesticides Steering Network
Pesticides Monitoring Network

Maximum Residue Levels
&
Consumers risks

- **MRL Reasoned Opinions**
- **Annual reports: CODEX & residues monitoring**

PESTICIDES PEER-REVIEW & MRL PROCESSES



CONCLUSION & REASONED OPINIONS

- Conclusions on Pesticides*
  - Identity and Phys/Chem properties
  - Mammalian Toxicology & non dietary health risks
  - Residues & Consumers risks
  - Environmental Fate and Behaviour
  - Ecotoxicology & environmental risks

- Reasoned Opinions on MRLs & Annual reports:
  - Residues & Consumers risks

*Some conclusions are limited to one or more areas

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The Peer-Review Process

Dossier submission

D/RAR
Draft/Review Assessment Report

EFSA

PEER REVIEW

EFSA,
RapporteurMS,
other MSs,
EU Commission,
Notifier, Public

1. Commenting phase

2. Evaluation of comments

3. Expert's consultation

EFSA Conclusion

EFSA Risk Assessment

Commission +MSs
Standing Committee on Plants, Animals, Food and Feed

Approval/Non Approval

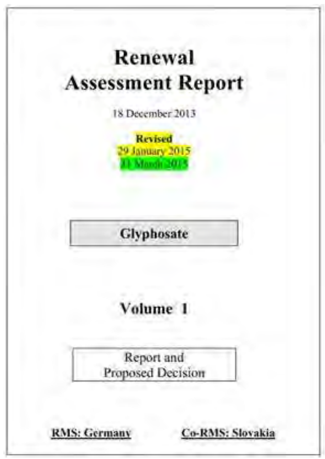
National authorisation PPP by MSs

efsa European Food Safety Authority

ALL AVAILABLE EVIDENCE DISCUSSED AND PRESENTED

RMS → Comments → EFSA

Mandatory GLP studies + Scientific literature + other evaluations



RMS evaluation, updates are highlighted

Comments, responses, meeting reports, MSs views

Critical concerns, data gaps. Validated endpoints

EFSA PEER-REVIEW OUTPUTS

- **Conclusions on Pesticides**
  - New active substances
  - AIR-II and III renewals
  - Confirmatory data
  - Reviews under Art 21
- **Technical reports**
  - Basic substances
  - Confirmatory data
  - Assessment of Endocrine Disruption
  - Recurrent issues: Ecotoxicology, Toxicology

Ecotoxicology

- Mammals
- Aquatic organisms
- Bees
- Soil Organisms
- Risk assessment for uses in protected structures
- PPR Opinion on Non-Target Terrestrial Plants
- Aspects of the new data requirements
- Evaluation and validity of studies performed to older versions of test guidelines using the criteria given in the latest version
- Literature data for the risk assessment

Toxicology

- New data requirements
  - GLP status
  - Analytical methods
  - Toxicokinetics and comparative metabolism
  - Phototoxicity/photomutagenicity
- Genotoxicity testing
- Toxicological profile of metabolites and impurities
- Endocrine disruptive properties
- Proposals for classification and labelling
- Literature search
- Panel recommendations

SPECIFIC REQUEST FROM EC

- **Recently published**
  - Risk of neonicotinoids foliar uses to bees
  - Diflubenzuron (metabolite 4-chloroaniline)
  - Call for data for Risk assessment for bees
  - Protocol of assessing the need of herbicides to control serious danger to plant health
- **On going and new requests**
  - Need to control serious danger to plant health for several flumioxazin
  - Protocol of assessing the need of insecticides to control serious danger to plant health
  - Assessment of negligible (human) exposure for flupyrsulfuron-methyl, pymetrozine
  - Updated risk of neonicotinoids/fipronil to bees
  - Risk of glyphosate for animal health

EFSA SCIENTIFIC ASSESSMENT

- **Substance ID**
- **Hazard assessment**
- **Phys-chem. Properties**
- **Env. Fate properties**

Classification (CLP)
Hazard approval criteria

(Eco)Toxicological profile:
CMR, Endocrine effects, PBT, POP

- Hazard characterisation
- Exposure assessment
- Risk characterisation

Risk based approval criteria

HAZARD BASED NON-APPROVAL CRITERIA

Annex II, Regulation 1107/2009

- Is or has to be classified as
  - **Mutagen category 1A and 1B**
  - **Carcinogen category 1A and 1B**
  - **Toxic for reproduction category 1A and 1B**
- Has endocrine properties which may cause adverse effects on humans
- Is a persistent organic pollutant (POP)
- Is persistent, bioaccumulative and toxic (PBT) or very-P and very-B (vPvB)
- Has endocrine properties which may cause adverse effects on the environment

EXCEPTIONAL APPROVAL HAZARDOUS PESTICIDE A.S.

- Carcinogen Category 1A or 1B
- Toxic to reproduction Category 1A or 1B
- Endocrine properties which may cause adverse effects on humans

  "*unless the exposure of humans under realistic proposed conditions of use, is negligible*".

- Carcinogen Category 1B with threshold
- Endocrine properties which may cause adverse effects on humans or non-target organisms

  "is necessary to control a serious danger to plant health which cannot be contained by other available means"

ANNEX II POINT 3.6.5 OF REGULATION 1107/2009/EC

Endocrine Disrupters criteria

Interim criteria

Shall be considered to have ED properties

- Carc Cat 2
- Repro Cat 2

May be considered to have ED properties

- Repro Cat 2
- Toxic effects on endocrine organs

Scientific assessment

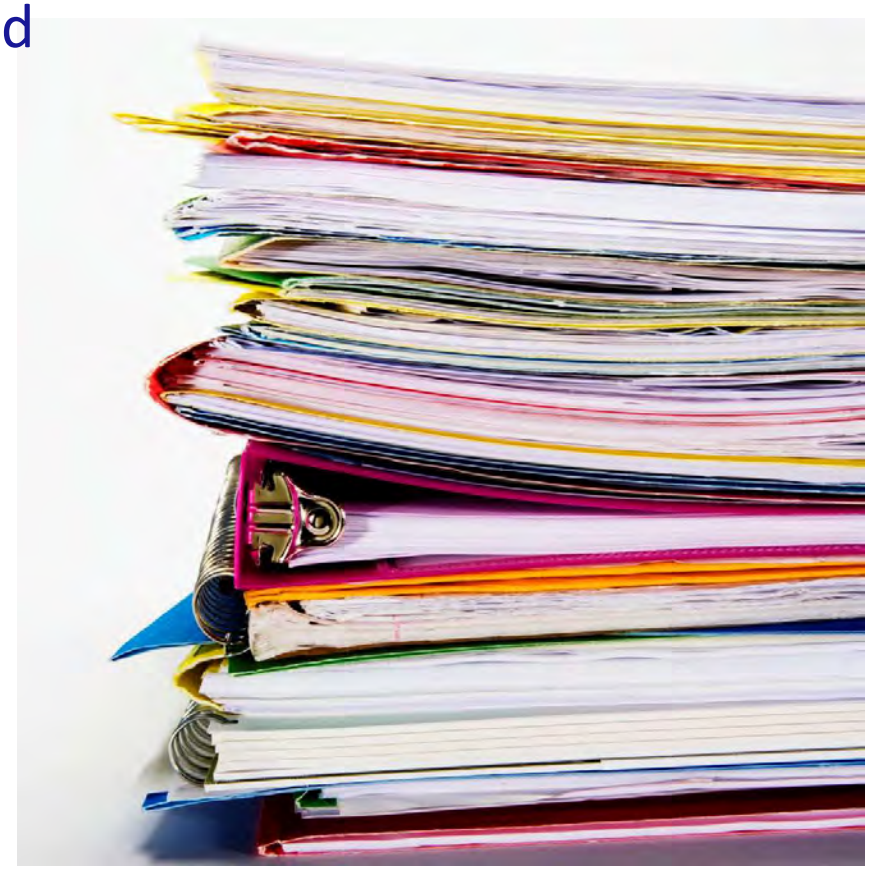
- Based on WHO definition
- Following the EFSA Scientific Committee opinion

- Adverse effects resulting from endocrine modes of actions

SCIENTIFIC ASSESSMENT

- Based on WHO definition
- Following the EFSA Scientific Committee opinion (2013)
- Test methods: OECD revised Conceptual Framework for the identification of EDs
- Integrating available published PR literature

→ Adverse effects resulting from endocrine modes of actions



ED CRITERIA - DEVELOPMENTS

- **Technical report** compiling the assessment of endocrine effects in the EFSA Conclusions (EFSA Supporting publication 2015:EN-867)
- EFSA summarises the **assessment** of potential endocrine effects in the Conclusions as of 2014:
  - the hazard assessment related to the application of the interim criteria
  - the risk assessment related to the identification of relevant adverse effects which could be related to endocrine mediated mechanisms
- **EC proposal** setting out scientific criteria for the determination of ED properties in plant protection products (June 2016).

COMMISSION PROPOSED CRITERIA (JUNE 2016)

- **Based on**
  - 2002 WHO definition for endocrine disruptors
  - 2009 WHO definition of adverse effects as endorsed by EFSA in its Scientific Opinion on endocrine disruptors (2013)
- **Applying**
  - Weight of evidence methodology provided for in Regulation (EC) No 1272/2008
  - OECD guidance document on standardised test guidelines for evaluating chemicals for endocrine disruption

COMMISSION DRAFT CRITERIA

Approval criteria

- An a.s., safener or synergist shall only be approved, if it is not considered to have endocrine disrupting properties that data may cause adverse effect in humans, unless the risk to humans/non-target organism from exposure to that a.s. is negligible

IDENTIFICATION OF AN ED

- all available relevant scientific evidence
- a WoE on ED mediated adverse effects considering whether or not the effects are adverse, the MoA, together with the biological plausibility of the causal link between the adverse effect and the endocrine mode of action.
- Adverse effects or endocrine MoA that are non-specific secondary consequences of other toxic effects shall not be considered for the identification of the substance as endocrine disruptor.
- Relevance for humans or population level for non-target organisms

PESTICIDES: ENDOCRINE DISRUPTION

Current & future activities

- Scientific feasibility and practicalities for implementing the criteria proposed in June
  - Scientific alignment with ECHA
  - Assessment with MS experts
- Priorities in the endocrine area:
  - Identification of ED mode of action and link with adverse effects
  - Biological plausibility of the pathway linking ED mode of action with adverse effect
    - Direct effects *vs.* secondary consequences
  - Relevance for humans and for non-target populations

ARTICLE 4(7)

- Evaluation of data concerning the necessity of the application of herbicide a.s. to control a serious danger to plant health
  - Ongoing application: flumioxazin Art. 4(7)

- EFSA established an ad hoc WG who proposed a methodology. Discussion with MS and EC (PSN, 10 March 2016).

Protocol for evaluation of data concerning the necessity of the application of herbicide a.s. to control a serious danger to plant health which cannot be contained by other available means, including non-chemical methods. *http://onlinelibrary.wiley.com/doi/10.2903/sp.efsa.2016.EN-1060/abstract*

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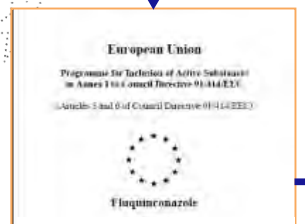
Scientific Cooperation: MRLs

Dossier submission



MRL Evaluation report

EFSA

Data gathering phase

EFSA Risk Assessment

Commenting phase

EFSA Reasoned Opinion

Commission +MSs
Standing Committee on Plants, Animals, Food and Feed

MRL setting

MRL ACTIVITIES

- Reasoned opinions on new proposals/modifications of existing MRL
  - Based on applications
- Reasoned opinions reviewing MRLs for approved/non-approved active substances
  - Based on work programme agreed at the PSN **Link**
- Reasoned opinions for ad-hoc EC Request under Art. 43
  - Dimethoathe, omethoate, coumafos, permethrin, oxytetracycline, streptomicin, flumequine, amitraz, thiabendazole, chlorpyrifos, atrazine, metalaxyl (-M), λ-cyhalothrin,…

MRL HIGHLIGHTS

- **New calculators covering new data requirements**
- **New Templates for Reasoned Opinions**
  - Methods of analysis
  - Residues nature and magnitude
  - Consumers risk assessment
  - MRL proposal
  - – Evaluation reports &

PRIMO risk assessments published as background documents


REASONED OPINION

Modification of the existing maximum residue level for cyantraniliprole in table grapes

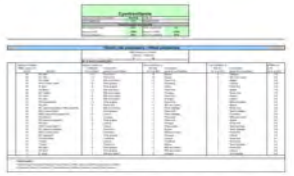
European Food Safety Authority (EFSA)

Abstract


Evaluation Report

Setting of MRL for cyantraniliprole in table grapes

Evaluating Member State: France



- **EFSA/FAO/WHO Workshop and Stakeholder Consultation on: Revisiting the International Estimate of Short-Term Intake (IESTI equations) used to estimate the acute exposure to pesticide residues via food**

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ANNUAL SCIENTIFIC REPORTS ON PESTICIDES RESIDUES

International harmonisation & Post-marketing monitoring

- Scientific support for EU Codex Committee on Pesticide Residues (CCPR)
  - General issues
  - Assessment of individual substances
    - Toxicological reference values
    - Residue definitions
    - CODEC MRL proposals
    - Consumers risk assessment
  - Published on Q3

- Annual Report on Pesticides Monitoring
- Compiles and report the MS monitoring programmes
  - Interactive report

  - Results of the EU coordinated programme
  - Results of the National control programme
  - Dietary exposure and dietary risk assessment

COOPERATION ACTIVITIES ON PESTICIDES R.A.

- EU wide: Pesticide Steering Network
  - Standard and dedicated meetings
  - Documents available upon request
- EFSA-MSs
  - Cumulative assessment, Operators-Workers, Epidemiology, microbial pesticides, co-formulants, plant-health,…
- EU-Bodies
  - Cooperation with EU Joint Research Centre
    - Environmental variability and modelling
  - Cooperation with ECHA on C&L, biocides, endocrine disruptors,…
    - ECHA-EFSA Topical Scientific Workshops
- International organisations
  - EFSA/WHO/FAO workshop on acute exposure estimations for consumers risk assessment, September 2015
  - EFSA/OECD workshop on developmental neurotoxicity

Thank you

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