bpia 2023 Annual Meeting

Anything New with Global Regulation of Biological Products

Moderator: Hank Krueger, Eurofins
Panel Speakers: Billy Smith, EPA;
Emma Babij, PMRA;
Jose Juanes, Eurofins;
Lisa Ortego, Bayer

What's New and What are the Biggest Challenges Facing your Organizations

Each speaker will introduce themselves, discuss what's new and discuss their biggest challenges,followed by questions

Emma – Canada
Billy – United States
Jose – Europe
Lisa – Innovating Microbial Pesticide Testing: European Conference Summary

Health Canada Santé Canada

Canada

Anything New with Regulation of Biopesticides in Canada?

BPIA Annual Meeting
February 22, 2023
Reno, NV

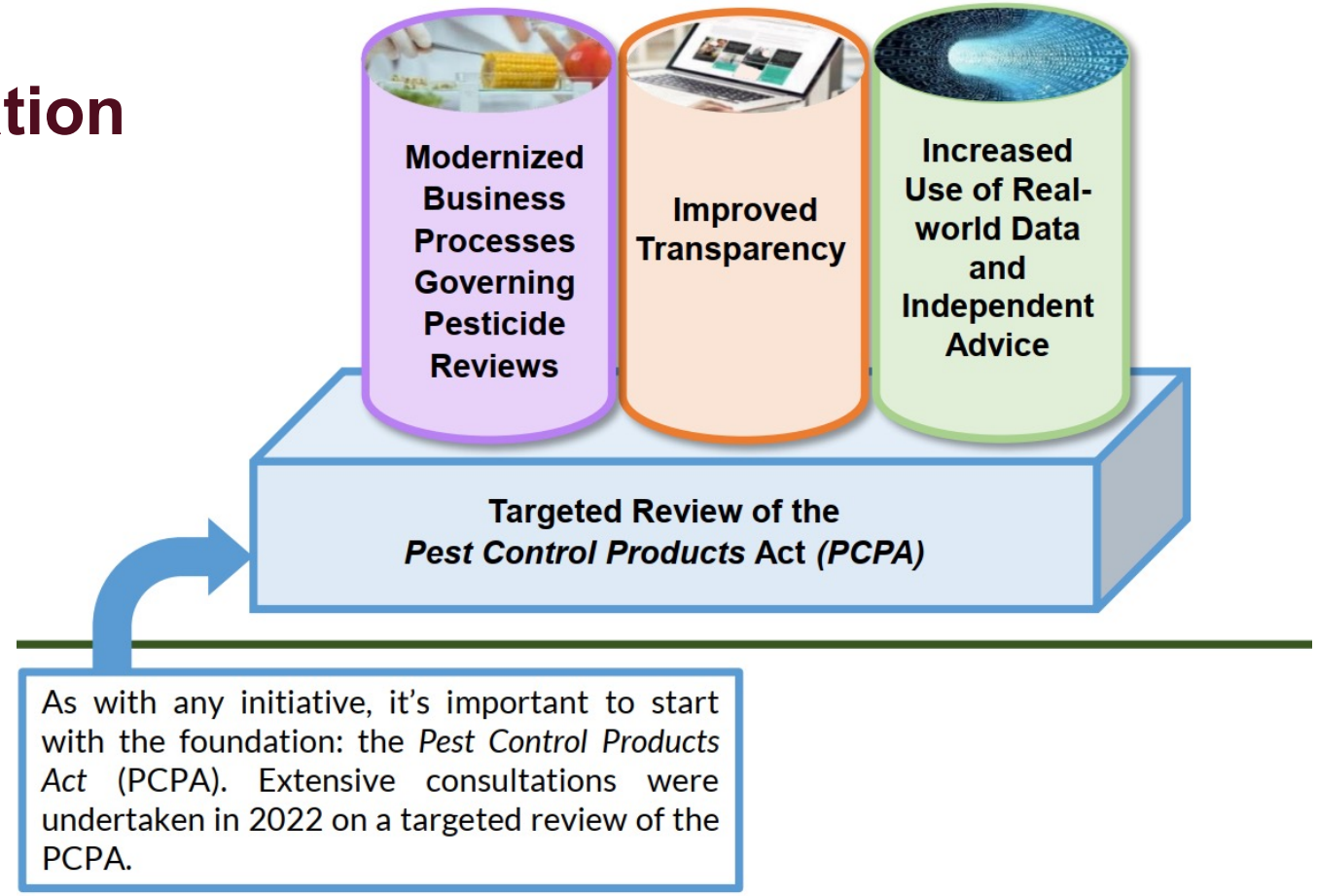
Emma Babij
Section Head, Microbial and Biochemical Evaluation Section
Health Evaluation Directorate
Pest Management Regulatory Agency (PMRA)
Health Canada

YOUR HEALTH AND SAFETY... OUR PRIORITY.

Outline

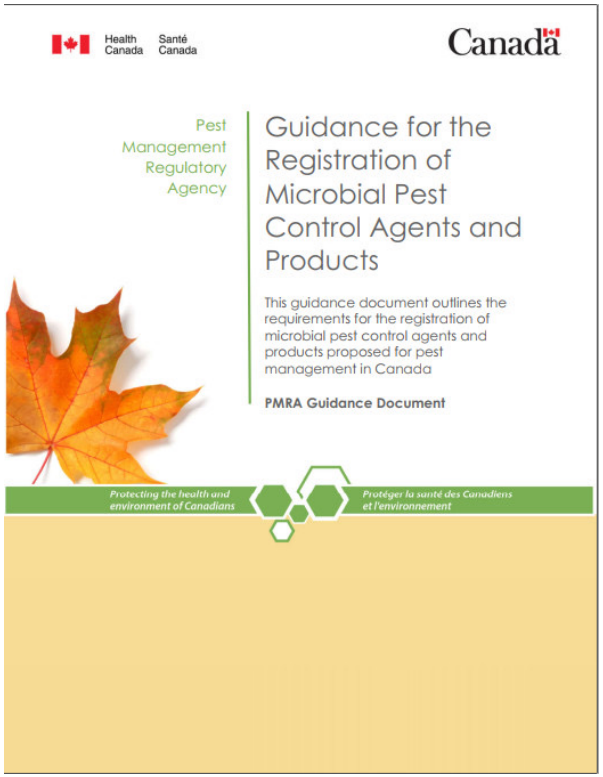
- Transformation at PMRA
- New guidance documents
- Food Grade Edible chemistry attestation forms
- Limits for residual solvents in Technical Grade Active Ingredients (TGAIs)
- Data requirements for biopesticides applied to cannabis and hemp
- Vertical farming
- OECD activities

Canada's Transformation Agenda

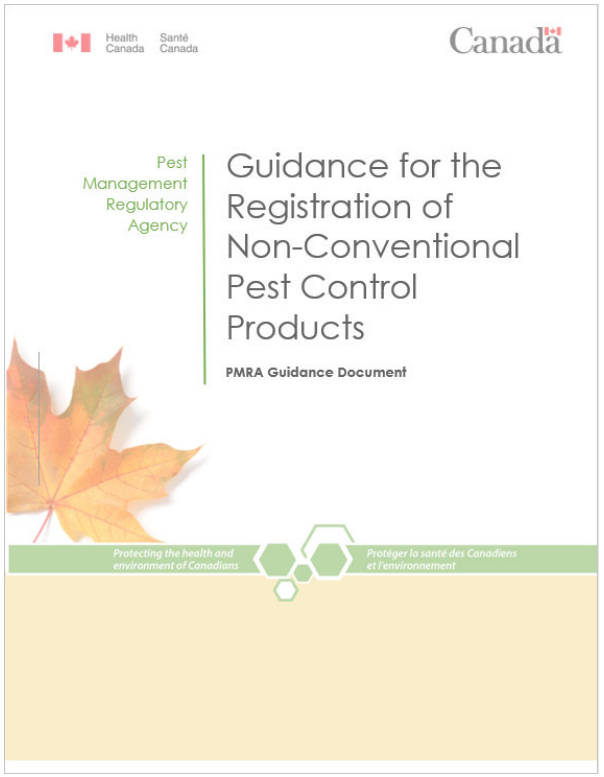


As with any initiative, it's important to start with the foundation: the *Pest Control Products Act* (PCPA). Extensive consultations were undertaken in 2022 on a targeted review of the PCPA.

Updated Guidance documents



COMING SOON



Food Grade Edible (FGE) Attestation Form

Attestation Forms

- PMRA has developed attestation forms to be completed by applicants for **FGE products**. The forms can be obtained during the pre-submission consultation or ordered by contacting the PMRA info line (pmra.info-arla@hc-sc.gc.ca).

Required DACOs

- Attestation form under data code (DACO) 2.16 for the TGAI and DACO 3.7 for the end-use product (EP).
- Certificate confirming Food Grade Edible classification submitted under DACO 0.8.8.
- Statement of Product Specification Form (SPSF) submitted under DACO 0.1.6003.

Chemistry Requirements

Since FGE products are fit for human consumption, PMRA requests the following:

- For TGAI: Physical-Chemical properties and levels of methyl eugenol and mycotoxins, if applicable.
- For EP: Physical-Chemical properties, Storage Stability and Corrosion Characteristics study.

PMRA limits for residual solvents in TGAIs

Residual solvent	Maximum PMRA general limit (ppm)	Required limit of quantitation (LOQ) (ppm)
carbon tetrachloride	--- (to be avoided)	1
1,2-dichloroethane	--- (to be avoided)	1
benzene	--- (to be avoided)	1
1,4-dioxane	4	1
chloroform	10	1
tetrahydrofuran	100	10
pyridine	200	100
hexane	290	100
dichloromethane	300	100
acetonitrile	410	100
N,N-dimethylformamide	500	100
N-methyl-2-pyrrolidone	530	100
chlorobenzene	600	100
cyclohexane	710	500
methylcyclohexane	1000	500
N,N-dimethylacetamide	1090	500
xylene	2170	1000
methanol	3000	1000
toluene	15000	1000

Biopesticides Used On Cannabis And Hemp

- To-date, mainly biopesticides have been registered for use on cannabis and industrial hemp grown for flowers
- Potential consumer exposure could include ingestion of edible oils or extracts, inhalation by smoking and vaping.
- Additional data/information required
  - **DACO 5.2 (Use Pattern/ Exposure Scenario):** The specific use pattern for cannabis and/or industrial hemp crops must be described in sufficient detail as well as the intended end use(s) of the harvested industrial hemp crop
  - **DACO 7.4.1 (Supervised Residue Trial Study):** The assessment of biopesticides will consider active ingredients, formulants, and any potential metabolites or reactive by-products of human health concern that may remain on consumable portions of the harvested crop. Alternatively, an acceptable scientific rationale to waive this data requirement may be provided.
  - **DACO 7.8.1 (Pyrolysis Study):** Required when there is potential for crop to be consumed through smoking/vaping. Alternatively, an acceptable scientific rationale to waive this data requirement may be provided.

Vertical Farming

- Vertical farm produces crops grown:
  - In appropriate media (hydroponically, aeroponically or in soil);
  - Indoors on vertically stacked or inclined layers and/or integrated in other vertical structures; and
  - Relying solely or largely on artificial lighting
  - ➢ This differs from greenhouse growing, for which there are registered pest control products. In a greenhouse, plants are generally grown in a single layer on horizontal benches, containers or troughs placed on the ground or suspended, relying largely on natural sunlight.
- Currently the use of pest control products in vertical farming (including those registered for use in greenhouses) in Canada is not permitted under the Pest Control Products Act
- PMRA is engaging with stakeholders to gain a better understanding of practices employed in vertical farming and considerations in assessing risk to human health and the environment

OECD Projects

- PMRA participates in various activities at the OECD level through membership in the Expert Group on Biopesticides and the Ad Hoc Expert Group on RNAi-based Pesticides
- Guidance Document on Bacteriophages published in late 2022 (OECD Series on Pesticides No. 108, ENV/CBC/MONO(2022)40)
- Working document on baculoviruses in progress
  - General guidance on considerations for preparing regulatory submissions
- Contaminants in microbial pest control products
  - The methodology section of the OECD Series on Pesticides No. 65, *Issue Paper on Microbial Contaminants Limits for Microbial Pest Control Products* (ENV/JM/MONO(2011)43) is being updated to include methods such as quantitative polymerase chain reaction (qPCR)
  - No change proposed to the list of pathogens or levels of detection

OECD Projects cont'd.

- RNAi-based pesticides
  - Ad Hoc Expert Group has published the OECD Working Document on *Considerations for the Environmental Risk Assessment of the Application of Sprayed or Externally Applied ds-RNA-Based Pesticides*, Series on Pesticides No.104 [ENV/JM/MONO(2020)26]
  - Working Document on human health and safety considerations nearing completion (aiming end of 2023)
  - In Canada, data requirements for dsRNA-based pesticides determined on a case by case basis
    - Pre-submission consultation required
    - Research authorizations required for any research conducted outside of laboratory

Challenges regulating biopesticides in Canada

Resources

Guidance for the Registration of Microbial Pest Control Agents and Products https://www.canada.ca/en/health-canada/services/consumer-product-safety/reports-publications/pesticides-pest-management/policies-guidelines/guidance-registration-microbial-pest-control-agent-products.html

Information Note: Vertical farming and pest control products https://www.canada.ca/en/health-canada/services/consumer-product-safety/reports-publications/pesticides-pest-management/fact-sheets-other-resources/vertical-farming-pest-control-products.html

OECD Working Document on Considerations for the Environmental Risk Assessment of the Application of Sprayed or Externally Applied ds-RNA-based Pesticides, Series on Pesticides No. 104 [ENV/JM/MONO (2020)26] https://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2020)26&doclanguage=en

OECD Guidance Document for the Regulatory Framework for the Microorganism Group: Bacteriophages, Series on Pesticides No. 108 [ENV/CBC/MONO(2022)40] https://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/cbc/mono(2022)40&doclanguage=en

Transforming the PMRA https://www.canada.ca/en/health-canada/corporate/about-health-canada/branches-agencies/pest-management-regulatory-agency/transforming.html

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"Anything New with Global Regulation of Biological Products"

Charles (Billy) Smith, Director
U.S. EPA Biopesticides & Pollution Prevention Division

USEPA – BPPD Staffing

- February 2023 – BPPD has 67 FTE across 5 branches
- BPPD currently working to hire an additional 3 FTE
  - Initial focus on hiring ecological risk assessors
- Ideal BPPD structure would include additional resources across multiple branches – 78 FTE
  - Based on BPPD workload analysis including data from Salesforce

BPPD Workload

BPPD FY23 Workplan Includes:

- PRIA Work – over 50 new AIs in house
  - Workload received similar over the past 5-years but nature of the work has changed = more new AIs
- Non-PRIA Work
  - Significant effort to reduce backlog over last two years
- Registration Review Work
  - Two Round 1 cases need to be completed
  - Significant effort to open Round 2 dockets
- Rule making - PIPs Final Rule, 25(b) Proposed Rule
- Biostimulants Guidance

BPPD Workload Continued

BPPD FY23 Workplan Includes:

- Process Improvements
  - Deficiency assessment (10-day and 75-day letter analysis)
  - Guidance for waiver development
  - Guidance for literature searches
  - Update Pre-Submission Guidance
  - Update Technical Screen Checklists
  - BPPD/AD SOP for antimicrobial uses for biochemicals
- Salesforce/Digital Transformation Development
- BioEconomy Executive Order Implementation

BPPD – Endangered Species Assessment

- Historically, significant percentage of biopesticides received “no effect” determinations (~75%)
- More recently, developments with ESA and biopesticides resulting in more “not likely to adversely affect” and a few “likely to adversely affect” determinations
  - Challenges with insecticides, both microbial and biochemical
  - Beneficial effects to plants (e.g., ISR/SAR induction in plants, certain PGRs)
- BPPD ramping up work on ESA, collaborating with EFED on tools and assessment methods
  - Upcoming hiring focused on scientists with eco backgrounds
- Will take time to make this a regular part of process
  - LAAs will be challenging to complete in PRIA V new AI timelines
  - NLAAs/NEs more likely to be completed in timeframes

Salesforce/Digital Transformation

Push to Digitally Transform OPP

- BPPD piloted Salesforce to track work, renegotiations, metrics development for several years
  - Transparency: provides significant insight into BPPD work
  - Allows for targeted process improvement that is metrics driven
- Future efforts:
  - Move all of OPP to Salesforce
    - Improve external customer experience
  - e-CSF
  - Electronic labeling

PRIA V Highlights

- **PRIA -Increase in fees and funding for OPP (+$11m for maintenance; +$6m for registration)**
- **FY23 appropriations - $11m increase, targeted at ESA**
- Omnibus - October 1, 2026, deadline extension (IDs with measures to reduce)
- Spanish Labeling for Pesticides
- Renegotiation Provisions for submissions
- Biopesticide table changes
  - Many BPPD PRIA Tables simplified
  - Additional time added to some codes (mostly 2 months)
  - New codes added, particularly for Table 17 (emerging technologies)
- Technical screen provisions
- Workforce analysis audit
- IT updates
- PRIA reporting/metrics

https://www.congress.gov/bill/117th-congress/house-bill/2617/text

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"Anything New with Global Regulation of Biological Products"

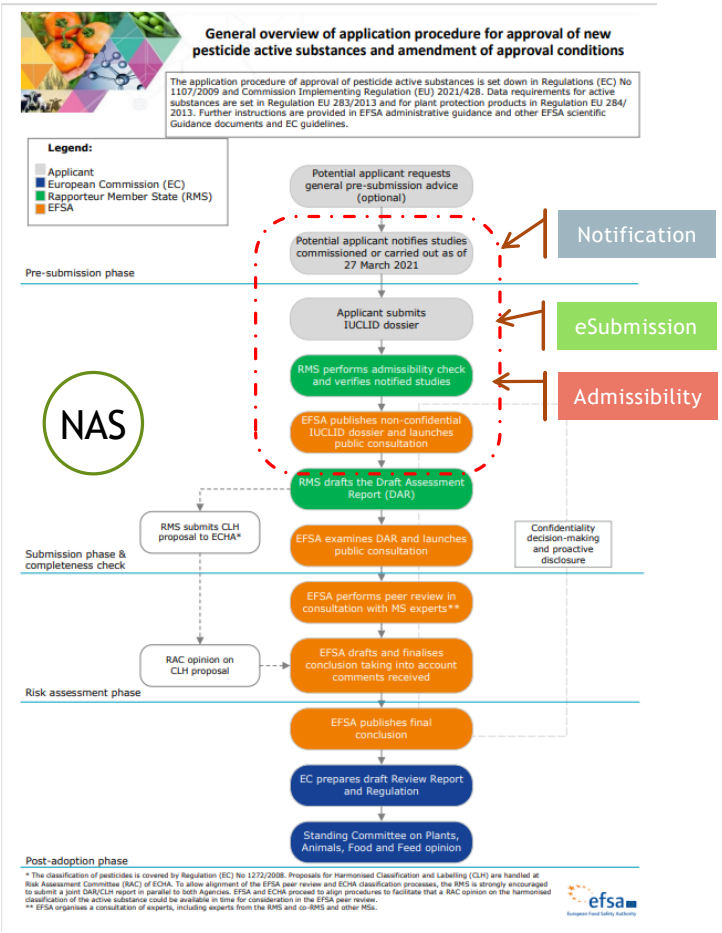
eurofins | agroscience regulatory

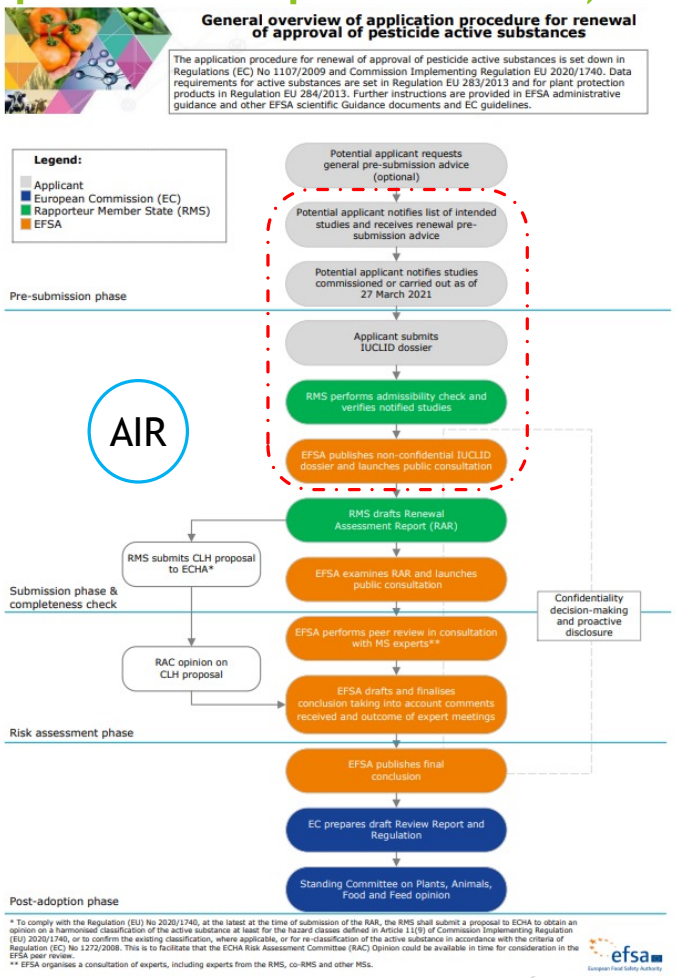
Jose Juanes, February 22

“Anything New with Global Regulation of Biological Products”

- Notification of studies
- IUCLID 6.0 software https://iuclid6.echa.europa.eu/
- Experiences with IUCLID dossier submissions (New active substances/Renewal of active substances)

EU (Active substances application procedure)





Source https://www.efsa.europa.eu/en/applications/toolkit

EU (Notification of studies)

Business operators

Role

- They act as potential applicant conducting presubmission activities linked to a future application for a regulated product in a specific regulated area.

Function

- Create pre-application IDs
- Studies from a pre-application ID
- Notify and co-notify studies
- The same qualification is assigned to consultants working on their behalf

Laboratory/CRO´s

Role

- Organisations such as laboratories/external testing facilities. They act as laboratories conducting studies commissioned by business operators

Function

- Only create, notify and conotify studies from the “Studies” section
- The same qualification is assigned to consultants working on their behalf

Preapplication ID and List of intended studies → IUCLID Dossier Header

Source: https://www.efsa.europa.eu/sites/default/files/2021-07/user-guide-notification-of-studies.pdf

EU (Regulatory Framework)

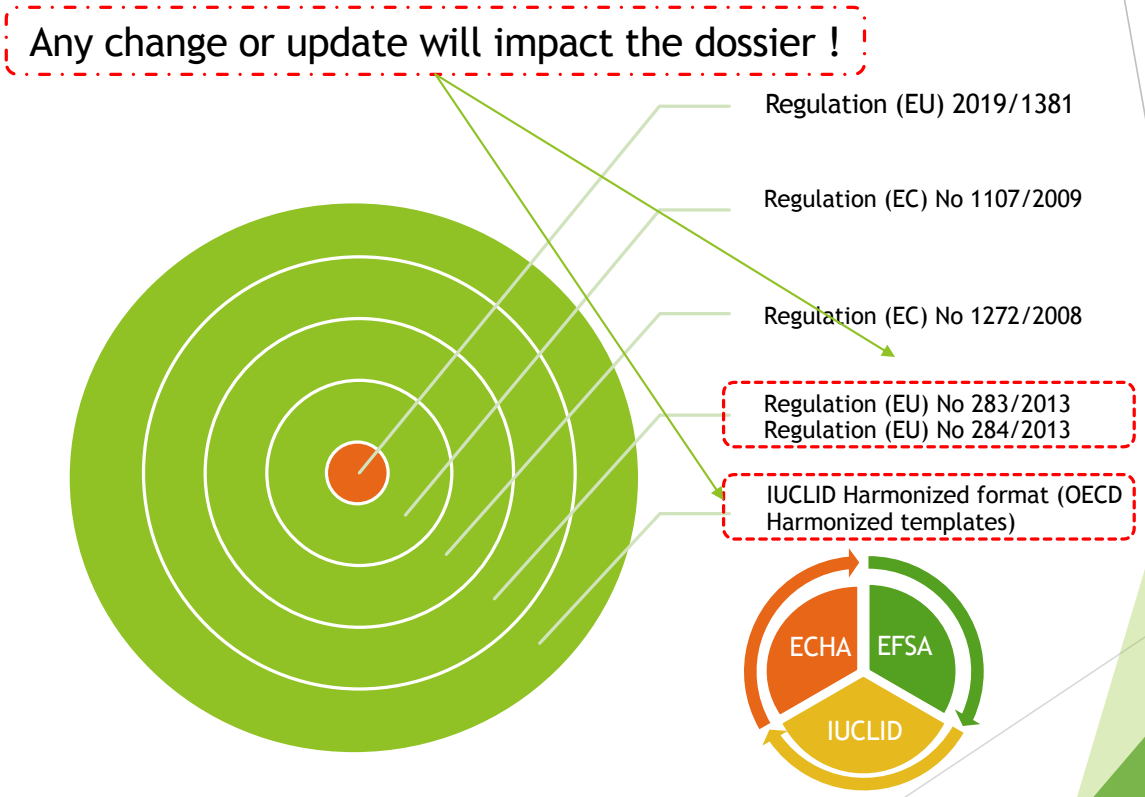
Regulation (EU) 2019/1381 of the European Parliament and of the Council of 20 June 2019 on the transparency and sustainability of the EU risk assessment in the food chain and amending Regulations (EC) No 178/2002, (EC) No 1829/2003, (EC) No 1831/2003, (EC) No 2065/2003, (EC) No 1935/2004, (EC) No 1331/2008, (EC) No 1107/2009, (EU) 2015/2283 and Directive 2001/18/EC.

Article 2

Adoption of standard data formats

The standard data formats for the approval of an active substance and those for the amendment to the conditions of such an approval, as proposed by the Authority, based on the IUCLID software package and linked with the central submission system to be established in accordance with Article 7(1) of Commission Implementing Regulation (EU) 2020/1740 of 20 November 2020,

are hereby adopted.



Data requirements in the EU (Regulatory Framework):

- Active substances

Regulation (EU) 283/2013

- Plant protection products

Regulation (EU) 284/2013

Part A: Chemicals including natural substances and semiochemicals

Biochemicals

- Botanicals = plant extracts
- Organic acids
- Plant hormones
- Semiochemicals (allelochemicals and pheromones)

Part B: Microorganisms (e.g. bacteria, fungi, protozoa), and viruses

Microbials

- Bacteria
- Fungi
- Protozoa
- Viruses
- Yeast

Update Data Requirements for Microbials (Applies from 21 November 2022)

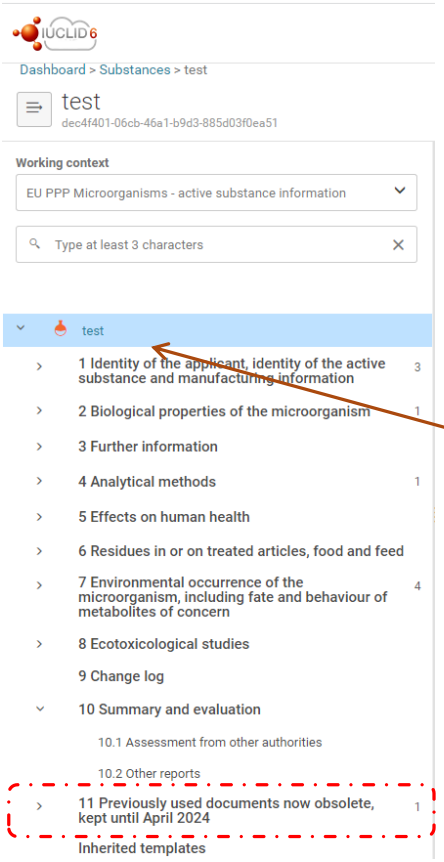
Active substance Regulation (EU) 2022/1439

- update data requirements to be used: transitional period between 21 Nov 2022 and 21 May 2023 - compulsory after 21 May 2023

Plant Protection Product Regulation (EU) 2022/1440

- it will depend on the data requirements used for the active substance

EU IUCLID Dossier (Table of contents and summaries)



Registration dossier

- Must contain in the form of study summaries or robust study summaries the physicochemical, biological properties, ecotoxicological and toxicological information, as well as all relevant available information.

Study summaries

- (robust) study summaries are reported in electronic formats called endpoint study records, which are based on the harmonised templates developed by the OECD

OECD Harmonised Templates

The OECD Harmonised Templates (OHTs) are standard data formats for reporting information used for the risk assessment of chemicals, mainly studies done on chemicals to determine their properties or effects on human health and the environment, but also for storing data on use and exposure. They are aimed at developers of database systems, as they prescribe the formats by which information can be entered into and maintained in a database. By using these templates, governments and industry are easily able to electronically exchange test study summary information.

The templates can be used to report summary test results for any type of chemical (e.g., pesticides, biocides, industrial chemicals, food/feed additives). The OECD Harmonised Templates cover endpoints and reporting elements which are grouped as follows:

Physico-chemical properties (incl. nanomaterials)	- OHTs 1 to 23-5 & 101 to 113
Environmental fate and behaviour	- OHTs 24 to 40 & 401
Effects on biotic systems	- OHTs 41 to 57
Health effects	- OHTs 58 to 84 & 86
Pesticide residue chemistry	- OHTs 85-1 to 85-10
Analytical methods	- OHT 87
Efficacy	- OHTs 88 & 89
Emissions from treated articles	- OHT 90
Intermediate effects	- OHT 201
Use and exposure information	- OHTs 301 to 306
Generic elements for all OHTs	- Literature reference - Test material information - Reference substance - Chemical inventory

EU IUCLID Database

IUCLID is a powerful database and was designed for regulatory purposes. REACh and Biocides registration/assessment experience is available and, in some cases, extrapolated to plant protection products.

Scientific data can be easily transferred for different regulatory purposes:

- ✓ Shift from a different regulatory geographical area context (OECD approach)
- ✓ Shift between EU regulations (REACh, BPR and Plant Protection Products)
- ✓ NAS/AIR (active substance) to expected dRR´s (product registrations)

If the electronic datasets contains good quality summaries and information we have:

- ✓ Traceability (Transparency)
- ✓ Expedited admissibility
- ✓ Electronic exchange
- ✓ Archiving
- ✓ Fast track dossier documentation(for example reference list, representative batches)
- ✓ Discussion during the evaluation process " Commenting tables", monography (DAR/RAR) or other evaluation formats.
- ✓ Possibility to reuse scientific data (common metabolites, etc.)

EU IUCLID Database

The adoption of IUCLID for the submission of dossiers has required a great effort on the part of authorities and industry, which goes beyond technical/scientific knowledge:

- Training for all users involved is required: software, complex dossiers, management of confidential data/CBI justifications: scientific work
- Training (regulatory process: dossier submission, resubmission, updates, dossier defence, commenting phase, etc.): regulatory work

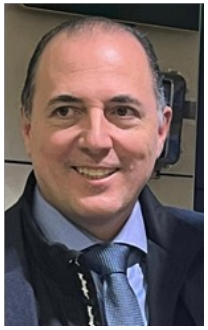
OECD Harmonize Templates in general fit for this purpose. New OHT templates must be developed or modified (such as example UV spectra).

Time and cost for dossier preparation has increased significantly due to the new implementation.

Summary

- Regulatory proceses evolves very fast worldwide (Data Requirements, guidelines, risk assessment approach, etc).
- The possibilities for greater coherence and efficiency on regulatory interactions between government, companies and citizens (Transparency Law) is granted with the use of IT tools (for example IUCLID).
- IUCLID involves a mix of information dissemination and transactional aspects required for an efficient evaluation of an active substance and representative product and work as a ”physical” enablers of burden reduction to bring products to market.
- Innovative thinking and skillful use of IT solutions like IUCLID are leading to new and more effective approaches for regulatory work and ideally for worldwide registrations following OECD format.

Do you have any question?



M. Sc. Jose Juanes is an analytical chemist with more than 25 years in the chemical industry. His work at Eurofins as Section Leader is to advice clients on product registration of active substances and plant protection products for the European region and worldwide, focusing on identity, manufacturing, five batch analysis, methods of analysis, physicochemical properties and storage stability of formulated products.
He has been involved in dossier submissions for conventional chemical, microorganisms, botanicals and semiochemicals in the EU since 2008 as project manager and regulatory expert.
He has extensive experience with preparation of IUCLID dossiers for substances and products under the EU regulatory framework (REACh, BPR, CLP and Plant Protection Products)
Jose Juanes contributes and leads several projects for implementation of IUCLID at Eurofins Agroscience Regulatory Europe to support effective solutions to customers with the registration procedures for new active substances and plant protection products.

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Questions?