8th meeting of the PSN IUCLID sub-group
22 November 2023

IUCLID FORMAT: HARMONISATION & CHANGES

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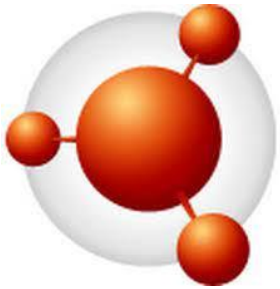
EUROPEAN FOOD SAFETY AUTHORITY

IUCLID RELEASE OCTOBER 2023

- IUCLID service release (version 7.10.1) went live on 30 October 2023



- **14 new** PPP Validation Assistant rules and improvement of 4 existing rules
- Open Validation Assistant report in a new tab
- Export/import fixes and performance improvement
- Literature reference cannot be imported with title more than 255 characters
- Improvement to the Comparison report

Release notes - IUCLID

THREE (PARALLEL) CONSULTATIONS ON IUCLID FORMATS

OECD (OHT/IUCLID Expert Group)

- **OHTs** (aka Endpoint Study Records)
- **Endpoint Summaries**

efsa EUROPEAN FOOD SAFETY AUTHORITY (PSN/EFSA staff)

- **EU PPP**

ECHA EUROPEAN CHEMICALS AGENCY (IUCLID Expert Group)

- **CORE** (endpoint summaries, flexible records/summaries)
- **Domain** (article, legal entity)

Backlog (IUCLID user requirements)

IUCLID FORMAT CHANGES – APRIL 2024

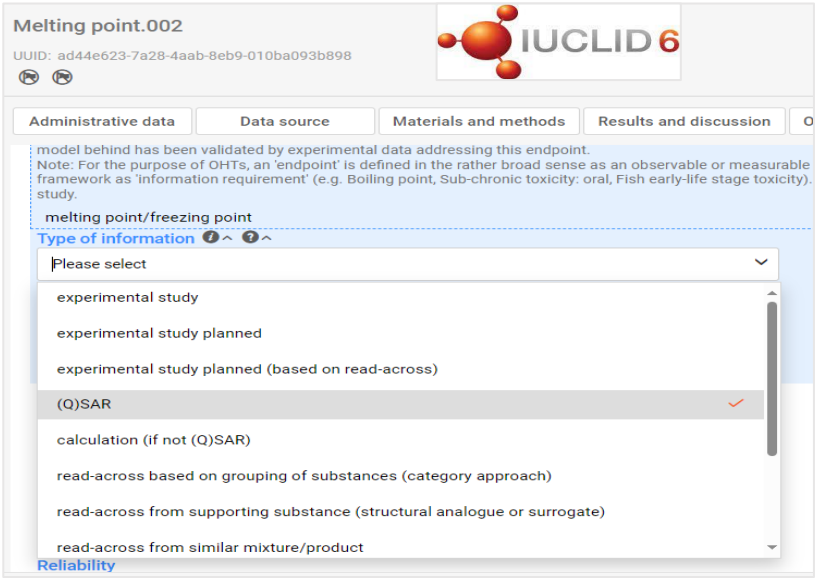
Provider	Name	IUCLID Backlog (#)
OECD	**REFERENCE_SUBSTANCE**	Adding InChI-key field (#2741)
OECD	ENDPOINT_STUDY_RECORD.**AcuteToxicityOral_QAF_Example** (**OHT 60**)	Adding specific fields to all OHTs to capture (Q)SARs studies according to OECD (Q)SAR assessment framework (QAF) project
OECD	FLEXIBLE_RECORD.**IntermediateEffects_v6.2** (**OHT 201**)	Harmonising attachments sections (original and sanitized) (#2730)
OECD	ENDPOINT_STUDY_RECORD.**AdsorptionDesorption**_v8.2 (**OHT 34**)	Removal of “Maximum occurrence (%)” (#2654)
OECD	ENDPOINT_SUMMARY.AdsorptionDesorption_v8.1	Adding fields to report pesticides related info (OC%, Soil pH. Kd, Kdoc, KF, Kfoc and 1/n) (#2149)
OECD	ENDPOINT_STUDY_RECORD.**MagnitudeResidInProcessedComm**_v6.1_2023-07-19_BfR_EFSA_rev.docx (**OHT85-9**)	EFSA-BfR proposal #2089#2467#2079#1786#2073#2466#2487#2067#2728
OECD	ENDPOINT_STUDY_RECORD.**ResiduesInRotationalCrops**_v8.4_2023-07-19-1_BfR_EFSA_rev.docx (**OHT85-5**)	
OECD	ENDPOINT_STUDY_RECORD.**OtherDistributionData**_v8.1 (**OHT 37**) ENDPOINT_STUDY_RECORD.**Hydrolysis**_v8.2 (**OHT 25**) ENDPOINT_STUDY_RECORD.**Phototransformation**_v9.1 (**OHT 26**) ENDPOINT_STUDY_RECORD.**PhototransformationInAir**_v9.1 (**OHT 24**) ENDPOINT_STUDY_RECORD.**PhotoTransformationInSoil**_v9.2 (**OHT 27**)	Harmonising results tables (2745)
OECD	ENDPOINT_SUMMARY.**FieldStudies**_v5.2 (**OHT 39**)	Updating cross-reference (#2765)

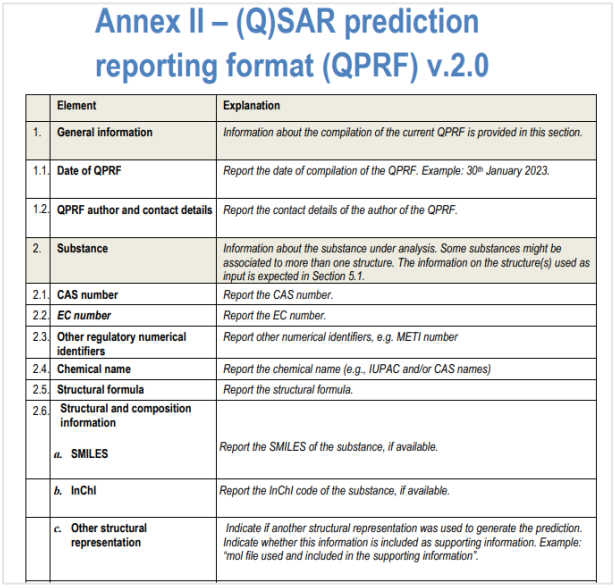
IUCLID FORMAT CHANGES – APRIL 2024

Provider	Name	IUCLID Backlog (#)
CORE	FLEXIBLE_RECORD.**AnalyticalInformation**	hHarmonising with current structure of ENDPOINT_STUDY_RECORDs (#2700)
CORE	ENDPOINT_SUMMARY.**Toxicokinetics_v7.0**	Alignment with list of endpoints (postponed to 2024/2025) (#2701)
CORE	FLEXIBLE_RECORD.**MixtureComposition_v8.3 (doc J)**	Add new check box “Authorised co-formulant”
CORE	FLEXIBLE_RECORD.**LiteratureSearch** FLEXIBLE_RECORD.**Packaging** FLEXIBLE_RECORD.**AssessmentOtherAuthorities**(EU PPP) FLEXIBLE_RECORD.**SubstanceComposition**	Harmonising attachments sections (original and sanitized) (#2730)
EU_PPP	DOSSIER.EU_PPP_**ACTIVE_SUBSTANCE_FOR_MIXTURES**_v4.2 DOSSIER.EU_PPP_**BASIC_SUBSTANCE**_v3.1 DOSSIER.EU_PPP_**MAXIMUM_RESIDUE_LEVELS**_v3.1 DOSSIER.EU_PPP_**MICROORGANISMS_FOR_MIXTURES**_v3.2	Dynamic field to capture submission update (#2744)
EU_PPP	FLEXIBLE_RECORD.GAP.**AdministrativeDataSummary**	Minor changes (#2726)
EU_PPP	FLEXIBLE_SUMMARY.**DefinitionResidueFate_v3.0**	Additions to reflect changes to the newly created Flexible Record Biomonitoring
EU_PPP	FLEXIBLE_SUMMARY.**ToxRefValues_v3.2**	Picklist harmonisation to allow OpenFoodTox db migration to IUCLID (#2811)
EU_PPP	NEW FLEXIBLE_SUMMARY.**Impurities**	New doc to report non-relevant impurities of a.s. as SUBSTANCE datasets (i.e., they should not be in the MIXTURE composition since they are not part of the formulation) (#2801)
EU_PPP	NEW FLEXIBLE_SUMMARY.**DefinitionResidueBiomonitoring**	New doc to report residue definition in body fluids and tissues needed for the LoE of PPP (#2805)

OHTS HARMONISATION TO REPORT (Q)SAR STUDIES IN IUCLID - BACKGROUND

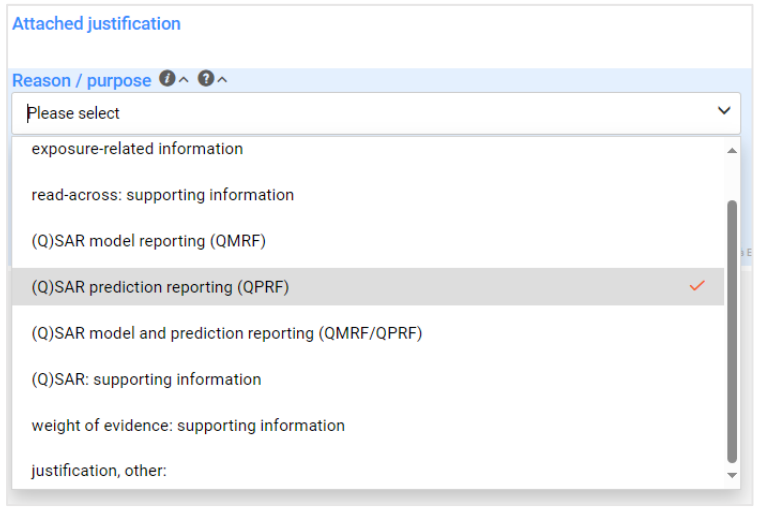
- Currently, **(Q)SAR results** are reported in IUCLID using the same fields as for "*Experimental Studies*";
- **(Q)SAR** specific fields are **not available in IUCLID** (e.g., applicability domain, analogues for the reliability assessment);
- **(Q)SAR** specific data can be reported using **free-text fields** and/or attaching **QPRF template limiting data extraction, mining and reuse**.





Annex II – (Q)SAR prediction reporting format (QPRF) v.2.0

	Element	Explanation
1.	**General information**	*Information about the compilation of the current QPRF is provided in this section.*
1.1	**Date of QPRF**	*Report the date of compilation of the QPRF. Example: 30th January 2023.*
1.2	**QPRF author and contact details**	*Report the contact details of the author of the QPRF.*
2.	**Substance**	*Information about the substance under analysis. Some substances might be associated to more than one structure. The information on the structure(s) used as input is expected in Section 5.1.*
2.1	**CAS number**	*Report the CAS number.*
2.2	***EC number***	*Report the EC number.*
2.3	**Other regulatory numerical identifiers**	*Report other numerical identifiers, e.g. METI number*
2.4	**Chemical name**	*Report the chemical name (e.g., IUPAC and/or CAS names)*
2.5	**Structural formula**	*Report the structural formula.*
2.6	**Structural and composition information**	
	a. **SMILES**	*Report the SMILES of the substance, if available.*
	b. **InChI**	*Report the InChI code of the substance, if available.*
	c. **Other structural representation**	*Indicate if another structural representation was used to generate the prediction. Indicate whether this information is included as supporting information. Example: "mol file used and included in the supporting information".*



OHTS HARMONISATION TO REPORT (Q)SAR STUDIES IN IUCLID - OBJECTIVES

To extend the current OHTs to report **(Q)SAR results** in **structured format** in IUCLID according to the **(Q)SAR Assessment Framework (QAF) (OECD, 2023)**:

- **Mapping QPRF fields** to OHTs structure
- **Implementing** additional fields in OHT format

PRINCIPLES FOR THE ASSESSMENT OF (Q)SAR PREDICTIONS AND RESULTS

1.Correct input
2. Substance within Applicability Domain
3. Reliable prediction(s)
4. Outcome fit for purpose

Annex II – (Q)SAR prediction reporting format (QPRF) v.2.0

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2.1.	**CAS number**	*Report the CAS number.*
2.2.	***EC number***	*Report the EC number.*
2.3.	**Other regulatory numerical identifiers**	*Report other numerical identifiers, e.g. METI number*
2.4.	**Chemical name**	*Report the chemical name (e.g., IUPAC and/or CAS names)*
2.5.	**Structural formula**	*Report the structural formula.*
2.6.	**Structural and composition information**	
	a. **SMILES**	*Report the SMILES of the substance, if available.*
	b. **InChI**	*Report the InChI code of the substance, if available.*
	c. **Other structural representation**	*Indicate if another structural representation was used to generate the prediction. Indicate whether this information is included as supporting information. Example: "mol file used and included in the supporting information".*

https://one.oecd.org/document/ENV/CBC/MONO(2023)32/ANN2/en/pdf

EXTENDED OHT

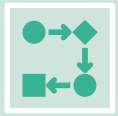
80.	**Additional information about applicability domain and reliability of (Q)SAR predictions**	**Header 2**		
81.	Fit within applicability domain		**Picklist values:** - iIn applicability domain - oOutside applicability domain - uUndefined applicability domain - aApplicability not assessed - other	Indicate if the substance fits within the applicability domain of the model defined by the model developers.
82.	Applicability domain methodology		**Free text**	Describe how the fit within the applicability domain was determined. Indicate if there is any additional known limitation of the applied model, not included in
83.	Reproducibility		**Picklist values:** - yYes - nNo - other:	Indicate if the prediction can be reproduced by others. This is usually the case for publicly available free and commercial models.
84.	Fit within the space defined by the training set of the model		**Picklist values:** - yYes - nNo - nNot assessed - other:	Indicate if the substance fits within the physicochemical, structural and response spaces defined by the training set of the model
85.	Mechanistic and metabolic considerations		**Free text**	Indicate mechanistic and metabolic considerations relevant for the predictions, if applicable.

OHTS HARMONISATION TO REPORT (Q)SAR STUDIES IN IUCLID - RESULTS

Structuring **QSAR** data to **improve** their **reporting** in IUCLID (i.e., **24 new fields** including picklist)

Reflecting the newly published **QPRF v.2.0 template** in OHTs/IUCLID format

Facilitating **Authorities** such as ECHA and EFSA in the **assessment** of QSAR data (e.g., under REACH; pesticides impurities, metabolites)



Possibility to reuse (structured) QSAR data for New Approach Methodologies (**NAMs**) developments.

HARMONISATION OF THE ENVIRONMENTAL FATE TEMPLATES

Currently the OECD Harmonised Template ”Biodegradation in soil” (OHT 30) makes use of the following result sections, comprised of repeatable blocks of fields:

- **”Material (mass) balance”**
- **”Disappearance time (DT) of parent compound“**

EFSA has proposed to align the usage of these result sections across the following environmental fate OHTs:

Hydrolysis (OHT 25)

Phototransformation in soil (OHT 27)

Phototransformation in water (OHT 26)

Biodegradation in water and sediment (OHT 29)

*”%total extractable” and “% Non extractable” not included in OHT 25
**Phototransformation in air (OHT 24) and Other distribution data (OHT 37) not changed as no OECD test guideline available

IUCLID - IMPURITIES

- FLEXIBLE_RECORD.MixtureComposition

Function → New picklist to report '**Relevant Impurities**'

1.4. Detailed quantitative and qualitative information on the composition of the plant protection product

1.4.1. ***Composition of the plant protection product***

For plant protection products the following information shall be reported:

— the content of the technical active substances (based on the specified minimum purity) and the declared content of pure active substances and, where relevant, the corresponding content of the variant (such as salts and esters) of the active substances,

— the content of safeners, synergists and co-formulants,

— the maximum content of relevant impurities, where appropriate.

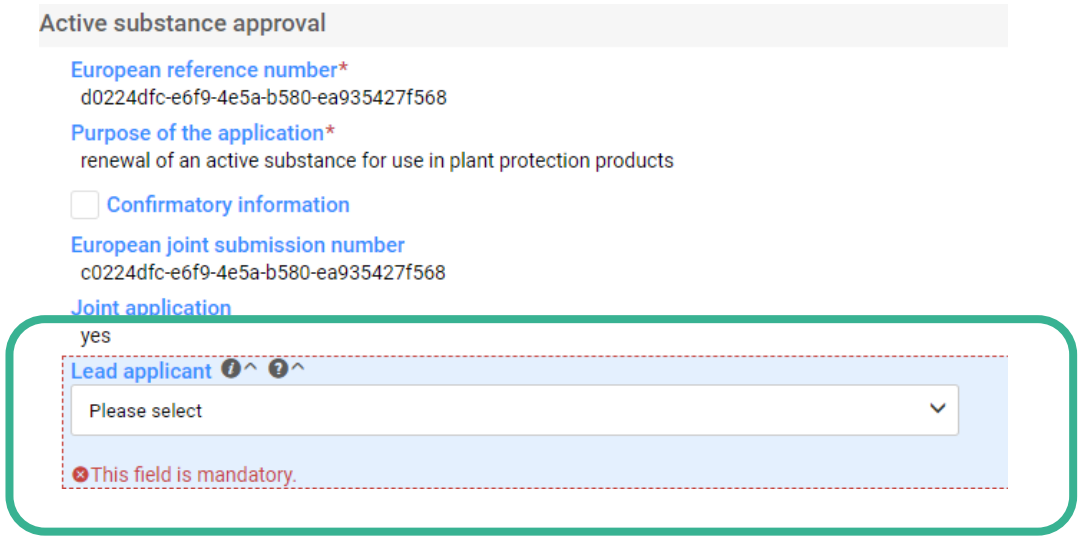
- Commission Regulation (EU) No 283/2013 - Any information including any known data on impurities shall be provided.

→ Proposed new **FLEXIBLE_SUMMARY.Impurities** to report information (dataset), if any, on impurities (*relevant, significant, not significant or theoretical*)

Line no.	Field name	Field type Display type	Picklist Freetext template	Help text	Remarks Guidance Cross-reference
7.	Link to impurity dataset	Link to entity (single) Display: Basic		If studies are performed on the impurity, link the corresponding substance dataset. If no studies are performed, link the reference substance.	**Cross-reference:** SUBSTANCE,REFERENCE_SUBSTANCE
8.	Code/Name of the impurity	Text (255 char)		Indicate the code or name of the impurity used to identify the impurity in the different studies provided in the dossier.	
9.	Type of Impurities	List (picklist) Display: Basic	**Picklist values:** -**Relevant** -Significant -Not significant -Theoretical	Indicate the type of impurity	
10.	Manufacturing plants	Link to entity (multiple) Display: Basic		Link the manufacturing plant(s) where the technical material containing the impurity was produced.	**Cross-reference:** FLEXIBLE_RECORD.Sites.ReferenceSite
11.	Remarks	Text (2,000 char.) Display: Basic			
12.	**Impurities**	**Block of fields (repeatable)** **End**			

IUCLID – JOINT SUBMISSION

- Currently the ‘Joint Submission’ technically implies that all members are considered as applicants
- The above is not suitable for companies who provide data by means of Letter of Access
- Proposal is to add a new role ‘Contributor’ to handle such cases



‘Lead Applicant’ field replaced by ‘Role in the Joint Submission’

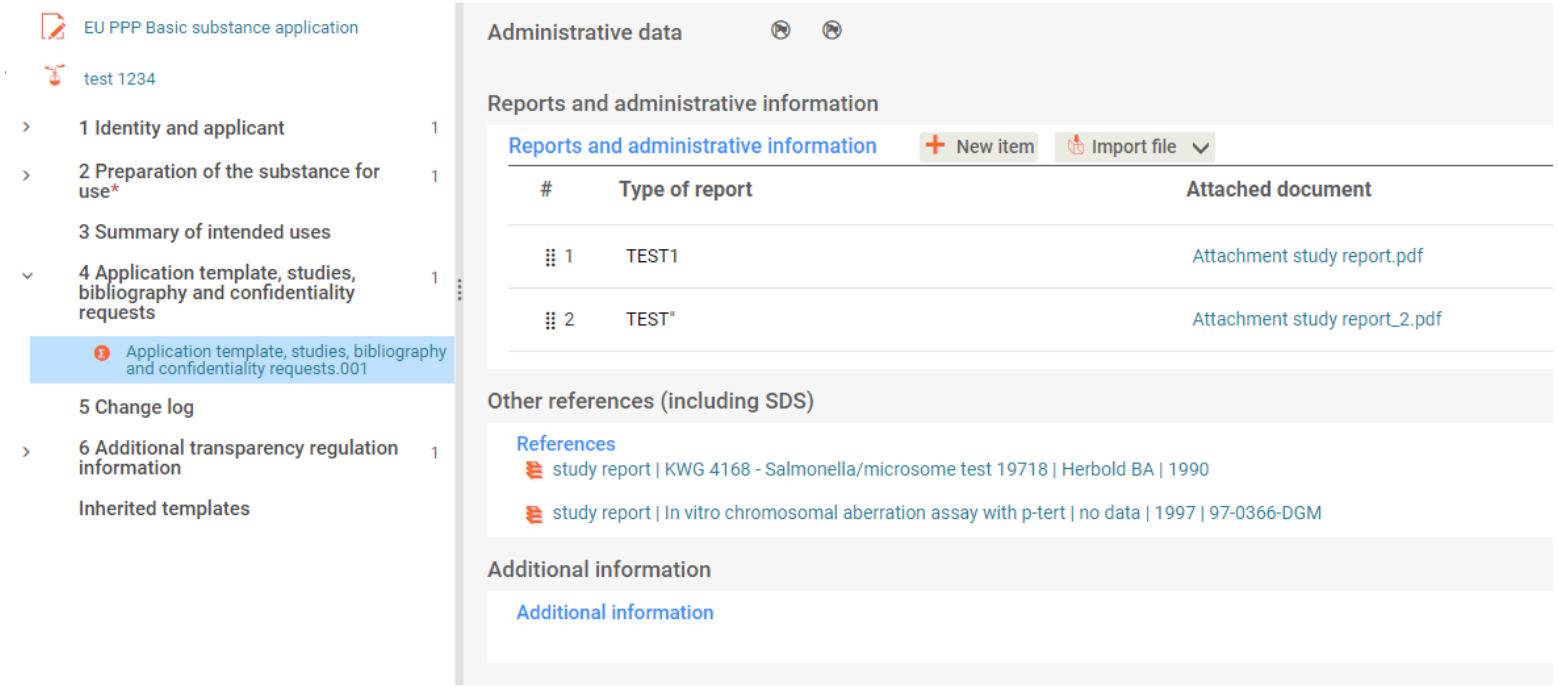
- Lead applicant
- Member applicant
- **Contributor**

ANALYTICAL METHODS

- EFSA‘s proposed changes to ENDPOINT_STUDY_RECORD.AnalyticalMethods only limited to update the list of Endpoints
- Several comments received during OECD consultation going beyond the proposed changes
- EFSA suggests creating new backlog items, if not yet done, so that any proposal can be carefully analysed for next round of format changes

3.	Endpoint	List sup. (picklist with remarks) Display: Basic	**Picklist values:** - analysis of the microorganism as manufactured (QC) - analytical methods - analytical profile of batches - methods for post-approval control and monitoring purposes - methods for providing information on possible variability of seed stock/active micro-organism - methods for providing information on purity of seed stock/active micro-organism - methods for relevant impurities and/or metabolites of concern - methods for risk assessment - methods for significant impurities

BASIC SUBSTANCE APPLICATIONS



- Simplified Table of Content
- Studies and any supporting documentation is attached in section 4 → no structured data
- No Validation Assistant rules
- No documents generated through Report generator

BASIC SUBSTANCE APPLICATIONS

EFSA proposes to update the Table of Content (ToC) of Basic Substance applications

Possible option which would require less effort would be to use the ToC of the existing ‘Active Substance’ dataset

Any change needs to be agreed with the European Commission

Timeline: Plan is to implement any change in April 2025

IUCLID IMPROVEMENT ACTIVITIES

❑ Active participation to the OECD improvement activities

- **#1 User interface improvements**
  - Searching functionalities (e.g., improving IUCLID User Interface? Other solutions e.g., cloud analysis tools and pipelines)
- **#2 IUCLID Reporting**
- **#3 Using the same dataset for multiple recipients**
  - Standardisation of data and harmonisation of VA rules
  - lifecycle management to address data stability during long evaluation processes and prevent data loss during migrations.
- **#4 Data availability / Dissemination**
  - EU PPP, OpenFoodTox, Genotox data
- **#5 Use of ontologies / extension of the format**
  - EFSA's FOODEX2 catalogue (PPP commodities, EPPO codes)
  - Substance Identifiers (list of reference substances from OpenFoodTox)

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