IT tools training

Read-across in IUCLID 6

Luxembourg
09 April 2018

Margot Mägi
Valérie Lasseigne-Phrakonkham
Directorate of Registration
European Chemicals Agency

Read-across in general

What is read-across?

WHAT?

- **Read-across (RA):** technique for predicting endpoint information for a substance (**target substance**), by using data on the same endpoint from (an)other substance(s), (**source substance**(**s**))

  - ✓ **Source substance - From** which the information is used to predict for another chemical that has similar properties

  - ✓ **Target substance** – **For** which the information is predicted based on the information of chemicals with similar properties

Using Read-across: Why, how?

WHY?

- **REACH's intention**
  - Minimise the new tests on vertebrate animals, but still ensure the safe use of chemicals

HOW?

- **Fill data gaps via applying read-across (source / target)**
  - Assessing the (eco)toxicology of the **target chemical** by using the data from a **source chemical** with similar physico-chemical and (eco) toxicity profile
  - Possibility to apply to all endpoints

Two approaches to report read-across

- **Category approach**

  - RA applied between several substances that have **structural similarity**

  - These substances are **grouped together** on the basis of defined structural similarity and differences

  - **A trend or regular pattern** on the properties can be defined because the properties vary in a clearly predictable way (E.g.: boiling point steadily increases with the length of the molecule hydrocarbon chain)

Two approaches to report read-across

- **Analogue approach**

  - RA applied between a **small number** (1-2) of structurally similar substances

  - The **trend or regular pattern** on the properties **cannot be claimed** due to small number of substances involved

  - Mostly just relies on that the **result for one chemical is the same** as for another

Category approach

Category approach

- **Source data**

  Experimental data from the group of substances is provided in the category member substance datasets. These source substances and the target substance are to be linked together in a **category object**

- **Target data**

  Outcome of the read-across is provided as an **endpoint study record** in the substance dataset of the registered substance

Category approach: example

- **Substances A, B and C**
  - Boiling point and Particle size distribution: substance **A** contains the **target records** and substances **B and C source records**
  - Melting point / freezing point and Density: substance **A and B** are the **source records** and substance **C** contains the **target records**

	A	B	C
2 Melting point / freezing point	1 ●	2 ●	
3 Boiling point		2 ●	1 ●
4 Density	1 ●	2 ●	
5 Particle size distribution (Granulometry)		2 ●	1 ●

Category approach in 3 steps

Step 1: Prepare the substance dataset that will be the **category members** with the experimental data available

Step 2: Create the **category object** (=**source**); link all the category members and provide the justification for the category; select the endpoints for which the category will be used

Step 3: Start filling in the read-across records (=**target**) for the endpoints with the data gaps

Category approach:
Category object (1/7)

- At least one **category object (source)** must exist in the dossier including:

  - Information on the category hypothesis, applicability domain and category justification in the field **Category rationale** or attached in the table Reports

  - **Category members** that are linked to the category object

  - The list of the **Category documents**

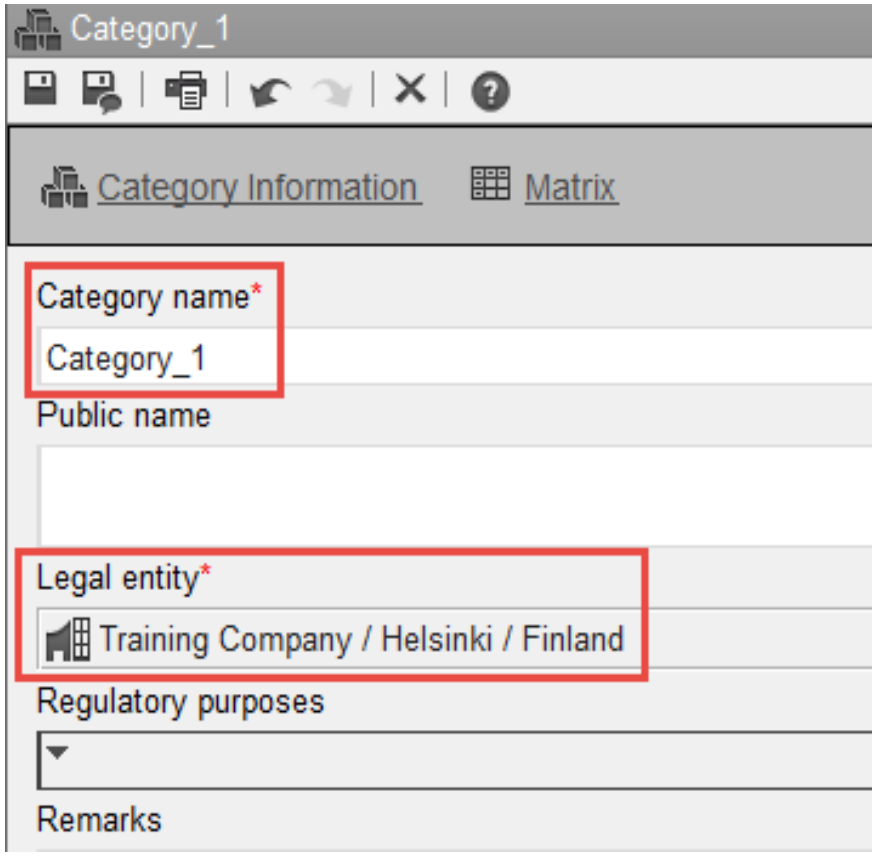
Category approach:
Category object (2/7)

- Create a new **category object**

Category approach

Category object (3/7)

- **Category identification**
  - Enter a **Category Name**
  - Associate a **legal entity** (mandatory)

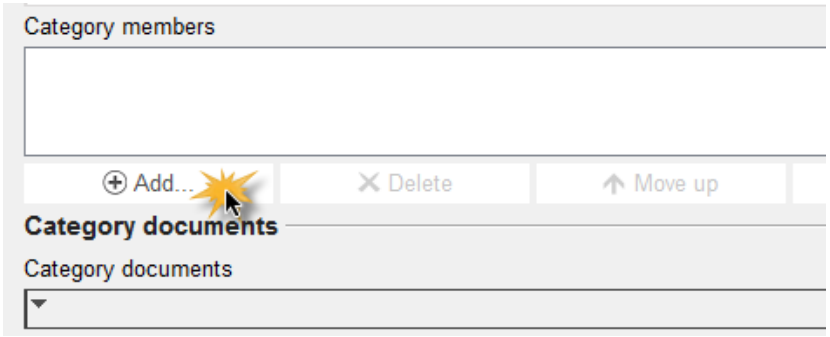


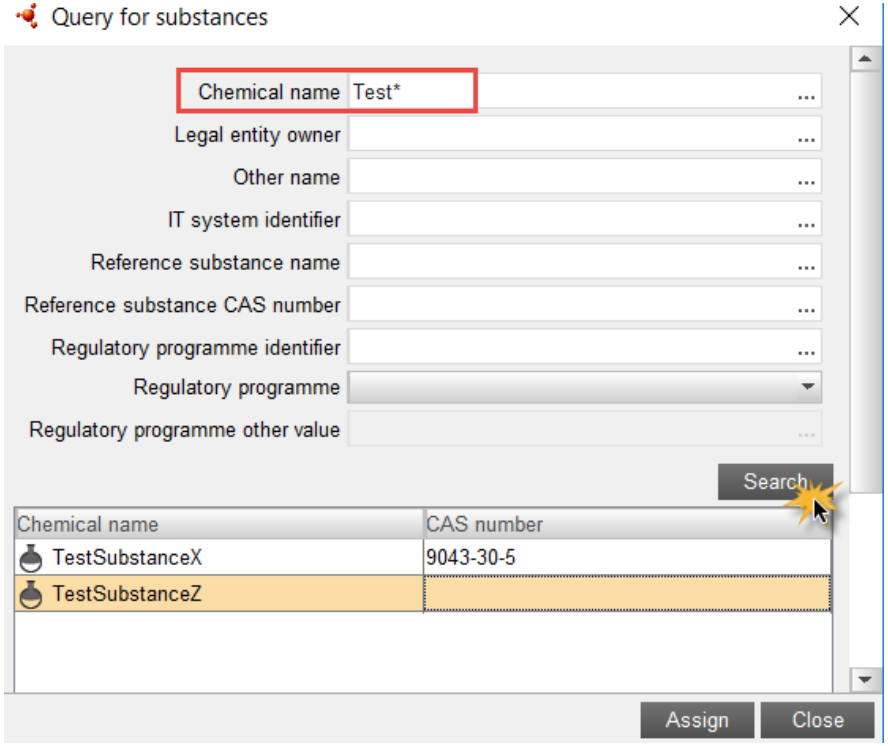
Category approach

Category object (4/7)

- **Category information**

  - Add the **category members**. Members must be linked to the category object.



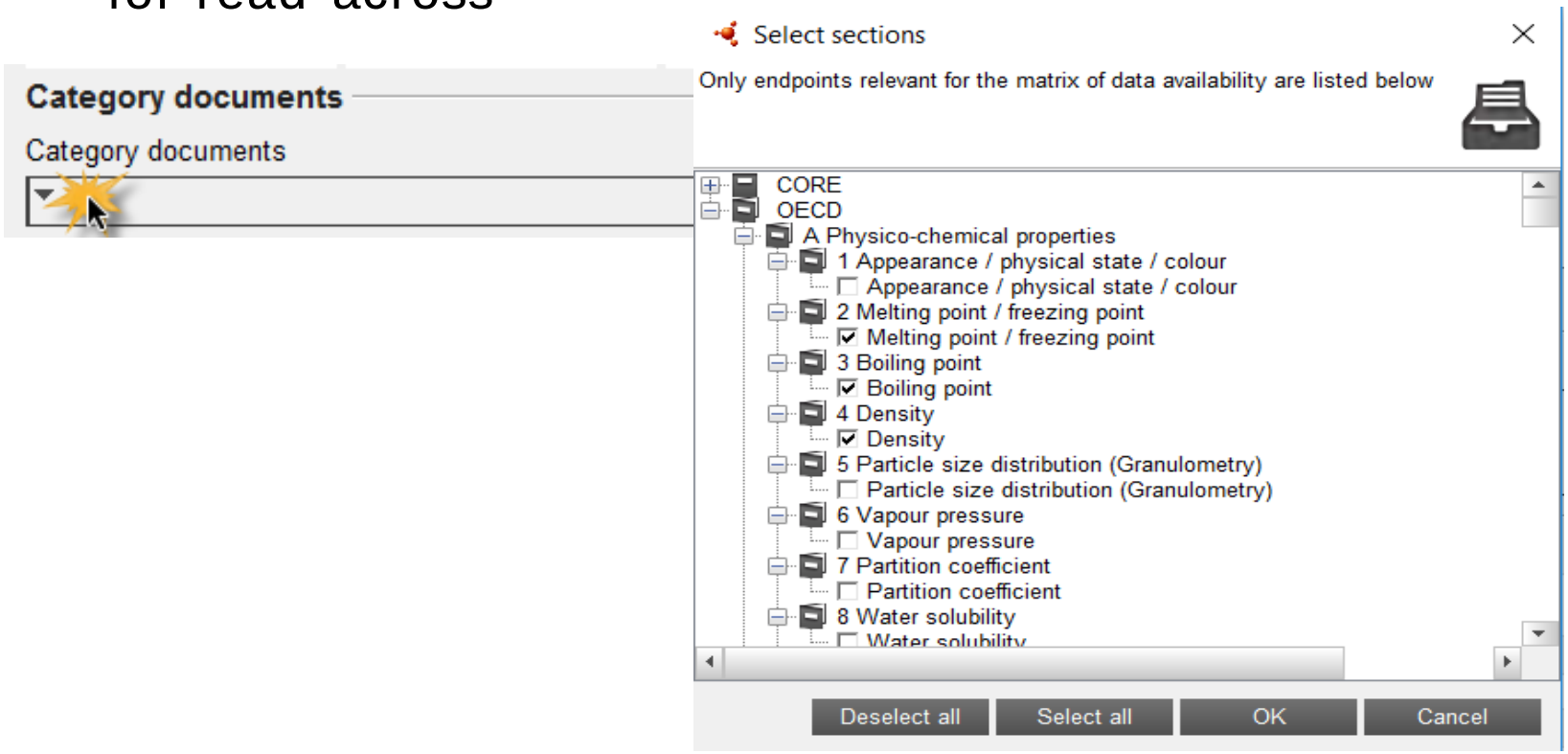


Category approach

Category object (5/7)

- **Category documents**

  - Select from the **Category documents** the endpoints for read-across

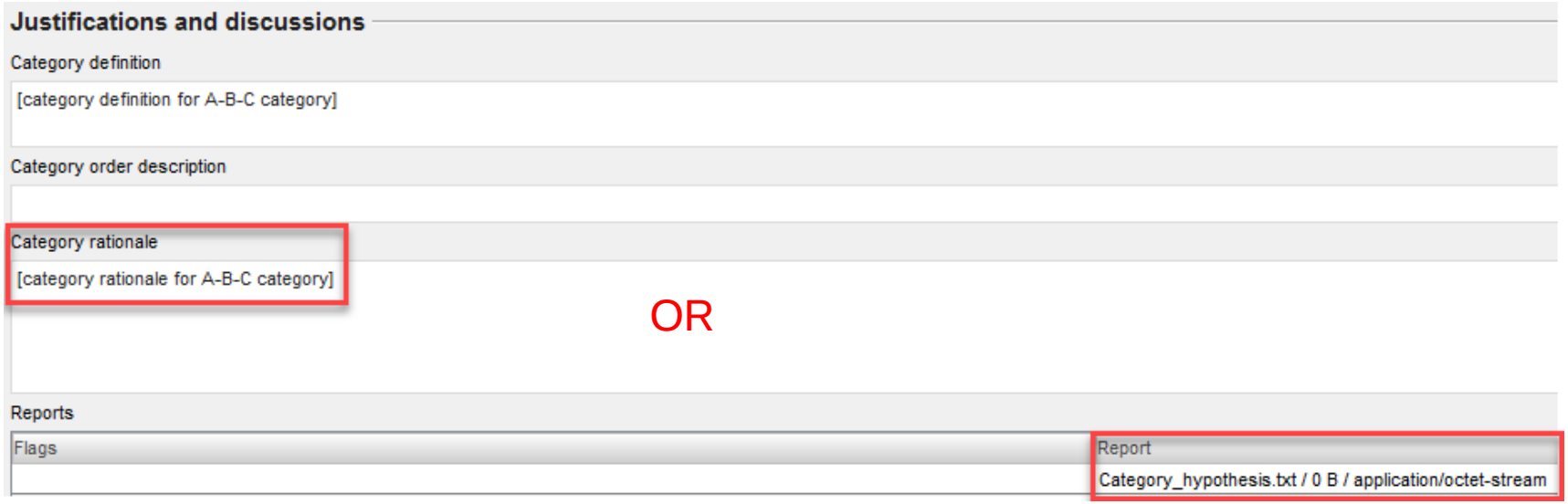


Category approach

Category object (6/7)

- **Category rationale**

  - Provide the category hypothesis, applicability domain and category justification in the **Category rationale** field as a free text or as an attachment in the table Reports

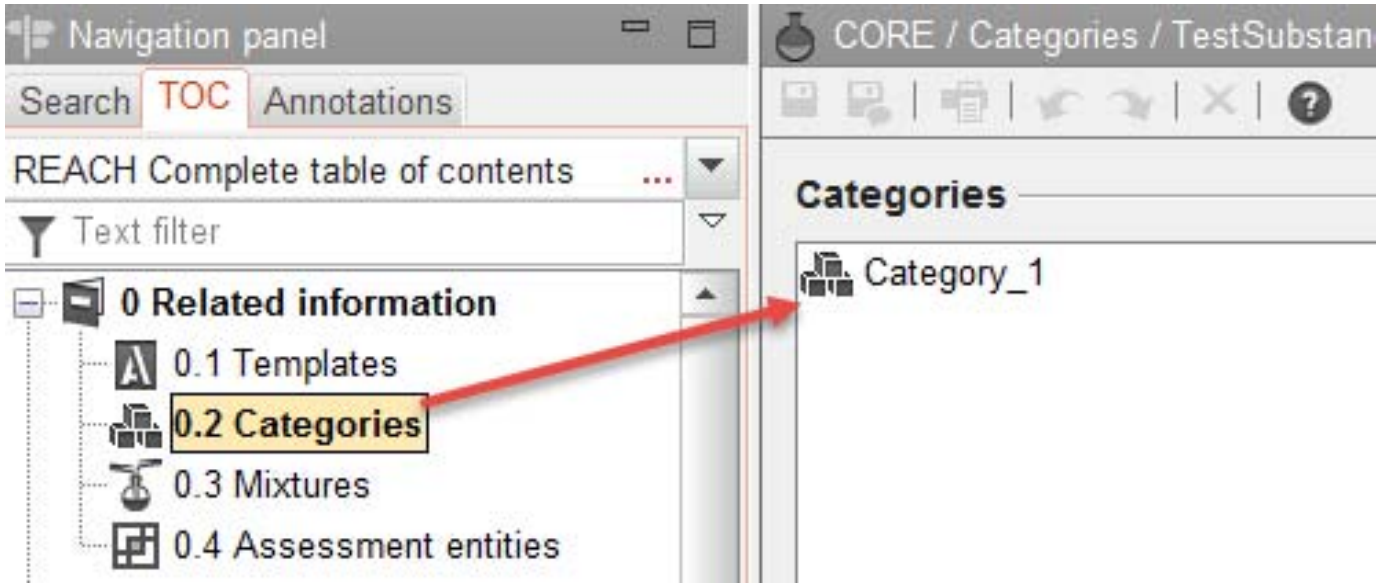


Category approach

Category object (7/7)

- **Section 0.2 – Substance dataset**

  - Link the Category object in the target substance dataset in section 0.2 Categories:



Category approach:
Target record (1/3)

	Endpoint study record	Target record
i	Administrative data	X
	Endpoint	X
	Type of information	X
	Adequacy of study	X
	Robust study summary Used for classification Used for SDS	X
	Study period	
	Reliability	
	Rationale for reliability incl. deficiencies	
	Data waiving	
	Justification for data waiving	
	Justification for type of information	X
	Attached justification	X
	Cross-reference	
ii	Data source	
iii	Materials and methods	
iv	Test materials	X
v	Result and discussion	X
vi	Overall remarks, attachments	X
vii	Applicant's summary and conclusion	x

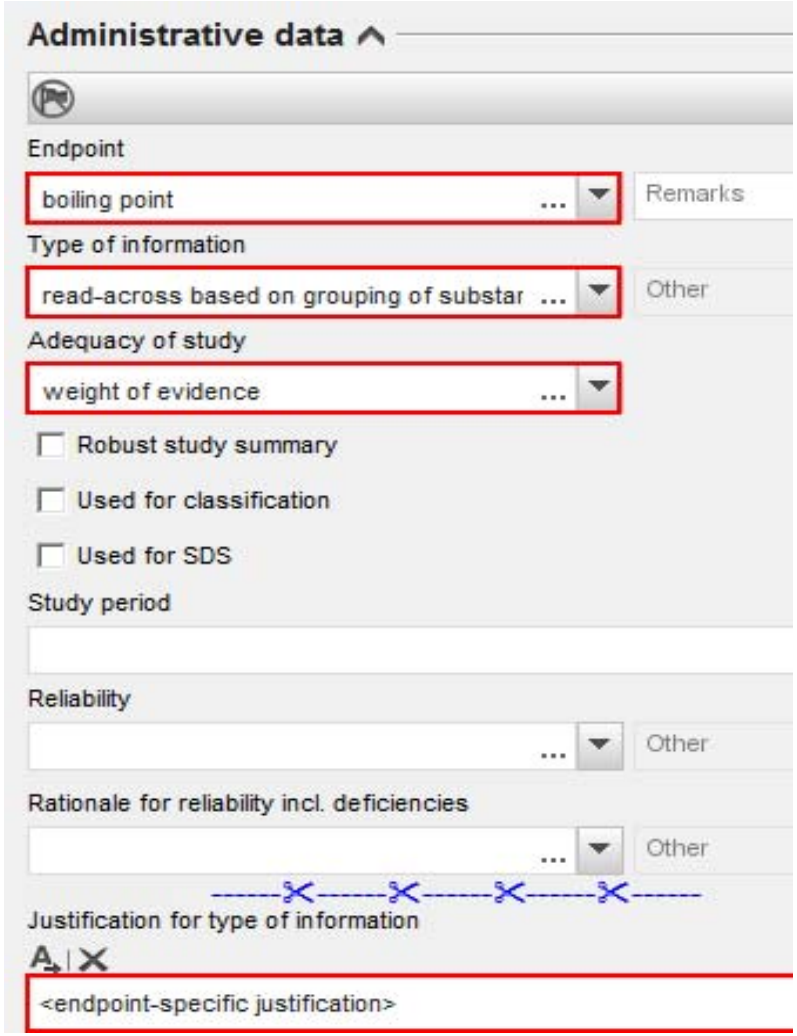
Category approach:
Target record (2/3)

- **Administrative data**

- **Type of information:** set to "read-across based on grouping of substances (category approach)"

- **Adequacy of study:** set to the appropriate value depending on how you use the read-across to fulfil the information requirement (typically "key study" or "weight-of-evidence")

- **Justification for type of information:** contains an endpoint-specific justification



Category approach:
Target record (3/3)

- **Materials and methods**
  - **Test material information**: The target record reflects the substance that is in scope of the registration (section 1.1)

- **Results and discussion**
  - The results in the target record may be identical to the source endpoint study record if read-across is truly one-to-one.
  - May be differences between the source and target chemicals, which influence the numerical result (e.g. molecular weight)

- **Applicant's summary and conclusion (optional)**
  - Main conclusions of the approach
  - In the *Executive summary* field, summarise the justification for the read-across approach and the applicability of the result

Analogue approach

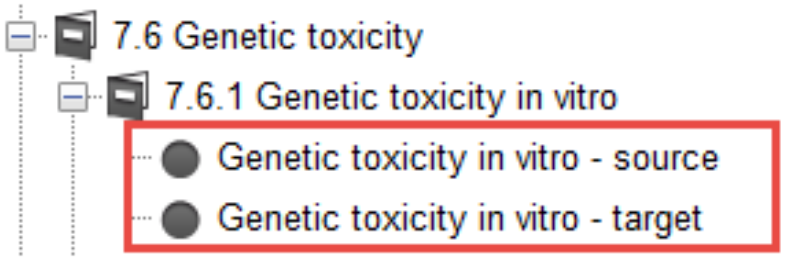
Analogue approach

- **Two records must exist in the <u>same endpoint</u>**

  - **Source data:** endpoint record that includes all the experimental data about the tested chemical

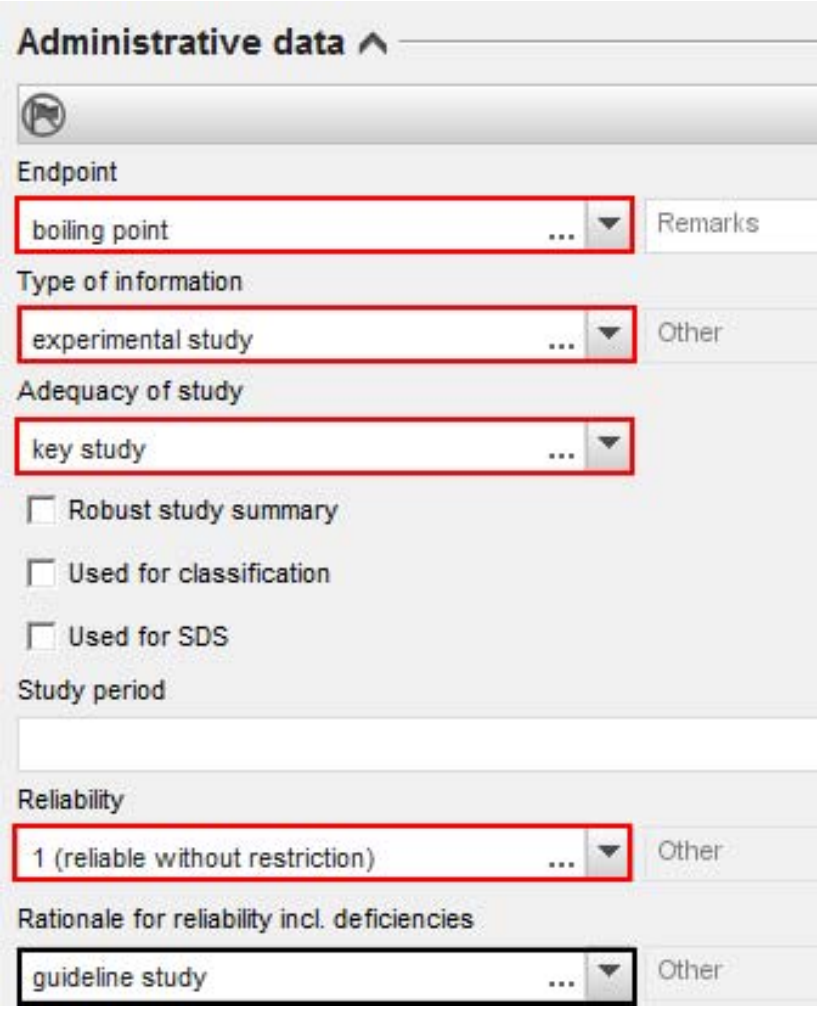
  - **Target data:** endpoint record that includes read-across information and data about the read-across target material

    → *Usually the substance that is in scope of the registration*



Analogue approach:
Source record

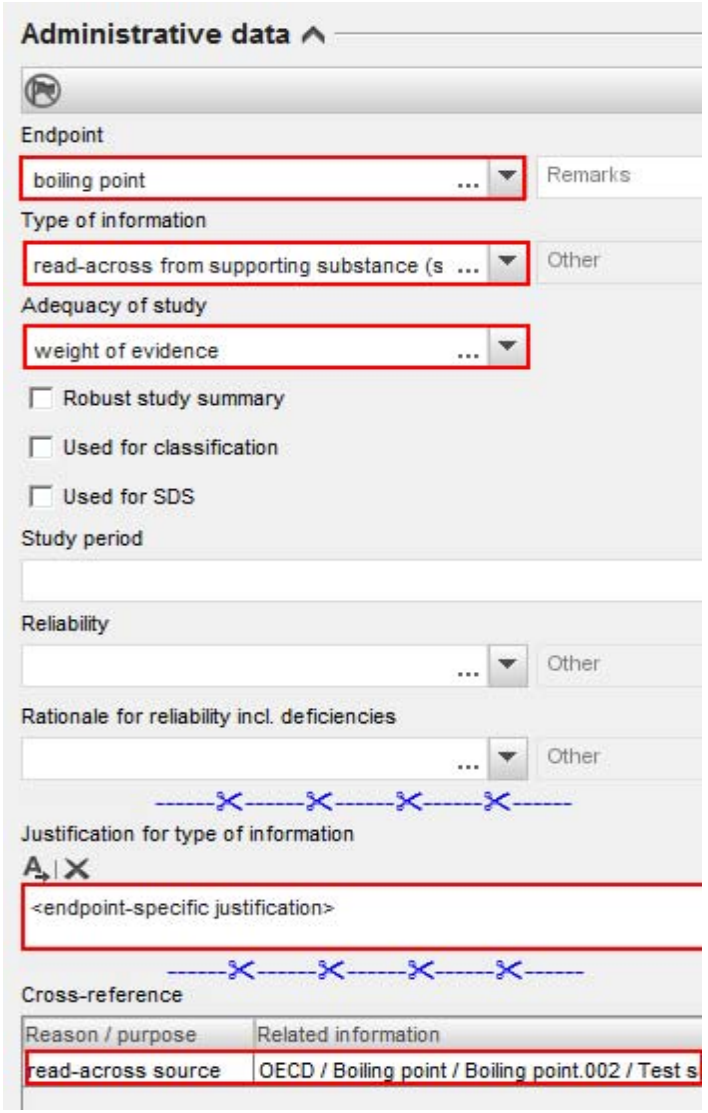
- **Type of information:** set to “experimental study”
- **Adequacy of study:** set to “key study”
- Fill in the source record as a normal experimental study record
- The **test material** information identifies the substance on which the test was done



Analogue approach:

Target record (1/3)

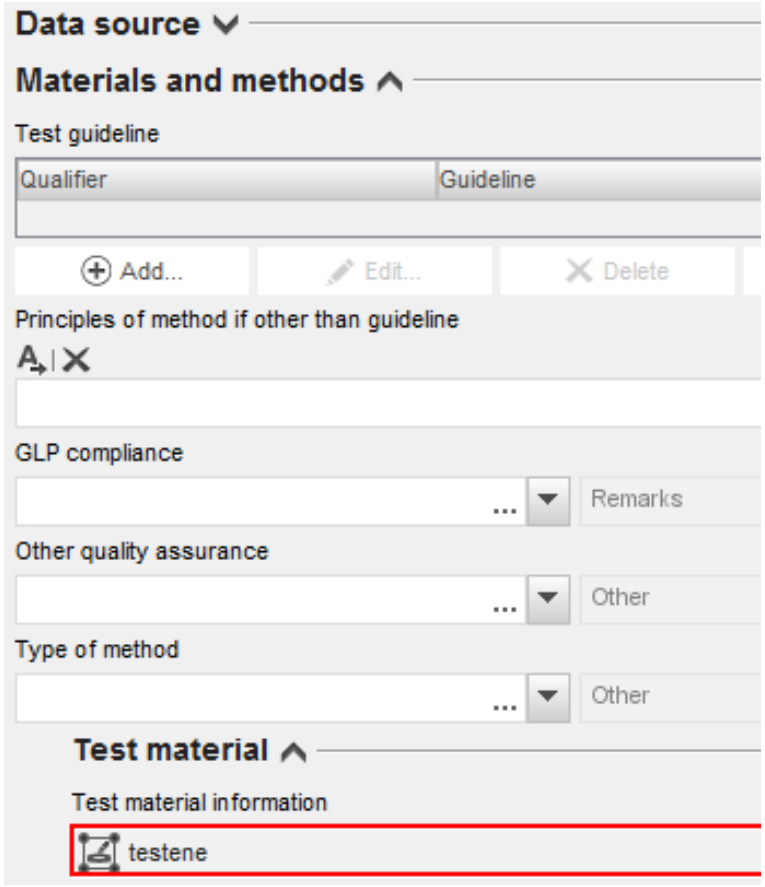
- **Type of information:** set to “read-across from supporting substance (structural analogue or surrogate)”
- **Adequacy of study:** set to the appropriate value depending on how you use the read-across to fulfil the information requirement (typically “**key study” or “weight-of-evidence**”)
- **Justification for type of information:** add the endpoint-specific justification in the field
- **Cross-reference:** link to the endpoint study record which contains the source data



Analogue approach:
Target record (2/3)

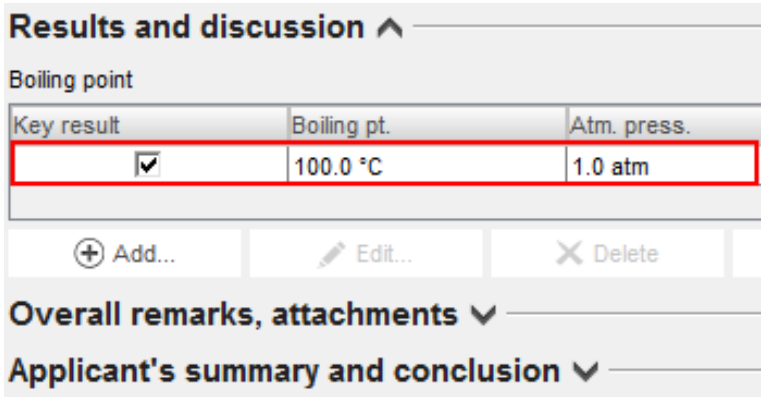
- **Test material information:** this is the *read-across target material*, to which the prediction is made
  - ➢ Not the material that was tested

- The material that was tested is reported in the source record.



Analogue approach:
Target record (3/3)

- **Results and discussion:** fill in the result for the read-across target material
- **Applicant's summary and conclusion':** indicate (if applicable) how estimated *effects relate to C&L* criteria for the target substance, and how results impact distribution of the target material
- **Executive summary:** briefly summarise read-across approach and applicability of results in the (optional)



Analogue approach: Source and target records are not identical

	Endpoint study record	Source record	Target record
i	Administrative data	X	X
	Endpoint	Same	Same
	Type of information	experimental study	X
	Adequacy of study	Key study	Key Study or Weight of Evidence (if used to fulfil information requirements)
	Robust study summary Used for classification Used for SDS	X	X
	Study period	X	
	Reliability	X	
	Rationale for reliability incl. deficiencies	X	
	Data waiving		
	Justification for data waiving		
	Justification for type of information		Endpoint-specific justification for read-across
	Attached justification		X
	Cross-reference		Link to source reference
ii	Data source	X	
iii	Materials and methods	X	
iv	Test materials	Tested material	Read-across target material (main constituent of registered substance, component of more complex substance, etc.)
v	Result and discussion	Experimental result	Result for target material
vi	Overall remarks, attachments	X	X
vii	Applicant's summary and conclusion	GHS criteria and implications for distribution of substance for source material. Executive summary of experimental study	GHS criteria and implications for distribution of substance for target material. Executive summary of read-across approach

Analogue approach:
Filling the source and target records

- **Main differences between source and target records**

  - **Experimental study related information** expected in the source record only
  - **Data waiving fields remain empty** for both
  - **Justification** for the type of information and the cross-reference fields must be filled in the target record only
  - **Cross reference**: link to the source endpoint study records
  - **Test materials and Results and discussions** are mandatory for both

Summary

Category approach in a nutshell

- Category read-across requires a **category object**
- The source data is expected to be present in the **category member datasets**
- **No linking** between target and sources is needed; the category matrix shows the endpoints that are in scope of the read-across
- Read-across justification is **provided both** in the category object (basis for grouping) **AND** in each target record (endpoint-specific justification)

Analogue approach in a nutshell

- **Only** the registered substance dataset is present
- The source data **must be inserted** into the dataset as experimental study records
- Source records **must be linked** to the target record
- Each target record must contain the **full justification** for the read-across

Support

- Read-across Assessment Framework (RAAF)
  https://echa.europa.eu/documents/10162/13628/raaf_en.pdf

- Guidance document
  https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment

- Practical Guides
  https://echa.europa.eu/web/guest/practical-guides

ECHA
EUROPEAN CHEMICALS AGENCY

Thank you!

Subscribe to our news at
echa.europa.eu/subscribe

Follow us on Twitter
@EU_ECHA

Follow us on Facebook
Facebook.com/EUECHA