GENOTOXIC SUBSTANCES IN PRINTED PAPER AND BOARD FOOD CONTACT MATERIALS

A prioritisation strategy based on non-animal methods

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Promoters:
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sciensano

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PAPER AND BOARD + **PRINTING INKS**

Printed paper and board

Widely & Frequently used

Major cause of contamination by FCM

Thousands of non (recently) safety-evaluated substances

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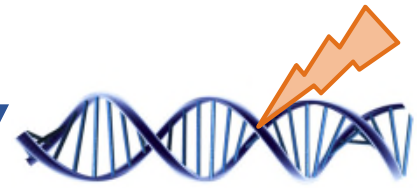
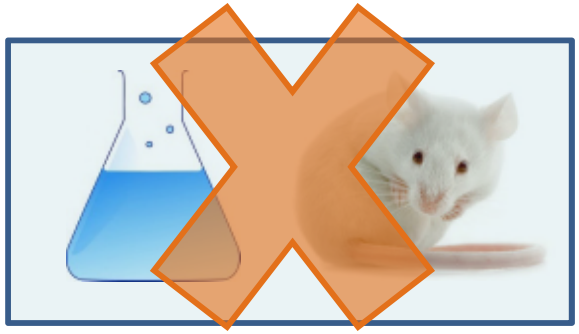
AIM:

PRIORITISATION STRATEGY

Genotoxicity



METHODOLOGY

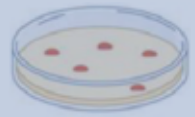


Step 1:
Database compilation

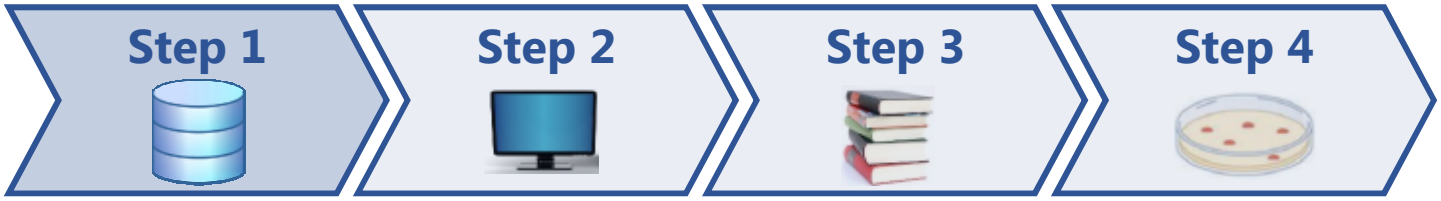
Step 2:
In silico
prediction

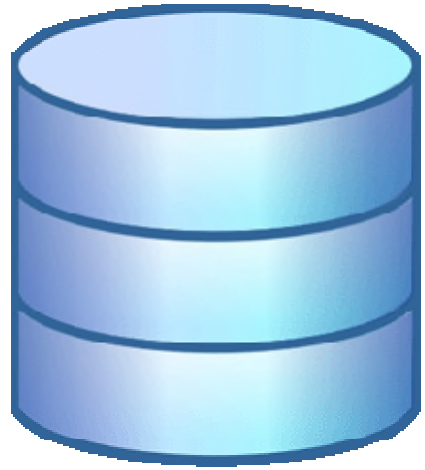
Step 3:
Literature review

Step 4:
In vitro
testing



NON-ANIMAL METHODS

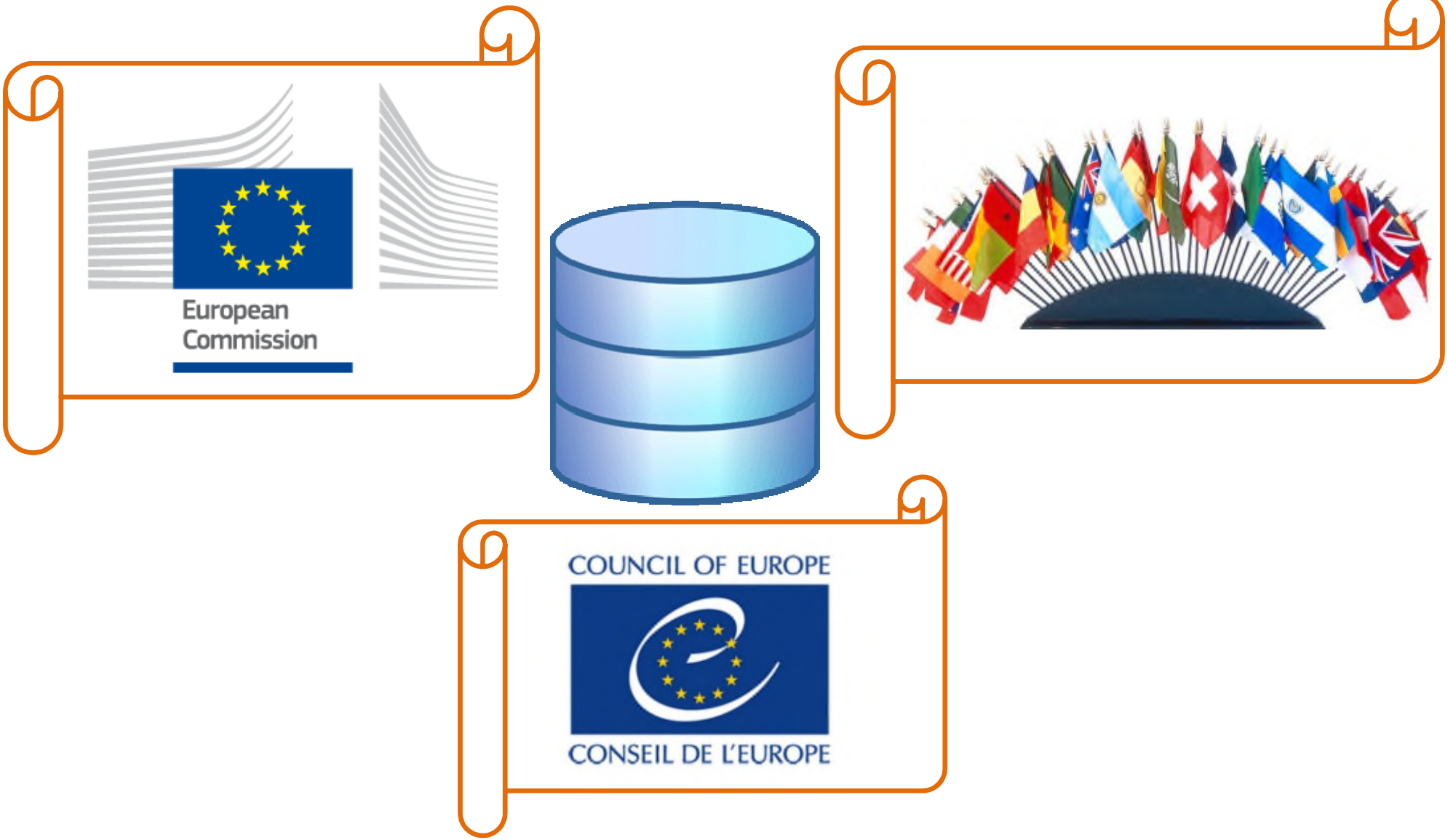


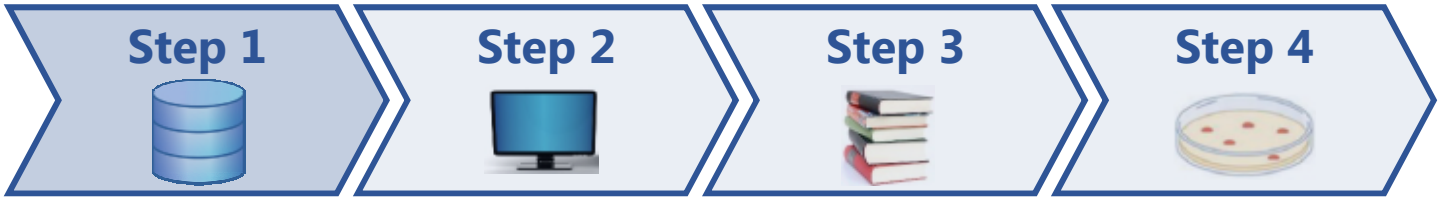


STEP 1: DATABASE COMPILATION

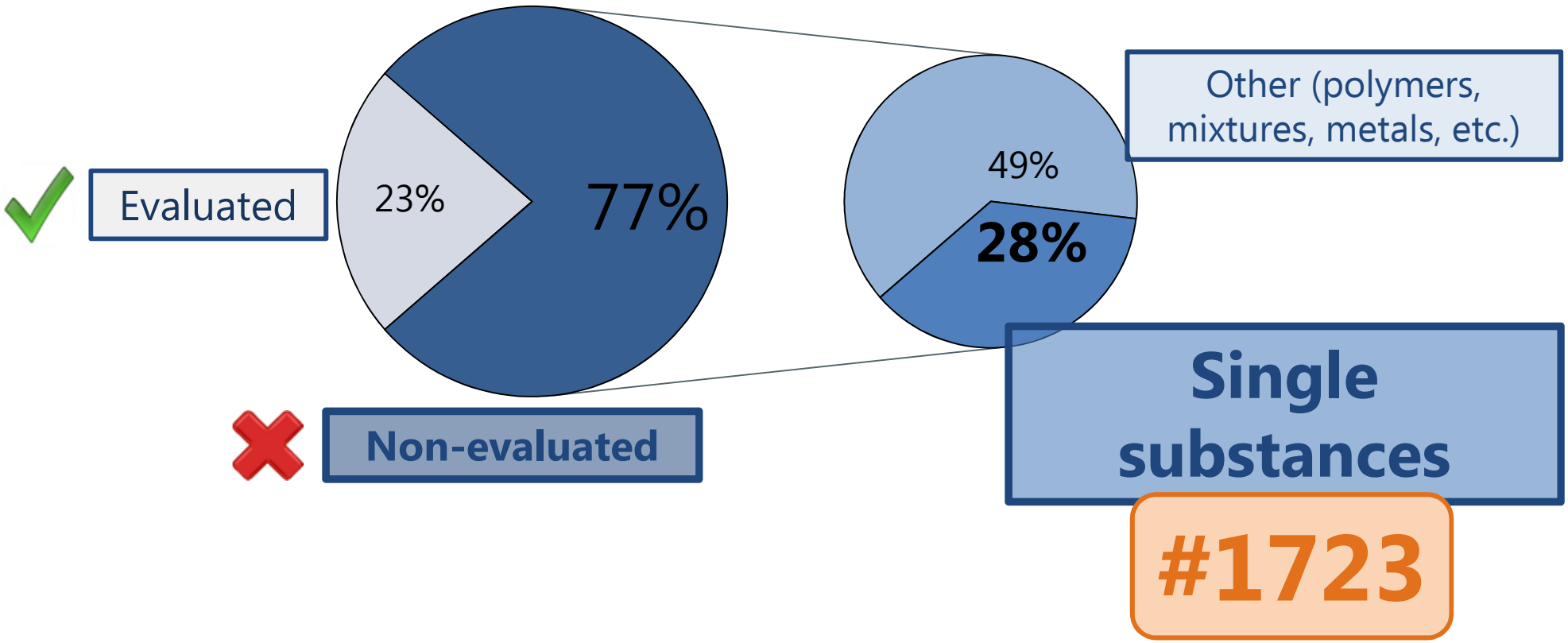
Van Bossuyt M, Van Hoeck E, Vanhaecke T, Rogiers V & Mertens B* (2016)*
Printed paper and board food contact materials as a potential source of food contamination.
*Regulatory Toxicology and Pharmacology 81: 10-19. *Equal contribution*

Step 1 Step 2 Step 3 Step 4




Step 1
Step 2
Step 3
Step 4

∑ = 6073


Evaluated
23%
77%
Non-evaluated
49%
28%
Other (polymers, mixtures, metals, etc.)
Single substances
#1723

STEP 2: *IN SILICO* PREDICTION

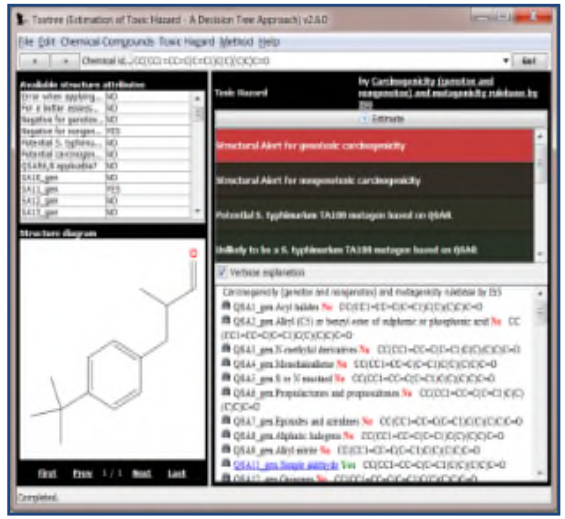
1. *Van Bossuyt M, Van Hoeck E, Raitano G, Manganelli S, Braeken E, Ates G, Vanhaecke T, Van Miert S, Benfenati E, Mertens B* & Rogiers V* (2017)*
(Q)SAR tools for priority setting: a case study with printed paper and board food contact material substances.
Food and Chemical Toxicology 102: 109-119.

2. *Van Bossuyt M, Van Hoeck E, Raitano G, Vanhaecke T, Benfenati E, Mertens B* & Rogiers V* (2018)*
Performance of in silico models for mutagenicity prediction of food contact materials. *Toxicological Sciences 163(2): 632-638*

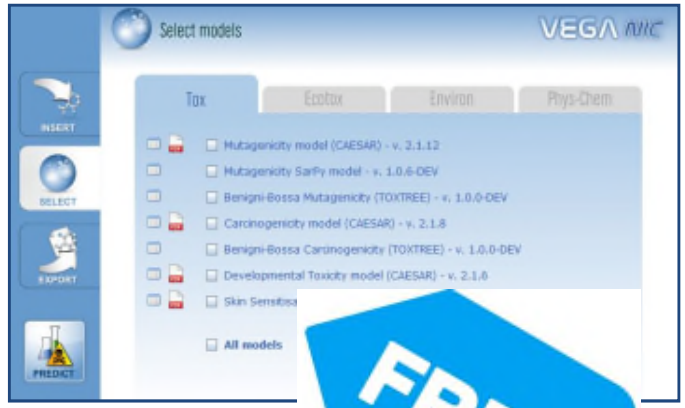
*Equal contribution

Step 1 | Step 2 | Step 3 | Step 4

Toxtree

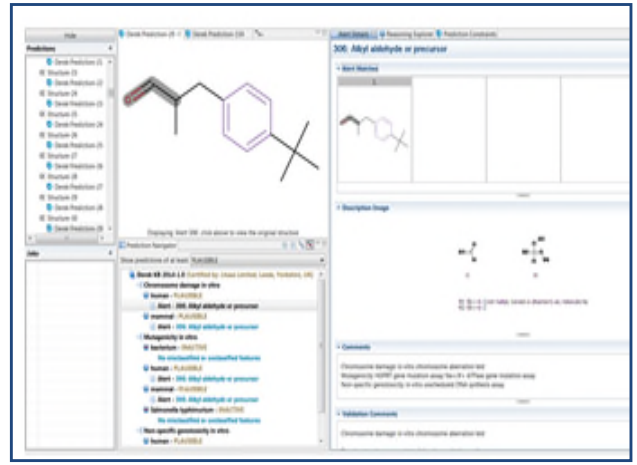


VEGA

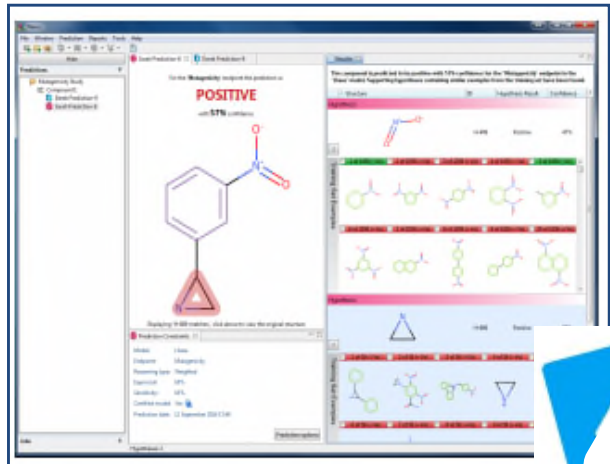


FREE

Derek Nexus



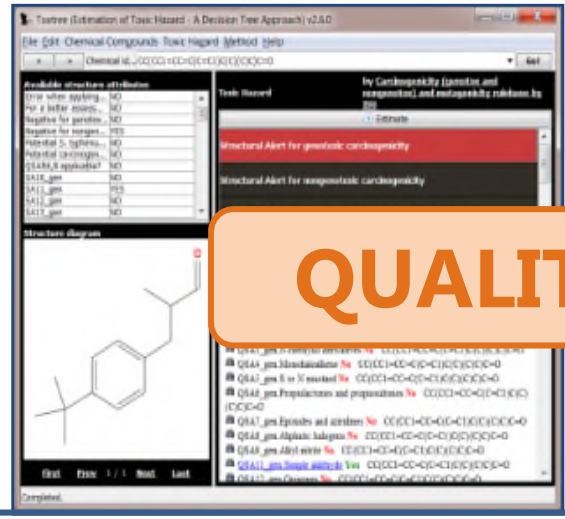
Sarah Nexus



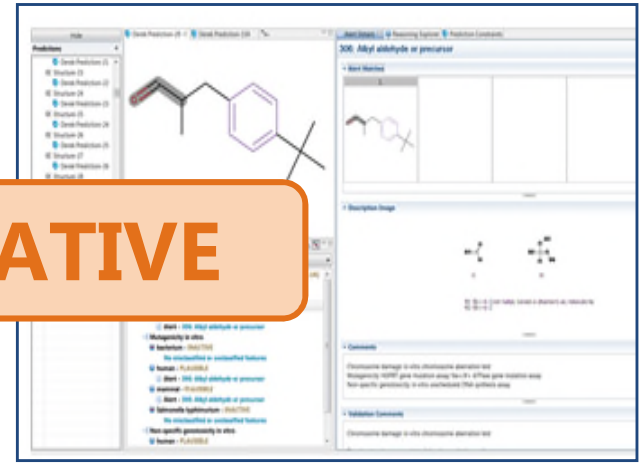
€£$

Step 1 Step 2 Step 3 Step 4

Toxtree

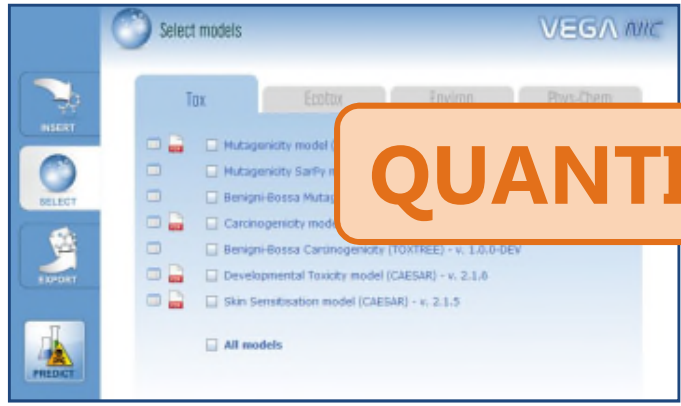


QUALITATIVE



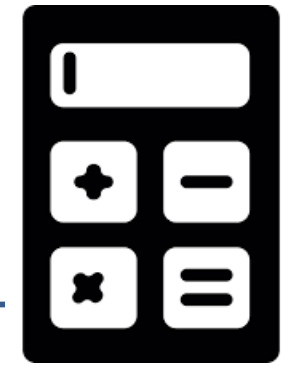
Derek Nexus

VEGA

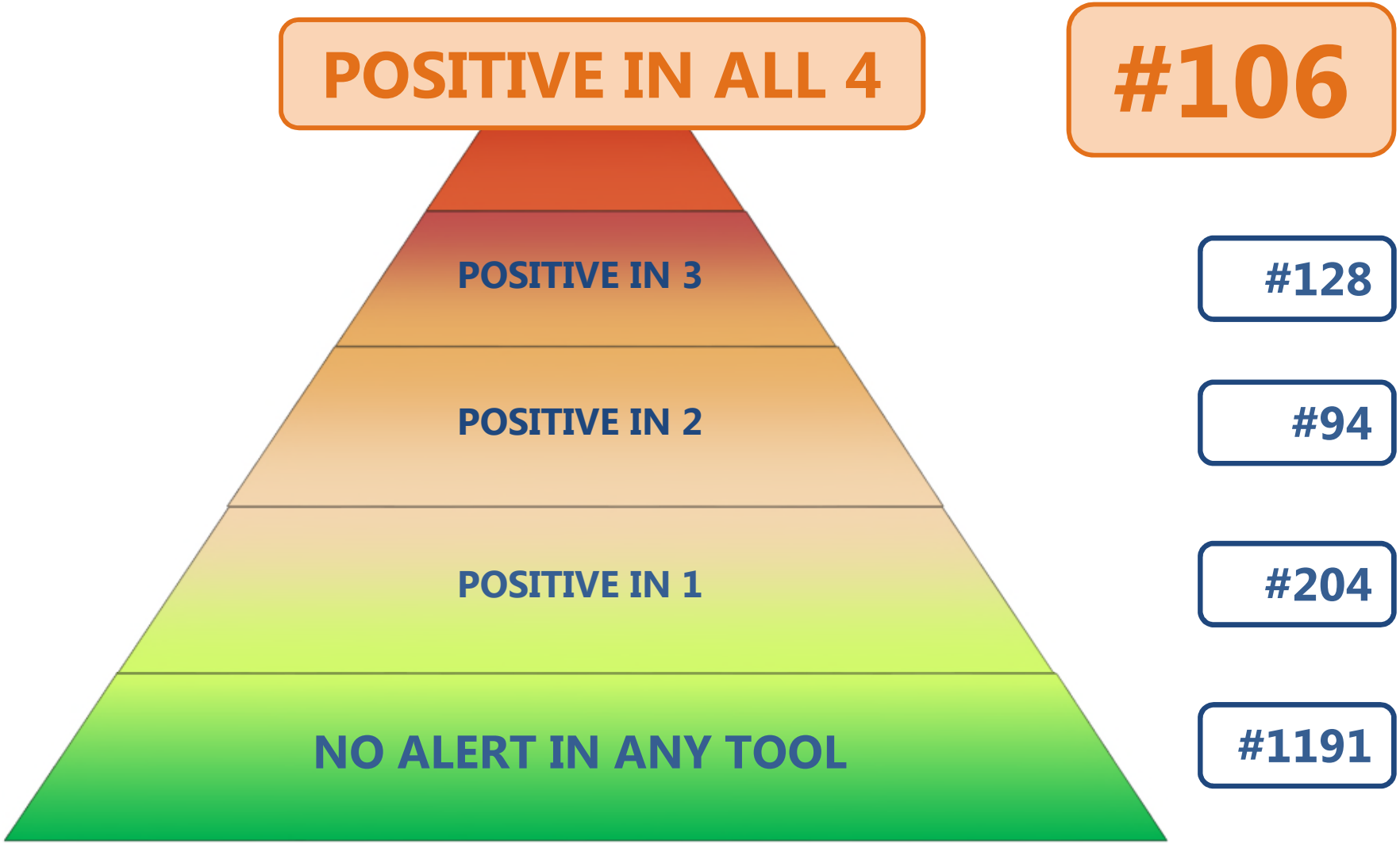


QUANTITATIVE

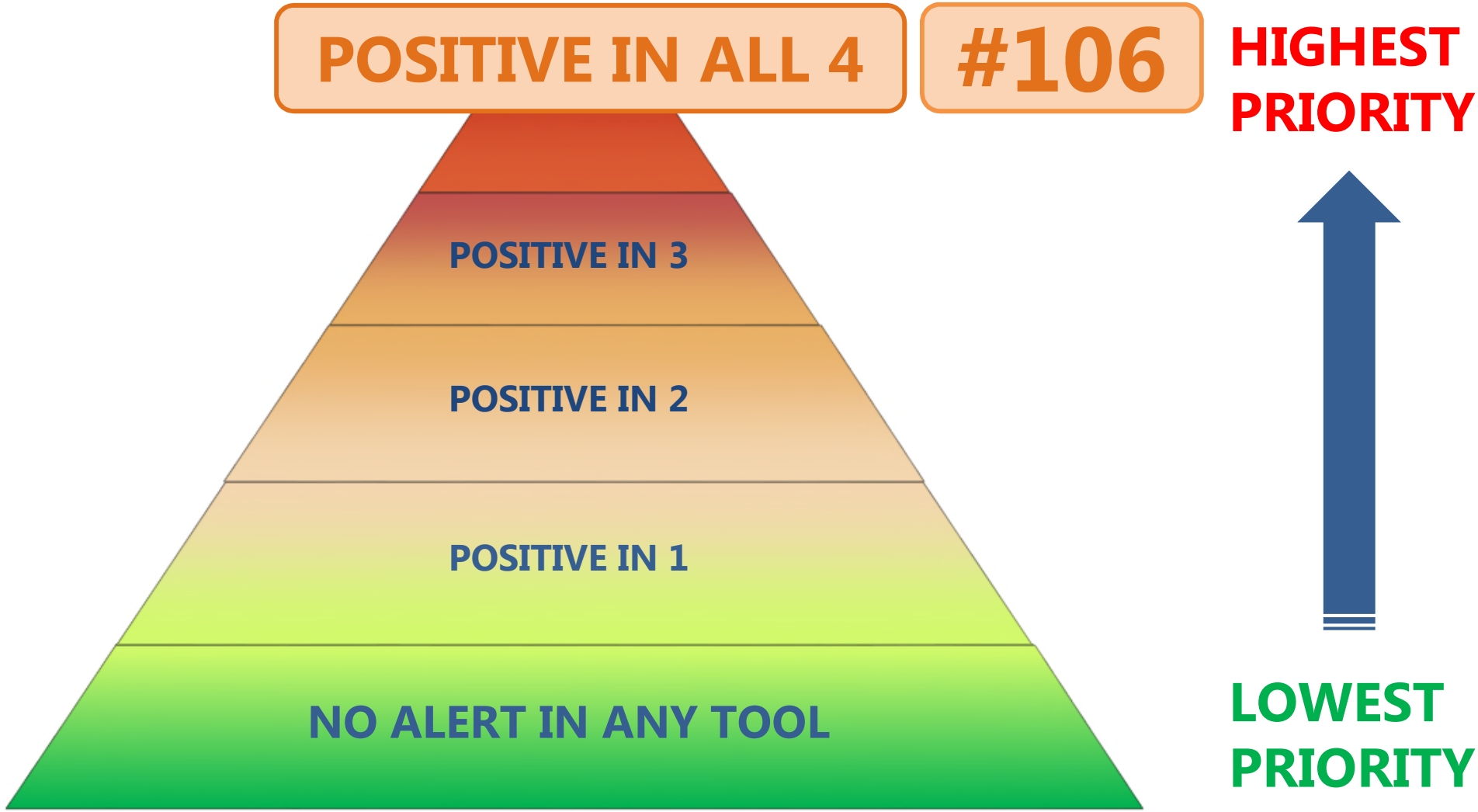
Sarah Nexus



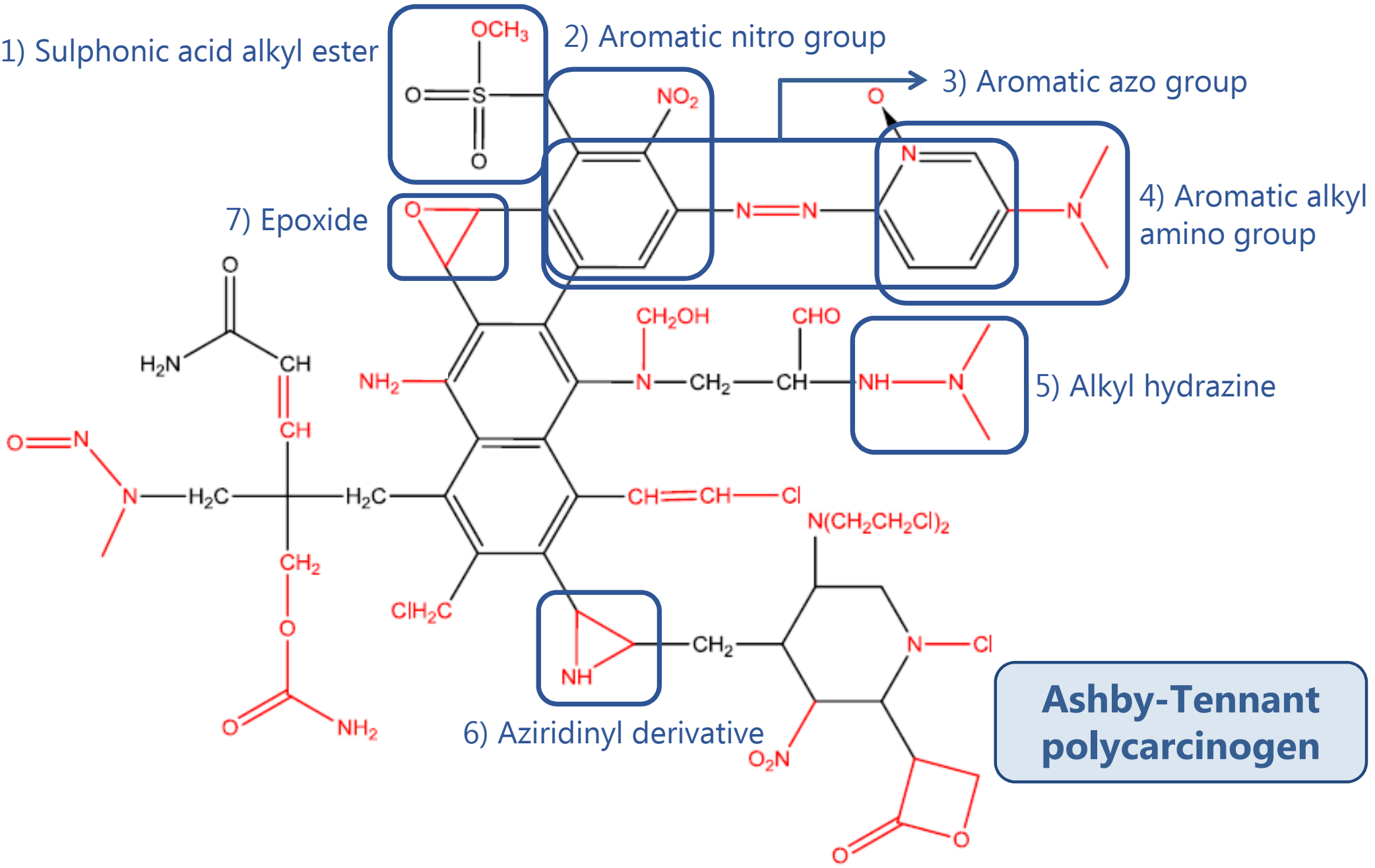
Combination of gene mutation prediction results




Step 1
Step 2
Step 3
Step 4


POSITIVE IN ALL 4
#106
HIGHEST PRIORITY
POSITIVE IN 3
POSITIVE IN 2
POSITIVE IN 1
NO ALERT IN ANY TOOL
LOWEST PRIORITY

Step 1 | Step 2 | Step 3 | Step 4



STEP 3: LITERATURE REVIEW

*Van Bossuyt M, Van Hoeck E, Vanhaecke T, Rogiers V * & Mertens B**
Prioritising substances of emerging concern for in-depth safety evaluation based on their genotoxic potential: the example of printed paper and board food contact materials.
Submitted to Toxicology Letters.

Step 1 → Step 2 → Step 3 → Step 4

PRIORITY SUBSTANCES (#106)

Official evaluation available

NO official evaluation available

Genotoxic *in vivo*

Inconclusive

Not genotoxic *in vivo*

Data collection from existing databases

EURL ECVAM European Union Reference Laboratory for Alternatives to Animal Testing

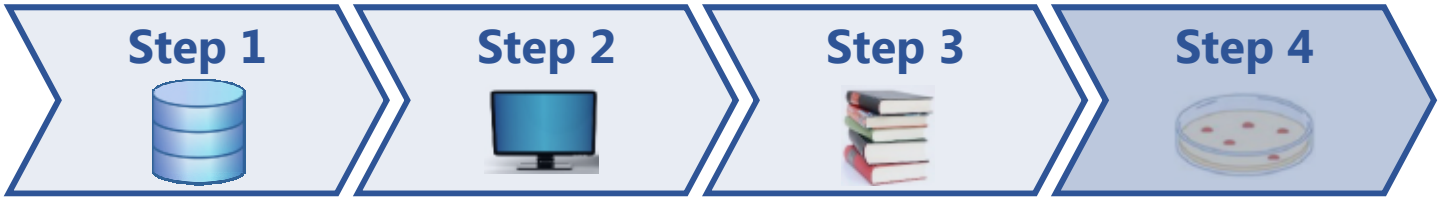
ECHA EUROPEAN CHEMICALS AGENCY

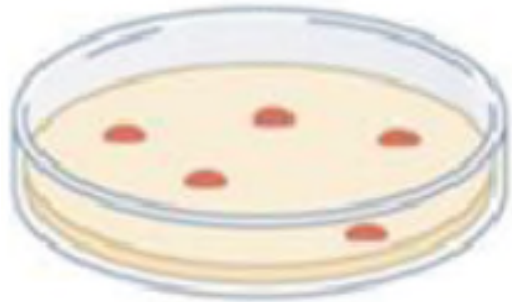
EURL ECVAM
European Union Reference Laboratory for Alternatives to Animal Testing

ECHA
EUROPEAN CHEMICALS AGENCY

Step 1 | Step 2 | Step 3 | Step 4

Gene mutation data are lacking!





STEP 4: *IN VITRO* TESTING

*Van Bossuyt M, Van Hoeck E, Vanhaecke T, Rogiers V * & Mertens B**
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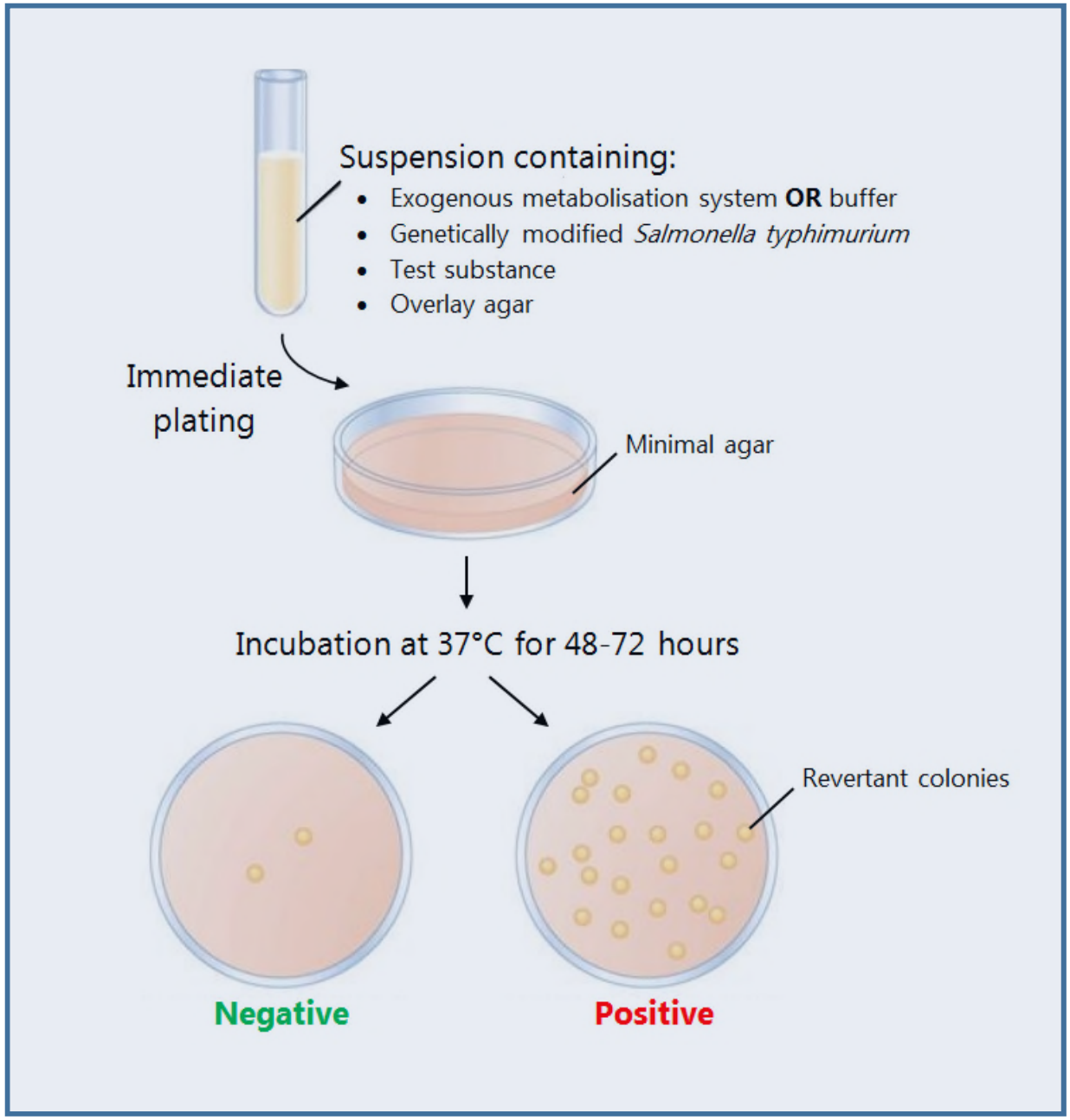
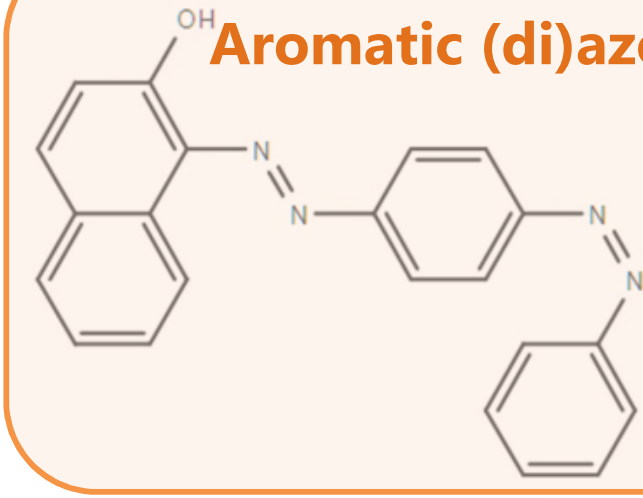
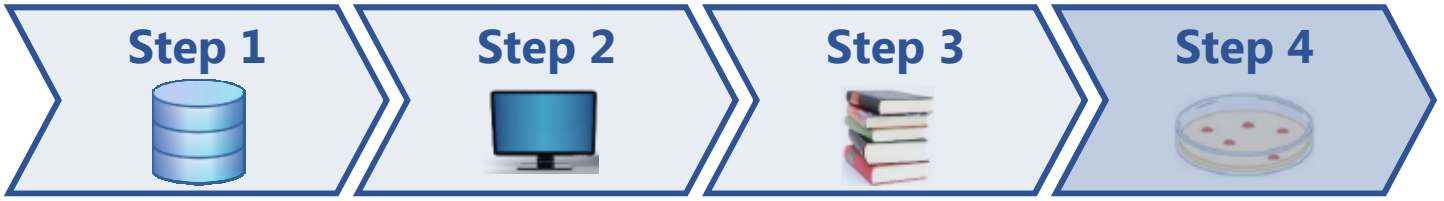


Aromatic (di)azo



1. ≠ Metabolisation system
2. Additional cofactors
3. Pre-incubation 30’



Negative in NON-OFFICALLY VERIFIED gene mutation test

CONCLUSION

Step 1:
Database compilation
#123

Step 2:
In silico
prediction
#106

Step 3:
Literature review

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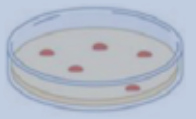
In vitro
testing



Future perspectives

- For a full safety evaluation, **additional aspects** need to be investigated

FCM-related

- Actual use
- Type of food
- Conditions of use
- …

TOX-related

- Other genotoxic endpoint
- Other toxicological endpoints
- …

- This prioritisation strategy can be extended to **other substance types/groups**

THANK YOU FOR YOUR ATTENTION!