

In-silico predictions a practical case of Reach Registration

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Dyestaff Cooperation (1)

In 2012 a Group of 10 – 12 Italian SMEs, delivering dyes to textile, leather and paper industries, set up a Reach Consortium coordinated by Centro Reach Srl with the aim to find an economically sustainable way to register the most number of substances they had on the market at that time

- over 600 mainly below 10 t/y –

In a 2. stage also a Dutch company joined while some of the founding members left the Cooperation

Dyestaff Cooperation (2)

The cost proposed at that time by the LR/Data Owners to purchase all the LoAs (several million €) went much beyond the financial capacity of these SMEs even reducing significantly the number of substances to register.

Key market point to consider here – dyes destined to fashion sector has continuous fluctuations!

Particular colour effects depend on different combination of primary colours and other tones; need to have available a significant range of tones/colours and manage an important number of dyeing techniques

Dyestaff Cooperation (3)

Negotiations for LoAs with LR/Data Owners organized in 3 big EU Consortia failed.

Dyestaff Cooperation decided to try exploit available NTM, in particular in-silico testing solutions like (Q)SAR and Read-Across, to cover most of the safety data needed for endpoints (mainly for lowest tonnage-band) required by Registration dossiers and Risk Assessment in REACH, trying to avoid as much as possible “need for citation of LR data”

Strong and long-lasting cooperation with M Negri Institute in support of these SMEs was a crucial basis for this strategy.

Dyestaff Cooperation (4)

Under REACH the joint submission of registration dossier is compulsory for registrants of the same substance.

Dyestaff Companies had to go for Opt-Out procedure in order to submit separately substance information in compliance with article 11(3) of Reach and to produce independently technical and scientific acceptable information being cheaper than other information made available with LoAs.

Dyestaff Cooperation (5)

Finally in 2018 Dyestaff Cooperation members submitted over 100 registrations thanks to significant support of NTM methods but were obliged to cite also certain number of data coming from animal testing data from the LR.s.

How did the companies compile the registration dossiers with the technical support of C. Maculan?

REACH registration dossier (1)

Regulation EC 1907/2006, REACH, defines that a producer or importer of a chemical substance in a quantity higher than 1 t/y, has the obligation to register the substance with the European Chemicals Agency ECHA. The registration contains scientific information of the chemical-physical, toxicological and ecotoxicological type of substance.

REACH registration dossier (2)

Dyestaff Companies had mainly the need to obtain the registration of their substances in the tonnage-band 1-10 tpa delivering the technical and scientific data required by Annex VII of the Regulation

REACH registration dossier (3)

Information required for standard registration of 1-10 tonnes a year (Annex VII of REACH)	
Non-vertebrate animal endpoints	Vertebrate animal endpoints
Description of the state of the substance at 20°C / 101.3 kPa	Acute toxicity: oral
Melting/freezing point	
Boiling point (if applicable)	
Relative density	
Vapour pressure (if applicable)	
Surface tension (if applicable)	
Water solubility	
Partition coefficient	
Flash-point	
Flammability	
Explosive properties	
Self-ignition temperature	
Oxidising properties	
Granulometry (if applicable)	
<i>In vitro</i> skin irritation/corrosion	
<i>In vitro</i> eye irritation	
Skin sensitisation	
<i>In vitro</i> gene mutation in bacteria	
Short-term toxicity on invertebrates	
Growth inhibition study aquatic plants	
Ready biodegradability (if applicable)	

REACH registration dossier (4)

The cooperation with M Negri Institute allowed Dyestaff Companies to develop data regarding the endpoints:

- Ready biodegradability
- In vitro skin irritation/corrosion
- In vitro eye irritation
- Skin sensitisation
- In vitro gene mutation in bacteria
- Short-term toxicity on invertebrates
- Growth inhibition study aquatic plants
- Acute toxicity: oral

REACH registration dossier (5)

Depending on the chemical structure of each substance subject to registration and to the availability of experimental data from substances with similar chemical structures, M Negri Institute delivered us in-silico elaborations considering the scientifically best solutions ((Q)SAR and/or Read-Across) on a case-by-case basis to produce the technical-scientific data required by the Reach Regulation for the previously mentioned endpoints in the registration dossiers.

REACH registration dossier (6)

Working context
REACH Registration 1 - 10 tonnes, standard rec

Type at least 3 characters X

> 6.1.3 CLUSTER 10

UUID: 4a30a4d1-e2e9-4f2e-9f59-605bd73ff3ac

Category documents Justifications and discussions

Category name*
6.1.3 CLUSTER 10

Public name
None

Legal entity*
Cristina Bocu

Regulatory purposes
EU: REACH

Remarks
None

Category members

- Acid Blue 129 (29-172-00-110) | Acid Blue 129 | 1,3,6-trisulfonate sodium salt of 4-amino-2-naphthol-6-sulfonate
- Acid Blue 129 (29-172-00-110) | Acid Blue 129 | 1,3,6-trisulfonate sodium salt of 4-amino-2-naphthol-6-sulfonate
- Acid Blue 129 (29-172-00-110) | Acid Blue 129 | 1,3,6-trisulfonate sodium salt of 4-amino-2-naphthol-6-sulfonate
- Acid Blue 129 (29-172-00-110) | Acid Blue 129 | 1,3,6-trisulfonate sodium salt of 4-amino-2-naphthol-6-sulfonate
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- Acid Blue 129 (29-172-00-110) | Acid Blue 129 | 1,3,6-trisulfonate sodium salt of 4-amino-2-naphthol-6-sulfonate

Category documents

Category documents

- 6. Ecotoxicological information
 - 6.1. Aquatic toxicity
 - 6.1.3. Short-term toxicity to aquatic invertebrates
 - Short-term toxicity to aquatic invertebrates

Example:

read-across based
on grouping of
substances (category
approach)

REACH registration dossier (7)

Working context
REACH Registration member of a joint subm...

REACH Registration member of a joint submission - general case

- 1 General information*
- 2 Classification & Labelling and PBT assessment
- 3 Manufacture, use and exposure*
- 4 Physical and chemical properties
- 5 Environmental fate and pathways
- 6 Ecotoxicological information
- 7 Toxicological information
 - 7.1 Toxicokinetics, metabolism and distribution
 - 7.2 Acute Toxicity
 - 7.3 Irritation / corrosion
 - 7.3.1 Skin irritation / corrosion
 - 7.3.2 Eye irritation
 - Eye irritation.01
 - Eye irritation.apar
 - Eye irritation.target**
 - Eye irritation...
 - Eye irritation...
 - 7.4 Sensitisation
 - 7.5 Repeated dose toxicity
 - 7.6 Genetic toxicity
 - 7.7 Carcinogenicity
 - 7.8 Toxicity to reproduction
 - 7.9 Specific investigations
 - 7.10 Exposure related observations in humans
 - 7.11 Toxic effects on livestock and pets
 - 7.12 Additional toxicological information
- 8 Analytical methods
- 11 Guidance on safe use
- 12 Literature search

Eye irritation.target
UUID: c4f89333-a185-4e16-8545-55ca6648c398
None None

Administrative data | Data source | Materials and methods | Results and discussion | Overall remarks, attachments | Applicant's summary and conclusions

read-across from supporting substance (structural analogue or surrogate)

Adequacy of study
weight of evidence

- Robust study summary
- Used for classification
- Used for SDS

Study period
2020

Reliability
2 (reliable with restrictions)
Rationale for reliability incl. deficiencies
study well documented, meets generally accepted scientific principles, acceptable for assessment

Data waiving
None
Justification for data waiving
None

Justification for type of information
1. HYPOTHESIS FOR THE WEIGHT OF EVIDENCE APPROACH
See the paragraph 2 in the attached document 7.3.2-...reasoning.pdf
2. SOURCE AND TARGET CHEMICAL(S) (INCLUDING INFORMATION ON PURITY AND IMPURITIES)
See the paragraph 3 in the attached document 7.3.2-...reasoning.pdf
3. WEIGHT OF EVIDENCE JUSTIFICATION
See the paragraph 6 in the attached document 7.3.2-...reasoning.pdf
4. DATA MATRIX
For the details on data matrix see the paragraph 4 attached document 7.3.2-...reasoning.pdf

Attached justification + New Item Import file

#	Attached justification	Reason / purpose
1	7.3.2-...ClusteringMethod.pdf	read-across: supporting information
2	7.3.2-...reasoning.pdf	read-across: supporting information

Cross-reference + New Item Import file

#	Reason / purpose for cross-reference	Related information
1	read-across source	Eye irritation ...
2	read-across source	Eye irritation ...

Example:

read-across from
supporting substance
(structural analogue
or surrogate)

REACH registration dossier (8)

Working context

REACH Registration member of a joint submission

Type at least 3 characters

- REACH Registration member of a joint submission - general case

1 General information* 4

2 Classification & Labelling and PBT assessment 1

3 Manufacture, use and exposure* 21

4 Physical and chemical properties 14

5 Environmental fate and pathways 1

6 Ecotoxicological information 6

7 Toxicological information 11

- 7.1 Toxicokinetics, metabolism and distribution
- 7.2 Acute Toxicity 1
- 7.3 Irritation / corrosion 7
 - 7.3.1 Skin irritation / corrosion 2
 - Skin irritation / corrosion 2
 - Skin irritation / corrosion 2
 - 7.3.2 Eye irritation 5
 - 7.4 Sensitisation 2
 - 7.5 Repeated dose toxicity
 - 7.6 Genetic toxicity 1
 - 7.7 Carcinogenicity
 - 7.8 Toxicity to reproduction
 - 7.9 Specific investigations
 - 7.10 Exposure related observations in humans
 - 7.11 Toxic effects on livestock and pets

Skin irritation / corrosion.001.COPY

UUID: bcf94c26-d3f3-463e-9e73-b311a51d7ea0

None None

Administrative data | Data source | Materials and methods | Results and discussion | Overall remarks, attachments | Applicant's summary and

Administrative data None None

Endpoint

skin irritation: in vivo

Type of information

(Q)SAR

Adequacy of study

weight of evidence

Robust study summary

Used for classification

Used for SDS

Study period

2020

Reliability

2 (reliable with restrictions)

Rationale for reliability incl. deficiencies

results derived from a valid (Q)SAR model and falling into its applicability domain, with limited documentation / justification

Data waiving

None

Justification for data waiving

None

Justification for type of information

The prediction has been carried out by means of QSAR prediction, using the following models:

Attached justification

#	Attached justification	Reason / purpose
1	7.3.1 - CS 213 219 0 - Prediction.pdf	(Q)SAR: supporting information
2	7.3.1 - CS 213 219 0 - QMRF - LeadScope - papers.txt	(Q)SAR: supporting information

Example:

(Q)SAR

Thank You For Your Attention