

# How to bring your registration dossier in compliance with REACH – Tips and Hints Part 4

## Hydrolysis

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# REACH information requirement

## Annex VIII

<b>COLUMN 1</b> <b>STANDARD INFORMATION REQUIRED</b>	<b>COLUMN 2</b> <b>SPECIFIC RULES FOR ADAPTATION FROM COLUMN 1</b>
<b>9.2.2.1. Hydrolysis as a function of pH.</b>	9.2.2.1. The study does not need to be conducted if: <ul style="list-style-type: none"><li>— the substance is readily biodegradable, or</li><li>— the substance is highly insoluble in water.</li></ul>

## Hydrolysis as a function of pH: what?

“The hydrolysis test should be performed at pH values of 4, 7 and 9.”

- Section 1.8.3, Method C.7, Commission Regulation (EC) No 440/2008.

## Hydrolysis as a function of pH: how?

- Report data at all of these 3 pH values:  
pH = 4 ... pH = 7 ... pH = 9
- QSAR data also need to be obtained at these 3 pH values
- Very fast, very slow, or no hydrolysis: still need to report all 3 pH values
  - (How? Explained later.)

# Hydrolysis as a function of pH: how in IUCLID?

Dissipation half-life of parent compound			
pH	Temp.	Hydrolysis rate constant	Half-life
4	25 °C	> 0.08 — < 0.14 min <sup>-1</sup>	> 5 — < 9 min
7	25 °C	0 h <sup>-1</sup>	> 2 yr
9	25 °C	0.35 min <sup>-1</sup>	ca. 2 min

## Using QSAR

- You still need to report at all 3 pH values
- Attach QMRF and QPRF ...
  - QSAR Model Report Format
  - QSAR Prediction Report Format
- ... at the endpoint study record for **hydrolysis**

# Using QSAR: QMRF and QPRF in IUCLID

Attached background material

Attached document	
QMRF_Hydrolysis_Dr.WhoLabs2013.pdf / 10.26 KB (application/octet-stream)	QMRF for hydrolysis
QPRF_Hydrolysis_esters_DrWhoLabs2013.pdf / 10.3 KB (application/octet-stream)	QPRF for the registered substance

Attached full study report

Attached full study report

Information

<input type="button" value="QMRF_Hydrolysis_Dr.WhoLabs2013.pdf / 10.26 KB"/> <input type="button" value="QPRF_Hydrolysis_esters_DrWhoLabs2013.pdf / 10.3 KB"/>	Remarks
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ECHA Practical guide 5: How to report (Q)SARs

[http://echa.europa.eu/documents/10162/13655/pg\\_report\\_qsars\\_en.pdf](http://echa.europa.eu/documents/10162/13655/pg_report_qsars_en.pdf)

## Reporting format: use numbers

- Fill in quantitative fields
- This helps in ECHA's evaluation
- This also helps when ECHA publishes data for the public



## Reporting format: very fast, very slow

- Very fast hydrolysis can be reported as:  
**half-life < 1 min**  
**half-life: ca. 2 min**
- Very slow or no hydrolysis:  
**half-life > 2 a**  
**rate: ca. 0**

# Reporting format: examples

pH

Temp.  °C

Hydrolysis rate constant  min<sup>-1</sup>

Half-life  min

St. dev.

Type (pseudo-)first order (= DT50)

pH

Temp.  °C

Hydrolysis rate constant   min<sup>-1</sup>

Half-life   min

St. dev.

Type (pseudo-)first order (= DT50)

# REACH adaptations in general

- Adaptations need to be based on
  - either Annex XI
  - or Column 2 in the relevant annex
- Be clear which one you are relying on
- Explain why

## Weight-of-evidence

- One study record for each piece of evidence
- Endpoint summary: your own conclusion
- At least 2 independent pieces of evidence

# Weight-of-evidence: example

5.1.2 Hydrolysis

**Hydrolysis - weight of evidence summary**

Weight of evidence-QSAR calculation

Weight of evidence-Read across

Key value for chemical safety assessment

Half-life for hydrolysis  h at the temperature of  °C

Discussion

Considering the combined weight of evidence of all the pieces of information available, we can derive a half life for the sub

Administrative Data

Purpose flag

Data waiving

Justification for data waiving

Study result type

Reliability

Administrative Data

Purpose flag

Data waiving

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# REACH adaptations for hydrolysis


- Column 2 for hydrolysis (Annex VIII, section 9.2.2.1):
  - readily biodegradable, or
  - highly insoluble in water
- Annex XI: Read the criteria carefully, and justify adequately according to these.


# REACH adaptations for hydrolysis


## Example for a properly structured justification




Administrative Data





Purpose flag    robust study summary  used for classification  used for MSDS

Data waiving  

Justification for data waiving  

Study result type     Study period  

Reliability  

Rationale for reliability incl. deficiencies  



*"According to Annex VIII of REACH, Column 2, section 9.2.2.1, the study does not need to be conducted if the substance is highly insoluble in water. The measured water solubility is under the analytical threshold of 0.01 ng/L, and hence the substance can be considered highly insoluble."*

# REACH adaptations based on hydrolysis

- Based on
  - column 2: e.g. water solubility, adsorption/desorption; or
  - Annex XI, section 2 (technically not possible)
- Submit a proper endpoint study record for hydrolysis
- Provide sufficient evidence for such an adaptation



Thank you!

<http://echa.europa.eu/contact/helpdesk-contact-form>