

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

Part 1

Hints and Tips on Physico-chemical, environmental and human health related endpoints

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15:00 - 17:00 Helsinki Time (GMT +3)

Physico-chemical endpoint

Partition coefficient – Log Kow

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Partition coefficient: recommendations 1(7)

- REACH Information requirements

| | Column 1 | Column 2 |
|------------------|--|---|
| Annex VII | 7.8. Partition coefficient n-octanol/water | The study does not need to be conducted if the substance is inorganic. If the test cannot be performed (e.g. the substance decomposes, has a high surface activity, reacts violently during the performance of the test or does not dissolve in water or in octanol, or it is not possible to obtain a sufficiently pure substance), a calculated value for log P as well as details of the calculation method shall be provided. |

If the substance is not inorganic, **at least a calculated value for log K_{ow}** as well as details of the calculation method **must be provided** for the registered substance.

Partition coefficient: recommendations 2(7)

- Choosing experimental method
 - Each experimental method has its own applicability range. To be considered reliable, the value obtained for $\log K_{ow}$ should be within the range of applicability of the method used.
 - Shake Flask Method (OECD TG 107/EU A.8): **$-2 < \log K_{ow} < 4$**
 - HPLC method (OECD TG 117/EU A.8): **$0 < \log K_{ow} < 6$**
 - Slow-Stirring Method (OECD TG 123): **up to $\log K_{ow}$ 8.3**

Partition coefficient: recommendations 3(7)

- Complex mixtures
 - HPLC method is generally the preferred method.
 - Log K_{ow} ranges can be provided for UVCB substances, but:
 - Ranges have to be concrete and narrow to be able to reflect their significance in the risk assessment.
 - An indication of the proportion of the substance should be provided.

Partition coefficient: recommendations 4(7)

- Each endpoint study record should contain only one study.

The screenshot displays the 'Administrative Data' section of a study record in the REACH database. On the left, a tree view shows the hierarchy of endpoints, with '4.7 Partition coefficient' and its sub-entry 'waiving.Partition coefficient' highlighted with a red box. The main panel shows the following fields:

- Purpose flag:** [Empty]
- Data waiving:** study technically not feasible
- Justification for data waiving:** According to REACH Regulation (Annex XI.2) testing of a specific endpoint may be omitted, if it is technically not feasible. The log Kow of the lead component is calculated to be [redacted] (Hansch, 1995).
- Study result type:** [Empty]
- Reliability:** [Empty]
- Rationale for reliability incl. deficiencies:** [Empty]

A red box highlights the justification text, and a red arrow points from this box to a larger red box below the screenshot.

This study should be in another endpoint study record with adequate and reliable documentation for the calculated value

- For complex substances, if studies for the different constituents are provided, they should be present in different endpoint study records.

Partition coefficient: recommendations 5(7)

- Weight of Evidence
 - This approach requires data from **several** and **independent** sources.
 - If using secondary sources, the original data source should be consulted.

| |
|---|
| 4 Physical and chemical properties |
| Physical and chemical properties |
| 4.1 Appearance/physical state/colour |
| 4.2 Melting point/freezing point |
| 4.3 Boiling point |
| 4.4 Density |
| 4.5 Particle size distribution (Granulometry) |
| 4.6 Vapour pressure |
| 4.7 Partition coefficient |
| Partition coefficient, Key Study - H |
| Partition coefficient, Supporting |
| 4.8 Water solubility |
| 4.10 Surface tension |
| 4.11 Flash point |
| 4.12 Auto flammability |
| 4.13 Flammability |
| 4.14 Explosiveness |
| 4.15 Oxidising properties |
| 4.17 Stability in organic solvents and |
| 4.21 Dissociation constant |
| 4.22 Viscosity |

| Reference type | Author | Year | Title | Bibliographic s... |
|----------------------------|-------------------------------|------|--|---|
| review article or handbook | Hansch C, Leo A and Hoekman D | 1995 | Exploring QSAR - Hydrophobic, Electronic and Steric Constants, p60 | ACS Professional Reference Book, American Chemical Society, Washington, DC, USA |

Add... Edit... Delete Move up

| Reference type | Author | Year | Title | Bibliographic s... |
|----------------------------|----------------|------|---|---------------------------------|
| review article or handbook | Lide, D. (Ed). | 2008 | CRC Handbook of Chemistry and Physics, 89th Edition., p 16-44 | CRC Press Inc. Boca Raton. USA. |

Add... Edit... Delete Move up

| Type | Partition coefficient | Temp. | pH |
|---------|-----------------------|-------|----|
| log Pow | 3.42 | | |

Add... Edit... Delete Move up Move down

Are the sources of these two databases different?

Partition coefficient: recommendations 6(7)

- Estimated log K_{ow}
 - The substance falls within the applicability domain (descriptor, functional groups)
 - Adequate and reliable documentation is provided (QMRF, QPRF)

| Attached background material | |
|--|---------|
| Attached document | Remarks |
| <input type="button" value="Add..."/> <input type="button" value="Edit..."/> <input type="button" value="Delete"/> <input type="button" value="Move up"/> <input type="button" value="Move down"/> | |

| Attached full study report | |
|--|--|
| Attached full study report | |
| <input type="button" value="Add..."/> <input type="button" value="Edit..."/> <input type="button" value="Delete"/> <input type="button" value="Move up"/> <input type="button" value="Move down"/> | |

Documentation can be attached to the ESR

Partition coefficient: recommendations 7(7)

- Ionisation
 - If the substance can dissociate, values for K_{ow} have to be provided for the neutral and dissociated forms.
- Hydrolysing substances
 - Annex VII, 7.8. Column 2 requires a calculated value for $\log K_{ow}$ if the test cannot be performed.
 - If the rate of hydrolysis is very fast, it is strongly recommended to provide $\log K_{ow}$ values for the hydrolysis products.

Partition coefficient: guidance

- Guidance on information requirements and chemical safety assessment
 - Chapter R.7a: Endpoint specific guidance
 - Chapter R.6: QSARs and grouping of chemicals
- Practical guide 2: How to report weight of evidence
- Practical guide 4: How to report data waiving
- Practical guide 5: How to report (Q)SARs