

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

Part 1

Hints and Tips on Physicochemical, environmental and human health related endpoints

27 September, 2012 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, <u>at least</u> 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  $K_{\text{ow}}$  should be within the range of applicability of the method used.
    - Shake Flask Method (OECD TG 107/EU A.8): -2 < log K<sub>ow</sub> < 4</li>
    - HPLC method (OECD TG 117/EU A.8):  $0 < log K_{ow} < 6$
    - Slow-Stirring Method (OECD TG 123): up to log K<sub>ow</sub> 8.3



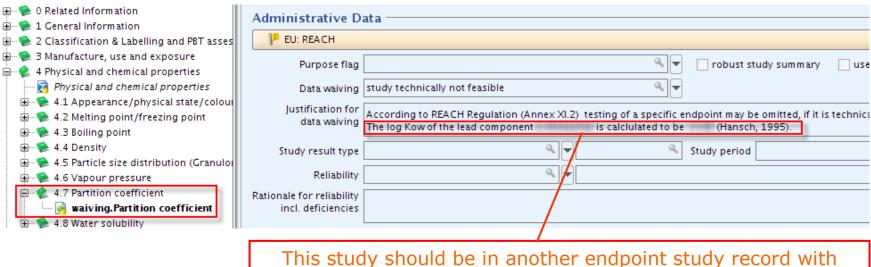
## Partition coefficient: recommendations 3(7)

- Complex mixtures
  - HPLC method is generally the preferred method.
  - Log K<sub>ow</sub> 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 <u>only</u> one study.



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

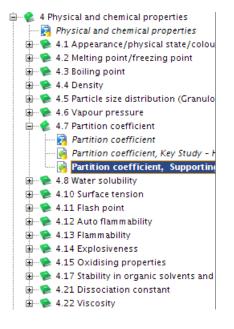
6

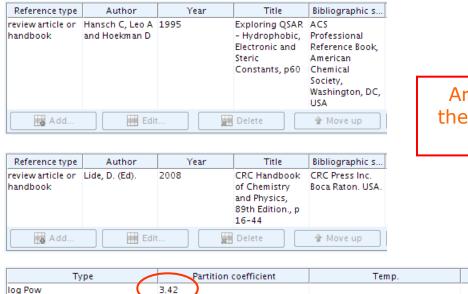
 For complex substances, if studies for the different constituents are provided, they should be present in different endpoint study records.



## Partition coefficient: recommendations 5(7)

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





Delete.

♠ Move up

Move down

Are the sources of these two <u>databases</u> different?

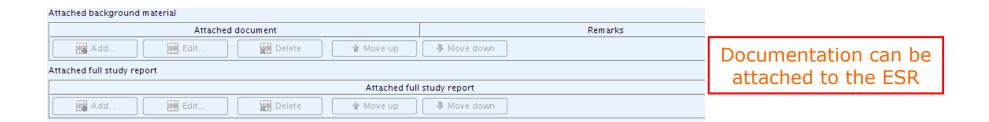
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## Partition coefficient: recommendations 6(7)

- Estimated log K<sub>ow</sub>
  - The substance falls within the applicability domain (descriptor, functional groups)
  - Adequate and reliable documentation is provided (QMRF, QPRF)





## Partition coefficient: recommendations 7(7)

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