

# Applicability Domains

## What can we do about it?

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# What is an applicability domain?

- Any toxicology test has limitations and these include physically unsuitable materials, solubility considerations etc.
- The limitations may also include specific types of chemistry which are documented not to be assessed correctly.
- Alternatively, it might be that a test is suitable for certain substances/formulations but has not been formally validated for that purpose.
- By describing properly these matters in effect we are developing applicability domains

# Consider a QSAR...

- A quantitative structure activity relationship for the skin sensitizing potency of aldehydes and ketones has been developed (Patlewicz et al, 2003).
- Does it predict the activity of alcohols or esters?
- No! The applicability domain of the QSAR has been defined by the substances used to develop it.

# Consider the LLNA...

- The local lymph node assay was developed with >200 substances as an alternative to guinea pig tests and was formally accepted as a complete replacement for them by ICCVAM/ECVAM
- Consequently, in contradistinction to the QSAR we have to try to discover and then to fully characterize those domains where the LLNA does not apply
- How we approach this is the topic of Break Out Group 2