

Case Study Handout: Facilitator

1. **Student Handout #1.** Start with method A and prompt comments about the numbers presented there. Some ideas for conversation:
 - a. How do you feel about the % (and that it isn't 100%); what might be a good % to be comfortable with a method (i.e., is 50% enough, 75%?).
2. Move to method B or C (depending on table assignment) with same questions.
3. **SPOILER!!!** Provide the information that Method A is actually the animal test (commonly known as the Local Lymph Node Assay, or LLNA) compared to human sensitization data: how does this change the point of view for what is acceptable (if at all)?
4. **SPOILER!!!** Provide the **Student Handout #2 (pink sheet)**. The previously provided information had methods compared to the LLNA positives and negatives, but the new table also has the human data: how does this change the point of view for what is acceptable (if at all)?
5. Additional discussion (as time allows):
 - a. These methods are all approved for use to support the hazard assessment for skin sensitization globally (especially in the US and Europe).
 - b. Do you think this method should be used to support product labelling?
 - c. What additional information would you like to know (as the regulator) to increase confidence in accepting these methods (or others). Examples include (suggested in the ICCVAM validation framework, but this is intended as a flexible model that might not be appropriate for all methods):
 - 1) Context of Use (COU): Establishing COU, or the intended utilization of a novel alternative method (NAM), includes crafting a statement that fully and clearly describes the way the NAM is intended to be used and its regulatory purpose (if applicable).
 - 2) Biological Relevance: The relevance of a NAM describes the relationship between the test and the effect in the target species and whether the test method is meaningful and useful for a defined purpose, with the limitations identified.
 - 3) Technical Characterization: Technical characterization is a key component of developing NAMs for widespread use. It includes an assessment of sources of variability in the NAM, designing the assay to include relevant control measurements, evaluating the range of test substances for which the assay can be used (i.e., the applicability domain), and developing a suitable statistical data analysis approach.
 - 4) Data Integrity is a key aspect of ensuring that information derived from NAMs is trustworthy and reliable.
 - 5) Information Transparency: Transparency facilitates trust in the use of NAMs and thereby hastens the pace of an agency's regulatory decision-making process and potential regulatory acceptance or qualification.
 - 6) Independent Review: Information and data supporting the NAM's COU, biological relevance, and technical characterization may be scientifically reviewed by independent third parties (whose members do not have conflicts of interest).