Applicability domain of read-across

In this guide

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34. The applicability domain of a method refers to the chemical, biological, or functional space where its predictions or measurements are considered reliable. For read-across, EFSA highlights that defining this domain means identifying suitable similar substances.

35. A clearly defined applicability domain is especially important for category-based read-across, which relies on patterns across multiple substances within a category. This allows the same prediction to apply to several target substances, provided they meet the category criteria. In contrast, analogue-based read-across is more limited, as its outcome applies only to the specific target substance unless another substance is very closely related.

36. After identifying similar substances, filters are often applied to refine the selection. These filters help define the boundaries of the read-across and should be explicitly stated. The domain is more clearly established when data interpolation is used.

37. EFSA advises using multiple source substances to strengthen read-across, as this increases the number of matching features and expands the applicability domain. If only one source is used, it must be highly similar to the target, with minimal differences that could affect the outcome.

38. Read-across is always endpoint-specific. Therefore, the applicability domain depends on the availability and density of chemical and biological data for the specific toxicological endpoint.