When do you need an OEB vs. an OEL?

We often get asked, "When do I need an OEB or occupational hazard categorization (OHC) report vs. an OEL monograph?" Well, let me explain.

Occupational exposure band reports are intended for early stage compounds with limited or no human data. The objective of an OEB report is to assign an early stage compound to a control band, without providing a specific numerical OEL or numerical acceptable daily exposure (ADE) (aka permitted daily exposure (PDE) value). And while the expert occupational toxicologist may perform some "back of the envelope" calculations to determine the appropriate control band assignment, it is unwise to present these calculations in the OEB report since the numbers will significantly change as the compound moves through development. In addition, the expert occupational toxicologist authoring the OEB report may also employ a "read-across" or professional judgement approach to similar compounds based on the compound of interest's specific molecular structure.

In general, the control band assignment in an OEB report tends to be conservative and is more focused on what controls are necessary to protect employees and prevent cross-product contamination. At this stage of development there is still significant uncertainty in determining a specific numerical value for the OEL and ADE. OEB reports are of value because the frequency of exposure is non-routine, the batch sizes are small, the number of employees potentially exposed is limited, and the turnaround is rapid. With regards to calculating an ADE (or PDE) for compounds at this stage, as recommended in ISPE's Risk-MaPP document (2nd Edition, p 39), an estimated ADE can be determined by taking the bottom of the control band, in $\mu g/m^3$, and multiplying by a factor of 10 to estimate the ADE. We use a factor of 5 (based on ECHA's factor for human variability) since that would result in a more conservative ADE.

The advantages of an OEB report include:

- Can be performed for early stage compounds with limited data;
- The turnaround for an OEB report can be done in a matter of days vs. weeks for a detail OEL monograph;
- Are useful for contract development and manufacturing organizations (CDMOs) that have a high throughput of early stage compounds;
- The cost of authoring an OEB report for a proprietary compound (typically 2-3 pages) is significantly lower than the cost of authoring a fully documented OEL monograph (typically 10+ pages); and
- A fully developed investigators brochure is not required for an OEB report.

The disadvantages of an OEB report include:

- It is conservative and may require more controls than are ultimately found to be necessary;
- In order to assign a compound to a specific control band, the control band cutoffs (upper and lower limits) must be determined; and
- If the OEB changes, either up or down, the end users may be upset because the control band changed. This is an interesting phenomenon where, even if you warned them that the OEB is provisional, and could change as more toxicology information becomes available, people can get mentally anchored to a specific OEB assignment.

Now on the other hand, as a compound moves through drug development, and either has completed or nearing completion of Phase 2b clinical trials, a fully documented occupational exposure limit/acceptable daily exposure (aka. Permitted Daily Exposure) monograph should be developed. At this stage of development, there will be adequate human data (including pharmacokinetics data, longer-term studies, larger population studies, reproductive toxicology studies, etc.) to perform a specific determination of the OEL and ADE.

The advantages of an OEL/ADE monograph include:

- Provides a specific numerical value for the OEL and ADE that can be used during containment design, industrial hygiene monitoring and cleaning validation studies;
- Is fully documented, with numerous scientific references and calculations; and
- The numbers are not likely to change unless there is an unexpected adverse human event.

The disadvantages of an OEL/ADE monograph include:

- Needs a fully developed investigator's brochure or an equivalent level of information; and
- Requires a detailed review of all the available data, thus taking longer to determine and is, therefore, more expensive.

The use of OEB and OEL/ADE reports each have their own place and purpose. It is important that the end users, such as contract development and manufacturing organizations (CDMOs), understand what is required at each stage of drug development. If an organization wants more accurate numbers for an OEL or ADE, the only solution is to provide more accurate and complete data.

Reference: When do you need an occupational exposure band vs. an occupational exposure limit? (affygility.com)