DOs of OELs and ADEs

DO understand that OELs and ADE values can change over time. As new toxicological information becomes available, it can change views regarding the hazard profile of a compound. When this new information is reviewed and considered, it may result in a revision of the OEL and ADE. In addition, the ”default” uncertainty/adjustment factors used by the toxicology community may change, or new regulatory guidance may be published that requires the OEL or ADE to be updated.

DO understand that an OEL or ADE value without the underlying documentation is worthless. This documentation should provide a clear description of the hazards identified for the compound and demonstrate how they are considered in deriving an OEL and ADE.

DO understand that adhering to OELs and ADEs is just one part of a risk assessment management toolbox. Reducing the probability of exposure or the probability of cross-contamination through improving engineering and personal protective controls and procedures plays a big role in reducing risk.

DO perform containment validation and industrial hygiene monitoring to understand process-specific exposure levels and ensure that exposure levels are safe.

DO understand that OELs and ADEs are not precise numbers. This makes the quality groups cringe, but it is the truth. OELs and ADEs are an extrapolation from a “known dose” (such as a NOAEL or a therapeutic dose) to an “unknown dose” that is believed to be protective over a long period of time for a daily exposure scenario. As such, there are many assumptions that are entered into the basic OEL and ADE equations.

DO understand that as an industrial hygiene practice and given the uncertainties associated with the calculations, the rounding of the OELs and ADEs do not necessarily follow mathematical rounding rules for significant digits.

DO understand that the goal of professionals that establish OELs and ADEs is to reduce uncertainties, not increase them. The more you increase the composite adjustment factor, the more you are indicating that you really don’t know much about the compound. With more toxicological and human relevant data, uncertainty can be significantly reduced.

DO understand that the vast majority of OELs are not based on actual worker exposures. In fact, only a handful of OELs actually incorporate any data from actual worker exposures. Toxicology information from animal data and, depending on the state of development of the compound, human clinical data, are used to determine the OEL and ADE.

DO understand that departmental biases may enter into the discussions when selecting OELs and ADEs. Typically, the manufacturing groups want “higher numbers” because they believe they can make anything and don’t like the expense, hassle, and contract manufacturing operation (CMO) limitations of additional engineering controls. On the other hand, the quality groups typically want “low numbers” just to be certain they are being protective enough. However, establishing scientifically appropriate health-protective levels is the goal.

DO understand that setting OELs or ADEs unreasonably low can result in unnecessary costs in the form of additional engineering controls, loss of productivity, ergonomic hazards, project delays, elaboration of analytical methods, and even the requirement for dedicated equipment or facilities.

DO understand that when a safety data sheet (SDS) for an active pharmaceutical ingredient (API) says that the OEL is “not available”, or that it is “not-listed” by OSHA, ACGIH, or AIHA, it does not mean that it is “nonhazardous.” Similarly, if a compound is not listed as being a carcinogen by ACGIH, OSHA or National Toxicology Program (NTP), it does not mean that it is not carcinogenic, only that it is not currently listed. In many cases, this can mean that the compound has not been tested for carcinogenicity.

DON’Ts of OELs and ADEs

DON’T get into the practice of “OEL/ADE shopping” to try and justify whatever cause you or your organization may be supporting. It is important to review OEL/ADE documentation that is generated by toxicology professionals and understand if it makes logical sense.

DON’T get into the practice of comparing OEL and ADE values without having the underlying documentation to review. OELs and ADEs can vary among consulting firms, or pharmaceuticals companies. In addition,

sometimes old values that were derived prior to having currently available information can be found. Without having the most recent underlying documentation to review, you cannot say one number is correct, as opposed to another number, lower or higher, that may have been derived based on potentially out-of-date information.

DON'T assume that a lower OEL or ADE is a better or more accurate number. Again, review the underlying documentation to see how the number was derived and if current best practices and most recent data were used. Sometimes OELs and ADEs are lower when less information is available for a compound due to uncertainty. As this information becomes available, the OEL and ADE may increase if hazards are found not to exist.

DON'T just accept piling adjustment factors on top of each other. When reviewing the data set for a specific compound, there are many different factors that are being evaluated. However, just because there are many factors, doesn't mean that you will use all of them in the final calculations. You must consider what is important and what has been adequately addressed by other adjustment factors. This is where professional judgement by trained toxicologists becomes very important.

DON'T believe that the ADE = 10 times the OEL. That was an old "rule of thumb" that someone mentioned in a presentation once. It ended up on the internet, and now some accept it as an absolute truth-it is not. The OEL is for a worker exposure scenario, which means employees ranging from approximately 18 to 65 years of age, of generally good health, and with exposures that are typically 8 to 10 hours per day, 5 days per week. ADEs are for the entire population, including sensitive populations, such as those with compromised health, and those individuals that may be on daily medication for their entire lifetime. In addition, the more current regulatory guidance for ADEs uses slightly different "defaults" for the adjustment factors than those that have been traditionally used for OELs.

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Reference: Affygility OEL Guidance Document, v9, Jun2022