

# Risk Assessment for Pharmaceuticals

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exposure is kept below the NOEL. For genotoxic active substances with non-threshold mechanism of action, any level of exposure carries a risk. An acceptable level for non-threshold related genotoxicants has been established as Threshold of Toxicological Concern (TTC) of 1.5 µg/person/day, which is associated with a theoretical cancer risk of 1 additional cancer in 100,000 patients when exposed over a life time [10]. When additional information about mechanism of action of carcinogens became available, it became apparent that NOELs may exist for some carcinogens. This resulted in development of the concept of benchmark dose approach. In addition to the approaches described so far, several other approaches have been used to set OELs. For example, use of the therapeutic dose and the use of an incremental increase in some level of endogenous biologic activity for hormones [11]. In the case where OELs can be estimated by several approaches, one has to judge the most appropriate approach especially if the various approaches result in OELs that differ significantly [11,12].

The duty of toxicologist entrusted with setting OELs/ADEs is to derive a value that is safe for workers/patients yet without reaching so overly protective values that resources are unreasonably consumed.

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