Current topics on nonclinical safety assessment of human pharmaceuticals from an European perspective

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Regulation of human pharmaceuticals in Europe was not generally established until the thalidomide disaster around 1960, more than 50 years ago. The political willingness to have harmonized criteria on a more European level arose already soon, resulting in a first Directive 65/65. Harmonized pharmacological and toxicological criteria were established 10 years later in Directive 75/318. It took another 10-15 years before the Committee on Proprietary Medicinal Products started as an advisory committee to the European Commission, and its member states.

The tasting of harmonization did also result in an initiative to start a global process with Japan and the United States in 1989, with the first International Conference on Harmonisation in Brussels in November 1991.

The starting point for assessment of new human pharmaceuticals is always to understand the clinical relevancy of the toxicity data, instead of focusing on full characterization of the toxicity of a substance up to the lethal level. This can be illustrated in the choice for dose selection.

Restriction of use of animals. The discussion about the protection of animals for scientific purposes is always important in the EU. A recent directive (2010/63) renewed the previous one after 25 years, further emphasizing that animals should only be used when clearly needed. In the legislation around cosmetics animal data are no longer allowed for regulatory purposes. Stimulation of in vitro approaches is therefore important in the research activities. Reproduction toxicity, carcinogenicity and sensitization are actual topics with promising perspectives to reduce animal use.