Overview of pharmacology-induced mechanisms of carcinogenesis by drug classes based on the analysis of the data set from the three parties

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Predicting the outcome of life-time carcinogenicity studies in rats based on chronic (6-month) toxicity studies in this species is possible in some instances. This should reduce the number of such studies and hence have a significant impact on the total number of animals used in safety assessment of new medicines. From a regulatory perspective, this should be sufficient to grant a waiver for a carcinogenicity study in those cases where there is confidence in the outcome of the prediction.

Pharmacological properties are a frequent key factor for the carcinogenic mode of action of some pharmaceuticals, but data-analysis on a large dataset has never been formally conducted. We have conducted an analysis of a dataset from based on the perspective of the pharmacology of 255 compounds from industrial and regulatory sources.

It is proposed that a pharmacological, class-specific, model may consist of an overall causal relationship between the pharmacological class and the histopathology findings in rats after 6 months treatment, leading to carcinogenicity outcome after 2 years. Knowledge of the intended drug target and pathway pharmacology should enhance the prediction of either positive or negative outcomes of rat carcinogenicity studies.

The goal of this analysis is to review the pharmacological properties of compounds together with the histopathology findings from the chronic toxicity study in rodents in order to introduce an integrated approach to estimate the risk of human carcinogenicity of pharmaceuticals.