Profiler for cohort of concern (v1.0)

ProtoICH by ProtoQSAR

ProtoICH

ProtoICH is a computational (*in silico*) tool specially focused on **ICH M7 Guideline**, aimed to reduce the potential carcinogenic risk of impurities. ICH M7 Guideline proposes the use of computational methods as an alternative for mutagenicity assays. It requires the prediction by means of two computational metodologies: a **statistical method (QSAR)** and an **expert-rule based method**. Moreover, it requires the detection of aflatoxins, N-nitrosamines and azoxy compounds (carcinogenicity **cohort of concern**).

Endpoint

Cohort of concern for high potency mutagenic carcinogens

The cohort of concern comprises three families of chemicals (aflatoxins, N-nitroso and alkyl-azoxy compounds) that require special consideration in the ICH M7 regulation, because of their risk of high mutagenic carcinogenecity effect. They are excluded of the generic limit of 1.5 µg/day/lifetime and, according to the ICH M7 guidelines, they trigger follow-up measures that are not triggered by the existence of other structural alerts.

Rules

This model is an expert rule-based system, formed by a set of 6 rules (structural alerts) related to structural characteristics of the three categories of compounds included in the cohort of concern

COC1.-Aflatoxins:

Aflatoxins are a family of mycotoxins produced by *Aspergillus flavus*, *Aspergillus parasiticus*, and related fungi which are known to be mutagenic.

COC2.-N-nitrosoamines:

The structure is a N-Nitroso compound (N-nitrosamines or N-nitrosamides).

COC3.-Azoxy:

Azoxy compounds contain a functional group with the structure RN=N+(O-)R.

COC1bis.-Aflatoxin derivatives:

This alert implies that the substance structure does not correspond to one of the main aflatoxins, but it is strongly related.

COC2bis.-N-nitrosoamine derivatives:

The structure is a derivative of an N-Nitroso compound (N-nitrosamines or N-nitrosamides).

COC3bis.-Azoxy derivatives:

Alkyl hydrazines and alkyl azides have been shown to directly convert into azoxy compounds.