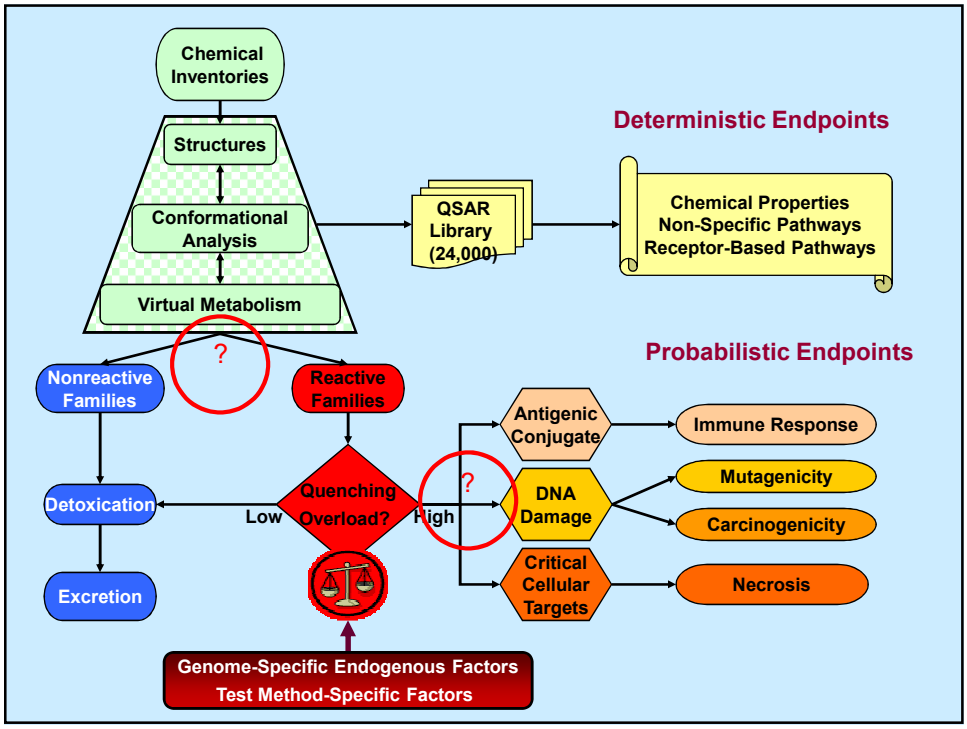


Probabilistic Models

$$P_{effect} = P_1 \times P_2 \times P_3 \times P_4 \times \ldots P_n$$

Forecasting distinct probabilities of low incident outcomes like idiosyncratic hepatic failure requires probability distributions for critical steps rather than effects under standard conditions

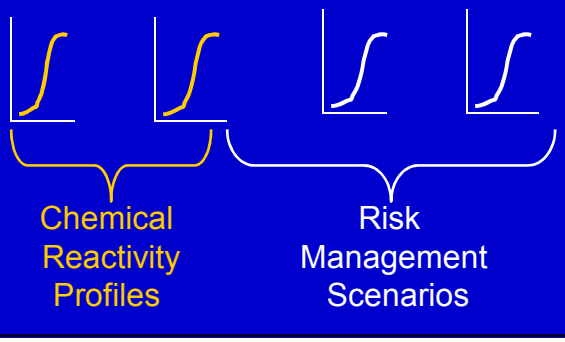
Exposure of the individual
Delivery rate to liver
Formation of reactive metabolites
Exceed detoxification rates
Covalent binding with proteins
Formation of neoantigens
Immune system recognition
Formation of cytotoxic antibodies
Interaction with hepatocytes
Overwhelm repair mechanisms
Liver Function Impairment
Liver Failure

--after Li (2002)

Probabilistic Models for Prioritization

Prioritization does not require explicit estimates of toxicity but rather a reliable ordering with respect to explicit risk management scenarios

$$P_{effect} = P_{chem} \times P_{exposure} \times P_{environ} \times P_{genetic}$$



Simulated 2-Acetylaminofluorene Metabolism