ILS Establishes and Qualifies Genetic Toxicology Screening Assays

Rationale and Strategies for In Vitro Screening Assays

- There is a clear need to establish early in drug development, rapid assessments of genotoxic potential prior to the conduct of GLP compliant regulatory studies for FDA Investigational New Drug Applications.
- ILS has established a strategy for rapid assessment of genotoxic potential that includes:
  - Quantitative Structure Activity Relationship (QSAR)
  - Mini-Ames bacterial mutation testing
  - *In vitro* micronucleus (MN) assay
- Early Identification of potential genotoxicity with pre-clinical candidates is an essential component of drug development.
- These non-GLP assays are utilized early in drug development for: lead optimization among candidate molecules, prediction of likely results of GLP regulatory-compliant OECD Guidance assays, investigation of mode-of-action and, assessing relative potency to define a threshold of toxicological concern (TTC).

Genetic Toxicology Screening Assays Include

- CQuantitative Structure Activity Relationships
  - QSAR models are highly predictive of potential response in the bacterial mutations assay and are part of the ICH M7 decision tree assessment of genotoxic potential.
- Mini-Ames in two or three test strains; S. *typhimurium* TA98, TA100, and *E.coli* WP2 *uvrA* pKM101
  - The mini-Ames test uses two or three bacterial tester strains that are OECD 471 compliant and are highly predictive of the results obtained from OECD compliant bacterial mutation assay.
- *In vitro* MN assay in human TK6 cells, 96-well format
  - The 96-well format *in vitro* MN uses human p53 proficient TK6 cells and is conducted under experimental conditions as required in OECD 487 GLP compliant assays.

Benefits

- Genetic toxicology screening studies are abbreviated versions of regulatory-compliant assays:
  - Require milligram amounts of test compound
  - Lower cost
  - Saves time and resources during drug development
  - Non-GLP profiling

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