2. TOXICOLOGY TESTS: POINTS TO CONSIDER

Several Offices within the FDA have Pre-Investigational New Drug Application Consultation Programs. These programs are designed to foster early communications between sponsors and the Agency. Advice may be requested for any aspect of drug development. All such communications are considered "informal" under 21CFR 10.90(b)(9) and do not obligate the Agency or sponsor.

As defined in CFR 312.23(a)(8), a sponsor filing an Investigational New Drug (IND) application must provide the results of pharmacological and toxicological studies of the drug involving laboratory animals and/or in vitro tests, which can provide the basis for the conclusion that it is reasonably safe to conduct the proposed clinical investigations. As drug development proceeds, the sponsor is required to submit informational amendments, as appropriate, with additional information pertinent to safety.

As per the regulation [CFR 312.23(a)(8)], the IND filing must include:

i. Pharmacology and Drug Disposition. A section describing the pharmacological effects and mechanism(s) of action of the drug in animals, and information on the absorption, distribution, metabolism, and excretion of the drug, if known.
ii. Toxicology. An integrated summary of the toxicological effects of the drug in animals and in vitro. Depending on the nature of the drug and the phase of the investigation, the description is to include the results of acute, subacute, and chronic toxicity tests; tests of the drug's effects on reproduction and the developing fetus; genetic toxicity testing; any special toxicity test related to the drug's particular mode of administration or conditions of use (e.g., inhalation, dermal, or ocular toxicology); and any in vitro studies intended to evaluate drug toxicity.

It is not unusual for the Agency to request draft/final study reports for the pivotal studies conducted in support of the initial IND, especially for new molecular entities.

Regulatory pharmacology and toxicology guidances involving animal models published by the International Committee on Harmonization (ICH) and/or the US Food and Drug Administration (FDA) Center for Drug Evaluation and Research (CDER) include the following http://www.fda.gov/cder/PharmTox/guidances.htm):

Pharmacology:

- Pharmacokinetics: Guidance for Repeated Dose Tissue Distribution Studies; ICH-S3B (Mar 1995).
- Toxicokinetics: The Assessment of Systemic Exposure in Toxicity Studies; ICH-S3A (Mar 1995).