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Introduction to Toxicological Studies - Medistri

🚀 Introduction to Toxicological Studies

The toxicological studies provide a consistent definition of the circumstances under which it is necessary to undertake studies on new drugs and/or devices. The recommendations take into account the known risk factors as well as the intended indications and duration of exposure. Following standards such as ISO 10993 also helps to uncover potential risks like carcinogenicity, genotoxicity and reprotoxicity. Additionally, following standards can increase sensitivity and reduce the number of animals required for overall safety evaluations.

Toxicology is the scientific study of adverse effects that occur in living organisms due to chemicals. It involves observing and reporting symptoms that arise following exposure to toxic substances. It is the characterization of the toxicity profile of a drug or device, by identifying its impact on the organ structure and/or its functionality.

👉 Toxicological risk is defined as the probability of a specified degree of an adverse reaction occurring in response to a specified level of exposure. Toxicological hazard is defined as the potential for a chemical substance or material to cause an adverse biological reaction, taking into account the nature of the reaction and the dose required to elicit it.

Toxicology studies help to determine the margin of safety of a drug or device - it's a reference in guiding the parameters for clinical trials to maximize safety and minimize risk. Not only do toxicology studies frame trial guidance related to duration, administration routes, and dose escalation, they also help to set the parameters for clinical monitoring (i.e., which organs to assess closely). With toxicology studies, we can also:

- Assesses the severity and reversibility of toxicity.
- Understand the relationship between dose ranges and exposure.
- Determine if (and to what degree) the biologic's toxicity is dose-dependent.
- Check which species can be tested.
- Comprehend how chemical or physical agents interact with living organisms that may trigger perturbations in cell function and/or structure or that may initiate repair mechanisms at the molecular, cellular, and/or tissue levels.

The ISO 10993 standard series specifies a process through which the manufacturer of a medical device can identify biological hazards associated with the medical device, estimate and evaluate the risks associated with these hazards, control these risks, and monitor the effectiveness of the controls throughout the life cycle of the medical device.

ISO 10993-17:2002 specifies the determination of allowable limits for substances leachable from medical devices. It is intended for use in deriving standards and estimating appropriate limits where standards do not exist. It describes a systematic process through which identified risks arising from toxicologically hazardous substances present in medical devices can be quantified.

The process, requirements, criteria and methods specified in this standard are intended to yield the following information, which are useful in the overall biological risk assessment of the final product:

- The presence of constituents that are a potential source of harm to health.
- A worst-case exposure estimate(s) for each chemical constituent(s) to determine whether or not it could cause appreciable harm to health.
- Derivation of a tolerable intake or tolerable contact level, to a chemical constituent over a specified time period, on the basis of body mass or surface area, that is considered to be without appreciable harm to health.
- An evaluation of exposure data for each chemical constituent(s) that is/are without appreciable harm to health, or alternatively, is or could be a harmful dose.

As outlined in ISO 10993-17, risks associated with exposure to identified leachables are managed by quantifying the associated risks and limiting exposure within tolerable levels. The process of establishing these tolerable levels can be broken down into the following key steps:

- Conduct comprehensive literature searches the critical health endpoint.
- Determine a point-of-departure (usually a NOAEL).
- Derive a Tolerable Intake (TI), specific for the route of entry and duration of exposure.
- Calculate the Tolerable Exposure (TE) for the target patient subgroups.

If appropriate, modify the initial TE to account for utilisation, benefit etc
Compare the final TE with the estimated worst-case exposure of the potential leachable and calculate a Margin of Safety (MOS).

Lastly, the latest revision of ISO 10993-17 extends the previous version by clarifying when a toxicological risk assessment is necessary, how to calculate worst case exposure of a chemical constituent, and when the probability of occurrence of harm to health should be addressed by other means. (e.g. frequency dose-response (if available), probabilistic dose-response, or biological test).

ISO 10993-1 and ISO 10993-18 are international standards that provide guidelines for the biological evaluation of medical devices.

👉 ISO 10993-1 describes chemical information as an essential first step in assessing biocompatibility – before biological testing. As of 2018, "chemical information" is required for all devices.

The primary aim of the ISO 10993-1 is the protection of humans from potential biological risks arising from the use of medical devices. It is compiled from numerous International and national standards and guidelines concerning the biological evaluation of medical devices. It is intended to describe the biological evaluation of medical devices within a risk management process, as part of the overall evaluation and development of each medical device.

👉 ISO 10993-18 describes a process for characterizing a device (or material):

- Identification of its materials of construction.
- Characterization of the material composition (i.e., chemical constituents).
- Report constituent information to support assessment of the potential for patient risk in clinical use.

ISO 10993-18 specifies a framework for the identification, and if necessary, quantification of constituents of a medical device, allowing the identification of biological hazards and the estimation and control of biological risks from material constituents, using a generally stepwise approach to the chemical characterization

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These standards provide a global framework for evaluating the potential toxicological risks associated with the materials used in medical devices, and help manufacturers to identify and mitigate any potential risks. They help manufacturers ensuring that medical devices are safe for patients and they directly reduce the risk of adverse reactions.

Toxicology studies are an essential part of drug development and require the contributions of skilled scientists and specialists. Medistri possesses an in-depth comprehension of the Toxicological Studies that will meet your regulatory requirements.

🎯 To learn more about Medistri's Toxicological Studies, visit on our website at www.medistri.swiss or directly contact our team at contact@medistri.swiss.

- The Medistri Team

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