
Preface

Developmental toxicity is defined as the study of adverse effects on the developing organism that may result from exposure to drugs/chemicals prior to conception (either parent), during prenatal development, or postnatally to the time of sexual maturation.

The thalidomide disaster is widely believed to be the catalyst that promoted regulatory agencies around the world, including the US FDA, to initiate requirements for new drugs to be thoroughly tested in animals prior to being sold in the marketplace.

At that time, developmental toxicity studies conducted in animals were inappropriately designed and insufficient to detect a teratogenic signal.

We currently rely on animal testing to predict the potential for drugs or chemicals to cause developmental toxicity in humans. Rodents (rats and mice) and rabbits are the most relevant species used in developmental toxicity testing, dogs and minipigs are rarely used, and nonhuman primates may be used for biologics, especially for monoclonal antibodies.

Manifestation of developmental and reproductive toxicity may include adverse effects on onset of puberty, gamete production and transport, reproductive cycle normality, sexual behavior, fertility, gestation, parturition, lactation, structural abnormalities, premature reproductive senescence, and modifications of other functions that are dependent on the integrity of the reproductive systems.

Evaluation of developmental and reproductive toxicology endpoints is an integral part of the safety assessment process for compounds with potential use in women of childbearing age or females that might be exposed during pregnancy as well as men of reproductive potential.

This volume covers metabolism and drug-drug interactions during pregnancy, critical periods of developmental toxicology, in vivo and alternative methods to assess potential developmental toxicity for drugs and chemicals, and effects of chemicals on testes and mammary glands. The in vivo assessments are guideline-driven and are required for submissions for product approval.

On the other hand, alternative methods for developmental toxicity testing have been sought because of the pressure to reduce the number of animals used in health research. Alternative in vitro methods include cell cultures, zebra fish, c-elegans, organ cultures, and embryo cultures and embryonic stem cells. These test systems can provide invaluable information and decrease the number of animals used in studies. The design of in vitro alternatives with good predictivity of in vivo effects is challenging, as embryo-fetal development is a continuous process of a precisely orchestrated sequence of events and any alternative assay in the field of developmental toxicity represents only part of the complexity of the whole developing conceptus and its maternal environment. Currently, the alternative methods are not used for regulatory submissions but mainly for screening and mechanistic studies.

Finally, I would like to thank all the authors/coauthors for their hard work and timely contributions. Likewise, I would like to extend my sincerest thanks and appreciation to David Casey and the entire Springer publishing team who worked tirelessly in the publication of this volume.

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