

**ECETOC Document**

**No 5**

**Teratogenicity - Definition**

**June 1980**

TERATOGENICITY - DEFINITION

---

ECETOC established a Task Force Teratogenicity which was asked to define a chemical teratogen in terms which are scientifically correct and which also serve in the classification of potential teratogens for practical, legislative purposes, for example in the 6th Amendment.

In attempting to do this, definitions produced by other scientists were considered. As a basis for discussion the following definition by the Scientific Committee of the European Commission was considered.

"Substances or Preparations which can produce or increase the frequency of non-hereditary congenital malformations or defects in the progeny".

Some fundamental remarks can be made on this definition.

- 1) The word "Preparations" should be deleted because a teratogenic effect observed in a preparation is caused by one or more chemical substances, and therefore it is scientifically unsatisfactory not to be able to relate an observed teratogenic effect to a well-defined chemical substance in the preparation.
- 2) "Non-hereditary congenital" is in the first place repetitive. Congenital according to Webster's dictionary means "acquired during development in the uterus and not through heredity". That means after implantation.

The use of the adjective "non-hereditary" is wrong, because :

2.1. A marked increase in the occurrence of a malformation which is believed to be of a "genetic" nature, due to the exposure to a chemical, might also be considered to be a teratogenic effect.

2.2. Up till now in many cases there is no scientific knowledge whether normally-occurring abnormalities are genetically determined or not.

- 3) The use of the words "malformations or defects" is misleading. "Malformations" is mostly used for severe morphological alterations, while the effects of teratogenic substances should be considered on a broader basis. The adding of the word defects is rather confusing because it is undefined.

./.

A general remark to this definition is that it is liable to misinterpretations because on the one hand it attempts to be complete and on the other hand undefined words are being used.

Teratology is a special part of reproductive toxicology and should not be confounded with embryo - or foeto-toxicity. Embryo - and foeto-toxicity can manifest itself by various degrees of growth-retardation, variations (eg skeletal) and in extreme cases lethality.

It should also be emphasized that teratology should be differentiated from maternal toxicity.

The ECETOC task force defined a teratogen in a clear and short definition, usable for legislative purposes.

The words used can be specified in separate footnotes.

The following definition is proposed :

"A CHEMICAL SUBSTANCE SHOULD BE DEFINED A TERATOGEN WHEN, AFTER MATERNAL EXPOSURE TO IT, DETECTABLE STRUCTURAL AND FUNCTIONAL ABNORMALITIES ARE CAUSED IN THE PROGENY,"

Under "exposure to a chemical substance" we include exposure to agents prior to pregnancy which persist in the dam and manifest teratogenic effects in her offspring, as well as exposure to chemicals during pregnancy.

Abnormalities include direct observable structural abnormalities and also functional abnormalities which are only observable post-natally.

The observed abnormalities should be judged according to a sound scientific scrutiny. The occurrence and the nature of the abnormalities in the treated group of test animals should be assessed in comparison with the nature and the frequency of the spontaneous abnormalities in the test system.

As all toxicological experiments are made with animals, it is important to bear in mind that animal data give only an indication of the potential effects in humans.