JUL-3 1989

TSCA SECTION 8(E)

QUESTIONS & ANSWERS

PUBLISHER'S NOTE: Published by the US EPA and dated July 3, 1989.

Q. Does Section 8(e) of TSCA intend the submission of animal test information: (a) when a determination of "substantial risk" has been made, or (b) where merely a finding of positive animal test results useful in the further assessment of human risk has been determined?

A. TSCA Section 8(e) requires the timely submission of evidence (including preliminary evidence) from animal studies that implicates the tested chemical as causing serious toxicologic effects (e.g., cancer, neurotoxicity, birth defects). A decision to report the observance of such serious toxicological effects should not hinge in any way on a judgement of either the actual or potential exposure to the chemical or a judgement about the degree of relevancy of the findings to an overall assessment of human risk. In other words, the decision to report under Section 8(e) in such cases should be based simply on the observance of the serious toxicologic effects.

Q. What criteria should be used to determine if the results from cancer bioassay studies in animals should be submitted to EPA under Section 8(e)? For example, when should animal studies showing only a significant increase in benign tumors over controls be submitted?

A. Reporting of benign and/or malignant tumors should take place, for example, when either statistically or biologically significant increases over controls are observed. The observation of such increases are made in many cases at interim sacrifices performed typically during long term exposure studies in animals.

Q. How should reproductive, or developmental toxicity data be evaluated for possible TSCA Section 8(e) submission if maternal toxicity is also present?

A. Statistically or biologically significant increases in teratogenic effects or other serious embryotoxic or fetotoxic effects (e.g., significant embryo or fetal lethality, spontaneous abortion) should be reported under Section 8(e) regardless of the level of maternal toxicity observed in the study.

Q. What criteria should be used to determine which reproductive/developmental effects observed in animal tests are reportable under section 8(e)? For example, should developmental effects that are reversible, such as reduced birth weight and/or incomplete ossification, trigger reporting?

A. In addition to teratogenic effects, serious adverse developmental effects (e.g., significant embryo or fetal lethality, significantly reduced fetal/birth weights, significantly retarded/incomplete skeletal ossification) should be reported. In addition, serious adverse effects on the male/female reproductive system (e.g., significant testicular or ovarian atrophy, significantly reduced fertility, sterility) should be reported.

Q. What criteria should be used in determining if the results of acute toxicity studies constitute information that reasonably supports a conclusion of substantial risk?

A. Criteria used to determine Section 8(e) reporting in the case of acute/subacute toxicity findings will depend on the nature of the effects observed and the dose at which the effects occurred. For example, information that shows a tested chemical to be extremely toxic (e.g., causes lethality at very low doses) by, for example, inhalation, dermal application or oral administration should be reported. On the other hand, the reporting of information showing a chemical to be moderately toxic will depend on the degree of actual or potential exposure to the tested chemical. Information showing a chemical to be slightly or minimally toxic on an acute/subacute basis is not considered typically to be reportable. In addition to extreme toxicity, certain other serious toxicological effects (e.g., neurotoxicity, adverse reproductive system effects) seen in an acute or subacute animal study should be reported under Section 8(e).

Q. When evaluating subchronic studies in animals, what criteria should be used to determine reportability of adverse effects? For example, should increased or decreased organ(s) size in the absence of histopathological changes be reported?

A. Serious toxic effects (e.g., neurotoxic effects, serious reproductive system effects) observed during the conduct of subchronic studies should be reported. This includes readily observable serious effects or serious effects seen only as the result of gross and/or histopathological examination. As is the case for acute and subacute toxicity studies, the degree of the observed toxicity is important. The more serious (or significant) the observed effect, the less heavily one should consider actual/potential exposure for reporting and vice versa.

Q. What criteria constitute evidence of reportable neurotoxicity in animal studies? For example, are reversible effects such as narcosis or effects observed in the presence of marked systemic toxicity considered reportable?

A. Typically, neurotoxic effects that are observed in dying animals are not, in and of themselves, considered by EPA to be reportable under Section 8(e) of TSCA. In many cases, however, already reportable data regarding extremely or highly toxic (lethal) substances will be accompanied by information concerning observed neurotoxic affects. In short or long term exposure studies in which serious neurotoxic signs and symptoms (e.g., convulsions, sleep induction, motor dysfunction, narcosis, behavioral dysfunction) are seen in non-moribund animals, however, specific reporting of the neurotoxic effects should take place.

Q. What criteria should be applied in determining whether positive results of in vivo or in vitro mutagenicity assays trigger Section 8(e) reporting?

A. Serious in vivo genotoxicological effects (e.g., gene or chromosomal mutations) are reportable in and of themselves under Section 8(e). On the other hand, a positive in vitro genotoxicity test, when considered alone, is usually insufficient to cause reporting under Section 8(e). However, EPA believes that such information is of value in assessing the possible risk(s) posed by exposure to the tested chemical or mixture. Further, the Agency believes that a positive in vitro genotoxicity test result, in combination with other information (e.g., knowledge of actual/potential exposure to and/or high production of the tested chemical), would suggest the need, in many cases, to conduct further studies designed to determine the toxicity of or the exposure to that chemical. EPA expects the results of such additional studies to be considered also for submission under TSCA Section 8(e).