

with or alter absorption of the toxic substance, and

(D) Dose.

(3) *Assessment of Risk.* This section on quantitative risk assessment applies to estimates of risk for substances that are toxic by reason of their carcinogenicity.

(i) Generally, the study leading to the highest risk should be used in the risk assessment; however, other factors may influence the choice of study.

(ii) Risk should be based on the maximum likelihood estimate from a multistage model (such as Global83 or later version) unless the maximum likelihood estimate is not linear at low dose, in which case the 95% upper confidence limit on risk should be used.

(iii) For systemic carcinogens, if estimates of human risk are made based on animal data, a factor derived from dividing the assumed human weight (70 kg) by the average animal weight during the study and taking that to the $\frac{1}{3}$ power should be used. There is the possibility that this factor may be changed, using the $\frac{1}{4}$ power instead of the $\frac{1}{3}$ power, as part of a unified Federal regulatory approach. If such an approach is adopted, it will apply here.

(iv) When dose is expressed as parts per million, and the carcinogen acts at the site of contact, humans and animals exposed to the same amount for the same proportion of lifetime should be assumed to be equally sensitive.

(v) If no experimental study having the same route of exposure as that anticipated for human use of a substance is available, a study by another route of exposure may be used. Pharmacokinetic methods may be used if sufficient data are available.

(vi) When exposure scenarios are different from those used in the underlying study upon which estimates of risk are based, proportionality should be applied. If pharmacokinetic methods are used to adjust for risks at high versus low exposure levels, level-time measures should not be combined without taking the non-linearity into account.

(4) *Acceptable Risks*—(i) *ADI for Carcinogens.* The maximum acceptable daily intake (“ADI”) is that exposure of a toxic (by virtue of its carcinogenicity) substance that is estimated

to lead to a lifetime excess risk of one in a million. Exposure refers to the anticipated exposure from normal lifetime use of the product, including use as a child as well as use as an adult.

(ii) *ADI for Neurotoxicological and Developmental/Reproductive Agents.* Due to the difficulties in using a numerical risk assessment method to determine risk for neurotoxicological or developmental/reproductive toxicants, the Commission is using a safety factor approach, as explained below.

(A) *Human Data.* If the hazard is ascertained from human data, a safety factor of ten will be applied to the lowest No Observed Effect Level (“NOEL”) seen among the relevant studies. If no NOEL can be determined, a safety factor of 100 will be applied to the Lowest Observed Effect Level (“LOEL”). Both the NOEL and LOEL are defined in terms of daily dose level.

(B) *Animal Data.* If the hazard is ascertained from animal data, a safety factor of one hundred will be applied to the lowest NOEL. If no NOEL can be determined, a safety factor of one thousand will be applied to the lowest LOEL. Both the NOEL and LOEL are defined in terms of daily dose level.

[57 FR 46665, Oct. 9, 1992]

§ 1500.210 Responsibility.

The provisions of these regulations (16 CFR subchapter C of chapter II) with respect to the doing of any act shall be applicable also to the causing of such act to be done.

§ 1500.211 Guaranty.

In the case of the giving of a guaranty or undertaking referred to in section 5(b)(2) of the act, each person signing such guaranty or undertaking, or causing it to be signed, shall be considered to have given it. Each person causing a guaranty or undertaking to be false is chargeable with violations of section 4(d) of the act.

§ 1500.212 Definition of guaranty; suggested forms.

(a) A guaranty or undertaking referred to in section 5(b)(2) of the act may be:

(1) Limited to a specific shipment or other delivery of an article, in which case it may be a part of or attached to