**Section 302.654 Determining the Risk Associated Intake**

The Risk Associated Intake (RAI) is the maximum amount of a substance that if ingested daily for a lifetime, is expected to result in the risk of one additional case of human cancer in a population of one million. Where more than one carcinogenic chemical is present, the RAI must be based on an allowed additive risk of one additional case of cancer in a population of one hundred thousand. The RAI must be derived as specified in subsections (a) through (c).

a) For those substances for which a human epidemiologic study has been performed, the RAI equals the product of the dose from exposure in units of milligrams of toxicant per kilogram body weight per day (mg/kg-d) that results in a 70-year lifetime cancer probability of one in one million, times the average weight of an adult human of 70 kilograms (kg). The resulting RAI is expressed in milligrams toxicant per day (mg/d). If more than one human epidemiologic study is available, the lowest exposure level resulting in a 70-year lifetime probability of cancer equal to a ratio of one in one hundred thousand must be used in calculating the RAI.

b) In the absence of an epidemiologic study, for those toxic substances for which a carcinogenic potency factor (CPF) has been derived from studies of mammalian test species, the risk associated intake is calculated from the equation:

RAI = K/CPF

Where:

|  |  |  |
| --- | --- | --- |
| RAI | = | Risk associated intake in milligrams per day (mg/d); |
| K | = | A constant consisting of the product of the average weight of an adult human, assumed to be 70 kg, and the allowed cancer risk level of one in one million (1/1,000,000); and |
| CPF | = | Carcinogenic Potency Factor is the risk of one additional cancer per unit dose from exposure. The CPF is expressed in units of inverse milligrams per kilogram - day (l/mg/kg-d) as derived in subsections (b)(1) through (b)(7). |

1) Only those studies that fulfill the data requirement criteria of Section 302.606 must be used in calculating the CPF.

2) The linear no-threshold dose-response relationship developed in the same manner as in the USEPA document "Mutagenicity and Carcinogenicity Assessment of 1,3-butadiene", incorporated by reference in 35 Ill. Adm. Code 301.106, must be used in obtaining the unit risk, defined as the 95th percentile upper bound risk of one additional cancer resulting from a lifetime exposure to a unit concentration of the substance being considered. The CPF must be estimated from the unit risk in compliance with subsection (b)(7). In calculating a CPF, the Agency must review alternate scientifically valid protocols if so requested.

3) If in a study of a single species more than one type of tumor is induced by exposure to the toxic substance, the highest of the CPFs is used.

4) If two or more studies vary in either species, strain, or sex of the test animal, or tumor type, the highest CPF is used.

5) If more than one tumor of the same type is found in some of the test animals, these should be pooled so that the dose-response relationship is dose versus number of tumors per animal. The potency estimate for this dose-response relationship is used if it is higher than estimates resulting from other methods.

6) If two or more studies are identical regarding species, strain, and sex of the test animal, and tumor type, the highest of the CPFs is used.

7) Calculation of an equivalent dose between animal species and humans using a surface area conversion, and conversion of units of exposure to dose in milligrams of toxicant per kilogram of body weight per day (mg/kg-d), must be performed as specified in the USEPA document "Mutagenicity and Carcinogenicity Assessment of 1,3-butadiene", incorporated by reference in 35 Ill. Adm. Code 301.106.

c) If both a human epidemiologic study and a study of mammalian test species are available for use in subsections (a) and (b), the risk associated intake is determined as follows:

1) When the human epidemiologic study provides evidence of a carcinogenic effect on humans, the RAI is calculated from the human epidemiology study as specified in subsection (a).

2) When the mammalian study provides evidence of a carcinogenic effect on humans, but the human epidemiologic study does not, a cancer risk to humans is assumed and the risk associated intake is calculated as specified in subsection (b).

(Source: Amended at 47 Ill. Reg. 4437, effective March 23, 2023)