

**Department for Environment, Food and Rural Affairs  
and the Environment Agency**

**CONTAMINANTS IN SOIL:  
COLLATION OF TOXICOLOGICAL DATA AND  
INTAKE VALUES FOR HUMANS.  
INORGANIC CYANIDE**

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This publication details the derivation of Tolerable Daily Soil Intakes or Index Doses for inorganic Cyanide. The report has been written for technical professionals who are familiar with the risks posed by land contamination to human health but who are not necessarily experts in risk assessment. It is expected to be of use to all parties involved with or interested in contamination, but in particular to those concerned with the assessment of land contamination.

## **Keywords**

Tolerable Daily Soil Intake, Index Dose, land contamination, risk assessment, human health, inorganic cyanide.

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## 1 Introduction

- 1.1 This report, one of a number on the assessment of risks to human health from contaminants in soil, presents key data and expert opinions on the toxicology and intake of inorganic cyanide. It may be necessary to update this report in the future to incorporate new toxicological data as science advances.
- 1.2 The aim is to derive tolerable daily intakes (TDIs), which in turn are needed to derive Soil Guideline Values (SGVs) for inorganic cyanide, that is, concentrations of inorganic cyanide in soil that will pose no significant threat to health.
- 1.3 There is a general discussion of TDIs in CLR9 *Contaminants in Soils: Collation of Toxicological Data and Intake Values for Humans. Consolidated Main Report*. Reference to CLR9 is necessary to understand the concepts and terms used in this report (Department for Environment, Food and Rural Affairs, DEFRA, and Environment Agency, 2002a).
- 1.4 The computer model used for deriving Soil Guideline Values is described in CLR10 *The Contaminated Land Exposure Assessment Model (CLEA): Technical Basis and Algorithms* (DEFRA and Environment Agency, 2002b). The derivation of the Soil Guideline Value for inorganic cyanide is given in SGV 6 *Guideline Values for Inorganic Cyanides Contamination in Soils* (DEFRA and Environment Agency, 2002c).
- 1.5 In general, the literature up to December 1997 has been reviewed in this report. In addition, the August 2001 record of the Integrated Risk Information System (IRIS) was consulted (USEPA, 2001).

## 2 Identity

- 2.1 Hydrogen cyanide (HCN), also known as prussic acid, is a colourless, flammable gas or liquid (boiling point, 26°C). It has a bitter almond smell, which, however, cannot be recognised by 20% of the population. Both the acid and alkali metal salts are highly soluble and toxic compounds, and their toxicity has ensured a role in homicide, suicide and gas chamber executions.
- 2.2 HCN is mainly used in the manufacture of other chemicals such as methyl methacrylate. It has also been used as a fumigant and rodenticide. Cyanide salts are used in metal refining, cleaning and electroplating. Organic cyanides, called nitriles, are important industrial chemicals used in synthesis and to form polymers such as polyacrylonitrile (“Orlon”).
- 2.3 Hydrogen cyanide may be given off when nitrogen-containing plastics such as polyurethane are burned, and it is also a by-product of blast furnaces, coke ovens, petroleum refining and metallurgy.
- 2.4 Cyanide also occurs naturally in the fruits, seeds and foliage of many plants, most notably in almonds and cassava (manioc).
- 2.5 The fate of cyanides in water can vary widely. HCN and alkali metal cyanides may be lost by volatilisation, and sparingly soluble metal cyanides such as the copper and silver salts can be expected to be lost by sedimentation. Below pH 9, most free cyanide would convert to the highly volatile hydrogen cyanide. Water-soluble complexes such as ferrocyanide may undergo photodecomposition, but are expected to have long half-lives and may therefore be transported over long distances.
- 2.6 The fate of cyanides in soils has been inadequately studied, but may be expected to be pH-dependent. With low sorption and high water solubility, cyanides are likely to leach readily from soils. In spite of this, cyanides are rarely detected in groundwater (USEPA, 1984; ATSDR, 1997).
- 2.7 Many micro-organisms both utilise cyanide and are capable of degrading cyanides and their organic equivalents, the nitriles. It has been proposed that industrial and waste waters could be detoxified by this method (Knowles, 1988; Ingvorsen *et al*, 1988).
- 2.8 This report concentrates on the toxicity of “free” inorganic cyanides. Not all cyanide at a contaminated site may be in the form of free cyanide, and therefore it may not be appropriate to use the TDIs derived here to derive Soil Guideline Values for total cyanide content. For example, Shifrin *et al* (1996) noted that the most prevalent forms of cyanide at former manufactured (town) gas sites are “the relatively nontoxic iron-complexed forms, such as ferric ferrocyanide, rather than the highly toxic free cyanide forms”.

### 3 Toxicity

- 3.1 Reviews of the literature on the toxicity of cyanide have been published by Way (1984), Shifrin *et al* (1996), the World Health Organization (WHO, 1996), the Agency for Toxic Substances and Disease Registry (ATSDR, 1997) and the United States Environmental Protection Agency (USEPA, 1984, 1985, 2001). This section is largely based upon these reviews; particular mention is made of those studies which have been used in deriving TDIs. In general, the primary literature has not been consulted.
- 3.2 **Absorption.** Cyanides are rapidly absorbed from the lungs, gastrointestinal tract and the skin. Humans retain about 60% of hydrogen cyanide in the lungs after normal inhalation. Three dogs given lethal doses of cyanide by gavage died at 8, 21 and 155 min after treatment, and had absorbed 17, 24 and 72% respectively of the administered dose. Rats given 2 mg CN kg<sup>-1</sup> bw (milligrams of cyanide per kilogram of body weight) by gavage absorbed about 53% of the cyanide within 24 h. Dermal absorption has been demonstrated in acute studies with guinea pigs and dogs.
- 3.3 **Metabolism.** Cyanide is metabolised primarily in the liver by conversion to the much less toxic thiocyanate in a reaction catalysed by the enzyme rhodanese. A minor pathway involves the combination of cyanide with the amino acid cystine, and subsequent conversion to 2-aminothiazoline-4-carboxylic acid. Cyanide can form complexes with some metal ions, and the cobalt complex reacts with hydroxocobalamin to form cyanocobalamin (vitamin B<sub>12</sub>).
- 3.4 Cyanide toxicity results from inhibition of cytochrome oxidase, thereby limiting the absorption of oxygen at the cellular level. Human poisonings usually involve massive doses, much above that required to inhibit cytochrome oxidase. The central nervous system is a major target of acute cyanide toxicity, with a short period of stimulation evidenced by rapid breathing, followed by depression, convulsions, paralysis and possibly death. Sub-lethal doses can produce dizziness, headache, confusion, nausea and numbness. Excess thiocyanate resulting from chronic cyanide exposure may inhibit iodine accumulation by the thyroid. Cyanide exposure coupled with iodine deficiency may be related to the thyroid disorders of goitre and cretinism.
- 3.5 **Acute oral toxicity.** The average fatal oral dose for humans has been estimated to be 1.52 mg CN kg<sup>-1</sup> bw. This value results from tissue analysis at autopsy, and is an absorbed dose. The lowest reported fatal oral dose for humans is 0.56 mg kg<sup>-1</sup> bw (Gettler and Baine, 1938). The average fatal dose for dermal exposure has been estimated to be 100 mg kg<sup>-1</sup> bw.
- 3.6 **Repeated oral toxicity.** The only information on the chronic ingestion of any foodstuff or substance containing cyanide concerns improperly prepared cassava (also known as manioc or tapioca). The leaves and outer parts of the roots contain the glucoside linamarin, from which HCN is released by enzymatic hydrolysis. The cyanide concentration can vary considerably depending upon the cultivar and the processing, with values up to 1500 mg kg<sup>-1</sup> reported in fresh roots. Effective processing can reduce the value in prepared products to significantly lower levels.

- 3.7 Over 70% of the calorific content of some tropical diets is provided by cassava, and the ingestion of cassava is associated with tropical ataxic neuropathy. This is a diffuse degenerative disease characterised by optic atrophy, nerve deafness and ataxia. An outbreak of over 1000 cases of partial paralysis was reported in Mozambique, where the estimated daily cyanide intake via cassava ingestion was about 0.2–0.45 mg kg<sup>-1</sup> bw. The symptoms could not definitively be attributed to chronic cyanide exposure because the patients and the unaffected members of the community had similarly high blood levels of thiocyanate (Casadei *et al*, 1984; Cliff *et al*, 1984).
- 3.8 The metabolism of cyanide to thiocyanate is implicated in the other manifestation of cassava ingestion, the increased incidence of goitres and other thyroid effects. Thiocyanate greatly inhibits the accumulation of iodine by the thyroid, and these tropical diets are also deficient in iodine (Bowman and Rand, 1980; USEPA, 1984, 2001; Way, 1984; Smith, 1996).
- 3.9 Unfortunately, adequate dose–response data are not available from the studies of cassava-ingesting populations, and therefore the estimation of an oral TDI has had to use data from laboratory studies.
- 3.10 In a two-year study, groups of rats were given food fumigated with HCN to produce doses of 4.3 and 10.8 mg CN kg<sup>-1</sup> bw day<sup>-1</sup> (Howard and Hanzal, 1955). There were no changes observed in growth rate, histopathology, haematology, or gross signs of toxicity. Because of the volatility of hydrogen cyanide, the diets were prepared every other day, and analysed at the beginning and end of each two-day period.
- 3.11 A reduced weight gain and decreased thyroid activity were observed in male rats given 30 mg CN kg<sup>-1</sup> bw day<sup>-1</sup> as potassium cyanide in the diet for 11.5 months (Philbrick *et al*, 1979). In a parallel study, diets deficient in methionine, vitamin B<sub>12</sub> and iodine produced primary myelin degeneration in the spinal cord when supplemented with thiocyanate at a level of 67 mg kg<sup>-1</sup> bw day<sup>-1</sup>.
- 3.12 A 90-day drinking-water study of sodium cyanide was conducted by the National Toxicology Program (NTP, 1993). Groups of 10 male and 10 female rats received sodium cyanide at dose levels of 0.2 to 12.5 mg CN kg<sup>-1</sup> bw day<sup>-1</sup>. The toxicity observed in the male rats at the highest tested dose included a decrease in left testis weight, spermatid heads and counts. The 12.5 mg kg<sup>-1</sup> bw day<sup>-1</sup> dose was judged to be the “lowest observed adverse effect” level (LOAEL), and the next lowest dose for the male rats, 4.5 mg kg<sup>-1</sup> bw day<sup>-1</sup>, was taken as the “no observed adverse effect” level (NOAEL).
- 3.13 Potassium cyanide was administered for 24 weeks by gavage to groups of three juvenile swine just prior to the daily meal of a cassava-free commercial diet, a dosage schedule specifically designed to maximise the absorption of the cyanide (Jackson, 1988). Cyanide dosage levels were 0, 0.4, 0.7 and 1.2 mg kg<sup>-1</sup> bw day<sup>-1</sup>. Increasing cyanide treatment was found to lead to increased ambivalence and longer response time to various stimuli, as indicated by changes in aggressive feeding pattern, fighting, rooting and pica. The investigator suggested an influence of dietary cyanide on cerebral function. She also questioned whether the findings of increasingly more passive, non-aggressive and ambivalent behaviour in pigs were relevant for humans.

- 3.14 Copper cyanide has been tested in a 90-day oral study in rats. Administration was by gavage at doses of 0, 0.5, 5, 15 and 50 mg copper cyanide  $\text{kg}^{-1}$  bw  $\text{day}^{-1}$ . Deaths, kidney and liver injury and severe haemolytic anaemia were the main toxic effects of the highest tested dose. Liver and kidney pathology were present at 15 mg  $\text{kg}^{-1}$  bw  $\text{day}^{-1}$  (the LOAEL), and the NOAEL was considered to be 5 mg  $\text{kg}^{-1}$  bw  $\text{day}^{-1}$  (USEPA, 1986, 2001).
- 3.15 **Repeated inhalation toxicity.** Although the cyanides possess a high acute toxicity, and are used in large quantities in industry, few problems have been recorded with occupational exposures. This is undoubtedly because extra care has been taken in the use of cyanides as a consequence of their known toxicity.
- 3.16 The effect of chronic cyanide inhalation in three electroplating factories was studied by El Ghawabi *et al* (1975). The most frequent symptoms reported were headache, weakness, changes in taste and smell, giddiness, throat irritation, vomiting and shortness of breath. While none of the 36 workers demonstrated any clinical signs of hypo- or hyperthyroidism, 20 exhibited thyroid enlargement. All workers showed a much greater uptake of radioiodine than in the controls. The lowest breathing zone cyanide concentration in the three factories was 6.4 ppm ( $7 \text{ mg m}^{-3}$ ).
- 3.17 The long-term exposure of workers to HCN fumes in a silver reclaiming facility produced a range of symptoms involving the central nervous system, and some indication of an influence on thyroid function (Blanc *et al*, 1985). There was no quantitative information on exposure levels.
- 3.18 Inhalation of cyanide in tobacco smoke by heavy smokers has been associated with the condition known as tobacco amblyopia, characterised by a loss of visual acuity, vitamin B<sub>12</sub> deficiency, and an inefficient metabolism of cyanide to thiocyanate. Administration of the cyanide antagonist hydroxocobalamin results in a reversal of the visual disturbance (USEPA, 1985; Way, 1984).
- 3.19 **Reproductive toxicity.** There was a slightly reduced body weight gain in the offspring of 20 female rats that had been given potassium cyanide in the diet for 19 days before mating and throughout gestation and lactation. The cyanide intake of the adults was about 10 mg  $\text{kg}^{-1}$  bw  $\text{day}^{-1}$ . The offspring were on the same dietary concentration for 28 days after weaning (Tewe and Maner, 1981). In a Japanese study, a dose of 0.05 mg  $\text{kg}^{-1}$  bw  $\text{day}^{-1}$  of cyanide in the drinking water of rats decreased the fertility rate and survival of the second generation and produced a 100% mortality in the third generation (Amo, 1973). The USEPA noted that these data “are not consistent with the body of available literature” (USEPA, 2001).

## 4 Carcinogenicity

- 4.1 There are no human or animal data available on the carcinogenicity of cyanide.
- 4.2 The International Agency for Research on Cancer (IARC) has not considered cyanide. The USEPA considers that it is not classifiable as a carcinogen (USEPA, 1985, 2001).

## 5 Derivation of a tolerable daily intake

### The recommendations of JECFA

- 5.1 In their 25th report, the Joint FAO/WHO Expert Committee on Food Additives (JECFA) evaluated cyanide that occurs naturally in certain flavouring agents, particularly those derived from the fruits and other parts of *Prunus* species (WHO, 1981). The Committee decided that hydrogen cyanide and its salts should not be used as food additives, and that the amount of cyanide in finished foods as the result of using natural flavouring agents containing cyanide should be kept to the lowest level necessary to achieve the desired organoleptic effect. JECFA did not produce a toxicological monograph, but referred to an earlier one prepared by a WHO expert group on pesticides, which in 1965 had evaluated hydrogen cyanide as a food fumigant. At that time, an acceptable daily intake for humans of cyanide arising from the fumigation of food was said to be  $0.05 \text{ mg kg}^{-1} \text{ bw}$ , and was based on the findings of Howard and Hanzal (1955), which were described as showing a “maximum no-effect” level of  $5 \text{ mg kg}^{-1} \text{ bw day}^{-1}$ .

### The WHO guidelines for drinking-water quality

- 5.2 A WHO Review Group (WHO, 1996) noted that “there are a very limited number of toxicological studies suitable for use in deriving a guideline value”, and that there was some indication “that pigs might be more sensitive than rats”. The LOAEL of  $1.2 \text{ mg CN kg}^{-1} \text{ bw day}^{-1}$  reported in the pig study of Jackson (1988) and an uncertainty factor of 100, consisting of factors of 10 each for inter- and intra-species variation, was used to derive a TDI of  $12 \mu\text{g kg}^{-1} \text{ bw}$ . The top dose was described by the Review Group as a “clear effect level” but “because of doubts over the biological significance of the observed changes”, the additional factor of 10 normally used when basing a TDI on a LOAEL rather than a NOAEL was not considered necessary.
- 5.3 As exposure to other sources of cyanide was said to be generally small, a 20% allocation of the TDI to drinking water was made, resulting in a guideline value of  $70 \mu\text{g L}^{-1}$ , which was considered protective of both acute and chronic exposure.

### The recommendations of the USEPA

- 5.4 The USEPA (2001) derived an oral reference dose (RfD) for hydrogen cyanide and its sodium, potassium, calcium, silver and zinc salts of  $20 \mu\text{g CN kg}^{-1} \text{ bw day}^{-1}$ . This was based upon the rat studies of Howard and Hanzal (1955) and Philbrick *et al* (1979) (paragraphs 3.10 and 3.11). In the two-year feeding study of Howard and Hanzal, no signs of toxicity were found at the maximum tested dose, said by the USEPA to be  $10.8 \text{ mg kg}^{-1} \text{ bw day}^{-1}$ , which was therefore designated as the NOAEL. The introduction of an uncertainty factor of 100, consisting of factors of 10 each for species extrapolation and to protect sensitive populations, and a further “modifying factor” of 5, produced the RfD. The modifying factor was used “to account for the apparent tolerance to cyanide when it is ingested with food rather than when it is administered by gavage or by drinking water”. The USEPA assigned a “medium” degree of confidence in the RfD, as ideally the database on free cyanide needed strengthening with additional chronic/reproductive studies.
- 5.5 The RfD for insoluble cuprous cyanide was based upon the 90-day gavage study in rats (USEPA, 1986). An uncertainty factor of 1000, composed of factors of 10 each for intra- and inter-species variation and 10 for extrapolation of a chronic limit from sub-chronic data, was applied to the NOAEL of  $5 \text{ mg kg}^{-1} \text{ bw day}^{-1}$  to arrive at an RfD of  $5 \mu\text{g kg}^{-1} \text{ bw day}^{-1}$  for cuprous cyanide.
- 5.6 The study of El Ghawabi *et al* (1975) (paragraph 3.16) was used by the USEPA (2001) to derive a reference dose (RfC) for chronic inhalation exposure to hydrogen cyanide. The lowest mean concentration of hydrogen cyanide of  $7 \text{ mg m}^{-3}$  observed in the factories studied was designated as a LOAEL. This concentration was converted from an occupational exposure to one relevant for chronic exposure by the general public (by correcting for the ratio of the daily respiratory volume at work to that for the entire day,  $10 \text{ m}^3$  compared to  $20 \text{ m}^3$ , and for the working week of 5 days to the 7 days applicable to the general population). To the resulting concentration of  $2.5 \text{ mg m}^{-3}$ , an uncertainty factor was applied to arrive (after rounding) at the RfC of  $3 \mu\text{g m}^{-3}$ . The uncertainty factor was composed of a factor of 10 for inter-individual variation, 10 for the lack of a NOAEL, 3 for the lack of multigenerational reproduction studies, and 3 for the key study being less than chronic duration.

### The recommendations of the ATSDR

- 5.7 The ATSDR (1997) derived an MRL (minimal risk level) for oral exposure of up to one year to cyanide from the 13-week drinking-water study of sodium cyanide conducted by the NTP (1993) (paragraph 3.12). Based upon the effects on the testes and sperm of the rats,  $12.5 \text{ mg CN kg}^{-1} \text{ bw day}^{-1}$  was identified as a LOAEL, with  $4.5 \text{ mg kg}^{-1} \text{ bw day}^{-1}$  considered the NOAEL. An uncertainty factor of 100, consisting of factors of 10 each for inter- and intra-species variability, and rounding was used to arrive at the MRL of  $50 \mu\text{g kg}^{-1} \text{ bw day}^{-1}$ .
- 5.8 No MRL was derived for chronic cyanide exposure because of the limitations of the oral database. The human studies of cassava eaters lacked quantitative information on exposure, and the only available chronic oral study in rats (Howard and Hanzal, 1955) was considered unsuitable because it “found no treatment related effects”.

- 5.9 The limitations in the available information on the inhalation toxicology of cyanide precluded the derivation of any inhalation MRLs. The occupational study by El Ghawabi *et al* (1975) was discounted because the workers may have been exposed to other chemicals.

## Conclusions

- 5.10 The 13-week rat study conducted under the NTP programme was the study favoured by the ATSDR, which used an uncertainty factor of 100 and the NOAEL of  $4.5 \text{ mg CN kg}^{-1} \text{ bw day}^{-1}$  to derive “an intermediate duration” MRL. An additional uncertainty factor of 3, to take account of the fact that sub-chronic study was used to estimate a safety limit relevant to chronic exposure, would produce a  $\text{TDI}_{\text{oral}}$  of  $15 \mu\text{g CN kg}^{-1} \text{ bw}$ .
- 5.11 The only published report of a chronic feeding study on cyanide, that of Howard and Hanzal (1955), was used by the USEPA as the basis of their RfD. The statistical power of this poorly reported study is probably very low, as only a small (and unspecified) number of the treated rats were examined in any detail. An additional problem is an uncertainty over the exact dose delivered to the animals. In both respects, the NTP experiment (and report) is a firmer basis for the estimation of a TDI.
- 5.12 The WHO believed “there is some indication” that the pig is more sensitive to cyanide’s toxicity than the rat, and therefore favoured the pig study of Jackson (1988) in the derivation of a TDI of  $12 \mu\text{g CN kg}^{-1} \text{ bw}$ . The study, with group sizes of only three, suffers from a lack of statistical power, and both the WHO and the investigator herself have expressed doubt as to whether the effects observed have a relevance to humans. Despite these weaknesses the TDI estimated by the WHO is in good agreement with that derived above from the NTP study, and is chosen here as the  $\text{TDI}_{\text{oral}}$ .
- 5.13 There are few studies upon which a TDI for exposure by inhalation might be based. Most inhalation studies have involved either acute or very short-term exposure. The extensive metabolism of cyanide in the liver, and therefore the importance of the first-pass effect, means that it would not be appropriate to extrapolate from oral studies. The best available study of the effect of the inhalation of cyanide is the occupational study of El Ghawabi *et al* (1975), which was used by the USEPA in deriving their RfC.
- 5.14 Based upon their RfC for hydrogen cyanide of  $3 \mu\text{g m}^{-3}$ , an inhalation volume of  $20 \text{ m}^3$  and an adult body weight of  $70 \text{ kg}$ , the recommended inhalation  $\text{TDI}_{\text{inh}}$  is  $0.9 \mu\text{g CN kg}^{-1} \text{ bw day}^{-1}$ .
- 5.15 The recommended TDIs are for “free”, soluble cyanides. Thus the USEPA study on the insoluble copper cyanide (paragraph 3.14) is not relevant here.
- 5.16 Not all cyanide at a contaminated site may be in the form of free cyanide, and therefore guidelines based upon free cyanide should not be used for total cyanide content (see paragraph 2.8).
- 5.17 The TDIs derived here are appropriate for chronic exposure. When assessing the risks from contaminated soils, it will also be necessary to take account of the risks from short-term exposure to inorganic cyanide, which may be important given its acute toxicity. The lowest

reported fatal oral dose for humans is  $0.56 \text{ mg CN kg}^{-1} \text{ bw}$ , which is nearly 50 times greater than the recommended  $\text{TDI}_{\text{oral}}$  of  $12 \mu\text{g CN kg}^{-1} \text{ bw}$ . Given the steepness of the dose–response curve for acute exposure, and the speed and efficiency of detoxification (see references in paragraph 3.1), ingestion of a bolus dose of cyanide equivalent to the TDI would not be expected to cause any acute toxicity.

## 6 The intake of cyanide from food, water and air

- 6.1 The major source of cyanide in food is cyanogenic glycosides, the most notable example being cassava, which is only important for some tropical diets. The other edible plants that can provide hydrogen cyanide include: almonds and pits from stone fruits, soybeans, spinach, lima (broad) beans, maize, millet and sweet potatoes. Reported levels of cyanide include: soy protein products,  $0.07\text{--}0.3\ \mu\text{g g}^{-1}$ ; cereal grains and products,  $0.001\text{--}0.45\ \mu\text{g g}^{-1}$ ; lima beans,  $0.1\text{--}3\ \mu\text{g g}^{-1}$ ; and canned unpitted fruits,  $0\text{--}4\ \mu\text{g g}^{-1}$  (ATSDR, 1997).
- 6.2 The Flavourings in Food Regulations 1992 (Statutory Instrument, 1992) limit the concentration of HCN in food to which flavourings have been added. The limit is  $1\ \text{mg kg}^{-1}$ , except for: nougat and marzipan at  $50\ \text{mg kg}^{-1}$ , tinned stone fruit at  $5\ \text{mg kg}^{-1}$ , and alcoholic drinks at  $1\ \text{mg kg}^{-1}$  for each 1% of alcohol by volume.
- 6.3 If foods were eaten which contained the maximum allowable concentration of cyanide according to The Flavourings in Food Regulations 1992, 1 mg of cyanide would be provided by 20 g of marzipan or 200 g of tinned plums. One standard measure of a plum brandy at the limit would provide over 5 mg of cyanide.
- 6.4 There are no total diet data for cyanide, and as cooking destroys most of the small amounts of cyanide present, the intake in normal diets is expected to be quite low (WHO, 1984a), and difficult to estimate.
- 6.5 The Ministry of Agriculture, Fisheries and Food (MAFF, 1998) has made an estimate of cyanide intake for the Council of Europe's Committee of Experts on Flavouring Substances. The consumption figures were based on the British Adults Study (MAFF, 1990), which was a seven-day weighted diary study of 2197 adults in private households. Two intake estimates were calculated: one based upon the maximum concentrations permitted in the regulations; the other on levels actually reported in the scientific literature and from industry. For the worst-case scenario, the mean and 97.5th percentile consumer intakes were calculated to be  $6.02$  and  $37.0\ \mu\text{g kg}^{-1}\ \text{bw day}^{-1}$  respectively. Using the actual data, the mean and 97.5th percentile intakes were estimated to be about  $4.2$  and  $28\ \mu\text{g kg}^{-1}\ \text{bw day}^{-1}$ .
- 6.6 Based upon the available concentration data, the mean daily intake (MDI) for an adult weighing 70 kg is accordingly estimated to be about  $300\ \mu\text{g day}^{-1}$ . For a six-year-old child, ingesting 62% of the adult dietary intake (DEFRA and Environment Agency, 2002a), the MDI would be about  $190\ \mu\text{g day}^{-1}$ . While these estimates are not based upon actual measured cyanide intakes by British adults, they are the best available estimates of average dietary intake of cyanide. The recommended TDIs would allow for the occasional ingestion of Christmas cake or tinned plums at the statutory maximum cyanide concentrations.
- 6.7 Chlorination of potable waters at neutral or alkaline pH will reduce cyanide concentrations to very low levels (WHO, 1984b), though the levels will depend upon the choice of final disinfectant. Cyanogen chloride (CNCl) is formed by the reaction of humic substances with chloramine. When it is used as the disinfectant, the levels of cyanogen chloride in drinking water are found to be 4–15 times those found when chlorine is used as the disinfectant. One

study of 35 water suppliers in the USA reported median cyanogen chloride concentrations of 0.45–0.80  $\mu\text{g L}^{-1}$  (ATSDR, 1997).

- 6.8 In one report, the mean cyanide concentration of most surface waters in the USA was less than 3.5  $\mu\text{g L}^{-1}$ ; another study reported a range of less than 5 to 80  $\mu\text{g L}^{-1}$  (ATSDR, 1997).
- 6.9 Based upon the reported concentration of cyanide in non-urban air of about 190  $\text{ng m}^{-3}$  (ATSDR, 1997), the daily intake of a non-smoking adult breathing 20  $\text{m}^3 \text{day}^{-1}$  would be about 0.06  $\mu\text{g kg}^{-1} \text{bw day}^{-1}$ .

## 7 Other sources

- 7.1 Cigarette smoke contains cyanide, and the effects of heavy smoking have been mentioned above. The levels of cyanide in tobacco smoke vary considerably, with reports of 10 to 550  $\mu\text{g}$  per cigarette for the inhaled smoke, with up to half the concentration found in the non-inhaled or sidestream smoke (ATSDR, 1997).
- 7.2 The supposed cancer cure laetrile is made from apricot stones, and contains amygdalin, which can be broken down yielding benzaldehyde and HCN. A number of cases of serious toxicity and several deaths have resulted from the ingestion of laetrile (Bowman and Rand, 1980; Way, 1984; Smith, 1996).
- 7.3 Malfunctioning catalytic converters can produce HCN, as does the combustion of various plastics such as polyurethane (Way, 1984). This can present a serious hazard to firemen and others exposed to smoke from both domestic and commercial premises.

## 8 Conclusions

- 8.1 Tolerable daily intakes derived from oral and inhalation studies (that is,  $\text{TDI}_{\text{oral}}$  and  $\text{TDI}_{\text{inh}}$ ) of free, soluble cyanides and the oral and inhaled mean daily intakes (MDIs) are summarised in Tables 8.1 and 8.2.
- 8.2 The oral tolerable daily soil intake (TDSI) is defined as the difference between the  $\text{TDI}_{\text{oral}}$  and the oral MDI ( $\text{TDI} - \text{MDI}$ ). As an example, the MDI for a 70 kg adult is equivalent to 4.2  $\mu\text{g kg}^{-1} \text{ bw day}^{-1}$  and therefore the TDSI would correspond to 7.8  $\mu\text{g kg}^{-1} \text{ bw day}^{-1}$ . Similarly, for a 20 kg child (aged six) who ingests 62% of the adult dietary intake, the TDSI would be 2.7  $\mu\text{g kg}^{-1} \text{ bw day}^{-1}$  (see DEFRA and Environment Agency, 2002a, for further details).

**Table 8.1  $\text{TDI}_{\text{oral}}$ , oral MDI and TDSI for an adult and six-year-old child**

| $\text{TDI}_{\text{oral}}$<br>( $\mu\text{g kg}^{-1} \text{ bw day}^{-1}$ ) | Oral MDI<br>( $\mu\text{g day}^{-1}$ ) | TDSI for an adult<br>( $\mu\text{g kg}^{-1} \text{ bw day}^{-1}$ ) | TDSI for six-year-old child<br>( $\mu\text{g kg}^{-1} \text{ bw day}^{-1}$ ) |
|---|--|--|--|
| 12  | 300                                    | 7.8  | 2.7  |

- 8.3 The recommended inhalation TDI for an adult is 0.9  $\mu\text{g kg}^{-1} \text{ bw}$ . The approximate inhalation MDI for a non-smoker is 0.06  $\mu\text{g kg}^{-1} \text{ bw}$ . A regular smoker would easily exceed the  $\text{TDI}_{\text{inh}}$ .

**Table 8.2 TDI<sub>inh</sub> and inhaled MDI**

| <b>TDI<sub>inh</sub></b><br><b>(<math>\mu\text{g kg}^{-1} \text{ bw day}^{-1}</math>)</b> | <b>Inhaled MDI</b><br><b>(<math>\mu\text{g day}^{-1}</math>)</b> |
|---|--|
| 0.9   | 0.06   |

8.5 The TDIs are derived for chronic exposure to free cyanide. As cyanide has a high acute toxicity, short-term exposure may be an important consideration when assessing the risks from soils contaminated with cyanide (see DEFRA and Environment Agency, 2002b, for further detail).

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