



INFOTOX (Pty) Ltd

Established 1991

Retrieval and scientific interpretation of ecotoxicological information

P O Box 98092 Waterkloof Heights 0065 SOUTH AFRICA

Tel: (012) 346 4668 Fax: (012) 460 0650 Cell: 082 416 5864

e-mail: info@infotox.co.za

**Prepared on behalf of Marsh Environmental Services
A Division of Marsh Vikela (Pty) Ltd**

Community Health Risk Assessment The Proposed Co-processing of Secondary Materials in Cement Kilns at PPC Dwaalboom

Report No 074-2007 Rev 1.0

**W C A van Niekerk PhD QEP (USA) Pr Sci Nat (Environmental Science)
M H Fourie PhD HPCSA (Medical Biological Scientist)
G Mouton BA (Social Science)**

October 2007

Copyright Warning and Intellectual Property

Copyright of all text and other matter in this document, including the manner of presentation, is the exclusive property of INFOTOX (Pty) Ltd. It is a criminal offence to publish this document or any part of the document under a different cover, or to reproduce and/or use, without written consent, any technical procedure and/or technique contained in this document. The intellectual property reflected in the contents resides with INFOTOX (Pty) Ltd and shall not be used for any project or activity that does not involve INFOTOX (Pty) Ltd, without the written consent of INFOTOX (Pty) Ltd.

This report has been prepared by INFOTOX (Pty) Ltd with all reasonable skill, care and diligence within the terms of the Agreement with the Client. The report is confidential to the client and INFOTOX (Pty) Ltd accepts no responsibility of whatsoever nature to third parties whom this report, or any part thereof, is made known. Any such parties rely upon the report at their own risk.



12 October 2007

Executive summary

The cement factory of PPC Dwaalboom (PE) was commissioned in 1928 and is situated approximately 3 km southwest of Dwaalboom in the North West Province. Currently, the factory manufactures Ordinary Portland Cement (OPC) and Surebuild cement. The plant consists of one long dry rotary kiln, which is not equipped with a pre-heater. The clinker is cooled by a planetary cooler. All of the exhaust gas streams, i.e. from the raw mill, finishing mill and kiln, pass through electrostatic precipitators (ESPs) to minimise dust emissions from the factory.

Investigations have been conducted to assess potential health impacts associated with air emissions of the existing coal-fired operations on neighbouring communities and to estimate potential health impacts when coal is replaced with alternative fuels. The emissions inventory for the existing and proposed plant operations was provided by Marsh Environmental Services, a division of Marsh Vikela (Pty) Ltd. These emission rates were subsequently used by Airshed Planning Professionals (Pty) Ltd in dispersion simulations to determine ambient air concentrations of airborne substances in residential areas in the proximity of the PPC factory. Sources of pollutants included the Dwaalboom Stack Kilns 1 and 2, stockpiles, vehicle entrainment from paved and unpaved roads, and mining operations. Dispersion simulations were undertaken for two scenarios at PPC Dwaalboom namely:

- Scenario A: Current operating conditions at PPC Dwaalboom (excluding background concentrations); and
- Scenario B: Future operations at PPC Dwaalboom including the usage of secondary materials (excluding background concentrations).

INFOTOX (Pty) Ltd was commissioned by Marsh Environmental Services to conduct a human health risk assessment on the basis of the simulated air concentration data. The scope of the investigation was limited to generic exposure scenarios, not taking specific characteristics of the population into account. This report presents the results of cancer and noncancer risk assessment, including a statement of uncertainties. It also presents a review of cancer unit risk factors and noncancer reference concentrations from the latest international peer-reviewed literature.

The main pollutants of concern resulting from current operations at PPC Dwaalboom include SO₂, NO₂, CO, HCl, HF, As, heavy metals and dioxins from the two kilns, and PM₁₀ (particulates with aerodynamic diameter equal to or smaller than 10 µm) and total suspended particulates (TSP). Annexure 1 of this report describes an overview of toxicological properties of the substances of interest and provides background data in support of the selection of guideline concentrations that were used in the assessment.

The study initiated by Marsh Environmental Services has indicated that co-processing of secondary materials as fuels in cement kilns at PPC Dwaalboom would not lead to any noteworthy changes in emissions of hazardous substances from the operations. Therefore, based on the assumptions that underlie the study and the available data on the air pathway of exposure, there would be no difference between current health risks associated with the PPC production plant and the scenario where alternative fuels would substitute coal as the energy source for fuelling the kiln.

The human health risk assessment has been based on the assumption that emissions of toxic substances from the PPC factory would not exceed internationally-acceptable emission

guidelines. This would however depend on the characteristics of the kiln and other auxiliary equipment at the factory. Generally, the efficiency of a kiln in combusting fuels that contain organic substances is expressed as a DRE (destruction and removal efficiency) value. This has to be obtained through a trial burn, which entails the demonstration that a facility is in compliance with regulatory requirements.

Furthermore, there has to be acceptance criteria for alternative fuels with regard to maximum permissible levels of halogens, metalloids and metals. The current human health risk assessment has assumed that these considerations have been, or will be, covered in the overall alternative fuels assessment for the PPC Dwaalboom factory. The assumption that stack emission guidelines will be met can be justified more fully when acceptance criteria have been developed for alternative fuels. The current dispersion modelling and risk assessment have been limited to the demonstration that operation within the respective stack emission guidelines would not lead to unacceptable risks through the air pathway of exposure. This is not surprising, because there is a tacit assumption in the setting of stack emission guidelines that these would be protective to human health within a large margin of safety.

It should be noted that the assessment has been based only on the air pathway of exposure. However, there are other factors that have to be considered. Mercury, for example, is a global issue and the introduction of alternative fuels should not increase releases of mercury. Also, the primary concern about lead is not exposure through inhalation, but ingestion of lead by children. Should the alternative fuels programme release more lead into the environment than the current operations, deposition of lead and its contribution to house dust in residential areas might lead to unacceptable risks to children, even at modelled air concentrations that might be acceptable for the inhalation route of exposure. Cadmium should be considered on the same basis.

Table of contents

1	Introduction	1
2	The risk assessment process.....	2
3	Hazard identification.....	5
4	Toxicological assessment	6
4.1	Hospitalisation rates and mortality.....	6
4.2	Toxicological parameters for carcinogens and systemic toxicants	8
5	Exposure assessment.....	10
5.1	The study area	10
5.2	Summary of modelled air concentrations.....	11
6	Human health risk assessment	13
7	Human health risk interpretation	15
8	Uncertainty analysis	16
9	Conclusions and recommendations	16
10	References.....	17
Annexure 1		
1	Particulates	20
2	Carbon monoxide (CO)	22
3	Sulphur dioxide (SO ₂).....	24
4	Nitrogen oxides (NO _x)	26
5	Hydrochloric acid.....	28
5.1	Acute toxicity	28
5.2	Chronic toxicity.....	28
6	Hydrofluoric acid	29
6.1	Acute toxicity	29
6.2	Chronic toxicity.....	29
7	Antimony	30
7.1	Cancer risk assessment	30
7.2	Noncancer risk assessment	30
8	Arsenic	31
8.1	Cancer risk assessment	31
8.2	Noncancer risk assessment	31
9	Cadmium.....	32
9.1	Cancer risk assessment	32
9.2	Noncancer risk assessment	32
10	Chromium.....	33
10.1	Cancer risk assessment	33
10.2	Noncancer risk assessment	33

11	Cobalt.....	34
11.1	Cancer risk assessment	34
11.2	Noncancer risk assessment	34
12	Copper	35
12.1	Cancer risk assessment	35
12.2	Noncancer risk assessment	35
13	Lead	36
13.1	Cancer risk assessment	36
13.2	Noncancer risk assessment	36
14	Manganese	38
14.1	Cancer risk assessment	38
14.2	Noncancer risk assessment	38
15	Mercury	40
15.1	Cancer risk assessment	40
15.2	Noncancer risk assessment	40
16	Nickel	41
16.1	Cancer risk assessment	41
16.2	Noncancer risk assessment	42
17	Vanadium pentoxide	43
17.1	Cancer risk assessment	43
17.2	Noncancer risk assessment	43
18	Polychlorinated dioxins, furans and PCBs	44
18.1	Cancer risk assessment	44
18.2	Noncancer risk assessment	45
19	References.....	45

List of tables

Table 4.2.1:	Summary of toxicological parameters of carcinogens and noncarcinogens for use in health risk quantification.	9
Table 5.2.1:	Summary of modelled air concentrations for gases, metalloids, metals and dioxins for the current operations.	11
Table 5.2.2:	Summary of modelled air concentrations for gases, metalloids, metals and dioxins for the proposed operations with co-processing of secondary materials.	12
Table 6.1:	Summary of exposure levels for gaseous pollutants for scenario A.	13
Table 6.2:	Summary of exposure levels for gaseous pollutants for scenario B.	13
Table 6.3:	Summary of risk assessment for metalloids, metals and dioxins for Scenario B.	14

List of figures

Figure 1.1:	Study area for the community health risk assessment associated with emissions from the PPC Dwaalboom cement factory (Liebenberg-Enslin and Olivier, 2007).	1
Figure 5.1.1:	Location of sensitive receptors in relation to the PPC Dwaalboom cement factory.	10

1 Introduction

The PPC Dwaalboom cement factory was commissioned in 1984. It is located in the North West Province approximately 60 km west-southwest of Thabazimbi. There is currently one coal-fired kiln in operation at PPC Dwaalboom. A second kiln is under construction. All of the exhaust gas streams pass through electrostatic precipitators (ESPs) to minimise dust emissions from the factory. Limestone is mined at the on-site quarry and transported via truck to the processing plant.



Figure 1.1: Study area for the community health risk assessment associated with emissions from the PPC Dwaalboom cement factory (Liebenberg-Enslin and Olivier, 2007).

Investigations were initiated to assess potential health impacts associated with air emissions of the existing coal-fired operations on neighbouring communities and to estimate potential health impacts when coal is replaced with alternative fuels. The emissions inventory for the existing and proposed plant operations was provided by Marsh Environmental Services, a division of Marsh Vikela (Pty) Ltd. These emission rates were subsequently used by Airshed Planning Professionals (Pty) Ltd in dispersion simulations to determine ambient air concentrations of airborne substances in residential areas in the proximity of the PPC factory.

The following sources of pollutants were included:

- Dwaalboom Stack Kiln 1 (existing);
- Dwaalboom Stack Kiln 2 (under construction);
- Stockpiles;
- Vehicle entrainment from paved and unpaved roads; and
- Mining operations.

Dispersion simulations were undertaken for two scenarios at PPC Dwaalboom namely:

- Scenario A: Current operating conditions at PPC Dwaalboom (excluding background concentrations); and
- Scenario B: Future operations at PPC Dwaalboom including the usage of secondary materials (excluding background concentrations).

“Background concentrations” refer to the current status of ambient air in the region. No ambient monitoring data were available for the region and no information on the emission rates from sources in the vicinity of PPC Dwaalboom was available. The scenarios simulated are therefore for PPC operations only. There are however no significant sources of atmospheric emissions in the vicinity of PPC Dwaalboom and the modelled ambient air concentrations can be regarded as a close reflection of actual air quality.

INFOTOX (Pty) Ltd was commissioned by Marsh Environmental Services to conduct a human health risk assessment on the basis of the simulated air concentration data. The scope of the investigation was limited to generic exposure scenarios, not taking specific characteristics of the population into account. This report presents the results of cancer and noncancer risk assessment, including a statement of uncertainties. It also presents a review of cancer unit risk factors and noncancer reference concentrations from the latest international peer-reviewed literature.

2 The risk assessment process

The original paradigm for regulatory human health risk assessment in the USA was developed by the USA National Research Council (NRC, 1983). This model has been adopted and refined by the US Environmental Protection Agency (USEPA) and other agencies in the world as published under the International Programme on Chemical Safety (IPCS, 1999) and is widely used for quantitative health risk assessments. The paradigm essentially divides human health risk assessment into a number of logical steps, as is outlined below.

- **Hazard assessment** is the identification of chemical and biological contaminants suspected to pose hazards and a description of the types of toxicity that they may evoke. Coal is the most common fuel used in the cement industry. Similar to the raw materials used in the manufacture of cement, coal can contain significant quantities of metals and halogens. Alternative fuels may contain higher or lower concentrations of these substances, and may contain compounds that could lead to different combustion products. The hazard assessment step has to identify these substances of interest. This part of the current study was conducted by Marsh Environmental Services.

- **Toxicological assessment** (dose-response assessment) addresses the relationship between levels of biological exposure and the manifestation of adverse health effects in humans, and/or how humans can be expected to respond to different doses or concentrations of contaminants. This is a quantitative assessment that distinguishes between carcinogens and noncarcinogens. Risk quantification for airborne carcinogens uses a cancer unit risk factor for each substance, whereas risks to noncarcinogens are characterised against reference concentrations (RfCs) or tolerable concentrations in air (TCAs).

The cancer unit risk factor (IRIS, 2006a) for inhalation is an upper-bound excess lifetime cancer risk estimated to result from continuous exposure to an agent at a concentration of 1 $\mu\text{g}/\text{m}^3$ in air. The interpretation of unit risk would be as follows: if unit risk = 2×10^{-6} per $\mu\text{g}/\text{m}^3$ [$(\mu\text{g}/\text{m}^3)^{-1}$], 2 excess cancer cases (upper bound estimate) are expected to develop per 1 000 000 people if exposed daily for a lifetime to 1 μg of the chemical in 1 m^3 of air.

USEPA defines a reference concentration (RfC) (IRIS, 2006a) as *an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. It can be derived from a no-observed-adverse-effect level (NOAEL), a lowest-observed-adverse-effect level (LOAEL), or benchmark concentration, with uncertainty factors generally applied to reflect limitations of the data used.* RfCs are generally used in noncancer health-risk assessments. Their primary use is to evaluate increments of exposure from specific sources when background exposures are low. Exceedence of the RfC is not a statement of risk. The term tolerable concentration in air (TCA) has a meaning similar to the RfC, describing a threshold concentration (IPCS, 1999).

RfCs and TCAs are useful because they represent a health risk goal below which there is likely to be no appreciable risk of noncancer effects over a lifetime of exposure.

Cancer unit risk factors and reference concentrations (or tolerable concentrations in air) have to be obtained from credible peer reviewed sources and the validity of the values has to be assessed prior to application in risk assessment. Annexure 1 of this report provides INFOTOX reviews of the available toxicological and epidemiological information that support the selected risk parameters.

- **Exposure assessment** includes a description of the environmental pathways and distribution of hazardous substances, identification of potentially exposed individuals or communities, the routes of direct and indirect exposure, and an estimate of concentrations and duration of the exposure. In screening health risk assessments, potentially affected communities may be identified, but the quantification of exposure is generic. That is, specific community characteristics are not identified or considered. For the assessment of airborne contaminants, the inhalation route of exposure is the only consideration. Indirect pathways of exposure may be referred to, but are not included in exposure quantification at the screening level, which has been the scope of this INFOTOX report. Airshed Planning Professionals (Pty) Ltd has provided air concentrations of substances for interpretation of community exposures (Liebenberg-Enslin and Olivier, 2007).

- **Risk characterisation** involves the integration of the components described above, with the purpose of determining whether specific exposures to an individual or a community might lead to adverse health effects.

Cancer risk is expressed as a unitless number, e.g. 1×10^{-5} or in scientific notation, 1.0E-05, indicating one cancer case in a population of a hundred thousand. The calculations refer to excess risk, i.e. risks due to exposure to the particular substance, over and above the background cancer risks that members of the community may be subjected to. In the calculation of cancer risk according to the USEPA paradigm (USEPA, 1989) all cancer risks from the individual carcinogens are added, irrespective of target organ, across all pathways and routes of exposure.

The cancer risk for exposure to a particular compound i through inhalation is calculated according to Equation 2.1:

$$Risk_i = UF_i \times C_i \quad (2.1)$$

Where:

Risk _{<i>i</i>}	Refers to excess cancer risk associated with exposure to substance <i>i</i>
UF _{<i>i</i>}	Inhalation unit risk factor for substance <i>i</i>
C _{<i>i</i>}	Concentration of the substance in air

The risk of exposure to noncarcinogens is expressed through a hazard quotient (HQ), which is the exposure concentration averaged over the period of exposure divided by the reference concentration or tolerable concentration in air. Where a HQ exceeds 1, health effects may occur and the situation requires further investigation.

$$HQ_i = \frac{C_i}{(RfC_i \text{ or } TCA_i)} \quad (2.2)$$

Where:

HQ _{<i>i</i>}	Hazard quotient for a particular substance <i>i</i>
C _{<i>i</i>}	Exposure concentration for substance <i>i</i>
RfC _{<i>i</i>} or TCA _{<i>i</i>}	Reference concentration or tolerable concentration of the substance in air

In the assessment of exposure to multiple chemicals, hazard quotients are added for those substances that have effects on the same target organ system. The addition of hazard quotients for a particular exposure scenario assumes that the mixture of components additively act on a common biological target by a common mechanism or mode of action, and that less-than-additive (e.g., antagonistic interactions) or greater-than-additive (e.g., synergism or potentiation) interactions, do not occur among the components of the mixture. The sum of the hazard quotients is then expressed as a hazard index.

As exposure levels approach threshold levels for toxic effects, a hazard index approach is likely to give a more complete assessment of health hazards than an approach that only examines hazard quotients for individual components in a mixture. The hazard quotients are summed to derive the hazard index for common health effects as follows:

$$HI = HQ_A + HQ_B + HQ_C + \dots \quad (2.3)$$

Where:

HI	Hazard index, a unitless number
HQ _A , etc	HQs of individual substances that act on the same target organ system

- Uncertainty analysis** identifies the nature and, when possible, the magnitude of the uncertainty and variability inherent in the characterisation of risks. The results of any risk assessment reflect scientific uncertainty associated with limitations in available data and assumptions that are made in the absence of such data, and the variability in exposure and toxicological response expected, given the diversity within the human population. The assumptions and limitations that form part of all risk characterisations should be explicitly discussed. Uncertainty analysis demonstrates the level of confidence in the outcome of the risk assessment and indicates whether additional data might be required, or whether elements of the precautionary principle should be applied.

3 Hazard identification

The main pollutants of concern resulting from current operations at PPC Dwaalboom are sulphur dioxide (SO₂), nitrogen oxides (NO_x), PM₁₀ (particulates with aerodynamic diameter equal to or smaller than 10 µm), total suspended particulates (TSP), carbon monoxide (CO), and the halogen compounds hydrochloric acid (HCl) and hydrofluoric acid (HF). The assessment of future operations included additional pollutants, viz. arsenic and heavy metals, total organic carbon and dioxins.

The emissions inventory of substances that are relevant to burning of coal and alternative fuels in cement kilns was provided by Marsh Environmental Services. These substances have been reviewed for toxicological properties and summaries are presented in Annexure 1 of this report. Total suspended particulates are monitored in the environment for pollution management purposes and generally TSP levels are not assessed in terms of potential impacts on human health. Similarly, the measurement of total organic carbon is not compound-specific and cannot be used in health risk assessment. Thallium (Tl) was not included in the reviews because it is of low significance in cement kiln emissions and very little has been documented on its toxicity.

Comparison of ambient air concentrations of airborne substances against air quality guidelines or standards forms part of the hazard identification step in the risk assessment paradigm. Exceedence of an air quality guideline or standard in itself is not a statement of risk, but it indicates in a qualitative manner that the situation requires assessment of potential risk in more detail. Clearly, in the case of large exceedences of guidelines or standards, immediate corrective action should be triggered.

It should be noted that ambient air quality guidelines are not always based entirely on health-risk considerations and in many cases these cannot be used as surrogates for reference

concentrations or tolerable concentrations in air, as is understood in risk assessment terminology (see Section 2 above). Furthermore, some of the air quality standards of states in the USA, in particular, have questionable scientific basis. These have simply been derived by dividing occupational exposure limits by arbitrary numbers, which cannot be justified scientifically. Any discussion of air quality guidelines or standards that may be considered in the assessment of environmental impact (e.g. in an environmental impact assessment) if relevant, should lead to the selection of preferred guideline concentrations, based on assessment of the underlying data and science that support the standard or guideline.

The South African Department of Environmental Affairs and Tourism (DEAT) have issued ambient air quality guidelines to support receiving environmental management practices. These have been adopted as standards in the Air Quality Act but are currently under revision (SANS, 2003). The local ambient air quality standards are available for criteria pollutants that are commonly emitted, such as sulphur dioxide (SO₂), lead (Pb), oxides of nitrogen (NO_x), carbon monoxide (CO) and particulates. A review of air quality guidelines and standards has been documented by Liebenberg-Enslin and Olivier (2007).

4 Toxicological assessment

4.1 Hospitalisation rates and mortality

Assessment of health risks associated with exposure to carcinogens and systemic toxicants is normally conducted on the basis of documented toxicological information on cancer slope factors (or inhalation unit risk factors) and noncancer reference doses or reference concentrations in the low exposure region. The fundamental understanding in these assessments is that the likelihood of adverse health effects occurring at exposures below the risk-based concentrations is remote, as has been outlined in the USEPA definitions presented in Section 2 above. In the case of contaminants that are abundant in ambient air, the use of reference concentrations as defined by USEPA (as well as similar guidance by other agencies) to assess potential impacts of industrial sources has limitations, because background concentrations (without considering the sources under investigation) may already have adverse impacts on health. The so-called criteria pollutants are relevant in this regard. These are managed through ambient air quality standards or guidelines.

Air concentrations of compounds that exceed the ambient air quality guidelines and standards indicate that adverse health conditions may develop, but simple comparisons between exposure concentrations and guidelines are inadequate to quantify health outcomes. In general, predicted or measured impacts of industrial emissions on air quality are used as a basis to quantify impacts on health. This is achieved by calculating the potential increase in hospital admissions or in mortality due to specific causes, associated with increased air concentrations of specific toxic compounds. These calculations are based on results of studies reported in the international scientific literature, in which statistical methods were used to compare changes in hospitalisation or mortality rates with changes in air quality.

This process relies on the availability of health data quantifying the risk of health effects associated with changes in air concentrations of relevant compounds. Such health data are obtained through the interpretation of epidemiological studies of environmental exposure to the various compounds. In the case of air pollutants, hospitalisation rates for respiratory or

cardiovascular causes provide a measure of associated illness that is mostly applied in epidemiological studies. It is important to note that it is common to observe increases in hospitalisation rates even when the largest body of the air data do not exceed the environmental air quality guidelines. Estimation of impacts of air pollutants on health may therefore not be restricted to areas in which the guideline concentrations are exceeded, but should also include areas in which concentrations are within limits.

Dab *et al.* (1996) conducted groundbreaking studies on the effects of airborne pollutants on health effects in an average population of 6 140 000 Parisians. The Paris data were registered during the study period of 1987 to 1992, and reflected the effects of several environmental pollutants, including black smoke, particulates, sulphur dioxide, nitrogen dioxide, and ozone. Other studies using large-scale data sets have also shown a fairly consistent relationship between air pollutant levels and respiratory diseases in a variety of communities in the industrialised world. Luginaah *et al.* (2005) and Fung *et al.* (2005) have published the most recent data on the association of ambient air pollution, including NO₂, CO, PM₁₀ and SO₂, with respiratory and cardiovascular hospitalisation rates in the town of Windsor, Ontario, Canada.

The studies by Luginaah *et al.* (2005) and Fung *et al.* (2005) used hospitalisation data available from 1995 through 2000 to quantify the association between ambient air pollution and respiratory hospitalisation, with corrections made for ambient temperature, humidity and change in barometric pressure. The statistical techniques incorporated important modifications in methodology developed since 2002. A significant relationship between the daily maximum concentrations of pollutants and hospital admissions for respiratory disease was shown. The study related increases of pollutant concentrations with the risk of hospital admission. The authors provided relative risk ratios (RRs) for hospitalisation associated with increased pollutant concentrations. The percentage change in the mean number of daily hospitalisations is calculated as $(RR-1) \times 100\%$. The unit of increase of pollutant concentrations used in the statistical analysis was the interquartile range (IQR). The IQR is the difference between the 75th and the 25th percentile of all concentrations of a specific pollutant recorded during the study period. The authors succeeded in developing a statistical model that could predict the percentage change in the mean number of daily hospitalisations based on the size of the increase in air pollutant concentrations.

Studies published prior to 2002 should be reassessed when there is an intention to use these as a basis for the quantification of the observed health effects, because estimates were potentially biased upward (*i.e.*, higher than they should be) due to previously undiscovered errors in some statistical techniques and software packages (Fourie *et al.*, 2006).

The scope of this INFOTOX study did not include a survey of historical and current hospitalisation and death rates for residents in the study area and control areas. Any extrapolations from literature data are thus likely to result in estimations with limited accuracy, due mostly to the perceived differences in socioeconomic status, health status and the accessibility and quality of health care in South Africa as compared to the European, North American and tropical Asian countries (Taiwan) from which the reported studies originated. These limitations could therefore result in either over- or underestimation of the background hospitalisation or death rates in the study area, and subsequently of the absolute numbers of additional daily hospitalisations, or of deaths, associated with measured and predicted air pollutants.

There is thus a fundamental difficulty in using the published relationships between increases in hospitalisation rates and mortality due to various causes for the prediction of the manifestation of such events in relation to air quality data in South Africa. At best, the documented relationships should be used for qualitative interpretations. The approach is nevertheless useful, as it clearly indicates situations where there should be concern over health impacts, although quantitative data may not be available. INFOTOX follows this approach in risk assessment relating to the criteria gaseous pollutants.

4.2 Toxicological parameters for carcinogens and systemic toxicants

Table 4.2.1 provides a summary of toxicological parameters of carcinogens and noncarcinogens for use in health risk quantification. Carbon monoxide was assessed only for its acute effects. Nitrogen dioxide, hydrochloric acid and hydrofluoric acid were assessed for both acute and chronic effects. Sulphur dioxide is assessed against a daily guideline concentration, because epidemiological dose-response information is available for that averaging period. Cancer risk is assessed in terms of exposure averaged over a lifetime, whereas chronic exposure to systemic toxicants is averaged over the period of exposure.

The chemical forms of metal emissions are uncertain and in some cases various possibilities were considered (e.g. nickel). Mercury was considered to be primarily in the form of elemental mercury where the inhalation route was considered; this would provide the most conservative estimate of risk. Vanadium was assessed as the pentoxide, which is the most likely chemical form. V_2O_5 is also the vanadium compound that has been shown to have the most significant adverse health effects. Background information on toxicological parameters is provided in Annexure 1.

Table 4.2.1: Summary of toxicological parameters of carcinogens and noncarcinogens for use in health risk quantification.

Substance	Carcinogens		Noncarcinogens		
	Unit risk	Reference	Guideline	Averaging time	Reference
	($\mu\text{g}/\text{m}^3$) ⁻¹		$\mu\text{g}/\text{m}^3$		
Gaseous pollutants					
PM ₁₀	Not assessed as a carcinogen		50	24-hour	WHO, 2005
			20	Annual	
CO	Not assessed as a carcinogen		30 000	1-hour	WHO, 2000
SO ₂	Not assessed as a carcinogen		20	24-hour	WHO, 2005
NO ₂	Not assessed as a carcinogen		200	1-hour	WHO, 2000; WHO, 2005
			40	Annual	
			RfC or TCA		
			$\mu\text{g}/\text{m}^3$		
HCl	Not assessed as a carcinogen		2 600	1-hour	NRC, 2004
			20	Annual	IRIS, 2006b
HF	Not assessed as a carcinogen		800	1-hour	NRC, 2004
			14	Annual	OEHHA, 2003
Metalloids and metals					
Antimony	Not assessed as a carcinogen		2.0	Annual	USEPA, 2006
Arsenic ¹	4.3E-03	IRIS, 2006c	1.0	Cancer, annual	Baars <i>et al.</i> , 2001
Cadmium	1.8E-03	IRIS, 2006d	0.3	Annual	WHO, 2000
Chromium	4.0E-02	WHO, 2000	0.3	Annual	Chemrisk, 1998
Cobalt	Not assessed as a carcinogen		0.1	Annual	ATSDR, 2004
Copper	Not assessed as a carcinogen		1.0	Annual	Baars <i>et al.</i> , 2001
Lead	Not assessed as a carcinogen		0.25	Annual	Fourie <i>et al.</i> , 2003
Manganese	Not assessed as a carcinogen		0.15	Annual	WHO, 2000
Mercury	Not assessed as a carcinogen		0.3	Annual	IRIS, 2006e
Nickel	2.4E-04 to 4.8E-04	ITER, 2006	0.02 to 0.2	Annual	ITER, 2006
Vanadium	Not assessed as a carcinogen		1.0	24-hours	WHO, 2000
Polychlorinated dibenzodioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and polychlorinated biphenyls (PCBs)					
Total TEQ	214	NAS, 2004			

¹ Also refer to the RIVM (Baars, 2001) risk-based concentration of 1 $\mu\text{g}/\text{m}^3$ for carcinogenic effects of arsenic.

5 Exposure assessment

5.1 The study area

The study area is shown in Figure 5.1.1 (Liebenberg-Enslin and Olivier, 2007).

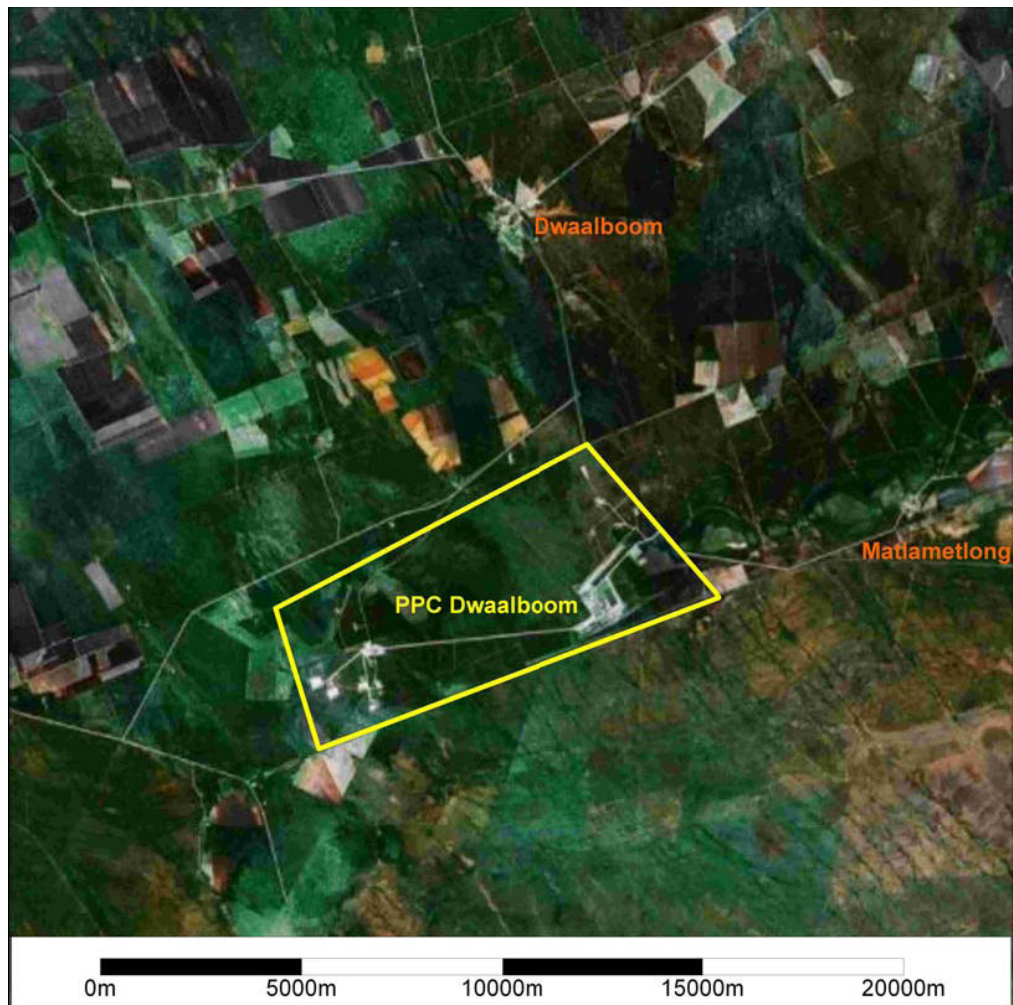


Figure 5.1.1: Location of sensitive receptors in relation to the PPC Dwaalboom cement factory.

The area surrounding the PPC Dwaalboom factory and mine consists primarily of agricultural activities with a low population count. The nearest residential area to the site is the community of Matlametlong, located approximately 7 km to the east of the PPC plant. The town of Dwaalboom is located approximately 9 km to the north of the plant. The residential areas are small and the entire areas were considered as sensitive receptors. It was not considered necessary to refine the study through identification of specific receptors such as schools, hospitals, etc.

5.2 Summary of modelled air concentrations

Modelled ambient air concentrations of contaminants associated with the PPC Dwaalboom plant are summarised in Table 5.2.1.

Table 5.2.1: Summary of modelled air concentrations for gases, metalloids, metals and dioxins for the current operations.

Substance	Averaging time	Plant boundary	Matlametlong	Dwaalboom
Gaseous pollutants ($\mu\text{g}/\text{m}^3$)				
PM ₁₀	24-hour	180.0	15.0	23.0
	Annual	27.0	0.5	2.0
NO ₂ ²	1-hour	12.3	7.7	3.3
	Annual	1.5E-01	2.0E-02	7.2E-02
SO ₂	24-hour	3.0E-02	3.3E-01	2.3E-01
CO	1-hour	100.0	46.3	22.5
HCl	1-hour	0.81	0.37	0.18
	Annual	1.0E-02	1.0E-03	4.0E-04
HF	1-hour	5.0E-02	2.1E-02	1.0E-02
	Annual	5.0E-04	6.0E-05	2.3E-04
Metalloids and metals ($\mu\text{g}/\text{m}^3$)				
Antimony	Annual	No data	No data	No data
Arsenic	Annual	No data	No data	No data
Cadmium	Annual	No data	No data	No data
Chromium	Annual	No data	No data	No data
Cobalt	Annual	No data	No data	No data
Copper	Annual	No data	No data	No data
Lead	Annual	No data	No data	No data
Manganese	Annual	No data	No data	No data
Mercury	Annual	No data	No data	No data
Nickel	Annual	No data	No data	No data
Vanadium	24-hour	No data	No data	No data
Polychlorinated dibenzodioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and polychlorinated biphenyls (PCBs) ($\mu\text{g}/\text{m}^3$)				
Total TEQ	Annual	No data	No data	No data

² Assuming that 10% of the NO_x concentrations be regarded as NO₂ (Liebenberg-Enslin and Olivier, 2007).

Table 5.2.2: Summary of modelled air concentrations for gases, metalloids, metals and dioxins for the proposed operations with co-processing of secondary materials.

Substance	Averaging time	Plant boundary	Matlametlong	Dwaalboom
Gaseous pollutants ($\mu\text{g}/\text{m}^3$)				
PM ₁₀	24-hour	180.0	15.0	23.0
	Annual	27.0	0.50	2.00
NO ₂ ³	1-hour	12.3	7.7	3.34
	Annual	0.15	0.02	0.07
SO ₂	24-hour	5.0E-02	3.3E-01	2.3E-01
CO	1-hour	100.0	46.3	22.5
HCl	1-hour	1.20	0.55	0.27
	Annual	1.5E-02	2.0E-03	6.0E-03
HF	1-hour	1.0E-01	5.5E-02	2.7E-02
	Annual	1.5E-03	1.6E-04	5.9E-04
Metalloids and metals ($\mu\text{g}/\text{m}^3$)				
Antimony	Annual	6.0E-04	8.0E-05	2.9E-04
Arsenic	Annual	6.0E-04	8.0E-05	2.9E-04
Cadmium	Annual	7.0E-05	1.0E-05	3.0E-05
Chromium	Annual	6.0E-04	8.0E-05	2.9E-04
Cobalt	Annual	6.0E-04	8.0E-05	2.9E-04
Copper	Annual	6.0E-04	8.0E-05	2.9E-04
Lead	Annual	6.0E-04	8.0E-05	2.9E-04
Manganese	Annual	6.0E-04	8.0E-05	2.9E-04
Mercury	Annual	7.0E-05	1.0E-05	3.0E-05
Nickel	Annual	6.0E-04	8.0E-05	2.9E-04
Vanadium	24-hour	9.5E-03	3.26E-03	2.34E-03
Polychlorinated dibenzodioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and polychlorinated biphenyls (PCBs) ($\mu\text{g}/\text{m}^3$)				
Total TEQ	Annual	1.7E-10	2.0E-11	6.0E-11

Concentrations smaller than 0.1 are presented in scientific notation. Except for PM₁₀, airborne concentrations of the substances that were selected for study were similar at the plant boundary and the closest sensitive receptor. PM₁₀ concentrations at the nearest receptor are less than 20 per cent of the concentrations at the fence line.

³ Assuming that 10% of the NO_x concentrations be regarded as NO₂ (Liebenberg-Enslin and Olivier, 2007).

6 Human health risk assessment

Tables 6.1 and 6.2 provide summaries of predicted air concentrations for scenarios A and B against guideline concentrations for PM₁₀, NO₂, SO₂ and CO. See Section 4.1 for an explanation of the approach for assessment of potential risks associated with exposure to these substances. Generally, carbon monoxide should be a non-issue in the assessment of emissions from cement kilns, because it is kept very low in the kiln and in fact is one of the control parameters in the process. Scenario A refers to current operating conditions at the PPC Dwaalboom cement factory where emissions from the factory were considered in isolation (no background ambient air levels of the substances were available for consideration). Scenario B reflects the situation where secondary materials would be co-processed in the kiln. No data were available for emissions of metals and dioxins for the current scenario (scenario A). See Table 6.3 for arsenic and metals. For substances that would be present at concentrations that normally are well below health thresholds, hazard coefficients (HQs) have been calculated for noncarcinogens and cancer risks were calculated for the carcinogenic substances.

Table 6.1: Summary of exposure levels for gaseous pollutants for scenario A.

Substance	Guideline	Averaging time	Plant boundary	Matlametlong	Dwaalboom
Gaseous pollutants (µg/m³)					
PM ₁₀	50	24-hour	180	15	23
	20	Annual	27	0.5	2
NO ₂	200	1-hour	12.3	7.7	3.34
	40	Annual	0.15	0.02	0.072
SO ₂	20	24-hour	0.03	0.33	0.23
CO	30 000	1-hour	100	46.25	22.54
Noncancer hazard quotients					
HCl		1-hour	3.12E-04	1.42E-04	6.92E-05
		Annual	5.00E-04	5.00E-05	2.00E-04
HF		1-hour	6.25E-05	2.63E-05	1.30E-05
		Annual	3.57E-05	4.29E-06	1.64E-05

Table 6.2: Summary of exposure levels for gaseous pollutants for scenario B.

Substance	Guideline	Averaging time	Plant boundary	Matlametlong	Dwaalboom
Gaseous pollutants (µg/m³)					
PM ₁₀	50	24-hour	180	15	23
	20	Annual	27	0.5	2
NO ₂	200	1-hour	12.3	7.7	3.34
	40	Annual	0.15	0.02	0.072
SO ₂	20	24-hour	0.05	0.55	0.23
CO	30 000	1-hour	100	46.25	22.54
Noncancer hazard quotients					
HCl		1-hour	4.62E-04	2.12E-04	1.04E-04
		Annual	7.50E-04	1.00E-04	3.00E-04
HF		1-hour	1.25E-04	6.88E-05	3.38E-05
		Annual	1.07E-04	1.14E-05	4.21E-05

Table 6.3: Summary of risk assessment for metalloids, metals and dioxins for Scenario B.

Metalloids and metals						
	Plant boundary		Matlametlong		Dwaalboom	
	Cancer risk	Noncancer HQ	Cancer risk	Noncancer HQ	Cancer risk	Noncancer HQ
Antimony	Not a carcinogen	3.00E-04	Not a carcinogen	4.00E-05	Not a carcinogen	1.45E-04
Arsenic	2.58E-06	6.00E-04	3.44E-07	8.00E-05	1.25E-06	2.90E-04
Cadmium	1.26E-07	2.33E-04	1.80E-08	3.33E-05	5.40E-08	1.00E-04
Chromium	2.40E-05	2.00E-03	3.20E-06	2.67E-04	1.16E-05	9.67E-04
Cobalt	Not a carcinogen	6.00E-03	Not a carcinogen	8.00E-04	Not a carcinogen	2.90E-03
Copper	Not a carcinogen	6.00E-04	Not a carcinogen	8.00E-05	Not a carcinogen	2.90E-04
Lead	Not a carcinogen	2.40E-03	Not a carcinogen	3.20E-04	Not a carcinogen	1.16E-03
Manganese	Not a carcinogen	4.00E-03	Not a carcinogen	5.33E-04	Not a carcinogen	1.93E-03
Mercury	Not a carcinogen	2.33E-04	Not a carcinogen	3.33E-05	Not a carcinogen	1.00E-04
Nickel	1.44E-07 to 2.88E-07	3.00E-03 to 3.00E-02	1.92E-08 to 3.84E-08	4.00E-04 to 4.00E-03	6.96E-08 to 1.39E-07	1.45E-02 to 1.45E-03
Vanadium	Not a carcinogen	9.50E-03	Not a carcinogen	3.26E-03	Not a carcinogen	2.34E-03
Polychlorinated dibenzodioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and polychlorinated biphenyls (PCBs)						
Total TEQ	3.64E-08		4.28E-09		1.28E-08	

7 Human health risk interpretation

The study initiated by Marsh Environmental Services has indicated that co-processing of secondary materials as fuels in cement kilns at PPC Dwaalboom would not lead to any noteworthy changes in emissions of hazardous substances from the operations. Therefore, based on the assumptions that underlie the study and the available data on the air pathway of exposure, there would be no difference between current health risks associated with the PPC production plant and the scenario where alternative fuels would substitute coal as the energy source for fuelling the kiln.

For hydrochloric and hydrofluoric acids, the calculated hazard quotients for both acute and chronic exposures at sensitive receptors were orders of magnitude below 1. These clearly indicated insignificant health risks.

Table 6.3 has shown that the total cancer risk associated with exposure to arsenic and metals would be lower than a few cases in a hundred thousand, even when all the cancer risks were added. In the calculation of cancer risk according to the original USEPA paradigm, all cancer risks from the individual carcinogens have to be added, irrespective of target organ, across all pathways and routes of exposure. This is a conservative way of assessing cancer risks. It should be noted that the highest risk was allocated to chromium in the hexavalent state. This is a large overestimate, because very little, if any, chromium would actually be in the Cr (VI) state.

Acceptability of risk is a judgement decision based on many factors, i.e. the number of people exposed, the consequences of the risk, the degree of control over exposure, risk options, and community priorities, among others. The break point between acceptable and unacceptable risk is generally understood to be between 10^{-4} and 10^{-6} , i.e. between one in ten thousand and one in a million. USEPA has adopted different cancer risk criteria in different programmes (USEPA, 2003). In the nationwide quality criteria programme for water, acceptable risk was defined as ranging between 1×10^{-4} and 1×10^{-7} . In the USEPA Superfund waste disposal programme, acceptable risk can be as high as 1×10^{-4} . The concept of 10^{-6} (one in a million) was originally an arbitrary number proposed by the USA Food and Drug Administration more than 20 years ago as a screening level of “essentially zero” or “insignificant” risk (Kelly, 1991). Because the background cancer risk in many parts of the world is about 1 in four, that is, 250 000 cases in a population of a million, one additional case in a million will not be detectable in a statistical evaluation (250 001 cases against 250 000). Cancer risks associated with exposure through inhalation can therefore be regarded as insignificant.

Similarly, noncancer risks as reflected in the calculated hazard quotients, are very low. Generally, hazard quotients are orders of magnitude below 1 and even if hazard quotients were added to determine a total hazard index, very low health risks through the inhalation route of exposure are indicated.

Dioxin emissions were of special concern and require specific discussion. The cancer risk at receptor locations associated with exposure to dioxins from the PPC Dwaalboom factory under conditions where secondary materials were used as supplementary fuel was shown to be approximately 6 cases in million ($6.4E-06$). Dioxin concentrations in ambient air have been shown to range from below 1 fg TEQ/m^3 to several hundred fg TEQ/m^3 (Fiedler, 1999). Without taking exposure of members of a community to indirect sources of dioxins (such as food) into

account, background exposure to air would in itself already lead to a cancer risk of higher than one in a hundred thousand, if the most recent USEPA cancer slope factor were used to calculate a unit risk factor for inhalation. It should be made clear that the USEPA upper bound slope factor has a very specific application. It allows the calculation of the high end (greater than 95 per cent) of the probability of cancer risk in the population. This means that there is a greater than 95 per cent chance that the calculated cancer risks will be less than the upper bound. The contribution from the PPC Dwaalboom factory to risk through inhalation under conditions of usage of alternative fuels would be insignificant against this background.

8 Uncertainty analysis

The assessment of exposure to emissions from the PPC cement factory under current conditions and where alternative fuels were utilised has been based on emissions data relevant to the process, which have been submitted by Marsh Environmental Services to Airshed Planning Professionals for dispersion modelling. INFOTOX has used these data without review of assumptions and scientific basis. It should be noted that the predicted impacts only reflect the concentrations from PPC operations (plant processes, vehicle entrainment on both paved and unpaved roads. Wind erosion of stockpiles and the mining operations) with no background sources included since no information was available. Incremental risks are however very low and would make a very small, if any, contribution to the overall exposure of the community.

The available information did not include background levels of dioxins in the assessment and also did not consider cumulative depositions and associated risks. Generally, this level of detail is not covered in a screening health risk assessment, as has been the purpose of this INFOTOX human health risk assessment. Following the highest calculated cancer risk of 3.64 cases in a hundred million (3.64E-08) associated with dioxins at the plant boundary (see Table 6.3), assuming operation of the plant within stack emission guidelines, it should be concluded that the overall risk due to dioxins would be low. Even if risks through indirect pathways as a result of accumulation in the food chain were 10 times higher than through inhalation, the cancer risk would still be very low.

The dispersion modelling data did not cover the 10-minute averaging periods for SO₂. WHO (2005) has a 10-minute guideline for sulphur dioxide. It is not expected that the absence of 10-minute data would affect the conclusions in this report, because the highest daily SO₂ concentration for the alternative fuels scenario was less than 3 per cent of the guideline value.

9 Conclusions and recommendations

The overall impression of this study is that the PPC Dwaalboom factory has very little, if any, impacts on human health in the study area. Although guideline concentrations for particulates are exceeded at the factory boundary, the area of impact due to the plant on its own is relatively small and sensitive receptors would not be exposed to concentrations where health effects would be observed. It is however not possible to interpret the exposure information in more detail, for reasons that have been explained in Section 4.1. The introduction of alternative fuels would have insignificant effects on emissions from the PPC factory.

The human health risk assessment has been based on the assumption that emissions of toxic substances from the PPC factory would not exceed internationally-acceptable emission

guidelines. This would however depend on the characteristics of the kiln and other auxiliary equipment at the factory. Generally, the efficiency of a kiln in combusting fuels that contain organic substances is expressed as a DRE (destruction and removal efficiency) value. This has to be obtained through a trial burn, which entails the demonstration that a facility is in compliance with regulatory requirements.

Furthermore, there has to be acceptance criteria for alternative fuels with regard to maximum permissible levels of halogens, metalloids and metals. The current human health risk assessment has assumed that these considerations have been, or will be, covered in the overall alternative fuels assessment for the PPC factory. The assumption that stack emission guidelines will be met can be justified more fully when acceptance criteria have been developed for alternative fuels. The current dispersion modelling and risk assessment have been limited to the demonstration that operation within the respective stack emission guidelines would not lead to unacceptable risks through the air pathway of exposure. This is not surprising, because there is a tacit assumption in the setting of stack emission guidelines that these would be protective to human health within a large margin of safety.

It should be noted that the assessment has been based only on the air pathway of exposure. There are other factors that have to be considered, however. Mercury, for example, is a global issue and the introduction of alternative fuels should not increase releases of mercury. Also, the primary concern about lead is not exposure through inhalation, but ingestion of lead by children. Should the alternative fuels programme release more lead into the environment than the current operations, deposition of lead and its contribution to house dust in residential areas might lead to unacceptable risks to children, even at modelled air concentrations that might be acceptable for the inhalation route of exposure. Cadmium should be considered on the same basis.

10 References

ATSDR, 2004. Toxicological Profile for Cobalt. Agency for Toxic Substances and Disease Registry. US Department of Health and Human Services, Public Health Service. April. <http://www.atsdr.cdc.gov/toxprofiles/tp33.html>.

Baars A J, Theelen R M C, Janssen P J C M, Hesse J M, Apeldoorn M E van, Meijerink M C M, Verdam L and Zeilmaaker M J, 2001. Re-evaluation of human-toxicological maximum permissible risk levels. RIVM report no. 711701025, National Institute of Public Health and the Environment, Bilthoven, The Netherlands, March 2001, p 62-65. <http://www.rivm.nl/bibliotheek/rapporten/711701025.pdf> or <http://www.rivm.nl/en/> .

ChemRisk, A Service of McLaren/Hart Inc, 1998. Documentation Package - Chromium (VI) Inhalation Reference Concentration. Pittsburgh, PA.

Dab W, Medina S, Quénel P, Le Moullec Y, Le Tertre A, Thelot B, Monteil C, Lameloise P, Priard P, Momas I, Ferry R and Festy B, 1996. Short term respiratory health effects of ambient air pollution: results of the APHEA project in Paris. *Journal of Epidemiology and Community Health*, 50 (suppl 1), S42-S46.

Fiedler H, 1999. Compilation of EU Dioxin Exposure and Health Data: Task 2 – Environmental Levels. Report produced for European Commission DG Environment and UK Department of the Environment, Transport and the Regions (DETR).

Fourie M H, Van Niekerk W C A and Mouton G, 2003. Technical Background Document for the Development of a National Ambient Air Quality Standard for Lead. Report prepared on behalf of the Chemical and Allied Industry Association. INFOTOX Document number 005-2003.

Fourie M H, Van Niekerk W C A and Mouton G, 2006. Assessment of Health Risks Associated with Two New Rotary Kilns for Direct Reduced Iron at Mittal Steel Vanderbijlpark Steel. Prepared on behalf of Mittal Steel. INFOTOX Report No 010-2006 Rev 1.0.

Fung K Y, Luginaah I, Gorey K M, Webster G, 2005. Air pollution and daily hospital admissions for cardiovascular diseases in Windsor, Ontario. *Canadian Journal of Public Health*, 96:29-33.

IPCS, 1999. Principles for the Assessment of Risks to Human Health from Exposure to Chemicals. Environmental Health Criteria 210. International Programme on Chemical Safety (IPCS). A cooperative agreement between UNEP, ILO, FAO, WHO, UNIDO, Unitar and OECD.

IRIS, 2006a. Glossary of IRIS Terms. Integrated Risk Information System, US Environmental Protection Agency, Washington DC, USA.

IRIS, 2006b. Hydrogen chloride (CASRN 7647-01-0), last revised 1 July 1995. Integrated Risk Information System. Online. National Center for Environmental Assessment, Washington, DC. <http://www.epa.gov/iris/>.

IRIS, 2006c. Arsenic, inorganic (CASRN 7440-38-2), last revised 10 April 1998. Integrated Risk Information System. Online. National Center for Environmental Assessment, Washington, DC. <http://www.epa.gov/iris/>.

IRIS, 2006d. Cadmium (CASRN 7440-43-9), last revised 1 June 1992. Integrated Risk Information System. Online. National Center for Environmental Assessment, Washington, DC. <http://www.epa.gov/iris/>.

IRIS, 2006e. Mercury, elemental (CASRN 7439-97-6), last revised 1 May 1995. Integrated Risk Information System. Online. National Center for Environmental Assessment, Washington, DC. <http://www.epa.gov/iris/>.

ITER, 2006. International Toxicity Estimates for Risk Database. Toxicology Excellence for Risk Assessment & Concurrent Technologies Corporation. <http://tera.org/iter/>.

Kelly K E, 1991. The myth of 10^{-6} as a definition of “acceptable risk”. 84th Annual Meeting of the Air and Waste Management Association, Vancouver.

Liebenberg-Enslin H and Olivier C, 2007. Air Dispersion Modelling for the Proposed Co-processing of Secondary Materials in Cement Kilns at PPC Dwaalboom. Report No APP/07/MES-03 Rev 0.0, Airshed Planning Professionals (Pty) Ltd. Prepared for Marsh Environmental Services, A Division of Marsh Vikela (Pty) Ltd.

Luginaah I N, Fung K Y, Gorey K M, Webster G and Wills C, 2005. Association of ambient air pollution with respiratory hospitalization in a government-designated “area of concern”: The case of Windsor, Ontario. *Environmental Health Perspectives*, 113:290–296.

NAS, 2004. Draft review. Exposure and Human Health Reassessment of 2,3,7,8-Tetrachlorodibenzo-p-Dioxin (TCDD) and Related Compounds National Academy Sciences (NAS).

NRC (National Research Council), 1983. Risk Assessment in the Federal Government: Managing the Process. Committee on the Institutional Means for the Assessment of Risks to Public Health. Washington, DC: National Academy Press.

NRC, 2004. Acute Exposure Guideline Levels for Selected Airborne Chemicals: Volume 4. Subcommittee on Acute Exposure Guideline Levels, Committee on Toxicology, National Research Council. National Academies Press, Washington, DC.

OEHHA, 2003. Determination of Noncancer Chronic Reference Exposure Levels. Fluorides Including hydrogen fluoride, chronic toxicity summary. [Office of Environmental Health Hazard Assessment, California Environmental Protection Agency.](#)

SANS, 2003. South African National Standard, Ambient air quality — Limits for common pollutants, SANS 1929:200x Edition 1, Published by Standards South Africa, Pretoria.

USEPA, 1989. Risk Assessment Guidance for Superfund. Volume I. Human Health Evaluation Manual (Part A). Interim Final. EPA/540/1-89/002. US Environmental Protection Agency.

USEPA, 2003. Exposure and human health reassessment of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) and related compounds. Draft document EPA/600/P-00/001. US Environmental Protection Agency, National Center for Environmental Assessment, Office of Research and Development, Washington, DC.

USEPA, 2006. EPA response to 9-11. Metals in air. Reference to antimony. OST/www.epa.gov/wtc/metal/.

WHO, 2000. Air Quality Guidelines - Second Edition Chapter 6.12 Vanadium. WHO Regional Office for Europe, Copenhagen, Denmark. www.euro.who.int/document/aig/6_12vanadium.pdf.

WHO, 2005. WHO air quality guidelines global update. Report on a Working Group meeting, Bonn, Germany, 18-20 October 2005. World Health Organisation, WHO Regional Office for Europe, Copenhagen, Denmark.

ANNEXURE 1

1 Particulates

Particulate matter (PM) may be classified by aerodynamic size as “coarse” particles of less than 10 µm aerodynamic diameter (PM₁₀), “fine” particles less than 2.5 µm diameter (PM_{2.5}) and “ultrafine” particles less than 0.1 µm diameter (PM_{0.1}). Over the past decade, overwhelming evidence has accumulated indicating that airborne particulate matter, including total suspended particles (TSP), PM₁₀ and PM_{2.5} exert a range of adverse health effects. The identified health effects are diverse in scope, severity, duration, and clinical significance. The key health effect categories associated with particulate matter have been reviewed by Van Niekerk and Fourie (2004) and Morawska *et al.* (2004) and are:

- Premature mortality;
- Aggravation of respiratory and cardiovascular disease (as indicated by increased hospital admissions and emergency room visits, school absences, work loss days, and restricted activity days);
- Changes in autonomic nervous system function and cardiovascular risk factors such as blood pressure, C-reactive protein and endothelial dysfunction;
- Changes in systemic blood markers;
- Changes in lung function and increased respiratory symptoms;
- Changes to lung tissues and structure; and
- Altered respiratory defence mechanisms.

Although mechanisms by which particles cause effects have not been clarified, there is general agreement that the cardio-respiratory system is the major target of PM effects. The epidemiological studies provide evidence that several subpopulations are more susceptible to the effects of air pollution containing PM. The observed effects in these subpopulations range from decreases in pulmonary function reported in children to increased mortality reported in the elderly and in individuals with cardiopulmonary disease. Such subpopulations may experience effects at lower levels of PM than the general population, and the severity of effects may be greater. Morawska *et al.* (2004) reviewed the subpopulations that appear to be at greatest risk due to exposure to ambient PM and emphasised the following:

- Individuals with respiratory disease (e.g., COPD, acute bronchitis) and cardiovascular disease (e.g., ischemic heart disease) are at greater risk of premature mortality and hospitalisation;
- Individuals with infectious respiratory disease (e.g., pneumonia) are at greater risk of premature mortality and morbidity (e.g., hospitalisation and aggravation of respiratory symptoms). Also, exposure to PM may increase individual susceptibility to respiratory infections;
- Elderly individuals are also at greater risk of premature mortality and hospitalisation for cardiopulmonary causes;
- Children are at greater risk of increased respiratory symptoms and decreased lung function; and
- Asthmatic children and adults are at risk of exacerbation of symptoms and increased need for medical attention.

According to Morawska *et al.* (2004), studies on PM₁₀ and PM_{2.5} indicate that there is no threshold in particle concentrations below which health would not be jeopardised. This has been presented in the World Health Organisation Guidelines for Air Quality (WHO 2000), which showed a linear relationship between PM₁₀ and PM_{2.5} and various health indicators (including mortality, hospital admissions, bronchodilator use, symptom exacerbation, cough, peak expiratory air flow) for concentration levels from 0 to up to 200 µg/m³.

Schwartz (2004) studied the associations of ambient concentrations of particles with mortality data derived from 14 USA cities. In response to several reports indicating that the software used to control for season and weather in some of the previous studies had deficiencies, Schwartz applied an alternative study design in order to avoid previous statistical problems. His results indicated a robust association between a 10 µg/m³ increase in PM₁₀ and a 0.36 per cent increase in daily deaths from natural causes that occurred in the cities included in the study.

Other recent studies indicating associations between PM₁₀ and/or PM_{2.5} levels and deaths are those of Iwai *et al.* (2005), Dominici *et al.* (2003) and Filleul *et al.* (2005). Dominici *et al.* (2003), made an important contribution to the subject by showing that associations between particulate matter and mortality do not imply only an advance in the timing of death by a few days for a restricted subpopulation of frail individuals (the “harvesting hypothesis”), but indicates a health impact on a wider selection of the population. Iwai *et al.* (2005) reported correlations with age-adjusted death rates of ischaemic heart disease or hypertensive heart disease in both genders. A correlation was also noted with death rates of lung cancer, pneumonia, asthma, or chronic bronchitis/emphysema only in females, and with death rates from breast, endometrial and ovarian cancer.

The study for the PPC Dwaalboom cement factory focused only on the PM₁₀ fraction of particulates. The South African limit value for PM₁₀ averaged over 24 hours is 75 µg/m³ and the target value is 50 µg/m³ (SANS, 2003). The annual average limit is 40 µg/m³ and the target value is 30 µg/m³.

The current USEPA primary standard for the annual arithmetic mean is 50 µg/m³ and the 24-hour averaging primary standard is 150 µg/m³.

The most recent guidelines for exposure to airborne particulates are available from the World Health Organisation (WHO, 2005). Guidelines have been proposed for PM_{2.5} and PM₁₀ as annual mean and 24-hour mean values. The annual mean guideline for PM_{2.5} is 10 µg/m³ and for PM₁₀, 20 µg/m³. These represent the lowest concentrations at which total mortality and mortality as a result of cardiopulmonary and lung cancer have been shown to increase with more than 95 per cent confidence in response to exposure to PM_{2.5}. WHO (2005) recommended use of the guideline for PM_{2.5}, but additional guidelines have to be considered for the PM₁₀ fraction. These are 20 µg/m³ for the annual mean and 50 µg/m³ for the 24-hour mean. These were based on the relation between 24-hour and annual particulate matter levels.

Seeing that PM₁₀ was modelled in this study, the WHO air quality guideline of 50 µg/m³ for a 24-hour mean and an annual mean guideline of 20 µg/m³ were used by INFOTOX as screening guidelines.

2 Carbon monoxide (CO)

CO is a colourless, odourless and tasteless gas. It is a trace constituent of the atmosphere, with background levels normally ranging between 0.01 and 0.2 mg/m³. There are many domestic as well as industrial sources of carbon monoxide. It is a product of incomplete combustion of carbon-containing fuels and can also be produced by industrial and biological processes. It is produced both by natural processes (for example, from volcanoes and burning vegetation) and by human activities (for example, the incomplete combustion of fuel from motor vehicles).

Carbon monoxide is absorbed through the lungs and is perhaps the best-known example of a chemical agent that decreases the oxygen transport of the blood and produces hypoxia, a condition in which there is an inadequate supply of oxygen to the tissues. The toxic effects of carbon monoxide are due to the fact that it binds 220-times more tightly to haemoglobin than does oxygen, forming carboxyhaemoglobin (COHb) rather than oxyhaemoglobin (Hall, 1996). High exposures to CO can cause acute poisoning, with coma and collapse occurring at COHb levels of over 40 per cent.

More recently, the scientific interest in carbon monoxide has shifted towards the association between chronic exposure to ambient carbon monoxide concentrations and health effects such as cardiovascular and respiratory disease (Hall, 1996, IPCS, 1999 and Timbrell, 1991). Ambient exposures to CO are several orders of magnitude lower than those associated with acute poisoning. However, some exposures in urban settings have been shown to adversely affect the heart, brain and central nervous system (Hall, 1996; IPCS, 1999 and Timbrell, 1991).

The effects of carbon monoxide on the heart and its association with cardiovascular disease have been reported in both animal and human studies. Environmental exposure to inhaled carbon monoxide has been reported to increase the risk of coronary artery disease (Leaf and Kleinman, 1996). The greatest concern at typical ambient carbon monoxide exposure levels is that certain cardiovascular effects are likely to occur in a small, but significant, segment of the general population. Chronic angina patients are viewed as the most sensitive risk group for carbon monoxide exposure, but the adverse health consequences of low-level carbon monoxide exposure are difficult to predict in the at-risk population of individuals with ischaemic heart disease. At high carbon monoxide concentrations, excessive increases in haemoglobin and haematocrit may impose an additional workload on the heart and compromise blood flow to the vascular tissues, resulting in ischaemic injury to the myocardium (IPCS, 1999, Timbrell, 1991 and Hall *et al.*, 1996).

For many years it was considered unlikely that carbon monoxide could have any direct effects on lung tissue, except at extremely high concentrations associated with carbon monoxide poisoning (IPCS, 1999). However, recent studies have indicated such direct effects. Lin *et al.* (2003) assessed the associations between short-term exposure to gaseous pollutants and asthma. They studied the hospitalisation rate among boys and girls aged 6 to 12 years and concluded that increased asthma hospitalisations in boys were associated with ambient carbon monoxide exposures at comparatively low levels. Tenias *et al.* (2002) also described an increase in hospital admissions for chronic obstructive pulmonary disease associated with increases in ambient carbon monoxide concentrations.

There is no doubt that exposure to high levels of carbon monoxide lead to severe neurotoxicity with lasting effects (IEH, 1998). However, the evidence for lasting (long-term) effects occurring at lower levels of exposure is poor. While there are as yet no epidemiological studies on this aspect, there is experimental evidence that carbon monoxide can affect the brain even at very low levels (Amitai *et al.*, 1998 and Putz, 1979). As early as 1963, Schulte (1963) reported that certain psychomotor abilities of volunteers exposed to carbon monoxide were affected at COHb levels of 5 per cent. Using tests of cognitive abilities, subjects showed an increasing number of errors and increased completion time as COHb levels increased, the effect becoming apparent at 5 per cent COHb. The results emphasise that even before clinical symptoms are reported (around 20 per cent COHb), cognitive skills can be affected.

Recent epidemiological studies have found effects in susceptible groups at levels lower than previously thought to be of concern. Anaemic persons are more susceptible to carbon monoxide than are individuals with normal levels of haemoglobin. Increased metabolic rate enhances the severity of symptoms in carbon monoxide poisoning; this is why children succumb earlier than adults when exposed to a given concentration of the gas. CO readily crosses the placenta, putting the foetus at risk (Gilman *et al.*, 1990). Persons with a history of coronary heart disease, pulmonary heart disease, cerebrovascular disease, thyrotoxicosis and smokers would be expected to be at an increased risk from exposure (Mackison *et al.*, 1981).

Patients with reproducible exercise induced ischemia appear to be the best established as a sensitive group within the general population that is at an increased risk for experiencing the health effects of concern (i.e., decreased exercise duration due to exacerbation of cardiovascular symptoms) at ambient or near-ambient carbon monoxide concentrations (IPCS, 1999). Identifiable probable risk groups can be categorised by gender differences; by age (e.g., foetuses, young infants and the elderly); by genetic variations (e.g., haemoglobin abnormalities); by pre-existing disease, either known or unknown, that already decrease the availability of oxygen to critical tissues; or by the use of medications, recreational drugs or alterations in environment (e.g., exposure to pollutants or high altitude) (IPCS, 1999).

All of the major environmental regulators regulate carbon monoxide. The South African air quality standards are 40 000 $\mu\text{g}/\text{m}^3$ (1-hour limit) and 10 000 $\mu\text{g}/\text{m}^3$ (8-hour limit) (SANS, 2003). The WHO has developed a comprehensive set of guidelines associated with four different averaging times, ranging from 15 minutes to 8 hours. The guidelines are based on the health endpoint of carboxyhaemoglobin (COHb) formation, with the aim of not exceeding the critical COHb level of 2.5 per cent in blood of exposed individuals. This is lower than the level of 5 per cent at which Schulte (1963) observed effects on cognitive abilities. The guidelines and standards of the other regulating bodies are in close agreement with the WHO guidelines, which are therefore recommended as screening guidelines for CO.

The hourly guideline for CO of 30 000 $\mu\text{g}/\text{m}^3$ was used by INFOTOX to screen the modelled daily CO concentrations, since a 24-hour guideline has not been developed by any of the regulatory bodies.

3 Sulphur dioxide (SO₂)

The respiratory tract is the primary target organ system affected by exposure to sulphur dioxide. Acute responses occur within the first few minutes after commencement of inhalation. Effects include reductions in lung function parameters and symptoms such as wheezing or shortness of breath (WHO, 2000). There is an extremely large variability of sensitivity to SO₂ exposure, both among normal individuals and those with asthma, but people with asthma are the most sensitive group in the community. Exacerbation of symptoms among sensitive patients arises when concentrations of SO₂ exceed 250 µg/m³ (24-hour average). Children exposed to sulphur dioxide at concentrations in the range 250 to 500 µg/m³ (24-hour averages) were shown to have more cough than children living in other communities (Dodge, 1983).

It has been demonstrated that there is a link between respiratory hospital admission rates and SO₂ concentrations. Even at low daily levels not exceeding the World Health Organisation's interim target 125 µg/m³ (WHO, 2000), effects on mortality (total, cardiovascular and respiratory) and on hospital emergency admissions for total respiratory causes and chronic obstructive pulmonary disease (COPD), have been demonstrated (WHO, 2000, Walters *et al.*, 1994 and Anderson *et al.*, 1998). Some of the more prominent research findings in this field are reviewed below.

Dab *et al.* (1996) assessed daily pollution levels in Paris for the period 1987 to 1992, as part of a multi-city European Project (*Air Pollution and Health: An European Approach (APHEA)*). The APHEA study is the largest epidemiological multi-centre study on asthma admissions in Europe and showed that increased 24-hour SO₂ concentrations were associated with an increase in hospital admissions for asthma and COPD. Anderson *et al.* (1998) and Stedman *et al.* (1999) illustrated similar effects on hospitalisation rates for respiratory diseases in the UK, as did Luginaah *et al.* (2005) in Canada. Schwartz *et al.* (1996) described a similar trend amongst elderly people in the USA. In Barcelona, it was shown that 100-µg/m³ increases in the daily average of SO₂ in summer were associated with a 15 per cent increase in cardiovascular mortality (Saez, 1993). In these studies, 24-hour averages never exceeded 160 µg/m³. The respiratory effects of SO₂ were revisited in the APHEA 2 study (Sunyer *et al.*, 2003). This study is more comprehensive than the first and an expert group conducted statistical analysis. Eight cities in the APHEA 2 group were able to provide hospital admissions data: Barcelona, Birmingham, London, Milan, the Netherlands (considered as a city because of its relatively small size and relative homogeneity in air pollution levels), Paris, Rome, and Stockholm. The results of the APHEA 2 study confirmed an association between SO₂ and hospital admissions for asthma in children.

In addition, Fung *et al.* (2005) studied the short-term effects of SO₂ on daily cardiac hospital admissions in the town of Windsor, Ontario, Canada and reported the strongest positive effect among the age group of 65 years and older.

All of the major environmental authorities regulate sulphur dioxide. Guidelines and standards are based on the prevention of respiratory effects and usually cover three distinct time periods, namely a short-term (less than 1 hour), daily and annual guideline or standard. The UK has developed the most comprehensive set of guidelines associated with four different averaging times, ranging from 15 minutes to an annual mean, including a specification for a winter mean

(1 October to 31 December). However, the UK annual mean and winter mean have been adopted for the protection of vegetation and ecosystems. The UK and WHO have adopted the same 24-hours guideline value of 125 $\mu\text{g}/\text{m}^3$, which is more conservative than the USEPA standard of 365 $\mu\text{g}/\text{m}^3$. The USEPA standard is however not based on only health risk considerations. South Africa has adopted the same guidelines as WHO (2000) (SANS, 2003).

WHO has recently revised its 2000 guidelines for sulphur dioxide (WHO, 2005). In consideration of the uncertainty of the role of SO_2 in the observed health effects, the difficulty in achieving levels that are certain to be associated with no effects, and the need to provide greater protection than what has been offered by the 2000 guidelines, WHO proposed a new guideline of 20 $\mu\text{g}/\text{m}^3$ as a 24-hour mean. The 10-minute mean remained unchanged at 500 $\mu\text{g}/\text{m}^3$. An annual guideline was not considered necessary, because compliance with the 24-hour guideline would assure acceptable levels for chronic exposure.

INFOTOX used the WHO (2005) 24-hour guideline of 20 $\mu\text{g}/\text{m}^3$ for screening of hourly SO_2 values. Modelling data were not available for 10-minute exposures.

4 Nitrogen oxides (NO_x)

NO₂ is a pungent, acidic gas. Corrosive and strongly oxidising, it is one of several oxides of nitrogen (NO_x) that can be produced as a result of combustion processes. In most countries, motor vehicles, industrial activities and the generation of electricity account for a large percentage of the anthropogenic production of nitrogen oxides. Combustion of fossil fuels converts atmospheric nitrogen and any nitrogen in the fuel into its oxides, mainly nitric oxide (NO) but with small amounts (5 to 10 per cent) of NO₂. NO oxidises to NO₂ in the atmosphere. This reaction is catalysed in the presence of O₃. In the presence of sunlight, NO_x, including NO₂, react with volatile organic compounds to form photochemical smog. The main source of NO₂ resulting from human activities is the combustion of fossil fuels (coal, gas and oil).

Exposure to nitrogen dioxide (NO₂) has been shown to cause reversible effects on lung function and airway responsiveness. It may also increase reactivity to natural allergens. Inhalation of NO₂ by children increases their risk of respiratory infection and may lead to poorer lung function in later life (NZME, 2002). NO₂ levels of about 940 µg/m³ (0.5 ppm) increase susceptibility to bacterial and viral infection of the lung (reviewed by the WHO, 2000). Generally, normal healthy individuals are not affected by subchronic exposure to NO₂ concentrations less than 1 880 µg/m³ (1.0 ppm), but there are indications that chronic obstructive pulmonary disease sufferers are affected by exposure to 560 µg/m³ (0.3 ppm). Individuals with asthma are much more susceptible to a bronchoconstrictive response and they are likely to be the most sensitive subjects.

At least two studies have found associations between stroke admissions and NO₂ (Tsai *et al.*, 2003 and Ponka *et al.*, 1996). Some earlier studies have however reported a lack of association with stroke admissions (Wong *et al.*, 1999; and Poloniecki *et al.*, 1997). A link between respiratory hospital admission rates and NO₂ concentrations has been demonstrated (Dab *et al.*, 1996; Anderson *et al.*, 1998; Thompson *et al.*, 2001) on the basis of epidemiological studies. The relationship between the 24-hour level of NO₂ and admissions for asthma was the strongest association observed in the study by Dab *et al.* (1996). Luginaah *et al.* (2005) recently confirmed the relationship between NO₂ and daily hospital admissions for respiratory diseases in a government-designated "area of concern" in Ontario, Canada.

Filleul *et al.* (2005) studied the long-term effects of air pollution on mortality in 24 areas from seven French cities. The authors showed that mean long-term (annual to 3-yearly) concentrations of NO₂ and NO were significantly related to non-accidental mortality, with consistent patterns emerging for deaths due to lung cancer or cardiopulmonary causes.

All of the major environmental agencies regulate specifically nitrogen dioxide (NO₂). Guidelines and standards are based on the prevention of lung function changes and usually state an hourly and an annual guideline or standard. Canada has developed a comprehensive set of guidelines associated with three different averaging times, namely a one-hour guideline, a 24-hour guideline and an annual mean (Health Canada, 2005). Guidelines are designated as a maximum desirable level, a maximum acceptable level and a maximum tolerable level. South Africa has proposed a maximum hourly average of 200 µg/m³ and an annual average of 40 µg/m³ (SANS, 2003). The UK has adopted an annual mean for nitrogen oxides as a group, with the aim of protecting vegetation and ecosystems. The WHO (2000) guidelines are based on the protection of lung function in asthmatics and are the most conservative NO₂ guidelines. The UK

has adopted the WHO guidelines on a provisional basis, but the terms of the provisional adoption is not clear. The USEPA standard is based on other considerations besides the health risk.

INFOTOX referred to the UK and WHO guidelines in this assessment as screening values (200 $\mu\text{g}/\text{m}^3$ as an hourly mean, and 40 $\mu\text{g}/\text{m}^3$ as an annual mean). WHO has not considered it necessary to revise the guidelines for NO_2 in their global update (WHO, 2005).

5 Hydrochloric acid

5.1 Acute toxicity

Hydrochloric acid is a respiratory irritant and is corrosive. When inhaled, it is absorbed in the nasal passages and when the scrubbing capacity of the upper respiratory tract is saturated, it may enter the lower respiratory tract. Based on a study of exposure of exercising male and female asthmatics to hydrochloric acid (Stevens *et al.*, 1992), a guideline concentration for irritation effects was derived (NRC, 2004). Exposure to HCl at 1.8 ppm (2.6 mg/m³) for 45 minutes resulted in a no-observed-adverse-effect level (NOAEL). The asthmatic subjects were considered a sensitive subpopulation, because exercise would enhance HCl uptake and exacerbate irritation. Therefore, no uncertainty factor was applied to account for sensitive individuals and no uncertainty factor for extrapolation from animals to humans was necessary. Because mild irritant effects generally do not vary much over time, the no-effect level would be protective for exposures up to 8 hours.

INFOTOX used the guideline of 2.6 mg/m³ to assess acute exposure to HCl.

5.2 Chronic toxicity

USEPA has evaluated the noncancer inhalation toxicity data for hydrochloric acid and derived a reference concentration (RfC) of 0.02 mg/m³ (IRIS, 2006a). The interpretations were based on the development of hyperplasia of nasal mucosa larynx and trachea in a chronic inhalation exposure study in rats. The lowest-observed-adverse-effect level (LOAEL) of 10 ppm (15 mg/m³) was converted to a human equivalent concentration [LOAEL(HEC)] of 6.1 mg/m³. An uncertainty term that includes a factor of 300 was applied to obtain the RfC of 0.02 mg/m³: 3 for interspecies differences, 10 for intraspecies extrapolations, and 10 to extrapolate from a LOAEL to a NOAEL.

INFOTOX used the USEPA RfC of 0.02 mg/m³ to assess chronic exposure to HCl.

6 Hydrofluoric acid

6.1 Acute toxicity

Hydrofluoric acid is a severe irritant to the eyes, skin and nasal passages. The guideline concentration for acute exposure is based on the threshold for pulmonary inflammation [3 ppm (2.45 mg/m³) for 1 hour] (NRC, 2004), as established by the observation of inflammatory parameters in the broncoalveolar fluid of 20 healthy exercising adults. There were no changes in lung function and only minor symptoms of irritation were noted at that concentration. The subjects were healthy exercising adults, but two of them had increased immune parameters. An intraspecies uncertainty factor of 3 was applied to account for atopic individuals, leading to a guideline concentration of 1 ppm (0.8 mg/m³) for acute exposure to HF. NRC (2004) reviewed various other studies, which supported the guideline concentration. Because mild irritant effects generally do not vary much over time, the exposure guidance concentration would be protective for exposures up to 8 hours.

INFOTOX used the guideline concentration of 800 µg/m³ to assess acute exposure to HF.

6.2 Chronic toxicity

OEHHA (2003) reviewed occupational fluoride exposure data for the employment period of each of 74 male workers in a study conducted by Derryberry *et al.* (1963). A statistically significant relationship was shown between airborne fluoride concentration and the incidence of minimal bone density increases. A concentration of 1.98 mg HF/m³ was considered a LOAEL for chronic skeletal fluorosis, and 1.13 mg HF/m³ was considered a NOAEL. A benchmark concentration (BMC05) of 0.37 mg/m³ was derived by fitting the probit model to the log dose in the USEPA's BMDS (version 1.3) software, for the individual mean air exposure data and incidence data.

Adjusting for exposure continuity and utilising an intraspecies uncertainty factor of 10 resulted in a chronic reference exposure level for HF of 14 µg HF/m³.

INFOTOX used this value to assess chronic exposure to airborne HF.

7 Antimony

7.1 Cancer risk assessment

Evidence for carcinogenic action in laboratory animals was judged by the International Agency for Research on Cancer (IARC, 2006) as sufficient for antimony trioxide (Group 2B), and limited for antimony trisulfide (Group 3). In humans, antimony trioxide is considered a possible carcinogen. The problem is that the studies used to assess carcinogenesis, both in occupational settings and experimental animal studies, involved impurities that are carcinogenic.

There is inadequate evidence for carcinogenicity of antimony and INFOTOX does not assess the substance as carcinogenic.

7.2 Noncancer risk assessment

USEPA derived a reference dose (RfD) of 0.0004 mg/kg-day, based on a rat study in which the subjects were administered potassium antimony tartrate in water (IRIS, 1998). Interpretations were based on longevity, blood glucose, and cholesterol. Since there was only one level of antimony administered, a NOEL was not established. A decrease in mean heart weight for the males was noted. No increase in tumors was observed as a result of treatment. An uncertainty factor of 1 000 (10 for interspecies conversion, 10 to protect sensitive individuals, and 10 because the effect level was a LOAEL and no NOEL was established) was applied to the LOAEL of 0.35 mg/kg-day. There is a low confidence in this RfD, but this is the best information available and is used by INFOTOX in the assessment of oral exposure to antimony. There are no US Environmental Protection Agency or World Health Organization guidelines for chronic inhalation exposure to antimony. If the oral data are extrapolated across routes of exposure, assuming similar bioavailability and health endpoints, a provisional guideline concentration of 0.5 µg/m³ can be derived for inhalation. This is an approximation in the absence of any data. The screening concentration used in the USEPA response to 9-11 is 2 µg/m³ (USEPA, 2006), which is in the same range as the extrapolated value.

INFOTOX therefore uses the USEPA screening guideline of 2 µg/m³ for assessment of chronic exposure to antimony through inhalation.

8 Arsenic

8.1 Cancer risk assessment

In its evaluation of arsenic as a contaminant in drinking water, the International Agency for Research on Cancer (IARC, 2002) classified arsenic (primarily inorganic, as arsenate and to a lesser extent arsenite) as carcinogenic to humans (Group 1) on the basis of sufficient evidence for an increased risk for cancer of the urinary bladder, lung and skin. Human inhalation studies have reported inorganic arsenic exposure to be strongly associated with lung cancer. The United States Environmental Protection Agency (USEPA) has classified inorganic arsenic into Group A (carcinogenic to humans) (IRIS, 2006b). The cancer weight of evidence classification is based on all routes of exposure.

USEPA used a mathematical model, using data from an occupational study of arsenic-exposed copper smelter workers, to estimate the probability of a person developing cancer from continuously breathing air containing a specified concentration of inorganic arsenic. USEPA calculated an inhalation unit risk estimate of $4.3 \times 10^{-3}(\mu\text{g}/\text{m}^3)^{-1}$.

An Expert Panel reviewed USEPA's arsenic assessment and concluded that one mode of action is unlikely to be operative for arsenic, that arsenic and its metabolites do not appear to directly interact with DNA, and that for modes of action regarded as plausible, the dose-response would either show a threshold or would be nonlinear (ITER, 2006).

The Netherlands National Institute of Public Health and the Environment (RIVM) derived a tolerable concentration in air (TCA) of $0.001 \text{ mg}/\text{m}^3$ (Baars *et al.*, 2001). RIVM notes that lung cancer occurs in humans at concentrations greater than $0.01 \text{ mg}/\text{m}^3$. However, RIVM indicates that the mechanism for tumours is not directly genotoxic, so a threshold exists for this effect. Therefore, RIVM elected to call the value a tolerable concentration in air (TCA), not a cancer risk value, and applied an uncertainty factor of 10 to account for intrahuman variability. RIVM indicates that the TCA is protective of cancer effects.

INFOTOX used the USEPA slope factor to estimate cancer risk, but it should be noted that this factor is likely to overestimate cancer risk considerably. Therefore, the RIVM TCA of $1 \mu\text{g}/\text{m}^3$ was also used to provide better perspective on the potential cancer risks.

8.2 Noncancer risk assessment

Chronic inhalation exposure to inorganic arsenic in humans is associated with irritation of the skin and mucous membranes (dermatitis, conjunctivitis, pharyngitis, and rhinitis). No chronic inhalation exposure studies have been performed in animals for any inorganic arsenic compound. USEPA has not established a Reference Concentration (RfC) for inorganic arsenic.

INFOTOX therefore did not assess arsenic for noncarcinogenic effects.

9 Cadmium

9.1 Cancer risk assessment

USEPA classified cadmium as B1 (probable human carcinogen) and estimated a cancer unit risk of $1.8E-03$ per $\mu\text{g}/\text{m}^3$ (IRIS, 2006c). The cancer weight-of-evidence classifications are based on all routes of exposure.

The Netherlands National Institute of Public Health and the Environment (RIVM) concluded that humans exposed to cadmium via inhalation are apparently at a higher risk of lung cancer, but the available data do not allow an unambiguous discrimination between a direct carcinogenic effect of cadmium and an effect from other carcinogens or environmental and/or lifestyle factors. Therefore, RIVM considers cadmium as "probably carcinogenic to humans by the inhalatory route." The International Agency for Research on Cancer (IARC) classified cadmium as carcinogenic to humans (Group 1), based on sufficient evidence of carcinogenicity of cadmium and cadmium compounds in humans, sufficient evidence of carcinogenicity of cadmium compounds in experimental animals, and limited evidence of carcinogenicity of cadmium metal in experimental animals. The IARC evaluation considers the evidence of carcinogenicity in humans and experimental animals, as well as other data relevant to the evaluation of carcinogenicity and its mechanisms.

Health Canada classified cadmium as Group II (probably carcinogenic to humans) and calculated a TC05 of $5.1E-3$ mg/m^3 . (TC05 refers to a tumorigenic concentration with 5 per cent response). USEPA considered using the Takenaka et al. (1983) study that Health Canada used, but felt the use of available human data was more reliable because of the species variations in response and the type of exposure (cadmium salt vs. cadmium and cadmium oxide) (ITER, 2006).

INFOTOX followed the USEPA preference and used the cancer unit risk of $1.8E-03$ per $\mu\text{g}/\text{m}^3$ in this assessment.

9.2 Noncancer risk assessment

The US Agency for Toxic Substances and Disease Registry (ATSDR, 1999), Health Canada (1996a, 1996b) and Environment Canada and Health Canada (1994) have evaluated the noncancer inhalation toxicity data for cadmium. Health Canada considered carcinogenicity to be the endpoint of concern and developed an inhalation cancer risk estimate, as discussed in Section 8.1 above. ATSDR did not derive a chronic inhalation minimal risk level.

Cadmium, whether absorbed by inhalation or via contaminated food, may give rise to various renal alterations (WHO, 2000). The lowest estimate of the cumulative exposure to airborne cadmium in industrial workers leading to an increased risk of renal dysfunction (low-molecular-weight proteinuria) or lung cancer is 100 $\mu\text{g}/\text{m}^3$ -years for an 8-hour exposure. Extrapolation to a continuous lifetime exposure gives a value of around 0.3 $\mu\text{g}/\text{m}^3$.

This was used by INFOTOX as a guideline concentration to protect against renal effects.

10 Chromium

10.1 Cancer risk assessment

Chromium (VI) compounds are toxic and carcinogenic, but the various compounds have a wide range of potencies. The bronchial system is the major target organ for carcinogenic effects of chromium (VI) compounds. IARC has stated that for chromium and certain chromium compounds there is sufficient evidence of carcinogenicity in humans (Group 1).

USEPA (IRIS, 2006d) has classified chromium (VI) as Group A (known human carcinogen by the inhalation route of exposure). Health Canada also classified chromium (VI) as a carcinogen Group I (human carcinogen). The USEPA cancer unit risk is 1.2E-2 per ($\mu\text{g}/\text{m}^3$).

The estimated lifetime risks based on various epidemiological data sets are relatively consistent in the range of 1.3E-01 to 1.1E-02 (WHO, 2000). As a best estimate, the geometric mean of the risk estimates of 4.0E-02 was taken by WHO (2000) as the incremental unit risk resulting from a lifetime exposure to chromium (VI) at a concentration of 1 $\mu\text{g}/\text{m}^3$.

INFOTOX used this cancer unit risk factor in the current assessment.

10.2 Noncancer risk assessment

Only ChemRisk (1998) and USEPA (IRIS, 2006d) have derived chronic inhalation risk values for hexavalent chromium. USEPA derived a RfC of 0.0001 mg/m^3 for chromium (VI) particulates based on lower respiratory effects of hexavalent chromium particulates in rats (Glaser *et al.*, 1990). A benchmark dose of 0.016 mg/m^3 was used (Malsch *et al.*, 1994) and multiplied by the regional deposited dose ratio (RDDR) of 2.16 (the RDDR for particulates to account for differences between rats and humans), for an adjusted concentration of 0.034 mg/m^3 . An uncertainty factor of 300 was applied (10 for variation in human population, 10 for subchronic to chronic and 3 for pharmacodynamic differences not accounted for by the RDDR).

ChemRisk derived a RfC for chromium (VI) particulates of 0.0003 mg/m^3 based on the same study, endpoint and uncertainty factor as USEPA, but differed in that it selected the arithmetic average of benchmark concentrations for the pulmonary inflammation endpoint. This average was selected, rather than the most conservative value, to ensure that the RfC is not driven by wide confidence intervals due to poor model fit. This accounts for the 3-fold difference in values between ChemRisk and USEPA. An independent peer review panel through TERA's ITER Peer Review program has approved the ChemRisk value and supporting documentation (ITER, 2006).

INFOTOX used the RfC of 0.3 $\mu\text{g}/\text{m}^3$ to assess noncancer risks associated with inhalation of chromium (VI).

11 Cobalt

11.1 Cancer risk assessment

The US Agency for Toxic Substances and Disease Registry (ATSDR) and The Netherlands National Institute of Public Health and the Environment (RIVM) evaluated the carcinogenicity data for cobalt. RIVM concluded that cobalt is not genotoxic and therefore, developed risk values based on noncancer endpoints. ATSDR has published a Toxicological Profile for Cobalt (ATSDR, 1992) but did not assess cancer potency or perform cancer risk assessments.

INFOTOX therefore did not assess cobalt as a carcinogen.

11.2 Noncancer risk assessment

ATSDR (2004) and RIVM (Baars *et al.*, 2001) have evaluated the noncancer inhalation toxicity data for cobalt. ATSDR derived a minimal risk level (MRL) of 0.0001 mg/m³ based on a NOAEL of 0.0053 mg/m³ for decreases in several measures of respiratory function in diamond polishers (Nemery *et al.*, 1992). The chronic inhalation MRL was derived by adjusting the NOAEL of 0.0053 mg/m³ for intermittent exposure (8 hours/24 hours x 5 days/7 days), resulting in an adjusted NOAEL of 0.0013 mg/m³, and then dividing by an uncertainty factor of 10 (for human variability). ATSDR noted that this MRL may not be protective for individuals already sensitive to cobalt.

RIVM derived a tolerable concentration in air (TCA) of 0.0005 mg/m³ using a LOAEL of 0.05 mg/m³ for interstitial lung disease in humans (Sprince *et al.*, 1988 as cited in ATSDR, 1992) and an uncertainty factor of 100 (10 for extrapolation from a LOAEL and a factor of 10 for intrahuman variability). The ATSDR and RIVM values differ by a factor of 5 because ATSDR based its new chronic inhalation MRL on a more recent study (Nemery *et al.*, 1992).

INFOTOX used the more recent MRL of 0.1 µg/m³ to assess noncancer risks associated with exposure to cobalt in this study.

12 Copper

12.1 Cancer risk assessment

USEPA has evaluated the carcinogenicity data for copper and classified it as D (not classifiable as to human carcinogenicity) (IRIS, 2006e). The cancer weight of evidence classification is based on all routes of exposure. RIVM determined that copper is not considered a genotoxic compound. Consequently, RIVM derived a risk value based on a threshold approach (Baars *et al.*, 2001).

INFOTOX therefore did not assess copper as a carcinogen.

12.2 Noncancer risk assessment

ATSDR (1990) and RIVM (Baars *et al.*, 2001) have evaluated the noncancer inhalation toxicity data for copper. ATSDR did not derive any inhalation minimal risk levels (MRLs) due to inadequate data. The occupational studies on copper could not be used to derive an MRL due to poor exposure characterisation and/or lack of controls.

RIVM derived a tolerable concentration in air (TCA) of 0.001 mg/m³ based on a NOAEC of 0.6 mg/m³ for lung and immune system effects in rabbits from a short-term toxicity study (Johansson *et al.*, 1984, as cited in ATSDR, 1990). RIVM used an uncertainty factor of 100 (10 each for intra- and interspecies variability), and a factor of 6 (5/7 x 6/24) to adjust for continuous exposure.

INFOTOX used this TCA of 1 µg/m³ to assess noncancer risks associated with inhalation of copper in this study.

13 Lead

13.1 Cancer risk assessment

A number of studies have been performed on workers occupationally exposed to lead, often at high levels (LDAI, 2001). Exposure to lead (and its inorganic compounds) gives a possible increased risk of contracting certain cancers, namely of the lungs, the stomach and perhaps also the kidneys. However, the results of these studies are not conclusive because the individuals were also exposed to other substances, such as chromium, arsenic, or certain hydrocarbons at work, and cigarette smoke, which are all known to cause cancers. There have not been studies on lead exposure in the general population and the occurrence of these cancers.

Animal experiments have found that long term exposure to high doses of lead acetate through ingestion have caused kidney cancer in rats and mice at high doses (IRIS, 2006f), brain cancer in rats, and lung cancer in mice. No studies relating to exposure through inhalation have been published. The relevance of the animal studies to humans is questionable (ACSH, 1997). All of the available human studies lacked quantitative exposure information, as well as information on the possible contribution from smoking. The studies also included exposures to other metals such as arsenic, cadmium, and zinc for which no adjustment was done (IRIS, 2006f). Nevertheless, the International Agency for Research on Cancer (IARC, 2004) has classified inorganic lead and lead compounds as probably carcinogenic to humans (Group 2A). IARC (2004) reasoned that lead is a toxic metal and that genetic toxicity one of its expressions. There is, however, insufficient evidence for its direct interaction with DNA. The genetic effects of lead may be mediated in part by increases in and modulation of reactive oxygen species. Furthermore, lead can interact with proteins, including those involved in DNA repair, which may be responsible for the enhancement of genetic toxicity caused by other agents. These actions could result in mutation, cell proliferation and changes in gene expression, all of which might contribute to a carcinogenic response under conditions of sustained exposure.

Although ATSDR, IARC and USEPA have reviewed the carcinogenicity of lead and its compounds, inadequate dose-response information is available to assist in the derivation of a cancer unit risk factor. Furthermore, the greatest concern for the general population is that low levels of lead exposure appear to cause a decrease in the intellectual development of young children. This is considered a priority in risk assessment where exposure to lead may occur.

INFOTOX has therefore not assessed lead as a carcinogen in this study.

13.2 Noncancer risk assessment

A small number of adults occupationally exposed to lead have in the past shown increased risk of kidney damage, nerve damage, infertility and, possibly, a small increase in blood pressure and the risk of contracting certain cancers at high levels of exposure. However, currently such effects are rarely observed. The greatest concern for the general population is that lower levels of lead exposure, which some of the general population may receive, appear to cause a small decrease in the intellectual development of young children. Children are more vulnerable

because their nervous system is developing and they absorb more lead than adults because of behavioural and physiological differences. There is no accepted threshold level, but the body of evidence to date does not find any effect below 10µg/dl blood lead. Individuals whose diet is lacking in iron or calcium absorb more lead than those who are well nourished.

The relationship between lead levels in air and levels of lead absorbed by the body (blood lead levels) is complex, but evidence suggests that the air concentration for the general population should not be above 1 µg/m³ (UK DETR, 1998). To allow for some individuals being more vulnerable, the UK Expert Panel on Air Quality Standards recommended a safety factor of 50 per cent per cent and a further safety factor of 50 per cent to allow for uncertainties, resulting in a recommended value of 0.25 µg/m³. The UK Expert Panel on Air Quality Standards believed at this level any effects on health, even to vulnerable individuals, will be too small to be detectable. This recommendation has, however, been criticised by industry as not being based on sound science.

Fourie *et al.* (2003) reviewed the scientific literature for the purpose of developing a national ambient air quality standard for South Africa. It was concluded that the UK recommended value of 0.25 µg/m³ has acceptable scientific basis and can be applied to the South African population, including vulnerable individuals.

INFOTOX adopted this guideline concentration (0.25 µg/m³) to assess risks associated with exposure to lead.

14 Manganese

14.1 Cancer risk assessment

There has been no incidence of lung tumours among occupationally exposed individuals at high doses of Mn_3O_4 (cited in Abbott, 1987). Intratracheal instillation of MnO_2 dust into hamsters also did not show any increase in the incidence of lung cancer. The likelihood of manganese oxides being lung carcinogens appears to be small (ATSDR, 2000). USEPA has classified manganese as Group D in the standard carcinogen classification, inferring that it is not classifiable as to human carcinogenicity. (IRIS, 2006g). This category is used for substances where there is inadequate evidence of carcinogenicity in human and animal studies.

INFOTOX did not assess manganese as a carcinogen in this study.

14.2 Noncancer risk assessment

USEPA derived a lowest-observed-adverse-effect level (LOAEL) from an occupational-lifetime integrated respirable dust concentration of manganese dioxide (MnO_2), based on the 8-hour time-weighted average (TWA) occupational exposure multiplied by individual work histories in years. The occupational LOAEL was then adjusted for non-occupational exposure and a safety factor of 1 000 was applied (a factor 10 to protect sensitive individuals, 10 for using a LOAEL instead of a no-observed-adverse-effect level (NOAEL), and 10 to account for database limitations relating to less-than-chronic periods of exposure in the occupational studies, and the lack of reproductive and developmental toxicity data). Following this approach, the USEPA reference concentration for airborne manganese is $0.05 \mu g Mn/m^3$ (IRIS, 2006g).

The World Health Organisation derived an air concentration guidance value for manganese based on the same epidemiological data used by USEPA (Roels *et al.*, 1992), following the benchmark dose approach. After adjustment to continuous exposure, a safety factor of 50 was applied (a factor 10 for interindividual variations in sensitivity, and a factor 5 for potential developmental effects in children). At $0.15 \mu g Mn/m^3$, the WHO guidance value is three times higher than the USEPA value.

The USEPA and WHO guidelines are the most prominent to consider in manganese health risk assessments, because these agencies are considered reputable and their data have been peer reviewed. Various other authors have published guideline concentrations for manganese in air, either as independent interpretations of published data, or as critical reviews of the USEPA and WHO documents. It appears that the USEPA number of $0.05 \mu g Mn/m^3$ is considered to be over-conservative by several reviewers. Even from within USEPA, using several methods of interpretation of the same data, it has been suggested that the best estimates for a reference concentration for manganese fall in the range 0.09 to $0.2 \mu g Mn/m^3$ (Davis *et al.*, 1998). Even the lowest value in this range is higher than the official RfC (IRIS, 2006g). Crump *et al.* (1994) suggested that a reference concentration of $3 \mu g Mn/m^3$ is scientifically defensible, based on the same data that were used by USEPA for setting the reference concentration of $0.05 \mu g Mn/m^3$.

A review by scientists in the reputable National Institute of Public Health and the Environment

(RIVM) in Bilthoven, The Netherlands, is particularly important to note. In response to a request from the WHO European Centre for Environment and Health, approaches for deriving an ambient air guideline concentration for manganese were reviewed (Slob, Janssen and Pieters, 1996). It was concluded that a benchmark dose of 26 $\mu\text{g}/\text{m}^3$, as derived from the study by Roels *et al.* (1992) was a better basis for calculating a guideline concentration than the LOAEL of 50 $\mu\text{g}/\text{m}^3$ from the same study, as used by USEPA in deriving a reference concentration. An uncertainty factor of 10 for using a LOAEL instead of a NOAEL was considered unnecessary, because the benchmark dose can be treated as a NOAEL. The application of additional uncertainty factors is warranted only when there are clear indications that endpoints other than neurotoxicity may be more sensitive to exposure. In the case of manganese, there are no well-established developmental and reproductive effects in humans. Limitations in chronic exposure information were considered insufficient to show the need for additional uncertainty factors. The reviewers found an uncertainty factor of 1 000 excessive, and concluded that the previous WHO guidance value of 1 $\mu\text{g Mn}/\text{m}^3$ (WHO, 1987) is adequately protective for the toxicological endpoints of concern.

Although it is agreed that the WHO guideline of 0.15 $\mu\text{g Mn}/\text{m}^3$ is overly conservative, INFOTOX adopted this guideline to assess risks associated with exposure to manganese in this study.

15 Mercury

15.1 Cancer risk assessment

The US Agency for Toxic Substances and Disease Registry (ATSDR, 1999), Health Canada, Toxicology Excellence for Risk Assessment (ITER, 2006), and National Institute of Public Health and the Environment (RIVM) (Baars *et al.*, 2001) have evaluated the carcinogenicity data for elemental mercury. USEPA has classified mercury as D (not classifiable as a human carcinogen). The cancer weight of evidence classification is based on all routes of exposure.

USEPA has classified mercury chloride (inorganic mercury) as C (possible human carcinogen) (IRIS, 2006h). The cancer weight of evidence classification is based on all routes of exposure. RIVM determined that the available data do not allow a clear conclusion on the genotoxic potency of inorganic mercury. However, assuming that repair mechanisms can protect cells up to a certain level of exposure, a threshold mechanism of action is to be expected and a risk value can be proposed using a threshold approach.

INFOTOX did not assess inorganic mercury as a carcinogen in this assessment.

15.2 Noncancer risk assessment

ATSDR (1999), RIVM (Baars *et al.*, 2001), and USEPA (IRIS, 2006h) have evaluated the noncancer inhalation toxicity data for metallic (elemental) mercury. USEPA derived a reference concentration (RfC) of 0.0003 mg/m³, while ATSDR and RIVM both derived risk values of 0.0002 mg/m³. USEPA used a LOAEL of 0.025 mg/m³ as a time-weighted average to represent exposure for the convergence of a number of studies, some of which extrapolated blood levels from biological monitoring. Using this time-weighted average and taking occupational ventilation rates and workweek into account results in a LOAEL (HEC) of 0.009 mg/m³. ATSDR and RIVM relied upon the LOAEL/LOAEC of 0.026 mg/m³ identified in a study conducted by Fawer *et al.* (1983) and adjusted this to a continuous exposure concentration. ATSDR, RIVM, and EPA all used the same choice of uncertainty factors, resulting in risk values that are just slightly different.

INFOTOX used the USEPA RfC of 0.3 µg/m³ to assess exposure to mercury in this study, assuming that exposure through inhalation would be to elemental mercury (mercury vapour).

16 Nickel

16.1 Cancer risk assessment

The carcinogenicity of nickel in occupationally-exposed individuals has been well documented. Increases in the risk of mortality from lung or nasal cancers were observed in several cohorts of nickel refinery workers (ATSDR, 2005). Studies in other nickel industries, including nickel mining and smelting, nickel alloy production, stainless steel production, or stainless steel welding, which typically involve exposure to lower concentrations of nickel, have not found significant increases in cancer risks.

In most of the studies, workers were exposed to several nickel species, thus making it difficult to compare carcinogenic potential across nickel species. The strongest evidence of carcinogenicity (increased lung cancer risks) has been observed for sulphidic nickel. There is weaker evidence that high concentrations of oxidic nickel, particularly when there is co-exposure to soluble nickel, is also carcinogenic. Soluble nickel compounds do not appear to be carcinogenic in the absence of exposure to other carcinogenic agents (TERA, 1999). There is no evidence that exposure to low levels of nickel is carcinogenic in humans.

The conclusions drawn from the occupational exposure studies are supported by animal inhalation studies. Significant increases in the incidence of lung tumors were observed in rats chronically exposed to nickel subsulphide or nickel oxide. The carcinogenic response was stronger for nickel subsulphide compared to nickel oxide. In contrast, no increases in lung tumour incidences were observed in rats exposed to nickel sulphate; however, the highest concentration tested was lower than the cancer effect levels for nickel subsulphide or nickel oxide.

Although the evidence is sufficient to consider less-soluble nickel compounds as carcinogens following occupational inhalation exposure, it is not clear how environmental exposure to nickel may affect cancer risk. Nickel concentrations in the environment are much lower than those that were associated with cancer in the occupational setting. Nickel emitted from high-temperature combustion sources is also more likely to be in the form of a mineral lattice rather than the more active nickel refinery dust that contains nickel subsulphide, the form of nickel most consistently associated with cancer. Studies linking nickel uptake from the environment and cancer incidence in the general population are not available.

The US Department of Health and Human Services has determined that metallic nickel may reasonably be anticipated to be a human carcinogen and nickel compounds are known to be human carcinogens. Similarly, IARC (1997a) classified metallic nickel in Group 2B (possibly carcinogenic to humans) and nickel compounds in Group 1 (carcinogenic to humans). USEPA has classified nickel refinery dust (IRIS, 2006i) and nickel subsulphide (IRIS, 2006j) in Group A (human carcinogen). However, nickel has a high melting point (1 453 °C) and it is unlikely that it would be emitted from a cement kiln in the vapour form that would condense primarily as the metal on particulates. Exposure to metallic nickel is therefore unlikely. Other nickel compounds have not been classified by the USEPA as to their carcinogenicity. Based on the occupational

data, inhalation unit risk levels of $2.4 \times 10^{-4} (\mu\text{g}/\text{m}^3)^{-1}$ and $4.8 \times 10^{-4} (\mu\text{g}/\text{m}^3)^{-1}$ were derived by USEPA for nickel refinery dust and nickel subsulphide, respectively.

Although there is great uncertainty about the form in which nickel may be emitted from cement factories, INFOTOX applied these cancer unit risk values as a range to assess the risk of exposure to nickel compounds.

16.2 Noncancer risk assessment

Health Canada derived a tolerable concentration (TC) of $0.02 \mu\text{g Ni}/\text{m}^3$ for nickel oxide based on the lowest-observed-effect level (LOEL) of $0.02 \text{ mg}/\text{m}^3$ for increases in the number of granulocytes and lymphocytes in the lungs of rats (ITER, 2006; Spiegelberg *et al.*, 1984). An uncertainty factor of 1 000 was applied (10 for intraspecies variation, 10 for interspecies variation, and 10 for the less-than-chronic study and minimal effects at the LOEL). Health Canada also derived a tolerable concentration for nickel sulphate of $0.0035 \mu\text{g Ni}/\text{m}^3$ based on a study by Dunnick *et al.* (1989) and additional evaluation of the literature up to August 1993.

ATSDR (2005) evaluated the noncancer toxicity of various forms of nickel, and derived a chronic minimal risk level (MRL) based on nickel sulphate. This MRL pertains to the soluble nickel compounds (i.e., nickel chloride, nickel sulphate, and nickel nitrite), but ATSDR stated that this value would also be protective against the toxicity of other nickel compounds (i.e., the less-soluble compounds, including nickel oxide, nickel subsulphide, and metallic nickel). ATSDR's chronic minimal risk level (MRL) for the inhalation of nickel is $0.09 \mu\text{g}/\text{m}^3$, and is based on a NOAEL(HEC) of $0.0027 \text{ mg}/\text{m}^3$ for chronic active inflammation and lung fibrosis in rats exposed to nickel sulphate. ATSDR used an uncertainty factor of 30 (3 for extrapolation from animals to humans with dosimetric adjustment and 10 for human variability). The ATSDR MRL may be used for screening assessment but is not intended to be used for quantitative health risk assessment.

TERA (ITER, 2006) derived a reference concentration (RfC) for soluble nickel salts of $0.2 \mu\text{g Ni}/\text{m}^3$ based on data from the same study as ATSDR. TERA calculated a benchmark concentration and used a smaller uncertainty factor than ATSDR. An independent peer review panel through TERA's ITER Peer Review Program has reviewed and approved the TERA risk values.

RIVM (Baars *et al.*, 2001) derived a tolerable concentration in air (TCA) of $0.05 \mu\text{g}/\text{m}^3$ for nickel oxide based on a duration-adjusted NOAEC of $0.005 \text{ mg}/\text{m}^3$ for respiratory effects in rats (the same studies as used by ATSDR as well as additional studies), and an uncertainty factor of 100 (10 each for intra- and interspecies extrapolation).

INFOTOX used the range of 0.02 to $0.2 \mu\text{g Ni}/\text{m}^3$ to assess noncarcinogenic risks associated with exposure to nickel compounds.

17 Vanadium pentoxide

17.1 Cancer risk assessment

The Office of Environmental Health Hazard Assessment (OEHHA) of the California Environmental Protection Agency has added vanadium pentoxide (orthorhombic crystalline form) to the list of chemicals known to the state to cause cancer (OEHHA, 2005). The decision was based on an inhalation study on rats and mice conducted under the National Toxicology Program of the US Department of Health and Human Services (NTP, 2002). An increased incidence of bronchiolo-alveolar neoplasms was observed in male and female mice and male rats. Exposures were at high doses and the data do not unambiguously indicate a potential for human carcinogenicity at low environmental levels. No cancer slope factor has been proposed.

The International Agency for Research on Cancer (IARC, 2003) evaluated vanadium pentoxide as possibly carcinogenic to humans (Group 2B). The overall evaluation was reached on the basis of *sufficient evidence* as to the carcinogenicity of vanadium pentoxide in experimental animals (the NTP study), in the absence of data on human cancer.

Because evidence for the carcinogenicity of vanadium pentoxide is insufficient, INFOTOX did not assess vanadium pentoxide as a carcinogen.

17.2 Noncancer risk assessment

Numerous studies have reported acute and chronic respiratory effects during occupational exposure, mainly due to exposure to vanadium pentoxide (WHO, 2000). Most of the reported clinical symptoms reflect irritative effects of vanadium on the upper respiratory tract. Only at high concentrations (above 1 mg V/m³) were more serious effects of the lower respiratory tract observed, such as bronchitis and pneumonitis.

Available data from occupational studies suggest that the lowest-observed-adverse-effect level of vanadium can be assumed to be 20 µg/m³, based on chronic upper respiratory tract symptoms (WHO, 2000). Since the adverse nature of the observed effects on the upper respiratory tract were minimal at this concentration and a susceptible subpopulation has not been identified, WHO (2000) selected a protection factor of 20. Therefore, below 1 µg V/m³ (averaging time 24 hours) environmental exposure to vanadium is not likely to have adverse effects on health.

INFOTOX adopted this guideline for the assessment of health risks associated with exposure to vanadium.

18 Polychlorinated dioxins, furans and PCBs

18.1 Cancer risk assessment

The term *dioxin* or *dioxins* refers to a range of polychlorinated dibenzo-p-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs), and a range of coplanar polychlorinated biphenyls (PCBs) that have dioxin-like toxicity.

USEPA (2001) has characterised 2,3,7,8-TCDD as a “*human carcinogen*” based on the weight of evidence of animal and human studies; other dioxin-like compounds, i.e., other polychlorinated dibenzo-p-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs), and dioxin-like polychlorinated biphenyls (PCBs) have been classified as “*likely human carcinogens*.” The US Department of Health and Human Services determined that “*it is reasonable to expect that 2,3,7,8-TCDD may cause cancer*” (ATSDR, 1998). The International Agency for Research on Cancer determined that 2,3,7,8-TCDD is a “*known human carcinogen*” (IARC, 1997b).

In order to derive an overall toxicity value for a mixture of dioxin and furan congeners, the concept of toxicity equivalency factors (TEFs) was introduced. TEFs are estimates of the toxicity of dioxin-like compounds relative to the toxicity of 2,3,7,8-tetrachloro-p-dibenzodioxin (TCDD), which is assigned a TEF of 1. 2,3,7,8-TCDD is the most toxic congener, and most scientific studies have focussed on the toxicology and health effects associated with this compound (USEPA, 1989; USEPA, 1994).

The 2,3,7,8-TCDD toxicity equivalent (TEQ) for a mixture of dioxins and furans is determined by multiplying the concentrations of the individual congeners with their TEF values, and summing the products. WHO has listed TEFs for the coplanar PCBs, and these were used to calculate TEQs for the stack emission samples.

The data on which USEPA has derived an inhalation cancer slope factor of 1.5×10^5 (mg/kg-day)⁻¹ and an inhalation unit risk estimate of 3.3×10^{-5} (pg/m³)⁻¹ for 2,3,7,8-TCDD were based on USEPA data in HEAST (1997) and USEPA (1985). The US Environmental Protection Agency has continued to work towards completion of its reassessment of dioxin exposure and human health effects entitled, *Exposure and Human Health Reassessment of 2,3,7,8-Tetrachlorodibenzo-p-Dioxin (TCDD) and Related Compounds* (the dioxin reassessment). On October 29, 2003, the Interagency Working Group on Dioxin (IWG) officially requested that the National Academy of Sciences (NAS) review USEPA’s draft dioxin reassessment. In this review, it was confirmed that “*The Agency, although fully recognizing the range and the public health-conservative nature of the slope factors that make up the range, suggests the use of 1×10^{-3} per pg TEQ/kg-day as an estimator of upper bound cancer risk for both background intakes and incremental intakes above background*” (NAS, 2004).

Assuming the validity of extrapolation across oral and inhalation routes of exposure and using the same relationship that has been employed to derive the previous USEPA unit risk factor for inhalation [33 (μg/m³)⁻¹], an updated unit risk factor of 214 (μg/m³)⁻¹ can be derived.

INFOTOX applied this updated cancer unit risk factor in the assessment of cancer risks associated with exposure to dioxins.

18.2 Noncancer risk assessment

The dioxin group of compounds have been characterised as developmental, reproductive, immunological, endocrinological, and carcinogenic hazards. The deduction that humans are likely to respond with noncancer effects from exposure to dioxin-like compounds is based on the finding that these compounds impact cellular regulation at a fundamental level and on the demonstration of adverse effects among a broad range of species. For example, because developmental toxicity following exposure to TCDD-like congeners occurs in fish, amphibians, reptiles, birds, and mammals, it is likely to occur at some level in humans.

It is not currently possible to state exactly how or at what levels individuals will respond with specific adverse impacts on development or reproductive function, but the analyses of available cohort data and laboratory animal studies suggest that some effects may occur at or near background levels. USEPA and other agencies have therefore not recommended a noncancer reference concentration. Because exceeding the RfC is not a statement of risk, comparing an incremental exposure to an RfC when the RfC has already been exceeded by average background exposures has little value for evaluating possible risk management options. In addition, the calculation of an RfC (with its traditional focus on a single “critical” effect) distracts from the large array of effects associated with similar body burdens of dioxin.

INFOTOX did therefore not consider the assessment of exposure to dioxins with regard to noncarcinogenic effects.

19 References

Abbott P J, 1987. Methylcyclopentadienyl Manganese Tricarbonyl (MMT) in Petrol: The Toxicologic Issues. *Sci Tot Env*, 67: 247-255.

ACSH, 1997. Lead and Human Health. American Council on Science and Health.

Amitai Y, Zlotogorski Z, Golan-Katzav V, Wexler A and Gross D, 1998. Neuropsychological impairment from acute low-level exposure to carbon monoxide. *Archives of Neurology*, 55:845-848.

Anderson H R, Ponce de Leon A, Bland J M, Bower J S, Emberlin J and Strachan P, 1998. Air pollution, pollens, and daily admissions for asthma in London 1987-92. *Thorax*, 53:842-848.

ATSDR, 1998. Draft Update Toxicological Profile for Chlorinated Dibenzo-p-dioxins. Prepared by Research Triangle Institute for U.S. Department of Health and Human Services, Agency for Toxic Substances Disease Registry (ATSDR), Atlanta, GA. 677 pp +appendices.

ATSDR, 1990. Toxicological Profile for Copper. ATSDR report no. TP90-08, Agency for Toxic Substances and Disease Registry, US Public Health Service, Atlanta (Georgia), USA.

ATSDR, 1992. Toxicological Profile for Cobalt. ATSDR report no. TP-91/10. Agency for Toxic Substances and Disease Registry. US Department of Health and Human Services. US Public Health Service, Atlanta (Georgia), USA.

ATSDR, 1999. Toxicological Profile for Cadmium. Agency for Toxic Substances and Disease Registry. US Department of Health and Human Services, Public Health Service. July. Available at <http://www.atsdr.cdc.gov/toxprofiles/tp5.html> .

ATSDR, 1999. Toxicological Profile for Mercury. Agency for Toxic Substances and Disease Registry. US Department of Health and Human Services, Public Health Service. March. <http://www.atsdr.cdc.gov/toxprofiles/tp46.html>.

ATSDR, 2000. Toxicological Profile for Manganese. Update. Agency for Toxic Substances and Disease Registry. US Department of Health and Human Services, Public Health Service. September. <http://www.atsdr.cdc.gov/toxprofiles/tp151.html>.

ATSDR, 2004. Toxicological Profile for Cobalt. Agency for Toxic Substances and Disease Registry. US Department of Health and Human Services, Public Health Service. April. <http://www.atsdr.cdc.gov/toxprofiles/tp33.html>.

ATSDR, 2005. Toxicological Profile for Nickel. Final, August 2005. Agency for Toxic Substances and Disease Registry, US Department of Health and Human Services, Public Health Service.

Baars A J, Theelen R M C, Janssen P J C M, Hesse J M, Apeldoorn M E van, Meijerink M C M, Verdam L and Zeilmaker M J, 2001. Re-evaluation of human-toxicological maximum permissible risk levels. RIVM report no. 711701025, National Institute of Public Health and the Environment, Bilthoven, The Netherlands, March 2001, p 62-65. <http://www.rivm.nl/bibliotheek/rapporten/711701025.pdf> or <http://www.rivm.nl/en/> .

ChemRisk, A Service of McLaren/Hart Inc, 1998. Documentation Package - Chromium (VI) Inhalation Reference Concentration. Pittsburgh, PA.

Crump K S, Shipp A M, Clewel H J and Gentry P R, 1994. Critical Review of EPA's Revised Manganese RfC. Prepared for Ethyl Corporation by ICF Kaiser, Ruston, Louisiana.

Dab W, Medina S, Quénel P, Le Moullec Y, Le Tertre A, Thelot B, Monteil C, Lameloise P, Priard P, Momas I, Ferry R and Festy B, 1996. Short term respiratory health effects of ambient air pollution: results of the APHEA project in Paris. *Journal of Epidemiology and Community Health*, 50 (suppl 1), S42-S46.

Davis M D, Jarabek A, Mage D T and Graham J A, 1998. The EPA Health Risk Assessment of Methylcyclopentadienyl Manganese Tricarbonyl (MMT). *Risk Analysis*, 18, (1), 57.

Derryberry O M, Bartholomew M D, and Fleming R B L, 1963. Fluoride exposure and worker health - The health status of workers in a fertilizer manufacturing plant in relation to fluoride exposure. *Arch. Environ. Health*, 6:503-514.

- Dodge R, 1983. The respiratory health and lung function of Anglo-American children in a smelter town. *American Review of Respiratory Disease*, 127:158-161.
- Dominici F, McDermott A, Zeger S L, Samet J M, 2003. Airborne Particulate Matter and Mortality: Timescale Effects in Four US Cities. *American Journal of Epidemiology*, 12:1055-1065.
- Dunnick J K, Elwell M R, Benson J M, 1989. Lung toxicity after 13-week inhalation exposure to nickel oxide, nickel subsulfide, or nickel sulfate in F344/N rats and B6C3F1 mice. *Fund Appl Toxicol*, 12:584-594.
- Environment Canada, Health Canada, 1994. Priority substances list assessment report: cadmium and its compounds. Ottawa. Ministry of Public Works and Government Services. http://www.hc-sc.gc.ca/ewh-semt/pubs/contaminants/psl1-lsp1/index_e.html.
- Fawer R F, de Ribaupierre Y, Guillemin M P, Berode M and Lob M, 1983. Measurement of hand tremor induced by industrial exposure to metallic mercury. *J. Industrial Medicine* 40:204-208. March.
- Filleul L, Rondeau V, Vandentorren S, Le Moual N, Cantagrel A, Annesi-Maesano I, Charpin D, Declercq C, Neukirch F, Paris C, Vervloet D, Brochard P, Tessier J F, Kauffmann F, Baldi I, 2005. Twenty five year mortality and air pollution: results from the French PAARC survey *Occupational and Environmental Medicine*, 62:453 – 460.
- Fourie M H, Van Niekerk W C A and Mouton G, 2003. Technical Background Document for the Development of a National Ambient Air Quality Standard for Lead. Report prepared on behalf of the Chemical and Allied Industry Association. INFOTOX Document number 005-2003.
- Fung K Y, Luginaah I, Gorey K M, Webster G, 2005. Air pollution and daily hospital admissions for cardiovascular diseases in Windsor, Ontario. *Canadian Journal of Public Health*, 96:29-33.
- Gilman A G, Rall T W, Nies A S and Taylor P (eds.), 1990. *Goodman and Gilman's The Pharmacological Basis of Therapeutics*. 8th ed. New York, NY:Pergamon Press, p.1619.
- Glaser U, Hochrainer D, Steinhoff D, 1990. Investigation of irritating properties of inhaled Cr(VI) with possible influence on its carcinogenic action. In: *Environmental Hygiene II*. Seemayer, NO;
- Hall S K, 1996. Toxic responses of the blood. In: Hall, S.K., Chakraborty, J. & Ruch, R.J. *Chemical Exposure and Toxic Responses*. New York: CRC Lewis publishers, p. 106.
- Health Canada, 1996a. Health-Based Tolerable Daily Intakes/Concentrations and Tumourigenic Doses/Concentrations for Priority Substances. Ottawa: Ministry of Supply and Services Canada. H46-2/96-194E.
- Health Canada, 1996b. Canadian Environmental Protection Act. Priority Substances List. Supporting Documentation: Health-Based Tolerable Daily Intakes/Concentrations and Tumourigenic Doses/Concentrations for Priority Substances. (unpublished). This is the supporting document for Health Canada (1996a).

Health Canada, 2005. Regulations Related To Health And Air Quality: National Ambient Air Quality Objectives (NAAQOs). Last updated: 2004-10-01. http://www.hc-sc.gc.ca/ewh-semt/air/out-ext/reg_e.html#3.

Heast, 1997. Health Effects Assessment Summary Tables. FY 1997 Update. Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, US Environmental Protection Agency. Cincinnati, OH.

IARC, 1997a. Nickel and nickel compounds. International Agency for Research on Cancer (IARC) Monographs. Volume 49. Summaries and Evaluations. <http://monographs.iarc.fr/ENG/Monographs/vol49/volume49.pdf>.

IARC, 1997b. Polychlorinated dibenzo-para-dioxins and polychlorinated dibenzofurans. Vol. 69, IARC monographs on the evaluation of carcinogenic risks to humans. International Agency for Research on Cancer (IARC), World Health Organisation (WHO), Lyon, France.

IARC, 2002. Some Drinking-water Disinfectants and Contaminants, including Arsenic. International Agency for Research on Cancer (IARC) Monographs. Volume 84. www.iarc.fr/ENG/Databases/index.php.

IARC, 2003. Cobalt in Hard-metals and Cobalt Sulfate, Gallium Arsenide, Indium Phosphide and Vanadium Pentoxide. IARC Monographs on the Evaluation of Carcinogenic Risks To Humans, Volume 86.

IARC, 2004. Inorganic and organic lead compounds. Volume 87 of the IARC Monographs, Lyon, France: International Agency for Research on Cancer. <http://monographs.iarc.fr/ENG/Meetings/vol87.php>.

IARC, 2006. Antimony trioxide, antimony trisulfide. Volume 47 of the IARC Monographs, 1989, Lyon, France: International Agency for Research on Cancer. <http://monographs.iarc.fr/>. Last revised September 2006.

IEH, 1998. IEH assessment on indoor air quality in the home (2): carbon monoxide. Institute for Environment and Health. Norwich: Page Bros.

IPCS, 1999. Environmental Health Criteria 213: Carbon Monoxide. International Programme on Chemical Safety, World Health Organisation, Geneva.

IRIS, 1998. Antimony (CASRN 7440-36-0). Integrated Risk Information System. Online. National Center for Environmental Assessment, Washington, DC. <http://www.epa.gov/iris/>.

IRIS, 2006a. Hydrogen chloride (CASRN 7647-01-0), last revised 1 July 1995. Integrated Risk Information System. Online. National Center for Environmental Assessment, Washington, DC. <http://www.epa.gov/iris/>.

IRIS, 2006b. Arsenic, inorganic (CASRN 7440-38-2), last revised 10 April 1998. Integrated Risk Information System. Online. National Center for Environmental Assessment, Washington, DC. <http://www.epa.gov/iris/>.

IRIS, 2006c. Cadmium (CASRN 7440-43-9), last revised 1 June 1992. Integrated Risk Information System. Online. National Center for Environmental Assessment, Washington, DC. <http://www.epa.gov/iris/>.

IRIS, 2006d. Chromium (VI) (CASRN 18540-29-9), last revised 3 September 1998. Integrated Risk Information System. Online. National Center for Environmental Assessment, Washington, DC. <http://www.epa.gov/iris/>.

IRIS, 2006e. Copper (CASRN 7440-50-8), last revised 1 July 1995. Integrated Risk Information System. Online. National Center for Environmental Assessment, Washington, DC. <http://www.epa.gov/iris/>.

IRIS, 2006f. Lead and compounds (inorganic) (CASRN 7439-92-1), last revised 1 November 1993. Integrated Risk Information System. Online. National Center for Environmental Assessment, Washington, DC. <http://www.epa.gov/iris/>.

IRIS, 2006g. Manganese (CASRN 7439-96-5), last revised 1 December 1996. Integrated Risk Information System. Online. National Center for Environmental Assessment, Washington, DC. <http://www.epa.gov/iris/>.

IRIS, 2006h. Mercury, elemental (CASRN 7439-97-6), last revised 1 May 1995. Integrated Risk Information System. Online. National Center for Environmental Assessment, Washington, DC. <http://www.epa.gov/iris/>.

IRIS, 2006i. Nickel refinery dust, last revised 1 January 1991. Integrated Risk Information System. Online. National Center for Environmental Assessment, Washington, DC. <http://www.epa.gov/iris/>.

IRIS, 2006j. Nickel subsulfide (CASRN 12035-72-2), last revised 1 January 1991. Integrated Risk Information System. Online. National Center for Environmental Assessment, Washington, DC. <http://www.epa.gov/iris/>.

ITER, 2006. International Toxicity Estimates for Risk Database. Toxicology Excellence for Risk Assessment & Concurrent Technologies Corporation. <http://tera.org/iter/>.

Iwai K, Mizuno S, Miyasaka Y, Mori T, 2005. Correlation between suspended particles in the environmental air and causes of disease among inhabitants: Cross-sectional studies using the vital statistics and air pollution data in Japan. *Environmental Research* 99:106–117.

Johansson A, Curstedt T, Robertson B, Camner P, 1984. Lung morphology and phospholipids after experimental inhalation of soluble cadmium, copper, and cobalt. *Environ Res*, **34**: 295-309; as cited in ATSDR, 1990.

LDAI, 2001. On-line Fact Book, Lead Development Association International.
www.ldaint.org/factbook/.

Leaf D A & Kleinman M T, 1996. Urban ectopy in the mountains: carbon monoxide exposure at high altitude. Archives of environmental health, 51:283-290.

Lin M, Chen Y, Burnett R T, Villeneuve P J and Krewski D, 2003. Effect of short-term exposure to gaseous pollution on asthma hospitalisation in children: a bi-directional case-crossover analysis. Journal of Epidemiology and Community Health, 57:50-55.

Luginaah I N, Fung K Y, Gorey K M, Webster G and Wills C, 2005. Association of ambient air pollution with respiratory hospitalization in a government-designated "area of concern": The case of Windsor, Ontario. Environmental Health Perspectives, 113:290–296.

Mackison F W, Stricoff R S, and Partridge L J(Jr). (eds.), 1981. NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) Publication No. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office.

Malsch P A, Proctor D M, Finley B L, 1994. Estimation of a chromium inhalation reference concentration using the benchmark dose method: a case study. Regul Toxicol Pharmacol, 20:58-82.

Morawska L, Moore M R & Ristovski Z D, 2004. Health Impacts of Ultrafine Particles. Canberra: Australian Department of the Environment and Heritage.

NAS, 2004. Draft review. Exposure and Human Health Reassessment of 2,3,7,8-Tetrachlorodibenzo-p-Dioxin (TCDD) and Related Compounds National Academy Sciences (NAS).

Nemery B, Casier P, Roosels D, Lahaye D and Demedts M, 1992. Survey of cobalt exposure and respiratory health in diamond polishers. Am Rev Respir Dis, 145:610-616.

NRC, 2004. Acute Exposure Guideline Levels for Selected Airborne Chemicals: Volume 4. Subcommittee on Acute Exposure Guideline Levels, Committee on Toxicology, National Research Council. National Academies Press, Washington, DC.

NTP, 2002. Toxicology and Carcinogenesis Studies of Vanadium Pentoxide (CAS No. 1314-62-1) in F344/N Rats and B6C3F1 Mice (Inhalation Studies). NTP Technical Report Series No. 507. NIH Publication No. 03-4441. National Toxicology Program, US Department of Health and Human Services, Public Health Service, National Institutes of Health, NTP, Research Triangle Park, NC.

NZME, 2002. 2002 Ambient Air Quality Guidelines. New-Zealand Ministry for the Environment.
<http://www.mfe.govt.nz/publications/air/ambient-air-quality-may02/html/index.html>.

OEHHA, 2003. Determination of Noncancer Chronic Reference Exposure Levels. Fluorides Including hydrogen fluoride, chronic toxicity summary. Office of Environmental Health Hazard Assessment, California Environmental Protection Agency.

OEHHA, 2005. California Regulatory Notice Register (Register No. 2004, No. 29-Z). Chemical Listed Effective February 11, 2005. The Office of Environmental Health Hazard Assessment (OEHHA) of the California Environmental Protection Agency.

Poloniecki J D, Atkinson R W, Leon A P, Anderson H R, 1997. Daily time series for cardiovascular hospital admissions and previous day's air pollution in London, UK. *Occupational and Environmental Medicine*, 54:535-540.

Ponka A, Virtanen M, 1996. Low-level air pollution and hospital admissions for cardiac and cerebrovascular diseases in Helsinki. *American Journal of Public Health*, 86:1273-1280.

Putz V R, 1979. The effects of carbon monoxide on dual-task performance. *Human Factors*, 21:13-24.

Roels H A, Ghyselen P, Buchet J P, Ceulemans E and Lauwerys R R, 1992. Assessment of the permissible exposure level to manganese in workers exposed to manganese dioxide dust. *Br J Ind Med*, 49:25-34.

Saez M, 1993. Relationship between weather, temperature, air pollution and mortality in Barcelona. *European Respiratory Journal*, 6:346.

SANS, 2003. South African National Standard, Ambient air quality — Limits for common pollutants, SANS 1929:200x Edition 1, Published by Standards South Africa, Pretoria.

Schulte J H, 1963. Effects of mild carbon monoxide intoxication. *Archives of Environmental Health*, 7:524-530.

Schwartz J, 2004. The effects of particulate air pollution on daily deaths: a multi-city case crossover analysis. *Occupational and Environmental Medicine*, 61:956-961.

Schwartz J, Spix, C., Touloumi, G., Bachárová, L., Barumamdzadeh, T., Le Tertre, A., Piekarksi, T., Ponce de Leon, A., Pönkä, A., Rossi, G., Saez, M. & Schouren, J.P. 1996. Methodological issues in studies of air pollution and daily counts of deaths or hospital admissions. *Journal of Epidemiology and Community Health*, 50 (Suppl):S3-S11.

Slob W, Janssen P and Pieters M, 1996. Review of the Proposed Air Quality Guidelines for Manganese. European Centre for Environment and Health, Bilthoven, The Netherlands. Report No ICP EHH 018 VD96.2/12, 8 October 1996.

Spiegelberg T, Kordel, W and Hochrainer D, 1984. Effects of NiO inhalation on alveolar macrophages and the humoral immune systems of rats. *Ecotox Environ Safety*, 8:516-525.

Sprince N L, Liver L C, Eisen E A, Greene R E and Chamberlin R I, 1988. Cobalt exposure and lung disease in tungsten carbide production: A cross-sectional study of current workers. *Am Rev Respir Dis*, 138:1220-1226. As cited in: ATSDR, 1992.

Stedman J R, Linehan E & King K, 1999. Quantification of the Health Effects of Air Pollution in

the UK for the Review of the National Air Quality Strategy. A report produced for The Department of the Environment, Transport and the Regions. Report No AEAT-4715 Issue 1. London: Department of the Environment, Transport and the Regions.

Stevens B, Koenig J Q, Rebolledo V, Hanley Q S and Covert D S, 1992. Respiratory effects from the inhalation of hydrogen chloride in young adult asthmatics. *JOM*, 34:923-929.

Sunyer J, Atkinson R, Ballester F, Le Tertre A, Ayres J G, Forastiere F, Forsberg B, Vonk J M, Bisanti L, Anderson R H, Schwartz J, Katsouyanni K, 2003. Respiratory effects of sulphur dioxide: a hierarchical multicity analysis in the APHEA 2 study. *Occup Environ Med* 2003, 60:e2 (<http://www.occenvmed.com/cgi/content/full/60/8/e2>) (electronic paper).

Takenaka S, Oldiges H, Konig H, Hochrainer D and Oberdorsater G, 1983. Carcinogenicity of cadmium chloride aerosols in W rats. *J Nat Cancer Inst*, 70: 367-373.

Tenias J M, Ballester F, Perez-Hoyos S, Rivera M L, 2002. Air pollution and hospital emergency room admissions for chronic obstructive pulmonary disease in Valencia, Spain. *Archives of Environmental Health*, 57:41-47.

TERA, 1999. Toxicological Review of Soluble Nickel Salts. Toxicology Excellence for Risk Assessment. Prepared for Metal Finishing Association of Southern California, Inc, US Environmental Protection Agency and Health Canada. March 1999. <http://www.tera.org/vera/Nickel%20Doc%20page.htm>.

Thompson A J, Shields M D & Patterson C C, 2001. Acute asthma exacerbations and air pollutants in children living in Belfast, Northern Ireland. *Archives of Environmental Health*, 56:234-241.

Timbrell J A, 1991. Biochemical mechanisms of toxicity: specific examples. In: Timbrell, J.A. *Principals of Biochemical Toxicology*, 2nd edition. Washington D.C.: Taylor & Francis. p. 342.

Tsai S S, Goggins W B, Chiu H F, Yang C Y, 2003. Evidence for an association between air pollution and daily stroke admissions in Kaohsiung, Taiwan. *Stroke* 2003: 2612-2616.

UK DETR, 1998. UK Department of the Environment, Transport and the Regions, Expert Panel on Air Quality Standards: Lead.

USEPA, 1985. Health Assessment Document for Polychlorinated Dibenzo-p-Dioxin. Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, US Environmental Protection Agency. Cincinnati, OH. EPA 600/8-84-014F.

USEPA, 1989. Interim Procedure for Estimating Risks Associated with Exposures to Mixtures of Chlorinated Dibenzo-p-dioxins and Dibenzofurans (CDDs and CDFs) and 1989 Update. Risk Assessment Forum, EPA/625/3-98/016. NTIS, Springfields, VA; PB90-145756.

USEPA, 1994. Estimating Exposure to Dioxin-like Compounds. EPA/600/6-88/005, Office of Research and Development, Washington DC, US Environmental Protection Agency.

USEPA, 2001. Exposure and Human Health Reassessment of 2,3,7,8-Tetrachlorodibenzo-p-Dioxin (TCDD) and Related Compounds. Parts I-III. Draft. Prepared by the National Center for Environmental Assessment, Office of Research and Development, Washington, DC. EPA/600/P-00/001 Bb, Bc, Bd, Be, Bg. Available from: <http://www.epa.gov/ncea> .

USEPA, 2006. EPA response to 9-11. Metals in air. Reference to antimony. OST/www.epa.gov/wtc/metal/.

Van Niekerk W C A and Fourie M H, 2004. Ultrafine Particles: Aggravating Exposure Factor? Proceedings of the Tenth International Ferroalloys Congress, INFACON X, February 2004, Cape Town, South Africa. (Available on the Proceedings CD.)

Walters S, Griffiths R K & Ayeres J G, 1994. Temporal association between hospital admissions for asthma in Birmingham and ambient levels of sulphur dioxide and smoke. *Thorax*, 49:133-140.

WHO, 1987. Air Quality Guidelines for Europe, Europe Series No 23.

WHO, 2000. Air Quality Guidelines - Second Edition Chapter 6.12 Vanadium. WHO Regional Office for Europe, Copenhagen, Denmark. www.euro.who.int/document/aiq/6_12vanadium.pdf.

WHO, 2005. WHO air quality guidelines global update. Report on a Working Group meeting, Bonn, Germany, 18-20 October 2005. World Health Organisation, WHO Regional Office for Europe, Copenhagen, Denmark.

Wong T W, Lau T S, Yu T S, Neller A, Wong S L, Tam W, Pang S W, 1999. Air pollution and hospital admissions for respiratory and cardiovascular diseases in Hong Kong. *Occupational and Environmental Medicine*, 56:679-683.