National Environment Protection (Ambient Air Quality) Measure

Report of the Risk Assessment Taskforce

Appendix 2

Review of Risk Assessment Methodologies Applicable to Ambient Air Quality

by

HERMA Risk Consultants Pty Ltd

(Report 99/147)

October 1999

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ISBN 0-642-323-208

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Acknowledgements

The author is grateful for useful discussions and information provided by a number of colleagues in Australia, Canada and the USA. In particular, thanks are due to the following individuals for their contributions:

Robert Lee, David Brenner, Susan Munroe, Shirley Deviesseux, Andrea Hinwood, Lynette Denison and Andrew Langley.

The author has also benefited from participation in a Technical Workshop on Risk Assessment Methodologies convened by the NEPC, and held in Melbourne on 23 July 1999.

Finally, the author wishes to thank the Risk Assessment Taskforce, and Professor Steve E. Hrudey of the University of Alberta, Canada, for their peer review of the draft, and for useful comments.

Prologue

"*The Air we receive at our birth and resign only when we die*
is the first necessity of our existence"

The Times, London, 17 February 1881.

"*We grow weary of speculations about the Air*"

Robert Angus Smith
"The Beginning of Chemical Climatology"
Longman, Green & Co., London, 1872

"*All models are wrong, but some are useful*"

George E. P. Box
"Robustness in the Strategy of Scientific Model Building"
in Launer, R. L., & G. N. Wilkinson (Eds.), "Robustness in Statistics"
Academic Press, New York, 1979

1. EXECUTIVE SUMMARY

HERMA Risk Consultants have completed a systematic review of existing international risk assessment methodologies which might be applicable to ambient air quality in Australia. The broad aim of the review was to explore the current, practical state-of-the-art in health-based risk assessment (HRA) of ambient air pollutants, with regard to its potential applicability to the derivation of ambient air quality guideline values for use in the standard-setting process.

Amongst current approaches to HRA, the following key methodologies were reviewed on the basis of their potential relevance to ambient air quality:

- United States Environmental Protection Agency (USEPA)
- California Air Pollution Control Officer's Association (CAPCOA)
- Integrated Exposure Uptake Biokinetic (IEUBK) Model (Lead)
- Health and Welfare Canada
- World Health Organisation (WHO)
- United Kingdom Expert Panel on Air Quality Standards (UK)
- The Ricci and Beer Approach
- National Environmental Health Forum (NEHF) [ENHealth Council]
- Contaminated Sites National Environment Protection Measure (Soil NEPM)

These nine methodological approaches include five frameworks (Canadian, WHO, UK, NEHF & Soil NEPM), three modelling approaches (USEPA, CAPCOA & Ricci/Beer), and only one true model (IEUBK). However, these are not exact distinctions, as the categories tend to overlap in some cases. CAPCOA, for example, essentially consists of two separate models that form the overall modelling approach. The methodologies were each reviewed against a common set of 26 criteria (covering key elements of exposure assessment, health effects data, risk characterisation & modelling) to provide a basis for evaluating their potential usefulness in developing NEPC ambient air quality standards.

The results of the review indicate that no single HRA methodology is completely suited to the development of ambient air quality standards in Australia. All nine approaches have advantages, disadvantages and limitations, and we believe that it will not serve the overall interest to make a single, all-encompassing "off the shelf" choice. Rather, we consider that flexibility is the key, and in order to maintain consistency, suitable approaches should, if possible, build on the existing approaches for HRA in Australia. Moreover, in recognition of the need to consider criteria pollutants separately from air toxics, and in order to facilitate an open and transparent standard-setting process, we believe that serious consideration should be given to the development of two specific, but complementary HRA approaches for ambient air quality:

A criteria pollutants modelling approach, based on the WHO methodology, and taking into account the detailed findings of this review.

An air toxics modelling approach, based on the future NEHF framework, and taking into account the detailed findings of this review.

2. INTRODUCTION

HERMA Risk Consultants Pty Ltd (HERMA) has been commissioned by the National Environment Protection Council (NEPC), on behalf of its Risk Assessment Task Force (RATF), to conduct a review of existing international risk assessment methodologies which might be applicable to ambient air quality in Australia[1]. The broad aim of this review is to explore the current, practical state-of-the-art in health-based risk assessment (HRA) as applied to ambient air pollutants, with regard to its potential usefulness in the setting of NEPC ambient air quality standards.

This report documents the results and rationale of the overall review process, and provides a sound basis for the determination of possible future directions for the setting of ambient air quality standards in Australia. In this regard, we have attempted to provide an objective evaluation of the inherently subjective application of a range of HRA tools to the ambient air environment.

Whilst a report of this type cannot avoid the use of technical jargon altogether, we have made a conscious attempt to keep such terminology to a minimum, with important terms being explained within the body of the report, as applicable.

Please note that throughout the report, all superscript numerals within the text refer to specific references cited in corresponding numerical order within Section 9.

3. PURPOSE AND SCOPE

This study was designed to systematically review the following international HRA frameworks, modelling approaches and incorporated models, as they relate to ambient air pollutants:

- United States Environmental Protection Agency [(US) EPA] methodology
- California Air Pollution Control Officers' Association (CAPCOA) approach
- Integrated Exposure Uptake Biokinetic (IEUBK) Model for lead in children
- Canadian methodology (Health and Welfare Canada)
- World Health Organisation (WHO) methodology
- United Kingdom (UK) Expert Panel on Air Quality Standards
- Ricci / Beer approach (Australia)
- National Environmental Health Forum (NEHF) approach (Australia)
- Contaminated Sites National Environment Protection Measure (NEPM) approach (Australia)

These methodologies were each reviewed against a common set of key criteria, as set out in Appendix 1, to provide a basis for evaluating their potential usefulness in developing NEPC ambient air quality standards. In this regard, the review has largely focused on the capacity of existing HRA methodologies to be employed in the development of ambient air quality standards, rather than on the general aspects of any particular HRA approach. A limited search and preliminary assessment of the peer-reviewed scientific literature was also undertaken to overview relevant current developments and emerging issues.

4. BACKGROUND

The National Environment Protection Measure (NEPM) for ambient air[2] was made on 26 June 1998. This NEPM provides a set of national ambient air quality standards for six priority (or "criteria") pollutants, with provision for a monitoring protocol for the assessment of ambient air quality. The priority pollutants include carbon monoxide (CO), nitrogen dioxide (NO_2), ozone (O_3), sulphur dioxide (SO_2), lead (Pb), and respirable particulate matter (PM_{10}).

During the development of the ambient air quality NEPM, an attempt was made to carry out a health risk assessment on the six pollutants being considered[3,4]. It was acknowledged at the time that a risk assessment approach had not been used before in Australia for the purpose of setting ambient air quality standards. After detailed analysis of the risk assessment process employed, and taking into account both expert and key stakeholder advice on the matter, it became clear that in order for the results of the risk assessment to be useful in evaluating the respective merits of the range of standards under consideration, the process required an ability to estimate incremental changes in risk for the range of possible standards for each pollutant. The NEPC concluded at the time that neither the methodology nor the available information sets allowed this to be undertaken5. In view of this, the outcomes of the health risk assessment process were not used in the development of the NEPM air quality standards.

Subsequently, the NEPC agreed that there was a need to investigate the possibility of developing a risk assessment approach that might be used in the review of ambient air quality standards and in the development of any future air quality standards. Accordingly, one of the future actions specified in the NEPM was the establishment of a Risk Assessment Taskforce (RATF)5 to "investigate a risk assessment approach to guide the application of [future ambient air quality] standards, to report within 3 years".

The NEPC Committee subsequently established the RATF, with 4 government representatives, 2 industry and 2 environment group representatives, with a Chair and executive officer from NEPC. In order to fulfil the RATF Terms of Reference (ToR), a three-stage plan of work was developed:

> **Stage 1** involves this project to review current risk assessment models; a review by RATF of epidemiological data and accompanying studies; and the development of a consultation strategy required to implement risk assessment.
>
> **Stage 2** involves consultation with key stakeholders on the outcomes of the Stage 1 work.
>
> **Stage 3** involves consideration by the RATF of stakeholder feedback from Stage 2, and the preparation of a final report and recommendations to the NEPC Committee for their consideration and action.

The ToR for the RATF require that an evaluation of "the adequacy of current risk assessment models for their applicability in the NEPC context and to assess the desirability and the viability of developing a standard methodology for risk-based approaches" be carried out.

On this basis, the present review has been designed to facilitate a technical evaluation of currently available risk assessment methodologies (incorporating existing frameworks, modelling approaches and models) and to provide information on their potential usefulness in developing NEPC ambient air quality standards.

It is acknowledged by the RATF that a significant body of work has already been generated towards developing a generic framework for the application of health risk assessment in a number of settings (e.g., the NEHF approach in Australia). It is not intended that the present review will focus on the general aspects of any particular framework for risk assessment, but will concentrate on the capacity of existing ("off the shelf") risk assessment methodologies to be employed in setting ambient air quality standards. In this regard, significant air quality issues such as exposure assessment and risk characterisation are expected to form a major focus for the review.

In order to draw on key stakeholder expertise and knowledge of HRA, a one-day Technical Workshop was convened by NEPC and held in Melbourne on 23 July 1999. The Workshop provided a general discussion and information exchange forum on risk assessment, and attempted to focus on the potential applicability of various HRA approaches in the setting of ambient air quality standards. This proved to be very difficult.

5. RATIONALE FOR HEALTH RISK ASSESSMENT

In general terms, ***risk*** is simply a function of the ***probability*** of an undesirable action or event occurring (i.e., how likely is it to happen?) and the ***consequence/s*** of the event (i.e., how bad is it when it happens?). In the context of this review, ***risk*** can therefore be expressed as *the likelihood of occurrence of a discrete level of harm, under a specific set of conditions, in a defined exposure situation*. This is not to be confused with the term ***hazard***, which is merely the *potential for harm.* Thus, the use of highly hazardous chemicals in industry, for example, might result in either a *significant risk* to health where uncontrolled (high-level) worker exposure occurs, or a *negligible risk* to health where worker exposure is minimised or prevented by some means.

In a practical sense, it is clear that the term *risk* always implies *uncertainty*, and the concept of risk is inherently probabilistic in nature. Risk assessment is therefore concerned with making technical decisions as to the nature and magnitude of a risk, where there is uncertainty both as to whether the undesirable action or event will happen, and what its consequences will be if it did happen. On this basis, ***health risk*** is generally a function of chemical/pollutant ***concentration*** (*C*), the degree of human ***exposure*** to that concentration (*E* - intake or uptake) and the toxic ***potency*** (or "harmfulness") of the pollutant (*P*). Conceptually, the basis of HRA is that health risk is a continuum, the magnitude of which may be quantitatively estimated at a given point by appropriate mathematical manipulation of the numerical variables that describe *C*, *E* and *P*.

In health risk assessment, the "undesirable event" of interest is the (probability of) induction of a defined adverse health effect within a particular human population in a specified exposure scenario, and the "consequence" of interest is the likely magnitude and extent of the adverse effect.

Therefore, HRA cannot be performed without firstly specifying the critical health endpoint or adverse outcome of interest; for example, lung cancer, asthma aggravation, throat irritation, etc. Such health outcomes can either be objective and measurable (e.g., 15% decrease in lung function from exposure to ozone) or subjective and anecdotal (e.g., transient nose and throat irritation from low-level exposure to sulphur dioxide).

HRA is currently a complex, immature, but continually evolving discipline that has generated increasing worldwide attention and interest over the past 20 years or thereabouts[6], particularly in its application to a range of diverse environmental and public health problems associated with chemical pollution of food, water, soil and air resources.

The usefulness of HRA is predicated in its major function as a versatile and powerful ***decision tool for risk management*** - in setting environmental and public health priorities, and in facilitating the allocation of scarce financial and infrastructural resources to achieve positive environmental cost-benefit outcomes. However, HRA is only *one* of the inputs required for making risk management decisions, and it may not be the most important input in any given situation.

We believe that the primary purpose of any HRA exercise is to provide a *transparent and complete-as-possible* set of information to facilitate the subsequent risk management decision-making process. In this regard, HRA process transparency is an essential requirement to enable informed community consultation and input to take place, and to facilitate effective peer review.

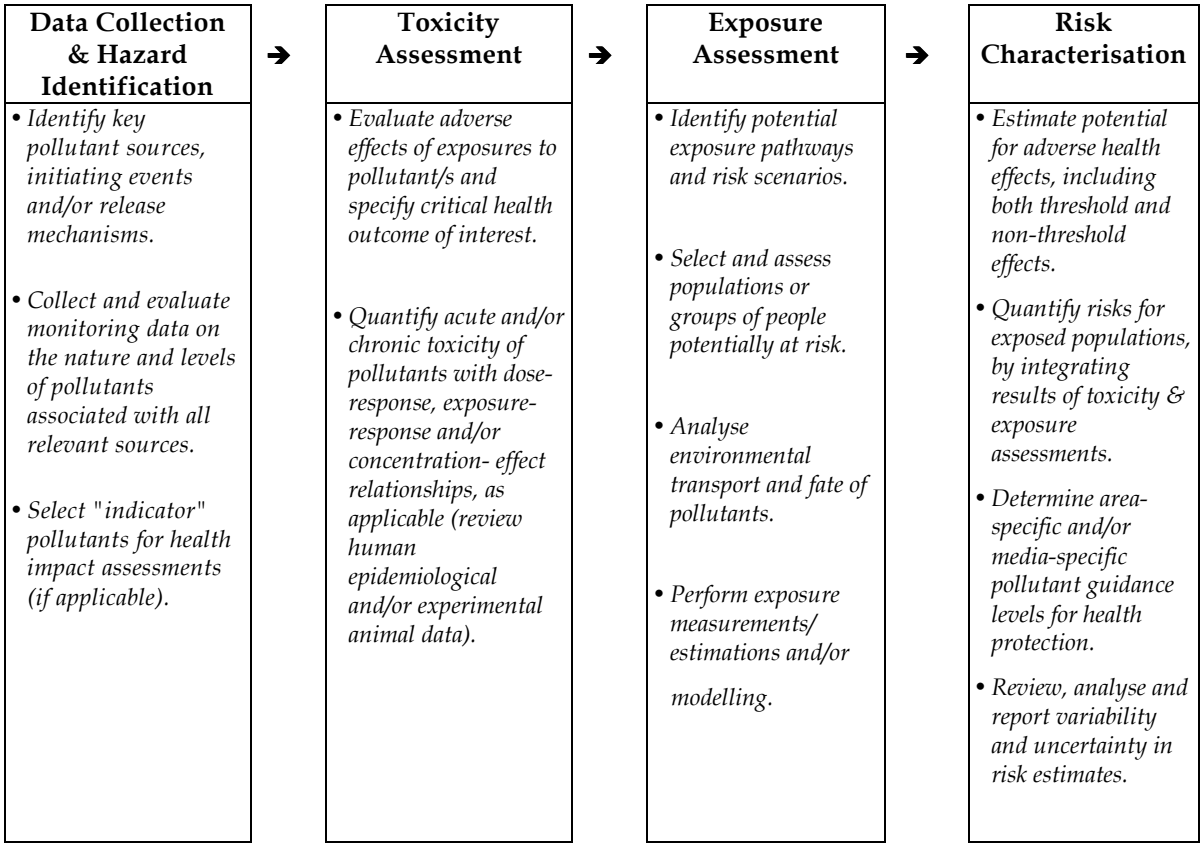
The basic, four-step framework for HRA, shown in *Figure 5-1* on the following page, can be broadly applied to all classes of environmental chemical hazard, although the specific procedures for doing so may be very different. Thus, the detailed approach to be taken and the specific methods required for any particular risk assessment will vary, for example, with the nature of the pollutant, the types of environmental media involved, the range of human activities being considered, the needs of the risk manager and many other factors. Therefore, in practice, the actual application of the risk assessment process will always depend upon the specific context in which it is used.

This means that there can be no single modelling approach specified for HRA that can be used for every conceivable application. The actual approach taken always needs to be tailored to the specific application, which in turn depends on accurate formulation of the health risk problem to be addressed. As will be discussed later, the use of professional (or expert) judgement is a key requirement in every facet of the HRA process.

As a fundamental rule, all HRA's tend to suffer from a relatively high degree of uncertainty. For example, it is generally found that the statistically calculated uncertainty associated with most chronic HRA's is at least 2-3 orders of magnitude, or higher (i.e., there is at least a hundredfold to a thousandfold spread between the high and low plausible estimates of risk).

However, the actual uncertainty may be even larger, due to continuing controversy over the fundamental assumptions of virtually all HRA's, such as the validity of extrapolating the results of animal toxicology studies to prediction of human health risks.

Figure 5-1
Overall Process Framework and Components of HRA



This well known, generally accepted overall framework for HRA was first enunciated by the U.S. National Academy of Sciences (National Research Council)[7] in 1983. Since then, this key framework has formed the foundation for the regulatory development in most western countries (particularly in North America), of a range of "generic" as well as "specific" frameworks, guidelines, modelling approaches and models for quantifying human health risks arising from exposure to environmental chemical contaminants. To date, the range of available risk-based approaches reflects the specific underlying regulatory and policy objectives of the particular countries involved, and this greatly influences the application context of any particular approach. Consequently, (so far as we are aware), no attempt has been made to develop any international uniformity in this regard.

For the purposes of this review, all of the HRA methodologies of interest fall into one of three distinct categories, which we have chosen to define as follows:

> ***HRA Framework*** - a broad-brush overview approach to HRA, providing overall methodological guidelines, but few specific procedural and application details. Sometimes used for qualitative screening purposes in HRA problem formulation, but generally requires subsequent development of an appropriate *modelling approach* to be of practical use. Provides the basic HRA substructure upon which to build specific modelling approaches and models.

HRA Modelling Approach - a more detailed, mathematically-based, problem-specific methodology derived from a framework by the risk assessor, incorporating targeted data collection, and employing purpose-designed computer spreadsheets or sub-models for automating risk calculations. High degree of professional judgement required in data collection, in selection of data inputs, in mathematical manipulation (setup & use of spreadsheets) and in interpretation of risk outputs.

HRA Model - a highly detailed, data-intensive, computerised methodology specifically designed for a particular (stated) purpose. All data input requirements are fully specified and encoded within the software, and the model outputs are generally fixed. May include built-in provision for sensitivity analysis and/or uncertainty analysis. Generally decreases (but does not eliminate) the need for professional judgement, but may encourage indiscriminate use as a "black box" by inexperienced users, with the consequent danger of model applications being stretched beyond their intended use, and subsequent potential for generation of meaningless risk data. Successful use requires a detailed understanding of model application constraints, the validity and limitations of model/data inputs, and the uncertainty inherent in model outputs.

Note that this hierarchical classification represents a logical derivation scheme from *framework* to *modelling approach* to *model*, and in theory at least, provides for potentially decreasing reliance on professional judgement going down the list.

These HRA methodologies have largely focused on food, water and soil contamination applications, to a much greater extent than air pollution applications, which have generally proven more difficult and problematic to deal with. As a rule, *deterministic* HRA methodologies have been most commonly used in these applications, i.e., a single numerical point estimate is used to represent a selected "plausible" or "worst-case" value for each of the HRA input parameters, thereby yielding an output consisting of a corresponding single point estimate of the risk (generally in the form of a summary statistic such as the 95th percentile or "upper bound" value).

In the context of this review, a "model" represents a conceptual, often abstract simplification of complex, real-world physicochemical and biological systems interacting within some sort of hazard scenario. Computerised mathematical models are commonly used in science, since they enable an otherwise complex real system to be broken down into a series of much simpler key components, thereby facilitating empirical analysis and predictive application. However, all HRA models generally represent some degree of oversimplification of the actual interaction of humans with environmental pollutants, due largely to the marked complexity and variability of the resultant human/exposure/risk systems, and the current inability of science to fully characterise such systems.

On this basis, we consider that HRA modelling, in any of its forms, realistically requires a systematic and judicious interactive application of science (X%) and professional judgement (Y%), with the respective proportions of X and Y varying depending on the strength and completeness of the available data sets (usually, $Y>X$). Professional judgement is an essential key requirement for risk assessment because the available scientific data are often incomplete, inaccurate or conjectural, resulting in the need to introduce numerous qualifying assumptions (based on speculation, best guesses or "defaults") in an effort to fill in data gaps.

With good science and sound professional judgement, HRA can be (and has been) a powerful tool for risk management decision-making. However, even with the best science, application of poor professional judgement in data collection and interpretation for toxicity and exposure assessment in particular, can turn HRA into a meaningless, and sometimes hazardous exercise.

This is especially so if poorly characterised uncertainties resulting in gross overestimation or underestimation of risk are propagated through the HRA process, leading to misguided and inappropriate risk management interventions being implemented as a result.

It is therefore important to appreciate that the need to exercise "sound professional judgement" in problem formulation and selection of appropriate data inputs for any HRA methodology, introduces a critical subjective component into what appears, on face value, to be an entirely objective scientific exercise. This built-in subjectivity can give rise to the propagation of significant compounding uncertainties throughout the HRA process. Coupled with this, it is well recognised that substantial inter-individual variability exists within all human populations, and, as a result, each HRA input parameter is usually best characterised by a range or distribution of possible values. Proper identification, analysis and reporting of the variability and uncertainty inherent in any HRA thus becomes an essential prerequisite for the generation of meaningful risk data[8,8a]. In this regard, it is important to distinguish between uncertainty due to *variability* and *uncertainty* due to lack of scientific knowledge, as follows[8-9]:

> ***Variability*** - represents the natural diversity or heterogeneity between individuals within a specified population of humans, which is usually not reducible through further measurement or study. For example, different adults will inhale different volumes of air each day, no matter how many specific measurements are made of lung ventilation rates. In this context, there is simply no such thing as an "average" adult human population, for example.
>
> ***Uncertainty*** - represents a lack of complete knowledge or scientific data with respect to key HRA process parameters outlined in Figure 5-1 (and associated models), which might be reducible through further measurement or study. For example, we may not know the inhalation exposure distribution for a pollutant within a given population, but we may be able to gain additional (albeit still incomplete) information through direct measurement of personal exposures within that population.

Consequently, in recent years, the traditional *deterministic* approach to HRA has become increasingly recognised as being deficient, in that it effectively ignores the significant variability and uncertainty inherent in the HRA process, and therefore does not reflect the true probabilistic nature of *risk*. In order to address these deficiencies, a number of *probabilistic* approaches to HRA have been developed over the past 10 years or so, particularly in the USA[9-10]. In essence, a *probabilistic* approach treats the HRA input parameters as *random variables* (i.e., multiple numerical values that belong to an overall plausible range or distribution of values), and thus yields a corresponding range or probability distribution of risk estimates. This approach is generally superior in that it provides a more complete set of risk information, and therefore forms a better basis for the subsequent risk management decision-making process.

We therefore consider that any serious discussion of risk assessment methodologies for ambient air quality, needs to clearly distinguish between subjective and objective data input requirements, and demands full consideration of relevant approaches for adequate characterisation of variability and uncertainty.

6. RISK ASSESSMENT AND AMBIENT AIR QUALITY

Despite significant international research efforts conducted over many years, the quantitative relationship between ambient air quality and public health risk remains a complex issue, details of which have become increasingly controversial in recent times. The complexities are currently characterised by a number of important (but largely unanswered) questions[11-13]. Chief amongst these are the issues of what actually constitutes an "adverse" health effect; the problem of relating ambient pollutant concentrations to actual human exposures; the design and interpretation of epidemiological studies; the potential ambiguity of concentration-effect, exposure-response and dose-response functions; and the difficulties in identifying thresholds of individual susceptibility to air pollutants. These issues are of fundamental importance to risk assessment, in that they greatly influence the uncertainties of many of the key data inputs to the HRA process, and therefore determine the practical usefulness, or otherwise, of the final risk estimates.

As a starting point for this review, we consider that the following simple health risk scheme is conceptually appropriate for examining the risks of human exposure to ambient air pollutants, as applied to the determination of ambient air quality guidelines:

				(population)					(interaction)
MOBILE SOURCES	➢	(fate & transport)		(activities/contact)		(lung)			
(air monitoring stations)	➢	**AMBIENT CONCENTRATIONS**	➢	**INHALATION EXPOSURE**	➢	**"DOSE"**	➢	**RISK**	
STATIONARY SOURCES	➢	(air dispersion)		(short & long-term)		(intake/update, including multimedia exposures)			

On this basis, key methodological requirements for any ambient air risk assessment modelling approach would be expected to include at least the following:

- Adequate characterisation of pollutant emissions from all relevant sources, and selection of the pollutant of interest
- Collection & analysis of air monitoring data, with special consideration of monitoring locations, averaging times and limits of detection
- Air dispersion modelling to determine atmospheric fate & transport of pollutant/s
- Availability of adequate epidemiological and experimental data to delineate the form and function of the dose-response curve for each pollutant of interest
- Identification of exposed population/s via, for example, demographic data
- Identification of sensitive sub-groups within population/s (eg. from hospital admissions/emergency room data)
- Personal exposure data collection via breathing zone air monitoring, and correlation with data from fixed monitoring stations and results of air dispersion modelling (i.e., overall inhalational exposure modelling)

- Delineation of the critical health outcome of interest due to the pollutant
- Identification and assessment of additional (non-inhalation) multimedia exposure
- sources for the pollutant, together with indoor inhalation exposure potential, for *total exposure* estimation purposes
- Delineation of mechanisms, levels and duration of exposures to determine human intake/uptake rates
- Identification and delineation of potential pollutant mixture interaction effects on health outcomes
- Determination of the variability (probability) of the health outcome within the specified population (this is the quantitative measure of risk, which is actually a probability distribution)
- Derivation of corresponding (risk-based) ambient air quality guideline levels for health protection of the specified population/s
- Provision for integrated uncertainty analysis of the risk results

These can also be considered as minimum qualitative "boundary conditions" that need to be met. Bearing in mind that the useful expression of the risk would be expected to depend on joint statistical considerations of pollutant dispersion and human population / exposure characteristics, the above is a rather simplistic representation of a complex, dynamic and interactive phenomenon. Within this scheme, we consider that exposure assessment is the most critical component, and the applicability of any risk assessment model to the setting of ambient air quality standards would be largely influenced by whether the necessary input data were available, and how well the exposure modelling can integrate pollutant dispersion patterns with human population activity patterns.

However, because of wide variations in ambient air pollutants and resultant exposure levels within urban areas, coupled with increasingly mobile and dynamic population patterns, it is extremely difficult to accurately assess or predict actual human exposure to such pollutants, and most of the available exposure data have a high level of associated uncertainty[3,14-15]. Consequently, there are significant knowledge gaps in terms of concentrations and distribution of ambient air pollutants; the physicochemical processes that influence their atmospheric transport and fate, quantitative human exposure patterns, and actual human health impact[14-15].

It is also important to distinguish between the (technically-based) *estimation of ambient air quality guideline levels for pollutants* and the (regulatory-based) *setting of ambient air quality standards,* for public health protection purposes. The most that any HRA approach can hope to achieve is to provide, within specified uncertainty bounds, risk-based *guideline estimates* for ambient air quality. Given such air quality guidelines, it is then up to regulatory authorities (in consultation with communities) to make the subsequent risk management decisions in setting "appropriate" air quality standards, (also taking into account relevant social, political, economic and policy considerations). Consequently, *standard setting* as such is fundamentally a political and social process, and is necessarily the responsibility of risk managers such as regulators and policymakers. The HRA process itself does not set ambient air quality standards. Moreover, because the "science" component of HRA is incapable of providing all the answers; regulators, policymakers and communities need to know the nature and magnitude of the uncertainties involved in order to best utilise HRA outputs within a rational decision framework.

7. RISK ASSESSMENT METHODOLOGIES

Numerous environmental HRA frameworks/guidelines, modelling approaches and models have been developed over the years in many countries for specific purposes, and to suit specific pollutants. Amongst current approaches to HRA, the available key methodologies of potential relevance to ambient air quality applications are as follows, divided respectively into their countries of origin:

United States of America:

- (US) EPA methodology[16-24] based on the National Ambient Air Quality Standards Exposure Models [NEM] and probabilistic versions of NEM [pNEM].
- California Environmental Protection Agency (Cal/EPA) approach, based on the CAPCOA guidelines[25-33].
- (US) EPA IEUBK model for lead in children[34-40].

Canada:

- Canadian methodology (Health & Welfare Canada)[41-43].

Europe:

- WHO methodology[44-48].

United Kingdom:

- UK approach (Expert Panel on Air Quality Standards)[49].

Australia:

- Ricci and Beer approach[3,4].
- NEHF (ENHealth Council) methodology[50].
- Contaminated Sites NEPM methodology[51,52].

Each of the above methodologies is outlined in the following *sub-sections 7.1-7.9* , and reviewed in tabular form, according to the key criteria detailed in *Appendix 1*. It should be noted that the format of the review criteria in *Appendix 1* specifically assumes that each methodology is wholly available in the form of a cookbook-style *computerised model*. Since this only applies to a very few of the above methodologies, we have taken the liberty of addressing the criteria in a more general, flexible manner in the case of those methodologies that fall under our definition of HRA *frameworks/guidelines* and *modelling approaches*.

7.1 United States Environmental Protection Agency

The (US) EPA is responsible for setting, reviewing and revising National Ambient Air Quality Standards (NAAQS) under the legislative framework of the federal Clean Air Act. Primary NAAQS have been set for widespread (*criteria* or *priority*) pollutants including carbon monoxide, sulphur dioxide, ozone, nitrogen dioxide, respirable particulate matter, lead and total hydrocarbons.

These standards were originally established not on a strict HRA basis, but on the basis of Agency review of the relevant scientific evidence on health effects, originally presented in specific *criteria documents* for each pollutant. Each *criteria document* provides a summary evaluation of relevant epidemiological, experimental, and human clinical data on the empirical relationship between pollutant exposure and adverse health effects. It is instructive to note that the Clean Air Act requires NAAQS to be set *at levels that protect the most at-risk (i.e., most sensitive) populations*, with an *adequate margin of safety*, under a 5-yearly standards review process.

Against this background, and as part of the standards review and revision requirements of the Clean Air Act, the Ambient Standards Branch of the (US) EPA's Office of Air Quality Planning and Standards has utilised complex exposure modelling protocols to evaluate public health risks associated with existing NAAQS, and with attainment of various alternative NAAQS for specific pollutants. A number of computer-based exposure models have been used as tools for this purpose, notably the continually developing series of NAAQS Exposure Models (NEM), and their probabilistic refinement (pNEM).

These models are applicable to criteria pollutants that are directly or indirectly associated with area or mobile sources, and each exposure model is specifically designed to evaluate one particular pollutant only. The exposure models are based on specific algorithms that simulate pollutant concentrations in relevant micro-environments of exposure (outdoor, indoor, in vehicles, etc); human time/activity patterns; and commuting patterns. The general NEM framework is summarised as follows:

- Identify and define the population/s at risk, including appropriate exposure districts, and the exposure period of interest
- Divide the population at risk into a comprehensive series of cohorts
- Develop an exposure event sequence for each cohort for the exposure period
- Estimate the pollutant concentration, lung ventilation rate and physiological indicator or biomarker (if applicable) associated with each exposure event
- Extrapolate the cohort exposure estimates to the population/s at risk

It is noteworthy that an integrated mass balance model is employed within pNEM to estimate pollutant concentrations indoors and within motor vehicles. To date, we are aware of two specific pNEM models that have been used to estimate exposures of urban populations to ozone (pNEM/O_3) and carbon monoxide (pNEM/CO) respectively, the resultant data being subsequently used in HRA's under the Clean Air Act.

A particulate matter risk assessment has also recently been completed for two sample locations (Philadelphia County, PA; and Southeast Los Angeles County, CA) involving application of concentration-response functions to data on daily ambient respirable particulate levels in each location.

In each of the above three cases, the overall HRA modelling approach used was derived from the original NAS/NRC risk assessment framework of 1983, but was empirically developed to suit the particular pollutant under study, for the specific regulatory purpose required under the Clean Air Act. Therefore, there is no single HRA modelling approach or model within the basic (US) EPA air quality standards framework that can be used in the review of all ambient air quality standards. Each model is uniquely developed for (and tailored to the specific needs of) each pollutant under study.

In this regard, the (US) EPA's Office of Air Quality Planning and Standards, in conjunction with the Office of Research and Development, and the Environmental Models Subcommittee of the Science Advisory Board, is currently engaged in an extensive, ongoing research program involving model development, review and refinement activities. In recognition of the many limitations and uncertainties inherent in the currently available air quality HRA approaches based on NEM and pNEM, the (US) EPA is in the process of developing a number of (more complex) improved models, notably the modular TRIM modelling system (TRIM = Total Risk Integrated Methodology). TRIM is expected to be completed by late 2000.

Although TRIM is still currently under development, and few specific details are available, we understand that the TRIM methodology is designed to provide the (US) EPA with a more flexible modelling system for assessing public health and environmental risks resulting from multimedia, multipathway exposure to a wide range of air pollutants, and thereby meet the risk assessment requirements of the "criteria pollutants" program, as well as the so-called "air toxics" program. Again, the major impetus for development of TRIM has been regulatory, as exemplified by the fact that beginning in 2002, the (US) EPA will need to implement its "residual risk" program, as required under the Clean Air Act Amendments of 1990 (this program involves some 188 specified air toxics). On this basis, TRIM is intended to be used to calculate the residual risk from air emissions from stationary (fixed point, mainly industrial) sources, after prescribed regulatory emission controls have been put into place. This means that TRIM could have significant implications for the regulation of air toxics in the USA in future.

In addition to being capable of performing multipollutant, multimedia, multipathway risk assessments, the TRIM modelling system has been designed to enable integrated characterisation of uncertainty and variability, and to be capable of performing tiered, iterative HRA's, depending on the completeness of the available input datasets. The design of TRIM includes six integrated modules, comprising environmental fate & transport; exposure event; pollutant uptake; biokinetics; dose-response; and risk characterisation modelling. The (US) EPA's Office of Air Quality Planning and Standards intends to replace the existing models that they use with TRIM, although there may be two components in the final version, one for air toxics, and the other for NAAQS. This appears to be a sensible approach, and it will be instructive to see whether the "improved" HRA modelling design specifications built into TRIM are actually borne out in practice, once the modelling system is available for use.

Table 7-1
(US)EPA METHODOLOGY
Based on pNEM/O_3 & pNEM/CO Models

REVIEW CRITERIA	RESULTS & COMMENTS
Model Inputs	
Exposure Assessment:	
Air Quality/Exposure Data	Model specifies required pollutant concentration data from fixed monitoring stations, census tract population data, commuting pattern data, human activity data from time-activity diary studies, meteorological data, and human lung ventilation rate data. High, population-specific input data requirement.
Data Quality Guidelines?	None specified. Assume based on professional judgement
Sensitive Populations	Model considers the general population of a study area, together with discrete (sensitive) subpopulations such as outdoor children and outdoor workers (ozone - exertion-related) and people with cardiovascular disease (carbon monoxide).
Health Effect Data:	
Inclusion Criteria for Toxicity &/or Epidemiological Data	None specified. Pollutant -specific evaluation based on professional judgement.
Health Endpoint Selection	Based on scientific evaluation of epidemiological and clinical databases for each pollutant. Range of endpoints considered, based on critical effects observed in controlled human exposure studies (eg. ozone acute health endpoints: lung function decrements; onset of respiratory symptoms such as cough, pain on breathing, etc).
Dose-response Assessment	Probabilistic exposure-response relationships for (e.g.) ozone acute endpoints derived from controlled human exposure data, by fitting a function to the data using regression techniques, and then estimating a statistical 90% *credible interval* (defined by 0.05 & 0.95 fractiles) about the fitted (predicted) response rate at those ozone levels required for the HRA calculations. Linear extrapolation of the dose response functions generally used.
Risk Modelling	
Elements of Inputs for Risk Characterisation	Not readily identifiable; assume based on professional judgement. For e.g. ozone, product of ozone exposure concentration and "**E**quivalent **V**entilation **R**ate" used as index of dose [where **EVR** = (ventilation rate)/(body surface area)] for each exposure event. Probabilistic exposure distributions over defined population of interest calculated by multiple simulation runs of pNEM model.
Deterministic or Probabilistic Approach?	Both available. Probabilistic (pNEM) approach greatly favoured over deterministic (NEM) approach.
Default Parameters Used	Not entirely clear. Appears to include default air exchange rate/decay rate parameters for mass balance model component of pNEM, and default (age & activity-based) ventilation rates used to calculate EVR. Emphasis on use of exposure-specific data.
Use of Safety Factors?	Not used and not applicable.
Uncertainty Analysis?	Partially built into pNEM model in the form of a variety of probabilistic elements representing variability/uncertainty in pollutant exposure factors. However, for pollutants such as e.g. ozone and particulate matter, the most important factor influencing uncertainty is whether or not a threshold really exists.
Sensitivity Analysis?	Not explicitly addressed; assume based on professional judgement.
Model Validation?	No evidence of adequate validation of existing model applications.

REVIEW CRITERIA	RESULTS & COMMENTS
Risk Modelling cont	
Model Acceptance?	Specifically used by (US) EPA under federal Clean Air Act. No evidence of use or general acceptance of model outside this regulatory sphere.
Pollutants Assessed?	Mobile source criteria pollutants such as carbon monoxide, ozone, particulate matter, lead, and nitrogen dioxide.
Inhalation-Specific or Multimedia Model?	Inhalation only.
Analysis of Threshold vs Non-Threshold Pollutants	Method assumes (via Clean Air Act) that criteria pollutants are *threshold pollutants*. There is no provision for assessing non-threshold pollutants within the methodology.
Model Transparency, Simplicity and Ease of Understanding	Basic modelling scheme transparent, but method details are somewhat complex and difficult to follow. Exposure modelling not entirely clear due to multiple levels of data-intensive input requirements and some mathematical complexity associated with encoded exposure algorithms.
Model Outputs – Risk Estimates	
Form of Risk Estimate	Risk = expected fractional response rate within exposed population at a particular pollutant concentration. 2 types of risk measures: e.g. for ozone: HEADCOUNT RISK = no. of people or no. of times an individual experiences some adverse event such as decreased lung function or cough or chest pain, etc. BENCHMARK RISK = probability that a benchmark response of say, 5% or 10% is experienced within a population for a specified number of times, in a specified period, at some location within a geographic region, under a particular ozone concentration.
Criteria for Risk Acceptability?	Variable depending on specific model (specific pollutant), & based on professional judgement. Implicitly suggested within the model as a minimal response, but not specified or defined in any way, since such criteria constitute a risk management consideration (i.e., what proportion of the population should be protected?)
Characterisation of Uncertainty in Risk Estimates	Risks represented by probability distributions over a range of risk measures. This accounts for the considerable uncertainty in exposure estimates, and in the degree of health endpoint response at particular exposure levels.
Other	
Software Details	No integrated program available for HRA; pNEM program written in IBM "JCL " language. Proprietary program, not public domain, and not available commercially.
Hardware Requirements	IBM-type mainframe computer environment.
Associated Costs	No information available.
Running Time for Risk Model	Requires considerable computer time, typically several days or more, for multiple runs of pNEM model and associated components

7.2 California Air Pollution Control Officers' Association

The California EPA is responsible for administering the State Air Toxics "Hot Spots" Information and Assessment Act of 1987, as amended in 1992. The legislation requires, amongst other things, quantification and reporting of toxic air emissions from stationary sources (i.e., factories & industrial facilities, etc.); and the conduct of risk assessments, as necessary, to determine the near-source (localised) human health impacts of facility emissions. Currently, there are over 600 "airborne toxic" substances identified in the Act which are subject to these requirements. The legislation also requires that the risk assessments should be conducted according to HRA methods specified jointly by the Cal/EPA and the CAPCOA. However, this apparently has nothing to do with the setting of ambient air quality standards for the State, and does not involve criteria pollutants.

As defined under the Air Toxics "Hot Spots" Act, each HRA must include a comprehensive analysis of the dispersion of toxic substances emitted into the atmosphere, the subsequent human exposure potential, and a quantitative evaluation of associated individual and population health risks.

To this end, the CAPCOA and Cal/EPA have developed a comprehensive set of Risk Assessment Guidelines, which provide procedures for use in the preparation of HRA's under the Air Toxics "Hot Spots" Act. Moreover, these guidelines are designed to be used in conjunction with two computerised air quality models, namely the HRA Version 2.0e risk assessment model developed by Cal/EPA, and the Industrial Source Complex Short Term Phase 3 -Refined analysis (ISCST3) air dispersion modelling program developed by the (US) EPA. Both are public domain models that are readily available from Cal/EPA without restriction. The overall CAPCOA HRA scheme was generally derived from standard (US) EPA risk assessment practice.

The CAPCOA procedures involve firstly, an estimation of maximum short-term ground level concentrations and deposition rates of each pollutant emitted from a facility using ISCST3, followed by calculation of potential cancer risk, together with acute and chronic hazard indices for non-cancer health effects (as applicable), using the HRA 2.0e program.

The primary rationale behind the CAPCOA guidelines is to specify a consistent approach to the assessment of risk, in order to provide a basis for comparison of different pollutant sources with one another, and thereby facilitate the determination of priorities for control. On this basis, the CAPCOA emphasises that its guidelines are only intended to provide a rough "yardstick" approach to HRA, and that the resultant risk estimates should not be construed as actually representing the expected rates of disease in the exposed population.

Consistent with this "yardstick" philosophy, and in common with the policy underlying many regulatory risk assessment procedures developed and used in the USA, the CAPCOA methodology utilises a series of conservative default toxicologic factors and exposure parameters, in the form of deterministic point estimates. The emphasis, then, is on the use of a large number of "health protective" default exposure assumptions, with little reliance on site-specific data. This approach is taken in order to ensure that exposures and risks approach an "upper bound" situation, and that underestimation of exposure and risk does not occur. In fact, this type of approach generally tends to result in significant overestimation of risk.

Whilst aiming for such "over-protection" is one possible way of dealing with situations involving minimal data (and the high degree of uncertainty) in HRA, independent studies have suggested that this approach is likely to result in overly conservative and therefore unrealistic risk assessments, which do not facilitate optimum risk management decision making.

This fundamental point was well illustrated in a recent independent study conducted in California33 to examine the degree of conservatism in the CAPCOA approach, by utilising a tandem probabilistic HRA methodology and comparing the risk outputs of both. In applying these methods to an assessment of public health risks from air pollutants emitted from a food processing facility, it was found that the CAPCOA methodology (using the recommended default point estimates) resulted in risk estimates that were greater than the 99.99th percentile risk predicted by the probabilistic methodology (using a range & distribution of input parameter estimates).

Nonetheless, we consider that the CAPCOA approach, with its basis in modelling point source emissions of air toxics for facility risk-ranking purposes, would be unsuitable for application to the development of NEPC ambient air quality standards.

Table 7-2 -CAPCOA Approach

REVIEW CRITERIA	RESULTS & COMMENTS
Model Inputs	
Exposure Assessment:	
Air Quality/Exposure Data	Exposure estimates based on ISCST3 or similar model outputs. Requires quantitative pollutant emission and release data from facility; meteorological data for local area, and receptor population locations in local area.
Data Quality Guidelines?	None specified. Assume based on professional judgement.
Sensitive Populations	Specifies location-based identification of sensitive receptor sites such as schools, daycare centres, and hospitals; but provides no further procedural detail.
Health Effect Data:	
Inclusion Criteria for Toxicity &/or Epidemiological Data	None specified. Includes default (US) EPA toxicity parameters (cancer unit risks and reference exposure levels) for a comprehensive list of substances.
Health Endpoint Selection	Provides prescriptive listing of carcinogens, and includes list of health endpoints to be considered in a hazard index (e.g., ammonia endpoint = respiratory effects).
Dose-response Assessment	Not specified. Prescribes use of (US) EPA dose-response summary parameters (including cancer unit risks & reference exposure levels) for a list of specified substances.
Risk Modelling	
Elements of Inputs for Risk Characterisation	Easily identifiable. Inhalation cancer risk = product of pollutant air level at a given receptor and pollutant-specific unit risk factor. Non-inhalation cancer risk = product of average daily dose (ADD) of pollutant at a given receptor and pollutant cancer slope factor. ADD determined using results of dispersion modelling and defined multipathway exposure algorithms. Noncancer health hazards evaluated via comparison of exposure/dose with listed default *reference exposure levels* (hazard index ratio approach) for both inhalation & multipathway exposures.
Deterministic or Probabilistic Approach?	Deterministic only; generally based on concept of *maximum exposed individual*.
Default Parameters Used	Large range specified, including a full suite of exposure and toxicity parameters. Significant uncertainty associated with use of default parameter values.
Use of Safety Factors?	Not used and not applicable.
Uncertainty Analysis?	Not specified. Model acknowledges existence of major sources of uncertainty in all risk assessments, but does not include requirements or methods for its estimation.
Sensitivity Analysis?	Not explicitly addressed.
Model Validation?	No evidence of adequate validation.
Model Acceptance?	Specifically used in California, USA for Cal/EPA regulatory purposes. Limited use on a case-by-case basis in NSW, Australia. No other evidence of general use or acceptance of model, other than limited ad-hoc use by some consultants.
Pollutants Assessed?	Applicable to some 600 specified airborne toxic substances, including both organic and inorganic compounds, that may be emitted into the atmosphere by industry.
Inhalation-Specific or Multimedia Model?	Comprehensive multimedia, multipathway model.

REVIEW CRITERIA	RESULTS & COMMENTS
Risk Modelling cont	
Analysis of Threshold vs Non-Threshold Pollutants	Threshold pollutants (non-carcinogens) assessed using an acceptable daily exposure/dose-type approach (i.e., comparison with *reference exposure levels*), based on existence of a threshold of exposure below which effects are unlikely to occur. Non-threshold pollutants (carcinogens) assessed using specified cancer potency slope factors or unit risk factors, assuming a linear non-threshold dose-response model, based on the concept of a discrete risk associated with any level of exposure.
Model Transparency, Simplicity and Ease of Understanding	A relatively straightforward, reasonably transparent model, due largely to its systematic, easy-to-follow procedures and extensive use of a range of specified default input parameters. Analogous to a "cookbook" approach.
Model Outputs - Risk Estimates	
Form of Risk Estimate	Multiple measures of risk generated, including: Maximum Offsite Cancer Risk (at any location); Maximum Individual Offsite Cancer Risk (at an existing receptor); Individual Excess Cancer Risk (inhalation & multipathway); Population Excess Cancer Burden (inhalation & multipathway); Maximum Acute & Chronic Non-cancer Hazard Indices (for each health endpoint). Emphasises "upper bound" risks only.
Criteria for Risk Acceptability?	Not included or explicitly addressed, apart from the suggestion that "total hazard indices of one or less are not considered to be indicative of public health impacts from non-cancer toxicity of the evaluated substances". A Risk Management issue.
Characterisation of Uncertainty in Risk Estimates	Not included.
Other	
Software Details	ISCST3 and HRA 2.0e are both public domain, MS-DOS based programs.
Hardware Requirements	IBM-compatible personal computer with 80286 or better CPU, MS-DOS Ver. 3.3 or later, with 640 kb memory, and a hard disk drive with minimum 600 kb free.
Associated Costs	Minimal. Both programs readily available from Cal/EPA (Air Resources Board) for US$20.00
Running Time for Risk Model	Variable, depending on computer hardware, number of pollutants & multipathway complexity, etc. May typically range from minutes to hours.

7.3 Integrated Exposure Uptake Biokinetic Model (Lead)

The (US) EPA IEUBK computer model for lead in children (version 0.99d) is designed to predict potential blood-lead levels in a hypothetical child or population of children, exposed to environmental lead from all sources, within a residential exposure setting. The model applies to children between the ages of 6 months to 7 years, and utilises either site-specific, or default information on lead concentrations in multiple environmental media (i.e., drinking water, soil, house dust & paint, air and food) to which the children might be continuously exposed. It is instructive to note that lead has been one of the most intensely studied pollutants of all time, and a rich empirical data-base exists for the metal, particularly with regard to its human epidemiology and toxicology.

The IEUBK model is conceptually simple and consists of four main modules:

- *Exposure Module:*
  Integrates lead concentrations in the various environmental media with the amount of lead entering a child's body. Environmental media-specific exposure rates are utilised together with lead concentration data, to estimate media-specific lead intake rates.

- *Uptake Module:*
  Integrates lead intake into the lungs or digestive system with the amount of lead absorbed into the child's blood.

- *Biokinetic Module:*
  Models the transfer and distribution of lead between blood and other body tissues, and its elimination from the body.

- *Statistical (Probability Distribution) Module:*
  Calculates the probability of a certain outcome, for example, a blood lead concentration exceeding a certain (user-selected) risk-based threshold in an exposed child based on the parameters used in the model. The model specifies a default risk-based threshold level of *10 micrograms lead per 100 millilitres of blood* (i.e., 10 $\mu g\ dL^{-1}$), which happens to be the same level as that recommended by the National Health & Medical Research Council (NH & MRC) in Australia.

The IEUBK model is best utilised by incorporating as much site-specific (or user-specified) data as possible into the exposure input variables, and collecting actual site population blood lead data wherever feasible. However, in many cases, this may not be possible, and the methodology provides an extensive set of default parameter values that may be used in those cases where site-specific data are not available, or where the user cannot specify a "better" value. Moreover, the model assumes a lognormal distribution of blood lead concentrations in any exposed population of U.S. children, and specifies a corresponding default geometric standard deviation of 1.6 (which is applied by the model to estimate the predicted lognormal distribution of blood lead values).

Therefore, the model basically utilises a set of "average" point estimates for exposure variables to calculate a corresponding point estimate of blood lead, which is assumed to be equivalent to the geometric mean blood lead concentration for the exposed population.

The model does this by simulating children's long-term lead exposure based on age-weighted input parameter assumptions for intake of food, water, air, soil, dust and paint, (corresponding to various defined or analysed lead concentrations); assuming continual growth on a year-to-year basis, under constant levels of exposure.

The (US) EPA stresses that the IEUBK model should be visualised as no more than a specific tool for making rapid calculations and recalculations of a complex set of algorithms that integrate multiple lead exposure, uptake and biokinetic parameters. In this regard, the model facilitates the assessment of the risk significance of varying blood-lead concentrations in lead-exposed children, and is useful in demonstrating how the risk may vary with changes in the input parameters. For example, in a site-specific assessment, it is crucial to consider potential lead exposure from contaminated soil and dust sources. Variables affecting this include the amount of soil transferred indoors as dust, the amount of soil or dust a typical child may ingest or inhale over a given time period, and the amount of lead absorbed from this source. In practice, it is found that the risk results are generally fairly sensitive to changes in any of these variables, i.e., changing the value of one variable can change the risk quite significantly.

On the basis of its current implementation of the IEUBK model, the (US) EPA has indicated that the intended use of the model for HRA purposes is limited to:

- Estimation of a geometric mean blood-lead concentration for a *typical child* up to 7 years of age, based on a long-term lead exposure estimate in and around a single residence.

- Provision of a basis for estimating the risk of elevated blood lead levels occurring in a *hypothetical child*; and/or prediction of likely changes in this risk from exposure to lead in multiple environmental media, following targeted action to reduce such exposure.

- Estimation of target clean-up levels for lead-contaminated soil or dust at specific residential sites.

- Estimation of hypothetical future blood-lead levels associated with lead-contaminated soil at currently undeveloped sites which are likely to undergo future residential development.

However, great care would need to be taken in any attempt to use the model to predict the mean blood lead level for an entire community, since estimates of "community averages" for the multimedia lead inputs could not be validly used. This is because a significant amount of exposure variability may occur between different homes in any given community. Given the basis of the IEUBK model, the preferred method would be to initially apply the model to individual homes, or to known homogeneous neighbourhoods, and then integrate the results to determine the respective neighbourhood or community mean. This would largely depend on the availability of appropriate site-specific and population-specific data.

Interestingly, the IEUBK model has been the subject of a significant amount of political, legal, social and scientific discussion amongst a broad spectrum of risk practitioners in the USA. The scientific discussions have centred largely around the issues of what constitutes the actual "at-risk" population (in practice), the availability of "sufficient" site-specific data for "valid" use of the model, problems of inadequate validation of model applications, and the extent of uncertainty, unreliability and misuse of the model (i.e., inappropriate use outside of specific contexts).

Clearly, there are major concerns in relation to the high input data requirement inherent in the model, and the potential problems arising from reliance on (US) EPA default input parameters, in the absence of population-specific and site-specific data. These concerns generally revolve around the broader issue that use of default parameters effectively ignores many of the site-specific, population-specific and exposure-specific nuances which influence the actual risk, thereby further contributing to uncertainty. In utilising default input parameter assumptions, the values are rarely population specific, and in fact, describe some hypothetical population which may not be even remotely comparable to the target population. Moreover, there is usually no rational basis for assuming that the (US) EPA default values are either accurate, or appropriate for any given application.

Since the blood-lead distribution predicted by the IEUBK model corresponds to a set of user-specified (including default) input values which collectively define discrete exposure scenarios at specific residential sites, the major application of the model (at least in the USA) has been in the development of target soil clean-up levels for lead-contaminated sites. The model has clearly not been designed for the derivation of ambient air quality standards for lead, and, so far as we are aware, has never been applied to ambient air.

However, from the point of view of air quality applications, we believe that it would be *theoretically* possible to utilise the model to generate a probability distribution of blood lead levels for a typical child, or group of children, exposed to a particular lead-in-air concentration, with concurrent lead exposures from other sources. From a practical HRA perspective, estimating blood lead levels that might result from residential environmental site exposures depends on appropriate integration of all relevant multi-media/multi-source exposures to lead. Specifically, it would be important to consider direct ambient air exposures and indoor air/dust exposures (which may include contributions from both soil and lead-based paint) on a site-specific basis, as well as any contributions from diet, drinking water, soil, or other local sources of lead exposure.

In using the IEUBK model to estimate blood lead levels, it is important to note that the risk attributable to air lead exposures would be dependent upon the existing level of exposures from other sources. In other words, the amount by which the total risk would be decreased if all exposures to lead in air were removed is not a constant, but varies with the level of existing non-air exposures. This is because the model derives "distribution" (rather than a simple point estimate) as an output whose shape and size is dependent on the predicted variability of exposures from each lead source. Consequently, with other factors being equal, the risks attributable to air will generally be higher in the presence of elevated lead exposures from other sources. Therefore, in applying the IEUBK model, the risk attributable to air lead may be predicted as the difference between the risk estimated when all sources of lead exposure are assessed, and the risk estimated considering only non-air related exposures.

Table 7-3
IEUBK MODEL (Lead)

REVIEW CRITERIA	RESULTS & COMMENTS
Model Inputs	
Exposure Assessment:	
Air Quality/Exposure Data	Model requires lead-in-air exposure concentrations (in µg m^{-3}) derived either from site monitoring or predictions based on site-specific source analysis such as those derived from relevant air dispersion modelling. Also requires lead concentration data for food, water, soil, dust, and paint.
Data Quality Guidelines?	Not explicitly included.
Sensitive Populations	Model only considers defined sensitive subpopulation of children between 6 months and 7 years of age.
Health Effect Data:	
Inclusion Criteria for Toxicity &/or Epidemiological Data	None specified.
Health Endpoint Selection	Based on (most sensitive) neurobehavioural adverse effects of low-level lead exposure in young children <5 years of age; specifically, that blood lead levels >10 µg dL^{-1} are associated with an increased risk of impaired intellectual and behavioural development in this age group.
Dose-response Assessment	Based on human epidemiology & pharmacokinetic studies. No discrete threshold for lead health effects. Linear dose-response relationship reflects long-term change in blood lead levels with change in environmental exposure concentrations and resultant lead body burden
Risk Modelling	
Elements of Inputs for Risk Characterisation	Easily identifiable. Biokinetic module integrates lead uptake predictions from all environmental sources and calculates age-specific blood lead levels based on a simple, 6-compartment biokinetic scheme.
Deterministic or Probabilistic Approach?	Not strictly either. Model uses deterministic point estimates for input parameters to derive a lognormal probability distribution of blood lead levels for a typical child or group of children.
Default Parameters Used	Virtually all input parameters are available as defaults, if the user so chooses. These are based solely on U.S. practice, and are generally conservative.
Use of Safety Factors?	Not used and not applicable.
Uncertainty Analysis?	Not explicitly specified or addressed. However, model output is based on the default assumption that variability in blood lead concentrations within a population group can be mathematically described by a lognormal distribution wholly defined by two parameters, namely, the geometric mean and the geometric standard deviation.
Sensitivity Analysis?	Automatically built into model. Simple procedure to selectively alter input parameter values to analyse effect on risk outputs, as in reviewing risk mitigation options
Model Validation?	Model has been partially validated, by comparing model output predictions with field measurements of blood lead levels in selected populations of children. In general, the model tends to overestimate geometric mean blood lead levels by up to 25%. This indicates significant variability in lead exposures within real populations.

REVIEW CRITERIA	RESULTS & COMMENTS
Risk Modelling	
Model Acceptance?	Most widely used (& generally accepted) lead model in the USA; not used in Canada; some evidence of limited use in Europe & Australia; but no evidence of general use or acceptance outside the USA.
Pollutants Assessed?	Specific to lead only.
Inhalation-Specific or Multimedia Model?	Comprehensive multimedia, multipathway model.
Analysis of Threshold vs Non-Threshold Pollutants	Not applicable. Treats lead as a non-threshold pollutant for the health endpoint of interest.
Model Transparency, Simplicity and Ease of Understanding	An elegantly simple, reasonably transparent model. (US) EPA guidance documents provide detailed explanations of all components of the model, together with systematic, easy-to-follow procedures for use. The seemingly complex set of exposure and risk algorithms are well documented and explained, as are the default input parameters and statistical distribution assumptions.
Model Outputs - Risk Estimates:	
Form of Risk Estimate	Lognormal probability distribution of blood lead concentrations centred around the predicted geometric mean blood lead level, and based on a selected (default) geometric standard deviation, which defines the spread of the distribution. Risk is calculated as the probability of exceeding the default blood lead level of 10µg dL^{-1}.
Criteria for Risk Acceptability?	Not explicitly included. User-selectable based on risk management requirements, for example, a hypothetical decision might be that *exposure to lead in air should be limited to levels such that a typical group of similarly exposed children would have an estimated risk of no more than say, 5% (0.05) of exceeding the 10 µg dL^{-1} blood lead level*. We emphasise that this would need to be a risk management decision.
Characterisation of Uncertainty in Risk Estimates	Not included, except for limited characterisation of variability, based on distribution.
Other	
Software Details	The model is a self-contained, MS-DOS based software package.
Hardware Requirements	IBM-compatible personal computer with 80286 or better CPU, MS-DOS Ver. 3.3 or later, with 640 kb memory, and a hard disk drive with minimum 500 kb free.
Associated Costs	Readily available from U.S. National Technical Information Service for about $400.
Running Time for Risk Model	Variable, depending on hardware, multimedia complexity, etc. Typically minutes to hours.

7.4 Health and Welfare Canada (Health Canada)

A generic approach for HRA has been developed in Canada to meet certain legislative requirements under the Canadian Environmental Protection Act (CEPA). This legislation requires that a listing of *priority chemical substances* be established for assessment to determine whether environmental exposure to them poses a risk to the health of Canadians or to the environment. In this regard, Health Canada has been tasked with the responsibility of assessing the risks to human health from environmental exposure to each *Priority Substance*, and developing comprehensive *Assessment Reports* publicly documenting the results of each assessment. In general, the development of HRA in Canada appears to have been influenced more by WHO approaches than by (US) EPA approaches.

It is instructive to note that each HRA is undertaken against a background of extensive external peer review, with full public and community consultation and involvement, to ensure that the assessment process is as open and transparent as possible. Since 1989, some 69 substances (both organic & inorganic) have been included in two separate federal Priority Substances Listings (i.e., PSL1 & PSL2), with 44 substances completed and 25 still undergoing HRA. The PSL/HRA program incorporates a number of important ambient air pollutants, including respirable particulate matter (PM_{10}), and air toxics such as benzene; polycyclic aromatic hydrocarbons; 1,3-butadiene; and formaldehyde.

The general HRA framework utilised by Health Canada for this purpose is based on determining whether or not a substance is "toxic" as defined under CEPA, viz., "*...a substance is toxic if it is entering or may enter the environment in a quantity or concentration or under conditions....constituting or that may constitute a danger in Canada to human life or health*". It is important to understand that this definition of "CEPA toxic" is a legal one which embodies the fundamental concept that harm is a function both of the true toxicity of the substance, and the extent of environmental exposure. In other words, *CEPA toxic* may be equated with *risk* in this context.

Whilst the Canadian approach has been continually evolving over the years to incorporate relevant advances in HRA methodology, the overall framework may be broadly summarised as follows, indicating some key areas of current evolutionary development:

> **Step 1:** *Identification of the critical adverse health effect associated with exposure to a Priority Substance.* To this end, a rather complex and cumbersome classification scheme has been utilised for substances, based on the nature of the critical effect. For example, in the PSL1 assessments, Priority Substances were classified into 6 main categories and 14 sub-categories, based on a weight-of-evidence scheme for carcinogenicity. A similar (unwieldy) multi-category scheme was also used for classification of substances in terms of their potential to cause inheritable human (germ-cell) mutations. However, in the more recent PSL2 assessments, greater emphasis is being placed on detailed descriptions of the weight-of-evidence of these effects, which more clearly outlines the nature of the supporting data, and allows for the increasing complexity of available data on mode of action for various substances. This is a much more rational approach, since chemical classification/listing schemes, on their own, generally provide little information, and tend to hide essential underlying scientific data.

Step 2: *Analysis of the dose-response relationship, based on the different types of critical effects.* This is based on a comprehensive review of *all available information* on the toxicology and epidemiology of the substance in question. Increasing emphasis is being placed on the use of benchmark doses or concentrations rather than "no-effect" or "low-effect" levels, resulting in greater convergence of approaches for characterisation of dose-response for cancer (non-threshold) and non-cancer (threshold) effects.

Step 3: *Determination of the extent to which the population (or certain subsets of the population) are exposed to the substance, incorporating development of multimedia, multipathway exposure estimates.* Multimedia exposure estimates have been derived based on standardised reference values for body weights; volume of air breathed; and ingestion rates for food, water & soil; together with information on population behaviour patterns and average levels of the Priority Substance in the various environmental media. Such estimates were derived for the general Canadian population, as well as (in some cases) for subgroups with potentially higher exposure. More recently, reference values for the intake parameters have been developed for six discrete population subgroups, namely infants (0-0.5 years); pre-schoolers (0.5-4 years); primary school children (5-11 years); teenagers (12-19 years); adults (20-59 years); and seniors (60+ years). Originally, only the first five subgroups were considered. Moreover, increased emphasis is being placed on tailoring the outcome of HRA to better meet risk management needs, including increasing use of probabilistic analysis, environmental fate modelling, and multimedia monitoring studies (in order to provide better characterisation of exposure).

Step 4: *Integration of the exposure with a measure of dose-response for the critical effect to determine whether the substance is "CEPA toxic" (i.e., what risk?).* In recognition of the considerable degree of uncertainty inherent in most HRA efforts, the need for more complete characterisation of the degree of confidence in the available data inputs is becoming a critical issue. To this end, more emphasis is being placed on qualitative and quantitative analysis of variability and uncertainty for measures of both exposure and effects, in order to properly qualify risk within discrete bounds of uncertainty.

Whilst the above provides an indication of the current status and direction of evolution of the Canadian approach to HRA, it should be noted that (so far as we are aware), the "new developments" have not yet been formalised in official policy, or in documented guidelines by Health Canada. On this basis, the existing 4-step Canadian HRA framework summarised above is detailed in Health Canada's 1994 guideline document entitled "*Human Health Risk Assessment for Priority Substances*". Key background information related to this is contained in a companion publication ("*Biological Safety Factors in Toxicological Risk Assessment*" - 1990), whilst a third publication ("*Health-Based Tolerable Daily Intakes/Concentrations and Tumorigenic Doses/Concentrations for Priority Substances*" - 1996) summarises the health-based measures of dose-response developed from risk assessments undertaken on PSL1 substances. Together, these three documents detail the overall Canadian approach to HRA, and have been utilised as the basis of the present review.

Health Canada emphasises that application of this HRA framework to specific substances on a case-by-case basis requires, above all else, the application of sound scientific (or professional) judgement on the part of the risk assessor/s.

Table 7-4
Canadian Methodology

REVIEW CRITERIA	RESULTS & COMMENTS
Model Inputs	
Exposure Assessment:	
Air Quality/Exposure Data	Framework utilises pollutant-specific concentration data (averages) in all environmental media, including ambient air. Multimedia approach to estimation of population "total daily intakes" emphasised. Default standard reference values for most exposure parameters are provided. Framework based on exposure of average members of general Canadian population.
Data Quality Guidelines?	Not specified. Assume based on pollutant-specific professional judgement.
Sensitive Populations	Not specifically addressed, although exposure categorizations within the framework include both young children and the elderly.
Health Effect Data:	
Inclusion Criteria for Toxicity &/or Epidemiological Data	No specific selection mechanism. Framework includes general qualitative summary overview on "usefulness" of various types of epidemiological & toxicological studies for CEPA purposes. Emphasises use of all available data on health effects
Health Endpoint Selection	Based on identification of pollutant-specific "critical effect" (i.e., the biologically significant effect expected to occur at lowest dose or concentration) from all available data. Utilises complex, multi-category classification system based on carcinogenicity & mutagenicity, to determine whether substances will be treated as "threshold or non-threshold toxicants".
Dose-response Assessment	For "threshold toxicants", an uncertainty factor (safety factor) is normally applied to the empirical no-effect or low-effect level for the critical endpoint to derive a tolerable daily intake (TDI) or concentration (TC). Alternatively, where data permit, a model-derived "benchmark dose" estimate of a specified incidence level (e.g. 5%) for the critical effect (above control levels) may be used. For "non-threshold toxicants" (mutagens & genotoxic carcinogens) a potency value is estimated as the tumorigenic dose or concentration which induces a 5% increase in cancer or mutation response (TD0.05 or TC0.05) associated with exposure (i.e., equivalent to a 1 in 20 risk level). Low dose extrapolation is not necessary; since potency is computed directly from the dose-response curve within (or close to) the experimental data range.
Risk Modelling	
Elements of Inputs for Risk Characterisation	Not readily identifiable in framework. Assume pollutant-specific requirements based on professional judgement.
Deterministic or Probabilistic Approach?	Generally deterministic.
Default Parameters Used	Standardised reference values based on Canadian population specified for age, body weight, air inhalation rates, food/water/soil intakes, & time spent indoors/outdoors.
Use of Safety Factors?	Used in TDI/TC derivation. Determined by professional judgement on a case-by-case basis, depending on the quality of the available datasets. Generally, factors of 1-10 used for intraspecies and interspecies variation; 1-100 to account for dataset inadequacies; and 1-5 to account for potential chemical interaction effects.
Uncertainty Analysis?	States that all sources of uncertainty should be considered, but provides no details.

REVIEW CRITERIA	RESULTS & COMMENTS
Risk Modelling (cont)	
Sensitivity Analysis?	Not explicitly addressed.
Model Validation?	Not applicable. Framework cannot be validated. Requires validation of each pollutant - specific application or derived model.
Model Acceptance?	Framework based on broad HRA principles used internationally in one form or other, particularly by WHO, and thus generally accepted in this sense. However, specific CEPA framework format is used & accepted only in Canada.
Pollutants Assessed?	Wide range, as documented in Canadian Priority Substances listings.
Inhalation-Specific or Multimedia Model?	Multimedia HRA framework.
Analysis of Threshold vs Non-Threshold Pollutants	For threshold pollutants, the value of the TDI or TDC is generally compared to the estimated daily intake of a pollutant (from all sources) for the various age groups in the Canadian population. For non-threshold pollutants, the $TD/TC_{0.05}$ is compared with the same daily Canadian exposure levels to derive a ratio known as the Exposure/Potency Index (EPI).
Model Transparency, Simplicity and Ease of Understanding	Basic framework relatively simple & easy to understand, except for substance classification rationale, which is complex, unwieldy and unclear.
Model Outputs - Risk Estimates	
Form of Risk Estimate	For threshold substances, ratio of daily intake to TDI yields a dimensionless "hazard index". For non-threshold substances, the risk estimate is provided by the EPI (i.e., the ratio between daily intake and TD/TC0.05).
Criteria for Risk Acceptability?	Implicitly included as follows: If estimated total daily intake of substance exceeds the TDI or TDC, the substance is considered "CEPA toxic". If intake is less than TDI/TC then substance is not considered to be CEPA toxic. Additionally, if EPI for substance is less than 2 x 10-6, there is generally no need for any further action. An EPI exceeding 2 x 10-4 indicates high priority for further action (i.e., review of options to reduce exposure); whilst an EPI value in between is of moderate priority.
Characterisation of Uncertainty in Risk Estimates	Not included. Qualitatively indicated by implying that the form of the risk estimates have been selected in order to decrease overall uncertainties (e.g. rejecting use of low-dose extrapolation, and opting not to establish a single "de-minimus" risk level).
Other	
Software Details; Hardware Requirements; Associated Costs; Running Time for Risk Model	Not included and not applicable.

7.5 World Health Organisation

The WHO, through its International Programme on Chemical Safety (IPCS), has long been actively engaged in the development and application of risk-based methodologies for public health protection purposes. Whilst the IPCS has based its overall approach to HRA on the general framework outlined in Fig. 5-1, there are fundamental differences in philosophy and scientific emphasis, resulting in methodologies which differ somewhat from USA-based approaches.

In this regard, whilst the (US) EPA has focused largely on the development and refinement of quantitative mathematical models for HRA and its components (for prescriptive regulatory applications); the IPCS has made much less use of such models, concentrating more on transparent documentation of the scientific data (e.g. in its *Environmental Health Criteria* documents), relevance of biomarkers & no-effect levels, and judicious application of "safety" (uncertainty) factors. Moreover, the IPCS has emphasised the use of risk-based approaches mainly in the development of voluntary *guidance values* for environmental chemical exposure limits (i.e., these are not formal standards or regulatory limits). In fact, the IPCS definition of *guidance values* illustrates the flexibility of HRA as used within the WHO context:

"***Guidance Values*** *are* (numerical) *values, such as concentrations* (of chemicals) *in air or water, which are derived after appropriate allocation of a* ***tolerable intake*** *among the different possible media of exposure. Combined exposures from all media at the guidance values over a lifetime would be expected to be* ***without appreciable health risk****. The aim of a guidance value is to provide* ***quantitative information from risk assessment for risk managers*** *to enable them to make decisions concerning the protection of human health*".

To this end, the IPCS has concentrated mainly on development of HRA approaches and guidance values for threshold pollutants (including non-genotoxic carcinogens with adequate mechanistic data), rather than non-threshold substances (largely genotoxic carcinogens & germ cell mutagens). This is the opposite to the situation in the USA, where quantitative cancer risk assessment has been a national priority for many years. The IPCS considers that in general, for non-threshold substances, selection of an appropriate HRA methodology is problematic, and involves considerable uncertainty. Moreover, current HRA approaches for non-threshold effects are not generally appropriate for the development of guidance values, because they require socio-political judgements of "acceptable" health risk (i.e., risk management decisions).

However, putting aside the question of acceptable risk, the IPCS undertakes careful evaluation of all relevant available data for non-threshold effects, in order to attempt to characterise the dose-response relationship using one or more of the currently available international methods (e.g. low dose risk extrapolation, relative potency ranking as in Canadian EPI approach, etc.) . This potentially enables appropriate guidance values to be developed by other authorities wishing to do so, by using the IPCS information.

The following provides a summary overview of the WHO/IPCS HRA process framework, and its application in the development of guidance values:

Step 1: Review, evaluation and summary documentation of all relevant available data on animal & human toxicity and human exposure of the pollutant.

Step 2: Derivation of a total Tolerable Intake (TI) for selected routes of exposure for threshold effects, on the basis of interpretation of available toxicity data. This involves application of various uncertainty ("safety") factors, generally to the no-observed-adverse-effect level (NOAEL) for critical endpoints. For non-threshold effects, characterisation of the dose-response relationship is carried out to the extent possible.

Step 3: Estimation of proportion of total intake originating from relevant media (e.g. food, water, ambient & indoor air, etc.), based on empirical exposure estimates for a consistent set of assumed intake values (using the "ICRP Reference Man" default values), in conjunction with data on representative average pollutant levels in the general environment. Mathematical fate & transport models may be used to estimate pollutant distribution through the various media, in the absence of adequate analytical data on pollutant concentrations.

Step 4: Allocation of proportions of the TI to the various exposure media, as determined in Step 3 (if pollutant is present in more than one environmental medium) to estimate relative multimedia contributions to exposure.

Step 5: Derivation of pollutant guidance values from intakes assigned to each medium, considering body weight, intake volume and (relative) absorption efficiency. Derivation is based on a (clearly defined) general exposure scenario, for a general population, using standard default exposure factors, and not necessarily representative of any national or local exposure conditions. Appropriate risk management input would be required for modification and adaptation of such guidance values to suit any specific local circumstances.

The risk-based framework outlined above has been applied by WHO to the derivation of various health-based ambient air quality guideline values, which provide a general preliminary basis for protecting public health from the adverse effects of air pollutants. Current (1997) WHO guideline values for a sample range of *priority pollutants*, *threshold pollutants* and *non-threshold pollutants* are summarised in Tables 7.5.1, 7.5.2 and 7.5.3 respectively, together with selected supporting HRA data.

Together, these data illustrate some of the technical difficulties and limitations inherent in the derivation of ambient air quality guideline values using such risk-based approaches. It is also interesting to note that the WHO treats ozone as a *threshold* pollutant, whilst the weight of epidemiological evidence increasingly suggests a *non-threshold* mode of action. This is an important source of uncertainty.

For non-threshold air pollutants such as respirable particulate matter (PM_{10} and $PM_{2.5}$) and genotoxic carcinogens, "guideline values" are not derived *per se,* but instead are presented indirectly in the form of "*% change-in-health-effect versus concentration*" relationships, which equate to *risk-concentration* relationships, from which *unit risks* may be derived, as applicable.

These risk-concentration relationships are usually (approximately) linear within a certain concentration range, and it becomes a risk management decision as to which concentration is actually chosen as the working "guideline value" in any particular application. (In this regard, a "*unit risk*" can be generally visualised as *an estimate of the excess risk resulting from a defined exposure to the non-threshold pollutant at a defined concentration interval [e.g., per µg m^{-3}] in air*).

Table 7.5.1
WHO Air Quality Guidelines for Some Priority (Threshold) Pollutants

POLLUTANT	AVERAGE AMBIENT AIR LEVEL (µg m^{-3})	HEALTH ENDPOINT	OBSERVED EFFECT LEVEL (µg m^{-3})	UNCERTAINTY FACTOR	GUIDELINE VALUE (µg m^{-3})	AVERAGING TIME
Carbon Monoxide	500-7000	Critical Level of COHb < 2.5% (carboxyhaemoglobin)	N/A	N/A	100,000 60,000 30,000 10,000	15 min. 30 min. 1 hour 8 hours
Lead	0.01-2	Critical Level of Blood Lead < 25 µg dL^{-1}	N/A	N/A	0.5	1 year
Nitrogen Dioxide	10-150	Slight Changes in Lung Function in Asthmatics	365-565	0.5	200 40	1 hour 1 year
Ozone	10-100	Respiratory Function Changes	N/A	N/A	120	8 hours
Sulphur Dioxide	5-400	Changes in Lung Function in Asthmatics	1000	2	500	10 min.
		Exacerbation of Respiratory Symptoms in Sensitive Individuals	250 100	2 2	125 50	24 hours 1year

As previously indicated, for PM_{10} and $PM_{2.5}$, the WHO has derived a range of linear relationships between the percent change of a range of acute human health endpoints and PM concentrations. These "health endpoints" include daily mortality, respiratory hospital admissions, and (for PM_{10}) bronchodilator use, lower-respiratory symptom exacerbation, cough, and peak expiratory flow. In this regard, the percent change in the selected health endpoint is directly related to the risk of health effects occurring.

However, in order for these *risk-concentration relationships* to be used in deriving ambient air quality standards for PM_{10} and $PM_{2.5}$, a "suitable" health endpoint needs to be selected from the available range (based on population-specific considerations), and a prior decision as to what constitutes an "acceptable risk" needs to be made (i.e., what % change in the selected health endpoint is acceptable to the exposed population) within a regulatory/consultative decision framework. Quite apart from the scientific uncertainties inherent in this approach, it is clear that such decisions would necessarily invoke complex value judgements including cost-benefit considerations, and would require appropriate risk management input in order to achieve any sort of resolution. In contrast, the air quality guideline values for priority pollutants in Table 7.5.1 uniformly assume a *minimal risk* without explicitly stating it, thereby facilitating more direct risk management application within the socio-political standard-setting process.

Table 7.5.2
WHO Air Quality Guidelines for Some Threshold Pollutants

POLLUTANT	AVERAGE AMBIENT AIR LEVEL ($\mu g\ m^{-3}$)	HEALTH ENDPOINT	OBSERVED EFFECT LEVEL ($mg\ m^{-3}$)	UNCERTAINTY FACTOR	GUIDELINE VALUE ($\mu g\ m^{-3}$)	AVERAGING TIME
Acrolein	15	Eye irritation in humans.	130×10^{-3}	2.5	50	30 min.
Diesel Exhaust	1-10	Chronic lung inflammation in humans.	0.139 (NOAEL)	25	5.6	1 year
		Chronic lung inflammation in rats.	0.23 (NOAEL)	100	2.3	1 year
Formaldehyde	$(1\text{-}20) \times 10^{-3}$	Nose & throat irritation in humans.	0.1 (NOAEL)	N/A	100	30 min.
Hydrogen Sulphide	0.15	Eye irritation in humans.	15 (LOAEL)	100	150	24 hours
		Odour (annoyance) threshold.	N/A	N/A	7	30 min.
Xylenes	1-100	CNS effects in human volunteers.	304 (NOAEL)	60	4800	24 hours
		Neurotoxicity in rats.	870 (LOAEL)	1000	870	1 year
		Odour (annoyance) threshold.	N/A	N/A	4400	30 min.

Note that a low uncertainty factor reflects a high quality toxicity data base (usually incorporating reliable human data), whilst a high uncertainty factor indicates much less confidence in the quality of the underlying data, usually based on animal studies alone.

Table 7.5.3
WHO Air Quality Guidelines For Some Non-threshold Pollutants

POLLUTANT	AVERAGE AMBIENT AIR LEVEL ($\mu g\ m^{-3}$)	HEALTH ENDPOINT	UNIT RISK ESTIMATES ($\mu g\ m^{-3}\ ^{-1}$)	IARC CANCER CLASS
Benzene	5-20	Leukaemia in exposed humans (workers)	$(4.4\text{-}7.5) \times 10^{-6}$	1
Diesel Exhaust	1-10	Lung cancer in rats	$(1.6\text{-}7.1) \times 10^{-5}$	
Polycyclic Aromatic Hydrocarbons (Benzo[a]pyrene)	$1\text{-}10 \times 10^{-3}$	Lung cancer in exposed humans	8.7×10^{-2}	1
Trichloroethylene	1-10	Cell tumours in testes of rats	4.3×10^{-7}	2A
Vinyl Chloride	0.1-10	Haemangiosarcoma in exposed workers. Liver cancer in exposed workers.	1×10^{-6}	1

(IARC = International Agency for Research on Cancer; a division of WHO).

In the case of the carcinogenic risk data presented in Table 7.5.3, a "unit risk" is strictly defined as *a model-derived estimate of the excess lifetime cancer risk resulting from continuous lifetime exposure to the carcinogen at a concentration of 1 μg* m^{-3} *in air.*

On this basis, whilst the WHO air quality guidelines are not standards *per se* (& should not be interpreted as such), they are "globally" designed to facilitate the risk management decision-making process, particularly in the setting of discrete ambient air quality standards to meet the differing requirements of specific (inter)national or local jurisdictions.

Consequently, it is important to note that in attempting to progress from guidelines to standards, key risk management policy options which must be addressed (amongst other considerations) include the questions of "which proportion of the general population" and "which susceptible population sub-groups" should be protected? Therefore, (inter)national standards might well be set either above or below the risk-based air quality guidelines.

Additionally, such "guidelines" and "standards" are by no means fixed entities, and are always subject to change as new information becomes available. In this regard, the WHO undertakes a program of revising and updating its guideline values and unit risk estimates whenever new scientific data and advances in HRA methodologies permit.

More significantly, the *guideline values* approach is part of an ongoing WHO/IPCS program which is attempting to *harmonise* HRA processes worldwide; with the aim that risk assessments performed in one country will in future be acceptable in other countries, thereby leading to more efficient use of resources, and more consistent HRA's. In this context, the definition of *harmonisation* includes an attempt to reach global agreement on basic HRA principles; an understanding of the HRA practices used by other countries in order to develop confidence in assessments using different approaches; and an overall aim of working towards globally beneficial convergence of the various HRA approaches.

We believe that this is a laudable and worthwhile aim, which would not only reduce duplication of work by scientists, but would also provide a greater transparency of approach (with potentially better understanding and involvement) for communities, thereby potentially facilitating the future development of risk-based consensus standards for ambient air quality.

Table 7-5-4
WHO Methodology

REVIEW CRITERIA	RESULTS & COMMENTS
Model Inputs	
Exposure Assessment:	
Air Quality/Exposure Data	Framework utilises pollutant-specific concentration data (averages) in all relevant environmental media, including ambient air. Multimedia approach to estimation of population "total intakes" emphasised. Default standard reference values for many exposure parameters are provided. Framework based on exposure of average members of a general population.
Data Quality Guidelines?	Not specified. Assume based on pollutant-specific professional judgement.
Sensitive Populations	Not explicitly addressed in any detail. Requires that sensitive population subgroups must be considered in framework applications, based on professional judgement
Health Effect Data:	
Inclusion Criteria for Toxicity &/or Epidemiological Data	No specific selection mechanism. Framework includes general procedures for extrapolation from a given toxicity database, including decision points for data adequacy, geared towards derivation of uncertainty factors. Emphasises use of all available epidemiological & toxicological data
Health Endpoint Selection	Based on identification of pollutant-specific "critical effect" (i.e., the biologically significant effect expected to occur at lowest dose or concentration) using all available data. In general, IARC Group 1 & 2A substances are treated as carcinogenic (non-threshold) compounds, while all other substances are treated as non-carcinogenic (threshold) compounds. Exceptions include PM_{10} and $PM_{2.5}$.
Dose-response Assessment	For non-carcinogens, an uncertainty factor (UF) is normally applied to the empirical no-effect or low-effect level for the critical endpoint to derive a tolerable intake (TI) or concentration (TC). Alternatively, where data adequacy allows, a model-derived "benchmark dose", defined as the LCL of the dose that produces a small increase (e.g. 5%) in the level of adverse effects may be used, to which UF's are applied to develop a TI. For carcinogens (& PM_{10}/$PM_{2.5}$) the "unit risk" model is normally used.
Risk Modelling	
Elements of Inputs for Risk Characterisation	Not readily identifiable in framework. Assume pollutant-specific requirements based on professional judgement.
Deterministic or Probabilistic Approach?	Deterministic only.
Default Parameters Used	Standard exposure defaults based on published "ICRP Reference Man" values for general population. Includes average body weights, respiratory volumes, and daily food, fluid & soil intakes.
Use of Safety Factors?	UF's used in TI derivation. Determined via a specific "decision tree" approach, depending on the quality and completeness of the available toxicity database. UF's between 1-10,000 can be applied, although a value of 100 has been most commonly used, comprising two factors of 10 each to account for intraspecies and interspecies variation. Each of these are subdivided further into factors which can incorporate appropriate data on toxicokinetics and toxicodynamics (where available).

REVIEW CRITERIA	RESULTS & COMMENTS
Risk Modelling (cont)	
Uncertainty Analysis?	Requires that guidance value estimates should clearly indicate the nature and sources of uncertainty, and the manner in which these have been taken into account.
Sensitivity Analysis?	Not addressed.
Model Validation?	Not applicable. Framework cannot be validated. Requires validation of each pollutant - specific application or derived model.
Model Acceptance?	Framework based on established HRA principles used internationally in one form or other, particularly in Europe, Canada & Australia, and thus generally accepted in this sense. Specific WHO framework format is accepted & used mainly in Europe.
Pollutants Assessed?	Wide range, as documented in WHO Environmental Health Criteria documents, and WHO air quality guidelines.
Inhalation-Specific or Multimedia Model?	Multimedia HRA framework.
Analysis of Threshold vs Non-Threshold Pollutants	For threshold pollutants, the value of the TI or TC is generally apportioned according to the estimated daily intake of a pollutant from all sources for an average population, to derive an appropriate guidance value. For non-threshold pollutants, linear *risk-concentration* relationships or *unit risks* are derived instead, providing information on the health effects associated with different levels of exposure, and an estimation of associated public health consequences.
Model Transparency, Simplicity and Ease of Understanding	Basic framework relatively simple, transparent & easy to understand.
Model Outputs - Risk Estimates	
Form of Risk Estimate	Generally, guidance values for threshold pollutants and unit risks for non-threshold substances. Provides a basis for standards development.
Criteria for Risk Acceptability?	Not explicitly addressed. Whilst guidance values are generally defined as minimal risk or "safe" levels of exposure, WHO considers that the question of "acceptable risk" is a risk management issue, particularly for non-threshold effects.
Characterisation of Uncertainty in Risk Estimates	Not explicitly included. Partially and indirectly addressed in specification of UF's for toxicity assessment; but not considered in exposure assessment, and overall requirements not addressed in any detail.
Other	
Software Details; Hardware Requirements; Associated Costs; Running Time for Risk Mode.	Not included and not applicable.

7.6 United Kingdom Expert Panel on Air Quality Standards

The Expert Panel on Air Quality Standards is a scientific advisory committee within the UK Department of the Environment, tasked with developing recommendations for ambient air quality standards, on the basis of evaluation of relevant scientific data. In undertaking this review, however, we have found little relevant information on the HRA approaches used by this group. Despite repeated attempts, we have been unsuccessful in our approaches to the UK Environment Agency, Department of Health and the Interdepartmental Liaison Group on Risk Assessment (ILGRA). A limited search of the published scientific literature also failed to turn up any material of relevance regarding the Expert Panel and its *modus operandi*.

Consequently, for the purpose of completing the present review, we have chosen to make the assumption that *any HRA approach used by the Expert Panel would most likely follow the WHO risk-based methodology*. Since the UK remains a key member of the European Union, and the WHO approach is used by the UK Department of Health, together with the Ministry of Agriculture, Fisheries and Food, we consider that this is a reasonable assumption to make under the circumstances.

On this basis, the review results are summarised on the next two pages, and the reader is referred to Section 7.5 for further details.

Table 7-6
UK Expert Panel on Air Quality Standards
(as per WHO)

REVIEW CRITERIA	RESULTS & COMMENTS
Model Inputs	
Exposure Assessment:	
Air Quality/Exposure Data	Framework utilises pollutant-specific concentration data (averages) in all relevant environmental media, including ambient air. Multimedia approach to estimation of population "total intakes" emphasised. Default standard reference values for many exposure parameters are provided. Framework based on exposure of average members of a general population.
Data Quality Guidelines?	Not specified. Assume based on pollutant-specific professional judgement.
Sensitive Populations	Not explicitly addressed in any detail. Requires that sensitive population subgroups must be considered in framework applications, based on professional judgement.
Health Effect Data:	
Inclusion Criteria for Toxicity &/or Epidemiological Data	No specific selection mechanism. Framework includes general procedures for extrapolation from a given toxicity data base, including decision points for data adequacy, geared towards derivation of uncertainty factors. Emphasises use of all available epidemiological & toxicological data.
Health Endpoint Selection	Based on identification of pollutant-specific "critical effect" (i.e., the biologically significant effect expected to occur at lowest dose or concentration) using all available data. In general, IARC Group 1 & 2A substances are treated as carcinogenic (non-threshold) compounds, while all other substances are treated as non-carcinogenic (threshold) compounds. Exceptions include PM_{10} and $PM_{2.5}$.
Dose-response Assessment	For non-carcinogens, an uncertainty factor (UF) is normally applied to the empirical no-effect or low-effect level for the critical endpoint to derive a tolerable intake (TI) or concentration (TC). Alternatively, where data adequacy allows, a model-derived "benchmark dose", defined as the LCL of the dose that produces a small increase (e.g. 5%) in the level of adverse effects may be used, to which UF's are applied to develop a TI. For carcinogens (& PM_{10}/$PM_{2.5}$) the "unit risk" model is normally used
Risk Modelling	
Elements of Inputs for Risk Characterisation	Not readily identifiable in framework. Assume pollutant-specific requirements based on professional judgement.
Deterministic or Probabilistic Approach?	Deterministic only.
Default Parameters Used	Standard exposure defaults based on published "ICRP Reference Man" values for general population. Includes average body weights, respiratory volumes, and daily food, fluid & soil intakes.
Use of Safety Factors?	UF's used in TI derivation. Determined via a specific "decision tree" approach, depending on the quality and completeness of the available toxicity database. UF's between 1-10,000 can be applied, although a value of 100 has been most commonly used, comprising two factors of 10 each to account for intraspecies and interspecies variation. Each of these are subdivided further into factors which can incorporate appropriate data on toxicokinetics and toxicodynamics (where available).
Uncertainty Analysis?	Requires that guidance value estimates should clearly indicate the nature and sources of uncertainty, and the manner in which these have been taken into account.

REVIEW CRITERIA	RESULTS & COMMENTS
Risk Modelling (cont)	
Sensitivity Analysis?	Not addressed.
Model Validation?	Not applicable. Framework cannot be validated. Requires validation of each pollutant - specific application or derived model.
Model Acceptance?	Framework based on established HRA principles used internationally in one form or other, particularly in Europe, Canada & Australia, and thus generally accepted in this sense. Specific WHO framework format is accepted & used mainly in Europe.
Pollutants Assessed?	Wide range, as documented in the WHO air quality guidelines, for example.
Inhalation-Specific or Multimedia Model?	Multimedia HRA framework.
Analysis of Threshold vs Non-Threshold Pollutants	For threshold pollutants, the value of the TI or TC is generally apportioned according to the estimated daily intake of a pollutant from all sources for an average population, to derive an appropriate guidance value. For non-threshold pollutants, linear *risk-concentration* relationships or *unit risks* are derived instead, providing information on the health effects associated with different levels of exposure, and an estimation of associated public health consequences.
Model Transparency, Simplicity and Ease of Understanding	Basic framework relatively simple, transparent & easy to understand.
Model Outputs - Risk Estimates	
Form of Risk Estimate	Generally, *guidance values* for threshold pollutants and *unit risks* for non-threshold substances. Provides a basis for standards development.
Criteria for Risk Acceptability?	Not explicitly addressed. Whilst guidance values are generally defined as "safe" levels of exposure, WHO considers that the question of "acceptable risk" is a risk management issue, particularly for non-threshold effects.
Characterisation of Uncertainty in Risk Estimates	Not explicitly included. Partially and indirectly addressed in specification of UF's for toxicity assessment; but not considered in exposure assessment, and overall requirements not addressed in any detail.
Other	
Software Details; Hardware Requirements; Associated Costs; Running Time for Risk Model	Not included and not applicable.

7.7 The Ricci and Beer Approach

During the development of the ambient air quality NEPM in 1997, an attempt was made to carry out a health risk assessment on the six priority pollutants being considered, for the purpose of evaluating the risk significance of the range of standards under consideration. To this end, Ricci and Beer developed a novel mathematical HRA modelling approach specifically for the pollutants under study, based on previous exposure modelling undertaken by Beer and Walsh. In general, the Ricci/Beer approach appears to consist of the following elements:

1. An ambient air quality review is undertaken and a suitable exposure measure defined such as pollutant concentration averaged over a specified time unit, or (for carbon monoxide & ozone), the number of hourly exceedances of daily maximum concentrations, utilising data from fixed point air quality monitoring stations representing selected capital city airsheds.

2. A population database is developed for Australia (using 1990 census statistics) and converted into a series of population densities for individual 1 km^2 exposure areas ("cells").

3. Population exposure modelling is undertaken by convoluting the statistical distribution of air quality data with the spatial population distribution in urban and industrial areas, to yield exposure measures comprising: "Repetitious Exposure" - frequency of exceedances in person-events per year; "Average Frequency of Exceedance" - number of events per year as a spatial average; and "Population Affected" - number of people affected by at least one defined exceedance event. A computer model for spatial interpolation is employed for these purposes, using a combination of $1/r^2$ interpolation between monitoring stations and defined boundary conditions for pollutant concentration parameters. This reportedly provides estimates of population-weighted exposure.

4. Exposure (concentration)-response functions are generated from selected reviews of epidemiological and other human data. (In the end, linear exposure-response models were assumed for each of the six pollutants, due to lack of adequate data).

5. The results of exposure assessment and toxicity evaluation are combined to yield probabilistic measures of health risk for ambient exposure to each of the six air pollutants. Convolution of the concentration-response and exposure probability functions yields a third (risk probability) distribution function which provides an estimate of the probable number of people affected.

We have found it somewhat difficult to determine the potential usefulness or applicability of the Ricci/Beer approach, and to properly interpret its rationale. The methodology is based almost entirely upon a series of complex mathematical, statistical and verbal arguments, which preclude an adequate characterisation and reconciliation of data inputs, selection criteria, modelling rationale and risk outputs. It appears to be an unusual theoretical approach, which tends to shroud model transparency within multiple layers of mathematical complexity, and unfortunately, we were unable to fully digest the underlying details of the approach.

Our difficulty in coming to terms with this approach suggests that other interested parties would also be likely to have similar difficulties, and this constitutes an important factor that needs to be considered in any proposed public health application of the methodology.

As discussed in *Section 4*, the NEPC had previously undertaken a detailed evaluation of the Ricci/Beer modelling approach during the development of the ambient air quality NEPM. Reportedly, after taking into account both expert and key stakeholder advice on the matter, it became apparent that in order for the results of the HRA to be useful in evaluating the respective merits of the range of standards under consideration, the process required an ability to estimate incremental changes in risk for the range of possible standards for each criteria pollutant. The NEPC concluded that neither the methodology nor the available data sets allowed this to be undertaken. In view of this conclusion, the outcomes of the Ricci/Beer approach were not used in the development of the NEPM air quality standards.

Table 7-7
Ricci and Beer Approach

REVIEW CRITERIA	RESULTS & COMMENTS
Model Inputs	
Exposure Assessment:	
Air Quality/Exposure Data	Modelling approach utilises air quality data from fixed monitoring stations, and population distribution data from census statistics.
Data Quality Guidelines?	Not included.
Sensitive Populations	Approach considers expected exposure of general (total) population only, and does not specifically target susceptible or high-risk sub-groups.
Health Effect Data:	
Inclusion Criteria for Toxicity &/or Epidemiological Data	None specified. Pollutant-specific evaluation based on professional judgement.
Health Endpoint Selection	Based on evaluation of epidemiological and human clinical databases for each pollutant. Range of endpoints considered, based on critical effects observed in relevant studies (e.g. carbon monoxide health endpoints: ischaemic heart disease; reduced birth weight).
Dose-response Assessment	Experimental data inadequate to define actual exposure-response model parameters. Therefore the simplifying assumption is made that linear exposure-response models are adequate to describe pollutant toxicity at "low" exposure levels. A range of empirical literature data relating exposure concentrations to selected human health endpoints was then used to build exposure-response functions for each of the six pollutants, depending on threshold/non-threshold response identification.
Risk Modelling	
Elements of Inputs for Risk Characterisation	Not readily identifiable in modelling approach. Elements of exposure probability functions and exposure-response functions hidden in mathematical complexity of approach.
Deterministic or Probabilistic Approach?	Not entirely clear. Modelling approach appears to use deterministic point estimates for input parameters to derive probability distribution functions.
Default Parameters Used	Not entirely clear. Modelling approach does not specify "default parameters" as such, but "indicates" inhalation rate assumption of 20 m3/day, and 24 hours/day ambient exposure.
Use of Safety Factors?	Not used and not applicable.
Uncertainty Analysis?	Not entirely clear. Modelling approach includes general theoretical discussion on uncertainty, and probability distribution functions are assumed to partially account for population variability. Overall approach appears to be lacking, however.
Sensitivity Analysis?	Not explicitly included.
Model Validation?	No evidence of validation of modelling approach, or its components.
Model Acceptance?	Not applicable. Approach recently developed and used in Australia for NEPM trial/experimental purposes only. Untested methodology of unproven validity.
Pollutants Assessed?	Ozone, Particulate Matter, Lead, Nitrogen Dioxide, Carbon Monoxide, Sulphur Dioxide.
Inhalation-Specific or Multimedia Model?	Inhalation only.

REVIEW CRITERIA	RESULTS & COMMENTS
Risk Modelling (cont)	
Analysis of Threshold vs Non-Threshold Pollutants	Not entirely clear, due to mathematical complexity.
Model Transparency, Simplicity and Ease of Understanding	Modelling approach complex and difficult to understand due to unusual theoretical mathematical/statistical treatment. Requires high-level understanding of applied mathematics to properly evaluate methodology used. Poor transparency overall.
Model Outputs - Risk Estimates	
Form of Risk Estimate	Product of exponential exposure probability curve and linear concentration-response function yields a (peak) health risk probability distribution function incorporating a maximum health risk value at some finite pollutant concentration. Values expressed in each case as an estimated number of people likely to be affected at a particular concentration. These are likely to incorporate significant uncertainty.
Criteria for Risk Acceptability?	Specific criteria not built into modelling approach, but contains a brief general theoretical and philosophical discussion on risk acceptability.
Characterisation of Uncertainty in Risk Estimates	Apparently not included, except for limited characterisation of variability, based on probability distributions.
Other	
Software Details; Hardware Requirements; Associated Costs; Running Time for Risk Model	No information.

7.8 National Environmental Health Forum (ENHealth Council)

In contrast to the prescriptive regulatory HRA framework that has dominated the North American approach, the development and use of HRA in Australia over the last 10 years has very much focused on "voluntary guidance" applications. Australian health and environmental authorities have made a concerted effort to develop practical working guidelines for risk assessment, emphasising the need for good science and consistent methodologies, against a background of community consultation. The increasing acceptance of HRA as a useful tool for environmental health risk management in this country has been a relatively recent occurrence, building on the initial Australian approaches of the early 1990's, which focused almost exclusively on soil contamination applications.

The general approach to development of HRA methodologies in Australia has been to select the "best" elements of established North American and European approaches (mainly WHO, Canadian & USEPA) and synthesise these into overall guideline-based frameworks, targeted to Australian environmental conditions and local data. In this regard, the National Environmental Health Forum ("ENHealth Council") has been instrumental in facilitating and promoting the development of such guidelines.

The most recent contribution to this ongoing effort is a draft document entitled "Guidelines for Environmental Health Risk Assessment" (hereinafter abbreviated to "GEHRA"). This lengthy document, which is based largely on the soil NEPM guidelines discussed in Section 7.9, presents a generic framework/guideline approach for HRA. It is designed to provide overall methodological and process guidance for risk assessors and others involved in the development and application of HRA techniques to environmental health problems. The emphasis of GEHRA is on facilitating process transparency and greater consistency in environmental health decision-making across Australia.

The GEHRA draft is based on a standard, 5-step process framework for HRA comprising: *issue identification, hazard identification, dose-response assessment, exposure assessment (for relevant population), and risk characterisation.*

The "guidance manual" format of GEHRA presents general guidelines for all of these steps, and incorporates a series of appendices summarising the various Australian approaches to risk assessment, together with general application guideline summaries for HRA of contaminated sites, air pollutants, food, and water. As a draft document, GEHRA is currently being revised and rewritten, and we note that a number of sections are largely incomplete, including the appendix on air pollutants. This review has been undertaken without pre-empting the content of the final version of the document.

As a general HRA framework, GEHRA does not provide a "cookbook" for specific applications such as ambient air quality standard setting. Whilst the guidelines contained within the document represent an excellent international distillation of soundly-based, general HRA principles and practices, GEHRA does not currently incorporate a HRA modelling approach for ambient air quality. It is still very much incumbent on the skills of the risk assessor to judiciously apply the principles contained in GEHRA, to the development of purpose-specific modelling approaches and/or models, tailored to the requirements of the particular environmental health issue/s being assessed.

Table 7-8
NEHF Approach

REVIEW CRITERIA	RESULTS & COMMENTS
Model Inputs	
	NOTE: *Draft GEHRA document does not specify or discuss air quality applications.*
Exposure Assessment:	
Air Quality/Exposure Data	Framework/guidelines discuss general aspects of exposure assessment, the need to consider all pathways, & the need to ensure applicability to the relevant population, but do not specify air quality requirements. Lists general input requirements for air dispersion modelling, but no specific treatment of subject.
Data Quality Guidelines?	Not specified. States that these need to be application-specific.
Sensitive Populations	Emphasises the need to identify and specifically consider sensitive sub-groups in all HRA's, but provides no details.
Health Effect Data:	
Inclusion Criteria for Toxicity &/or Epidemiological Data	Framework includes general discussions on analysis & evaluation of toxicology studies and use of epidemiology in HRA, but neither specifies inclusion criteria, nor provides a specific selection mechanism.
Health Endpoint Selection	Not specified, but generally based on evaluation of relevant epidemiological and toxicological data. Application-specific & pollutant specific requirement based on professional judgement.
Dose-response Assessment	Framework includes general discussion on dose-response assessment, covering threshold & non-threshold approaches, including mechanistic models and benchmark dose approaches. Favours basic WHO approach, with selected modifications. Application-specific & pollutant-specific requirement based on professional judgement.
Risk Modelling	
Elements of Inputs for Risk Characterisation	Not specifically identifiable in framework. Application-specific & pollutant-specific requirement based on professional judgement.
Deterministic or Probabilistic Approach?	Both approaches included and discussed. Framework favours deterministic approach.
Default Parameters Used	Standard range of exposure parameters included & discussed. Depending on specific application requirements, and availability of suitable application-specific & population-specific data. May include, for example, inhalation factors, ingestion factors, dermal factors, body weights, duration of residency, etc.
Use of Safety Factors?	General discussion on use in toxicity assessment as per WHO. No specific factors used.
Uncertainty Analysis?	General discussion only. Specifies that uncertainty analysis is required at each step of the HRA process.
Sensitivity Analysis?	General discussion only. No methodological or application details.
Model Validation?	Not applicable. Framework cannot be validated. Would require validation of each pollutant-specific application or derived model.
Model Acceptance?	Framework based on well-known, established HRA principles & approaches used internationally in one form or other, particularly in Europe, Canada & the USA, and thus generally accepted in this sense. GEHRA document basically constitutes a collation & synthesis of selected elements of existing international approaches, adapted for use within Australia.

REVIEW CRITERIA	RESULTS & COMMENTS
Risk Modelling (cont)	
Pollutants Assessed?	Applicable to virtually any pollutant that is present in environmental media (air, water, soil and food)
Inhalation-Specific or Multimedia Model?	Framework specifies multimedia, multipathway approach to HRA.
Analysis of Threshold vs Non-Threshold Pollutants	Threshold pollutants generally based on WHO tolerable intake (or acceptable daily intake) approach, for comparison with environmental dose. Various approaches are outlined for non-threshold substances, including USEPA, WHO, mechanistic and benchmark dose. Application-specific & pollutant-specific requirement based on professional judgement, and availability of relevant data.
Model Transparency, Simplicity and Ease of Understanding	Basic framework relatively simple, transparent and easy to understand. Some of the detail is complex, however, and requires a good knowledge of toxicology, epidemiology and HRA practice for proper understanding and application.
Model Outputs - Risk Estimates	
Form of Risk Estimate	Variable, depending on application-specific & pollutant-specific requirements, based on professional judgement. Framework discusses general principles of risk characterisation but does not provide "cookbook" details or techniques.
Criteria for Risk Acceptability?	Not applicable and not included. Requires appropriate risk management input.
Characterisation of Uncertainty in Risk Estimates	Framework emphasises the importance of integrated uncertainty characterisation with respect to scenario uncertainty, parameter uncertainty, and model uncertainty, and specifies uncertainty issues to be addressed at each HRA step. Suggests overall qualitative characterisation of uncertainty (i.e., low, moderate, high).
Other	
Software Details; Hardware Requirements; Associated Costs; Running Time for Risk Model	Not included and not applicable.

7.9 Contaminated Sites National Environment Protection Measure

In recognition of the importance of ensuring that appropriate processes are in place to properly assess potentially contaminated sites in Australia, the NEPC has recently developed a *Draft NEPM for the Assessment of Site Contamination*. This NEPM essentially constitutes a major review, revision and formalisation of the *1992 Australian and New Zealand Guidelines for the Assessment and Management of Contaminated Sites* (Australian & New Zealand Environment & Conservation Council and National Health & Medical Research Council).

The purpose of the NEPM is to "*establish a nationally consistent approach to the assessment of site contamination to ensure sound environmental management practices by regulators, community, assessors, contaminated land auditors, land owners, developers and industry.*" On this basis, the "desired environmental outcome" for this NEPM is to "*provide adequate protection of human health and the environment, where site contamination has occurred, through the development of an efficient and effective national approach to the assessment of site contamination.*" The NEPC is currently in the process of finalising this draft NEPM, and is expected to agree to make the Measure towards the end of 1999, or by early 2000.

A series of draft National Environment Protection Guidelines [Schedule B (1) to Schedule B (10)] form an integral part of the NEPM, and are included to provide general guidance on the possible means for achieving the "desired environmental outcome". Schedule B (4) is the key HRA guideline within the NEPM, and provides a consistent methodological framework for conducting site-specific risk assessments of contaminated land.

The focus of this framework is exclusively fixed upon localised soil contamination issues, and does not consider ambient air quality applications. The framework does consider the inhalation pathway as one of the local exposure routes for soil contaminants, particularly volatiles, but this is not relevant to ambient air quality.

The material in the Schedule B (4) HRA guideline is essentially the same as that in the draft NEHF (GEHRA) document reviewed in Section 7.8, with some differences in emphasis where required. In fact, the NEHF document appears to generally comprise an expanded version of Schedule B (4). We consider this to be a logical approach in terms of maintaining consistency. However, practical use of both sets of guidelines still requires the derivation of an application-specific/pollutant-specific modelling approach tailored to the requirements of the actual health risk problem to be addressed.

In this regard, it is clear that, as a methodological framework for soil and groundwater assessment, Schedule B (4) does not provide the tools required for the determination of ambient air quality standards, and of course, has not been designed for this purpose.

Table 7-9
Contaminated Sites NEPM Approach:

REVIEW CRITERIA	RESULTS & COMMENTS
Model Inputs	
	NOTE: *Draft guideline document does not specify or discuss air quality applications.*
Exposure Assessment:	
Air Quality/Exposure Data	Methodological framework discusses general aspects of exposure assessment, the need to consider all pathways, & the need to ensure applicability to the relevant population, but does not specify air quality requirements. Specifically designed for application to site-specific soil contamination problems.
Data Quality Guidelines?	Not specified. States that these need to be application-specific.
Sensitive Populations	Emphasises the need to identify and specifically consider sensitive sub-groups.
Health Effect Data:	
Inclusion Criteria for Toxicity &/or Epidemiological Data	Framework includes general discussion on toxicology appraisals, but neither specifies inclusion criteria, nor provides a specific selection mechanism.
Health Endpoint Selection	Not specified, but generally based on evaluation of relevant epidemiological and toxicological data. Application-specific & pollutant specific requirement based on professional judgement.
Dose-response Assessment	Framework includes general discussion on dose-response assessment, covering threshold & non-threshold approaches, including benchmark dose approaches. Favours basic WHO approach. Highlights modified benchmark dose approach for carcinogens. Requires high level of professional judgement.
Risk Modelling	
Elements of Inputs for Risk Characterisation	Not specifically identifiable in framework. Application-specific & pollutant-specific requirement based on professional judgement.
Deterministic or Probabilistic Approach?	Both approaches included and discussed. Framework favours deterministic approach.
Default Parameters Used	Standard range of exposure parameters included & discussed. Depending on specific application requirements, and availability of suitable application-specific & population-specific data. May include, for example, inhalation factors, ingestion factors, dermal factors, body weights, duration of residency, etc.
Use of Safety Factors?	General discussion on use in toxicity assessment as per WHO. No specific factors actually used.
Uncertainty Analysis?	General discussion only. Specifies that uncertainty analysis is required at each step of the HRA process.
Sensitivity Analysis?	General discussion only. No methodological or application details.
Model Validation?	Not applicable. Framework cannot be validated. Would require validation of each pollutant-specific application or derived model
Model Acceptance?	Framework based on well-known, established HRA principles & approaches used internationally in one form or other, particularly in Europe, Canada & the USA, and thus generally accepted in this sense. Methodology basically constitutes a collation & synthesis of relevant existing international approaches, adapted for use within Australia.
Pollutants Assessed?	Applicable to virtually any pollutant that is present in soil (& groundwater).

REVIEW CRITERIA	RESULTS & COMMENTS
Risk Modelling (cont)	
Inhalation-Specific or Multimedia Model?	Framework specifies multimedia, multipathway approach to HRA.
Analysis of Threshold vs Non-Threshold Pollutants	Threshold pollutants generally based on WHO tolerable intake (or acceptable daily intake) approach, for comparison with environmental dose. Various approaches are outlined for non-threshold substances, including (favoured) benchmark dose method. Application-specific & pollutant-specific requirement based on professional judgement.
Model Transparency, Simplicity and Ease of Understanding	Basic framework relatively simple, transparent and easy to understand.
Model Outputs - Risk Estimates	
Form of Risk Estimate	Variable, depending on application-specific & pollutant-specific requirements, based on professional judgement. Framework discusses general principles of risk characterisation but does not provide "cookbook" details or techniques.
Criteria for Risk Acceptability?	Not applicable and not included. Requires appropriate risk management input.
Characterisation of Uncertainty in Risk Estimates	Framework emphasises the importance of integrated uncertainty characterisation and specifies uncertainty issues to be addressed. Suggests overall qualitative characterisation of uncertainty (i.e., low, moderate, high).
Other	
Software Details; Hardware Requirements; Associated Costs; Running Time for Risk Model	Not included and not applicable.

8. DISCUSSION AND CONCLUSIONS

General Considerations

This review has examined nine methodological approaches to HRA for air pollutants which might be applicable to the derivation of ambient air quality guideline data for use in the standard-setting process. These have included five *frameworks* (Canadian, WHO, UK, NEHF & Soil NEPM)[41-52], three *modelling approaches* (USEPA, CAPCOA & Ricci/Beer)[3,4,16-33], and only one true *model* (IEUBK)[34-40]. However, these are not exact distinctions, as the categories tend to overlap in some cases. CAPCOA, for example, essentially consists of two separate *models* that form the overall *modelling approach*.

All nine methodologies have limitations, only three have been developed for Australian conditions, and we believe that none are immediately useable in their current form (i.e., "off the shelf") for the development of Australian air quality standards. However, as will be discussed later, several of the existing methodologies are potentially adaptable to the development of ambient air quality standards. The major unresolved issues (apart from methodological suitability for air pollutants) include exposure-response ambiguities in selection of subjective critical endpoints, exposure assessment and dose-response assessment limitations, poor or incomplete treatment of variability and uncertainty, and lack of adequate validation. Moreover, application of default point estimate input parameters, in any form, generally produces results which are not population-specific.

Modelling Considerations and Uncertainty

In this regard, the IEUBK model, which appears to be a reasonable HRA model for lead in children, has been calibrated only for U.S. conditions, and depends on input of detailed, population-specific data on multimedia lead exposures, which are rarely available in most cases. Moreover, the IEUBK model lacks the capability to undertake quantitative uncertainty analysis, a problem common to all of the methodologies reviewed, and one which we believe needs to be resolved if any of the existing methodologies are to be successfully adapted to ambient air quality applications in Australia.

However, this limitation takes on increased importance with models of the IEUBK-type, which are characterised by multiple (multimedia) exposure parameter variables that collectively determine the population dose (& hence risk) distribution. The ability of such models to accurately predict this distribution is directly influenced by the uncertainties inherent in problem specification, model formulation, parameter value estimation, and subsequent risk computation and interpretation activities. There are, however, a number of approaches to uncertainty analysis (and sensitivity analysis) that can be used to analyse parameter variance and its impact on model predictions.

Conceptually, all HRA models can be considered to produce a risk output that is a function of a number of input parameter variables operating over a specified time. Because populations are characterised by significant interindividual variability, and environmental distributions of pollutants are highly variable, then exposure *per se* will be best defined by a range of plausible input values.

Therefore, the usefulness of quantitative uncertainty analysis lies in the ability to determine the variation or range in the risk output, based on the *collective* variation of the input parameters. On the other hand, sensitivity analysis (basically an elementary form of uncertainty analysis), involves examining the effect on the risk output, by making *individual* changes to the value of *single* input parameters. In general, model calculations are of little value without a decent (quantitative) understanding of the associated uncertainty.

On this basis, Monte Carlo simulation analysis using commercially available software[53,54] has been most commonly used to characterise uncertainty and variability in probabilistic HRA applications[8,9,55,56]. This serves to greatly assist in the practical application of HRA results, by providing a more complete risk picture to risk managers, the public and other interested parties. For example, a probabilistic model "add-on" module has recently been successfully developed for the IEUBK model, using Monte Carlo simulation techniques for multiple variable uncertainty analysis[36].

In principle, Monte Carlo techniques should be applicable to any of the methodologies reviewed in the present study. Essentially, what is required is that each exposure input parameter be assigned a distribution that reflects either the interindividual variability in its value (within the target population), or the uncertainty in its value, or some combination of both[8]. The Monte Carlo process then randomly samples from these distributions and performs thousands of simulation iterations, involving repetitive random calculations to provide an output frequency distribution of risk values based on uncertainty.

A rational aim in the derivation of air quality guideline values should therefore be to provide such values in the form of a probability distribution of risk as a function of pollutant concentration, based on Monte Carlo analysis of variability and uncertainty. This would enable the risk manager and the community to see the full risk distribution in a population (against a plausible background of uncertainty), thereby providing a better basis for selection of risk information appropriate for setting standards.

Successful use of Monte Carlo techniques for these purposes depends, of course, on the availability of appropriate input parameter data, in the form of plausible probability distributions for exposure variables[56]. Whilst the available Monte Carlo simulation software is relatively straightforward and simple to use, suitable precautions would still need to be taken to ensure that it is used appropriately[57], and that the input data are suited to Australian conditions. Monte Carlo computer models can, of course, be subject to "black-box" type abuse, in similar ways to any other computer model.

Pollutant Considerations

There are two distinct classes or groups of pollutants that need to be considered in any discussion of the application of HRA methodologies to the setting of ambient air quality standards. These include the *criteria pollutants* and the *air toxics*, some general characteristics of which are outlined on the following page.

- *Criteria or Priority Pollutants:*

    - generally includes a standard suite of inorganic gases and particulate matter (ie CO, NO_2, O_3, SO_2, Pb, PM_{10})
    - largely characterised by *short-term (acute)* health endpoints, as exemplified by hospital admissions, sensory irritation, respiratory symptoms, etc, for which it is often difficult to identify a threshold of response
    - significant interindividual variability exists in subjective health responses (eg irritation, cough, etc.) at any given exposure level
    - health effects data based mainly on *human epidemiological* and clinical studies.

- *Airborne Toxic Substances (Air Toxics):*

    - generally includes a more diverse range of organic and inorganic gases and vapours (eg benzene, 1,3-butadiene, formaldehyde, hydrogen sulphide etc.)
    - largely characterised by long-term (chronic) health endpoints such as cancer, neurotoxicity, chronic lung inflammation, etc., with discrete non-threshold or threshold behaviour, depending on the pollutant in question
    - mainly characterised by clinically objective health responses
    - experimental toxicology studies form a large proportion of the health effects database.

On this basis, it is clear that the *criteria pollutants*, both collectively and individually, represent a special case for HRA, and should therefore be treated separately (and differently) to air toxics. This has been recognised by WHO, for example, in their concerted development of a comprehensive series of concentration-response and dose-response functions for the criteria pollutants, derived exclusively from the available human epidemiological and clinical database. Combined with targeted exposure modelling, these data could be utilised to facilitate the development of a relatively transparent HRA approach for ambient air quality standard-setting, based on the WHO framework for criteria pollutants.

HRA Methodologies for Setting Air Quality Standards

Theoretically, any of the *framework* methodologies reviewed could conceivably be used (ignoring the legal aspects of the Canadian approach) to develop specific modelling approaches and models suitable for ambient air quality applications, depending on professional judgement, and data availability. In practice however, assuming limited resources, the framework selection question boils down to one of convenience of adaptability and overall relevance &/or applicability to ambient air quality.

Of the existing frameworks, we consider that only the WHO and draft NEHF approaches would be versatile enough to be considered suitable in this context. For example, the WHO approach has long been applied to the derivation of ambient air quality guideline levels for a range of air pollutants, and in particular, has been extensively applied to the criteria pollutants. It would be preferable, however, to substitute population-specific data in place of the available defaults for exposure assessment, in order to best utilise this methodology.

We further note that the draft NEHF document is broadly compatible with the overall WHO approach. Moreover, we believe that the draft NEHF approach provides an excellent framework for the potential assessment of air toxics, emphasising as it does the state-of-the-art in dose-response assessment, including benchmark dose methodologies. We consider this to be an improvement over the existing WHO approach to air toxics, which relies on identification of no-effect levels, and use of low-dose risk extrapolation.

The *modelling approaches*, on the other hand, present detailed methodologies that are very different in scope, content and applicability. Of these, the CAPCOA approach is clearly unsuitable for ambient air quality standard-setting, since it has been designed solely for risk-ranking of industrial facilities, on the basis of assessment of localised, upper-bound health risks from point-source emissions of air toxics.

The (US) EPA and Ricci/Beer approaches focus on the criteria pollutants, but appear to have serious problems with methodological complexity and poor process transparency. However, the (US) EPA approach alone takes into account the important indoor as well as ambient exposures, including time spent in the various exposure microenvironments. These factors can have a significant influence on the reliability and population-specificity of the exposure assessment. Moreover, notwithstanding the merits (or the limitations) of the (US) EPA approach, the software that forms the basis of the approach is a hardware resource-hungry proprietary mainframe program, which does not appear to be available to any external organisation, even on a commercial basis. In practice, therefore, the possible adoption of the (US) EPA approach for criteria pollutants does not appear to present a realistic option for Australia at the present time.

In this regard, the practical usefulness of all HRA methodologies reviewed is summarised in Table 8.1, following, on the basis of potential applicability to ambient air quality standard-setting.

Methodological Issues & Practical Limitations

The determination of robust exposure-response functions associated with ambient air pollutants represents a significant challenge for the scientific community, and the use of epidemiological and other human data for this purpose has been the mainstay of current risk-based approaches to standard-setting, particularly for criteria pollutants. In this regard, despite the numerous problems associated with epidemiological studies of air pollutant health effects[11a], the resultant data have been preferentially used by the WHO, the (US) EPA and the NEPC in their respective derivations of ambient air quality guidelines and standards.

For all the methodologies reviewed, given a particular epidemiological (&/or toxicological) data base for the pollutant/s of interest, there is little doubt that exposure assessment is the most critical component of the entire HRA process, and many of the methodological limitations of the various approaches relate to exposure assessment deficiencies. Good exposure data are essential for HRA, and recent developments in probabilistic approaches to exposure assessment provide a valuable set of tools to assist risk assessors and others in properly addressing the inherent variability and uncertainty[57a], thereby providing a more rational basis for setting standards.

Table 8.1
Summary of Practical Usefulness of HRA Methodologies:

HRA METHODOLOGY	PURPOSE OF METHODOLOGY	INTENDED USE & APPLICABILITY	OVERALL TRANSPARENCY	USEFUL FOR SETTING AIR QUALITY STANDARDS?
(US) EPA	HRA modelling approach to meet legislative requirements of Clean Air Act	Determination & review of various risk-based NAAQS for criteria pollutants from mobile sources.	Poor - fair	Yes – for criteria pollutants.
(Cal)EPA/ CAPCOA	HRA modelling approach to meet legislative requirements of Air Toxics "Hot Spots" Act.	Determination of relative health risks of air toxics emissions from point sources, to enable risk-ranking of industrial facilities.	Good	No
IEUBK	HRA model for prediction of potential blood-lead levels in children, due to residential lead exposure from all sources.	Assessment of risk significance of varying blood-lead levels in children up to 7 years of age. Determination of target soil clean-up levels for lead-contaminated residential sites.	Good	No
Health Canada	HRA framework to meet legislative requirements of Canadian Environment Protection Act (CEPA).	Classification of priority chemical substances according to whether they are "CEPA-toxic" or not.	Fair - good	No
WHO	HRA framework for development of health-protective *guidance values* for environmental chemical exposure limits.	Determination of *minimal-risk* guidance values for chemicals in air or water, to provide quantitative information from risk assessment to risk managers, for public health decision making.	Good - excellent	Yes - for criteria pollutants in particular.
UK Expert Panel (per WHO)	HRA framework for development of ambient air quality standards.	Determination of ambient air quality standards based on WHO approach.	Refer WHO	Refer WHO
Ricci & Beer	Trial HRA modelling approach for development of initial draft ambient air quality NEPM.	Assessment of the risk significance of a range of possible air quality standards for criteria pollutants.	Poor	Theoretically possible (?) - for criteria pollutants.
NEHF	Generic HRA framework for overall environmental health risk assessment in Australia.	As a general methodological guidance manual for the conduct of broad-based environmental health risk assessments in the Australian context, encompassing all contaminated media.	Fair - good	Yes - for air toxics; with derivation of an appropriate modelling approach.
Contaminated Sites NEPM	HRA framework for conducting site-specific risk assessments of contaminated land in Australia.	Provides general methodological guidelines for site-specific HRA of contaminated land.	Good	No

Methodological Issues & Practical Limitations (cont)

Population exposure estimates for air pollutants are generally based on the identification and integration of a number of specific microenvironments of exposure where people spend their time, and a 24 hour day is suitably apportioned among the various microenvironments (e.g. indoor, outdoor, & travelling in vehicle).

Since most people generally spend 20% or less of their time outdoors[3,58,59], it appears that indoor air pollution may provide a significant contribution to population exposure in conjunction with ambient (outdoor) air. Given that indoor air quality is generally quite different to ambient air quality[60], it is important to consider all microenvironmental exposure sources in terms of their aggregate contribution to *total exposures*, in order that these may be taken into account in the derivation of ambient air quality guidelines and standards.

In this regard, it may be useful to consider the possibility of undertaking collaborative pilot studies with local health and environmental authorities, in order to develop a quantitative appreciation of the relative magnitude of "indoor" vs. "outdoor" exposures, using an indicator pollutant such as NO_2 or CO, for example. If such correlational pilot studies were undertaken using personal monitoring, valuable information could also be collected with regard to the reliability of regional (fixed-point) air monitoring in estimating population exposures, as discussed in the next paragraph.

The total exposure is estimated by adding together the microenvironmental exposures, which are determined using air quality data derived from fixed-point monitoring stations, exposure modelling, personal monitoring, or a combination of the three. It should be noted that each exposure monitoring method that is further removed from the human breathing zone will yield a correspondingly less reliable estimate of exposure. In this regard, the least representative samples are those derived from fixed monitoring stations, and the most representative samples are those derived from personal (breathing zone) monitoring. Air dispersion modelling is normally used to fill the gap, but this technique has its own pitfalls and limitations, which need to be thoroughly understood before the data can be used for exposure assessment[31].

All of the HRA methodologies reviewed focus on individual risks from single chemical pollutants only, and consider separate health endpoints for each. Considering the diversity of different pollutants present in ambient urban air, populations are usually exposed to complex mixtures of pollutants, rather than individual substances[61]. Where exposure occurs to ambient air mixtures of hundreds or thousands of different pollutants, the presence of one pollutant can affect the impact of another, and there is significant potential for the induction of interactive toxic effects such as pollutant synergism, potentiation or supra-additive effects[62].

Apart from simple additive effects of certain pollutants, the potential for multiple chemical interactions is difficult to assess and incorporate into current HRA modelling[63], but nonetheless needs to be taken into account as a potentially important risk factor[64] . The default assumption that each pollutant can be assessed individually therefore constitutes an additional (significant?) source of uncertainty in HRA.

In addition, most of the HRA methodologies have difficulty in dealing with non-cancer "irritant" effects of air pollutants, where the critical health endpoint is characterised by transient, subjective symptoms such as respiratory irritation, cough, pain on breathing, headache, etc. Because of the significant interindividual variability within populations, it would logically be expected that there would be a relatively wide variation in the responses of individuals for such effects. Thus, no two individuals are likely to react in the same way to any "irritation-producing" pollutant exposure level.

Conversely, no single individual is likely to react in the same way to a given exposure level on any two separate occasions. The presence or absence of a subjective reaction can be influenced by a wide range of additional lifestyle-based and environmental factors, and will very much depend on the previous experiences of the individual. Therefore, it cannot be logically argued that there exists a minimum pollutant exposure level below which subjective effects will not occur. Hence, it is not strictly possible to establish public health protective air quality standards on the basis of prevention of subjective health effects[65].

The final key issue worthy of emphasis is that of methodological ease of understanding and process transparency. The HRA methodologies reviewed have different levels of complexity, based on depth of technical detail, level of approach, documentation style, and extent of (explicit) explanation. The current trend appears to be towards the development of increasingly complex HRA methodologies, in the belief that greater complexity leads to better accuracy and predictive reliability. However, since HRA transparency is inversely proportional to its complexity, more complex methods and models generally become less transparent and more difficult to understand. This does not assist community consultation and generally tends to exclude valuable community input into the risk assessment process. The challenge is to keep methods and models reasonably simple, complete, and open, whilst at the same time maintaining the required scientific and technical robustness.

Conclusions

We do not consider it appropriate to recommend any single HRA approach as being completely suited to the development of ambient air quality standards in Australia. All have advantages, disadvantages and limitations, and we believe that it will not serve the overall interest to make a single, all-encompassing "off the shelf" choice. Rather, we consider that flexibility is the key, and in order to maintain consistency, suitable approaches should, if possible, build on the existing approaches for HRA in Australia. Moreover, in recognition of the need to consider *criteria pollutants* separately from *air toxics*, and in order to facilitate an open and transparent standard-setting process, we believe that serious consideration should be given to the development of two specific, but complementary HRA approaches for ambient air quality. These should include:

- A criteria pollutants modelling approach, based on the WHO methodology, and taking into account the detailed findings of this review.

- An air toxics modelling approach, based on the future NEHF framework, and taking into account the detailed findings of this review.

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APPENDIX 1
CRITERIA FOR REVIEW OF RISK ASSESSMENT METHODOLOGIES
(Incorporating Selected Terms & Definitions)

Model Inputs:
- Exposure assessment:
- What air quality or exposure data are required?
- Are guidelines on data quality included? Comment on their usefulness.
- How are sensitive populations treated?
- Health effect data:
- Does the method specify inclusion criteria for toxicity and/or epidemiological studies and data?
- What is the basis for selection of health endpoints?
- How are the dose-response relationships characterised? What method of extrapolation of the dose-response relationships is used?

Risk Modelling:
- Can the elements of the risk characterisation and inputs required be easily identified? If so, what are they?
- Is the method probabilistic or deterministic?
- What default parameters are used in the model?
- Are safety factors used, and if so, what is the basis for these?
- How is uncertainty treated?
- Does the methodology incorporate sensitivity analysis? In what form?
- Has the modelling been validated? Outline method of validation?
- Has the model received general acceptance within the scientific community and the public (including industry and non-government organisations)? What evidence of acceptance or otherwise is available?
- What pollutants can be assessed?
- What routes of exposure can be included in the model, or is it inhalation-specific?
- How are threshold versus non-threshold pollutants assessed?
- Is the risk modelling transparent? If not, indicate what isn't clear.
- Is the method easy to follow? If so, what are its strengths in this regard?

Model Outputs - Risk Estimates:
- What form does the risk estimate take?
- Are there criteria for risk acceptability built into the methodology? If so, what are they and how were they established?
- Is uncertainty incorporated into the risk estimates? If so, how is it characterised?

Other:
- Details of software, i.e., what language is used, is a full listing of the program available?
- Hardware requirements of the risk model?
- Costs associated with use of the risk model?
- Running time associated with use of the risk model?

SELECTED TERMS & DEFINITIONS

Model: Simplified description of a real system or situation devised to facilitate calculations or predictions. Usually developed in the form of a computerised mathematical program. Models are merely mimics of reality, and generally have significant limitations associated with their application and use.

Validation: 1. The process of assessing whether the predictions or conclusions reached in a HRA are "correct". 2. The process for establishing that a particular HRA model will provide reliable (reproducible) results.

Uncertainty: Imperfect knowledge concerning the present or future state of the system under consideration. Uncertainty is an important component of risk resulting from lack of knowledge about specific factors, parameters or models. This commonly includes uncertainty with respect to both HRA parameter values, and model formulations of risk scenarios. ***Parameter Uncertainty*** includes measurement errors, sampling errors, systematic errors and use of default values; ***Model Uncertainty*** is due to simplification of real-world processes, mis-specification of the model structure, model misuse and use of inappropriate surrogate variables; whilst ***Scenario Uncertainty*** covers descriptive errors, aggregation errors and incomplete analysis. All three types of uncertainty include errors in professional judgement.

Sensitivity: The variation in output of a mathematical model with respect to changes in the values of the model's input parameters. In this context, a sensitivity analysis attempts to provide a ranking of the model's input assumptions with respect to their contribution to model output variability or uncertainty.

Health Endpoint: An adverse effect manifested by a change in morphology, physiology, growth, development or life span of an individual, which results in an impairment of functional capacity, an impairment of the capacity to compensate for additional stress, or an increase in susceptibility to other environmental influences.

Safety Factor: Numerical factor applied to an observed or estimated toxic concentration or dose to arrive at a criterion, guideline or standard that is considered "safe". However, this term implies that application of such a "corrective" factor will ensure absolute safety. This is incorrect, and current practice dictates that the term "safety factor" should be replaced instead by "*uncertainty factor*".

Uncertainty Factor: Numerical factor applied to an observed or estimated toxic concentration or dose to accommodate the fact that the present knowledge of certain parameters may be insufficient to ensure absolute accuracy or precision.

Sensitive Populations: Sub-sets of a general population that, because of age or predisposition, are potentially more sensitive or susceptible to the health effects of pollutant exposure than the rest of the population. Sensitive populations generally include young children, the elderly, and those with pre-existing disease states, including asthmatics.

Deterministic Method: Calculation and expression of health risks as single numerical values or "single point" estimates of risk, where variability and uncertainty are usually only discussed in a qualitative manner. Deterministic results provide only a *partial* risk picture to risk managers.

Probabilistic Method: Calculation and expression of health risks using multiple risk descriptors to provide the likelihood of various risk levels. Probabilistic risk results approximate a full range of possible outcomes and the likelihood of each, which is often presented as a frequency distribution graph. This allows variability and uncertainty to be expressed quantitatively. The important practical distinction is that probabilistic methods have the capacity to provide results that offer a much more *complete* risk picture to risk managers.

Default Value: Pragmatic, fixed or standard (assumed) value for a HRA input parameter, used in the absence of relevant population-specific or site-specific data. Default values are not necessarily representative of any real population group, and may be associated with significant uncertainties in actual use.