GUIDANCE

Guidance for Human Health Risk Assessment

Volume III Human Health, Part B Risk Assessment

Draft Version 2.0
May 2015

LEGAL NOTE

This document aims to assist users in complying with their obligations under the Biocides Regulation. However, users are reminded that the text of the BPR is the only authentic legal reference and that the information in this document does not constitute legal advice. Usage of the information remains under the sole responsibility of the user. The European Chemicals Agency does not accept any liability with regard to the use that may be made of the information contained in this document.

Guidance for Human Health Risk Assessment for Biocidal Active Substances and Biocidal Products

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DOCUMENT HISTORY

Version	Comment	Date
Version 1.0.	First edition	December 2013
Version 1.1	Corrigendum covering the following: (i) Added Annex A, a Commission document on Substances of Concern (ii) Reformatting into ECHA corporate style (iii) Editorial revisions such as punctuation, spelling, etc. (iv) Correcting broken hyperlinks (v) Adding hyperlinks to list of abbreviations and section cross references	April 2015
Version 2.0	Update to Chapter 3 Exposure Assessment	xxx 2015

Comment [SJ1]: ECHA Secretariat will elaborate the text before publication. This update will be published as version 2.0. The

PREFACE

This document describes the BPR obligations and how to fulfil them.

The requirements explained in this Guidance will be updated over time to reflect developments agreed with the European Commission and the Member States. There may be a time lag in the application of the requirements for product authorisation, as explained in the Note for Guidance "Relevance of new guidance becoming available during the process of authorisation and mutual recognition of authorisations of biocidal products" (ref.: CA-July 12-Doc.6.2d-Final): [https://circabc.europa.eu/sd/a/03bce60b-cf04-49aa-8172-e9c6a75205a7/CA-July12-Doc.6.2.d%20-%20Relevance%20of%20new%20guidance.doc]. Applicants are advised to consult the receiving Member State for further details on the requirements specific to their application.

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Comment [SJ2]: TO NOTE:
The ToC will be updated at the end of the consultation procedure.

For this consultation (Chapter 3) please refer to TEMPORARY ToC at the beginning of Chapter 3

1 LIST OF ABBREVIATIONS

Comment [SJ3]: TO NOTE: Reviewed and updated in v1.1 published 29 April 2015.

Please refer to recently published version 1.1 April 2015 for up-to-date list.

Standard term / Abbreviation	Explanation
°C	Degree(s) Celsius (centigrade)
AAS	Atomic absorption spectrometry
ADI	Acceptable daily intake
ADME	Administration distribution metabolism and excretion
ADS	Additional data set
AEC	Acceptable Exposure Concentration
AEL	overall systemic limit value for the human population
AF	Assessment factor
AI	Active ingredient
AOEL	Acceptable Operator Exposure Level
ARfD	Acute Reference Dose
a.s	Active substance
ASTM	American Society for Testing and Materials
BCF	Bioconcentration factor
BPC	Biocidal Products Committee (ECHA body)
BPD	Directive 98/8/EC concerning the placing of biocidal products on the market (Biocidal Products Directive)
BPR	Regulation (EU) No 528/2012 concerning the making available on the market and use of biocidal products (Biocidal Products Regulation)
CA	Competent Authority
CAS	Chemical abstract (Service or System)
CAS registry number	A CAS registry number (Chemical Abstract Service index number) is a unique numerical identifier for chemical compounds, polymers, biological sequences, mixtures and alloys and does not have any chemical significance
Cat	Category
CDS	Core data set
CEFIC	European Chemical Industry Council
CEN	European Committee for Normalisation
CEPE	European Committee for Paints and Inks

Standard term / Abbreviation	Explanation
CIPAC	Collaborative International Pesticides Analytic Council Ltd.
CLP	Regulation (EC) No 1272/2008 on Classification, Labelling and Packaging of substances and mixtures
C&L	Classification and labelling
CO_2	Carbon dioxide
ConsExpo	The software model ConsExpo is a set of coherent, general models that enables the estimation and assessment of exposure to substances from consumer products that are used indoor and their uptake by humans.
CSA	Chemical safety assessment
CSR	Chemical safety report
d	Day(s)
dw	Dry weight
Doc	Document
DAD	Diode array detector
$DegT_{50}$	Period required for 50% degradation (define method of estimation)
$DegT_{50lab}$	Period required for 50% degradation under laboratory conditions (define method of estimation)
$DegT_{90}$	Period required for 90% degradation (define method of estimation)
DG	European Commission Directorate General
DG ENTR	European Commission Directorate-General for Enterprise
DG ENV	European Commission Directorate General for Environment
DG SANCO	European Commission Directorate-General for Health and Consumers
DIN (TTC,INT)	Deutsches Institut für Normung e.V. (German Institute for Standardisation)
$DisT_{50}$	Period required for 50% dissipation (define method of estimation)
$DisT_{90}$	Period required for 90% dissipation (define method of estimation)
$DisT_{90field}$	Period required for 90% dissipation under field conditions (define method of estimation)
DIT	Developmental Immunotoxicity
DMEL	Derived Minimal Effect Level
DNA	Deoxyribonucleic acid
DNEL	Derived No Effect Level
DNT	Developmental Neurotoxicity
DoA	Date of application

Standard term / Abbreviation	Explanation
Doc	Document
DPD	Dangerous Preparations Directive Directive 1999/45/EC concerning the approximation of the laws, regulations and administrative provisions of the Member States relating to the classification, packaging and labelling of dangerous preparations
DSC	Differential Scanning Calorimetry
DSD	Dangerous Substance Directive Directive 67/548/EEC on the approximation of laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances
DTA	Differential Thermo-Analysis
DWD	European Drinking Water Directive Directive 98/83/EC on the quality of water intended for human consumption
EC	European Communities or European Commission
EC_{50}	Median effective concentration
ECB	European Chemicals Bureau
ECD	Electron Capture Detector
ECETOC	European Centre for Ecotoxicology and Toxicology of Chemicals
ECHA	European Chemicals Agency
EC method	Test Method as listed in the Test Methods Regulation
EEC	European Economic Community
EFSA	European Food Safety Agency
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINCS	European List of (new or notified) Chemical Substances
EMA	European Medicines Agency
EN	European norm
EPA (DK)	Environmental Protection Agency of Denmark
EPA (USA)	Environmental Protection Agency of the United States of America
EPPO/OEPP	European and Mediterranean Plant Protection Organization
ESD	Emission Scenario Document, Guidance developed under the BPD tailored for biocides
EU	European Union
EWPM	European Wood Preservation Manufacturers

Standard term / Abbreviation	Explanation
FAO	Food and Agriculture Organization
FCM	Food contact material
FELS	Fish early-life stage
FID	Flame ionisation detector
f_{OC}	Organic carbon factor (compartment depending)
FOCUS	Forum for the Coordination of Pesticide Fate Models and their Use (European pesticide project for risk assessment)
FPD	Flame photometric detector
G	Gram(s)
GC	Gas chromatography
GI(T)	Gastrointestinal (tract)
GLP	Good laboratory practice
GPMT	Guinea Pig Maximisation Test
H	Hour(s)
Ha	Hectare(s)
HLC	Henry's Law Constant
HPLC	High performance (or pressure) liquid chromatography
HPT	Human Patch Test
HRIPT	Human Repeat-Insult Patch Test
IC_{50}	Median immobilisation concentration or median inhibitory concentration 1 (explained by a footnote if necessary)
ICP	Inductively coupled plasma
ICP-MS	Inductively coupled plasma mass spectrometry
ICP-OES	Inductively coupled plasma optical emission spectrometry
IHCP	Institute for Health and Consumer Protection (DG Joint Research Centre)
ILSI	International Life Sciences Institute
ILV	Independent laboratory validation
INDEX number	The INDEX number (format XXX-XXX-XX-X) is a European number attributed to substances listed on Part 3 of Annex VI to CLP Regulation (List of harmonised classifications and labelling).
INT	2-p-iodophenyl-3-p-nitrophenyl-5-phenyltetrazoliumchloride testing method (please refer to DIN)
IOBC	International Organisation for Biological Control of noxious animals and plants

Standard term / Abbreviation	Explanation
IPCS	The WHO International Programme on Chemical Safety
IR	Infrared
ISBN	International standard book number
ISO	International Standards Organisation
ISO (TC, SC, WG)	International Standards Organisation Technical Committee, Scientific Committee, Working Group
ISSN	International standard serial number
ITS	Integrated testing strategy
IUCLID	International Uniform Chemical Information Database
IUPAC	International Union for Pure and Applied Chemistry
JECFA	Joint Expert Committee on Food Additives and Contaminants
JMPR	Joint FAO/WHO Meeting on Pesticide Residues
JRC	Joint Research Centre
k	Kilo- or rate constant for biodegradation
K	Kelvin
Ka	Acid dissociation coefficient
Kb	Base dissociation coefficient
Kd	Desorption coefficient
kg	Kilogram(s)
K_{oc}	Organic carbon adsorption coefficient
K_{ow}	Octanol-water partition coefficient
K_P	Solid-water partitioning coefficient of suspended matter
kPa	Kilopascal(s)
Kst	Dust explosion constant
L	Litre(s)
$L(E)C_{50}$	Lethal concentration, median
LD_{50}	Lethal dose for 50% of the group of tested animals
LEL	Lower explosion limit
LLNA	Murine local lymph node assay
LOAEC	Lowest Observed Adverse Effect Concentration
LOAEL	Lowest Observed Adverse Effect Level
LOC	Limiting oxygen concentration

Standard term / Abbreviation	Explanation
log	Logarithm to the basis 10
LOQ	Limit of quantification
m	Metre
MAC	Maximum admissible concentration
mg	Milligram(s)
MIE	Minimum ignition energy
MIT	Minimum ignition temperature
MITI	Ministry of International Trade and Industry (Japan)
MMAD	Mass median aerodynamic diameter
MOE	Margin of Exposure
Mol	Mole(s)
MOS	Margin of Safety
MOTA	Manual of Technical Agreements of the Biocides Technical Meeting
MRL	Maximum residue limit
MS	Mass spectrometry
MSCA	Member State Competent Authority
MSn	A number of coupled mass spectrometers
MT	Material test
NESIL	Non Expected Sensitisation Induction Level
NGO	Non-Governmental Organisation
nm	Nanometre(s)
NMR	Nuclear magnetic resonance
no.	Number
NOAEC	No observed adverse effect concentration
NOAEL	No observed adverse effect level
NOEC	No observed effect concentration
NOEL	No observed effect level
NPD	Nitrogen phosphorus detector
OECD	Organisation for Economic Cooperation and Development
OEL	Occupational exposure limit
OH	Hydroxide
OPPTS	Office of Prevention, Pesticides, and Toxic Substances (U.S.-EPA)

Standard term / Abbreviation	Explanation
OSHA	European Agency for Safety and Health at Work
Pa	Pascal(s)
Para.	Paragraph
PBPK	Physiologically-based pharmaco(toxico)-kinetics
PEC	Predicted environmental concentration
pH	pH-value, negative decadic logarithm of the hydrogen ion concentration
pKa	Negative decadic logarithm of the acid dissociation constant
pKb	Negative decadic logarithm (to the basis 10) of the base dissociation constant
PNEC	Predicted no effect concentration
PPE	Personal Protective Equipment
PPP	Plant Protection Product
PPPD	Plant Protection Product Directive Directive 91/414/EC concerning the placing of plant protection products on the market
PPPR	Plant Protection Products Regulation, Regulation (EC) No 1107/2009 concerning the placing of plant protection products on the market
PT	Product-type
(Q)SAR	(Quantitative) structure activity relationship
r	Correlation coefficient
RA	Risk Assessment
RAC	Committee for Risk Assessment (ECHA body)
$rate_{a.s.}$	Use rate of active substance [kg /ha]
$rate_{metabolite}$	Application rate at which metabolite should be tested (kg/ha)
RC	Risk Characterisation
REACH	Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH)
rf.	Refer
RIVM	Rijksinstituut voor Volksgezondheid en Milieuhygiëne (Dutch National Institute of Public Health and Environmental Protection)
RMM	Risk Management Measures
RMS	Rapporteur Member State
RSD	Relative standard deviation

Standard term / Abbreviation	Explanation
RT	Respiratory tract
s	Second(s)
SAF	Safety Assessment Factor
S/L	Short-term to long-term ratio
SCAS	Semi-continuous activated sludge (inherent biodegradability tests)
SDS	Safety data sheet
SETAC	Society of Environmental Toxicology and Chemistry
SMEs	Small and medium-sized enterprises
SMILES	Simplified molecular-input line-entry system
STP	Sewage Treatment Plant
TC	Technical material In accordance with FAO manual (FAO, 2010), TC is usually the final product from preparation of the active substance prior to being formulated into an end-use product. This may contain a stabiliser and/or anti-caking or anti-static agents (if required) but no other additives. TC is usually ≥900 g/kg with solvent(s) removed during synthesis, with only residual amounts remaining (usually ≤10%) and no solvent added subsequently.
TMDI	Theoretical Maximum Daily Intake
Test Methods Regulation	Regulation (EC) No 440/2008 laying down test methods pursuant to the REACH Regulation
TK	Technical concentrate In accordance with FAO manual (FAO, 2010), TK may also be the final product from preparation of the active substance but it may contain additives (not formulants) in addition to a stabiliser, for example as safety agents. TK may also contain solvent(s) (including water), either deliberately added to a TC or not removed during preparation.
TG	Technical guideline(s), technical group(s)
TGD	Technical Guidance Document (EU, 2003)
TM	Biocides Technical Meeting, an established subsidiary body responsible for the implementation of the Biocidal Products Directive, together with the European Commission.
TNsG	Technical Notes for Guidance
TTC	2,3,5-Triphenyltetrazoliumchloride testing method (please refer to DIN)
UDS	Unscheduled DNA synthesis
UN	United Nations
UV	Ultraviolet
UVC	Unknown or variable composition, complex reaction products

Standard term / Abbreviation	Explanation
UVCB	Undefined or variable composition, complex reaction products or biological material
v/v	Volume per volume ratio
VDI	Verein Deutscher Ingenieure (The Association of German Engineers)
VIS	Visible
VMP	Veterinary Medicinal Product
w/w	Weight per weight ratio
w/v	Weight per volume ratio
WHO	World Health Organisation
µg	Microgram(s)

1

General Introduction

Comment [SJ4]: **TO NOTE**: This section is **NOT in the scope of this update** and is left in this document for reference ONLY and you are not required to comment.

The risk assessment process, in relation to human health entails a sequence of actions which is outlined below.

(1) Assessment of effects, comprising

(a) hazard identification: identification of the adverse effects which a substance has an inherent capacity to cause; and

(b) hazard characterisation: dose (concentration) - response (effects) assessment: estimation of the relationship between dose, or level of exposure to a substance, and the incidence and severity of an effect, where appropriate.

(2) Exposure assessment: estimation of the concentrations/doses to which human populations (i.e. users of biocidal products, general public) or environmental compartments (aquatic environment, terrestrial environment and air) are or may be exposed.

(3) Risk characterisation: estimation of the incidence and severity of the adverse effects likely to occur in a human population or environmental compartment due to actual or predicted exposure to a substance, and may include "risk estimation", i.e. the quantification of that likelihood. Combined exposure to multiple chemicals and dietary risk assessment should also be considered where relevant.

Risk assessment containing all steps must be carried out for all biocidal active substances.

Possible results of the risk assessment for active biocidal substances:

- Recommendation for the approval of an active substance for use in biocidal products

  (the approval shall, where appropriate, be subject to certain requirements).

- Recommendation for the non-approval of an active substance for use in biocidal products

The risk assessment for human health shall address the following potential toxic effects and human populations, considering each population's exposure by the inhalation, oral and dermal routes:

<u>Effects</u>

- acute toxicity;
- irritation;
- corrosivity;
- sensitisation;
- repeated dose toxicity;
- mutagenicity;
- carcinogenicity;
- toxicity for reproduction.

<u>Human population</u>

- Professional users (and industrial workers);
- Non-professional users (including the general public);
- General Public (humans exposed via secondary pathways).

The human exposure assessment is based on representative monitoring data and/or on model calculations. If appropriate, available information on substances with analogous use and exposure patterns or analogous properties is taken into account. The availability

of representative and reliable monitoring data and/or the amount and detail of the information necessary to derive realistic exposure levels by modelling, in particular at later stages in the life cycle of a substance (e.g. during and after use in mixtures and articles), will also vary. Again, expert judgement is needed.

The risk assessment should be carried out on the basis of all data available, applying the methods described in the following sections of the document. As a general rule for the risk assessment the best and most realistic information available should be given preference.

However, it may often be useful to conduct initially a risk assessment using exposure estimates based on worst-case assumptions. If the outcome of such an assessment is that the substance/biocidal product does not have unacceptable effects (for the population for which the risk assessment is carried out), the risk assessment for that human population can be stopped.

If, in contrast, the outcome is that a substance/biocidal product does have unacceptable effects (for the population for which the risk assessment is carried out) the assessment must, if possible, be refined.

General Principles

In essence, the procedure for the risk assessment for human health of a substance consists of comparing the exposure level(s) to which the population(s) are exposed or are likely to be exposed with the exposure level(s) at which no toxic effects are expected to occur.

Where possible, a risk assessment is conducted by comparing the exposure level, the outcome of the exposure assessment, with the relevant AEL or AEC (Acceptable Exposure Level or Concentration derived on the basis of threshold levels such as N(L)OAEL(C), BMD with the use of assessment factors), the outcome of the hazard characterisation. The exposure levels can be derived based on available monitoring data and/or model calculations. The N(L)OAEL values are determined on the basis of results from animal testing, or on the basis of available human data. For some effects N(L)OAEL and the corresponding AEL values are not usually available. For genotoxic substances it is considered prudent to assume that a threshold exposure level cannot be identified.

Also, for substances which are corrosive or skin/eye irritants, or skin sensitisers N(L)OAEL and the corresponding AEL values are often not available.

The derivation and use of dose-response relationships for each of the effects to be considered are discussed in detail in Chapter 2.

For both the exposure assessment and the effects assessment, data on physico-chemical properties including chemical reactivity may be needed. The data on physico-chemical properties are required, for example, to estimate emissions and the human exposure scenarios, to assess the design of toxicity tests, and may also provide indications about the absorption of the substance for various routes of exposure. The chemical reactivity may also be of importance, for example, in the estimation of the exposure of the substance, and also has an impact on its toxicokinetics and metabolism.

Dependent on the exposure level/AEL or AEC ratio the decision whether a substance presents a risk to human health is taken (if the ratio is above 1, exposure to the substance from the biocidal product is considered to have unacceptable effects and refinement of the assessment is needed). If it is not possible to identify a AEL or AEC, a qualitative evaluation is carried out of the likelihood that an adverse effect may occur.

The comparison of the exposure with the potential effects is done separately for each human population exposed, or likely to be exposed, to the substance, and for the critical effect. It should be noted that, in any particular human population, sub-populations may

be identified (e.g. with different exposure scenarios and/or different susceptibility) which may need to be considered individually during risk characterisation. Thus, exposure levels are derived separately for each relevant population/sub-population, and different AELs or AECs (derived on the basis of threshold levels such as NOAEL, LOAEL, BMD), where appropriate, are identified for the critical endpoints, and respective ratios of exposure level/AEL or AEC values are established.

The risk assessment process depends heavily upon expert judgement in the interpretation of exposure and effects. The risk assessor should focus the assessment on those effects of toxicological relevance to humans which may be expected at the predicted levels of exposure.

Requirements for further information on effects and on exposure are inter-related, and are to a large extent addressed in the toxicity testing strategies in the *Guidance on the BPR: Volume III Human Health, Part A Information Requirements*. However, when all the effects and all the expected human exposure patterns are considered, there may be indications for several tests, possibly using more than one route of exposure. Particularly when early and/or extensive further testing is being considered, it is important to ensure that either high quality and relevant measured exposure levels, or the best possible estimates of human exposure, are obtained so that the decision to test or not to test can be justified. In addition, it should be considered whether toxicokinetic, metabolic or mechanistic data/information, if obtainable, may be useful for defining which tests and which routes of exposure should be used, or such data may be useful in themselves in the assessment of the risks to human health. At any particular stage, integrated requirements for further testing must be developed, using professional judgement, so that the necessary information is obtained using the least amount of testing in animals.

CHAPTER 1

EFFECTS ASSESSMENT

HAZARD IDENTIFICATION

Chapter 2

EFFECTS ASSESSMENT

Hazard Characterisation

(Dose-Response / Concentration Relationship)

Chapter 3

Exposure Assessment

Contents

Comment [SJ5]: TO NOTE: This table of contents is for **REFERENCE ONLY** with this consultation. The ToC will be moved to the front of Vol III at the end of the update process

The ToC for Vol III Part B in full will be updated at the end of the consultation.

1 Introduction

The BPR requires risk assessment of biocidal products before these can be placed on the European Market. The estimation of human exposure is a fundamental element of the risk assessment process and requires quantification of the levels of exposure for both users of the biocidal product and others who may be exposed following its use.

Not all tasks that may be carried out with biocidal products are covered with suitable experimental exposure data or databases/approaches. In such cases suitable information on exposure is required (to be provided by industry to the evaluating CA)to build a risk assessment to indicate appropriate safety for humans during use.

Chapter 3 on Exposure Assessment presents a tiered approach (see section 2.4) for conducting exposure assessment with refinement options to be chosen using higher tier methodologies when needed.

This can be the case when risk is identified for specific exposure scenarios and refinement (as described in Chapter 4 Risk Characterisation), needs to be considered either for hazard or exposure assessment or for both.

This Chapter outlines the principles of exposure assessment and the procedure that needs to be followed for the assessment of exposure from biocidal products. It is applicable for both the review of active substances programme and for product authorisation applications.

For the actual estimation of exposure, additional technical guidance on types of generic models, calculations and default parameters is provided in the document Biocides Human Health Exposure Estimation Methodology available on ECHA website [add link to BPR Biocides WG webpage].

NOTE to the reader:

There are several references in this Chapter to the document Biocides Human Health Exposure Estimation Methodology (see link above) for further detailed information on the methodology and the reader is advised to read this Chapter in conjunction with the document on methodology.

Comment [SJ6]: TO NOTE:
A link will be added to this document/webpage before publication.

The methodology document is under development with the BPC Working Group and is planned for publication at the same time as this Guidance update.

2 General Principles of Exposure Assessment

2.1 INTRODUCTION

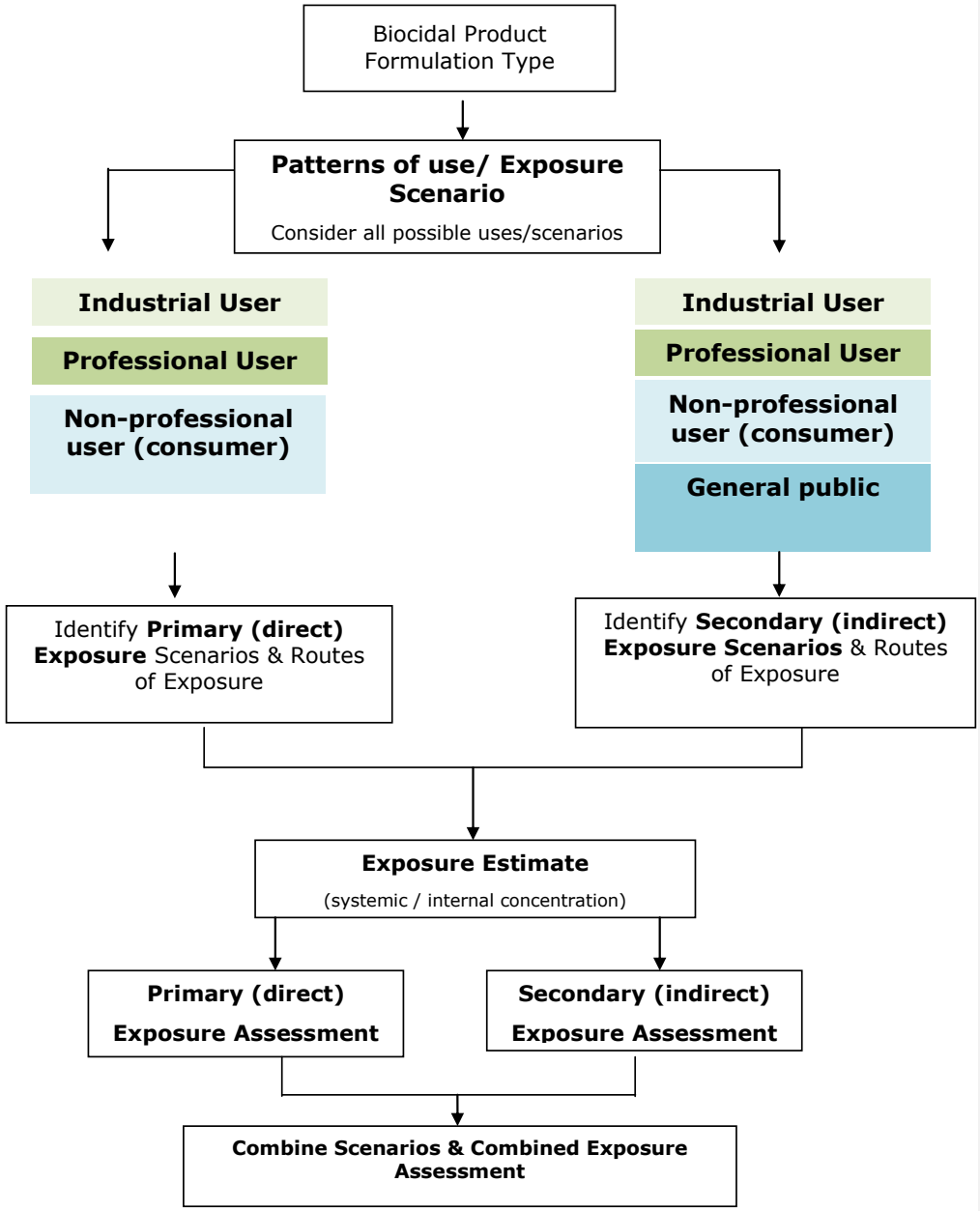
Comment [SJ7]: TO NOTE:
All formatting/style of headings will be updated to the standard ECHA style at the end of the consultation and incorporation of the updated Chapter 3 into Vol III/B.

There is no need to comment on formatting/style of headings

The fundamental concept underlying the approach for human exposure assessment is the need to establish the full range of human exposure situations that could occur from the use of a biocidal product and to consider all routes of exposure. The exposure assessment process therefore requires determination of the:

- Product type / formulation that will be the source of exposure;
- identification of the exposed population (industrial, professional, non-professional, general public);
- identification of exposure scenarios / patterns of use for each population including routes of exposure;
- calculation & quantification of potential chemical intake.

Figure 1 provides the general workflow for the exposure assessment.



Product type/formulation type

Understanding of the source of exposure is the first step in preparing the exposure assessment.

Identification of the product type(s) where the active substance is contained, is needed to enable mapping of the patterns of use with specific product type(s) and/or formulations and the corresponding exposure via different routes of each exposed population.

2.2 PATTERNS OF USE / EXPOSURE SCENARIO (IDENTIFICATION OF THE USES & USERS & EXPOSED POPULATION)

For the purpose of exposure assessment, the different types of potential users (intentional use of a biocidal product) as well as the exposure of individuals via secondary (indirect, unintentional exposure) pathways of exposure need to be considered. As a first step, depending on the product type a list of potential uses and releases enables identification of the populations/individuals that are likely to be exposed directly or indirectly to the biocidal product.

Regarding the potential exposed population from the use of biocidal products, these can be divided into four categories:

- Industrial users;
- Professional users;
- Non-professional users (consumers);
- General public (adults, infants, and children).

The industrial users are in essence a subcategory of the professional users (i.e. professional users performing tasks at industrial settings). For the structure of the guidance, in order to align with the Competent Authority Report (CAR) template, the terms "industrial users" and "professional users" are used to indicate the area where a task is performed (within or outside industrial settings respectively).

2.2.1 Industrial and Professional users

The industrial users (professional users involved in manufacturing, handling and/or packaging of actives or products in industry as well as those using biocidal products in their own processes at industrial settings, for example, manufacturers of timber cladding using wood preservatives or food companies using disinfectants.) or professional users (those using end-products outside industry) are users that come into contact with the biocidal product as a consequence of their professional life. In general the professional user is subject to EU and national worker protection legislation, such as the EU Chemical Agents Directive, (Directive 98/24/EC on the protection of the health and safety of workers from the risks related to chemical agents at work) and has residual risk controlled through control measures and the use of Personal Protective Equipment (PPE). However, some workers will have limited knowledge and skills to handle hazardous biocidal products – particularly if the use of biocidal products is not routinely required in their workplace (e.g. incidental use of slimicides, insecticides, irregular disinfection and use of products containing preservatives). The exposure conditions of these users might be similar to those of non-professional users. There are also trained professional users, who will have expert knowledge and skill in handling hazardous biocidal products and their pattern of use will show greater frequency and/or duration of use (e.g. pest control operators).

2.2.2 Non-professional users (consumers)

The non-professional user is the consumer, i.e. a member of the general public who may primarily be exposed to biocides by using a consumer product. The consumer is unlikely to take informed measures to control exposure and may not follow exactly the instructions for using the biocidal product. In addition, the non-professional pattern of use is expected to show a lower frequency and/or duration of use.

The consumer exposure assessment should normally address the intended uses of the product. However, since consumers may not accurately follow instructions for use of products or articles, a separate assessment of other reasonably foreseeable uses should also be made. For example, consumers will experience relatively high exposures when they use biocidal products in poorly ventilated indoor areas. When use under these circumstances is foreseeable, an exposure assessment for this situation should be carried out.

Another important aspect of consumer practice is the very limited use of PPE to control exposure. Consumers may not normally use PPE unless it is strongly recommended by the manufacturer and/or provided with the product. As a result only typical clothing should be assumed when carrying out consumer exposure assessments.

2.2.3 General Public (adults, infants, children)

The general public are the individuals that are likely to be inadvertently exposed to the biocidal active substance directly or indirectly via the environment and via different routes of exposure without actually using the biocidal product themselves.

The general public would cover both residents (those living in areas treated with biocides when longer exposure is expected) and bystanders (those adjacent to an area treated with a biocide that would be exposed for short periods, thus acute exposure).

The general public covers all adults, infants and children.

2.3 PRIMARY (DIRECT) AND SECONDARY (INDIRECT) EXPOSURE SCENARIOS

2.3.1 Principles

For each of the identified populations that are likely to be exposed to the biocidal product, it needs to be defined what type of exposure is expected. The type of exposure expected for each of the identified exposed populations should be characterised as primary (direct) or secondary (indirect). Primary exposure to biocidal products occurs to the individual who actively uses the biocidal products, i.e. the user. The user may be a professional at work or a non-professional. Professional users differ from non-professional users in a number of aspects and a distinction between the two is necessary in exposure assessments (see Section 3 of this Chapter for further information on primary exposure assessment).

Secondary exposure is exposure that may occur during or after the actual use or application of the biocidal product. For professional users it is useful to make a distinction between *intentional* secondary exposure scenarios and *incidental* secondary exposure scenarios. An intentional secondary exposure scenario is any secondary exposure incurred during a worker's regular employment duties, for example, a carpenter exposed to wood dust impregnated with a biocide. In most instances the professional users' flowchart will provide the most suitable approach for these scenarios. Incidental secondary exposure relates to any exposure not necessarily incurred during employment but resulting from the professional use of a biocide. Home laundering of contaminated work clothes is a typical example of incidental secondary exposure. In most instances these exposure scenarios are best assessed using the methodology for non-professional uses (consumers) as a realistic worst case with refinement options if

needed (see Section 4 of this Chapter for further information on secondary exposure assessment).

It is important to note that the user of a product may be subject to both primary and secondary exposure whereas the "non-user" (i.e the general public) will only experience secondary exposure. Primary exposures are invariably higher than secondary exposures, however, some specific subgroups of the population may experience higher secondary exposures because of their specific behaviour (e.g. children crawling on a treated carpet).

2.3.2 Routes of exposure

For both primary (direct) and secondary (indirect) exposure scenarios, human exposure can occur through any or all of the following exposure routes:

- inhalation route;
- dermal contact (dermal route);
- ingestion (oral route);
- eye contact (occular route).

The second step in the exposure assessment process is therefore to determine the likelihood of the biocides entering the body by the three major routes: being inhaled (inhalation), being absorbed through the skin (dermal), or being swallowed (ingestion). Although not a major route of exposure, the potential for exposure of the eyes will also need to be considered, particularly when handling irritant/corrosive substances. If in this second step it is indicated that exposure via one or more of the pathways does not occur, no further assessment is needed for that route of exposure and the conclusion can be mentioned in the risk assessment phase. Where one or more routes of exposure have been identified then an appropriate exposure assessment is required for each route..

Once all the exposure assessments from all possible routes have been explored, the systemic (internal) dose from these is calculated so that the single internal exposure value is compared with the corresponding AEL for quantitative risk characterisation.

2.3.2.1 Inhalation exposure

Inhalation exposure is often a small component of total exposure to biocides but can in some cases become the predominant route of exposure (e.g. use of a volatile material in an enclosed space). Inhalation exposure is usually derived from the airborne concentration in the breathing zone of the exposed individual. It may refer to the active substance or to the product in use and is expressed as mg/m^3 as a time weighted average concentration over a stipulated period of time. By its nature this concentration represents an assessment of potential exposure. The potential inhalation exposure can be reduced by technical measures such as local exhaust ventilation or by using respiratory protective equipment. The resulting actual exposure takes the effectiveness of these risk mitigation measures into account.Inhalation exposure stops at the end of the work shift when exposure ends.

2.3.2.2 Dermal exposure

Exposure to the skin is usually a significant aspect of human exposure to biocides and can be subdivided into **potential** or **actual dermal** exposure.

- Potential dermal exposure is the amount that deposits on the clothes or gloves and on exposed skin over some defined period of time. The most common metric

measurement for biocides is the amount of biocidal product that deposits per unit time (mg/min)[1] or task (mg/cycle);

- Actual dermal exposure is an estimate of the amount of contamination that actually reaches the skin. It is dependent on the effectiveness of clothing and is often expressed simply as a weight of biocidal product on skin (mg on skin).

  Actual dermal exposure arises through:

  - direct deposition on exposed skin such as the face;
  - permeation through clothing, penetration of clothing around fastenings, openings and along seams;
  - incidentally through contact with surfaces, and when putting on and taking off contaminated clothing (including protective gloves).

For the assessment of dermal exposure (professional and non-professional) it is estimated that the calculated external dose (mg/min x duration of exposure resulting in mg per person) will stay on the skin for the whole shift or even longer, since it is generally not possible to rely on personal cleaning procedures/ washing habits as a reducing factor. This means that for daily exposure, the skin contamination remains for that day, unless thorough cleaning of the skin can be assured.

2.3.2.3 Ingestion exposure

This is the amount entering the mouth other than that which is inhaled. There are no standard methods for quantifying exposure by ingestion but it can be inferred from biological monitoring studies. It is expressed as mg per event or mg/day. It is usually assumed that ingestion exposure in workplaces does not occur when good hygiene is assumed. This may not be true in all cases, especially when there is a regular contact between the contaminated skin and the mouth region. Unfortunately, at present there are no good or established ways to estimate oral exposure to humans, unless with biomonitoring (where oral, dermal and inhalation exposure are integrated).

2.3.2.4 Systemic exposure

The estimates of exposure, via the three major routes outlined above, relate to external exposure, i.e. the amount of the substance ingested, the amount in contact with the skin and the amount inhaled. For risk characterisation purposes, two approaches can be taken.

The first is to calculate the internal (systemic) body burden from these values. This conversion is based on the selection and use of a variety of physiological default values (e.g. body weight and breathing rate) for specific situations. As absorption data for the different routes of exposure are often not available, the calculation of systemic body burdens is subject to a high degree of uncertainty and requires expert judgement.

The second approach is to use route-specific external exposure data and compare that to limit values for each relevant route of uptake. These external values can be calculated from the systemic limit value (e.g. systemic AEL (AcceptableExposure Level)) using relevant absorption data for each route of uptake.

Guidance and default values regarding dermal absorption and physiological factors are given in Chapter 1 on Hazard Identification within the toxicokinetics section of this

[1] For liquids mg/min is often used interchangeably with ul/min for water based formulations with a density close to 1. For liquids more generally, expressing dermal exposure in ul/min and using a weight/volume concentration of active substance, will avoid the need for making a correction for density.

Guidance, as well as in the *Guidance on the BPR, Volume III Human health Part A Information Requirements*. In addition the "Default Human Factor Values for Human Health Exposure Assessment" within the Biocides Human Health Exposure Estimation Methodology should also be consulted.

The most appropriate way of assessing total systemic exposure is by biomonitoring, however, the measured levels of a substance or its metabolites are dependent on numerous factors which can result in inaccuracy/uncertainty of the method. Hence, biomonitoring and interpretation of its results is only reliable if detailed pharmacokinetic information on the substance/compound is available. For an exposure assessment, it is not usual to consider an active substance, but instead to consider a biocidal product containing the active substance. This may be a liquid or a solid andthe concentration may be given in percentage (for a solid) or as w/w or w/v for liquids. Care should be taken to interpret these values appropriately, as shown in the following example:

Example

Say the active substance concentration in the biocidal product is 0.56 % w/v. This means there is 0.56g of active substance in 100 ml of the biocidal product.

If the density of the biocidal product is 0.8g/ml then, 100ml of the biocidal product weighs 0.8 x 100 = 80g of biocidal product.

Consequently, for 0.56g of active substance in 100ml (i.e. in 80g of biocidal product) then in 1g of biocidal product there is 0.56 ÷ 80 = 0.007g of active substance.

Thus, there is 0.007 x 100 = 0.7g of active substance in 100g of biocidal product. This is equivalent to a concentration of 0.7% w/w active substance in the biocidal product.

An important further issue is to consider absorption for each relevant route of exposure. This again is not so much relevant for the active substance, but for the product type containing the active substance.

For inhalation, the absorption is usually taken as 100%, when no further details are known. The same may apply for dermal absorption, although the actual absorption may in practice be much lower and will also depend on the concentration in use; this may vary appreciably between concentrates and in-use dilutions. Further guidance on the use of dermal absorption values is provided within the *Guidance on the BPR, Volume III Human health, Part A Information Requirements* and Chapter 2 on Hazard Assessment within the toxicokinetics section of this Guidance.

2.4 TIERED APPROACH IN HUMAN EXPOSURE ASSESSMENT

It is useful to initially conduct an exposure assessment based on realistic worst case assumptions and to use default values when model calculations are applied. If the outcome of the risk assessment based on worst-case exposure assumptions is that the use of a biocidal product does not present risks (unacceptable effects), the assessment (for that human population) can be stopped and no further refinement of the exposure estimate is required. However, if the outcome is that the use of a biocidal product presents a risk (unacceptable effects), the assessment must, if possible, be refined using additional data and/or reasoned arguments based on expert judgement to allow a more informed decision.

This Tiered approach is a logical stepwise process to risk assessment and uses the available information thus reducing unnecessary requirements for human exposure surveys or studies. The three Tiers described below provide an illustration of how this iterative risk assessment process might progress.

The tiering scheme should be read together with Section on 3.3 of this Chapter regarding refinement options for exposure assessment.

The tiering (from low to higher tiers) can include either options regarding exposure controls (including PPE for professional users) or higher tier methodology (e.g. use of more complex mathematical models and probabilistic approaches versus deterministic ones used in lower tiers) or both.

Tier 1

This is the screening Tier in the risk assessment process and should be kept simple. The assessor should select the top end value from a single exposure study or the recommended indicative value from an empirical (database) model or a worst-case estimate from a mathematical exposure model. Tier 1 estimates should be based on realistic worst-case time budget information (i.e. frequency and duration of use) and must not take account of exposure reduction measures such as LEV or mechanical ventilation, or PPE, unless these measures have already been included in the measured data used for exposure assessment.

If this exposure assessment produces an unacceptable outcome in risk assessment, a refined exposure estimate will be required.

Tier 2

The second Tier in the exposure estimation process is more complex and requires further specific data and/or reasoned arguments to produce a more refined exposure assessment. The exposure studies/models are used in the same way as in Tier 1 but specific data on time budgets, transfer factors and the effects of exposure reduction measures (e.g. technical measures such as LEV or mechanical ventilation, or PPE) may be used to modify the exposure assessment. However, the use of PPE by non-professional users (consumers) should only be considered in very limited situations for example, where gloves are to be supplied with the product,such as antifouling products. The options for exposure reduction measures and appropriate defaults are discussed in Section 3.3 of this Chapter. Information on quantitative assessment of these measures is included in the Biocides Human Health Exposure Estimation Methodology document.

If, after this remodelling the predicted exposure is still unacceptable, then a third iteration of the exposure assessment will be required.

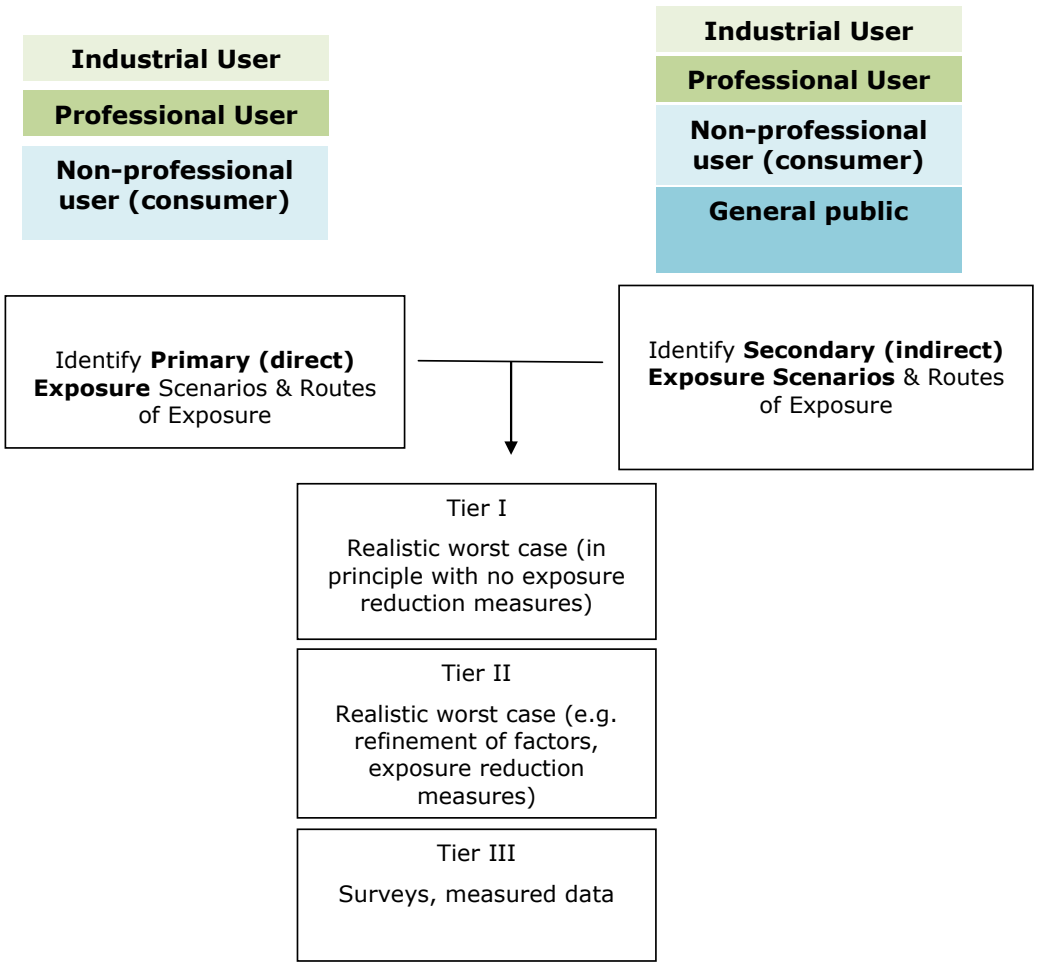
Tier 3

The most detailed level of risk assessment requires surveys or studies with the actual product or with a surrogate. The surveys must be representative, cover all the key tasks within the scenario and provide detailed information on patterns of use.

It should be noted that where biological monitoring is not included in the study, unless the specific scenario of the study is more representative than the generic model, simply generating further potential inhalation and dermal exposure data may not allow refinement of the exposure assessment. Obviously where no generic data, and hence a model are available, then a field study is required. Where field studies are done the OECD guidance on exposure studies[2] should be followed and biomonitoring studies should be carried out in accordance with the Helsinki Declaration (Describing the Ethical Principles for Medical Research Involving Human Subjects).

[2] OCDE/GD(97) 148 (OECD, Paris, France, 1997

Figure 2: Schematic representation of Tiering for exposure assessment



2.5 EXPOSURE ESTIMATION (TYPES OF EXPOSURE DATA / APPROACHES)

Although substance specific measured data (where available) are preferred over modelled data, it could contain considerable uncertainty due to temporal and spatial variations as well as deficiencies in the quality and/or quantity of the available measured data. In such circumstances it may be very useful to compare measured data with modelled exposure estimates. This will require a critical analysis of the results and reasoned arguments to explain the similarities or differences between the two estimates. The ultimate choice of exposure estimates should be made on the basis of the robustness/representativeness of the measured and/or modelled data for the situation/use scenario/conditions under consideration. This will require substantial expert judgement and should always be based on reasoned arguments.

2.5.1 Deterministic and Probabilistic Approaches

When performing estimation of exposure there are two approaches that can be followed. The first one is the deterministic approach which provides an estimate that is based on a single value for each model input and a corresponding individual value for a model output, without quantification of the cumulative probability or, in some cases, plausibility of the estimate with respect to the real-world system being modelled. This term is also used to refer to a model for which the output is uniquely specified based on selected single values for each of its inputs.

Another approach is the probabilistic analysis in which distributions are assigned to represent variability or uncertainty in quantities. The form of the output of a probabilistic analysis is likewise a distribution.

2.5.2 Product specific exposure data

Measured exposure data for the specific product and associated information describing these data may be available from workplace exposure assessments or dedicated monitoring surveys. The data should be accompanied by sufficient information to place the exposures in context with respect to the pattern of use and control. All data will require careful evaluation before use and should have been collected following good occupational hygiene practice, preferably applying standardised procedures particularly with respect to sampling strategy, measurement methods and analytical techniques.

2.5.3 Generic exposure data

Generic exposure data describes measured exposure data obtained from similar operations utilising similar biocidal products. The data are collected from worker exposure studies or, in the case of consumers, from simulation studies using analogous products. These data are used to develop simple (generic) database exposure models for particular product types and specific use scenarios.

Generic exposure modelling is a useful regulatory tool in this scheme, because of its ability to predict the likely levels of occupational exposure of users of biocides and to estimate the effect of changes in conditions of use on exposure. Where representative generic data and a suitable model exist, modelling is the initial, and often the only, basis for the exposure assessment. Generic exposure models may also be used instead of, or as well as, exposure data for the specific product if there is significant uncertainty associated with the quality and/or quantity of these data.

Generic exposure data can also be used to develop more complex computer based data models.

2.5.4 Mathematical models

In the absence of product specific and/or generic exposure data for a particular biocidal use/scenario Competent Authorities and Approval Holders should make use of the available mathematical exposure models for assessing human exposure to biocidal products. As in the case of generic exposure models, mathematical exposure models may also be used instead of, or as well as, exposure data for the specific product and generic models if there is significant uncertainty associated with the exposure estimates derived from the first two approaches.

Mathematical models are calculation routines that are based on the physico-chemical properties of a substance and the environment into which these substances are released. Although the basis for the calculation algorithm is scientific these models can be gross approximations of the real world as the full range of real variables cannot be accounted for and are therefore assigned very conservative defaults. However, although mathematical models are usually meant to be conservative, this does not hold true for all models or assessed scenarios. For some models and some scenarios, model outcomes

may also underestimate exposure substantially. In general, few of the models have been validated against real situations.

Generally, exposure models fall into one of three types:

1) mathematical mechanistic models: predict exposure levels from a mechanistic description of a process;
2) empirical/knowledge-based models: predict exposure levels based on an empirical database;
3) statistical mathematical models: predict exposure levels based on statistical relations.

Some of these types of models are further described within the Biocides Human Health Exposure Estimation Methodology document.

The use of exposure models requires the selection of various input parameters. Insufficiently detailed information on exposure scenarios or lack of sufficient data may require the use of default values. Input data or default values used for the calculations must be clearly documented. Computer programs have been developed to implement mathematical predictive models and empirical models. Statistical models have been developed using available data and appropriate statistical methods. Model choice should be justified by showing that the model uses the appropriate exposure scenario (e.g. as judged from the underlying assumptions of the model). Expert judgement may be required to check the realism of the exposure value derived from a model, particularly if default or realistic worst case values have been used. Modelling of exposure can be performed either by taking discrete values (point estimate) or distributions for the model variables (probabilistic modelling).

Mathematical Mechanistic Models

Commonly, mathematical models are based on mass balance equations. Mathematical mechanistic models are often used for assessing inhalative exposure to volatile compounds.

These can incorporate the physical and chemical properties of the substance, together with patterns of use. They are used to characterise the rate of release of the product into a space, and its subsequent behaviour. Mathematical models should cover all relevant processes or tasks contributing to exposure in a scenario. For many tasks, a number of models could be appropriate. The underlying assumptions for each model, and the processes it represents, help the assessor in model selection. More than one model can be run, to assure consistency. The advantages of mechanistic models are:

- the mechanisms and main processes are clearly stated;
- their inputs and outputs are clearly stated;
- they are well documented and can be validated;
- they can be improved using real life data.

However, if the underlying assumptions do not apply to the task, they can be poor approximations of the real world. Importantly:

- they make a number of simplifying assumptions, for example, instantaneous complete mixing of the substance in air;
- they account only for the main variables that affect exposure;
- care must be taken not to rely completely on point prediction.

Empirical Models

Empirical models are probably best described as models based on exposure measurements obtained from real situations. This type of model can be used to predict the likely exposure in other comparable situations, i.e. the informed use of generic data. If sufficient and high quality data are used in empirical models they are likely to account for the many variables that influence exposure.

The main advantage of empirical models is their amalgamation of multiple studies into a large data set, which reflects the distribution of results better than a small exposure study. The disadvantages include:

- uncertainties about the quality of the information fed into the model;
- uncertainties about input default settings;
- important factors that influenced the recorded exposure level may become hidden;
- the output from the model may be misapplied or misinterpreted;
- outputs may be imprecise, which can lead to skepticism over the answer.

Statistical Mathematical Models

Statistical models have not yet been used for EU exposure estimations. Such models use empirical relationships to predict exposures from statistical indicative distributions together with historical data. In principle, they reflect a combination of empirical and mechanistic models together with consideration of the distribution of the input parameters. One of the most important steps in the procedure is represented by the implementation of the probabilistic approach, which allows the use of distributions in the calculation.

Probabilistic techniques use distributions instead of point values for variables in model estimations. Distributions reflect the variability and the uncertainty of a variable. From this point of view it enables the assessor to introduce an additional approach to describe data quality. Probabilistic analysis may reveal the factors that really drive the exposure. It may also help to differentiate sub-populations with respect to exposure, and thus to identify groups of people at risk. Knowledge of the range and distribution of exposures allows the assessor to select from appropriate points in the distribution to inform the decision making process and to perform an appropriate sensitivity analysis.

Many exposure data are needed to establish a distribution and allow application of statistical methods. Probabilistic analysis therefore requires input data of sufficient number and quality. Otherwise, misinterpretations of the probability distribution that represents the variables, for example, underestimating the variance, can seriously hinder and prevent the interpretation of the outcome. In cases where the assessor has little data of low quality, a realistic worst case estimate of exposure in combination with expert judgment is preferable.

In summary, probabilistic assessments integrate distributions of exposure factors to produce an estimate of exposure. They increase insight in the uncertainty of the assessment (via uncertainty analysis) and the contribution of each exposure factor in the end result (via sensitivity analysis). If data quality are adequate, a probabilistic analysis is advocated, at least to underpin a deterministic presentation of the results.

2.5.5 Reverse reference scenarios

In the absence of suitable product specific data or generic exposure data or suitable mathematical model the reverse reference scenario can be used to determine the upper acceptable exposure level.

The reverse reference scenario can be used to determine an estimate of the maximum amount of exposure that might be acceptable and its likelihood of occurrence as a realistic worst case. Using the relevant No Observed Adverse Effect Level (NOAEL), it is possible to compute the amount of product that would lead to that dose by a specific route. That amount can be related to the amount of exposure that is realistically likely, as determined from experimental or other data. An example on how to use the reverse reference scenario is provided in Appendix 3 of this Chapter.

2.5.6 Suitability of exposure data sources

Any data source that describes relevant exposures can be used in the exposure assessment, when the detailed descriptions of the circumstances (contextual information) of the data source is available. The main criterion is the similarity in the tasks being considered. Good data are thus representative and robust, i.e. covering a reasonable large sample for the full range of circumstances. One might have a suitable exposure model or database with measurements at hand that cover similar scenarios. One might even have a series of measurements for the scenario to be assessed. The combination of all this information should really be done at expert level, covering all relevant parameters and circumstances, i.e. contextual information.

Another important issue is the combination of tasks, since human exposures are distributions, not single values. But single values must be drawn from the distributions in order to estimate exposures where no directly relevant data exist.

Distributions of human exposure data are commonly accepted as being approximately log-normal.

Exposure estimates for a single procedure can be reasonably estimated by a percentile from the data distribution. However, if the procedure is done several times, simple addition of percentile values can show gross deviations in the final estimate, especially with high or low percentiles.

This argument applies to:

- summing the data for several daily treatment cycles;
- summing the data for the inhalation and dermal exposure routes;
- adding the phase of use estimates;
- combining primary and secondary exposure;
- aggregate exposure from all sources of the particular chemical.

Example

Exposure in applying a product has a data set with a geometric mean of 20 units and a geometric standard deviation at 2.5. For a single application, the data distribution shows the following percentiles:

50^{th} 20
75^{th} 37
95^{th} 82

For four applications, simple multiplication gives:

50^{th} 80
75^{th} 148
95^{th} 328

But the percentiles for the distribution, properly combined, are:

50^{th} 103 (the simple multiplication gives 20 % under-estimate)
75^{th} 147
95^{th} 241 (the simple multiplication gives 30 % over-estimate).

Simple addition of percentiles for the routes, phases and cycles of exposure, exposure times or amounts used, and cumulative exposures, has the clear potential to provide an unacceptable estimate of exposure. The assessor needs to take great care to avoid gross errors in combining exposure.

An alternative to extracting values from data distributions is to use the entire data distribution in a probabilistic assessment. This is of particular importance for estimating combined exposure. The probabilistic estimation technique is currently not fully integrated in the risk assessment process (for more details see Ann. Occup. Hyg. 45 Suppl. 1, 2001).

3 Primary (Direct) Exposure Assessment for Industrial & Professional Users & Non Professional Users

In this section, a summary of the main components from the pattern of use that are needed in the different types of exposure scenarios is presented.

The essentials of exposure assessment for primary (direct) exposure for industrial/professional and non-professional users are:

- Product composition & physicochemical properties (physical state, concentration, vapour pressure of the active substance);
- Type of user: By whom the product will be used (for primary exposure);
- Duration and frequency of use (for each stage of use) (see Section 3.1 of this Chapter);
- Method of application / task: where and how the product will be used (see Section 3.2 of this Chapter);
- Expected exposure controls (see Section 3.3.1 of this Chapter);
- Refinement of exposure assessment if risk not acceptable (see Section 3.3 of this Chapter).

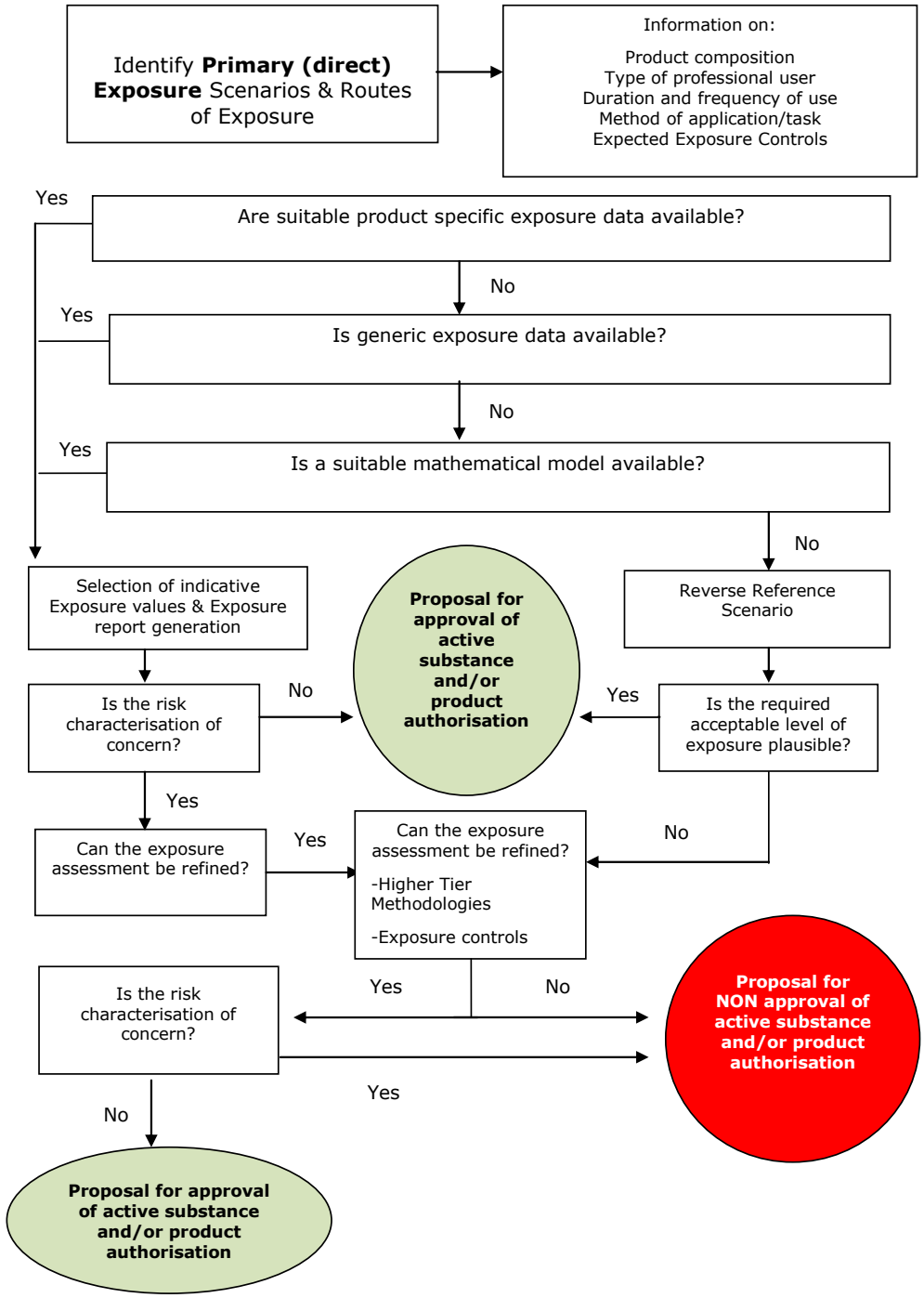
In Figure 3 a flow chart on how to perform in a stepwise approach primary (direct) exposure assessment for industrial/professional and non-professional users respectively is shown. Additional information on the methodology that applies in the Figure is available within the Biocides Human Health Exposure Methodology Document.

Depending on the data/information available at the time of the assessment, it maybe that suitable product specific exposure data are available.

In the absence of product specific data, the next choice would be the use of default parameters (generic exposure data) or specific models available for the exposure scenario under consideration.

When the exposure assessment estimate is compared to the corresponding hazard threshold, if no risk is identified no further refinement is needed. However if risk is identified, refinement of exposure should be performed. This can be done taken into account refinement of parameters (defaults) used in the exposure assessment (with appropriate justification), application of exposure control measures (for industrial/professional users this can also include PPE but this cannot be the case for non-professional users), generation of product specific data (e.g. measured data), or uncertainty assessment of the various steps of the exposure assessment performed.

Figure 3: Flow chart for primary (direct) exposure scenario/assessment **for industrial ,professional users, and non-professional users**



Information on the pattern of use can be gathered through surveys or generic data from similar products. Specific information on patterns of use for many biocidal product types is limited and those placing biocidal products on the market will need to conduct research into patterns of use directly with the users if actual or surrogate data are not available.

In the following overview table, the most relevant data requirements for primary (direct) exposure assessment are listed:

Table 1: Overview of requirements for primary (direct) exposure assessment

Data requirement	Priority	Comment
Product		
- physical properties	Essential	liquid / solid / in-situ generation / particle size, aerosol, volatility
- package details	Essential	volume, material, closure, bulk delivery.
- formulation details	Essential	active substance and co-formulants
- site inventory	Desirable	amount, delivery frequency
- storage information	Desirable	
Purpose of product		
- where used	Essential	location / system treated
- description of tasks	Essential	how used, application rates
- equipment used	Essential	pressures, volumes
Use environment		
- containment	Essential	barriers to exposure, ventilation
- pattern of control	Essential	full containment, LEV, segregation, dilution ventilation
- use pattern	Essential	closed system, within a matrix, non-dispersive, wide dispersive
Mixing and loading phase		
- task	Essential	Description
- frequency per task	Essential	events per day
- duration of task	Essential	event duration
- quantity used per task	Desirable	
- dilution rate	Essential	
Application phase		
- task	Essential	description, continuous / intermittent / event
- frequency per task	Essential	events per day
- duration of task	Essential	event duration
- quantity used	Essential	not always relevant
- area / volume treated	Essential	not always relevant
- timing	Desirable	seasonality etc.
Post-application phase		
- task	Essential	description, continuous / intermittent / event
- frequency per task	Essential	events per day
- duration of task	Essential	event duration
Disposal		
- task description	Desirable	e.g. strip old coatings, collect dead vermin

Comment [SJ8]: TO NOTE:
The table number (and all references to it) will be updated at the end of the consultation and incorporation of the updated Chapter 3 into Vol III/B.

Additionally it will be formatted in the ECHA style.

Data requirement	Priority	Comment
Primary exposure		
User sector	Essential	
- mode of exposure	Essential	inhaled / via skin / ingested, by task
- proximity to exposure source	Desirable	hand / arm's length / more distant
- operators per task	Desirable	
Data may be better expressed as ranges and likely values, rather than as single values.		

3.1 DURATION AND FREQUENCY OF USE (FOR EACH STAGE OF USE)

The frequency and duration of a task are major determinants influencing the level of exposure. The frequency of a task is variable and is critical in deciding whether the exposure is chronic or acute for risk characterisation purposes. Frequency of exposure should be expressed as events per day (with precision as to how many days per year the user of biocides is exposed).

Duration of exposure (duration intervals) should be expressed as minutes or hours per day.

When determining the pattern of use, by default a harmonised approach is followed. There are however cases where variability in pattern of use (e.g. different user groups; professional user versus non-professional user/consumer), across the EU may be based such as:

- regional differences;
- climatic differences.

Competent Authorities will need to ensure the relevance of a stated pattern of use, especially in product authorization and appropriate justification should be provided if it is not in line with the harmonized approach (see the Biocides Human Health Exposure Methodology Document for further information).

3.2 METHOD OF APPLICATION / TASK: WHERE AND HOW THE PRODUCT WILL BE USED

Primary exposure is experienced by industrial users, professionals and non-professionals (consumers) who use and apply a biocidal product. It is related to the task and the overall exposure scenario will consist of a series of tasks that can be allocated to three distinct phases of use:

1. Mixing & loading — Includes the tasks involved in delivery and handling of bulk ready-for-use and concentrate products, dilution of concentrates and/or the introduction of product to the application apparatus/system.
2. Application — Involves all uses of biocidal products, including application by hand, by hand-held tools, by dipping, by spraying, handling treated articles, and in machining. This phase of use can lead to the exposure of people who are present during the product application (secondary exposure).
3. Post-application — Includes exposure through separately cleaning and maintaining process equipment and tools. Secondary exposure is also included in the post-application phase.

The contribution to each route of exposure may vary considerably between these phases with any given biocidal product and method of application, given that mixing and loading can reflect exposure to a concentrate, application to a dilute product, post-application to vapour or dried residue and removal to waste material (e.g. removing and disposing of a preserved coating). In practice, exposure data often relate to full-shift sampling and therefore includes all three phases of use. However, it is important to ensure that each phase of use has been accounted for in the exposure assessment.

3.3 REFINEMENT OF EXPOSURE ESTIMATES

3.3.1 Exposure Controls

This Section introduces concepts of how to control exposure to biocides.

When undertaking an exposure assessment the assessor should seek to ensure that exposure to a biocide is prevented or controlled. Exposure can be prevented by a variety of means, including:

- Elimination;
- Substitution;
- Modification of a process or substance to reduce emission or release.

For biocides, with the myriad of application methods available, preventing exposure is not, in many cases, reasonably practicable. Exposure must therefore be controlled.

3.3.1.1 Control options

There are control options that evaluators can invoke, to abate exposure. In order of priority according to Dir. 98/24/EC, art.6, para.2, the options to consider are:

- structure related;
- engineering;
- technical (especially for consumers);
- administrative;
- personal.

Structure related control of exposure (applies to both residential environments and workplaces)

Structure related control means the reduction of exposure by inhalation afforded by general ventilation, for example, opening windows. Structure related control of exposure can also be achieved by spatial separation of the exposure source and the worker, for example, by installing control elements for a vacuum impregnation chamber in a seperate room. This can reduce inhalative as well as dermal exposure.

Engineering control of exposure (applies to workplaces only)

Engineering control in the professional setting means the abatement of exposure by local exhaust ventilation (LEV) at the point of emission, or by containment in pipework or other systems from which minor emissions only are anticipated.

Technical measures for control (for consumers)

Bait boxes and child-resistant fastenings are good examples of technical measures to reduce possible exposure.

Administrative control of exposure (applies to both residential environments and workplaces, but in different ways)

Residential administrative control means the exclusion of residents from treated spaces until aerosols have dispersed and surfaces are dry. All subsequent exposure is secondary.

Workplace administrative control has several levels to consider:

- proper supervision and training of workers;
- procedural plans, event planning (such as accidental spill procedures) and permits to work.

'Safe systems of work', 'emergency procedures' and 'permits to work' mean that hazardous biocides can be used with minimum risk. For example, the risk is likely to be high in operations such as maintenance and a 'permit to work' is needed. The permit sets out the steps to assure that situations are made safe before work starts, remains safe, and includes standby rescue and recommissioning procedures.

Personal control of exposure (applies to both residential environments and workplaces, but in different ways)

The personal approach refers to the use of PPE, which can be defined as 'all equipment which is intended to be worn or held by a person and which protects them against one or more risks to their health or safety'. The user, taking specific steps to limit inhalation and skin exposure, uses PPE as a means of reducing primary exposure. PPE is relevant to primary exposure only. The impact of the use of PPE as part of the exposure assessment is complicated and needs to address:

- proper functioning, i.e. designed and tested to result in reproducible, quantifiable reduction of exposure;
- proper use, i.e. wearers use PPE according to guidelines to ensure adequate protection under conditions of use.

Industrial workers, Professional workers and workplaces

Workers are covered by additional regulatory control mechanisms and as a consequence are more likely to use PPE if it is required. In many cases PPE has to be supplied and used at work wherever there are risks to health and safety that cannot be adequately controlled in other ways.

Non-professionals and the residential environment

While non-professional users may wear overalls, gardening or kitchen gloves, or even a dust mask, such usage cannot be assured and must not be assumed in exposure estimation. For example, non-professional users applying antifoulants to leisure craft in warm weather, would most likely be wearing sandals and shorts rather than long trousers and boots or the recommended protective clothing.In general, at besta user may wear a long sleeved shirt, long trousers and footwear, irrespective of any label stipulation. For inhalation exposure, no exposure reduction should be assumed

3.3.1.2 Use and Selection of Appropriate PPE

There are two points to acknowledge when considering the implications of using PPE in the field of biocides. These are:

- what default values for the protection offered by PPE, should be used when undertaking an exposure assessment (this requires proper functioning) ?
- what impact does the recommendation to use PPE have on the operator (this requires proper use) ?

It is also important to remember that we are primarily concerned with the user of the biocide, however for the use of PPE to be successful both employer and employee need to take an active part in the selection and use of PPE.

Default values for the use of PPE are available in the Biocides Human Health Exposure Estimation Methodology Document.

Specific requirements to consider when recommending use of PPE

There are eight key issues to consider when considering PPE as ; this selection will, briefly, address these issues. This Section should also be read in conjunction with the section on the principles of good control practice in Appendix 1 of this Chapter.

1. Provision of suitable PPE.

It must be remembered that PPE should always be regarded as the `last option' to protect against exposure to biocides. The provision of appropriate engineering controls and safe systems of work should always be considered first and this should be the basis of the users risk assessment. However, where there are no reasonably practicable other means of adequately controlling the risks, as will often be the case for the application of a biocide, then PPE will still be needed. The PPE which is provided should be appropriate for the risks involved and take into account ergonomic requirements (i.e. the nature of the job and the demands it places on the user), and the state of health of the person who may wear it.It must fit the wearer correctly and be effective to prevent or adequately control the risk.

2. Ensuring that where more than one item of PPE has to be worn to control risks, then the PPE is compatible and is effective against the risks.

Where the presence of more than one health and safety risk makes it necessary for a user to wear or simultaneously use more than one item of PPE, then the PPE must be compatible and continue to be effective against the risks, for example, certain types of respirators may not fit properly and give adequate protection if a safety helmet is worn.

3. Assessment of PPE to determine whether it is suitable.

Where PPE has to be provided to adequately control the risks, then an assessment has to be made to determine what PPE is suitable before it is chosen. This will ensure that the PPE is correct for the particular risks involved and for the circumstances of its use. The assessment should assess the risks to health which have not been avoided or sufficiently reduced by other means and should also define the characteristics the PPE must have in order to be effective against the assessed risks. It should then compare the characteristics of the PPE available against the defined effective characteristics needed. The person making the assessment of PPE should always seek the help from the manufacturer of the PPE and/or the manufacturer of the biocidal product when selecting PPE.

4. The maintenance and replacement of PPE.

Any PPE provided to users must be maintained in an effective and efficient condition and be in working order and in good repair. To ensure the equipment continues to provide the degree of protection for which it is designed, an effective maintenance system is essential and should include, cleaning, disinfection, examination, replacement, repair and testing as appropriate. The details of the maintenance procedures to be followed and their frequency should normally follow manufacturers' maintenance schedules and should be documented together with details of the person who has the responsibilities for carrying out the maintenance. Where appropriate, records of tests and examinations should also be kept;this may depend on the type of PPE, for example, gloves may only require periodic inspection by the user. Generally speaking, PPE should be examined to ensure it is in good working order before it is issued to the wearer and also be examined before it is put on and should not be worn if it is found to be defective or has not been cleaned. A sufficient stock of proper spare parts, where appropriate, should be available to wearers.

5. Provision of appropriate accommodation for PPE when it is not being used.

Where PPE is required, then appropriate accommodation when it is not being used has to be provided. Storage of PPE should be adequate to protect it from contamination, loss or damage by harmful substances, damp or sunlight. If it is likely that the PPE will become contaminated during use, then the accommodation should be separate from any provided for ordinary clothing. The accommodation required will obviously depend on the equipment and, in some cases, need not be complex or fixed, for example, pegs would be suitable for weatherproof clothing and safety spectacles could be kept by the user in a suitable carrying case.

6. Provision of adequate and appropriate information, instruction and training.

Employees have to be provided with adequate and comprehensible information, instruction and training in order that they know the risks which the PPE will avoid or limit, the purpose and manner in which the PPE is to be used and any action the employee has to take to ensure it remains in an efficient state, in efficient working order and in good repair. Everyone who is involved in the use or maintenance of PPE should be appropriately trained. A systematic approach to training, including the elements of theory as well as practice, in accordance with the recommendations and instructions supplied by the manufacturer, is required in order that: users are trained in its correct use; users know how to correctly fit and wear it and know its limitations; managers and supervisors are aware of why PPE is being used and how it is used properly, and training is given to those people who are involved in its maintenance, repair, testing and selection for use.

The instruction and training provided will obviously depend on the complexity and performance of the PPE but should typically include:

- An explanation of the risks present and why PPE is needed;
- The operation, performance and limitations of the equipment;
- List instructions on the selection, use and storage of PPE related to the intended use. Written operating procedures such as Permits to Work involving PPE should be explained;
- Factors which can affect the protection provided by the PPE, e.g. other PPE, personal factors, working conditions, inadequate fitting, defects, damage and wear;
- Recognition of PPE defects and arrangements for reporting loss or defects;
- Practice in putting on, wearing and removing the equipment;
- Practice and instruction in inspection and, where appropriate, testing of the PPE before use;
- Practice and instruction in the maintenance, which can be done by the user, such as cleaning and the replacement of certain components; and
- Instruction in the safe storage of equipment.

7. Ensuring that PPE provided to employees is properly used.

Employers have a duty to take all reasonable steps to ensure that any PPE equipment provided to users is correctly used and adequate levels of supervision should therefore be provided to ensure that the training and instructions are being followed. Users have a duty to ensure they use the PPE in accordance with any training and instructions they have received and to take all reasonable steps to ensure that the PPE is returned to the accommodation provided for it after use.

8. Duties on employees provided with PPE to report any loss or obvious defects to his employer.

All employees who have been provided with PPE have a duty to report immediately any loss or obvious defect to their employer. Arrangements should therefore be made to ensure that employees can report the loss of, or defects in, PPE and these arrangements should also ensure that defective PPE is replaced or repaired before the employee concerned re-starts work.

Protective gloves

Protective gloves are available in a wide range of materials; however, there is no single glove material (or combination of glove materials) able to provide unlimited resistance to any user or against any chemical substance or combination of chemical substances. There are three ways in which any protective glove will, at some stage, fail to protect the wearer from exposure to any chemical substance and these are:

- permeation – the process by which a chemical substance migrates through the protective glove at a molecular level;
- penetration – the bulk flow of a chemical substance through closures, porous materials, seams and pinholes or other imperfections in the protective glove;
- degradation – a damaging change in one or more physical properties of the protective glove as a result of exposure to a chemical substance.

Selecting suitable protective gloves

The selection of suitable protective gloves is a complicated procedure and the degree of protection they give is not always easy to establish. When choosing gloves, always seek expert help from the manufacturer/distributor of the chemical substance and protective glove. They can provide glove performance test data, which can be used to assist in predicting the permeation, penetration and degradation of specific glove materials by specific chemical substances.

There are four requirements which must be met for any protective glove to be considered suitable. The glove must:

- be appropriate for the risk(s) and the conditions where it is used;
- take into account the ergonomic requirements and state of health of the person wearing it;
- fit the wearer correctly, if necessary, after adjustments;
- either prevent or control the risk involved without increasing the overall risk.

Chemical protective gloves are Cat. III PPE in accordance with the PPE Directive (Directive 89/686/EEC the approximation of the laws of the Member States relating to personal protective equipment) and should be labeled with the Erlenmeyer flask symbol.

Selection should therefore take into consideration the wearer, the workplace conditions and the protective glove itself. Employees need to be trained in the correct way to put on, wear and then take off protective gloves to ensure maximum protection. If protective gloves are selected or worn incorrectly there is every possibility that this may increase the wearer's overall risk to health because:

- contaminant may get inside the glove to reside permanently against the skin, which could cause greater exposure than if a glove had not been worn at all;
- wearing a glove for extended periods can lead to the development of excessive moisture (e.g. sweat) on the skin, which in itself will act as a skin irritant;
- wearing gloves manufactured in natural rubber (latex) can cause an allergic reaction in susceptible individuals, causing the skin disease contact urticaria to occur.

Selecting protective gloves must be part of an overall health and safety risk assessment for the relevant tasks. The risk assessment must clearly demonstrate that exposure to the health risk is unavoidable and that other methods of control are not reasonably practicable. Gloves should be used as a control measure as a last optionwhere other methods of control are not reasonably practicable. This is because:

- gloves only protect the wearer – they do not remove the biocide from the workplace environment;
- some types of glove are inconvenient and interfere with the way people work;
- wearing gloves interferes with the wearer's sense of touch;
- the extent of protection depends upon good fit and attention to detail;
- if protective gloves are used incorrectly, or badly maintained, the wearer may receive no protection;
- for glove design to be effective, the glove needs to be used correctly in the workplace.

Glove selection is a complex issue and the importance of using a material which provides suitable and sufficient protection, depends on the nature of the chemical and extent of exposure. Where there is a choice of glove material, the extent of exposure to the chemical substance will be a significant factor in choosing between, for example, a neoprene glove or a less costly glove: if workers' gloves are significantly contaminated for extended periods, the neoprene glove may be required; if however, there is only occasional splashing of the chemical substance onto the glove, then the less costly glove may be adequate. Other factors to consider are the manual dexterity required for the job and the required physical length of the glove, for example are gauntlet gloves required?. If workers cannot do their job because the glove material is too thick or too stiff then they may decide not to wear them.

Always remember that if the inner surface of a glove becomes contaminated, it will not matter how much care, attention and expertise has gone into the selection process of the protective gloves, exposure will occur. If, for example, contaminated gloves are removed temporarily, then the operators' hands may become contaminated from handling the gloves;if the same pair of gloves is then put back on, there could be transfer of the chemical substance to the inside surface of the glove. To prevent this, the gloves should be thoroughly washed before being taking off.

Detailed information on the selection of chemical protective gloves can be found in the BG Information BGI/GUV-I 868 E "Chemical protective gloves" (DGUV, 2009). This document is available in English language on the homepage of the DGUV: [http://publikationen.dguv.de/dguv/pdf/10002/i-868-e.pdf]

Selecting suitable Respiratory Protective Equipment (RPE)

The decision to use Respiratory Protective Equipment (RPE) should only be made after a justification has been made via a risk assessment. Examples of when RPE can be used include:

- where an inhalation exposure risk remains after other realistic controls have been put in place (i.e. there is a residual risk);
- short term or infrequent exposures (e.g. cleaning of equipment) where it is decided that other controls at source are not reasonably practicable;
- when other control measures are being put in place (e.g. interim measures);
- where there is a need to provide RPE for safe exit from an area where hazardous substances may be released suddenly in the event of a control systems failure (e.g. use of sulphuryfluoride);

- emergency work or temporary failure of controls where other means of controls are not reasonably practicable.

Ideally, the approval of a biocidal product will not rely on the use of RPE. However, in some cases at the approval stage, for example, when there is residual risk, it may be necessary to recommend the use of RPE. This should not be because other control measures are inadequate on their own, but should be to provide additional protection. During the exposure assessment there is an assumption that the user of the product will have put into place all eight principles of good control practice (see Appendix 1 of this Chapter). When RPE is necessary there must be a system to demonstrate that selection of RPE has been made via a transparent and consistent procedure. Detailed information relating to selection of RPE can be found in HSE Guidance '*Respiratory protective equipment at work – A practical guide'* (HSE, 2013, available via http://www.hse.gov.uk/pubns/books/hsg53.htm).

3.3.2 Higher tier methodologies

Higher tier methodologies usually include more elaborate exposure assessment using probalistic approaches and/or more complex mathematical models. Also as part of refinement of the exposure estimate, uncertainty analysis is an option to allow understanding of the validity of the data that will be used.

Further Guidance for dealing with remaining uncertainty in exposure assessment and characterisation of human exposure models is available via the WHO/IPCS harmonisation work and can be further consulted for the exposure assessment of biocidal products:

1. "Guidance Document on Characterising and communicating uncertainty in exposure assessment" (available at: http://www.who.int/ipcs/publications/methods/harmonization/exposure_assessment.pdf)
2. "Harmonisation Project Document No: 3, Principles of Characterising and Applying Human Exposure Models"

   (available at: http://whqlibdoc.who.int/publications/2005/9241563117_eng.pdf)

4 Secondary Exposure Scenarios

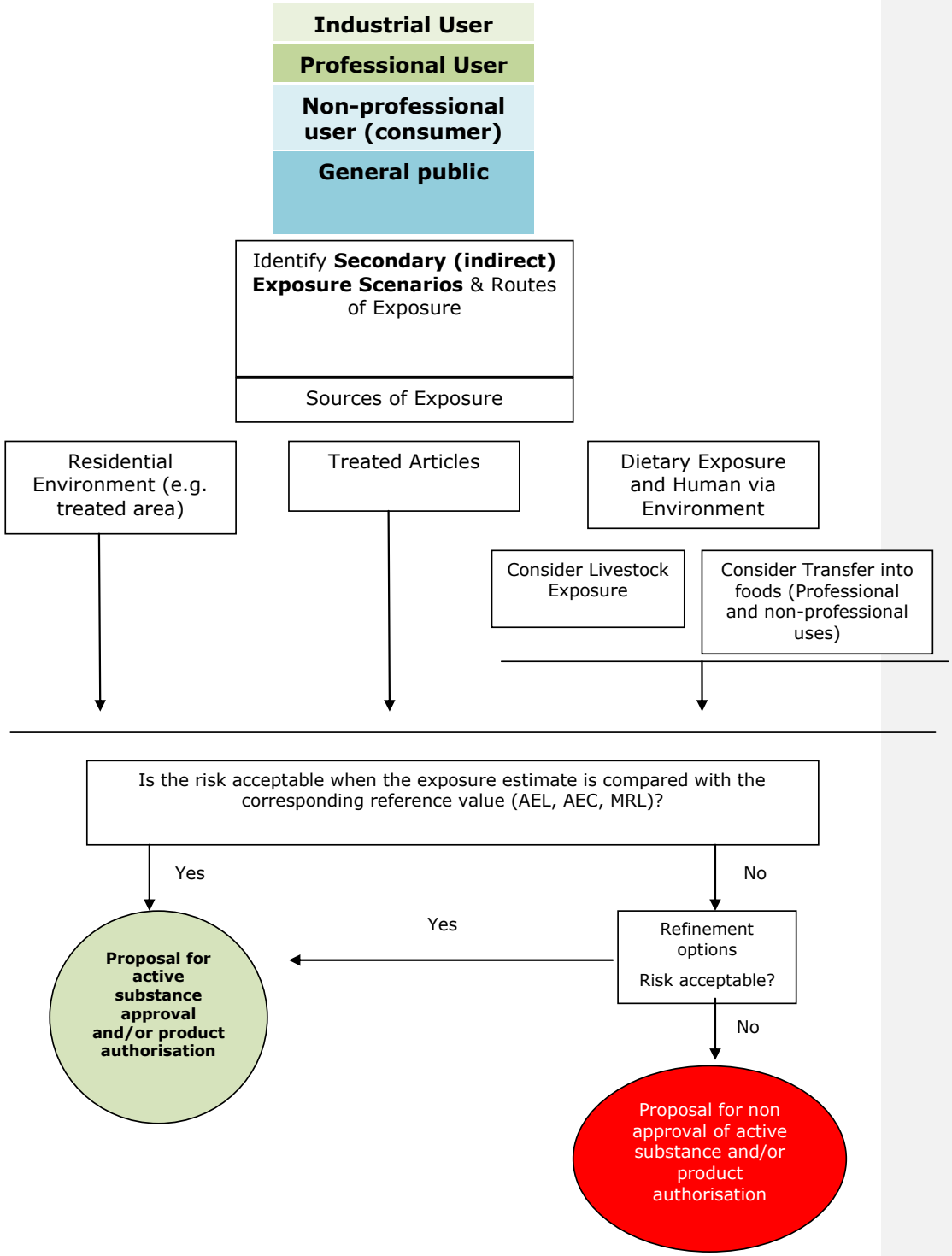
There can be three main categories that need to be considered as being potential source of secondary (indirect exposure).

These are environmental sources from the point of view of treated areas with biocidal products (e.g. a room fumigated with a biocidal product, swimming pool treated with disinfectants), treated articles and dietary exposure sources (covering potential of exposure via consumption of food where residues of biocidal products may be present).

Figure 4 provides an outline of the potential secondary exposure scenarios that need to be considered in the exposure assessment for each population.

When the exposure assessment estimate is compared to the corresponding hazard threshold, if no risk is identified no further refinement is needed. However if risk is identified, refinement of exposure should be performed. This can take into account refinement of parameters (defaults) used in the exposure assessment (with appropriate justification), generation of product specific data (e.g. measured data), or uncertainty assessment of the various steps of the exposure assessment performed.

Figure 4: Schematic flowchart of secondary (indirect) exposure assessment



4.1 RESIDENTIAL ENVIRONMENT

This includes exposure of people who are present during or following the use of a biocidal product (residents or bystanders). The post application phase is particularly important for non-professional exposure assessment because:

- some residues will remain in the treated area following application of the biocidal product;
- there can be prolonged contact in the residential environment because people live there;
- children, the elderly and other sensitive subgroups are present in the residential environment.

The task based approach does not apply to post application phase, because there are no well defined tasks in post application exposure. Instead, a scenario approach is proposed, containing the following two post-application scenarios for the residential environment:

1. Children playing on the floor where biocides have been applied. In this scenario, they transfer the biocide to their skin by contact with contaminated surfaces such as floors and walls. Oral contact may take place via hand-mouth transfer and toy-mouth transfer.
2. People present in the house after application, exposed to the residues in air and on surfaces.

The exposed population is anyone in the environment who may:

- inhale residual aerosols (sprays only, during or immediately after application);
- inhale vaporised biocide from deposits (any application); dermal contact deposits (both recently applied and dried);
- ingest dislodged deposits (inadvertently by adults, for example during smoking or eating/drinking; ingestion of dislodged deposits by infants).

Experience indicates that post application exposure of children may be the most important exposure to a biocidal substance. This is because children are a sensitive group (higher ventilation in relation to body weight, playing at ground level where the concentration of residues may be higher) and they may have a prolonged duration of contact, in the order of days to weeks. During application, concentrations are higher, but duration of contact is significantly shorter (minutes to tens of minutes typically).

In the above sense, post-application is subtly different from secondary exposure. The post application exposure is a consequence of the application of a biocide. It is secondary in the sense that the children are not aware of their exposure. However, the use of copper chrome arsenic (CCA)-treated wood, for instance, would constitute a secondary exposure but does not fit post-application exposure.

The mentioned defaults for frequency and duration of exposure should serve as a starting point for exposure assessment and should be used in the absence of accurate scenario data only. Whenever more detailed information for use scenarios is available, these data should be used instead, but always on the basis of a valid argument, for example, in case a survey has been carried out.

In addition to Table 1 (see Section 3 of this Chapter) the following elements should be considered / reported when performing secondary (indirect) exposure assessment:

Table 2 : **Data for Secondary (Indirect)Exposure Assessment**

Data requirement	Priority	Comment
Secondary exposure		
- population (acute phase)	Essential	include mode and likelihood of exposure
- population (chronic phase)	Essential	include mode and likelihood of exposure
- removal of product	Desirable	include mode of exposure

An overview of possible secondary exposure scenarios that might be considered when doing risk assessments for specific biocidal products in view of their uses within a certain Product Type, is available within the Biocides Human Health Exposure Methodology Document.

Additional information on secondary scenarios for consideration can be found within ECHA Guidance on IR & CSA R.15
http://echa.europa.eu/documents/10162/13632/information_requirements_r15_en.pdf

4.2 DIETARY EXPOSURE AND HUMAN VIA ENVIRONMENT

Indirect exposure of humans via the environment may occur by consumption of food (fish, crops, meat and milk) and drinking water, inhalation of air and ingestion of soil.

The indirect exposure is assessed by estimating the total daily intake of a substance based on the predicted environmental concentrations for (surface) water, groundwater, soil and air.

In addition to the overall calculation of indirect exposure from the environment there are three more specific areas where estimation of risk via exposure needs to be addressed for specific product types and specific guidance is currently under development:

1. Estimating Dietary Risk from Transfer of Biocidal Active Substances into Foods Non-professional Uses.

Relevant for the following product types:

- PT4 (Food and Feed area disinfectants)
- PT5 (Drinking water disinfectants)
- PT6 (Preservatives for product during storage)
- PT18 (Insecticides, acaricides & products to control arthropods)

2. Estimating Transfer of Biocidal Active Substances into Foods – Professional Uses.

Relevant for the following product types:

- PT3 (Veterinary hygiene products)
- PT4 (Food and Feed area disinfectants)
- PT8 (Wood preservatives)
- PT12 (Slimicides)
- PT14 (Rodenticides)
- PT18 (Insecticides, acaricides & products to control arthropods)
- PT19 (Repellents & attractants)

3. Estimating Livestock Exposure to Biocidal Active Substances

Relevant for the following product types:

- PT3 (Veterinary hygiene products)
- PT4 (Food and Feed area disinfectants)

- PT5 (Drinking water disinfectants)
- PT8 (Wood preservatives)
- PT12 (Slimicides)
- PT18 (Insecticides, acaricides & products to control arthropods)
- PT19 (Repellents & attractants)
- PT21 (Antifouling products)

4.3 TREATED ARTICLES

Articles treated with or incorporating biocidal products can lead to consumer and environmental exposure as well as exposure of professional users if chemical constituents of the active substances are released in any way. Exposure from treated articles during service life may be the most significant exposure to certain active substances (e.g. PT 7, 8, 9, 10). Specifically, articles consisting of different types of polymers can be used in a large range of consumer applications, which makes the exposure situation very complex. The diversity of applications has consequences for the exposure situation. Therefore, it can also be necessary to model the aggregated exposure of different articles used at the same time (please see further under section 5 of this chapter).

During direct contact with various materials that may have been treated with biocidal products, transfer may occur to the skin. This is due to the fact that the biocidal product may be dislodgeable, i.e. can be removed from the surface.

In addition to the dermal route of exposure, the possibility of transfer via the oral route should also be taken into account. This can be relevant for cases where an exposure scenario such as mouthing by infants or children or leaking from treated articles is identified .

In order to identify the potential that individuals may be exposed to an active substance via a secondary (indirect) route from treated articles, information from the patterns of use/exposure scenarios could also provide information on the potential of exposure from treated articles. In addition,the recommendations provided within the Biocides Human Health Exposure Estimation Methodology Document should be first consulted .

Furthermore, for specific product types and applications in relation to treated articles, guidance developed for the implementation of Commission Regulation (EU) No 10/2011 on plastic materials and articles intended to come into contact with food ("Food Contact Materials Regulation") or WHO for the work are of insecticides can be also considered for the secondary (indirect) exposure assessment via treated articles from biocides.

4.4 REFINEMENT OPTIONS

The principles described in Section 3.3 and the Tiering approach in Section 2.4 (both of this Chapter) apply, with the exception of use of PPE which is not applicable for secondary exposure scenarios.

5 Combined Scenarios & Combined Exposure Assessment

The (combined) scenario should cover a complete working day under realistic worst case conditions for each user type (industrial, professional, non-professional).

The estimated combined exposure for a job (for primary exposure related tasks) is added up from the exposure arising from the individual tasks through the different phases of use. In practice, the exposure estimates from the different routes of exposure

(inhalation, dermal, oral) per scenario are added together to provide a total systemic (internal) dose. If relevant the total estimates from different scenarios are combined to provide a total exposure estimate for each user type (industrial, professional, non-professional).

For instance, for industrial or professional users the tasks may include scenarios for handling concentrated material (mixing and loading), for spraying a formulation and for handling a wet object post-application. Appropriate selection from available data distributions should allow a realistic estimate of daily exposure from the combination of the scenarios which takes into account the time exposed.

It is important to recognize that simple addition of precautionary estimates can lead to gross errors and it should be considered if it is relevant and realistic to add primary and secondary exposure estimates before doing so..

Aggregate exposure to a specific substance includes both primary and secondary exposure and exposure to the same chemical in different products and matrices including treated articles .

Combined residential uses should also be considered if relevant (secondary exposure assessment), such as non-professional dietary exposure in combination with other non-professional or secondary exposure. This is particularly relevant for secondary exposure via treated articles.

It might not be feasible in all cases to aggregate the personal daily exposure to a chemical substance through all such sources. Further guidance on aggregate exposure assessment is provided in Chapter 4, Section 4.4of this Guidance.

For combined exposure assessment (cumulative and aggregate exposure assessment) principles please see Chapter 4, Section 4.4 (risk characterization for combined exposures) of this Guidance.

The principles of exposure assessment for combined exposure assessment are the same as for the exposure assessment from a single biocidal product.

The tiering approach needs to be followed both in terms of exposure refinement and hazard refinement where relevant.

6 Assessment of Data Quality

6.1 Criteria for quality assessment of reports concerning exposure data

The criteria to judge the quality of exposure surveys and study reports are set out below. It is not acceptable to use inadequate data from inadequate reports in exposure estimation and so it is imperative that all data generated are adhering to thoughtfully designed protocols and carefully conducted studies.

Initially, to build a database from past studies, it may be necessary to use less stringent quality criteria. However, these "barely adequate" data must, in time, be superseded by more acceptable data so that they can serve as entries into a generic data base. Inappropriate data may trigger over-conservative default assumptions.

6.2 Acceptability

Scientifically sound and well-documented state-of-the-art data are given preference over default assumptions. The conduct and reporting of studies must be in compliance with current test protocols and requirements.

Documentation is adequate when studies have been carried out in compliance with Good Laboratory Practice and Good Exposure Assessment (Hawkins et al., Am. Ind. Hyg. Ass. J. 53:34-41, 1992) , and defined in terms of the following eight components. All components should be present:

1. A detailed protocol, which bridges the study conduct and the conclusions that may be reached.
2. The study should be carried out with adequate and validated equipment by committed and qualified scientific and technical staff, described in terms of organisation, personnel, and resources.
3. A statement on the study model which bridges the actual observed data and the general application, be it deterministic, empirical or statistical.
4. A fully described study design, containing all forms of data handling (sampling, chemical and statistical analysis). It is essential not only to describe what is done and how, but also to show that the procedures are adequate for reaching the study goal.
5. A quality assurance procedure, including external audits.
6. A statement of overall uncertainty, indicating the errors due to variables in the study and possible bias.
7. All documents relevant to the study should be retained, the report indicating the absolute essential archiving.
8. The need for communication and confidentiality of results, when relevant or appropriate.

In practice it is recognised that a pragmatic approach to study acceptability would have to be developed to deal with the sparse data for exposure to biocides.

6.3 Criteria

Each study submitted should be evaluated by comparison with pragmatic data acceptability criteria as set out below.

This evaluation forms the basis for the decision whether or not to include a study in the database, which study information to include and which study exposure records (data points) to include in sub-sets for deriving surrogate values or distributions for use in predictive models. It would also form a basis for Competent Authorities to evaluate studies submitted in support of authorisation of specific biocidal products.

To provide transparency on the individual judgements, each study should be summarised in a standardised note format. The information in this summary should contain:

- study number (unique number);
- documentation (comment on adequacy or otherwise);
- contextual information about the scenario and tasks;
- database contribution (number of records);
- participants (number and definition);
- replicates (number per worker);
- time/surface/volume (relevant measure, as related to a work cycle or shift);
- equipment (and/or other relevant information);
- information, training;
- engineering measures in use;
- recommended (or in use) PPE;
- matrix-matched recovery data (field and laboratory);
- limits of detection and quantification;

- inhalation (technique and sampling media, collection efficiency, particle size, if applicable);
- dermal (body) (technique and sampling media);
- hands (technique and sampling media);
- bulk concentrate and in-use biocide concentrations;
- analytical aspects (technique and documentation);
- container size/type;
- formulation (type);
- activities involved;
- notes (other relevant information);
- judgement (proposed decision on inclusion of exposure records to be included);
- environmental conditions;
- calculations and data analysis;
- plausibility analysis;
- discussion of results.

The pragmatic acceptance criteria are set out in the following table. These are set out as essential requirements, desirable attributes and rejection criteria. For example, it is considered essential that a study report should contain a description of the aims of the work and, ideally, there should be a written protocol for the study, including a justification/ reasoning for the chosen design.

Table 3 Recommended pragmatic acceptance criteria for human exposure studies

Essential requirements	Desirable requirements	Rejection criteria
Aims of survey or study strategy[3]	Protocol for study	No stated objective
Identification of the process etc.	Full details of process, task, equipment, substance in use	No process or task description, substance unidentified
Number of subjects and samples	Number of unique subjects and samples	Many replicates (few subjects, many samples)
Work environment	Workplace information	No workplace information
Product used - form, packing, site delivery	Product form etc and in-use assay	No product details
Duration of task / tasks	Full pattern of use data and work-rate	No data for use duration
Sampling methods	Sampling methods validation	No clearly stated sampling methods
Analytical outline and recovery data	Analytical method, validation, recovery, storage, detection limits	No recovery data (unless obvious)
Task sampled - task and sampling match	Sampling data linked to task data	Sampling time and task or duration mismatch,

[3] GLP compliance of studies into exposure to biocidal products is at the moment no generic demand in the EU, as it is in the USA and Canada. Some Member States require GLP-compliant studies for pesticides.

Comment [SJ9]: TO NOTE: The table number (and all references to it) will be updated at the end of the consultation and incorporation of the updated Chapter 3 into Vol III/B.

Additionally it will be formatted in the ECHA style.

In-use product	Bulk biocidal product samples taken	Missing bulk information
M&L, application, or post-application information	M&L, application, or post-application sampling	No clear description of activity phase sampled
Controls, work clothing	Exposure controls and PPE used, laundry, etc	No data on work clothing or controls
Outline of disposal route	Detail of exposure route and recycling	No way of deducing disposal route
Data reported in full	Data reported in full	Data as summary (e.g. range and statistics)
Study date	Date	No indication

Notes on Table 3
M&L= mixing and loading;
PPE= personal protective equipment

Expert judgement will be required to evaluate whether certain aspects of a study do not fulfil some of the essential requirements.

Studies meeting any of the rejection criteria will still be evaluated to see if they contain any useful data on any aspect of exposure, such as the pattern of use or the environment in which the product was applied.

The assessor must report on the acceptability or otherwise of studies submitted. All studies that are reported in the present document have met the criteria of acceptability, unless noted otherwise.

In addition to the general desirable study characteristics set out above there are a number of specific contextual data items that should also be documented in a study report. These are shown in the following table. Some of the data indicated in this table can be important for the evaluation of the adequacy of studies, for example, a study on inhalation exposure towards a volatile substance would probably be rejected if it provides no information on the location and the ventilation.

Table 4 Desirable contextual human exposure data

Data item	**Desirable amount of detail to be recorded**
Emission of biocides	Either: solid/liquid aerosol, vapour, mist; spray, splash or spill
Location of biocide use	Inside or outside a building; volume of room
General ventilation	Details of general ventilation, e.g. good mechanical ventilation, poor mechanical ventilation, natural ventilation; details of weather conditions if outside
Physical properties of biocidal product	Some indication of the dustiness of solids being handled or the volatility of liquids; qualitative details of the viscosity of liquid biocidal products
Mass of product used	The total mass of product used during the task or tasks
Biocide concentration	Record of the concentration of the active biocide, both in use and before any dilution
Proportion of the task exposed to biocide	Percentage time the person is exposed (by inhalation or dermal contact) to the biocide
Time near to the source	Proportion of the task where the person is close (within 1m) to the source of the biocide
Description of the	Details of the process or activity; for example, handling contaminated

Comment [SJ10]: TO NOTE:
The table number (and all references to it) will be updated at the end of the consultation and incorporation of the updated Chapter 3 into Vol III/B.

Additionally it will be formatted in the ECHA style.

handling of the biocide	objects, spraying, brushing, wiping, immersion etc; details of the process, e.g. spray technology, spray pressure, nozzle diameter, etc
Process temperature	Temperature of the biocide in use
Description of local controls	Presence of local ventilation for inhalation risks, ideally with some comment on its likely effectiveness; details of any other control measures applied at the source
Housekeeping	Description of the apparent cleanliness of the area; details of any accidental splashes, spills, etc
Contaminated surfaces	Area of contaminated surfaces, concentration of biocide on surfaces, estimated personal contact rate (hands or body touches per hour) with surfaces.
Use of PPE	Type of respirator, gloves, clothing or other PPE worn while using biocide; brief description of training of people to use the equipment and administration of the PPE.
Physical activity involved with task	Categorised as: *rest* (e.g. sitting), *light* work (e.g. sitting or standing with moderate arm movements), *moderate* (walking with moderate lifting or pushing), *heavy* (e.g. intermittent heavy lifting with pushing or pulling), *very heavy* (e.g. shovelling wet sand).
Categorical (yes/no)	Inadvertent exposure of food through treatment/contamination

It is realised that most studies of human exposure to biocides that have previously been undertaken will not report detailed data for many of the above. However, it is considered that in the future further efforts should be made to collect such data.

7 Selection of Indicative Exposure Values

The following general 'rules' are presented for selection of indicative exposure values from available exposure data (see also Appendix 2 of this Chapter).

1. Moderate uncertainty. The dataset is sufficiently large and/or the variability sufficiently low that the exposure distribution can be characterised with a reasonable level of assurance. 90% confidence intervals for the 75th percentile are typically less than a factor of 2. For these datasets the 75th percentile is proposed as an indicative exposure value.

2. Considerable uncertainty. The dataset is of smaller size and/or the variability greater than for datasets of moderate uncertainty. The degree of confidence in the characterisation of the exposure distribution is lower with 90% confidence intervals for the 75th percentile typically greater than 2. For these datasets the 95th percentile is proposed as an indicative exposure value.

3. High uncertainty. The dataset is of small size and/or the variability is great. The lognormal approximation to the exposure dataset may not be verifiable and so confidence intervals based upon this assumption might be misleading. The exposure distribution is poorly characterised and so the maximum exposure value is proposed as an indicative value, or else none whatsoever.

It is important to note that the rules defined above only address the sampling uncertainty associated with each data set. The use of any generic data model is also subject to scenario and extrapolation uncertainty reflecting the degree of analogy between the assessment scenario and the circumstances represented by the data model. The strength of this analogy requires expert evaluation and might justify the use of a higher percentile.

8 Glossary of Terms

Comment [SJ11]: TO NOTE: This list will be reformatted into a table in the ECHA style before publication.

It is important that there is a clear understanding of the terms used in exposure assessment. This glossary was developed in conjunction with that in Annex III of the OECD guidance on the conduct of studies. Where no definition appears, that in the TGD applies. In addition, the definitions in the BPR apply and in doubtful cases override other definitions.

abuse is intentional misuse, for example inhaling aerosol propellant - as such, it is not included in exposure estimation.

active substance (a.s.) is the substance (or microorganism) that has an action on or against harmful organisms (Article 3(1)(c) BPR)..

actual dermal exposure is the amount of active substance or in-use biocide formulation (biocidal product) that reaches the skin through e.g. (work) clothing or gloves and is available for uptake through the skin.

application refers to using the in-use biocide(biocidal product).

biocidal product is is a substance or mixture that consists of, contains or generates one or more active substances and which has a biocidal intention (see full definition at Article 3(1)(a) BPR).

biological monitoring is the sampling of blood, urine, saliva or exhaled air at suitable times before, during and after the task, and analysing for the substance or a metabolite to determine the body dose. The sampling regime needs expert advice and ethical clearance.

bulk samples are samples of the biocide in use (and where necessary, the concentrate).

Bystanders are those who could be located within or directly adjacent to the area where a biocidal product has been applied; their presence is quite incidental and unrelated to work involving biocides, but whose position might lead them to be exposed for a short period of time (acute exposure); and who take no action to avoid or control exposure.

central tendency in a distribution is a value that describes best the central value. The central tendency may be used in exposure estimates where well trained operators show practically continuous use.

clothing can range from minimal (e.g. T-shirt and shorts) through to leisure wear, work clothing and coveralls, to impermeable suits. It includes PPE.

deterministic estimates are single-value, including worst-case estimates.

dislodgeable residues are post-application residues that are available for uptake through human contact with substances on surfaces.

empirical (database) model is a data distribution of exposures derived from site surveys or laboratory simulations, strongly associated with the biocide application task(s). The only inputs are new exposure data to reinforce the model. The outputs are "indicative exposure values" which when modified by pattern of use data, are compared with toxicological endpoint data. This is used in Tier 1 and Tier 2 assessments.

exposure reduction measures are techniques to reduce risk through substitution of products, controlling the product, its sectors for use, specifying in-use control measures.

exposure data (experimental) are personal samples (for inhalation and dermal exposure) and each is a data-point. It is unlikely that a sufficiently powerful data set would exist for meaningful statistics to apply to most scenarios.

exposure information includes the frequency and duration of exposure, the selection of products in preference to others on the market, and the patterns of use.

exposure models are used to predict exposure from databases, from statistical relationships and through mechanistic calculations. They provide information which, in conjunction with other data, leads to a quantitative estimate of exposure.

exposure via the environment is an element of secondary exposure. It includes bystanders and consumers, including children, who are inadvertently exposed to biocides by inhalation of plumes drifting off-site and ingesting contaminated food or water.

field blank samples are sampling media that are treated in the same way as monitoring media, without being exposed to the biocide in use.

foreseeable non-proper (incorrect) use is the use of biocidal products not in line with the instructions for use or without the consideration of some or all common and specific technical, operational and personal protective measures (e.g. the over-application or inadequate dilution of a biocide, common spillage scenarios, use without or with non-proper RPE and PPE). Accidents, malfunctions or deliberate misuse are not addressed.

likelihood of exposure is the expression of probability that exposure will occur at all. It can be quoted to reflect "none detected" values in exposure surveys and studies. See also LoD, LoQ.

in-use biocide is the product as it is being applied, whether or not diluted by the user, as a paint, a dust, a spray, a solid, a solution, or as a component of a fluid.

Industrial users are those involved in manufacturing, handling and/or packaging of actives or products in industry as well as those using biocidal products in their own processes at industrial setting, for example, manufacturers of timber cladding using wood preservatives or food companies using disinfectants.

ingestion arises from the swallowing of biocides. Ingestion can also occur through poor hygiene practice (e.g. through dislodging from contaminated skin to food or cigarettes, by hand-mouth contact, or through applying cosmetics).

inhalation exposure reflects the airborne concentration that is available in the breathing zone. The substance is then available for uptake via the lungs or following mucociliary elevator action from the gastrointestinal tract.

Intended use of a biocidal product means what is supposed to be used according to the manufacturer's specifications, instructions, and other information.

LoD, LoQ - limits of detection and quantitation are levels, below which the biocide cannot be detected, and cannot be measured accurately, respectively.

mathematical model is a tool whereby inputs by the user result in a prediction of exposure through calculation. This is used in Tier 1 and Tier 2 assessments.

mixing & loading - handling biocide concentrates, diluting them and where necessary, putting the in-use formulation into the application apparatus.

NOAEL - the no observed adverse effect level.

none-detected values from exposure studies - see likelihood of exposure, limits of detection.

non-professional applications where products are for non-professional user (consumer) application, and include examples where people in a workplace are not employed to use biocides (e.g. fly sprays in an office).

non-professional users are the general public - consumers - .There is an expectation – but little guarantee, that non-professionals will comply with instructions for use of a product. They have no access to controls or formal PPE.

penetration of PPE - that proportion of biocide that by-passes PPE, e.g. by soaking through seams and zips, being drawn in at the neck, cuffs and ankles by the "bellows

effect", that gets inside protective gloves by them being donned with contaminated hands.

permeation of PPE - the migration of biocide through the PPE barrier, e.g. solvent-based product through latex-based gloves.

personal monitoring is the sampling of a biocide during its application or mixing and loading, using samplers deployed on the person. See also static monitoring.

personal protective equipment (PPE) includes head, eye, respiratory (RPE), body, hand and foot protection that is designed to protect the wearer. The basic safety requirements that PPE must satisfy, in order to ensure the health protection and safety of users, are laid down in the Council Directive 89/686/EEC.

phases of activity are mixing & loading, application, post-application and removal of the biocide.

post-application covers the scenarios of sampling, maintaining and cleaning and may give rise to secondary exposure.

potential dermal exposure is the deposition of active substance or biocidal product on the outer surface of clothing and on any bare skin.

preparation or formulation is the biocidal product as placed on the market; the active substance with its coformulants, diluents, carrier materials and stabilisers.

primary exposure is that which occurs to the user (i.e. the person who applies the biocide).

probabilistic (stochastic) modeling is used to combine data in order to derive fair 'central tendency' and 'realistic worst case' values. It is based on distributions of parameters. See deterministic estimates.

professional users (e.g. employees and the self-employed) will handle biocidal products within the framework of statutory requirements. They are trained and skilled in the main objectives of their occupation and may have some experience and skill in the use of the PPE if that is necessary for their normal work. Not all professional users will have the knowledge and skills to handle hazardous biocidal products (e.g. incidental use of slimicides, insecticides, irregular disinfections and use of products containing preservatives).

protocols are detailed descriptions of the work to be undertaken in surveys or studies and the objectives to be achieved.

removal and disposal phase includes removing exhausted antifoulant coatings, disposing of used preservative fluids and burning treated timber.

Realistic worst case is the situation where the exposure is estimated using from a range of factors (i.e. duration, amount, exposure controls), where applicable, the ones that would be expected to lead to maximum amount of exposure. The realistic worst case does not include deliberate misuse.

Residents are those who live or work adjacent to an area that has been treated with a biocidal product; whose presence is quite incidental and unrelated to work involving biocides but whose position might lead them to be exposed; who take no action to avoid or control exposure and who might be in the location for 24 hours per day (longer term exposure).

risk assessment is the comparison of a predicted human dose from undertaking a task or tasks with appropriate toxicological endpoint values or NOAELs.

scenario is one or a number of well defined tasks for which exposure can be characterised.

secondary exposure is that which is not primary. It is characterised through the exposed person having little or no control over their exposure, which may be acute or prolonged. It includes re-entry to treated zones (contact with treated surfaces, inhalation of residual vapours, ingestion of residues).

trained professional users probably have specialised knowledge and skill in handling hazardous chemicals. Protective measures as foreseen in the European Communities regulations on safety and health at work (instruction, training, exposure control, PPE) should be observed. Qualification might be documented by the endorsement of management systems for occupational safety and health, by certification to branch-specific standards or by approval through competent authorities. The term specialised professional user has the same definition as trained professional user.

static monitoring is sampling of background atmospheric concentrations or deposition.

studies are short laboratory simulations of limited tasks, or workplace based small surveys to indicate a likely exposure pattern.

surrogates or tracers - e.g. strontium salts, dyes, fluorescent agents - are used in surveys and studies to enable analysts to trace the exposure pattern.

surveys are extensive measurement of exposure resulting from real biocide application tasks.

task covers the phases of use of a biocide. It is a unit of operation within one or several scenarios.

Tier 1 is a screening level risk assessment.

Tier 2 is a detailed risk assessment, taking into account patterns of work and risk management measures.

Tier 3 is the output of an individual exposure study, possibly generated as a result of a data requirement for product registration.

TWA - time weighted average exposure by inhalation.

user sectors: industrial, professional, non-professional and secondary.

ventilation has several meanings. It may be a control measure in the workplace; it may refer to passive air changes within a building; and it may refer to the human breathing rate. The context should be clear from the text.

visualisation involves the introduction of a coloured or fluorescent tracer to the biocide in-use formulation for post-exposure quantitation.

work clothing - work uniform or work wear is a set of clothes worn at work. They are not designed to protect the health and safety of the worker and do not constitute PPE. However, they do protect the wearer to some extent from dermal exposure.

Appendix1: Principles of Good Control Practice

The following text details the principles of good practice for the control of exposure to substances hazardous to health according to Directive 98/24/EC (especially Art.6/Paragraph 2) and the "Practical Guidelines of a non-binding nature on the protection of the health and safety of workers from the risks related to chemicals agents at work" (available at: http://bookshop.europa.eu/is-bin/INTERSHOP.enfinity/WFS/EU-Bookshop-Site/en_GB/-/EUR/ViewPublication-Start?PublicationKey=KE6805058). As such the principles should be followed when considering preventing / controlling exposure to biocides. The focus is on inhalation exposure.

The following table provides a good summary of "Specific prevention methods and their prioritisation" (as available within the "Practical Guidelines of a non-binding nature on the protection of the health and safety of workers from the risks related to chemicals agents at work" Chapter 3.1):

Table A1-1: Specific prevention methods and their prioritisation

Priority	**Objective**	**Area of Application**			
		Chemical agent	Process or installation	Workplace	Work method
1	*Risk elimination*	• Total substitution of the chemical substance	• Modification of the process • Use of intrinsically safe equipment (1)		• Automation
2	*Risk reduction-control*	• Partial substitution of the agent • Change of form or physical state (2)	• Closed process • Local extraction	• Safe storage • Segregation of dirty departments • Ventilation by dilution • Fire prevention	• Safe handing • Safe internal transport
3	*Worker protection*			• Eyebaths and showers • Fire protection • Explosion prevention and protection	• Respiratory, skin and eye PPE

(1) Applicable for eliminating the risk of fire or explosion
(2) For example, handling of a solid material in a wet state, in the form of a paste or gel or encapsulation may reduce inhalation risk

Adequate control

Considerable emphasis should be placed on using good control practice and that it would be considered adequate if:

- the principles of good control practice are applied;

- a workplace exposure limit is not exceeded.

The primary emphasis for achieving adequate control relies on the application of eight principles of good control practice.

Principles of good control practice

'To be effective in the long-term, control measures must be practical, workable and sustainable'.

There are eight principles (a - h) that have to be followed to develop effective control measures. The principles should be regarded as a 'package', which must all be properly applied in order to achieve effective, reliable and sustainable control of exposure. Applicants and evaluators cannot pick and choose which principles to apply – they are all important in achieving adequate control. Principle (a) is not more important than principle (h), although there is a logical progression in how they are presented and should be considered.

Principle a: Design and operate processes to minimise emission, release and spread of contaminants.

It is more effective to reduce the emission of a contaminant at source, rather than to develop ways of removing the contaminant from the workplace, once it has been released and dispersed. Clearly, with the way that many biocides are applied this approach is often not possible. However, it is possible to consider reducing in number the size, emission or release rate, as much as possible. Indeed it is often not possible to obtain adequate and reliable control unless this is done. Consequently, to identify how people are exposed during the application of biocides, it is essential to recognise the principal sources and how the contaminant is transferred within the workplace. It is easy to miss significant sources and causes of exposure. Application of biocides will lead to the emission and release of contaminants. The way this occurs and the scale of release needs to be understood because only then can alterations be developed to minimise emission, release and spread of the biocide. This is best done at the design stage. Other people, workers or bystanders, may be significantly exposed even though those applying are protected; for example, by wearing PPE. In such circumstances, the most practical option to protect those people not directly involved in application may be to segregate the process.

Once the number and size of sources has been minimised, consideration should be given to whether further reduction can be made by enclosing the process. If enclosure is possible (e.g. by sealing a building prior to fumigation), the enclosure should be big enough and robust enough to cope with the application process. For airborne contaminants, properly designed exhaust ventilation applied to the enclosure may be needed to minimise leakage into the workplace. Work methods should be designed and organised to minimise the number of people exposed, the duration, frequency and level of exposure. For example, when treating a large article with a wood preservative, containment may not be feasible; natural ventilation may, however, with the right precautions, be relied on to disperse vapour. Clearly this would be best done at the end of a shift, in controlled circumstances and when fewer people will be present.

In addition to identifying significant sources, it is essential to identify and consider all work groups and bystanders that may be exposed. It is easy to miss or underestimate the exposure of those engaged in non-routine activities such as work done by maintenance personnel and contractors. Control measures at the outset should be designed for ease of use and maintenance. If they include working methods that are difficult to follow or involve hardware that is difficult to repair, the control measures will probably not be maintained or sustained. Inevitably their effectiveness will fall and exposure will rise.

Principle b: Take into account all relevant routes of exposure – inhalation, skin absorption and ingestion – when developing control measures

The physical and chemical properties of a biocide, in the circumstances of use, have a great bearing on which route (inhalation, dermal or ingestion) of exposure, or combination of routes, is most important. If there is no exposure, there is no risk to health, but for many biocides the usage pattern nearly always leads to some exposure. There is therefore a need to consider:

- the health effects that the biocide can cause;
- the way the biocide is used;
- the degree of exposure;
- how exposure occurs.

An adequate risk assessment considers all routes by which the biocide might enter the body and, in the case of direct contact, how a biocide might affect the skin and eyes. In some cases, it might be immediately obvious that not all routes apply. Therefore, for the exposure assessment there is a need to:

- identify all sources and routes of exposure;
- rank these routes in order of importance.

Where inhalation is the most relevant route, the main focus for control will be sources of emission to air. Where the main concern is ingestion or effects on, or as a result of penetration through the skin, the main focus for control will be sources of contamination of surfaces or clothing and direct contamination of the skin. The exposure assessment should identify and, if possible, grade or rank the contribution of all routes of exposure to total exposure. In this way control effort can be directed at the main sources and causes of exposure. Skin contact should be prevented, if possible, where contamination may lead to skin absorption, ingestion or direct health effects on the skin. Regular cleaning of surfaces that can become contaminated, for example, the outside of a knapsack sprayer, should be undertaken. The frequency of cleaning should be based on the rate at which the surfaces become contaminated and how often skin is likely to come into contact with them. Gloves are often used to provide protection against skin contact with biocides. However, transfer of contamination from the outside of protective gloves to the inside is common. The risk assessment should identify the fact that if gloves are to be worn then users have to be trained in the correct technique for putting on and taking off their gloves. If biocides are applied in a room, which may become contaminated, and this contamination may contribute significantly to exposure, people should not increase their exposure by activities such as:

- eating;
- drinking;
- smoking;
- using cosmetics in the workplace.

If the workroom is liable to be contaminated, people should have clean areas to rest, eat or drink. Where skin contact is relevant it will be necessary to provide:

- adequate and accessible welfare facilities for washing and changing;
- laundered or disposable workwear. The frequency of laundering will depend on the degree of contamination and the hazardous nature of the biocide;
- separate storage for day-wear and work-wear;
- clean facilities;

- segregation of clean and dirty areas if the risk of contamination is severe.

It is good practice to keep workplaces clean, however cleaning methods should not lead to spread of contamination. If dust exposure from contaminated work clothing could be significant, clothing should be used that is made from low dust-retention and low dust-release fabric.

Principle c: Control exposure by measures proportionate to the health risk

The more severe the potential health effect and the greater the likelihood of it occurring, the stricter the measures to control exposure will be required. Control measures that are adequate will take into account the nature and severity of the hazard and the magnitude, frequency and duration of exposure. They will therefore be proportionate to the risk. The consequences of failing to control exposure adequately should be considered. If the health effects arising from exposure are less serious, such as simple, reversible irritation, and are not likely to cause long-term harm, it may be sufficient to reduce exposure by simple low-cost measures, such as replacing lids on vessels. In such cases, it may be unnecessary to go to greater trouble and expense to reduce the risks even further. Where the health effects arising from exposure are more serious then exposure will need to be reduced to low levels. How low these levels need to be will depend on the nature of the hazard, the likelihood of harm occurring and the degree of confidence in the information on potential health effects. The control measures necessary in this case might be extensive, take time to develop and implement, and be relatively costly. The measures should control the risk of both long-term (chronic) and short-term (acute) health effects.

Sometimes, control measures may be selected that reduce exposure more than is strictly necessary. Usually, this occurs because some controls are more convenient and acceptable. For instance, people may prefer to wear air-fed respiratory protective equipment rather than filtering devices, although the protection offered by the latter would be adequate, if well fitted. Such cases do not undermine the general principle that, overall, control measures should reduce exposure to a level which minimises any risk to health. Control measures should be kept under review to ensure they remain effective enough in the light of new information. Knowledge and understanding of the potential health risks from the biocide may change. Advances in the application process and control technology and work organisation may enable changes to be made to reduce exposure.

Principle d: Choose most effective and reliable control options, which minimise escape and spread of contaminant from sources

Some control options are inherently more reliable and effective than others. For example, the protection afforded by personal protective equipment (PPE) is dependent upon good fit and attention to detail. In contrast a very reliable form of control is changing the process so that less of the biocide is emitted or released. For example, application by brush may be easier to control than by spraying. The most effective and reliable control option for particular circumstances should be chosen and these should be directed at the main source and cause of exposure. There is a broad hierarchy of control options available, based on inherent reliability and likely effectiveness. These include:

- elimination of the biocide;
- modification of the biocide, application process and/or workplace;
- applying controls to the process, such as enclosure;
- ways of working to minimise exposure;
- equipment or devices worn by individuals.

Clearly, for many biocidal products, some of the above control options are not feasible. However, raising the profile of the hierarchy of control means that the Applicant should have considered the possibility of elimination and asked the question; can the biocide be eliminated or replaced with something else? Elimination means exposure cannot occur and, as an option, should always be considered first. If it were not possible to eliminate then a reliable form of control would be to change the process so that less biocide is released. Controls applied to the process might be effective, but will require maintenance and are unlikely to be as reliable as elimination. The key message is that there is a hierarchy of reliability of control options and this hierarchy is often linked to their effectiveness. Many of these decisions will be made by the user and not the Applicant.

Providing PPE, such as gloves or respirators, may appear to be a quick and easy option. In practice, it is likely to be the least reliable and effective option. Indeed, it may not actually be the cheapest if a PPE programme is compared like-for-like with the cost of providing other control options. What is required is the development of a set of integrated control measures that are effective and reliable enough to control exposure adequately. The 'hierarchy' of control should not be seen as a marker of reliability and effectiveness so rigidly that some control options are viewed automatically as 'good' while others are seen as 'bad'. This 'good-bad' view can hinder the development of what is needed, that is, effective, reliable, practicable and workable control measures. There is a large range of control options available. Each will have its own characteristics as to when it can be applied, how much it can reduce exposure, and how reliable it is likely to be. As a matter of principle, the aim should be to select from the most reliable control options. Again, it is important not to be too fixed in one's thinking as, in many cases, an effective set of control measures will turn out to be a mix of options – some more reliable than others.

Principle e: Where adequate control is not reasonably practicable by other means, provide suitable PPE in combination with other measures

Effective control measures usually consist of a mixture of process and/or workplace modifications; applied controls, such as LEV, and methods of working that minimise exposure and make the best use of controls. Sometimes the mix includes PPE, such as respirators, workwear or gloves. PPE tends to be less effective and reliable than other control options, because it:

- has to be selected for the individual;
- has to fit the individual and not interfere with their work or other PPE worn at the same time;
- has to be put on correctly every time it is worn;
- has to remain properly fitted all the time the individual is exposed;
- has to be properly stored, checked and maintained
- tends to be delicate and relatively easily damaged;
- fails to danger, sometimes without warning.

The possibility of failure at each of the steps needed for successful use of PPE makes it difficult to achieve sustained and effective exposure control across a population of people. Even if a reliable, defined sustained reduction in exposure is achieved using PPE, it offers no protection to others working nearby not wearing PPE. Control options, such as change of process or applied controls, are likely to be more effective and reliable than PPE. They will probably be cheaper long term, but it may take longer to plan and organise them. It is important not to rely solely on PPE as the only control option and believe exposure is adequately, effectively and reliably controlled. Unless, that is, PPE really is the only feasible control option. Normally, PPE should be used to secure

adequate control in addition to the application process, operational or engineering measures, and where adequate control of exposure cannot be achieved straight away, or solely by application or use of these other measures.

With respect to biocides PPE may be the essential element for controlling exposure; in which case a programme to organise and manage this element will be required. PPE, including RPE, requires proper:

- selection;
- fitting;
- use;
- storage;
- checking and maintenance;
- training for use.

A PPE programme involves the careful, routine training of the behaviour of people, including wearers and supervisors. If used, it must be set up carefully, managed properly and checked regularly. Clearly, the type of PPE provided should be both adequate and suitable. Adequate, in this context, means technically capable of providing the required degree of protection; appropriate selection is therefore very important. Suitable, means correctly matched to the needs of the wearer, the job and the work environment. Choice, comfort, user trials and supervision will all be important. Sometimes the PPE chosen may offer protection that is more than adequate, but is chosen for its suitability. For instance, an airline hood may be more comfortable and, therefore, more acceptable than a full-face mask, even though the additional protection is not indicated from the risk assessment. As with gloves, shoes and clothing, one size of respirator will not fit everyone. People must be offered a choice of device. This is especially the case for half-mask devices, which need a good and complete fit against the face of the wearer to work effectively.

Principle f: Check and review regularly all elements of control measures for continuing effectiveness

Once an effective set of workable control measures have been devised, they need to be put in place and managed. This includes training all relevant people in the use and maintenance of the control measures. The requirement for maintenance covers all elements of the measures to achieve effective and sustained control of exposure. These include any defined methods of working, for example, supervisory actions and record keeping, (i.e. the 'software' of control) as well as the 'hardware' of control, such as PPE. Certainly, whatever hardware is involved must be checked and must continue to function as intended. In addition a similar approach needs to be taken to check the actions people must take and the methods of working they need to adopt. The effectiveness of control measures should be checked regularly. Which checks, and how often, will depend on the particular control measures. The consequences if the measures fail or degrade significantly, should be considered. Process changes are likely to be more stable and reliable than, say, LEV. In turn, LEV is likely to be more stable and reliable than controls that rely on routine human behaviour. In practice, it is necessary to draw up a simple practical programme for checking essential elements in each set of control measures. For instance, it may be necessary to check every week that operators are still adopting the correct methods of working. Checking on the working of the LEV may only be needed every month. Checking the continuing effectiveness of the process changes may only be needed every six months.

It is however important not to miss the basic checks. It may be very obvious that an important element of a set of control measures has failed and the operator may well be in the best position to check this.

The frequency of checks should be adjusted to what is needed to keep the control measures effective. There is nothing more likely to cause people to ignore or not take checks seriously than routinely measuring and recording 'no change' over long periods of time. Checks have to have some purpose and meaning. Exactly what checks should be done will depend on:

- the control measures in use;
- how reliably they control exposure;
- how well characterised they are;
- the consequences of control degradation or failure.

When control measures are known to be reliable and effective, the focus of attention should be on checking the critical elements of the measures to ensure continued effectiveness. Where reliability and effectiveness are not known, it may, ultimately be necessary, to measure exposure to the biocide in question.

Principle g: Inform & train all employees on hazard and risks from substances and use of control measures

For control measures to be effective, operators need to know how to use them properly. Most importantly, operators need to know why they should be bothered to work in a certain way and use controls as specified; they need to be motivated. Motivation comes from understanding what the health risks are and, therefore, why the control measures are important. It also comes from the user having confidence in the control measures and believing that they will protect their health. If the health risk is serious and is chronic or latent in nature, a good appreciation of the risk is especially important. With latent or delayed risks, exposure can often be excessive, with no short-term warning, such as smell or irritation, to indicate that anything is amiss. People exposed during application of a biocide need to be told, clearly and honestly, why they should use the control measures, and the consequences, in terms of ill health, if they do not use them.

Operators need to know how control measures work to use them correctly, and to recognise when they are not working properly. This means training the operators that are directly involved, as well as supervisors and managers. This is so that everyone can identify when controls are being used in ways that reduce their effectiveness. It is important to know whether the individual is working in a way that reduces the effectiveness of control measures because:

- there is no other way of doing the job;
- because they do not know any better.

If the control measures are difficult to use or get in the way of doing the job, they will need redesigning. If the control measures are well designed and tested but are still misused, then the individual needs retraining and motivating. Most control measures involve methods of working, which means that, at the design stage, it is essential to ask workers and supervisors for their views on how best to do the work so exposure is minimised. They should be asked whether a proposed method of working is practical and how to get the best out of the proposed control measures. Easily followed, convenient and simple procedures, which minimise exposure, and are built-in to the working method, are more likely to be followed.

Principle h: Ensure introduction of control measures does not increase overall risk

Process changes, enclosures, ventilation, new methods of working, PPE and other changes to control exposure can introduce new risks. For instance, process changes may mean that equipment cannot be fully decontaminated before maintenance staff are given repairs to do. New methods of working may create risks of musculoskeletal injury. LEV has to be maintained, introducing possible risks of access and manual handling of

heavy parts, while PPE can restrict movement, feel and vision. People designing control measures should look for these 'new' risks and minimise them. They must not only focus on the risk from biocides hazardous to health. A good control solution is one which minimises the health risk while reducing maintenance burdens, being relatively foolproof, and not introducing other risk.

Appendix 2: Confidence Intervals for Percentiles of Exposure Distributions

The correct selection and use of exposure percentiles in a risk assessment is essential in order to avoid excessive conservatism whilst also providing reassurance that highly exposed workers are incorporated into the assessment. As uncertainty increases with small datasets it is generally the case that a higher percentile such as 90th, 95th or maximum exposure value will be used in place of a more moderate one such as a 75th percentile. Alternatively, a confidence interval may be calculated for a percentile to indicate the level of precision in the value and this supplementary information considered when making the assessment.

Assuming that a sample of *n* exposure measurements has a lognormal distribution with a geometric mean of exp (μ) and a geometric standard deviation of exp (σ) then an estimate of the *p*th percentile is given by:

$$\exp \{ \mu + z_p \sigma\}$$

Where z_p is the *p*th percentile from a standardized normal distribution N(0,1). For example, z_{75} = 0.6745, z_{90} = 1.2816.

An approximate standard error of log(*p*) can be calculated as:

$$\sqrt{\sigma^2 n^{-1} + z_\alpha{}^2 \sigma^2 (2n)^{-1}}$$

1-α% confidence intervals for exposure percentiles can then be calculated using the following formula:

$$\exp\left(\mu + z_p \sigma \pm z_{\frac{\alpha}{2}} \sqrt{\sigma^2 n^{-1} + z_p{}^2 \sigma^2 (2n)^{-1}} \right)$$

Example

A sample of size 10 with geometric mean 20 and GSD 5 has a 75th percentile of exp{log(20) + 0.6745 × log(5)} = 5.88.

The standard error of the log 75th percentile is $(\log(5)^2/10 + 0.6745^2 \times \log(5)^2 / 20)^{0.5}$ = 0.245.

A 90% confidence interval for the 75th percentile is then given by exp(log(5.88) ± 1.6449 × 0.245).

Often, rather than assuming a lognormal distribution, an empirical estimate of a percentile will be taken directly from the ranked exposure data. In these cases an approximate 90% confidence interval for the percentile is given by:

Lower endpoint: $\quad p / \exp\left(1.6449 \sqrt{\sigma^2 n^{-1} + z_p{}^2 \sigma^2 (2n)^{-1}}\right)$

Upper endpoint: $\quad p \times \exp\left(1.6449 \sqrt{\sigma^2 n^{-1} + z_p{}^2 \sigma^2 (2n)^{-1}}\right)$

Tables A2-1 and A2-2 give the multiplicative values required to obtain a 90% confidence interval for a 75th and 95th percentile of a variety of geometric standard deviations and sample sizes. For example for an empirical 75th percentile of 100 mg min^{-1} from a dataset of 50 measurements with a GSD of 6 a 90% confidence interval for the percentile is 63 mg min^{-1} (100 /v1.59) to 159 mg min^{-1} (100v×v1.59). Confidence

intervals become wider (less certain) with greater exposure variability and narrower with increasing sample size.

Table A2-1: Scaling factors to obtain a 90% confidence interval for a 75th percentile with a variety of sample sizes and GSDs

		Geometric standard deviation								
		2	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Sample size	**5**	1.75	2.45	3.10	3.71	4.31	4.88	5.45	5.99	6.53
	10	1.49	1.88	2.22	2.53	2.81	3.07	3.31	3.55	3.77
	20	1.33	1.56	1.76	1.93	2.08	2.21	2.33	2.49	2.56
	50	1.20	1.33	1.43	1.51	1.59	1.65	1.71	1.76	1.81
	100	1.13	1.22	1.29	1.34	1.39	1.43	1.46	1.49	1.52

Table A2-2: Scaling factors to obtain a 90% confidence interval for a 95th percentile with a variety of sample sizes and GSDs

		Geometric standard deviation								
		2	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Sample size	**5**	2.19	3.45	4.78	6.15	7.55	8.99	10.45	11.93	13.44
	10	1.74	2.40	3.02	3.61	4.18	4.72	5.25	5.77	6.28
	20	1.48	1.86	2.19	2.38	2.75	3.00	3.23	3.45	3.67
	50	1.28	1.48	1.64	1.78	1.90	2.00	2.10	2.19	2.27
	100	1.19	1.32	1.42	1.50	1.57	1.63	1.69	1.74	1.79

Appendix 3: Reverse Reference Scenario Example

This example reflects primary exposure of professional and non-professional remedial treatment of timber using wood preservative containing 0.5% active substance pastes by brush, trowel, caulking gun and gloved hand. This task is performed for approximately 30 minutes per day.

There are no generic exposure data for application of pastes. In the absence of generic data or a suitable mathematical model, an option is to assess the maximum exposure to the active substance, which would allow for an acceptable Assessment Factor (AF) based on an appropriate NOAEL and then assess the likelihood that exposures will exceed this level.

The maximum amount of active substance allowable can be calculated by dividing the NOAEL by the appropriate AF. Assuming a NOAEL of 25mg kg^{-1} d^{-1} and an AF of 100, the maximum amount of active substance is given by:

$$NOAEL/AF = 25/100 = 0.25mg\ kg^{-1}\ d^{-1}$$

For a non-volatile paste it is assumed that inhalation exposure is negligible and so assuming dermal absorption of 10%[4], to exceed an AF of 100, active substance contamination to the skin would need to exceed:

$$0.25\text{mg kg}^{-1}\text{ d}^{-1} \times 10 = 2.5\text{mg kg}^{-1}\text{ d}^{-1}$$

[Although in many cases the AF is 100, the value of the AF should always be considered first and 100 is not to be taken as a default.]

If the operator weighs 60 kg then active substance contamination would need to exceed:

$$2.5\text{mg kg}^{-1}\text{ d}^{-1} \times 60\text{kg} = 150\text{mg d}^{-1}$$

As the maximum concentration of active substance in the ready-for-use paste formulation is 0.5% w/w, then the weight of paste product containing 150mg active substance will be

$$150/0.5 \times 100 = 30{,}000\text{mg}$$

Assuming that dermal exposure will be predominantly to the hands and that gloves are worn, then rate of actual dermal exposure to the hands inside gloves is required to exceed:

$$30{,}000\text{ mg} / 30\text{ min} = 1{,}000\text{ mg min}^{-1}$$

The worked examples database for professional users contains approximately 400 measurements of actual hand exposure inside gloves across a wide range of tasks. The maximum exposure to an in-use formulation is 360mg min^{-1} with a 95th percentile of 23mg min^{-1}. On this basis, for chronic exposure, it is concluded that a margin of safety of a least 100 will be achieved. This calculation is presented in the standard format in Table A3-1.

[4] The correction for dermal absorption is only necessary if in the study the NOAEL is derived from absorption through the used route of uptake is 100% (e.g. an oral study). If the study were a dermal study, then there should not be a correction for dermal absorption.

Table A3-1: Presentation of reverse reference scenario exposure assessment in standard format

Application of curative pastes

Product	
active substance % w/w	0.50%
Potential body exposure	
Indicative value mg/min	0
Duration min	30
Potential dermal deposit mg	0
Clothing type	Cotton coveralls, 20% penetration
Clothing penetration %	20%
Actual dermal deposit [*product*] mg	0
Hand exposure	
Indicative value mg/min (actual)	1,000
Duration min	30
Potential hand deposit mg	30,000
Mitigation by gloves	None
Actual hand deposit [*product*] mg	30,000
Total dermal exposure	
Total dermal deposit [*product]* mg	30,000
Active substance mg	150
Dermal absorption %	10%
Systemic exposure via dermal route mg	15
Exposure by inhalation	
Indicative value m^3/min	0
Duration	30
Inhalation rate m^3/h	1.25
Mitigation by RPE	None
Inhaled [*product*] mg	0
Systemic exposure via inhalation route mg	0
Systemic exposure	
Total systemic exposure a.i. mg	15
Body weight kg	60
Systemic exposure mg kg^{-1} day^{-1}	**0.25**

Chapter 4

Risk Characterisation