

Human Exposure to Biocidal Products: Evolution of the Technical Notes for Guidance

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Overview

- Main changes and reasoning behind the changes
 - TNsG 2002
 - User Guidance 2004
 - Revised TNsG 2007

- Participants

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User Guidance

- Participants

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- Biocidal Products Directive 98/8/EC came into force in May 2000
- Specific guidance on exposure assessment for biocides
- HSE had previous extensive experience of exposure assessment for non-agricultural pesticides (wood preservatives, antifoulants, insecticides) and this experience along with the data that HSE had generated to support these assessments formed the core of the guidance document
- This guidance document was very comprehensive and incorporated a huge wealth of information that was relevant to biocides but wasn't always completely clear about which default values, data sets etc should be used
- Paper-based

Indicative distributions

Median deposit, mg.min ⁻¹		Percentile	Low 4 mg.min ⁻¹	Medium 20 mg.min ⁻¹	High 100 mg.min ⁻¹	Top 500 mg.min ⁻¹
Deposition profile	Narrow (GSD 3.40)	50%	4	20	100	500
		75%	9	46	225	1150
		95%	30	150	750	3750
	Intermediate (GSD 5.19)	50%	4	20	100	500
		75%	12	60	300	1500
		95%	60	300	1500	7500
	Wide (GSD 7.06)	50%	4	20	100	500
		75%	15	75	375	1850
		95%	100	500	2500	12500

Indicative distributions (2)

Deposition profile	Deposition rate			
	Low	Medium	High	Top
Narrow	Solvent based timber pre-treatment	Amateur antifoulant brushing		
	Cabbed orchard spraying	AF net deployment		
Medium		Water-based timber pre-treatment Antifoulant mix & load	Antifoulant spraying	Sheep dipping
Wide	Public hygiene insecticides (solid)	Public hygiene insecticides (liquid)	Remedial biocide spraying Uncabbed orchard spraying	

Launched the development of BEAT

Motivation for User Guidance

- Lack of consensus between member states over choice of exposure percentiles
 - Arguments were put forward that, depending upon the GSD and the relative levels of between and within worker variation, a significant proportion of workers could be over-exposed (long term average exposure greater than the level of concern) if the 75th percentile were used
 - 95th or 99th percentile proposed (for chronic exposure)

Motivation for User Guidance

- Counter arguments:
 - Unlike datasets of industrial inhalation exposure, the biocide data sets are of well-defined tasks with the same product, conditions etc. Most of the variation is therefore day-to-day, not between workers.
 - Using 95th percentiles for body, hands, inhalation along with conservative assumptions about the efficacy of PPE, bodyweights, dermal absorption is overly conservative.
 - No widespread evidence of ill-health or high levels of systemic exposure (biological monitoring)

Outcome: working group set up to develop User Guidance

User Guidance

Main changes for the 2004 User Guidance

- Streamlined
- Supplement TNsG not replace it
- Rules for selection of exposure percentiles
- Selection of the best data sets
- Revised flowchart
- Worked examples for rodenticides and wood preservatives

Selection of percentiles

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. 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 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.

Selection of percentiles

- An alternative would have been to use an upper confidence interval for the 75th percentile
 - Even for the largest datasets e.g. Public hygiene insecticide spraying and remedial wood preservatives (TNsG v1 spray models 1, 2) the upper confidence limit would have been considerably higher than values used previously
 - Applied to inhalation, body and hands along with other conservative assumptions could lead to possible problems with products previously considered safe

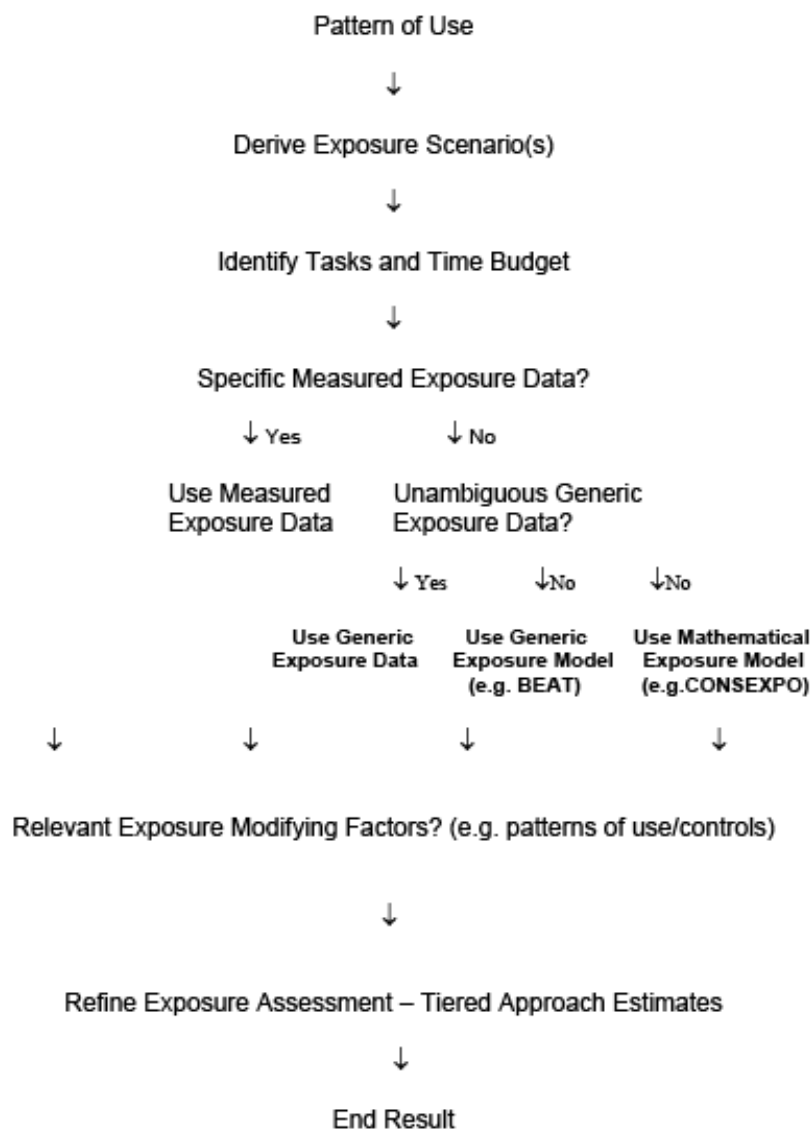
Selection of percentiles

- Philosophy behind criteria was sound:
 - Small data sets > greater uncertainty > more precaution
 - Introduced quantification of statistical uncertainties even if they weren't utilised in a nice manner
 - Should be viewed as an interim measure before the adoption of proper probabilistic methodologies?
- Criteria applied to the 'best' datasets in the TNsG v1 to produce streamlined tables of indicative exposure values (User Guidance Annex 4)

User Guidance: worked examples

- Comprehensive worked examples for wood preservatives and rodenticides
 - Wood preservatives has been assessed for many years and a number of workplace surveys conducted
 - Narrower range of products and exposure scenarios for rodenticides – reliance on theoretical calculations

User Guidance: flowchart



TNsG 2007: Aims

- Development of worked examples for each product type
- Development of a comprehensive list of formulation types for each of the 23 product types
- Development of a comprehensive description of patterns of use for all product types
- Development of a series of relevant secondary exposure scenarios covering all 23 product types.

TNsG 2007: further aims

- Development of a series of exposure databases and models that cover worker use scenarios.
- Development of screening models, such as CONSEXPO, and other approaches for estimation of consumer exposures.
- Written report for stakeholders
- Competitively tendered

Thinking behind TNsG 2007

- *There is an increasing proliferation of exposure data sets relevant to biocides. Presenting all these data in a revised user guidance will be confusing for applicants trying to identify appropriate exposure values for use in an exposure assessment.*
- *The user guidance tried to streamline the number of data models by selecting the 'best' data model from those presented in the TNsG. This may have created further confusion.*
- *Some datasets could be merged e.g. the existing data on antifoulant spraying and the riskofderm antifoulant spraying data set. However, currently there are no guidelines for deciding when this should be done and on what basis. Merging datasets could compromise transparency and the resulting deviations from earlier documents would cause confusion.*

Looking at Part II of the 2002 TNsG

- 1 SPECIFIC GUIDANCE ON EXPOSURE ESTIMATION - covered again in the user guidance
- 2.3 Options for exposure reduction and personal protective equipment (PPE) - to be re-visited during the current project
- 3.2 Patterns of use statements by biocidal product type - this is a key part of the current project
- 3.3 Database models - needs to be revised to include new data
- 3.4 Mathematical models - revised in the user guidance
- 3.5 Defaults for non-professional use and format for exposure estimation - this information will be used in the current project

Suggestion:

‘withdraw Part 2 of the TNsG and make the final report of the current project its replacement. We should consider how we could allow a more continuous revision of both the exposure data and the worked exposure scenarios - a web-based database being the obvious long term solution’

New data identified (2006)

- 11 data sets of measurements of exposure to biocidal products
- 10 data sets of measurements of tasks relevant to biocides
- Selection of data?

New biocide data (circa 2006)

Scenario	Dermal	Inhalation	N	Included in BEAT?
Antifoulant paint; spraying	Yes	Yes	18	Yes
Antifoulant paint; lineman	Yes	Yes	17	Yes
Antifoulant paint; mixing & loading	Yes	No	14	Yes
Laboratory disinfection; mixing & loading	Yes	No	16	Yes
Laboratory disinfection; large scale wiping	Yes	No	24	Yes
Laboratory disinfection; small scale wiping	Yes	No	6	Yes
Metal working fluids – machining (HSL)	Yes	No	31	Yes
Metal working fluids – machining (IOM)	Yes	Yes	8	Yes
Spraying of cleaning foam	Yes	No	12	Yes
Spraying of disinfectant foam – poultry housing	Yes	Yes	16	No
Wood preservatives (Austria)	Yes	Yes	80	No

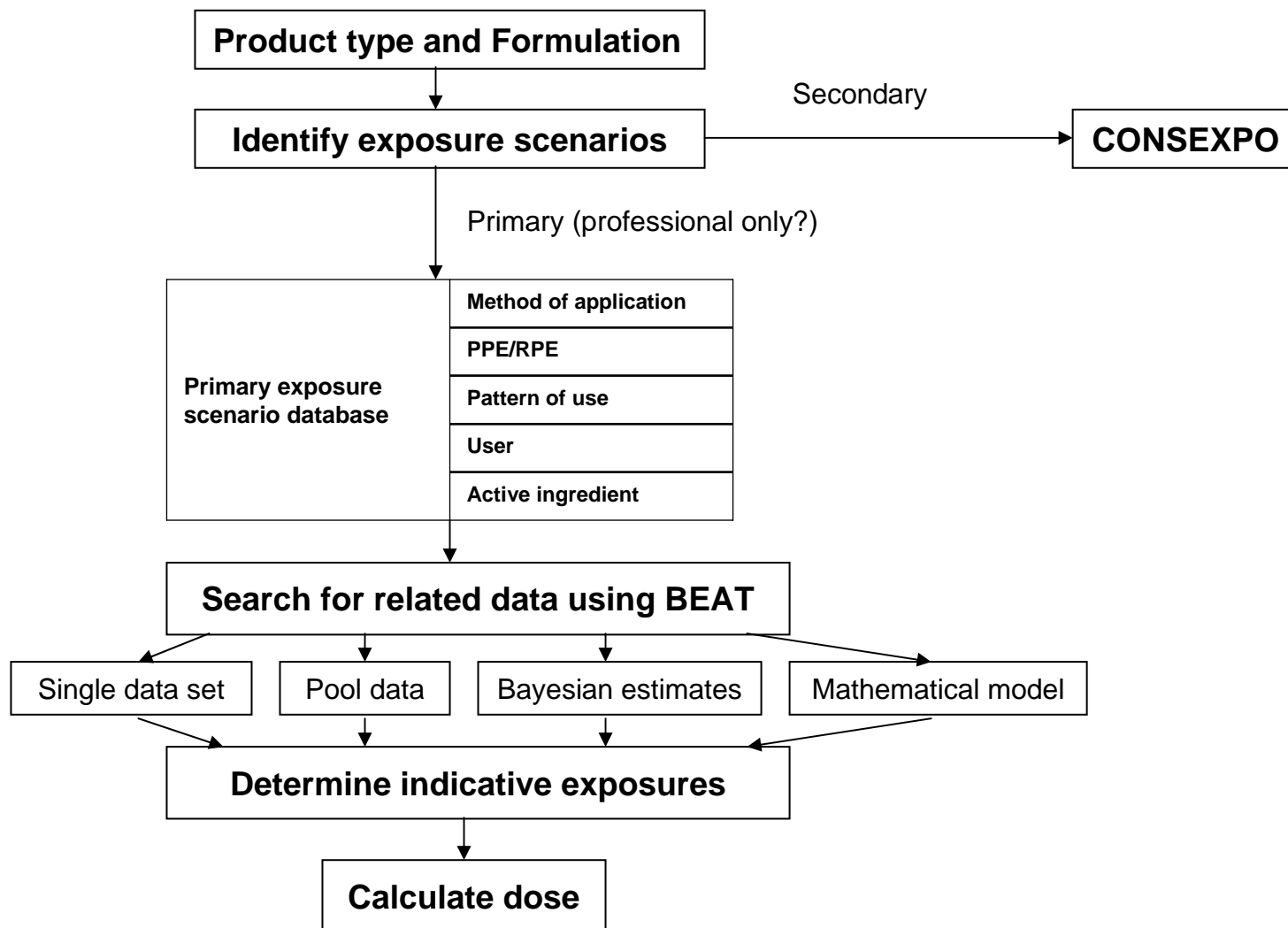
Data relevant to Biocides (circa 2006)

Scenario	Dermal	Inhalation	n	Included in BEAT?
Brushing; painting buildings	Yes	No	36	Yes
Mixing & loading; drug preparation	Yes	No	30	Yes
Mixing & loading; loading spray guns	Yes	No	30	Yes
Pouring; urine	Yes	No	30	Yes
Sawing of timber	Yes	No	29	Yes
Knapsack spraying; forestry	Yes	Yes	2	Yes
Airless pressure spraying; car bodies	Yes	No	30	Yes
Handling; forestry planting & packing	Yes	Yes	11	Yes
Handling; forestry planting	Yes	Yes	16	No

Way forward (project meeting 2006)

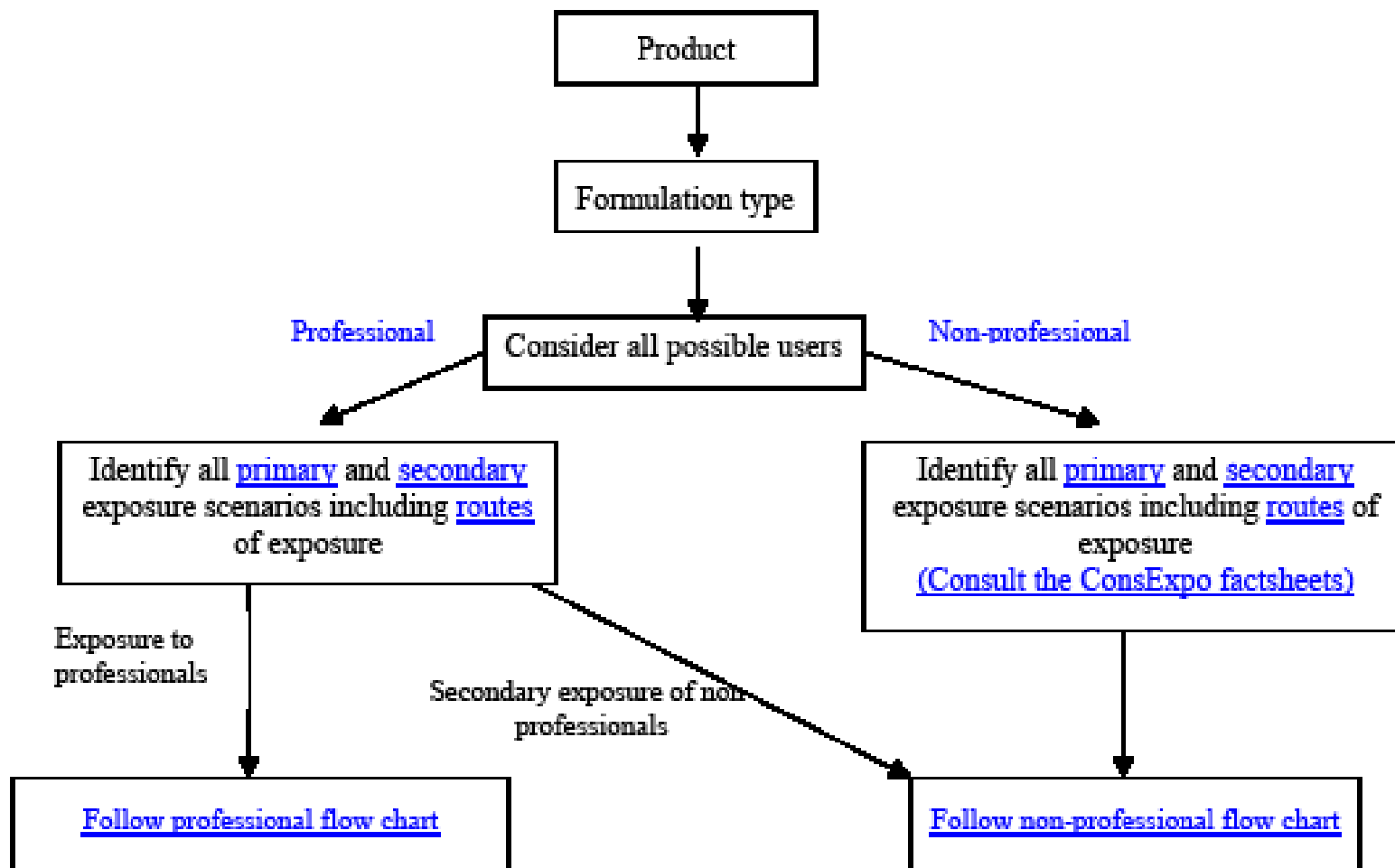
- Remove need to 'trawl' through TNsG
- Initiate a flow chart selection system
- Design a system that will continue to evolve
- Include all new exposure data & key existing ones and recommend that this database be the preferred source for obtaining indicative exposure values
- Develop a (primary) exposure scenario database for use by all biocide stakeholders that we populate with one example from each product type.
- Have the scenario database 'linkable' to BEAT, this would allow the BEAT rule-base to suggest suitable datasets but would not commit the user to the Bayesian exposure estimates

Flow chart – early version



Flowcharts: final versions

Figure 1: Identifying users and exposure scenarios



Flow chart for primary exposure to professional users

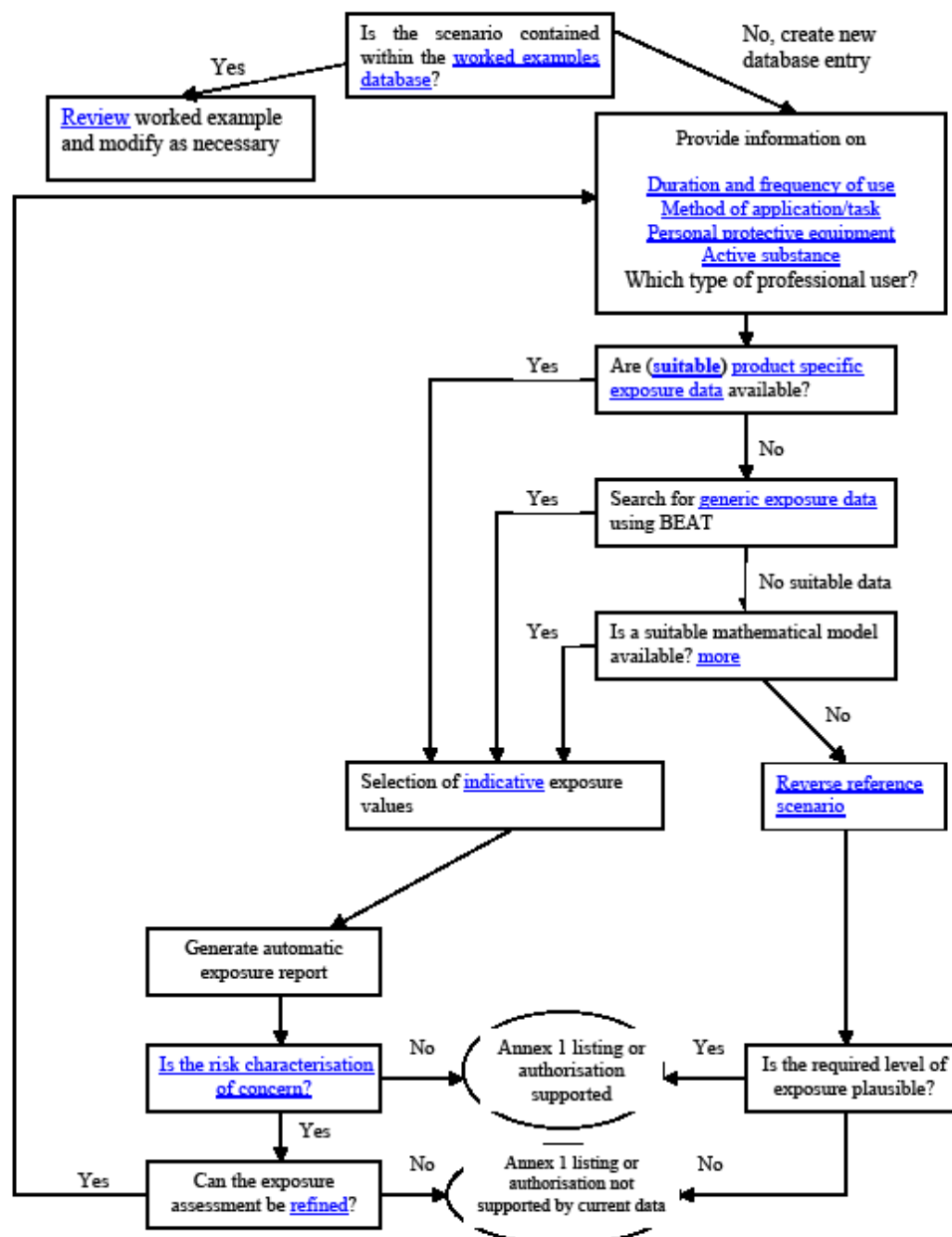
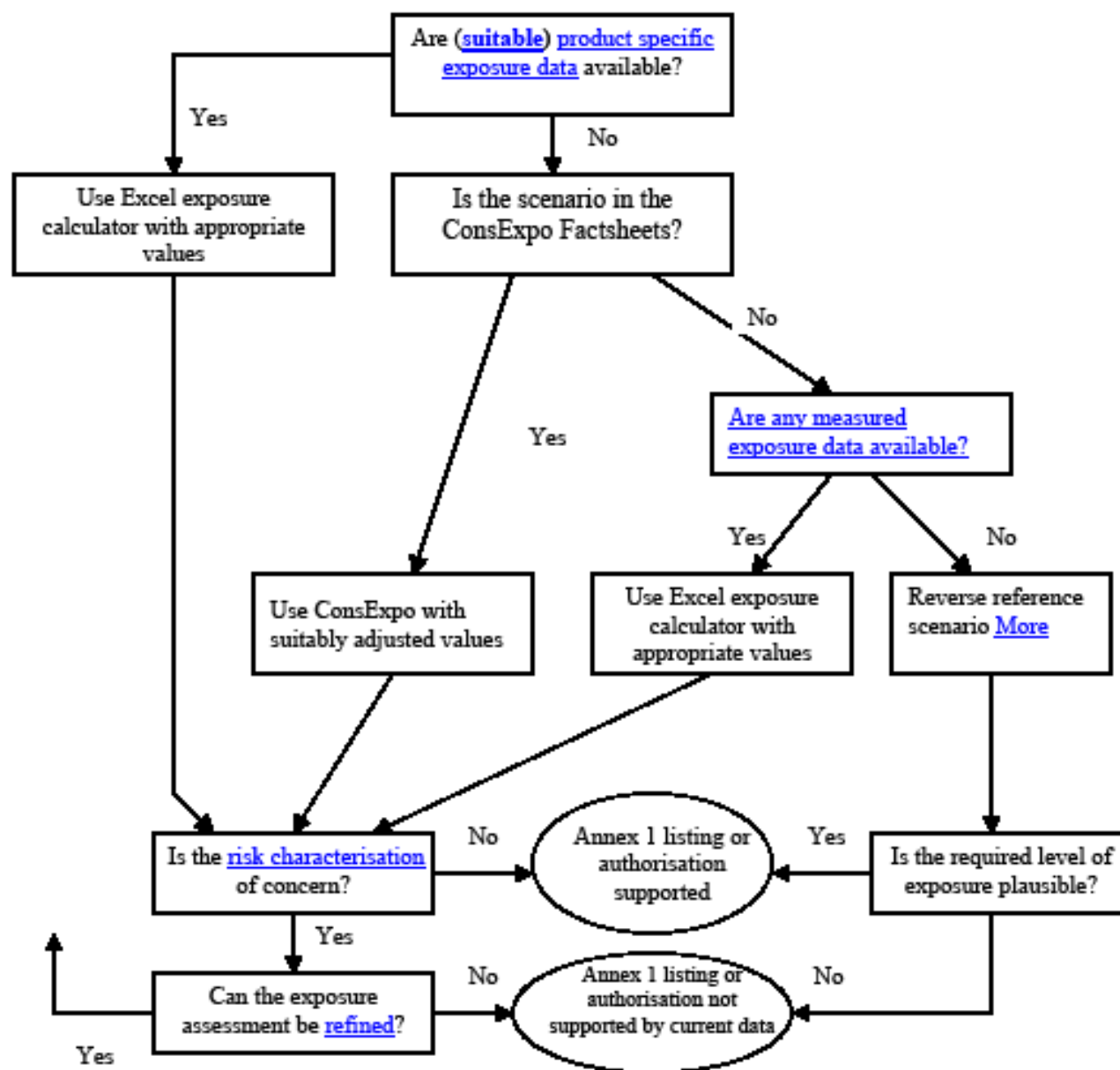


Figure 4: Flow chart for non-professional users



Worked examples database

- Existing TNsG and User Guidance
 - Written worked examples
 - Tables of summary exposure statistics for generic data
 - Difficult to find information
 - Not updateable
- Worked examples database
 - Primary exposure of professionals
 - Worked examples stored in electronic form
 - Electronic database of measured exposure data
 - Individual measurements
 - Contextual information
 - Photographs
 - Addition of new data
 - Search algorithms linking worked examples to measured data
 - Facility to export calculation of systemic dose to Excel

Worked examples database

- At least one worked example for each product type (30 in total)
- Information on
 - Tasks
 - Product
 - Task specific exposure determinants
 - Environment and control measures
 - PPE
 - Pattern of use – frequency and duration
 - Physiological parameters – bodyweight & respiration rate
 - Indicative exposure values
 - Active substance

Generic exposure data

- 70 scenarios
- 1200 potential body exposures
- 1200 hand measurements
- 600 inhalation measurements

- Contains most of the data described in the user guidance
- Other data in Annex 1 of draft report:
 - Mixing and loading of agricultural pesticides
 - Non-professional simulation studies
 - Volatile inhalation data

Selecting exposure values

- Product specific data
- Generic data
 - Large number of data already contained in the system
 - Rule base suggests analogous data sets
 - Body, hands and inhalation
 - Automatic calculation of percentiles
 - Standard – based upon fitted lognormal distribution
 - Bayesian integration of multiple datasets
- Indicative exposure values from other data sources may be used:
 - Annex 1
 - Mechanistic exposure models

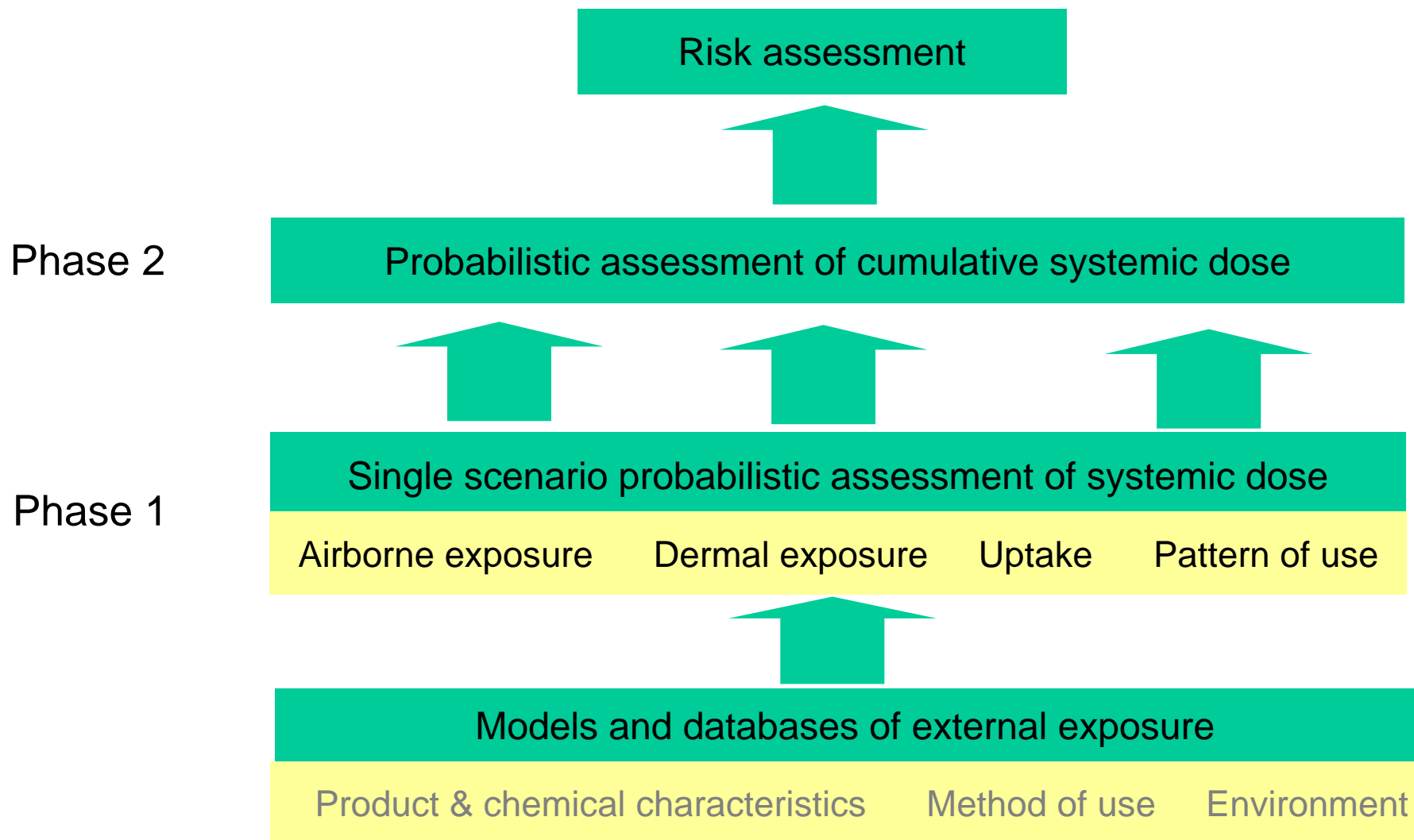
Further improvements

- Use pattern database
- Secondary exposure scenarios
- Inclusion of ConsExpo 4
- Complete set of information will be available on a CD
 - Also downloadable

Future developments ?

- New worked examples and data
 - Member states can add own scenarios/assessments
 - How are these incorporated into a new version?
- Probabilistic exposure assessments

Vision: A web-based hierarchy



Phase 1: Objectives

- Development of a web-based tool for probabilistic assessment of systemic dose from single occupational or consumer exposure scenarios
- Acute (single day) exposures
 - 2D Monte Carlo simulations **uncertainty x worker**
- Chronic (long-term average) exposures
 - '3D' Monte Carlo simulations **uncertainty x worker x day**
- Parametric and non-parametric characterisations of dermal and inhalation exposures
- Correlated external exposures
- Correlated physiological parameters
- Integration with existing databases of exposure data

Probabilistic exposure assessments

- First phase completed by HSL on behalf of HSE
 - Access presently restricted to HSE
 - Database to store assessments
- Choice of percentile & uncertainty
 - Still an issue but now relates to systemic exposure
 - Probabilistic assessments alongside current deterministic regulatory assessments ?

Concluding remarks

- Tension between writing prescriptive guidance, which leads to harmonisation, and gaining acceptance by all member states
- Tension between different users of the guidance:
 - Exposure assessors with a lot of experience and expertise do not need much guidance – desire is for their current approach to be compatible with guidance
 - Less experienced assessors want guidance that clearly sets out the approved methodology
 - Consultancy companies want to be confident that competent authorities will accept an assessment that follows the guidance

Concluding remarks

- We always tried to write the guidance in quite open terms i.e. not prescriptive allowing alternative defaults, data etc to be used, if justified
- Concern that member states should not seek to apply the guidance in a strict manner, though clearly consistency is important – more so between member states at any particular moment, than over time
- All the guidance is probably still useful – still some information that is only in TNsG v1
- Need for continued evolution

Acknowledgements

Joop van Hemmen



Thank you