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Treatment of exposure data in BEAT

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Oslo, February 24th 2009

Overview

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- Many of the underlying measurements in BEAT are the same as those underpinning the 2002 TNsG. Their treatment however differs.
- Present the main differences
  - Are some approaches better than others?
  - How big an impact on assessments might/ought these differences make?

Summary

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- Inclusion criteria
- Lognormal vs. empirical percentiles
- Selection of percentiles
- Treatment of non-detects
- Units/density correction
- Wood preservatives
  - Industrial pressure treatment
  - Austrian study

Inclusion criteria

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- BEAT originally designed as a task-based model for potential dermal exposure
  - Dermal exposure studies (with or without inhalation)
  - Measurements of potential dermal exposure or exposure inside gloves
  - Non-volatile
  - HSE biocide data, RISKOFDERM data, some TNO data, Austrian wood preservative study
- Excluded:
  - Agricultural studies e.g. EUROPOEM mixing and loading
  - Volatile inhalation data
  - Consumer exposure studies measured using fluorescence
    - Different body regions

Types of percentile

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- Earlier guidance indicated that both fitted and empirical percentiles were acceptable
  - Data models presented empirical percentiles
- BEAT provides percentiles based upon fitted lognormal distributions
  - Individual data points are available so empirical percentiles are also possible

Are exposures log-normally distributed ?

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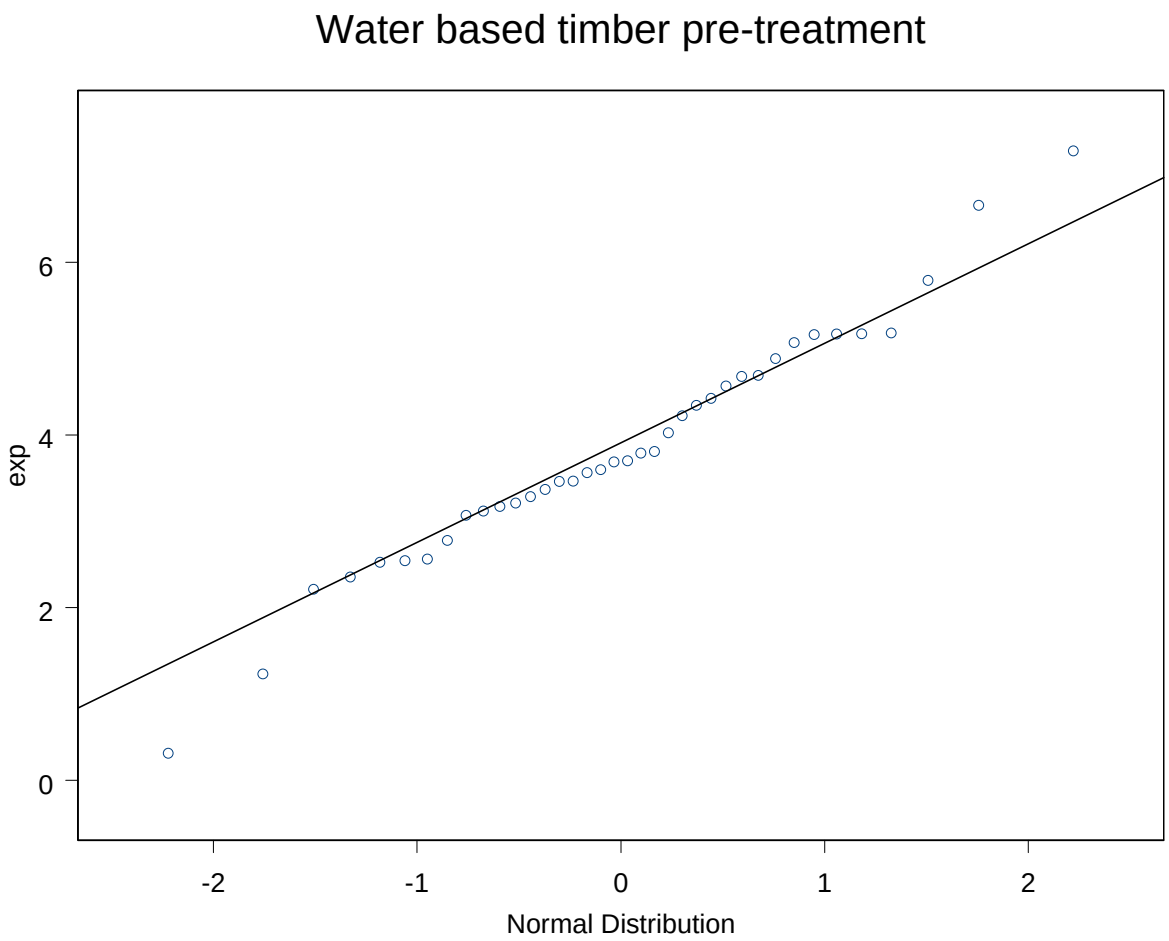
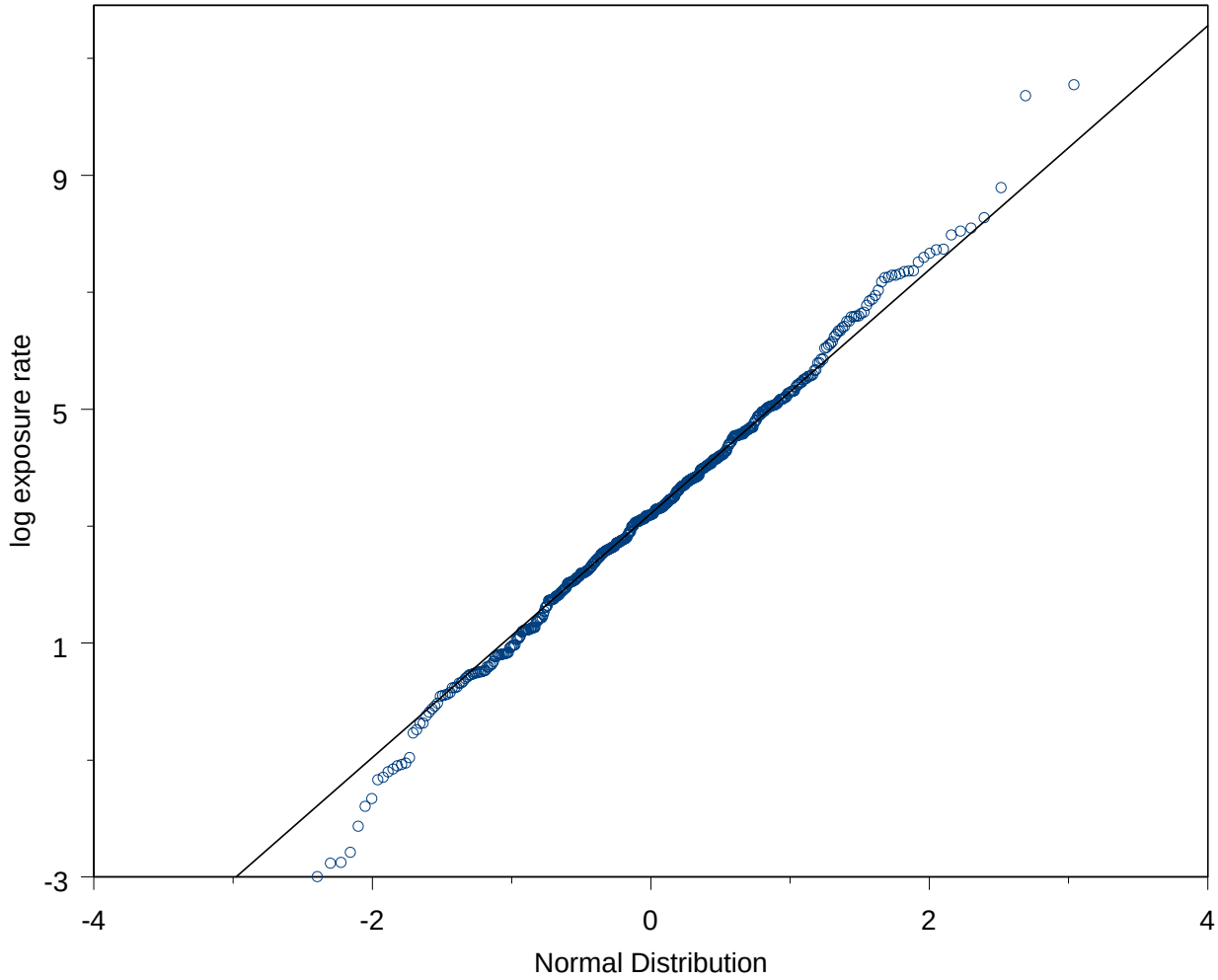
- Statistical goodness of fit tests, although available, are of limited use:
  - Small data sets > little power > rarely rejects lognormal hypothesis
  - Large data sets > small departures from log normality lead to rejection

- Do we assume a lognormal distribution unless there is evidence to the contrary **or** use non-parametric approach unless we can demonstrate a log normal distribution?
  - Why view data sets in isolation?

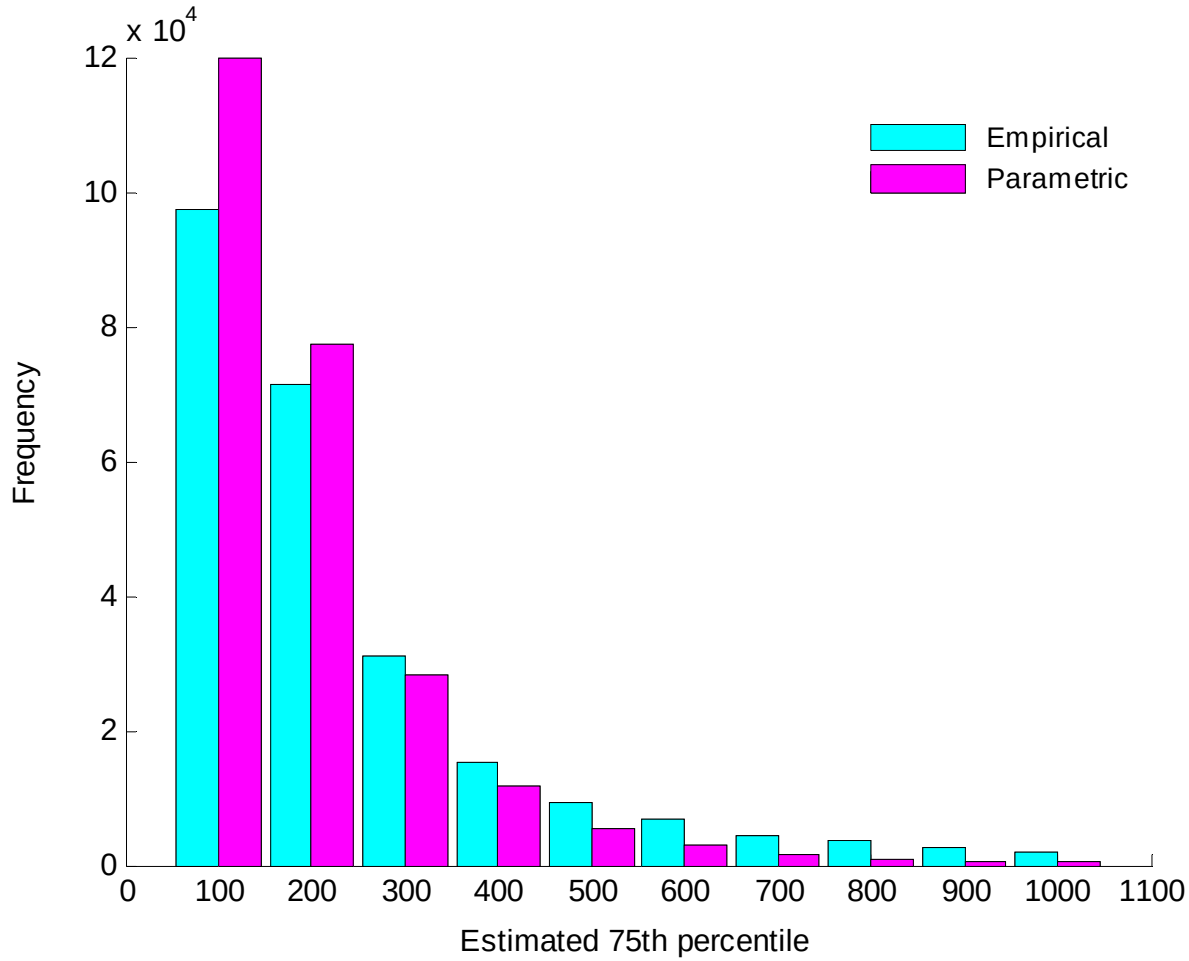
Dermal exposure to wood preservatives



Mixed distribution of 421 dermal measurements



Sampling distributions for estimators of the 75th percentile (n=10)



Selection of percentiles

- User guidance gave criteria for the 75th %ile, 95th%ile and maximum value
  - Criteria applied with an element of expert judgement to derive indicative values in Annex 4
- BEAT uses the first of these criteria to recommend either the 75th or 95th percentile
  - Applied strictly – but only a first recommendation

Selection of percentiles

- Fitted 95th percentile can sometimes exceed the maximum observed exposure
  - Dipping of timber articles: n=5, fitted 95th 1040 ul/min, max =444 ul/min
  - AF brushing: n=10, fitted 95th 63 ul/min, max 67 ul/min
  - Solvent based vacuum pressure treatment n=19, fitted 95th =25 ul/min, max =8.5 ul/min
- Not necessarily a bad thing - with small data sets the maximum value may vary enormously

  –*'according to the log-normal distribution even extreme exposure levels may occasionally occur. It is obviously not likely that such extreme exposure values are captured by small measurement series. Hence, selecting the highest values among limited measurement series is not a valid strategy'* TNsG v1 P2 1.6

Treatment of non-detects

- BEAT:
  - Fitting lognormal distributions: treated as censored (e.g. 0-1mg/m^3)
  - Histograms: half LOD substituted
  - Export: lower and upper bounds

- TNsG 2002:
  - Percentiles reported for non-zero results
    - e.g. Garden timber treatment 15 data, 9 zero values, 50th percentile of non-zero values =1.63mg/m^3 (TNsG v1 part 2, page 202)

Non detects in BEAT - detail

- For non-detects to be treated as censored the LOD must have been entered in the database
- Exposures recorded as ND are excluded from statistics
- Between Version 1.7 (June 2007) and V1.71 (May 2008) missing LODs determined from original sources
  - Mainly HSE public hygiene insecticide data set and solvent based vacuum treatment
  - Indicative exposures for worked examples not recalculated

Units and density correction

- 2002 TNsG and User guidance mg/min and mg/m^3
- BEAT
  - liquids: ul/min and ul/m^3
  - Solids: mg/min and mg/m^3
  - Incorrectly given as mg/min on histogram on ‘Statistics for measured scenarios’ form
- However, indicative exposures in 2007 TNsG (Annex 1) remain in mg/min
- History?
-

Units and density correction

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- Do the units matter?
  - Not for the majority of biocides which are water-based or have densities close to 1
  - Density antifoulants ranges from 1.3 to 2.5

- Analyte (mass)>conc. (w/w) > exposure (formulation, mass)
- Analyte (mass)>conc. (w/v) > exposure (formulation, volume)
- Provided the correct concentration is used in the exposure assessment to convert back from product to a.i. the same result should be obtained
- Density of product under review different to that in the exposure study?

Units and density correction

- Density of product under review different to that in the exposure study?
- If the same task is done with two liquids of similar viscosity but different densities should the exposure (distribution) be the same in terms of mass or volume?
  - If the assumption is mass then using mg/min requires no density adjustment
  - If the assumption is volume:
    - mg/min requires a density adjustment (requires densities of both the current product and products in measurement study)
    - ul/min does not require density adjustment, however w/v conc. must be used

Timeline of units in BEAT

- Originally in mg/min (mg/m^3) for liquids and solids
- RISKOFDERM project assumed equivalence of exposure in terms of volume (liquids)
- RISKOFDERM data imported into BEAT
  - IOM antifoulant data imported with w/v conc.
- Units displayed in BEAT changed to ul/min (worked examples)
  - Worked example for mixing and loading Afs prepared?
- Densities for products in HSE studies (prof. & amateur) obtained and conc. in BEAT database converted from w/w to w/v

Mixing and loading AF

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- Worked example in BEAT
  - Potential body exposure 107 ul/min (75th IOM dataset)
  - Potential hand exposure 462.7 ul/min (75th IOM dataset)
  - Inhalation exposure 13.64 ul/m^3 (95th HSE dataset)
- However BEAT gives this last value as 4.3 ul/m^3
  - Inhalation value derived before units re-calculated for HSE studies ?

Wood preservatives

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- Vacuum pressure treatment
- Expressed as a rate rather than per cycle
- Taking the exposures in mg/cycle and dividing by the nominal length of the cycle gives lower rates of dermal exposure than BEAT (when comparing empirical percentiles). However, looking at the durations of measurements indicates that in practice cycles are typically shorter than 180 minutes hence the higher rate when dividing the dermal deposit by the actual duration.
- Using the values in BEAT with a nominal cycle time of 180 minutes will be precautionary
- Total dermal depositions in BEAT have been checked for agreement with the original data spreadsheets

Wood preservatives

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- Austrian study (application by brush)
- Data converted from total exposure to active substance to rate of exposure to in-use fluid.
- Split into two datasets: solvent-based and water-based
- Insufficient detail to determine use rates
  - Use rate is a parameter in the BEAT similarity algorithm and, as missing determinants are ignored, this study may be promoted to a higher position in the search results

Wood preservatives

- Brush painting sheds and fences (TNsG v2 page 63)

Exp route	TNsG	Worked example (BEAT)	Suggested model data (BEAT)
Hands (potential)	5.91 mg/min (75^{th} %ile)	20.3 ul/min (75^{th} %ile)	116 ul/min (95^{th} %ile)
Body (potential)	16.9 mg/min (75^{th} %ile)	15 ul/min (75^{th} %ile)	85.5 ul/min (95^{th} %ile)
Air	1.63 mg/m^3 (75^{th} %ile)	1.03 ul/m^3 (75^{th} %ile)	41.8 ul/m^3 (95^{th} %ile)

Investigation showed:

5.91 mg/min is the 6^{th} out 10 values so NOT the 75^{th} %ile

4 measurements in the TNsG appear to be based upon an erroneous concentration (traced back to original report, correct in BEAT)

Maximum air level is 62 mg/m^3 not the 8.03 mg/m^3 reported in the TNsG v1 P2 p 202

Concluding remarks

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- BEAT does not force the use of percentiles based upon lognormal distributions though it certainly promotes their use
  - This is a much a legacy of the purpose for which BEAT was originally developed than a preference for a parametric approach
- As all the underlying data are readily accessible other approaches can easily be evaluated
  - Count down the displayed list to obtain empirical percentiles
  - Export data to Excel

Concluding remarks

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- Data in BEAT have been extensively checked against original records

- In some cases significant errors in the data summaries presented in the TNsG 2002 have been identified.
  - e.g. dipping data based upon patch results with highest values excluded as outliers
    - Analysis of complete coveralls suggests results should be retained

Concluding remarks

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- Indicative values differ through choice of percentile, use of lognormal distributions, treatment of density, treatment of duration and data errors

- Differences between empirical and fitted percentiles are generally well within the statistical uncertainties in the data
  - Similar (risk) outcomes ought to be obtained
  - However, as uncertainties not properly considered, this might not be the current situation
    - Probabilistic exposure assessments

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Thank you