A systematic review of validation studies on ECETOC TRA worker exposure predictions

Is the ECETOC TRA v3.1 worker tool sufficiently conservative?

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Agenda

- Introduction
  - ECETOC TRA tool
  - Evaluation of performance (2010 – 2020)
  - Objectives for review
- Approach
  - Constructing databases with measured exposures
  - Constructing ECETOC TRA estimates
  - Comparison of measured data with TRA estimate
- Results
  - Tool performance for estimating inhalatory exposure
  - Tool performance for estimating dermal exposure
- Conclusions

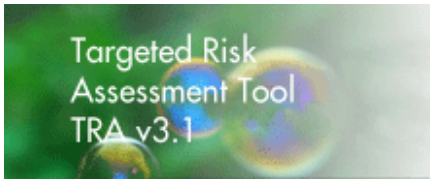
Introduction

ECETOC TRA* v3.1 worker tool

Developed by ECETOC, available on line, after registration: www.ecetoc.org/tra

ecetoc

EUROPEAN CENTRE FOR ECOTOXICOLOGY AND TOXICOLOGY OF CHEMICALS



TRA version 3.1 downloads

Download Consumer tool

- Consumer Tool user Manual

Download Integrated tool

- Integrated Tool User Manual (updated July 2017)

Supporting Documents

- TR 93: Targeted Risk Assessment (December 2004)
- TR 107: Addendum to TR 93 (December 2009)
- TR 114: ECETOC TRAv3: Background and Rationale for the Improvements (July 2012)
- TR 124: Addendum to TR114 : Technical Basis for the TRA v3.1 (June 2014)
- TR 131: Targeted Risk Assessment: Further Explanation of the Technical Basis of the TRA v3.1 (February 2018)
- FAQs – Download & Installation
- FAQs – Using the TRA Tool

Note: the online ECETOC TRA tools are updated in July 2017: version 3.1

** TRA: Targeted Risk Assessment*

Introduction

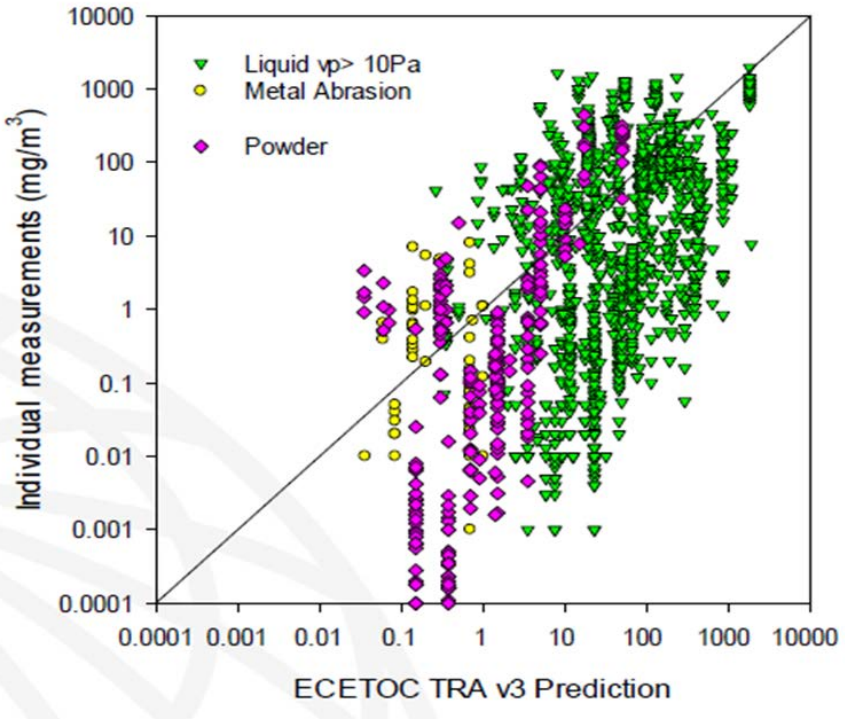
ECETOC TRA v3.1 worker tool

- Simple, easy to use, Tier 1 exposure tool
- Provides conservative estimate (75-percentile of exposure distribution) of both inhalatory (8hr TWA, peak) and dermal exposure (liquids, solids)
- Use of PROCs (Process Categories), type of setting (industrial/professional) and fugacity for providing base estimates. Further refinement of prediction using modifiers: e.g. ventilation, LEV, duration, concentration
- Widely used for REACH registrations but also for worker exposure assessments in the context of OSH

Evaluation of performance (2010 – 2020)

- Since 2010 several validation studies have been published on the performance of the ECETOC-TRA tool
- Most prominent one: the E-Team study (2014)
- Validation studies show mixed results
- Questions on validity of TRA tool as conservative screening tool

=> Installation of **ECETOC Expert Task Force**



E-TEAM project (2014): **E**valuation of **T**iered **E**xposure **A**ssessment **M**odels under REACH (www.eteam-project.eu , includes ECETOC-TRA, Stoffenmanager, EMKG Expo tool)

Introduction

Objectives

- Review published performance studies
  - inhalation exposure data + contextual information
  - dermal exposure data + contextual information
- Construction of TRA-estimates for scenario's with valid datasets
- Evaluation of TRA worker tool performance
- Identify potential tool improvements

Agenda

- Introduction
  - ECETOC TRA tool
  - Evaluation of performance by others
  - Objectives for review

- **Approach**
  - **Constructing databases with measured exposures**
  - **Constructing ECETOC TRA estimates**
  - **Comparison of measured data with TRA estimate**

- Results
  - Tool performance for estimating inhalatory exposure
  - Tool performance for estimating dermal exposure

- Conclusions

Approach

Constructing databases with measured exposures

- Identify studies that have evaluated ECETOC TRA and retrieve original publications with underlying datasets and workplace descriptions (where needed contacting the lead authors)

- Construct a database from published studies in Excel

- Develop a set of criteria for selecting valid (datasets in) studies, e.g:
  - Dataset should contain at least 6 measurements per scenario (N ≥ 6)
  - Quality of exposure data used (rating scale 1-4)
  - Quality of information elements (rating scale 1-4)
  - Representativity of measurements (e.g. reflecting personal exposure)
  - Sufficient information available to calculate a 75th percentile
  - Sufficient contextual information to assign PROC, setting, volatility, etc.

- Review process: lead reviewer, second reviewer, consensus

- Calculate 75th percentile (P75) for measured dataset with N $\underline{\geq}$ 6

Approach
Constructing ECETOC TRA estimates

- Based on available contextual information and complemented with generic industry knowledge
- Highlight any disagreement with original publication; provide justification for alternative selection
- If information on modifier was unclear, err on the side of conservatism, i.e., produce a lower TRA estimate
  - E.g., product with ~5% of substance: modelled as 1-5%, not 5-25% (TRA estimate would be 3x higher)
- Document all changes and decisions

Approach
Comparison of measured data with TRA estimate

- Measured data: 75th percentile (P75) of data (N $\geq$ 6) in dataset
- Data are log-normally distributed => comparison of logtransformed P75 and TRA estimate: log (P75) and log (TRA)
- Calculation of residuals: residual = log (TRA) – log (P75)

Note: negative residual means that TRA tool underestimates the measured P75

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Tool performance for estimating inhalatory exposure

Overview of datasets in database

- 14 published projects examining TRA performance (long-term inhalation exposure of workers)
- 129 valid scenarios covering 2272 measurements

Scenarios	# scenarios	# measurements
Liquids	119	2171
Solids	10	101
Not valid	10	60

Main sources	# scenarios	# measurements (illustr.)
E-team project	52	1045 (ART, NIOSH, SUVA)
CONCAWE	20	282
US NIOSH 2019	14	157
S. Lee (Korea)	18	103
Ishii (Japan)	7	72

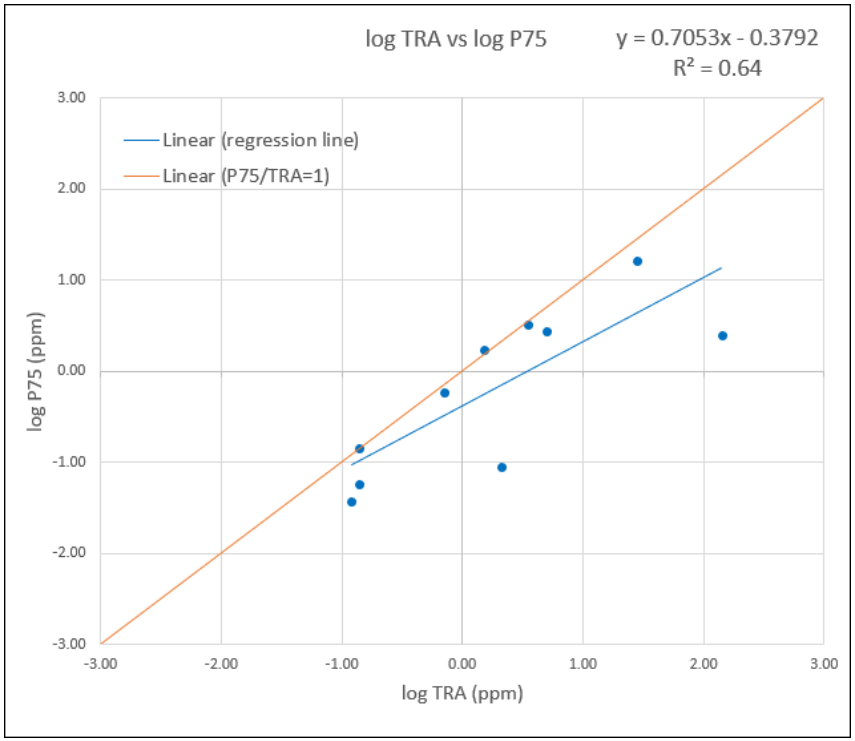
Tool performance for estimating inhalatory exposure

Changes in input variables for TRA estimate

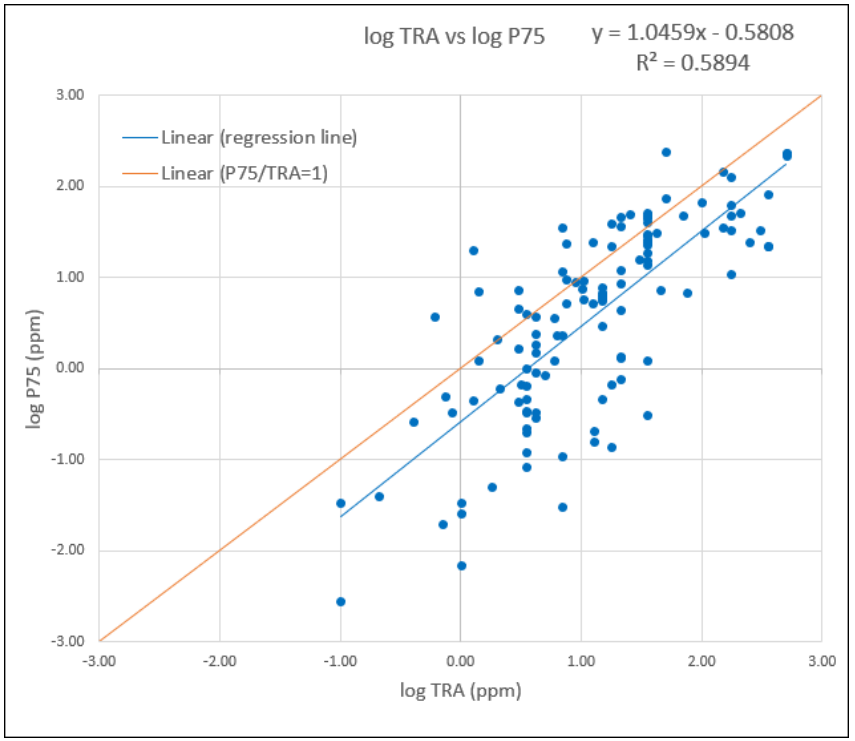
Parameter	Corrected (%)
PROC	25
Room ventilation status	16
Local exhaust ventilation	8
Setting (IND, PROF)	6
Application of duration factor	5
Concentration substance in product	3
Substance fugacity	1

Tool performance for estimating inhalatory exposure

Measured vs modelled exposure for solids and liquids



Solids

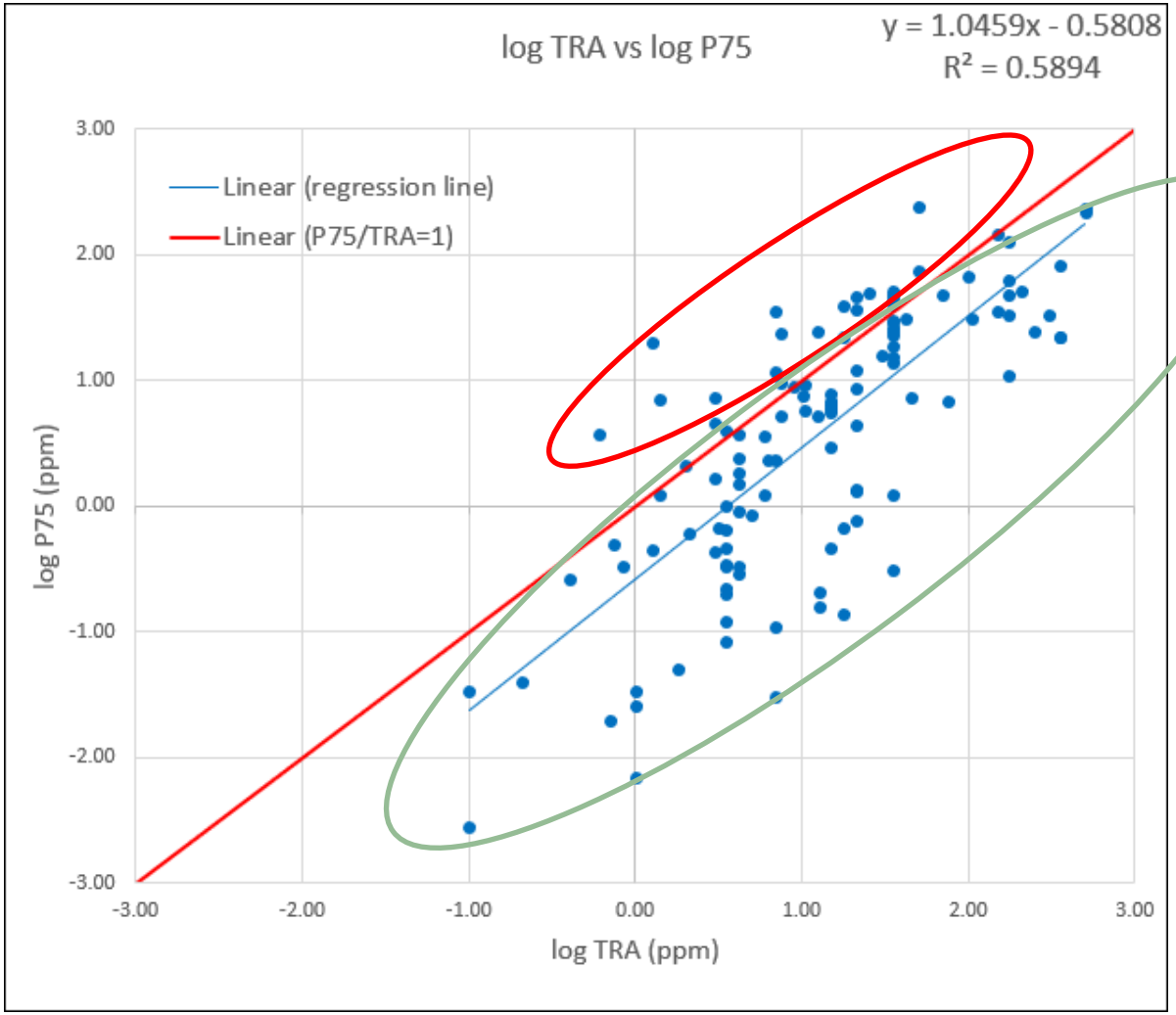


Liquids

Further analysis on liquids only (only 10 datapoints for solids)

Tool performance for estimating inhalatory exposure

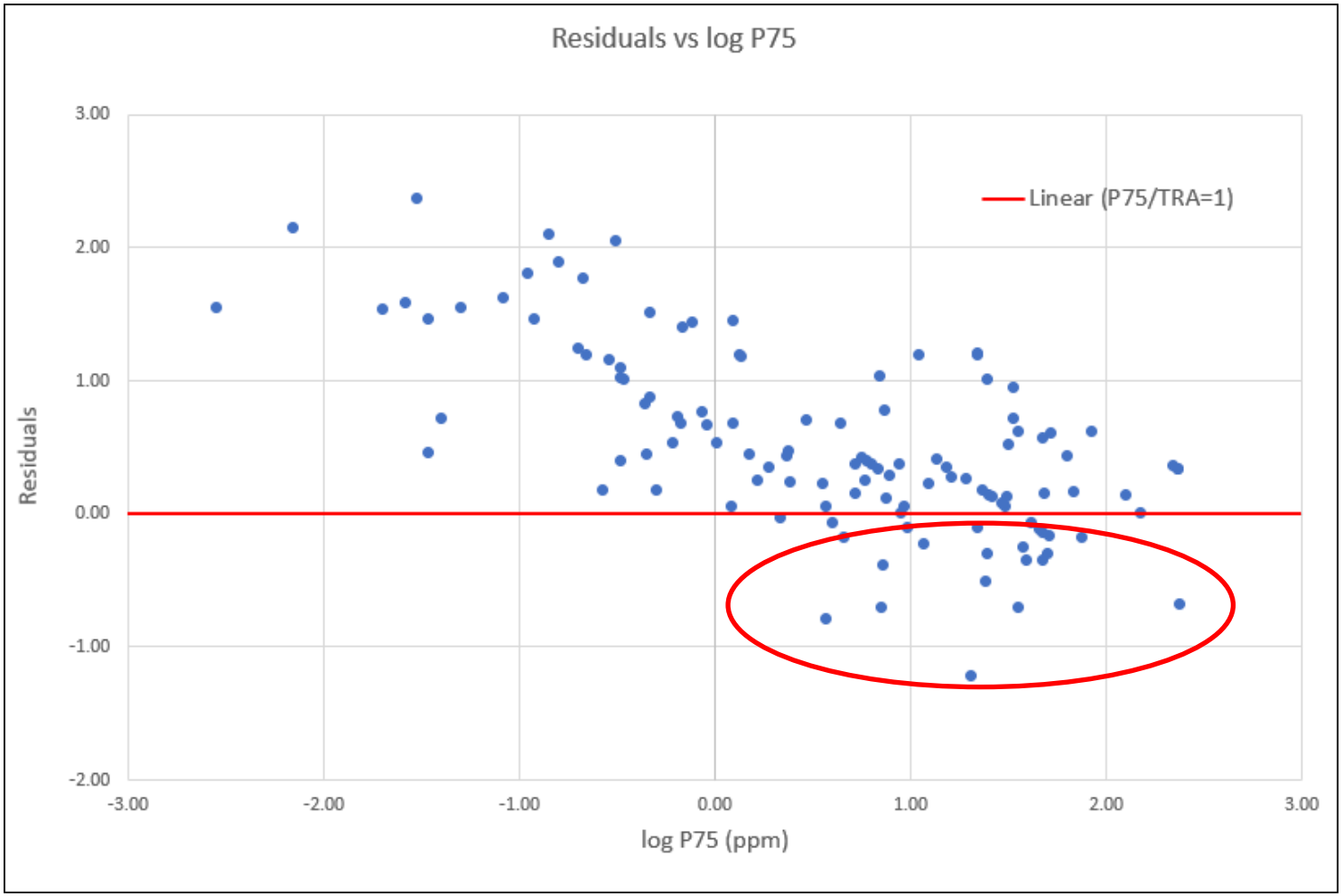
Measured vs modelled exposure for liquids only



23 out of 119 datasets with P75 > TRA (19 %)

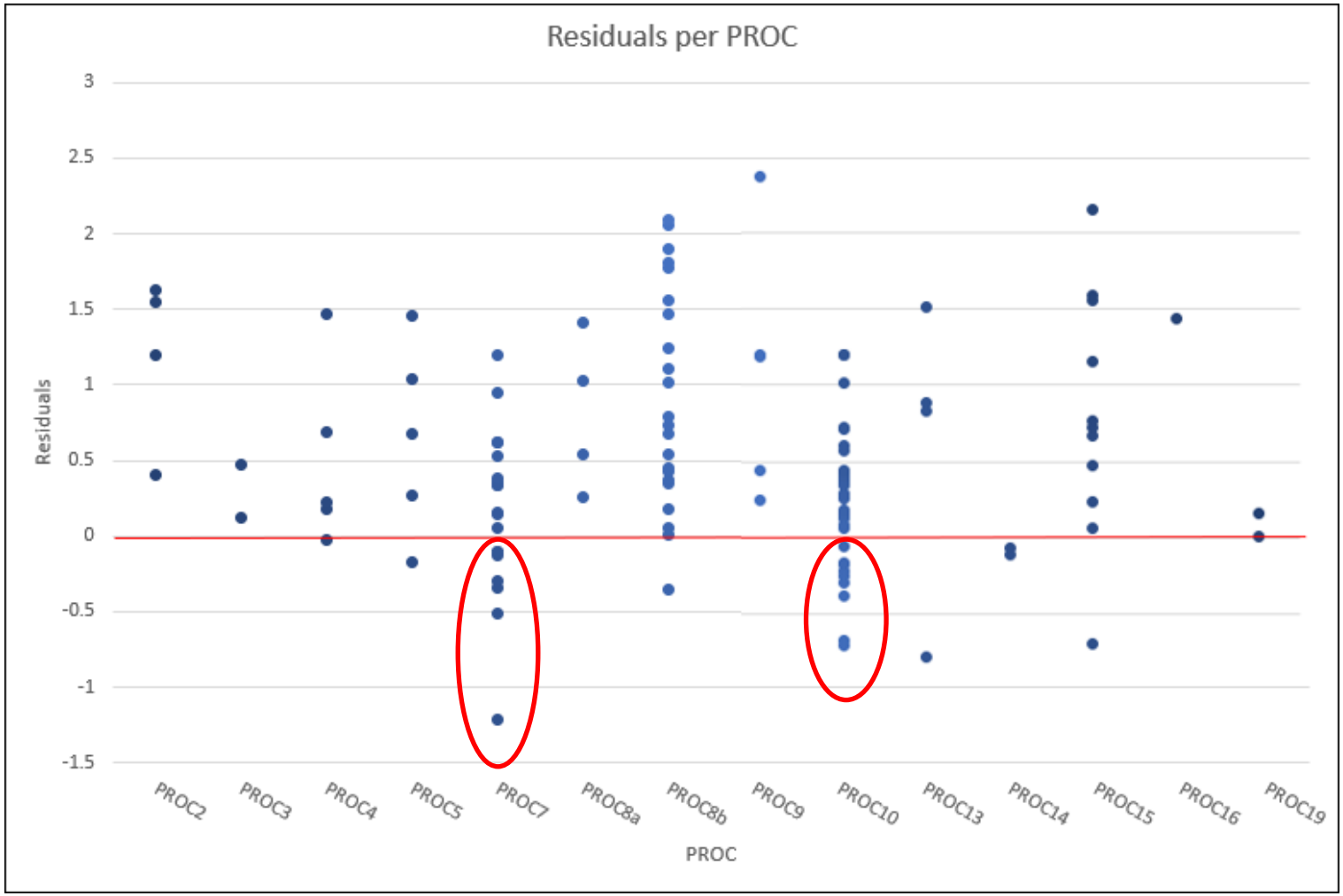
Tool performance for estimating inhalatory exposure

More underestimation at high exposure levels



Tool performance for estimating inhalatory exposure

Residuals per PROC



Tool performance for estimating inhalatory exposure

Probability of ‘false negatives’ for inhalatory risk ratio

- In the REACH risk assessment the outcome of the inhalatory exposure assessment is compared with the DNEL for inhalation:

  Risk Characterization Ratio (RCR) = Inhalatory exposure / $DNEL_{inhalation}$

  Note: DNEL: Derived No Effect Level

- If RCR < 1 than the risk is acceptable

- When applying the TRA in risk assessment, a ‘**false negative**’ is the situation

  – where the outcome of $RCR_{estimated\text{-}TRA} < 1$ (TRA/DNEL < 1)

  – while in reality $RCR_{measured\text{-}P75} \geq 1$ (P75 / DNEL ≥ 1)

Tool performance for estimating inhalatory exposure

Calculation of ‘false negatives’ for inhalatory risk ratio

- In the database (n=129) a selection has been made of the cases with $RCR_{estimated\text{-}TRA}$ < 1 (TRA/DNEL < 1) => n=80

  note: for 10 datasets no DNEL was available; instead the OEL (Occupational Exposure Limit value) has been used

- For these cases the P75/DNEL has been calculated; only for 3 of the 80 datasets the $RCR_{measured\text{-}P75} \geq 1$ (P75/DNEL $\geq$ 1)

- The probability of a ‘false negative’ outcome (based on comparison with the 75-percentile) is 3/129 = 2.3 %

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Tool performance for estimating dermal exposure

Overview of datasets in dermal database

- Dermal data used from 32 studies
- 82 valid scenarios covering 1719 measurements

Scenarios	# scenarios	# measurements
Liquids	21	881
Solids in liquids	36	554
Solids	25	284

Main sources	# scenarios	# measurements (illustr.)
Studies identified in Cefic LRI B16 project	52	1045 (ART, NIOSH, SUVA)
Cefic LRI B20 project (simulation of PROCs)	20	282

Tool performance for estimating dermal exposure

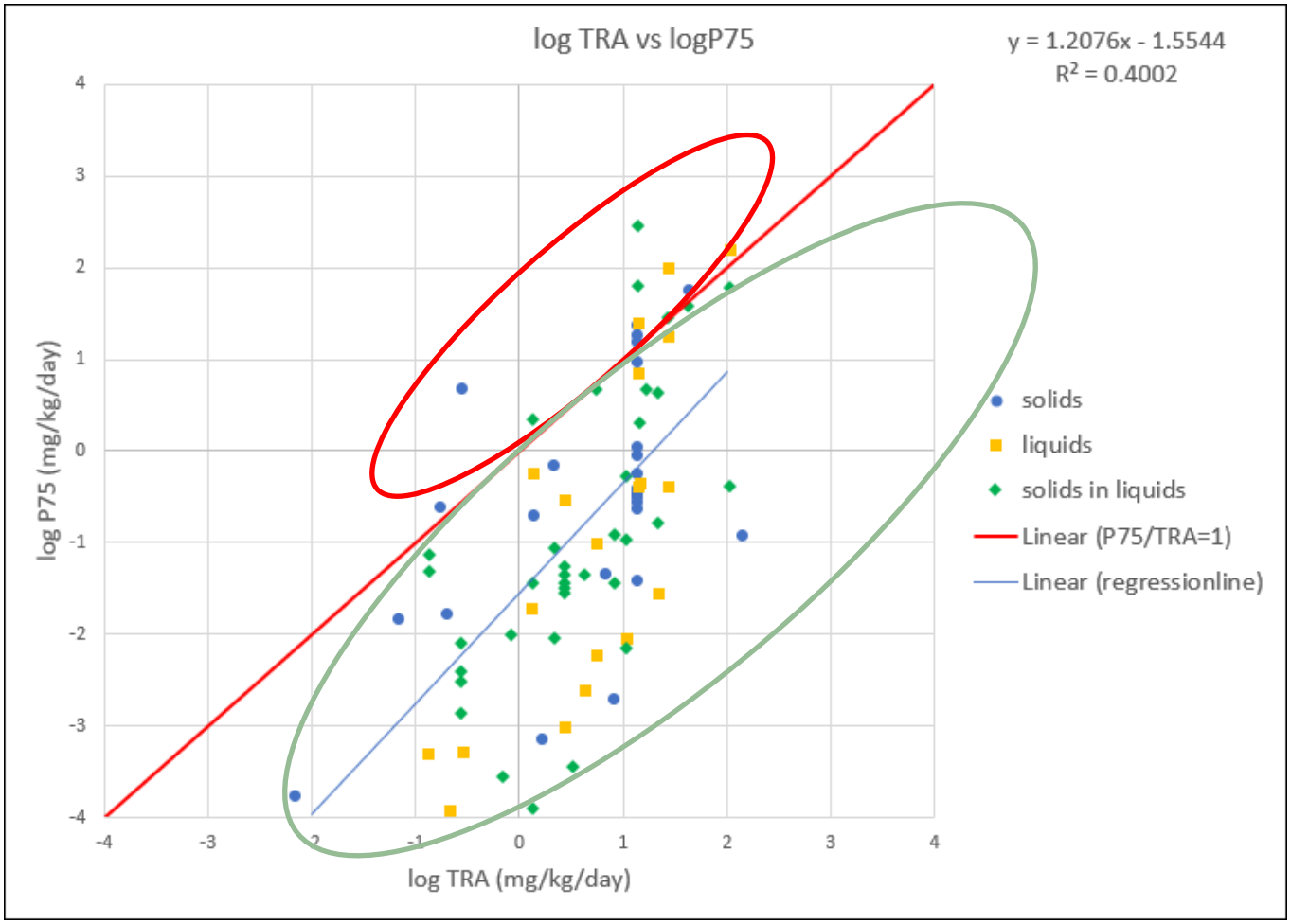
Changes in input variables for TRA estimate

Parameter	Corrected (%)
PROC	2
Local exhaust ventilation - dermal	6
Application of duration factor[#]	15
Dermal protection equipment	2

[#] *Duration factor only applies for medium and high volatile liquids and low dustiness solids*

Tool performance for estimating dermal exposure

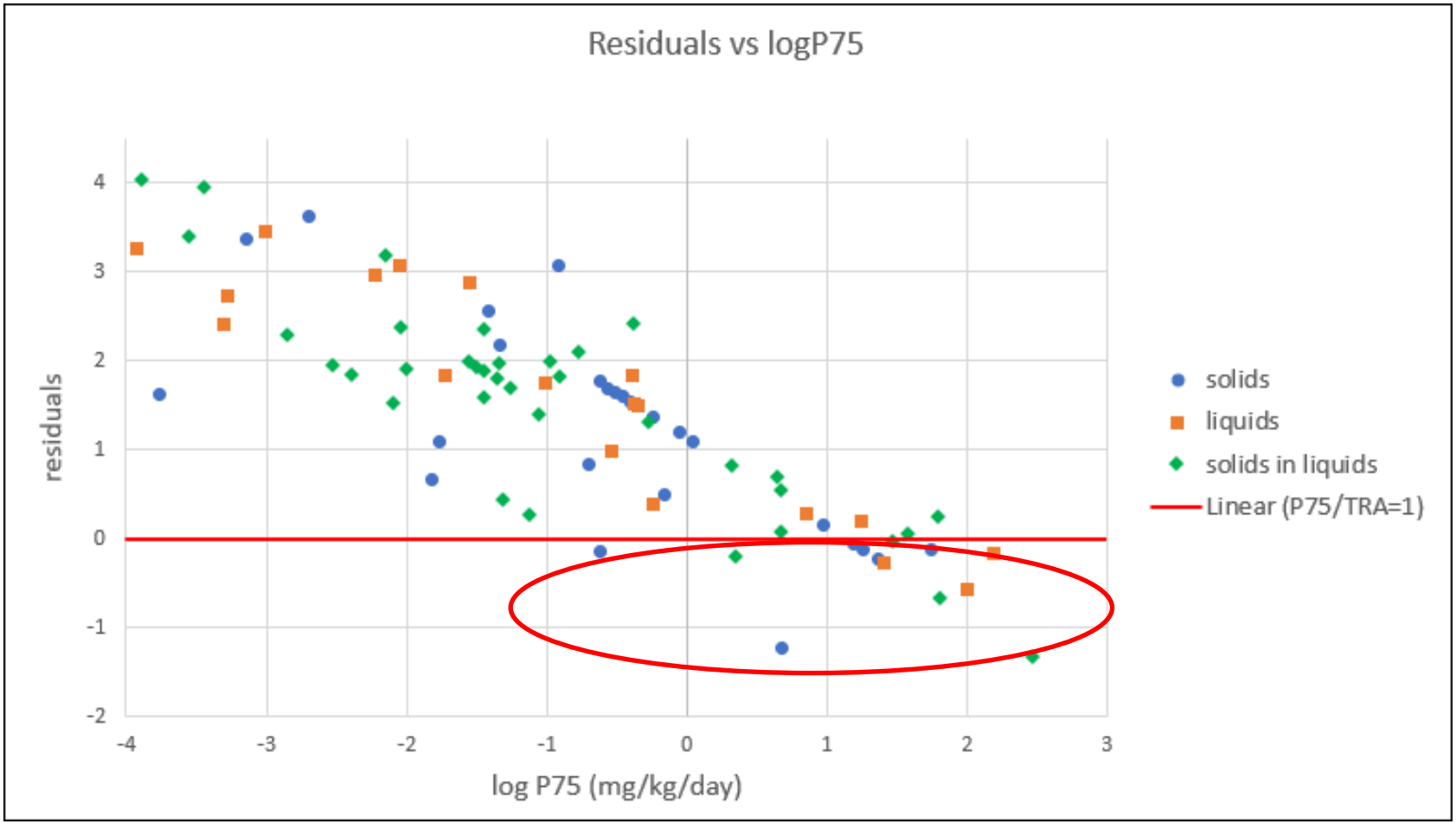
Measured vs modelled exposure



- 13 out of 82 datasets with P75 > TRA (16 %)

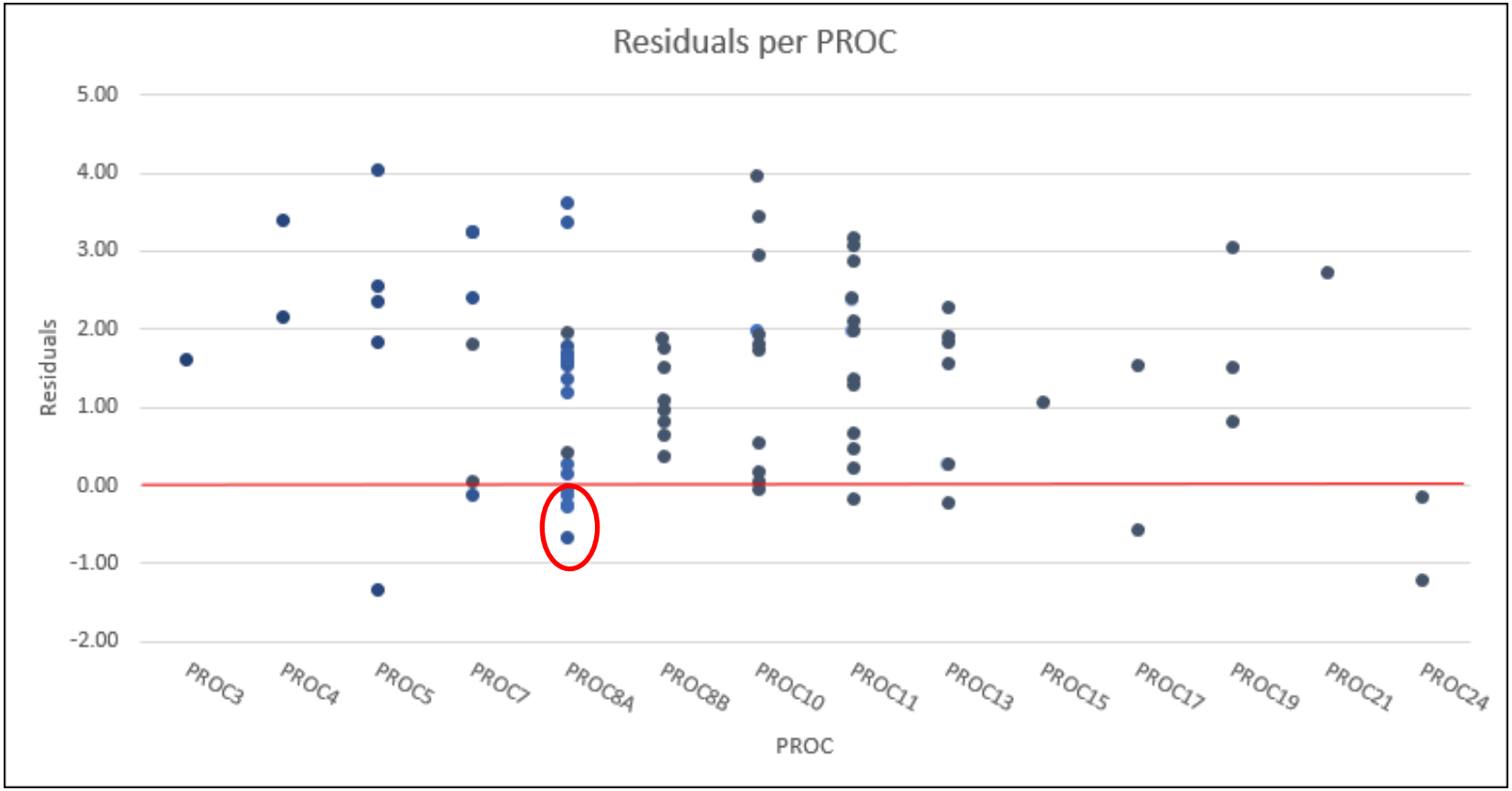
Tool performance for estimating dermal exposure

More underestimation at high exposure levels



Tool performance for estimating dermal exposure

Residuals per PROC



Tool performance for estimating dermal exposure

Probability of ‘false negatives’ for dermal risk ratio

- In the REACH risk assessment the outcome of the dermal exposure assessment is compared with the DNEL for dermal exposure:

  Risk Characterization Ratio (RCR) = Dermal exposure / $DNEL_{dermal}$

  Note: DNEL: Derived No Effect Level

- If RCR < 1 than the risk is acceptable

- When applying the TRA in risk assessment, a ‘**false negative**’ is the situation

  – where the outcome of $RCR_{estimated\text{-}TRA} < 1$ (TRA/DNEL < 1)

  – while in reality $RCR_{measured\text{-}P75} \geq 1$ (P75 / DNEL ≥ 1)

Tool performance for estimating inhalatory exposure

Calculation of ‘false negatives’ for dermal risk ratio

- In the database (n=82) only for 32 cases a dermal DNEL was available; for these datasets a selection has been made of the cases with $RCR_{estimated\text{-}TRA} < 1$ (TRA/DNEL < 1) => n= 24

- For these cases the P75/DNEL has been calculated; only for 1 of the 24 datasets the $RCR_{measured\text{-}P75} \geq 1$ (P75/DNEL $\geq$ 1)

- The probability of a ‘false negative’ outcome (based on comparison with the 75-percentile) is 1/32 = 3.1 %

Conclusions

Review published performance studies

- inhalation exposure data: 14 studies - 129 valid scenario's (2272 measurements)
- dermal exposure data: 32 studies - 82 valid scenarios (1719 measurements)

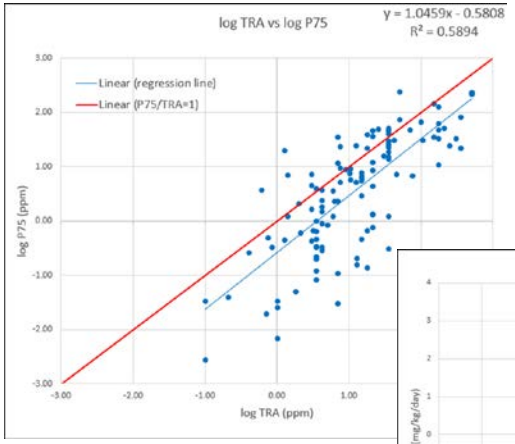
Construction of TRA-estimates for scenario's with valid datasets

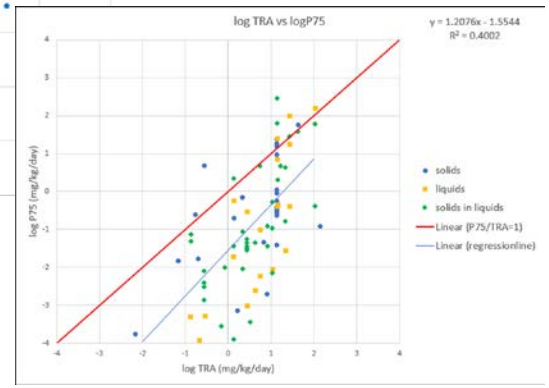
- correction input for inhalation estimate: PROC > Dilution ventilation > LEV > setting…
- correction input for dermal estimate: PROC > LEV > Duration > PPE

Evaluation of tool performance

- Inhalation estimates
  - sufficiently conservative
  - 'false negatives' low (2.3%)

- Dermal estimates:
  - sufficiently conservative
  - 'false negatives' low (3.1%)





Identify potential tool improvements

Improvements/modifications will be published soon

Acknowledgements

Members of the **ECETOC Expert Task Force**

Jan Urbanus (TF Chair)	Shell, BE – Brussels
Oliver Henschel	BASF SE, DE – Ludwigshafen am Rhein
Qiang Li	Clariant, DE - Sulzbach am Taunus
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