

**Practical learnings from an epidemiology study on TDI-related occupational asthma. Part I -
Cumulative exposure is not a good indicator of risk.**

Supplemental Information - 4

Background information on job functions

This Supplement provides some additional background on job functions in TDI production facilities and how they affect exposure metrics.

Distribution of TWA-8 values for job classes

Aggregation of data is not necessary to determine the cumulative exposure for each participant, since for most Plant/SEGs sufficient samples were taken. However, it is useful in addition to briefly compare the distributions of TWA-8 values for different groups of workers. For this purpose, clustering along the traditional job classes was used. Based on the authors' experience in chemical plants, personnel in support roles (Support-SEG)¹ in their present function spend a larger portion of their time indoors (e.g., in control rooms, offices or shops) and a smaller part in the plant near the TDI-containing processing equipment. They are usually not involved in direct line-breaking activities. Consequently, they rarely come into contact with "open" plant systems and are less likely to be near any incident or other event should these occur in the facility. Their risk of exposure is therefore low, as demonstrated by 90% of TWA-values being below detection limit (Middendorf et al, 2017). Personnel in maintenance-like roles (Maintenance-SEG) regularly perform activities whereby plant systems are intentionally opened (repair of piping and equipment, collection of samples, maintenance of instrumentation devices connected to plant systems). They are more prone to be confronted with residues of process liquids but can plan many of their activities in advance and can include adequate precautionary measures such as respiratory protection to prevent physical exposure. Field operators (Field-SEG) in their present function spend a large portion of their time in the plant near the TDI-processing equipment and are usually first responders who are likely to be near incidents that result in short peak exposures should these occur in the facility. Consequently, they are at risk for higher TDI exposure as well as for exposure to other chemicals in the plant². Exposure potentially

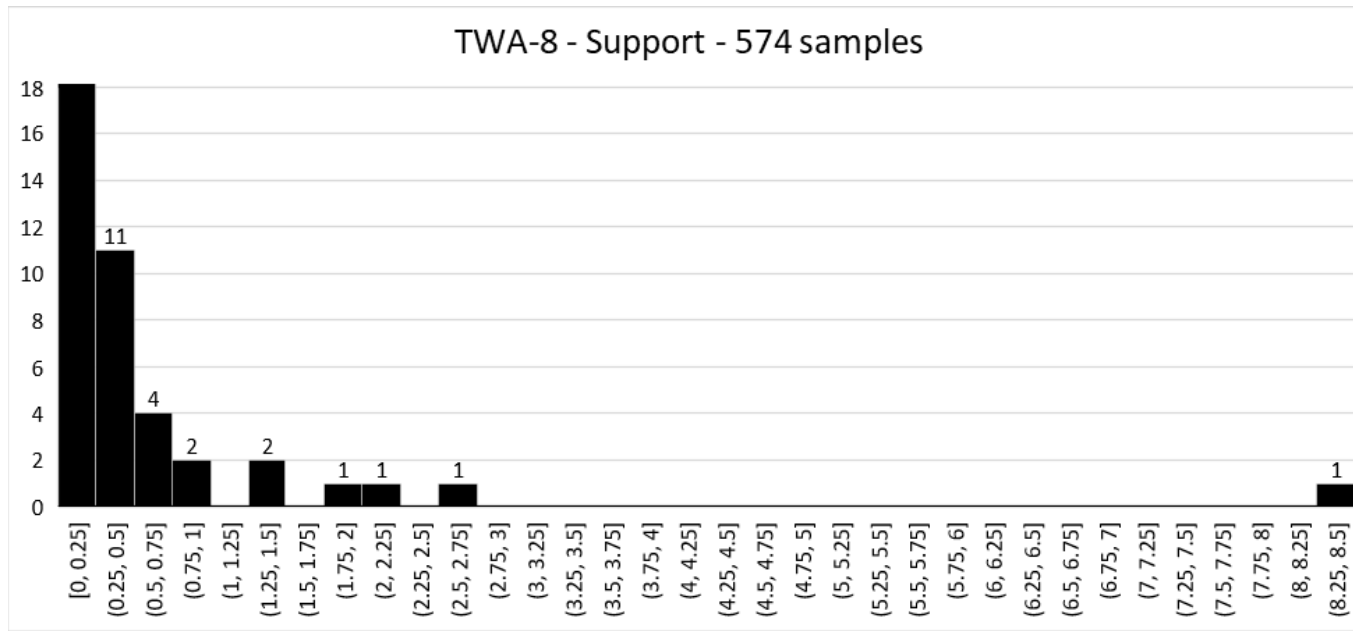
¹ Nomenclature: see Table S3-1 in Supplemental Information – 3.

² Ammonia as refrigerant, DCB (dichlorobenzene) as a solvent, chlorine, phosgene, and hydrochloric acid.

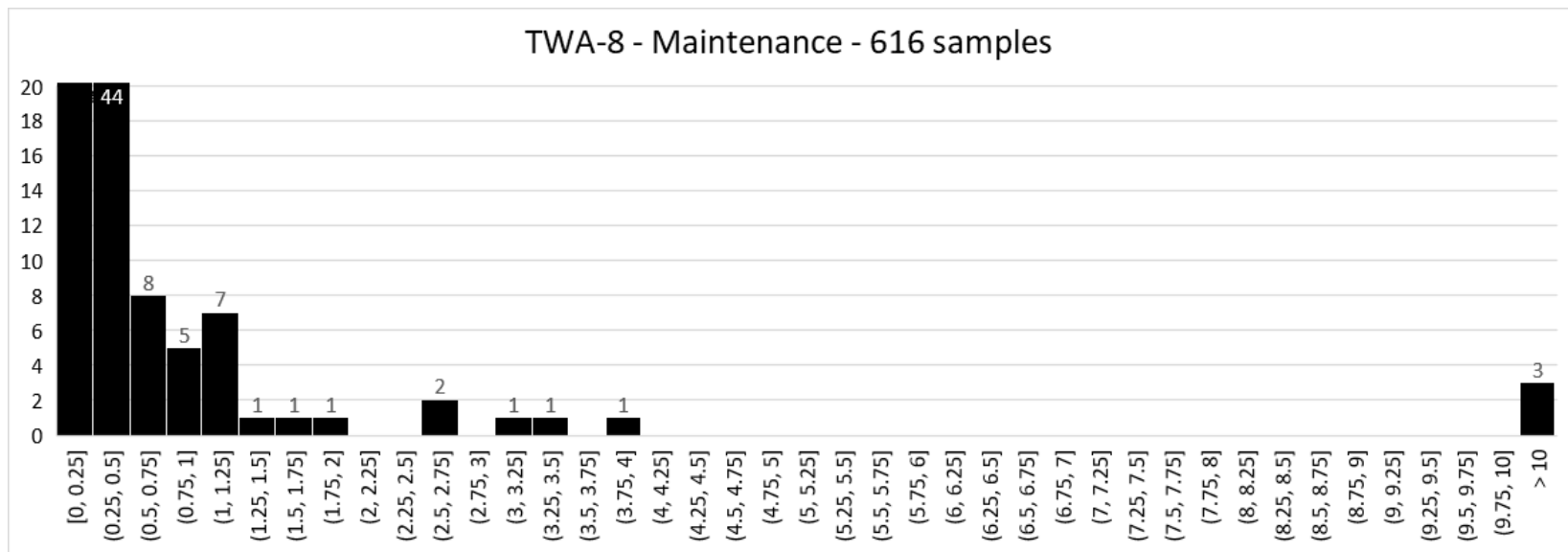
occurs without respiratory protection being used, because they may not notice significant peak concentrations since TDI odor is not perceived below 20-50 ppb (Henschler et al., 1962). Comments similar to the Field-SEG can be made for Loaders (Load-SEG). In addition, Loaders' jobs specifically include connecting and/or opening systems (trucks, railcars) and handling of other chemicals related to TDI-production (e.g., chlorine, hydrochloric acid). These specific loading activities can be planned and adequate protective measures can be taken.

As an illustration, **Figure S4-1** shows the distributions of the TWA-8 values (routine as well as non-routine samples, time-adjusted to an 8-hour TWA-value) for these function classes. The graphs are scaled so that the values on the x-axes match, and so that the (curtailed) y-axes' maximum scales correspond to about 3% of the total number of samples in order to give a better impression of frequencies. The right-most overflow group on the x-axis includes all samples that exceed the high-end of the x-axis scale.

The average for the Maintenance-SEG is significantly different (higher) from the one for Support-SEG ($P < 0.01$). The distribution is generally a bit broader than the Support-SEG distribution. Field-SEG, in turn, is significantly different (higher) from Maintenance-SEG ($P < 10^{-4}$). It is characterized by a very long "tail" (indicating peak exposure incidents). The difference between Load-SEG and Field-SEG almost reaches statistical significance ($P = 0.065$). Load-SEG shows a higher frequency of likely task-related values centered around a TWA-8 of 1 ppb, and a similar long tail. In general, the TWA-8 values that represent the background levels in the plants (e.g., **Figure S4-1A** and **S4-1B**) were below 2 ppb.

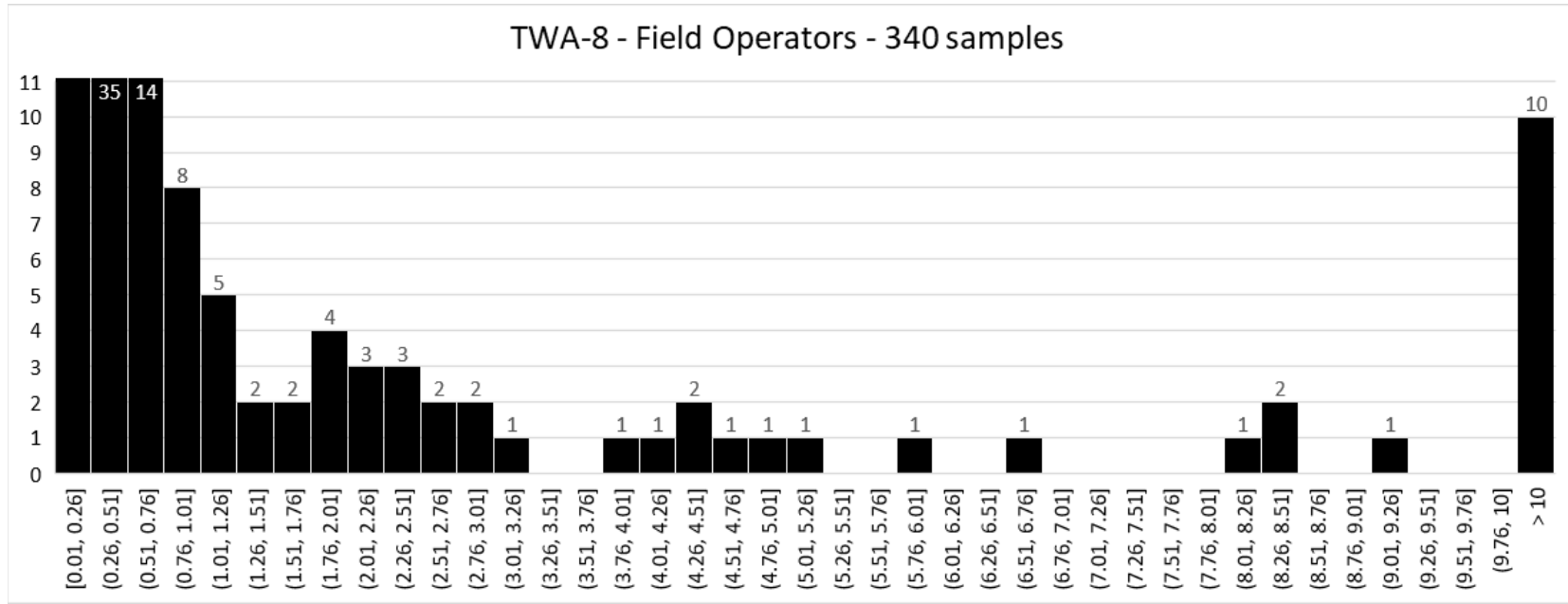


A.



B.

C.



D.

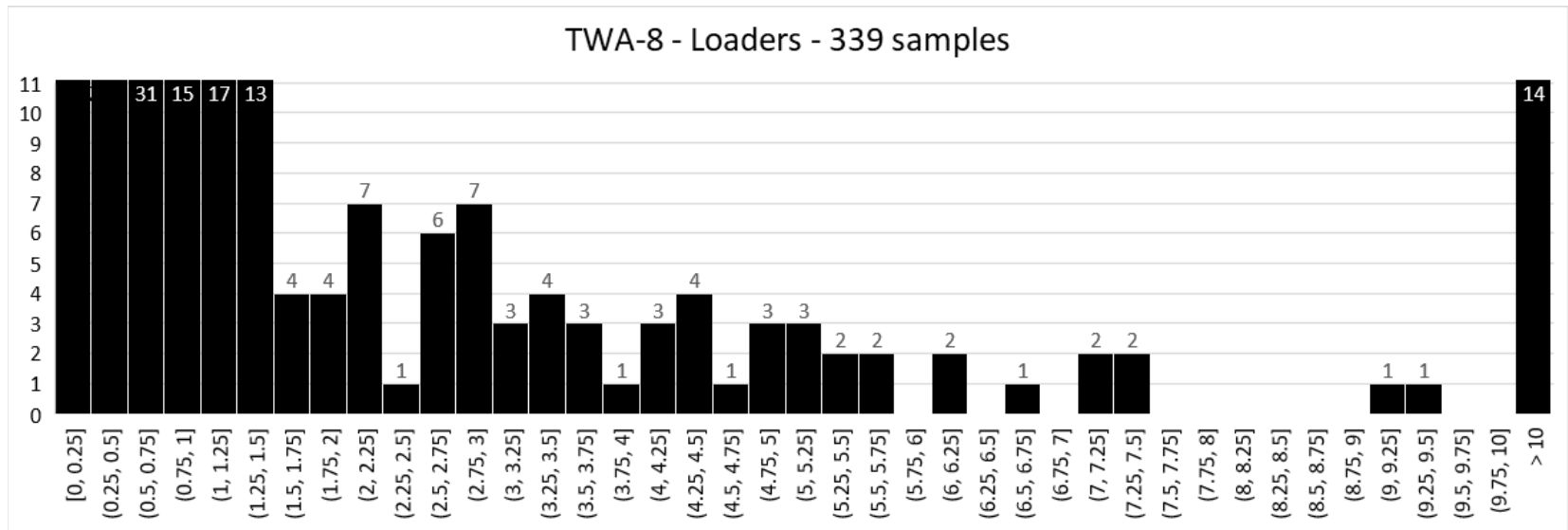


Figure S4-1 – Histograms of TWA-8-values (2,4- plus 2,6-TDI, time adjusted to 8 hours) for the following job classes: **A**. Support functions [Support-SEG], **B**. Maintenance functions [Maintenance-SEG], **C**. Field Operators [Field-SEG], and **D**. Loaders [Load-SEG]. X-axis: intervals of TWA-8 values [ppb]; y-axis: count, capped at approx. 3% of total number of samples. The average of **B** is significantly higher than that of **A** ($P < 0.01$); the average of **C** is significantly higher than that of **B** ($P < 10^{-4}$); the average of **D** is higher than that of **C** with a difference that approaches statistical significance ($P = 0.065$); the overflow group on the far right end of **D** contains 14 data points (truncated).

Role of dermal exposure

The main focus of the ACC-NIOSH study was on the effects of inhalation exposure. Middendorf et al. (2017: top of page S3) mentioned that dermal exposure was only expected to “occur sporadically”, which was one of the reasons not to investigate it further. Taking into account that the ACC-NIOSH study exclusively involved workers engaged in the production of TDI, we support the view that dermal exposure only represents a minor contribution.

Whereas in foam plants, manual handling of (foamed) products is part of the process, in the chemical production facilities, TDI is handled in closed systems. Therefore, exposure only occurs when production systems are intentionally or accidentally opened. Consequently, dermal exposure is not expected to occur on a regular basis.

It should also be noted that standard working attire in US Gulf Coast chemical production plants includes long-sleeved (and often liquid-repellent and/or flame retardant) clothing. Depending upon the task to be performed, this is complemented by the prescribed use of working or chemical-resistant gloves. This attire provides good protection against minor liquid residues or spills. Sudden (in the sense of “unexpected” – since expected potential liquid exposure would be addressed by donning chemical protective gear) large liquid spills that would soak clothing could pose a dermal exposure risk. These are, however, truly exceptional and rare occurrences that would inevitably be accompanied by significant inhalation exposure, since the vapor pressure of TDI at 25 °C (approx. 20 ppm) is about three orders of magnitude higher than the OSHA ceiling of 20 ppb (Allport et al., 2003: page 349, Figure 5.6.1). The dermal component of such occurrences cannot be separated out without significantly more detailed individual information about dermal contact.

Occupational exposure limits

At the time when the ACC-NIOSH study was conducted, the OSHA³ ceiling value for TDI was 20 ppb. This value is still in effect as of 2020.

At the time of the study, the TWA-8(hour) and STEL-15(minute) values recommended by the ACGIH⁴ were 5 ppb and 20 ppb respectively. ACGIH have updated their recommendation to 1 ppb and 5 ppb respectively in 2016 (ACGIH, 2016).

Different values may apply in other countries.

References in addition to those mentioned in the main paper

Allport DC, Gilbert DS and Outterside SM (2003) *MDI and TDI: safety, health and the environment. A source book and practical guide*. ISBN 0-471-95812-3. Chichester, UK: John Wiley & Sons.

American Conference of Governmental and Industrial Hygienists (ACGIH) (2016) *Toluene diisocyanate, 2,4- or 2,6- (or as a mixture) [newly adopted TLV documentation]*. Cincinnati, OH, USA: American Conference of Governmental and Industrial Hygienists.

Henschler D, Assmann W and Meyer KO (1962) Zur Toxikologie der Toluylen-diisocyanate. *Archiv für Toxikologie* 19: 364-387.

³ US Occupational Safety and Health Administration

⁴ American Conference of Governmental and Industrial Hygienists