Practical learnings from an epidemiology study on TDI-related occupational asthma. Part II - Exposure without respiratory protection to TWA-8 values indicative of peak events is a good indicator of risk.

Supplemental Information - 1

Sensitivity analyses

Choice of limit value

The choice of limit value to determine UP-frequencies could potentially impact model conclusions. The impact of selecting limit values of 1 ppb (UP-1), 2 ppb (UP-2), or 3 ppb (UP-3) on the significance of parameter estimates and goodness-of-fit for the logarithmic alternative model was investigated. The method used is that described in the "Methods" section.

Table S1-1 summarizes the results.

Groups as Table 1	UP-frequency (%)			Incidence
	UP-1	UP-2	UP-3	
Support-SEG	0.45	0.3	0.15	0
Others	2.4*	1.3*	0.8*	0.8
	5.1	4.4	3.4	1.2
	8.7	7.5	7.1	2.8
	Significance of			
Intercept	$P < 10^{-4}$	$P < 10^{-4}$	$P < 10^{-4}$	
Slope	$P < 0.05$	$P < 0.05$	$P < 0.05$	
Goodness-of-fit	$P < 0.05$	$P < 0.05$	$P < 0.05$	

Table S1-1 – *UP-frequencies at limits of TWA-8 values of 1 ppb (UP-1), 2 ppb (UP-2), and 3 ppb (UP-3). Corresponding significance of parameter estimates (intercept and slope) and goodness-of-fit for the logarithmic alternative model. Incidence per hundred person-years. *: average of range.*

Intercept and slope parameter estimates are significantly different from zero for the logarithmic alternate model up to a limit of 3 ppb. Goodness-of-fit is significant up to 3 ppb. Model validity is given up to 3 ppb as a limit value.

Note: In this particular study, TWA-8 values of 2-3 ppb are indicative of exposures approaching STEL allowances in force at the time of the study, not of plant background. The limit value in itself as well as the correlation with UP-frequency suggest a threshold below which induction of occupational asthma is not expected to occur. This is true up to a TWA-8 value of 3 ppb. Higher values were not investigated.

Use of unsmoothed data

Using fitted distributions could potentially impact model conclusions or validity. The significance of parameter estimates and goodness-of-fit for the logarithmic alternative model were investigated using:

- The approach described in the "Methods" section for UP-3-frequencies below 1%;
- A straight count of TWA-8 values above 3 ppb ratioed to the total number of samples for the SEGs with UP-3-frequencies above 1%.

Alternative assumption for Maintenance-SEG

The UP-3-frequency for the Maintenance-SEG (0.8%) has been used for those SEGs where only a limited number of samples was available. This assumption could potentially impact model conclusions and validity. The significance of parameter estimates and goodness-of-fit for the logarithmic alternative model were investigated using a 50% lower UP-3-frequency (0.4%).

Table S1-2 summarizes the results. Model validity is maintained for both alternative data assumptions.

Groups as Table 1	UP-3-frequency (%)			Incidence
	Smoothed	Straight count	Alt Maint	
Support-SEG	0.15	0.15	0.15	0
Others	0.8	0.8	**0.40**	0.8
	3.4	**2.9**	**2.9**	1.2
	7.1	**5.8**	**5.8**	2.8
	Significance of			
Intercept	$P < 10^{-4}$	$P < 10^{-4}$	$P < 10^{-4}$	
Slope	$P < 0.05$	$P < 0.05$	$P < 0.05$	
Goodness-of-fit	$P < 0.05$	$P < 0.05$	$P < 0.05$	

Table S1-2 – *UP-3-frequencies using the method described in the "Methods" section ("Smoothed"), the alternative method described above ("Straight Count"), and with the changed assumption for the Maintenance-SEG ("Alt Maint"). Corresponding significance of parameter estimates (intercept and slope) and goodness-of-fit for the logarithmic alternative model. Incidence per hundred person-years.*