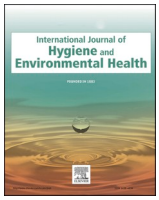
International Journal of Hygiene and Environmental Health 238 (2021) 113838

Contents lists available at ScienceDirect

International Journal of Hygiene and Environmental Health

journal homepage: www.elsevier.com/locate/ijheh



Estimating nickel exposure in respirable dust from nickel in inhalable dust

Cornelia Wippich *, Dorothea Koppisch, Katrin Pitzke, Dietmar Breuer

Institute for Occupational Safety and Health of the German Social Accident Insurance, Alte Heerstraße 111, 53757, Sankt Augustin, Germany

ARTICLE INFO

Keywords:
Nickel
Respirable dust
Inhalable dust
Aerosol
Exposure assessment
Regression analysis

ABSTRACT

The conversion of dust components is of high importance for retrospective evaluations of exposure levels, of occupational diseases or the time trend of occupational dust exposure. For this purpose, possibilities to convert nickel concentrations from inhalable to respirable dust are discussed in this study. Therefore, 551 parallel measurements of nickel concentrations in inhalable and respirable dust fractions were extracted from the exposure database MEGA (maintained at the Institute for Occupational Safety and Health of the German Social Accident Insurance) and investigated by linear regression analysis of ln-transformed concentrations. Inhalable dust is the most important predictor variable, showing an adjusted coefficient of determination (*adj.* R^2) of 0.767 (R^2 adjusted to sample size). Since multilinear regression analysis, cannot be applied, further description of data is gained by splitting the whole dataset into working activity groups (e. g. '*high temperature processing*', *adj.* R^2 = *0.628,*' *filling/transport/storage*' *adj.* R^2 = *0.741*, '*machining/abrasive techniques*', *adj.* R^2 = 0.777). From these groups, four task restrictive subgroups, so-called *'heuristic groups'*, can be derived by pooling similar working tasks with similar regression coefficients and enhanced quality measures (*adj.* R^2 between 0.724 and 0.924): '*welding (grinding time fraction [GTF] < 5%)*', '*welding (grinding time fraction [GTF] > 5%)*', '*high temperature cutting*' and '*grinding*'. For the working activity group '*high temperature processing*' and the heuristic group '*welding*' the determination of the grinding time fraction and its inclusion or exclusion from a dataset has a huge impact on the description of data and whether a transformation of nickel concentrations using the natural logarithm (ln) is necessary or not. In case of *GTF* < 5%, the conversions functions are linear, all other conversion functions are power functions with exponents between 0.713 and 0.986. It is possible to develop conversion functions for estimating the nickel concentration in the respirable dust fraction ($c_{R(Ni)}$) out of the nickel concentration in the inhalable dust fraction ($c_{I(Ni)}$). For the estimation of Nickel in respirable dust other studies, it is recommend to use the conversion functions of the heuristic trial and error groups. Limitations of the possibility to use the conversion functions are discussed.

1. Introduction

Nickel is one of the most commonly used elements in metal industry. Due to its physical and chemical properties, it has a wide field of application. The element is mainly used as an alloy to form chemical resistant materials, for nickel-cadmium batteries and as a catalyst in chemical and food industry (Genchi et al., 2020; Kasprzak et al., 2003). The exposure of workers through the inhalation of metal particles or fumes can be quite high. Nickel can cause allergic reactions, but it is also known to cause cancer in parts of the respiratory tract, like the lungs and the nose (Tsai et al., 1995; Andersen et al., 1996; Rahilly and Price, 2003).

In 1985, the International Committee on Nickel Carcinogenesis in man (ICNCM) was initiated, where the nickel forms causing cancer were determined and a dose-response relation was derived (Doll, 1990). This was the start of the nickel exposure evaluation, firstly based on the measurement of nickel and its compounds (Tsai et al., 1995; Andersen et al., 1996) in total dust. During the following years the carcinogenicity and toxicity of nickel was tested in various experiments and studies (Andersen et al., 1996; Grimsrud et al., 2002). Nickel and its compounds have been categorized as 'carcinogenic for humans' group 1 (IARC) (IARC, 2012) or group 1A (CLP) (ECHA, 2021), whereas metallic nickel and nickel alloys are categorized as 'possibly carcinogenic for humans' group 2B (IARC) (IARC, 1990) or Carc 2 (CLP) (ECHA, 2021) (Hughson et al., 2010; IARC, 2012).

Nickel was mainly measured in the inhalable dust fraction, based on

* Corresponding author.
E-mail addresses: cornelia.wippich@dguv.de (C. Wippich), dorothea.koppisch@dguv.de (D. Koppisch), katrin.pitzke@dguv.de (K. Pitzke), dietmar.breuer@dguv.de (D. Breuer).

https://doi.org/10.1016/j.ijheh.2021.113838
Received 8 March 2021; Received in revised form 1 September 2021; Accepted 1 September 2021
Available online 6 September 2021

a technical guide concentration [TRK], which was firstly established 1977 in Germany (BMAS, 1977). These legal values were adopted to the technical state of the art over the years. In 2004, a TRK of 0.05 mg m^{-3} (in inhalable dust) in droplets and for nickel and its compounds 0.5 mg m^{-3} (in inhalable dust) was valid. In 2005, all TRKs for carcinogenics were suspended. After several years, new limit values for nickel compounds due to its carcinogenic effects in respirable dust were established at 0.006 mg m^{-3} as exposure-risk-relationship (ERB) (AGS, 2021). Furthermore, nickel and nickel compounds are toxic and highly sensitizing; regarding these non-carcinogenic effects an occupational exposure limit value of 0.03 mg m^{-3} in inhalable dust was established. For nickel metal, additional an occupational exposure limit value of 0.006 mg m^{-3} in respirable dust has been valid since 2017 (AGS, 2020). Subsequently the number of parallel measurements of nickel in respirable and inhalable dust increased in the recent years. Apart from air monitoring, measurements of individual nickel concentrations in workers is also a common tool for assessing occupational health risks of workers. For biomonitoring of nickel in Germany, no threshold values in biological material was established so far, besides a reference value [BAR] of 3 µg Nickel/L urine (DFG, 2012). Since this study focusses on air monitoring, with respect to the legal limit values, biomonitoring will not be discussed in further detail.

The increase of measurements targeting respirable dust and its components was not unique in Germany but it was also an international trend to focus on the dust fraction with an associated limit value. When it comes to retrospective assessment, monitoring the development of nickel exposure and investigation of occupational diseases, it remains problematic if only data from inhalable dust is available. In order to be able to use the historical data, e.g. in epidemiological evaluations, a mathematically conversion of nickel concentrations in inhalable dust to nickel concentrations in respirable dust is desirable.

Other studies mainly focused on the ratio of “inhalable” to “total” dust (Tsai et al., 1995; Tsai and Vincent, 2001). Only a few studies target nickel in respirable dust (Tanaka et al., 1985; Roels et al., 1993).

In our recently published study, we offered a mathematical solution for converting inhalable dust into respirable dust and vice versa (Wippich et al., 2020) by using the exposure data from the nonpublic database MEGA. Using further data from the same database, we developed a method to determine a possible relation between nickel in inhalable dust and nickel in respirable dust depending on working environments, using similar methods and assumptions as in our past study.

2. Materials and methods

2.1. Exposure database MEGA

The data were obtained by the surveillance activity of the German Social Accident Insurance (Gabriel et al., 2010). The database MEGA holds over 3 million dataset with exposure data from over 870 hazardous substances, including additional information about the measurement procedure, the used equipment and the analytical method. It was established in 1972 and it is designed for the evaluation of occupational diseases, hazard and exposure analysis in specific types of industry, as well as time-dependent analysis of exposure to hazardous substances at work places.

2.2. Sampling systems

The most measurements in this study were performed using the samplers GSP and FSP. The FSP sampler is used to collect respirable dust, where a cyclone is used as a pre-separator for coarse particles. Smaller particles (with an aerodynamic diameter less than 10 µm) are separated on a cellulose nitrate filter (0.8 µm pore size) (Siekmann, 1998). In case of the GSP, inhalable dust is collected through a cone on a filter, directly without pre-separation (Riediger, 2001). Both, FSP and GSP can be used for personal and stationary sampling (Mattenklott and Möhlmann, 2011). Besides FSP and GSP, also the systems Gravikon PM4 and Gravikon VC-25 are used for the stationary measurement of inhalable and respirable dust. The system PM4 for respirable dust also uses a cyclone as a pre-separator for coarse particles. For the collection of inhalable dust, the sampling volume is drawn into a filter cassette with an annular gap nozzle onto a filter (Siekmann, 1998; Riediger, 2001). The Gravikon VC-25 system also uses two different sampling heads to collect both dust fractions. For respirable dust, an additional impactor is used. Similar to the PM4, the inhalable fraction is measured with the VC-25 by drawing the sampling volume through an annular gap onto a filter (Coenen, 1981) (Siekmann, 1998) (Riediger, 2001). The most common combination of sampling systems in this study is GSP (inhalable dust, sampling rate: 3.5 L/min) and FSP-10 (respirable dust, sampling rate: 10 L/min), providing 274 pairs of parallel personal measurements. The second highest abundance can be seen for the combination GSP-10 (inhalable dust, sampling rate: 10 L/min) and FSP-10 with 197 personal parallel measurements. For the complete list of used sampling systems, the sampling rate and the type of sampling, see Table 1.

All samplers used in this study are validated according to the international standards EN 13205, EN 1540 and comply with ISO 7708.

2.3. Analytical methods

The sampling systems were equipped with cellulose nitrate filters (0.8 µm pore size). These filters were shipped to the Institute for Occupational Safety and Health of the German Social Accident Insurance for gravimetric and quantitative metal analysis. The filters were conditioned for at least one day in the laboratory atmosphere at a fixed temperature and humidity.

Nickel was determined by inductively coupled plasma mass spectrometry (ICP-MS) after digestion with a mixture of nitric and hydrochloric acid. A detailed method description was recently published (Pitzke et al., 2020).

2.4. Data selection

The method of pair formation of inhalable and respirable dust follows mainly the same scheme, as in our previous study (Wippich et al. (2020)). However, in this work the pairs are formed from nickel in respirable and inhalable dust, which was measured in parallel.

Firstly, the datasets are extracted from the database MEGA. Between the years 1989 and September 2020, a total of 234 202 respirable fraction measurements, 123 118 inhalable fraction measurements and 32 882 nickel measurements were collected in total.

For the formation of parallel measured pairs of nickel in inhalable and nickel in respirable dust, first, measurements are excluded, if the concentration is below the limit of quantification. With this restriction 169 458 measurements of the respirable fraction, 95 328 measurements of the inhalable fraction and 22 941 total nickel measurements remain

Table 1
Measurement systems and sampling rates used for both dust fractions in parallel measurements.

sampler inhalable dust (sampling rate)	sampler respirable dust (sampling rate)	*n*	type of sampling
GSP (3.5 L/min)	FSP-10 (10 L/min)	274	Personal
GSP-10 (10 L/min)	FSP-10 (10 L/min)	197	Personal
GSP-10 (10 L/min)	FSP-10 (10 L/min)	31	Stationary
GSP (3.5 L/min)	FSP-10 (10 L/min)	28	Stationary
PM4-G (66.7 L/min)	PM4-F (66.7 L/min)	6	Stationary
VC-25 G (375 L/min)	VC-25 F (375 L/min)	5	Stationary
VC-25 G (375 L/min)	PM4-F (66.7 L/min)	4	Stationary
GSP (3.5 L/min)	PM4-F (66.7 L/min)	3	Stationary
GSP (3.5 L/min)	FSP-2 (2 L/min)	2	Personal
GSP-10 (10 L/min)	PM4-F (66.7 L/min)	1	Stationary

for the formation of pairs.

Parallel pairs are formed if:

- the nickel concentration ($c_{I(Ni)}$) and the concentration of inhalable dust (c_I), and the nickel concentration ($c_{R(Ni)}$)and the concentration of respirable dust (c_R) respectively, were analyzed from the same sample carrier (filter) and
- the measurements have the same report number, industrial sector, working activity, type of sampling and were executed at the same day (remaining pairs: $n = 1117$),
- the measurements were executed at the same time (starting and ending times of both measurements do not differ by more than 5 min) and the sampling duration was $\geq$ 2 h ($n = 1011$),
- the measurement procedure and the analytical process are standardized methods in the Measurement system for exposure assessment of the German Social Accident Insurance Institutions (MGU) ($n = 598$).

The industrial sector describes the type of industry where the measurement was executed, as *metalworking* or *electronic waste recycling* for example. With the parameter *working activity,* the task and the process were combined. The *type of sampling* consists of the two subgroups: *personal* and *stationary sampling.* It was considered necessary, that all these variables were concordant within a pair.

In Germany according to the Technical Guidance 402, the minimum number of samples which have to be taken during a work shift with constant exposure is dependent on the sampling duration. When the sampling duration is higher or equal 2 h, one measurement is sufficient (AGS, 2017). Therefore, only measurements with a sampling duration of higher or equal 2 h have been included.

One further restriction is placed on the dataset: Samples have been excluded if c_R was higher than c_I or c_{Ni} in the respirable fraction was higher than c_{Ni} in the inhalable fraction. Physically it is not possible, that $c_{R(Ni)}$ or c_R exceed $c_{I(Ni)}$ or c_I, respectively, because respirable dust is a subset of inhalable dust, but at work places, these cases can be observed occasionally. Measurements like that can result from incorrect sampling, particle movement, thermal effects or inhomogeneous materials. This criterion affects only 45 pairs of measurement. Further discussion on these values will be done later in this study.

After merging the datasets of nickel/inhalable fraction and nickel/respirable fraction and considering all previous described restrictions, a dataset of 553 pairs, gathered between the years 2011 and 2020 can be formed. The data has been collected in 105 different working activities and the majority of dust concentrations was recorded during 2 h-measurements. As described in section 'Statistical and mathematical methods', two leverage points have been eliminated, so the whole dataset (group 0, see Table 3) consist of 551 pairs of parallel measured nickel concentrations.

According to the approach in our prior study, the whole dataset is divided into activity groups (Wippich et al., 2020). For nickel, we found measurement pairs for the groups *'high temperature processing', 'filling/-transport/storage'* and *'machining/abrasive techniques'*. From these groups more restrictive subgroups, 'heuristic groups' are formed as well. The formation of these groups is described in section 'Statistical and mathematical methods'.

At the work place, there is often no spatial separation of welding and grinding. In many cases a mixture of dusts, produced through the same worker, who is grinding for a certain time-share of the shift, e.g. when smoothing the welding seam cannot be excluded. In such cases, as additional information '< 5 % grinding time fraction (GTF)' or '> 5 % grinding time fraction (GTF)' can be added to each measured dataset at welding workplaces. This also has been considered in the group formation.

2.5. Statistical and mathematical methods

All statistical analyses were performed using the statistical software IBM SPSS statistics, version 26 (IBM Corp.). For all tests, the significance level is fixed at $\alpha = 0.05$, equaling a confidence interval of 95 %.

The assumption of a normal or lognormal distribution had to be rejected at the significance level of 0.05, using the Lilliefors-corrected Kolmogorov-Smirnov test (Sachs, 2004) for nickel in both dust fractions. This is mainly caused by the heterogeneous working activities, which are included in the total dataset. To identify the effects of the *type*

Table 2
Descriptive statistics of respirable and inhalable nickel samples used in the study, with the amount of paired nickel concentrations (n) arithmetic mean (AM), standard deviation (SD), median, minimum measured concentration (Min), maximum measured concentration (Max).

ID	Group	Dust fraction	n	AM [mg m^{-3}]	SD [mg m^{-3}]	Median [mg m^{-3}]	Min [mg m^{-3}]	Max [mg m^{-3}]
0	*Entire dataset*	$c_{I(Ni)}$	551	0.079	0.303	0.005	$1.6*10^{-5}$	4.700
		$c_{R(Ni)}$	551	0.008	0.019	0.001	$5.8*10^{-7}$	0.190
1	*High temperature processing*	$c_{I(Ni)}$	250	0.021	0.050	0.003	$2.3*10^{-4}$	0.350
		$c_{R(Ni)}$	250	0.008	0.022	0.001	$5.8*10^{-7}$	0.190
1a	*High temperature processing (incl. welding GTF < 5%)*	$c_{I(Ni)}$	159	0.022	0.054	0.003	$2.3*10^{-4}$	0.350
		$c_{R(Ni)}$	159	0.010	0.026	0.001	$5.8*10^{-7}$	0.190
1b	*High temperature processing (incl. welding GTF > 5%)*	$c_{I(Ni)}$	159	0.022	0.054	0.003	$2.3*10^{-4}$	0.350
		$c_{R(Ni)}$	159	0.007	0.021	0.001	$1.2*10^{-4}$	0.190
2	*Filling/transport/storage*	$c_{I(Ni)}$	42	0.048	0.167	0.004	$3.0*10^{-4}$	1.000
		$c_{R(Ni)}$	42	0.004	0.008	0.001	$6.7*10^{-5}$	0.049
3	*Machining/abrasive techniques*	$c_{I(Ni)}$	198	0.133	0.326	0.012	$6.7*10^{-5}$	2.300
		$c_{R(Ni)}$	198	0.013	0.027	0.003	$5.4*10^{-5}$	0.190
α	*Welding*	$c_{I(Ni)}$	198	0.021	0.050	0.003	$2.3*10^{-4}$	0.350
		$c_{R(Ni)}$	198	0.007	0.021	0.001	$5.8*10^{-7}$	0.190
α1/ α2	*Welding (GTF < 5%)*	$c_{I(Ni)}$	91	0.018	0.041	0.003	$3.3*10^{-4}$	0.230
		$c_{R(Ni)}$	91	0.008	0.022	0.001	$5.8*10^{-7}$	0.170
α3/ α4	*Welding (GTF > 5%)*	$c_{I(Ni)}$	91	0.018	0.041	0.003	$2.3*10^{-4}$	0.250
		$c_{R(Ni)}$	91	0.004	0.007	0.001	$1.2*10^{-4}$	0.049
ß	*High temperature cutting*	$c_{I(Ni)}$	48	0.011	0.021	0.002	$4.7*10^{-4}$	0.100
		$c_{R(Ni)}$	48	0.005	0.012	0.001	$1.8*10^{-4}$	0.073
γ	*Grinding*	$c_{I(Ni)}$	156	0.196	0.641	0.015	$6.7*10^{-5}$	2.300
		$c_{R(Ni)}$	156	0.017	0.059	0.003	$5.4*10^{-5}$	0.190

Table 3
Regression coefficients k, C_0 with standard errors for Equation (2) or (4), range of standard errors for regression function $s_{Fit}(\ln(c_{R(Ni)}))$ within groups 1–3 for working activity and heuristic groups α - γ including group names as defined in Table 3; GTF = Grinding time fraction. To use the conversion functions concentrations have to be inserted in mg m^{-3}.

ID	Group	*n*	*R*	adj. R^2	C_0	k	$s_{Fit}(\ln(c_{R(Ni)}))$	conversion function
0	*Entire dataset*	551	0.876	0.767	−2.835 ± 0.090	0.726 ± 0.017	0.085–0.220	$c_{R(Ni)} = c_{I(Ni)}^{0.726} * e^{-2.835}$
	Working activities							
1	*High temperature processing*	250	0.793	0.628	−1.801 ± 0.239	0.870 ± 0.042	0.113–0.237	$c_{R(Ni)} = c_{I(Ni)}^{0.870} * e^{-1.801}$
1a	*High temperature processing (incl. welding GTF < 5%)*	159	0.759	0.573	−1.599 ± 0.348	0.906 ± 0.062	0.132–0.275	$c_{R(Ni)} = c_{I(Ni)}^{0.906} * e^{-1.599}$
1b	*High temperature processing (incl. welding GTF > 5%)*	159	0.922	0.851	−1.685 ± 0.165	0.881 ± 0.029	0.130–0,273	$c_{R(Ni)} = c_{I(Ni)}^{0.881} * e^{-1.685}$
2	*Filling/transport/storage*	42	0.864	0.741	−3.290 ± 0.368	0.746 ± 0.068	0.301–0.536	$c_{R(Ni)} = c_{I(Ni)}^{0.746} * e^{-3.290}$
3	*Machining/abrasive techniques*	198	0.822	0.777	−2.956 ± 0.124	0.713 ± 0.027	0.161–0.692	$c_{R(Ni)} = c_{I(Ni)}^{0.713} * e^{-2.956}$
	Heuristic groups							
α	*Heuristic groupsWelding*	198	0.758	0.573	−2.039 ± 0.286	0.834 ± 0.051	0.116–0.246	$c_{R(Ni)} = c_{I(Ni)}^{0.834} * e^{-2.039}$
α1	*Welding (GTF < 5%) ln-transformed*	91	0.620	0.377	−2.189 ± 0.628	0.820 ± 0.111	0.164–0.317	$c_{R(Ni)} = c_{I(Ni)}^{0.820} * e^{-2.189}$
α2	*Welding (GTF < 5%) not transformed*	91	0.852	0.724	0.001 ± 0.001	0.347 ± 0.023	0.004–0.021	$c_{R(Ni)} = c_{I(Ni)} * 0.347 + 0.001$
α3	*Welding (GTF > 5%) ln-transformed*	91	0.912	0.830	−2.094 ± 0.223	0.816 ± 0.039	0.159–0.345	$c_{R(Ni)} = c_{I(Ni)}^{0.816} * e^{-2.094}$
α4	*Welding (GTF > 5%) not transformed*	91	0.679	0.455	0.002 ± 0.001	0.143 ± 0.016	0.002–0.143	$c_{R(Ni)} = c_{I(Ni)} * 0.143 + 0.002$
ß	*High temperature cutting*	48	0.962	0.924	−0.829 ± 0.247	0.986 ± 0.042	0.210–0.350	$c_{R(Ni)} = c_{I(Ni)}^{0.986} * e^{-0.829}$
γ	*Grinding*	156	0.894	0.798	−2.997 ± 0.128	0.705 ± 0.028	0.182–0.493	$c_{R(Ni)} = c_{I(Ni)}^{0.705} * e^{-2.997}$

of sampling, of *working activity* and possible interactions between these two variables, a two-factor ANOVA was performed. Following our prior study (Wippich et al., 2020), for further evaluation of the variable *working activity*, the total dataset was split into working activity groups. The criterions to form these groups mainly base on the technical information, which also can be found in the database. For nickel, these groups are: *'high temperature processing'*, *'filling/transport/storage'* and *'machining/abrasive techniques'*. The ratio $c_{R(Ni)}/c_{I(Ni)}$ was calculated for

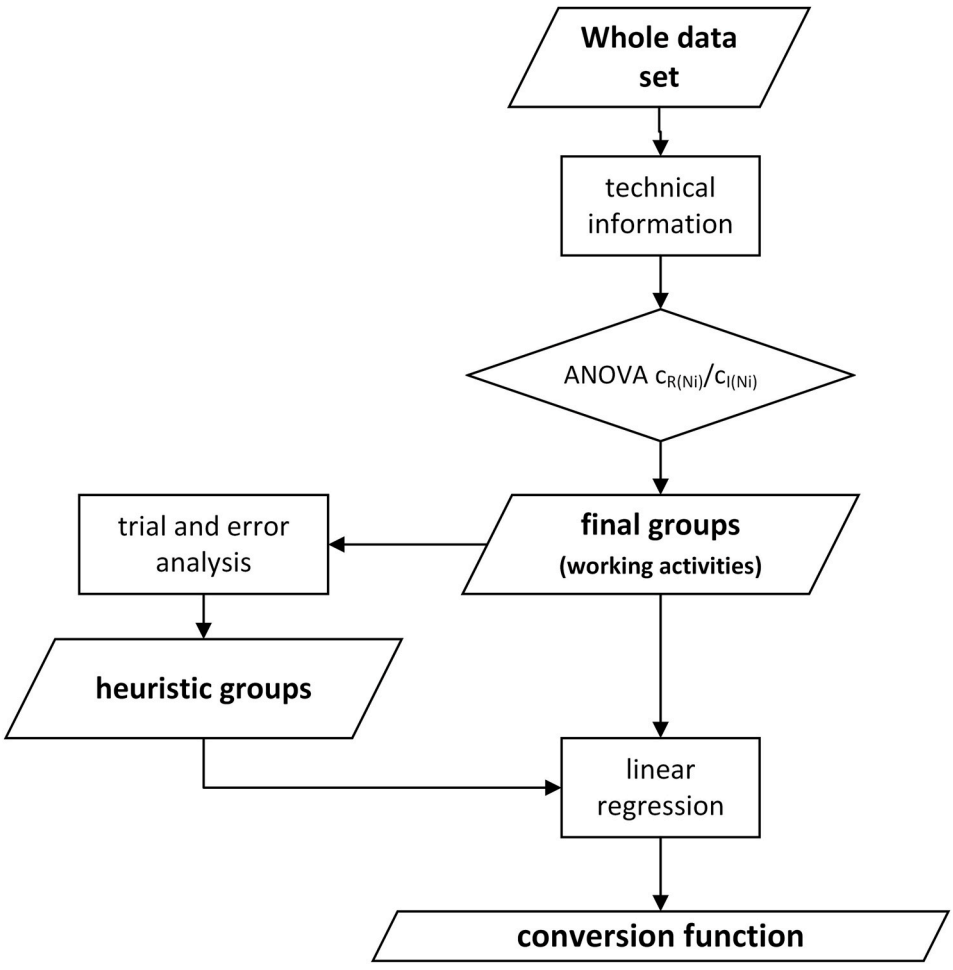


Fig. 1. Flowchart of the group formation steps and statistical tests (for each group distribution: Kolmogoroff-Smirnov, ANOVA: F-Test, Kruskal-Wallis test, variance homogeneity: Levene-test and graphical evaluation, post hoc tests: Games-Howell).

each group and homogeneity of variance was confirmed applying the Levene-Test ((Janssen and Laatz, 2017). To determine differences between the working activity groups, ANOVA, the non-parametric Kruskal-Wallis test and pair-by-pair comparisons using the Games-Howell post-hoc test (Sachs, 2004; Hilton and Armstrong, 2006) were conducted. The formation steps and statistical tests are shown in the flowchart (Fig. 1). This systematic approach leads to groups of parallel measured nickel concentrations in inhalable and respirable dust.

Similar, to evaluate the impact of the *type of sampling,* the total dataset was divided into the two subgroups *'stationary'* and *'personal'*. In the next step, the ratio of $c_{R(Ni)}$ and $c_{I(Ni)}$ was calculated for each pair in the two subgroups. Differences in both groups were compared by Median tests (with correction after Yates) and the non-parametric Mann-Whitney-U-Test for independent samples (Sachs, 2004; MacFarland and Yates, 2016; Haviland, 1990).

In each group the residuals of all analyses have been checked graphically (histograms) for normality and the absence of trends: There are no patterns discernible apart from the omission $c_{R(Ni)} > c_{I(Ni)}$ and all residuals are approximately normally distributed. Additionally each group has been checked for autocorrelation by performing a Durbin-Watson test (Sachs, 2004). These are prerequisites to perform a regression analysis. Before calculating the regression equations, possible leverage points are identified, and eliminated using the Cook's measure (Cook and Weisberg, 1982; Chatterjee and Hadi, 1989; Kleinbaum et al., 2014). In a next step, the groups are subjected to a linear regression analysis. The quality of regression parameters is evaluated using the correlation coefficient R and the adjusted coefficient of determination *adj.* R^2 (Janssen and Laatz, 2017):

$$adj.\ R^2 = R^2 - \frac{m}{n-m-1} * \left(1 - R^2\right) \tag{1}$$

This accounts for the number of variables m and the number of paired data n. Since in our case $n \gg m$, *adj.* $R^2 \approx R^2$.

This study describes in most cases a linear relationship between $ln(c_{R(Ni)})$ (natural logarithm of the nickel concentration in respirable dust) and $ln(c_{I(Ni)})$ (natural logarithm of the nickel concentration in inhalable dust):

$$ln\left(c_{R(Ni)}\right) = k \cdot ln\left(c_{I(Ni)}\right) + C_0 \tag{2}$$

where k is the slope and C_0 the intercept, which can be determined by regression analysis. C_0 and k are given with their standard errors (compare Table 3). We also calculated the range of the standard errors of the fitted regression function $s_{Fit}(ln(c_{R(Ni)}))$, for calculating the confidence intervals for the regression function at a given $ln(c_{I(Ni)})$ (Draper and Smith, 1998). Equation (2) can be transformed back into a function with the original concentrations:

$$c_{R(Ni)} = {c_{I(Ni)}}^{k} \cdot e^{C_0}. \tag{3}$$

From equation (3) two things can be derived: First, when $c_{I(Ni)}$ tends to zero, $c_{R(Ni)}$ also tends to zero. This is a necessary condition, since $c_{R(Ni)} \leq c_{I(Ni)}$. Second, the linear relation of $c_{R(Ni)}$ and $c_{I(Ni)}$ is included in equations (2) and (3) if the value 1 is included in the 95 % confidence interval of k. The worst-case assumption $c_{R(Ni)} = c_{I(Ni)}$ is included, if $C_0 = 0$ and $k = 1$.

In some cases, the correlation coefficient was better for untransformed data. In this cases a correlation between $c_{R(Ni)}$ and $c_{I(Ni)}$ was calculated:

$$c_{R(Ni)} = c_{I(Ni)} \cdot k + C_0 \tag{4}$$

In general it is possible to expand equation (2) or (4) with further covariates, such as *working activity* or *measurement system*, and perform a multilinear regression analysis. One prerequisite of a multilinear regression analysis is that all covariates have to be independent. In case of this study, $c_{I(Ni)}$ is influenced by all other possible covariates. Therefore, the prerequisite would be violated and this method cannot be applied.

From the working activity groups, more restrictive subgroups, so-called 'heuristic groups' (*'welding', 'high temperature cutting'* and *'grinding'*) were derived. These groups cannot be formed systematically. The working activity groups contain many subgroups which describe similar working tasks, such as *'wet grinding'* and *'dry grinding'* (from working activity group *'machining/abrasive techniques'*) or *'tungsten inert gas welding', 'metal active gas welding'* and *'arc welding'* (in working group *'high temperature processing'*) for example. These subgroups were pooled, when they showed similar regression coefficients and enhanced quality measures (higher R and *adj.* R^2) compared to their associating working activity group in order to form the so-called 'heuristic groups'.

3. Results

3.1. Nickel in inhalable and respirable dust: Description of the whole dataset

After two leverage points have been eliminated, simple linear regression analysis is performed on the whole dataset of 551 pairs of parallel nickel measurements. When only $c_{I(Ni)}$ is considered as predictor variable, one obtains $k = 0.726$ and $C_0 = -2.835$ in equation (2). The adjusted coefficient of determination *adj.* R^2 and correlation coefficient R are 0.767 and 0.876, respectively.

Fig. 2 shows a scatterplot of the log-transformed, parallel measured nickel concentrations in inhalable versus respirable dust and the 95% confidence interval. The cutoff values, resulting from the data selection for $c_{R(Ni)} > c_{I(Ni)}$ are clearly visible.

The arithmetic mean (*AM*) for nickel in inhalable dust is 0.07933 mg m^{-3}, for nickel in respirable dust 0.0077 mg m^{-3} respectively (Table 2). The lowest observed concentration of nickel in inhalable dust was $1.6*10^{-5}$ mg m^{-3} and for nickel in respirable dust $5.8*10^{-7}$ mg m^{-3}. The highest observed concentrations were 4.7 mg m^{-3} (Ni in inhalable dust) and 0.19 mg m^{-3} (Ni in respirable dust).

3.2. Exclusion of 'unphysical' nickel concentrations

With the restriction ($c_{R(Ni)}$ cannot be higher than $c_{I(Ni)}$), 45 parallel measurements were excluded. If one considers these measurements for linear regression, the quality measures for the whole dataset decrease slightly ($\Delta R = -0.038$; $\Delta adj.\ R^2 = -0.065$) in comparison to group 0. The regression coefficients vary by -0.069 (Δk) and -0.224 (ΔC_0), resulting in lower nickel concentrations in respirable dust with increasing amount of nickel in the inhalable dust fraction.

3.3. Type of sampling

For this study, 473 personal and 78 stationary measurements are considered. The high amount of personal measurements results from the requirements of the Technical Guidance 402, where exposure measurements should mainly be performed personally and stationary measurements only in exceptional cases, when a personal measurement is not possible (AGS, 2017). In the whole dataset, the median in both groups '*stationary*' (median = 0.322) and '*personal*' (median = 0.245), as well as the distribution of the ratio $c_{R(Ni)}/c_{I(Ni)}$ are not identical. The tests show significant differences (median test: $p = 0.036$; Mann-Whitney-U test: $p = 0.007$). In order to prove, if the differences actually result from the type of sampling, a two-factor ANOVA was done on the whole dataset. This ANOVA showed that the differences in the ratio $c_{R(Ni)}/c_{I(Ni)}$ result from the different working activities included in the whole dataset ($p = 0.007$), and do not result from the type of sampling ($p = 0.273$). The ANOVA also showed no interactions between *working activity* and *type of sampling* ($p = 0.308$).

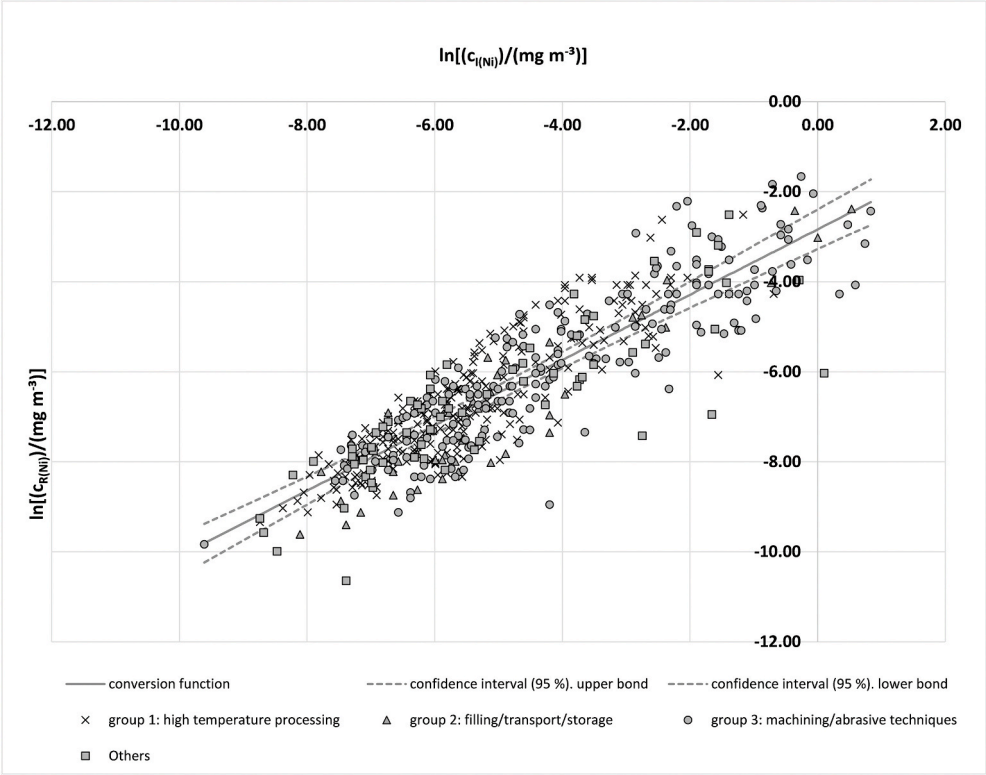


Fig. 2. Scatterplot $y = ln(c_{R(Ni)})$ versus $x = ln(c_{I(Ni)})$ for parallel measurements with their relating working activity group, the linear regression line and 95thconficence interval (equation (2)).

3.4. Working activity

In this study, three working activity groups are formed (Tables 2 and 3):

- *Group 1: high temperature processing* (such as welding, foundry, soldering)
- Group 2: *filling/transport/storage*
- Group 3: *machining/abrasive techniques* (such as grinding, milling, polishing)

As group 1 also contains all welding processes, as an additional information the Grinding time fraction (GTF) is given in most of the datasets concerning welding. Group 1 was divided into group 1a (high temperature processing *(incl. welding GTF < 5%)*) and group 1b (*high temperature processing (incl. welding GTF > 5%)*). These groups both contain 16 measurement pairs with no GTF information, and 52 datasets of further high temperature processes excluding welding, which is the reason for their similar AM, SD and median (Table 2). The purpose of group 1a and 1b is to highlight the impact of abrasive techniques during welding measurements. Comparing the minimum concentrations of group 1a and group 1b, lower concentrations of nickel in respirable dust were measured in group 1a ($5.8*10^{-7}$ mg m^{-3} for nickel in respirable and $1.2*10^{-4}$ mg m^{-3} for nickel in inhalable dust).

The highest concentrations of nickel in inhalable and respirable dust can be determined in group 3 *'machining/abrasive techniques'* ($c_{I(Ni)}$ = 2.300 mg m^{-3} and $c_{R(Ni)}$ = 0.1900 mg m^{-3}). The lowest concentrations of nickel in respirable dust can be found in group 1 *'high temperature processes'* ($c_{R(Ni)}$ = $5.8*10^{-7}$ mg m^{-3}) and of nickel in inhalable dust in group 3 *'machining/abrasive techniques'* ($c_{I(Ni)} = 6.7*10^{-5}$ mg m^{-3}). No significant difference of the ratio $c_{R(Ni)}/c_{I(Ni)}$ between group 2 (*'filling/transport/storage'*) and 3 (*'machining/abrasive techniques'*) can be determined ($p = 0.385$), whereas the ANOVA shows, that group 1 (*'high temperature processing'*) differs highly from the other two groups (in both cases: $p < 0.001$). In the next step, the groups 1–3 (Tables 2 and 3) are subjected to a linear regression analysis. The biggest dataset is group 1 *'high temperature processing'*. The regression coefficients, $k = 0.870$ and $C_0 = -1.801$, differ strongly from the other two groups and the differences are larger than the respective standard errors (Table 3).

Comparing *'high temperature processing'* to the whole dataset (group 0), the quality measures are lower in group 1 ($\Delta R = 0.083$; $\Delta adj.\ R^2 = 0.139$). This is caused by the GTF, as it can be seen in group 1a and 1b. Our model, using the ln-transformation and the linear regression analysis, results in high quality measures ($R = 0.922$; $adj.\ R^2 = 0.850$), for group 1b *'high temperature processing (incl. welding GTF > 5%)'*, exceeding the measures of group 0 (compare Table 3). Whereas high temperature processing datasets describing a GTF <5% show weaker quality measures than the entire dataset (group 0) ($R = 0.759$, $adj.\ R^2 = 0.573$, group 1a, Table 3).

The other working activity groups (*'filling/transport/storage'* and *'machining/abrasive techniques'*) show similar quality measures compared to the entire dataset (group 0, compare Table 3).

3.5. Heuristic groups

Apart from the systematic approach, three so-called heuristic groups were formed. These groups were formed from similar working task subgroups (see Table 4) to bigger groups, describing the same activity. The groups α *'welding'* and β *'high temperature cutting'* are subgroups of group 1 and γ *'grinding'* is a subgroup of group 3. Because of the small number of data pairs, it was not possible to form more heuristic groups.

Similar to working activity group 1 *'high temperature processing'*, the heuristic group α *'welding'* was divided according to the GTF. The groups α1 and α2 contain parallel nickel measurements during welding processes with a GTF < 5% (n = 91). For this dataset, a transformation with the natural logarithm results in a poor correlation of $c_{R(Ni)}$ and $c_{I(Ni)}$ ($R = 0.620$, $adj.\ R^2 = 0.377$, group α1 *'welding (GTF < 5%) ln-transformed'*). If one applies a linear regression to the non-transformed dataset (group α2

Table 4
Heuristic groups with listed special activities, materials and number of data pairs (*n*).

ID	Group name	Originating group no.	Working activities	n
α	Welding	1	gas-melt welding, laser welding/ manual arc welding with coated rod electrode/ arc welding, mixed arc process/ metal inert gas welding/ metal active gas welding/ metal welding, mixed welding processes/ plasma welding/ submerged arc welding/ mesh welding machines tungsten inert gas welding	198
β	High temperature cutting	1	flame cutting/ plasma cutting/ laser cutting	48
γ	Grinding	3	wet grinding dry grinding abrasive grinding sanding block grinding	156

'welding (GTF < 5%) not transformed'), a better description of the data can be achieved with $R = 0.852$ and *adj.* $R^2 = 0.724$. The groups α3 and α4 contain parallel nickel measurements during welding processes with a GTF > 5% (n = 91). Linear regression results in higher quality measures for the ln-transformed data (*adj* $R^2 = 0.830$ and $R = 0.912$ (group α3 '*welding (GTF > 5%) ln-transformed*'), in comparison to the untransformed data (*adj* $R^2 = 0.455$, $R = 0.679$; group α4 '*welding (GTF > 5%) not transformed*'). Group α 'welding' itself should be used in cases, where no information about the GTF during welding processes is known, since this group also contains 16 parallel measured pairs of nickel without information about the GTF.

The regression models of the heuristic groups α3 '*welding (GTF > 5%) ln-transformed*', β '*high temperature cutting*' and γ '*grinding*', show a better description of the data than those with the systematic approach (Table 3). The *adj.* R^2 are 0.830, 0.924 and 0.798 respectively. The standard errors of s_{Fit} increase with decreasing group size.

Although transformed data were used, a plot of the regression curve for the group β '*high temperature cutting*' shows a nearly linear relationship (Fig. 3). This corresponds to the fact that the value 1 lays within $k \pm$ standard error from this group. Applying linear regression on the untransformed concentrations in this group leads to a smaller correlation coefficient ($R = 0.565$). In addition to that, the relating working activity group 1 '*high temperature processing*' shows no linear relationship or more specifically, the value 1 does not lay within $k \pm$ standard error from this group. Therefore, no linear conversion function for group β is presumed and in Table 3 only equation (2) is described for this group.

Comparing just the heuristic groups with transformed nickel concentrations (groups α1, α3, β and γ, Table 3), the regression coefficients show a variety for both k ($0.705 \leq k \leq 0.986$) and C_0 ($-2.997 \leq C_0 \leq -0.829$). Figs. 3 and 4 show the regression functions with their relating 95 % confidence intervals in their valid working range. It can be seen from these figures, that each heuristic group shows a different conversion function. If one measures for example $c_{I(Ni)} = 0.03$ mg m^{-3}, the result for $c_{R(Ni)}$ is different in each group, such as $c_{R(Ni)} \approx 0.014$ mg m^{-3} for '*high temperature cutting*' or $c_{R(Ni} \approx 0.004$ mg m^{-3} for '*grinding*'.

4. Discussion

4.1. Identification of groups

Describing the whole dataset by means of equation (2) or (3), reveals that the most important variable is inhalable dust, already explaining 76 % of the variation in the dataset (Table 3, group 0) and, resulting in $k = 0.726$ and $C_0 = -2.835$. Considering working activity as an additional variable, it leads especially to the group '*high temperature processing*', which is described by $k = 0.870$ and $C_0 = -1.801$. All other working activity groups in this systematic approach combine many different dust-generating processes and lead to coefficients similar to those of the

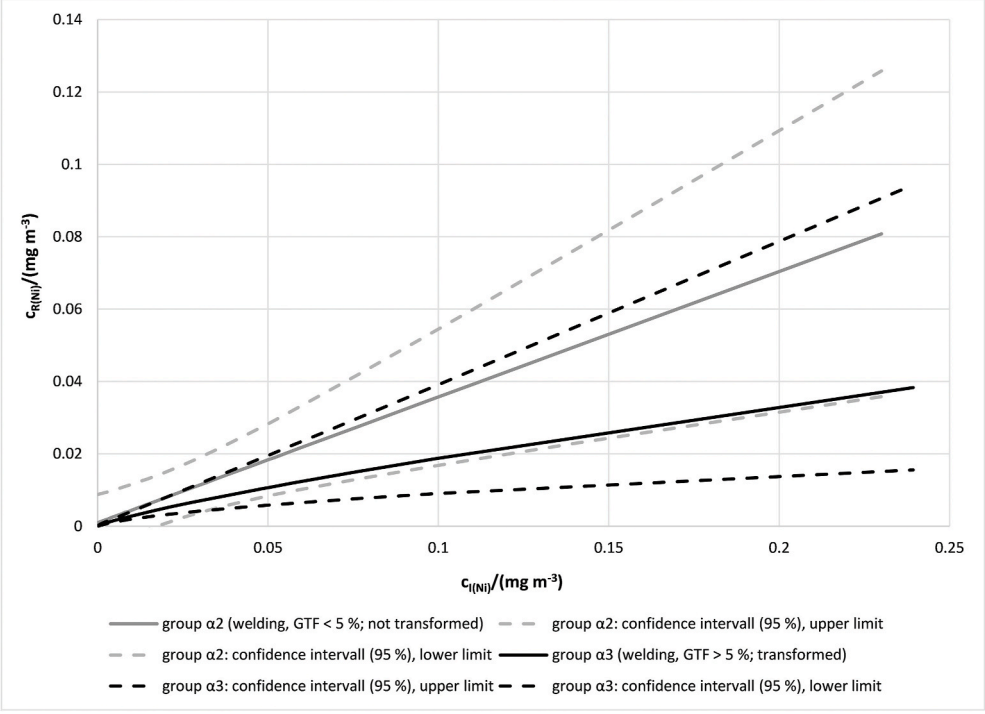


Fig. 3. Comparison of the determined conversion functions for the heuristic groups α2 *'welding, GTF < 5 %; not transformed'* and α3 *'welding, GTF > 5%; transformed'* with their 95 % confidence intervals.

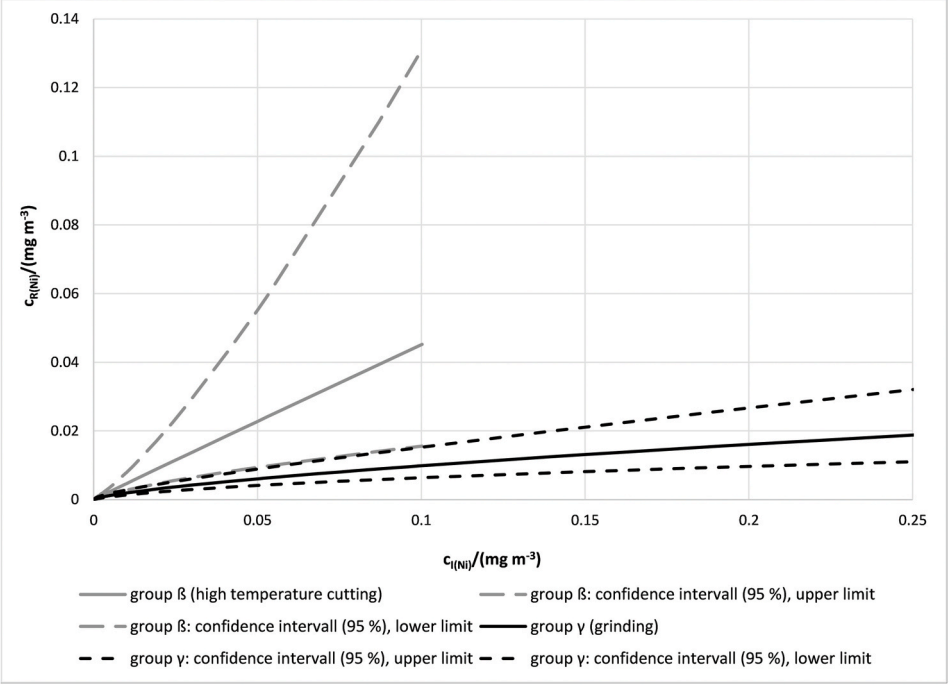


Fig. 4. Comparison of the determined conversion functions for the heuristic groups *ß 'high temperature cutting'* and *γ 'grinding'* with their 95% confidence intervals.

total dataset (Table 3).

The working activity groups *'high temperature processing'* and *'machining/abrasive techniques'* are mainly characterized by some large, specific subgroups. Group 1 is characterized by the subgroup *'welding'*, which represents 79 % of the data. 70 % of the presented data in group 3 contribute to the subgroup *'dry grinding'*. This shows that group 1 and 3 might not be representative for the whole working activity group which they are supposed to describe. In contrast to that, group 2 (*'filling/transport/storage'*) consists of heterogeneous data pairs with no dominant subgroup. However, this group consists of only 42 parallel measurements and we have limited information about the type of products that are transported or stored. Therefore, its validity is limited.

Since group 1 *'high temperature processing'* mainly consists of welding measurements, many datapoints contain additional information about the GTF. The groups 1a *'high temperature processing (incl. welding GTF < 5%)'* and 1b *'high temperature processing (incl. welding GTF < 5%)'* show similar descriptive statistics, at least for $c_{I(Ni)}$ (Table 2) because in both cases also data points without further information on GTF and other processes than welding are included. These two groups were created to highlight the impact of the GTF, when risk assessment is performed for workplaces with high temperature processes and other processes, such as abrasive techniques influence the measurements. The GTF is only given for welding processes, so the process specific groups α1 and α2 (*'welding GTF < 5%'*), as well as groups α3 and α4 (*'welding GTF > 5%'*) were formed.

4.2. Application of equations (2) and (3) or (4)

There are two limiting cases of equation (2):

- The worst-case assumption $c_{R(Ni)} = c_{I(Ni)}$, equivalent to $C_0 = 0$ and $k = 1$.
- The linear assumption for $c_{R(Ni)} > c_{I(Ni)}$, equivalent to $C_0 < 0$ and $k = 1$.

The worst-case assumption has not been observed in our dataset. Additionally all C_0 values for equation (2) throughout this study are negative ($-3.290 \leq C_0 \leq -0.829$).

All k values of this study are smaller than 1 ($0.347 \leq k \leq 0.986$), although the regression analysis does not prohibit $k > 1$. For equation (2), this indicates that $k < 1$ is a systematic effect. Which means, that the resulting function is not linear. The ratio $c_{R(Ni)}/c_{I(Ni)}$ is declining with increasing values of $c_{I(Ni)}$.

Table 3 shows that the concentrations of nickel in respirable dust are strongly dependent on the grinding time fraction. In the special case, that the GTF is lower than 5 %, the regression function shows a better description for untransformed data using equation (4). In contrast to that, if the GTF is higher than 5 %, a better description of the data can be achieved when the data is transformed. By this observation, we strongly recommend, to consider the GTF at the workplace when welding dust exposure is about to be evaluated.

A linear relation with $k = 1$ implies, that a single process is responsible for a constant ratio of emission for both dust fractions. One possible explanation for the finding of $k < 1$ in this study are agglomeration effects, which become more important with increasing concentrations (Rumpf et al., 1976; Koch et al., 1999). In addition, one can speculate that similar processes, which emit different concentrations of dust at different ratios, are coded as to the same working activity in the database.

4.3. Exclusion of 'unphysical' nickel concentrations

For this study pairs of nickel concentration are excluded when $c_{R(Ni)}$ is higher than $c_{I(Ni)}$. In fact, in some cases higher nickel concentrations are measured in respirable dust. This is possible as independent sampling systems for both dust fractions are used. Therefore, inhomogeneous materials, particle movement, thermal effects, incorrect sampling, wall deposits in FSP cyclones or the distance of the sampling systems to the source of emission can lead to higher nickel concentrations in respirable dust samples. In the result section, it was shown, that the exclusion of these data pairs does not have a large impact on the analysis at this stage, regarding the nickel concentration ranges of interest. However, to include these samples would introduce a bias the analysis toward a physically uncommon situation. Therefore, these values remain excluded.

4.4. Type of sampling

As ANOVA shows, the significant differences of $c_{R(Ni)}/c_{I(Ni)}$ found for the whole dataset (group 0) with the median and distribution tests, are caused by the different working activities which are included in the whole dataset and are not an effect of using different types of sampling.

However, one cannot exclude, that the type of sampling has an impact on the concentration, as it has been observed in various studies (Lillienberg and Brisman, 1994; Esmen and Hall, 2000; Lee et al., 2006; Klasson et al., 2016). Personal sampling systems collect occupational dusts in reduced distance to the source of exposure, while stationary systems can only be directed to the source. Personal sampling systems might collect larger, heavier particles directly after the source of emission, while the amount of those particles decreases with increasing distance and thus are collected to a lesser extend using stationary sampling systems. This cannot be proved using the technical information in the database MEGA, as it contains no information about the distance from the source of emission.

4.5. Application and limitations of results

Especially for the group welding, it cannot be excluded, that the nickel content of the welding material might influence the nickel concentration in inhalable and respirable dust, and therefore the conversion function resulting for welding (Kendzia et al., 2017). When different forms of welding are pooled it is possible, that the effect of different nickel contents is concealed.

The considered measurements in this study have to be representative for a whole 8-h shift with regard to the German limit values. This is a prerequisite for analyses and the data storage in the exposure database MEGA. According to the German Technical Guidance 402, one measurement during a 2-h measurement is sufficient, to report a representative exposure during the shift of a worker. It remains problematic, if the 2 h during which the measurements were executed, are not representative for the whole work shift, but monitors a part of a work shift (Kendzia et al., 2017). The restriction of 2 h-measurements is also a limitation, because at workplaces with high exposures, the sampler could be loaded with particles in a shorter time.

The given groups are heterogeneous considering the different working activities and subgroups. One has to be careful to use the model parameters in toxicological or epidemiological analyses without a careful check of applicability. The results in this study were derived for nickel dust-generating processes in the German industry between 2011 and 2020 and the working conditions described in the previous sections.

For the estimation of Nickel in respirable dust, we recommend to use the conversion functions of the heuristic groups if the concerning working activity matches to these groups. Special attention should be paid, if there is no spatial separation between welding and grinding at the evaluated work place. When welding processes with GTF < 5% are evaluated, we recommend to use the conversion function of group α2 (*'welding (GTF < 5%) not transformed'*). When the GTF is supposed to exceed 5 % at welding processes, we recommend to use the formula of group α3 (*'welding (GTF > 5 %) ln-transformed'*). When the GTF of a welding process is unknown, it is recommended to use function α (*'welding'*). In all cases, where other high temperature processes than welding (or high temperature cutting, group β) are to be evaluated, one should use the conversion function of group 1 *'high temperature processing'*. If the concerning working activity does not match the heuristic groups, the functions of the working activity groups could be used (group 1–3). If they are also not applicable, the use of group 0 is not recommended.

If one calculates $ln(c_{R(Ni)})$ using the regression coefficients in Table 3 for a given group and a given $ln(c_{I(Ni)})$, then the result has the confidence interval of $\pm 1.96 \cdot s_{Fit} ln(c_{R(Ni)})$. The smaller value of s_{Fit} (Table 3) is only valid around the mean value of $ln(c_{I(Ni)})$ (Table 3). This variance has to be added to the measurement uncertainty, which should be calculated for the dust sampling process, as well as the analytical process. The measurement uncertainty (u) for the overall process (sampling and analytics) of nickel is about 6.05 % (expanded measurement uncertainty (U): 12.1 %) for concentrations up to 0.003 mg m^{-3} and $u = 12.1$ % ($U =$ 24.2 %) for concentrations up to 0.012 mg m^{-3}. The calculations and estimation of measurement uncertainties comply with the demands and requirements in the international standards EN 482, ISO 21832 and ISO/IEC Guide 98–3:2008 (GUM).

The uncertainty of the measured concentrations is in this study limited to several percent of the measured value (European Committee for Standardization, 2010; Deutsches Institut für Normung, 2021). The concentrations themselves, on the other hand, cover up to an order of magnitude due to other influences such as the type of work and inter or intra worker effects. The difference of these two scales suggest that the estimates of the slope parameter are not severely biased (Draper and Smith, 1998). If such a bias existed, it would decrease the size of the slope parameter. However, a rigorous treatment of the effect of uncertainty in the concentrations is beyond the scope of this study, as it includes the transfer from the natural to a logarithmic scale in combination with non-constant uncertainties.

The conversion functions were calculated from measurements performed with the sampling systems listed in Table 1. Applying the functions on data associated with other sampling systems, other measurement uncertainties have to be taken into account and the overall uncertainty might differ. The applicability of the functions on such data can be assumed, when the sampling systems were validated by the same international standards.

4.6. Comparison with literature

In a study of Kendzia et al. (2017), the average occupational exposure to inhalable nickel was estimated, also using the exposure database MEGA. In this study a total of 8 052 personal measurements of Nickel, collected between the years 1990 and 2009 were evaluated and a median of $c_{I(Ni)} = 0.009$ mg m^{-3} was determined (Kendzia et al., 2017). In our study, for 551 measurements a median of $c_{I(Ni)} = 0.0047$ mg m^{-3} was calculated, although both studies used the same database. In our study, only nickel concentrations of inhalable dust were considered, when a relating nickel concentration of respirable dust was measured as well. Additional to that, in our study more requirements and restrictions were demanded for the dataset, such as the sampling time should be equal or higher than 2 h or the restriction of not using samples with measured concentrations below the limit of quantification and a restriction to the used sampling systems. Kendzia et al. (2017) evaluated different occupations, such as welders and metalworkers. The median for nine different welding processes ranged between 0.004 mg $m^{-3}$and 0.022 mg m^{-3} ($c_{I(Ni)}$). In our study, we pooled ten different welding processes, forming the heuristic group α *'welding'*, determining a median of 0.0034 mg m^{-3}. In the study of Kendiza et al. (2017) also the effect of different nickel content of the welding material is evaluated, in our study this was not possible due to insufficient data.

In a study of Weiss et al. (2013) the correlation of parallel measured nickel concentrations ($n = 228$) in respirable and inhalable dust during different welding processes were evaluated. In contrast to our study, values < LOQ have been included and were imputed with values randomly selected from a log-normal distribution using a bootstrap algorithm with 100 runs. A transformation of nickel concentrations with log_{10} was done instead of ln (natural logarithm). The study distinguishes between metals with a nickel content lower or higher 5 %, whereas the grinding time fraction in the measurements is neglected (Weiss et al., 2013). In our study the correlation coefficient is smaller for the heuristic group *welding* ($R = 0.758$ vs. $R = 0.850$). Considering the influence of the GTF on the correlation of $c_{I(Ni)}$ and $c_{R(Ni)}$, the correlation in group α2 ($R = 0.852$) is close to the one of Weiss et al. (2013) and in group α3 the correlation coefficient is even higher ($R = 0.912$). If one uses the conversion function of Weiss et al. (2013), considering $c_{I(Ni)} = 0.03$ mg m^{-3},

the resulting $c_{R(Ni)}$ is ≈ 0.016 mg m^{-3}. If one uses the functions from our study for group α or α3, $c_{R(Ni)}$ ≈ 0.007 mg m^{-3} is estimated and if one uses the function of group α2 0.011 mg m^{-3} respectively. The differences of the regression functions in the two studies and thus the estimated $c_{R(Ni)}$, increase with higher $c_{I(Ni)}$. Weiss et al. (2013) performed additionally multiple linear regression models to determine predictor variables for internal and external exposure. In our study, it was not possible to correlate such variables, as the exposure database MEGA does not contain biomonitoring measurements and these are not part of this study.

The study of Berlinger et al. (2019) describes workplace exposures during different hot work processes. In two different facilities inhalable and respirable dust measurements were performed, and among other elements also analyzed for the nickel content. Their study contains measurements for flame cutting and plasma cutting (Berlinger et al., 2019), which can be compared to our group β *'high temperature cutting'*, since this heuristic group contains both subgroups (see Table 4). A further group which can be compared is their group 'surface grinding' and our group γ *'grinding'*. The measurements of the two facilities in the study of Berliner et al. (2019) showed big differences in the measured concentrations, resulting in broad median ranges. The median range for nickel in inhalable dust in the groups 'flame cutting' and 'plasma cutting' is 0.038–0.180 mg m^{-3} and in respirable dust 0.025–0.140 mg m^{-3}. In our study the median is lower, for $c_{I(Ni)}$ it is 0.0021 mg m^{-3} and $c_{R(Ni)}$ 0.0012 mg m^{-3}, respectively. The maximum concentrations (Max) of $c_{I(Ni)}$ of the cutting groups vary between 0.051 and 0.480 mg m^{-3} ($c_{R(Ni)}$ = 0.030–0.550 mg m^{-3}), and the minimum concentrations (Min) of $c_{I(Ni)}$ between 0.023 and 0.100 mg m^{-3} ($c_{R(Ni)}$ = 0.015–0.060 mg m^{-3}). In our group β, $c_{I(Ni)}$ Max is 0.100 mg m^{-3} ($c_{R(Ni)}$ Max = 0.73 mg m^{-3}) and $c_{I(Ni)}$ Min is 0.00047 ($c_{R(Ni)}$ Min = 0.00018 mg m^{-3}). In our study, we cover a broader range of concentrations as it can be seen for our Min and Max concentrations. The different medians comparing both studies might result from the different number of measurements. Berlinger et al. (2019) calculated their parameters on the basis of 5–7 pairs of measurement (dependent on facility and cutting group), whereas we were able to use 48 parallel measured nickel concentrations. In case of grinding, the study of Berlinger et al. (2019) showed also big differences between the two facilities, medians of nickel in inhalable dust are 0.016 mg m^{-3} (facility 1) and 0.190 mg m^{-3} (facility 2). The median of facility 1 matches the median of our group γ *'grinding'* (0.015 mg m^{-3}). Berlinger et al. (2019) did not use linear regression to correlate nickel in respirable and inhalable dust, but calculated the ratio $c_{R(Ni)}/c_{I(Ni)}$ by 0.64 ± 0.14 (flame cutting), 0.75 ± 0.34(plasma cutting) and 1.22 ± 0.36 (surface grinding). As we cannot assume a linear correlation for these concentrations, we did not calculate any ratios. In addition, a ratio of 1.22 cannot result from our study, because of the restriction $c_{R(Ni)} > c_{I(Ni)}$.

5. Summary and conclusion

In summary, it is possible to develop conversion functions for estimating the nickel concentration in the respirable dust fraction out of the nickel concentration in the inhalable dust fraction. 551 data pairs were analyzed including different working activities. The given conversion functions can help occupational hygienists and risk assessors to estimate missing nickel concentrations for retrospective analyses which are often required for the assessment of occupational diseases or for epidemiological studies. The used data represents nickel exposure at work places in Germany and therefore, the conversion functions might be more applicable for German exposure data. The application of the conversion functions for data measured in other countries should be done with caution.

The study suggests that the data should generally be evaluated using linear regression of the log-transformed data shown in equation (2) or (3) with $k \leq 1$ and $C_0 < 0$, except for welding with a grinding time fraction (GTF) < 5 %, where a linear regression of the untransformed, original concentrations is feasible, using equation (4). With specific working conditions, it is possible to identify heuristic groups (α2, α3, β, γ) where 72 – 92 % of the variance in the data is accounted for by the regression functions. The bigger working activity groups 1 – 3 are less specific and the regression explains only 63 – 85 % of the variance.

For the estimation of Nickel in respirable dust, it is recommend to use the conversion functions of the heuristic groups if the concerning working activity matches these groups. When welding processes with GTF < 5 % are evaluated, we recommend to use the conversion function of group α2 (*'welding (GTF < 5 %) not transformed'*). When the GTF exceeds 5 %, we recommend to use the formula of group α3 (*'welding (GTF > 5%) ln-transformed'*). When the GTF of a welding process is unknown, function α (*'welding'*) should be used. In all cases, where other high temperature processes than welding (or high temperature cutting, group β) are to be evaluated, one should use the conversion function of group 1 *'high temperature processing'*. If the concerning working activity does not match the heuristic groups, the functions of the working activity groups could be used (group 1 – 3). In the next years, more measurements of nickel in respirable and inhalable dust will be performed and these new measurements will be used for further verification of the conversion functions found in this study. This study is the starting point for investigating further health related dust components, such as Cobalt and Manganese.

Declaration of competing interest

The authors declare no conflict of interest relating to the material presented in this article its contents, including any opinions and/or conclusions expressed, are solely those of the authors.

Acknowledgments

The authors thank the German Social Accident Insurance institutions for the provision of the data. All authors contributed substantially to the work and approved the final version of the manuscript. They also agree to take responsibility for the work.

References

AGS, 2020. Technische Regeln für Gefahrstoffe: arbeitsplatzgrenzwerte (TRGS 900). GMBl 1–69.
AGS, 2017. Technische Regeln für Gefahrstoffe: ermitteln und Beurteilen der Gefährdungen bei Tätigkeiten mit Gefahrstoffen: inhalative Exposition (TRGS 402). GMBl 43, 843–846.
AGS, 2021. Technische Regeln für Gefahrstoffe: risikobezogenes Maßnahmenkonzept für Tätigkeiten mit krebserzeugenden Gefahrstoffen (TRGS 910). GMBl 1–165.
Andersen, A., Berge, S.R., Engeland, A., Norseth, T., 1996. Exposure to nickel compounds and smoking in relation to incidence of lung and nasal cancer among nickel refinery workers. Occup. Environ. Med. 13, 708. https://doi.org/10.1136/oem.53.10.708.
Berlinger, B., Skogen, U., Meijer, C., Thomassen, Y., 2019. Workplace exposure to particulate matter bioaccessible and non-soluble metal compounds during hot work processes. J. Occup. Environ. Hyg. 16, 378. https://doi.org/10.1080/15459624, 2019.1594841, 86.
BMAS, 1977. Arbeitsschutz. BArbBl 128.
Chatterjee, S., Hadi, A.S., 1989. Influential observations, high leverage points, and outliers in linear regression. Stat. Sci. 379–416. https://doi.org/10.1214/ss/1177013622.
Coenen, W., 1981. Beschreibung der Erfassungs- und Durchgangsfunktion von Partikeln bei der Atmung - messtechnische Realisierung. Staub Reinhalt. Luft 41, 472–479.
Cook, R.D., Weisberg, S., 1982. Residuals and Influence in Regression. Chapman and Hall, New York, 0-412-24280-0.
Deutsches Institut für Normung, 2021. Exposition am Arbeitsplatz – Verfahren zur Bestimmung der Konzentration von chemischen Arbeitsstoffen – Grundlegende Anforderungen an die Leistungsfähigkeit. Deutsches Insitut für Normung, Berlin. https://doi.org/10.31030/3211072. DIN 482:2021-05.
DFG, 2012. Stoffliste. MAK- und BAT-Werte-Liste 2012.
Doll, R., 1990. Report of the international committee on nickel carcinogenesis in man. Report of the international committee on nickel carcinogenesis in man. Scandinavian J. Work. https://doi.org/10.5271/sjweh.1813. Environment & Health. Oxford.
Draper, N., Smith, H., 1998. Applied Regression Analysis. Wiley & Sons, New York, ISBN 978-0-471-17082-2.
ECHA, E.C.A., 2021. Nickel. 2021 Feb. Available from: URL: https://echa.europa.eu/de/substance-information/-/substanceinfo/100.028.283. (Accessed 11 February 2021). accessed.

Esmen, N.A., Hall, T.A., 2000. Theoretical investigation of the interrelationship between stationary and personal sampling in exposure estimation. Appl. Occup. Environ. Hyg 19, 114. https://doi.org/10.1080/104732200301935.

European Committee for Standardization, 2010. ISO 15767:2010-10. Workplace Atomospheres – Controlling and Characterizing Uncertainty in Weighing Collected Aerosols. European Commettee for Standardization, Brussels. https://doi.org/10.31030/1709485.

Gabriel, S., Koppisch, D., Range, D., 2010. The MGU - a monitoring system for the collection and documentation of valid workplace exposure data. Gefahrst. Reinhalt. Luft 43–49.

Genchi, G., Carocci, A., Lauria, G., Sinicropi, M.S., Catalano, A., 2020. Nickel: human health and environmental toxicology. Int. J. Environ. Res. Publ. Health 21, 1. https://doi.org/10.3390/2Fijerph17030679.

Grimsrud, T.K., Berge, S.R., Haldorsen, T., Andersen, A., 2002. Exposure to different forms of nickel and risk of lung cancer. Am. J. Epidemiol. 1123–1132. https://doi.org/10.1093/aje/kwf165.

Haviland, M.G., 1990. Yates's correction for continuity and the analysis of 2 x 2 contingency tables. Stat. Med. 9, 363–367. https://doi.org/10.1002/sim.4780090403.

Hilton, A., Armstrong, R., 2006. Post hoc ANOVA tests. Microbiologist 34–36, 09.

Hughson, G.W., Galea, K.S., Heim, K.E., 2010. Characterization and assessment of dermal and inhalable nickel exposures in nickel production and primary user industries. Ann. Occup. Hyg. 8–22. https://doi.org/10.1093/annhyg/mep068.

IARC, 1990. IARC monographs on the evaluation of carcinogenic risks to humans. Int. Agency Res. Canc. 49 (7). Chromium, Nickel and Welding, 978-92-832-1249-2.

IARC, 2012. Nickel and nickel compounds Chemical Agents and related occupations. In: IARC Monographs on the Evaluation of Carcinogenic Risks of Chemicals to Humans 100 C.

Janssen, J., Laatz, W., 2017. Statistsiche Datenanalyse mit SPSS: Eine anwendungsorientierte Einführung in das Basissystem und das Modul Exakte Tests. Springer Gabler Verlag, Berlin, ISBN 978-3-662-53477-9.

Kasprzak, K.S., Sunderman Jr., F.W., Salnikow, K., 2003. Nickel carcinogenesis. In: Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis, pp. 67–97. https://doi.org/10.1016/j.mrfmmm.2003.08.021.

Kendzia, B., Pesch, B., Koppisch, D., Van Gelder, R., Pitzke, K., Zschiesche, W., Behrens, T., Weiss, T., Siemiatycki, J., Lavoué, J., et al., 2017. Modelling of occupational exposure to inhalable nickel compounds. J. Expo. Sci. Environ. Epidemiol. 27, 427–433. https://doi.org/10.1038/jes.2016.80.

Klasson, M., Bryngelsson, I.-L., Pettersson, C., Husby, B., Arvidsson, H., Westberg, H., 2016. Occupational exposure to Cobalt and tungsten in the Swedish hard metal industry: air concentrations of particle mass, number, and surface area. The Annals of Occupational Hygiene 684–699. https://doi.org/10.1093/annhyg/mew023.

Kleinbaum, D.G., Kupper, L.L., Nizam, A., Rosenberg, E.S., 2014. Applied Regression Analysis - and Other Multivariable Methods. Cengage Learning, Boston, ISBN 978-128-505108-6.

Koch, W., Dunkhorst, W., Lodding, H., 1999. Design and performance of a new personal aerosol monitor. Aerosol. Sci. Technol. 231–246. https://doi.org/10.1080/027868299304282; 2-3.

Lee, S.-A., Adhikari, A., Grinshpun, S.A., KcKay, R., Shukla RR, T., 2006. Personal exposure to airborne dust and microogranisms in agricultural environments. J. Occup. Environ. Hyg. 30, 118. https://doi.org/10.1080/15459620500524607.

Lillienberg, L., Brisman, J., 1994. Flour dust in bakeries - a comparison between methods. Ann. Occup. Hyg. 75, 571. https://doi.org/10.1093/annhyg/38.inhaled_particles_VII.571.

Mattenklott, M., Möhlmann, C., 2011. Probenahme und analytische Bestimmung von granulären biobeständigen Stäuben (GBS). Gefahrst. Reinhalt. Luft 425–428.

MacFarland, T.W., Yates, J.M., 2016. Mann-Whintney U Test. Introduction to Nonparametric Statistics for the Biological Sciences Using R. Springer Interantional Publishing Switzerland, Basel, ISBN 978-3-319-30634-6.

Pitzke, K., Schwank, T., Wippich, C., 2020. Krebserzeugende Metalle (Arsen, Beryllium, Cadmium, Cobalt, Nickel) und ihre Verbindungen (ICP-Massenspektrometrie) (Loseblattsammlung Kennzahl: 7808). Deutsche Gesetzliche Unfallversicherung e. V. Berlin: Erich Schmidt. Available from: URL: https://www.ifa-arbeitsmappedigital.de/IFA-AM_7808. (Accessed 26 February 2021). accessed.

Rahilly, G., Price, N., 2003. Nickel allergy and orthodontics. J. Orthod. 74, 171. https://doi.org/10.1093/2Fortho.30.2.171.

Riediger, G., 2001. Geräte zur Probenahme der einatembaren Staubfraktion (E-Staub) (Loseblattsammlung Kennzahl 3010). Deutsche Gesetzliche Unfallversicherung e. V. Berlin: Erich Schmidt. Available from: URL: www.ifa-arbeitsmappedigital.de/3010. (Accessed 26 February 2021). accessed.

Roels, H., Van de Voorde, R., Vargas, V.M.M., Lauwerys, R., 1993. Relationship between atmospheric and urinary nickel in workers manufacturing electrical restistances using nickel oxide: role of the bioavailability of nickel. Occup. Med. 95–104. https://doi.org/10.1093/occmed/43.2.95.

Rumpf, H., Sommer, K., Steier, K., 1976. Mechanismen der Haftverstärkung bei der Partikelhaftung durch plastisches Verformen, Sintern und viskoelastisches Fließen. Chem. Ing. Tech. 4, 300. https://doi.org/10.1002/cite.330480408, 07.

Sachs, L., 2004. Angewandte Statistik. Springer Verlag, Berlin-Heidelberg-New York, ISBN 978-3-662-05744-5.

Siekmann, H., 1998. Geräte zur Probenahme der alveolengängigen Staubfraktion (A-Staub) (Loseblattsammlung Kennzahl 3020). Deutsche Gesetzliche Unfallversicherung e. V. Berlin: Erich Schmidt Verlag. Available from: URL: www.ifa-arbeitsmappedigital.de/3020. (Accessed 26 February 2021). accessed.

Tanaka, I., Ishimatsu, S., Matsuno, K., Kodama, Y., Tsuchiya, K., 1985. Biological half time of deposited nickel oxide aerosol in rat lung by inhalation. Trace Element Res. 10, 203. https://doi.org/10.1007/BF02917459.

Tsai, P.-J., Werner, M.A., Vincent, J.H., Maldonando, G., 1996. Worker exposure to nickel-containing aerosol in two electroplating shops: comparison between inhalable and total aerosol. Appl. Occup. Environ. Hyg 11, 484–492. https://doi.org/10.1080/1047322X, 1996.10389360.

Tsai, Perng-Jy, Vincent, James H., 2001. A Study of Workers' Exposures to the Inhalable and'Total' Aerosol Fractions in the Primary NickelProduction Industry using Mannequins to Simulate Personal Sampling. Annal. Occup. Hyg. 45 (5), 385–394. https://doi.org/10.1093/annhyg/45.5.385. In press.

Tsai, P.J., Vincent, J.H., Wahl, G., Maldonado, G., 1995. Occupational exposure to inhalable and total aerosol in the primary nickel production industry. Occup. Environ. Med. 99, 793. https://doi.org/10.1136/2Foem.52.12.793.

Weiss, T., Pesch, B., Lotz, A., Gutwinski, E., Van Gelder, R., Punkenburg, E., Kendzia, B., Gawrych, K., Lehnert, M., Heinze, E., et al., 2013. Levels and predictors of airborne and internal exposure to chromium and nickel among welders—results of the WELDOX study. Int. J. Hyg Environ. Health 216, 175–183. https://doi.org/10.1016/j.ijheh.2012.07.003.

Wippich, C., Rissler, J., Koppisch, D., Breuer, D., 2020. Estimating respirable dust exposure from inhalable dust exposure. Ann. Work Expos. Health 44, 430. https://doi.org/10.1093/annweh/wxaa016.