

ORIGINAL ARTICLE

# Modelling of occupational exposure to inhalable nickel compounds

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The aim of this study was to estimate average occupational exposure to inhalable nickel (Ni) using the German exposure database MEGA. This database contains 8052 personal measurements of Ni collected between 1990 and 2009 in adjunct with information on the measurement and workplace conditions. The median of all Ni concentrations was 9 µg/m<sup>3</sup> and the 95th percentile was 460 µg/m<sup>3</sup>. We predicted geometric means (GMs) for welders and other occupations centered to 1999. Exposure to Ni in welders is strongly influenced by the welding process applied and the Ni content of the used welding materials. Welding with consumable electrodes of high Ni content (>30%) was associated with 10-fold higher concentrations compared with those with a low content (<5%). The highest exposure levels (GMs ≥ 20 µg/m<sup>3</sup>) were observed in gas metal and shielded metal arc welders using welding materials with high Ni content, in metal sprayers, grinders and forging-press operators, and in the manufacture of batteries and accumulators. The exposure profiles are useful for exposure assessment in epidemiologic studies as well as in industrial hygiene. Therefore, we recommend to collect additional exposure-specific information in addition to the job title in community-based studies when estimating the health risks of Ni exposure.

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## INTRODUCTION

Exposure to nickel (Ni) is a widely distributed exposure circumstance in the production and processing of steel or alloys, for example, in foundry workers and welders. The International Agency for Research on Cancer classified exposure to metallic Ni and nickel-containing alloys as possibly carcinogenic (Group 2B).<sup>1</sup> Exposure to Ni and its compounds in Ni refining was classified as carcinogenic to humans (Group 1).<sup>2</sup> Compared with the production of nearly 800 million tons of steel, only 1.4 million tonnes of primary Ni are mined, smelted or refined currently in about 25 countries,<sup>3</sup> but not in Germany. Furthermore, Ni is used in the production of batteries and accumulators, and in some other applications.

Nickel occurs in the metallic form as oxides and mixed oxides (spinel) in welding fumes and in a variety of compounds in the ore or in industrial applications. Bioavailability is influenced by the solubility of the Ni species, where oxides and sulfides are poorly soluble compared with certain nickel salts.<sup>4</sup> The European Scientific Committee on Occupational Exposure Limits (SCOEL) considered both, soluble and insoluble particulate Ni compounds as carcinogenic to humans, but not metallic Ni.<sup>5</sup>

Several governmental and scientific agencies have recommended occupational exposure limits (OELs) for Ni and its compounds. The current 8 h time-weighted average permissible exposure limit (PEL) of the US Occupational Safety and Health

Administration for metallic Ni and insoluble Ni compounds is 1000 µg/m<sup>3</sup> in total dust.<sup>6</sup> SCOEL proposed 10 µg/m<sup>3</sup> for all forms of Ni in inhalable particles, excluding metallic Ni, to protect workers from Ni carcinogenicity.<sup>5</sup> However, Ni is a frequent cause of allergic contact dermatitis, induced by even smaller concentrations. In Germany, 6 µg/m<sup>3</sup> is the recent OEL for respirable Ni in its metallic form to protect workers from irritative effects.<sup>7</sup>

So far, dose–response relations of exposure to Ni with lung cancer were predominantly investigated in the Ni refining industry.<sup>8–11</sup> By contrast, welders comprise a much larger workforce and are exposed to Ni within a complex welding fume matrix consisting of spinels and metal oxides. It is yet challenging to disentangle the lung cancer risk associated with exposure to welding fume into its major components Ni, hexavalent chromium (Cr(VI)) and particulate matter. A welding-process exposure matrix was developed to estimate exposure to Ni and other agents in a cohort study of welders, but few measurements were available to support the quantitative estimates.<sup>12,13</sup>

The exploration of large exposure databases may improve exposure assessment.<sup>14</sup> Here we took advantage of the comprehensive exposure database MEGA (Messdaten zur Exposition gegenüber Gefahrstoffen am Arbeitsplatz)<sup>15</sup> to estimate the mean concentration of Ni related to job tasks and industrial settings, allowing for a refinement or validation of existing JEMs, especially for major welding processes.

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## METHODS

### Measurements of inhalable nickel

Airborne concentrations of inhalable Ni were compiled together with information on the duration of measurement, the analytical method, and the workplace in the MEGA exposure database at the Institute for Occupational Safety and Health of DGUV (IFA).<sup>15,16</sup> This analysis was based on 8052 personal Ni measurements taken between 1990 and 2009. Airborne dust was collected on glass fibre, quartz-glass fibre or cellulose nitrate filters with a GSP sampler operating at a flow rate of 3.5 l/min according to the European standard EN 481, to capture inhalable particles.<sup>17</sup> This particle fraction is defined as the mass fraction of particles, which can be inhaled by nose or mouth. Particles >100 µm are not included in this convention.

The filters were shipped to the central laboratory at IFA for quantitative Ni determination with different analytic methods. Ni was determined after digestion with standard digestion agent according to a protocol of Deutsche Forschungsgemeinschaft.<sup>18</sup> The filters were digested with a mixture of nitric and hydrochloric acid, and following dilution before quantitative analysis with different analytical techniques.

Flame atomic absorption spectrometry (FT-AAS) and graphite furnace AAS (ETA-AAS) were the standard methods in the early 1990ies. ETA-AAS achieves lower limits of quantification (LOQs). This more sensitive method was additionally applied to determine Ni, especially in low-exposure circumstances to comply with EN 482. Total reflection X-ray fluorescence and the more sensitive inductively coupled plasma mass spectrometry were increasingly applied as multi-element methods since 1996. Ni was also determined with inductively coupled plasma optical emission spectrometry since 2006.

Measurements below the LOQ were documented by their individual LOQs, which mainly depend on the analytical method used, pump flow rate and duration of sampling.

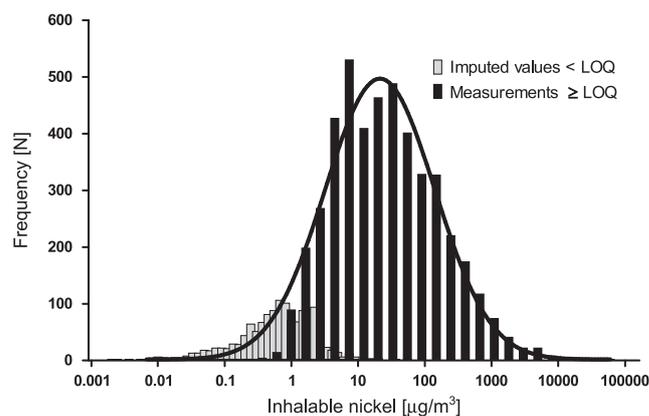
### Assessment of settings with occupational exposure to nickel

All workplaces were documented according to the national classification of occupations,<sup>19</sup> together with a description of job tasks and occupational settings. We classified welders by the predominantly applied welding process and the Ni content of the welding consumable or of the base material in consumable-free techniques (<5%, 5–30% and >30%). Another 12 occupational tasks were classified as “metal workers” (cutters,

metal sprayers, electroplaters, foundry workers, grinders, polishers, solderers or brazers, surface coaters, forging-press operators, scrap-metal workers and sinters). Other settings comprised the manufacture of accumulators and batteries, and rare exposure circumstances in the chemical industry and glass production. All assignments of measurements to the pre-defined job tasks were classified independently with 96% agreement (BK, BP and DK). A random subset of 100 ambiguous assignments was subjected to an additional rating (WZ). Measurements that could not be assigned to these settings were classified as “other occupations.”

### Statistical analysis

All calculations were performed with the statistical software SAS, version 9.4 (SAS Institute, Cary, NC, USA). We present the distribution of Ni concentrations with the fraction of measurements below LOQ, the 75th,



**Figure 1.** Density function of the concentrations of inhalable nickel (MEGA (Messdaten zur Exposition gegenüber Gefahrstoffen am Arbeitsplatz) database, 1990–2009).

**Table 1.** Distribution of personal measurements of inhalable nickel compiled in the German MEGA database between 1990 and 2009

Characteristics	N	N < LOQ (%)	Median (µg/m <sup>3</sup> )	P75 (µg/m <sup>3</sup> )	P90 (µg/m <sup>3</sup> )	P95 (µg/m <sup>3</sup> )
<b>Total</b>	8052	27	9	50	210	460
<b>Filter type</b>						
Quartz-glass fibre	1017	27	5	27	130	360
Cellulose nitrate	5747	25	10	53	220	480
Glass fibre	1288	34	10	60	220	420
<b>Analytical method</b>						
AAS	6023	23	10	60	230	500
ICP-OES	541	35	7	31	155	410
ICP-MS	732	30	4	20	99	270
X-ray fluorescence	756	45	7	39	160	350
<b>Time of measurement (years)</b>						
1990– < 1994	1639	28	10	50	200	420
1994– < 1999	2321	31	10	50	210	500
1999– < 2004	1889	21	9	50	240	460
2004–2009	2203	26	7	40	180	420
<b>Sampling time (hours)</b>						
< 2	1067	30	20	99	500	1200
2– < 3	5926	26	9	50	190	400
3– < 4	646	26	6	34	120	300
≥ 4	413	26	4	23	120	270

Abbreviation: AAS, atomic absorption spectroscopy; ICP-OES, inductively coupled plasma optical emission spectrometry; ICP-MS, inductively coupled plasma mass spectrometry; LOQ, limit of quantification; MEGA, Messdaten zur Exposition gegenüber Gefahrstoffen am Arbeitsplatz. P75, 75th percentile; P90, 90th percentile, P95, 95th percentile.

90th and 95th percentile. We refrained from the presentation of the 25th percentile, because 27% of all measurements were < LOQ. Multiple imputation was performed for measurements below LOQ according to the method used for measurements of Cr(VI).<sup>20,21</sup> Mixed-effects models were applied to the natural log-transformed Ni concentrations with imputed non-detects to assess the geometric means (GMs) of exposure to Ni in the various occupational settings with gas metal arc welding with solid wire (GMAW) as reference group. We adjusted by the Ni content of the welding material, duration of sampling (continuous and log-transformed) and calendar year (median-centered at 1999). We refrained from adjustment of the analytical method and type of filter, which are dependent on the anticipated exposure level and calendar year. We present GMs adjusted and not adjusted for the duration of sampling. The adjusted  $R^2$  was estimated for goodness-of-fit of the regression models.<sup>22</sup> We estimated the variability of Ni exposure between and within occupational settings using a simple one-way random-effects analysis of variance according to Loomis and Kromhout.<sup>23</sup>

## RESULTS

Characteristics of the 8052 personal measurements of inhalable nickel collected between 1990 and 2009 are shown in Table 1. Sampling on cellulose nitrate filter was the predominant type of particle collection ( $n=5747$ ). The major analytical method, especially in the earlier years, was AAS. Median duration of sampling was 2 h. The distribution of all concentrations (Figure 1) was skewed with a median concentration of  $9 \mu\text{g}/\text{m}^3$  and a 95th percentile of  $460 \mu\text{g}/\text{m}^3$ .

Table 2 presents the distribution of the measurements in welders ( $n=3055$ ) and other occupations. GMAW resulted in a median concentration of  $22 \mu\text{g}/\text{m}^3$  compared with  $5 \mu\text{g}/\text{m}^3$  in tungsten inert gas welding (TIG). A high Ni content of >30% of the welding material (mainly of the consumable) yielded a median Ni concentration of  $74 \mu\text{g}/\text{m}^3$  for GMAW and  $78 \mu\text{g}/\text{m}^3$  for

**Table 2.** Distribution of personal measurements of inhalable nickel in occupations with anticipated exposure (MEGA database, 1990–2009)

Occupation	Ni content of welding material (%)	N	N < LOQ (%)	Median ( $\mu\text{g}/\text{m}^3$ )	P75 ( $\mu\text{g}/\text{m}^3$ )	P90 ( $\mu\text{g}/\text{m}^3$ )	P95 ( $\mu\text{g}/\text{m}^3$ )
<i>Welder</i>							
GMAW	Total	1159	17	22	97	250	420
	Unknown	542	21	11	78	210	380
	< 5	156	34	5	20	55	110
	5–30	405	5	50	130	320	436
	>30	56	4	74	405	980	1600
FCAW	Total	93	25	7	29	55	155
	Unknown	66	29	5	10	30	50
	< 5	11	36	3	11	29	110
	5–30	16	0	40	139	312	460
	>30	0	—	—	—	—	—
TIG	Total	799	28	5	14	38	82
	Unknown	330	29	6	20	46	99
	< 5	18	50	4	6	19	40
	5–30	430	27	5	12	31	60
	>30	21	14	8	13	37	50
SMAW	Total	479	17	15	51	180	330
	Unknown	283	22	10	40	170	330
	< 5	34	21	5	45	210	1020
	5–30	140	14	20	61	143	245
	>30	22	5	78	270	520	630
Autogenous welding		20	15	6	10	65	404
Laser welding		35	37	4	10	35	40
Submerged arc welding		26	42	5	8	24	38
Plasma welding		64	18	14	63	130	280
Resistance welding		12	50	< LOQ	5	6	8
Others or not specified		368	26	18	60	190	320
<i>Metal worker</i>							
Cutter		259	18	19	120	630	1100
Metal sprayer		234	12	30	90	380	910
Electroplater		875	37	3	9	29	72
Foundry worker		350	34	6	25	170	450
Grinder		1291	22	21	120	470	1100
Chip-remove processor		133	42	5	30	170	360
Polisher/ molder		285	11	20	68	210	430
Solderer		80	63	< LOQ	9	43	160
Surface coater		112	52	< LOQ	12	95	160
Forging-press operator		68	18	39	150	300	360
Scrap-metal worker		197	65	< LOQ	10	50	120
Sinter		146	19	33	230	800	1100
<i>Other exposure circumstances</i>							
Chemical workers		183	45	7	35	230	1400
Manufacture of accumulators		50	4	20	60	175	350
Manufacture of batteries		219	8	30	130	370	570
Manufacture of glass		178	29	10	39	190	450
Other occupations		337	45	5	20	110	350

Abbreviation: FCAW, flux-cored arc welding; GMAW, gas metal arc welding; LOQ, limit of quantification; MEGA, Messdaten zur Exposition gegenüber Gefahrstoffen am Arbeitsplatz; SMAW, shielded metal arc welding; P75, 75th percentile; P90, 90th percentile; P95, 95th percentile; TIG, tungsten inert gas welding.

**Table 3.** Influence of occupation, year of measurement, Ni content of the welding material and sampling duration on the concentration of inhalable nickel (MEGA database, 1990–2009)

	N	Model with adjustment for sampling time ( $R^2 = 0.17$ )			Model without adjustment for sampling time ( $R^2 = 0.16$ )		
		Exp( $\beta$ )	95% CI	P	Exp( $\beta$ )	95% CI	P
<i>Intercept</i>	8052	44	36–54		27	23–33	
<i>Welder</i>							
GMAW	1159	1.00			1.00		
FCAW	93	0.51	0.31–0.83	0.0066	0.46	0.28–0.75	0.0020
TIG	799	0.21	0.17–0.26	< 0.0001	0.21	0.17–0.26	< 0.0001
SMAW	479	0.76	0.60–0.97	0.0260	0.83	0.66–1.06	0.1330
Autogenous welding	20	0.46	0.17–1.23	0.1232	0.48	0.18–1.28	0.1428
Laser welding	35	0.15	0.07–0.33	< 0.0001	0.16	0.07–0.35	< 0.0001
Submerged arc welding	26	0.17	0.06–0.44	0.0003	0.17	0.07–0.46	0.0004
Plasma welding	64	0.67	0.38–1.17	0.1629	0.74	0.42–1.31	0.3033
Resistance welding	12	0.07	0.02–0.30	0.0003	0.07	0.01–0.30	0.0003
Others or not specified	368	1.06	0.84–1.34	0.6319	1.12	0.89–1.42	0.3348
<i>Ni content of welding material (%)</i>							
< 5	238	0.21	0.15–0.30	< 0.0001	0.20	0.15–0.29	< 0.0001
5–30	1095	1.00			1.00		
> 30	118	1.98	1.30–3.01	0.0015	2.30	1.51–3.51	0.0001
Unknown or no welding process	6601	0.51	0.43–0.60	< 0.0001	0.51	0.43–0.61	< 0.0001
<i>Metal worker</i>							
Cutter	259	1.03	0.74–1.44	0.8603	1.18	0.85–1.64	0.3259
Metal sprayer	234	2.48	1.69–3.63	< 0.0001	2.78	1.89–4.07	< 0.0001
Electroplater	875	0.19	0.15–0.24	< 0.0001	0.18	0.15–0.23	< 0.0001
Foundry worker	350	0.53	0.41–0.67	< 0.0001	0.49	0.41–0.67	< 0.0001
Grinder	1291	1.82	1.48–2.23	< 0.0001	1.75	1.42–2.15	< 0.0001
Chip-remove processor	133	0.28	0.18–0.42	< 0.0001	0.28	0.19–0.43	< 0.0001
Polisher/ molder	285	0.81	0.50–1.32	0.4047	0.77	0.47–1.25	0.2826
Solderer	80	0.05	0.03–0.11	< 0.0001	0.06	0.03–0.11	< 0.0001
Surface coater	112	0.18	0.11–0.29	< 0.0001	0.19	0.12–0.31	< 0.0001
Forging-press operator	68	1.86	1.09–3.18	0.0220	1.86	1.08–3.18	0.0242
Scrap-metal worker	197	0.07	0.05–0.10	< 0.0001	0.08	0.05–0.11	< 0.0001
Sinter	146	1.51	1.03–2.20	0.0336	1.48	1.01–2.17	0.0436
<i>Other exposure circumstances</i>							
Chemical workers	183	0.51	0.35–0.73	0.0003	0.56	0.38–0.81	0.0020
Manufacture of accumulators	50	1.58	0.88–2.85	0.1273	1.69	0.93–3.06	0.0823
Manufacture of batteries	219	2.01	1.47–2.76	< 0.0001	2.05	1.49–2.82	< 0.0001
Manufacture of glass	178	1.13	0.88–1.45	0.3528	1.17	0.91–1.51	0.2259
Other occupations	337	0.51	0.42–0.60	< 0.0001	0.50	0.40–0.62	< 0.0001
Year of measurement (Ref = 1999)	8052	1.01	0.99–1.02	0.3638	0.99	0.98–1.01	0.4111
Sampling time (log(h))	8052	0.52	0.45–0.59	< 0.0001			

Abbreviation: CI, confidence interval; FCAW, flux-cored arc welding; GMAW, gas metal arc welding; MEGA, Messdaten zur Exposition gegenüber Gefahrstoffen am Arbeitsplatz; SMAW, shielded metal arc welding; TIG, tungsten inert gas welding.

shielded metal arc welding with coated stick electrodes (SMAW). Median concentrations of  $30 \mu\text{g}/\text{m}^3$  or higher were determined in metal sprayers, sinters, forging-press operators and battery-manufacturing workers. The majority of measurements in resistance welders, solderers or brazers, surface coaters such as flame sprayers and scrap-metal workers were below LOQ.

Table 3 depicts the adjusted effect estimates from the regression model as factors modifying the exposure level based on the measured and imputed Ni concentrations. GMAW served as reference group and had higher Ni concentrations than other welding processes such as flux-cored arc welding (FCAW), TIG, laser, submerged arc and resistance welding. The Ni content of the welding material (mainly of the consumable) was associated with a 10-fold difference of the airborne Ni concentration between low (< 5%) and high content (> 30%). Metal sprayers and workers in the production of batteries had at least

twofold higher concentrations than GMAW welders. No time trend in the Ni concentrations could be observed in the data investigated. The concentrations decreased with increasing sampling time.

Table 4 shows the model-based GMs for different occupational tasks estimated for the year 1999 with and without adjustment for the average sampling duration of 2 h. The Ni exposure levels varied widely by major welding process and Ni content of welding materials according to the pattern already found in the raw data: When adjusting for 2 h sampling time, high GMs were estimated for welding materials of high Ni content with GMAW ( $48 \mu\text{g}/\text{m}^3$ ; 95% CI 32–72  $\mu\text{g}/\text{m}^3$ ) and SMAW ( $37 \mu\text{g}/\text{m}^3$ ; 95% CI 24–57  $\mu\text{g}/\text{m}^3$ ), respectively. When estimating GMs for welders only, the corresponding mean concentrations were non-significantly higher for welding with consumables of high Ni content (GMAW:  $68 \mu\text{g}/\text{m}^3$ , 95% CI 47–101  $\mu\text{g}/\text{m}^3$ ; SMAW:  $45 \mu\text{g}/\text{m}^3$ , 95% CI 30–68  $\mu\text{g}/\text{m}^3$ )

**Table 4.** Model-based estimates of the geometric means of occupational exposure to inhalable nickel predicted for the year 1999 with and without adjustment for sampling time (MEGA database, 1990–2009)

Occupations	Ni content of welding material (%)	N	With adjustment for 2 h sampling time		Without adjustment for sampling time	
			GM ( $\mu\text{g}/\text{m}^3$ )	95% CI ( $\mu\text{g}/\text{m}^3$ )	GM ( $\mu\text{g}/\text{m}^3$ )	95% CI ( $\mu\text{g}/\text{m}^3$ )
<i>Welder</i>						
GMAW		1159	13	12–15	15	13–18
	< 5	156	5	4–7	6	4–8
	5–30	405	24	21–29	26	22–31
	> 30	56	48	32–72	61	40–92
FCAW		93	7	4–11	7	4–11
	< 5	11	3	2–5	3	2–5
	5–30	16	12	8–20	13	8–22
	> 30	0	–	–	–	–
TIG		799	3	2–3	3	3–4
	< 5	18	1	1–2	1	1–2
	5–30	430	5	4–6	6	5–7
	> 30	21	10	7–16	14	9–21
SMAW		479	10	8–13	12	10–15
	< 5	34	4	3–6	5	3–7
	5–30	140	19	15–24	22	17–28
	> 30	22	37	24–57	51	33–79
Autogenous welding		20	6	2–16	7	3–20
Laser welding		35	2	1–4	2	1–5
Submerged arc welding		26	2	1–6	3	1–7
Plasma welding		64	9	5–16	11	7–20
Resistance welding		12	1	0–4	1	0–5
Others or not specified		368	14	12–17	17	14–21
<i>Metal worker</i>						
Cutter		259	14	10–19	18	13–25
Metal sprayer		234	33	23–48	43	30–61
Electroplater		875	3	2–3	3	2–3
Foundry worker		350	7	6–9	7	6–9
Grinder		1291	24	21–29	27	23–31
Chip-remove processor		133	4	2–6	4	3–7
Polisher/ molder		285	11	7–17	12	7–19
Solderer		80	1	0–1	1	0–2
Surface coater		112	2	2–4	3	2–5
Forging-press operator		68	25	15–42	29	17–48
Scrap-metal worker		197	1	1–1	1	1–2
Sinter		146	20	14–29	23	16–33
<i>Other exposure circumstances</i>						
Chemical workers		183	7	5–10	9	6–12
Manufacture of accumulators		50	23	13–41	26	15–46
Manufacture of batteries		219	27	20–36	31	24–42
Manufacture of glass		178	15	12–19	18	14–22
Other occupations		337	7	6–8	8	7–9

Abbreviation: CI, confidence interval; FCAW, flux-cored arc welding; GM, geometric mean; GMAW, gas metal arc welding; MEGA, Messdaten zur Exposition gegenüber Gefahrstoffen am Arbeitsplatz; SMAW, shielded metal arc welding; TIG, tungsten inert gas welding.

(data not shown). Furthermore, high GMs were estimated in metal sprayers ( $33 \mu\text{g}/\text{m}^3$ ), in the manufacture of batteries ( $27 \mu\text{g}/\text{m}^3$ ) and in forging-press operators ( $25 \mu\text{g}/\text{m}^3$ ). The estimates of GMs were higher for most occupations when not adjusting for sampling time, but usually lower than the median concentrations. The variability of Ni concentrations between different occupational settings was high (98.1%), whereas the differences within the same setting were low (1.9%).

## DISCUSSION

Using a comprehensive data set of 8052 concentrations of inhalable Ni collected in workers' breathing zone, we estimated the average exposure level in occupations with recognized Ni exposure. Ni occurs mostly as oxides in welding fumes, but also in

a variety of compounds at other workplaces, for example, in Ni refining.<sup>4</sup> The concentrations were compiled as total Ni in the German exposure database MEGA,<sup>16</sup> together with supplemental information on sampling duration, analytical method, job task and related data. Notably, no data were available for Ni refining. The Ni concentrations were log-normally distributed, where the average should be presented by GM ( $13.7 \mu\text{g}/\text{m}^3$ ) or median ( $9 \mu\text{g}/\text{m}^3$ ) as a robust measure.

The arithmetic mean ( $132 \mu\text{g}/\text{m}^3$ ) is much higher due to few high concentrations. The 95th percentile was  $460 \mu\text{g}/\text{m}^3$  and 27% of all measurements were below LOQ. Nearly every other concentration of inhalable Ni was above the proposed OEL of  $10 \mu\text{g}/\text{m}^3$  of SCOEL.<sup>5</sup> The 95th percentiles for performing GMAW or SMAW with materials of high Ni content, grinders, cutters and sinters were higher than the current US PEL of  $1000 \mu\text{g}/\text{m}^3$ . There

is a large difference between recommended and permitted exposure limits. OELs can additionally vary by the form of Ni (elemental, soluble and insoluble compounds) and particle-size fraction (inhalable, respirable or total dust).<sup>24</sup> Exposure limits recommended by scientific committees are usually low, based on scientific evidence of health effects. Permitted limits can be adopted to follow these recommendations. The technical feasibility can be challenging. Welding techniques such as GMAW can hardly comply with  $10 \mu\text{g}/\text{m}^3$  as recommended by SCOEL.

We could not observe a time trend for the measurements between 1990 and 2009 in our data, whereas a decrease of 1.2% per year was found in a larger data set containing concentrations from 1977 to 2009.<sup>25</sup> As our data set was part of this analysis for the SYNERGY project (synergy.iarc.fr), we focus on the discussion of the exposure to Ni in welders, where we could use additional information from the MEGA database.

Our analysis can contribute to quantitative estimates of occupational exposure to airborne Ni in JEMs, especially for welders. In 1993, Gerin *et al.*<sup>12</sup> published a welding process exposure matrix for a cohort study of European welders, in which the job axis was stratified by major technique and type of steel welded. Whereas a limited number of measurements was available to derive the quantitative exposure levels of this JEM,<sup>13</sup> more than 3000 personal measurements for welders were compiled in this study based on MEGA. The welding process and Ni content of the material were major determinants of the average exposure concentration ranging between 1 and  $50 \mu\text{g}/\text{m}^3$  for the usual 2 h sampling duration. Welding with consumables of high Ni content (>30%) was associated with 10-fold higher concentrations compared with welding with consumables of low content (<5%). Our adjusted GMs of SMAW ( $37 \mu\text{g}/\text{m}^3$ ) and TIG ( $10 \mu\text{g}/\text{m}^3$ ) for welding materials of high Ni content were similar to the shift concentrations incorporated in the JEM of Gerin *et al.*<sup>12</sup> (30 and  $10 \mu\text{g}/\text{m}^3$ , respectively). The highest GM in welders was observed for GMAW ( $48 \mu\text{g}/\text{m}^3$ ) when working with consumables of high Ni content. Even higher average concentrations up to about  $100 \mu\text{g}/\text{m}^3$  can occur when welding with high-emission techniques such as GMAW or FCAW is performed in confined spaces.<sup>26,27</sup> The 8 h shift average of  $150 \mu\text{g}/\text{m}^3$  for GMAW applied to stainless steel in the JEM of Gerin *et al.*<sup>12</sup> is likely an overestimation. The application of a welding process JEM to population-based studies requires supplemental questionnaires to capture more detailed technical information on the welding process.<sup>28</sup> The job title “welder” is not sufficient to capture the wide range of Ni exposure occurring with different welding techniques. This, for example, is of major importance when investigating the dose-response relation between Ni in combination with Cr(VI) and lung cancer in welders.

The modelling of average exposure concentrations is pivotal in the development of quantitative JEMs. The strength of our model is the large number of airborne Ni concentrations and detailed information on job tasks and sampling. A challenge in using concentrations from exposure databases, also for monitoring exposure with regard to OELs, is the calculation of an 8 h shift exposure. In practice, welding is usually performed for less than 8 h. Measurements compiled in MEGA lasted on average 2 h and were preferentially conducted during the actual welding process. As a consequence, the GMs predicted from 2 h measurements are rather partial-workshift samples than full-shift time-weighted averages. As the duration of measurements is not independent from the exposure level, we estimated GMs with and without adjustment for sampling duration. As the duration of 62% measurements was 2 h, both GMs were mostly similar. The adjustment to a fixed sampling time of 2 h was based on the functional relation between sampling time and Ni concentration. However, this function can underestimate the concentration in certain exposure circumstances with a high airborne concen-

tration, where the filters are loaded within a shorter time. On the other hand, such a function may overestimate the concentration, for example, in few welders, as the arc time can be shorter than the duration of sampling. We further refrained from the implementation of the analytical methods into the model, as they can depend on the concentration. A more sensitive method was applied following concentrations < LOQ in the analysis of the respective sample with a standard method.

A major challenge is the estimation of mean exposure levels with regard to representativeness.<sup>20,29</sup> Measurements are usually not conducted as random samples of workplaces. Welding is more frequently applied to join parts of mild steel than of stainless steel.<sup>30</sup> However, welders of mild steel and job tasks with low exposure are less frequently monitored than workers with an anticipated high level of exposure. This can bias the estimate of the average exposure level towards higher concentrations, for example if the job title is simply “welder” and no other information available. This underlines the need for supplemental questionnaires when estimating occupational cancer risks, especially in community-based studies.

## CONCLUSIONS

This statistical analysis of inhalable Ni concentrations compiled in the German MEGA database aimed at providing exposure estimates for occupations with anticipated exposure. The exposure levels varied strongly between jobs. In welders, exposure was strongly influenced by the major technique and the Ni content of the processed material. High exposures could be also found in grinders, cutters, sinters and metal sprayers. These exposure profiles are useful for exposure assessment in epidemiologic studies and in industrial hygiene. In order to assess exposure to Ni and other occupational carcinogens in community-based studies, supplemental information on job tasks, workplaces and processed materials is essential in addition to job titles.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

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