Committee for Risk Assessment (RAC)

Committee for Socio-economic Analysis (SEAC)

Annex 3 to the Background Document

to the Opinion on the Annex XV dossier proposing restrictions on

N,N -dimethylacetamide (DMAC); 1-ethylpyrrolidin-2-one (NEP)

ECHA/RAC/RES-O-0000007225-77-01/F

ECHA/SEAC/[reference code to be added after the adoption of the SEAC opinion]

18 April 2023

IN THIS REPORT CONFIDENTIAL INFORMATION IS REDACTED - BLACKED OUT

1. Detailed evaluation of workplace exposure for DMAC and NEP – including confidential information

Table 1: Range of estimated exposure concentrations and measurement results for DMAC per exposure scenario - Details

Dossier Submitter					RAC					
PROC	Estimated exposure concentrations long-term		8h time weighted inhalation measure-ment results	Used reduction factors, OCs, PPE	Estimated exposure concentrations long-term			8h time weighted inhalation measurement results	Biomonitoring post-shift urine concentrations of NMAC	Remarks
	Inhalation	Dermal			Inhalation		Dermal			
	mg/m³	mg/kg bw/ day	mg/m³		ppm	mg/m³	mg/kg bw/day	mg/m³	mg/g creatinine (unless otherwise indicated)	
Industrial use of DMAC										
Manufacturing										
Low fugacity category										
1	0.036	0.034	<2.49	8h full shift, 100 % conc. no elevated temp → low fugacity, (Gloves)	0.01	0.036	0.03			
2	3.56	1.37			1	3.63	1.37			
3	10.69	0.69			3	10.89	0.69			
High fugacity category										
1	0.036	0.034		8h full shift, 100 % conc. Temp up to 180 °C → high fugacity, Gloves 90 %	0.01	0.036	0.03			
2	89.08	1.37			25	90.75	1.37			
3	178.16	0.69			50	181.5	0.69			
Formulation										
3	10.69	0.69	<0.07-<0.22	8h full shift, 100 % conc. no elevated temp → low fugacity, Gloves 90 % (not for PROC 3) LEV for PROC 4 & 5 (90 %)	3	10.89	0.69			
4	1.78	0.69			0.5	1.81	0.69			
5	1.78	1.37			0.5	1.81	1.37			
5 (no LEV)	17.82	1.37			5	18.15	1.37			
Charging and discharging										
Low fugacity category										
8a	3.56	1.37	<0.07-5.27	8h full shift, 100 % conc. Gloves 90 %,	1	3.63	1.37			
8b	0.89	1.37			0.25	0.91	1.37			

confidential

Dossier Submitter					RAC					
PROC	Estimated exposure concentrations long-term		8h time weighted inhalation measure-ment results	Used reduction factors, OCs, PPE	Estimated exposure concentrations long-term			8h time weighted inhalation measurement results	Biomonitoring post-shift urine concentrations of NMAC	Remarks
	Inhalation	Dermal			Inhalation		Dermal			
	mg/m³	mg/kg bw/ day	mg/m³		ppm	mg/m³	mg/kg bw/day	mg/m³	mg/g creatinine (unless otherwise indicated)	
8b (no LEV)	17.82	1.37		LEV (PROC 8b (95 %), otherwise 90 %)	5	18.15	1.37	[redacted]	[1]	[redacted]
9	1.78	0.69			0.5	1.81	0.69	[redacted]		
Medium fugacity category								[redacted]		
8a	17.82	1.37		8h full shift, 100 % conc. Elevated temp (40 °C) → medium, Gloves 90 % LEV (PROC 8b (95 %), otherwise 90 %)	5	18.15	1.37	[redacted]	confidential	
8b	4.45	1.37			1.25	4.53	1.37	[redacted]		
9	17.82	0.69			5	18.15	0.69	[redacted]		
Use as solvent in the production of agrochemicals, pharmaceuticals and fine chemicals										
1	0.036	0.034		8h full shift 100 % conc. No elevated temp → low Gloves 90 % (only for PROC 4) LEV 90 % (only for PROC 4)	0.01	0.036	0.03	No air or biomonitoring values are available.		No air or biomonitoring values are available.
2	3.56	1.37			1	3.63	1.37			
3	10.69	0.69			3	10.89	0.69			
4	1.78	0.69			0.5	1.81	0.69			
4 (no LEV)	17.82	0.69			5	18.15	0.69			
Use as solvent in the production of man-made fibres and films										
Low fugacity category								[redacted]	[2]	[redacted]
1	0.036	0.034	Maximum values >36	8h full shift 100 % conc. No elevated temp → low	0.01	0.036	0.03			
2	3.56	1.37			1	3.63	1.37			
3	10.69	0.69			3	10.89	0.69			

[1] Information confidential

[2] Information confidential

Dossier Submitter					RAC					
PROC	Estimated exposure concentrations long-term		8h time weighted inhalation measure-ment results	Used reduction factors, OCs, PPE	Estimated exposure concentrations long-term			8h time weighted inhalation measurement results	Biomonitoring post-shift urine concentrations of NMAC	Remarks
	Inhalation	Dermal			Inhalation		Dermal			
	mg/m³	mg/kg bw/ day	mg/m³		ppm	mg/m³	mg/kg bw/day	mg/m³	mg/g creatinine (unless otherwise indicated)	
4	1.78	0.69		Gloves 90 % (not for PROC 1-3) LEV 90 % (not for PROC 1-3) RPE (mentioned but not considered)	0.5	1.81	0.69	confidential		
13	3.56	1.37			1	3.63	1.37			
14	1.78	0.34			0.5	1.81	0.34			
19	3.56	14.14			1	3.63	14.14			
-	<9.5	-			xx	xx	xx			
Medium fugacity category[3]										
1	0.036	0.034		8h full shift,100 % conc. elevated temp → medium 120 °C (up to 300 °C)[3] Gloves 90 % (not for PROC 1-3), LEV 90 % (not for PROC 1-3), RPE (mentioned but not considered)	0.01	0.036	0.03			
2	17.82	1.37			5	18.15	1.37			
3	35.63	0.69			10	36.3	0.69			
4	7.13	0.69			2	7.26	0.69			
13	17.82	1.37			5	18.15	1.37			
14	17.82	0.34			5	18.15	0.34			
19	17.82	14.14			5	18.15	14.14			
Use as solvent in coatings										
Low fugacity category										
2	2.14	0.82	<3.6	8h full shift, 5-25 % conc. No elevated temp → low Gloves 90 % (not for PROC 1-3), LEV 90 % (not for	0.6	2.18	0.82	confidential		
7	10.69	2.57			3	10.89	2.57			
10	2.14	1.65			0.6	2.18	1.65			
13	2.14	0.82			0.6	2.18	0.82			

[3] Fugacity category should actually be "high" instead of "medium", as process temperature exceeds 100 °C, therefore the inhalation exposure values would be 5 times higher (except for PROC 1).

Dossier Submitter					RAC					
PROC	Estimated exposure concentrations long-term		8h time weighted inhalation measure-ment results	Used reduction factors, OCs, PPE	Estimated exposure concentrations long-term			8h time weighted inhalation measurement results	Biomonitoring post-shift urine concentrations of NMAC	Remarks
	Inhalation	Dermal			Inhalation		Dermal			
	mg/m³	mg/kg bw/ day	mg/m³		ppm	mg/m³	mg/kg bw/day	mg/m³	mg/g creatinine (unless otherwise indicated)	
				PROC 1-3)				[redacted]	[redacted]	[redacted]
Medium fugacity category								[redacted]	[redacted]	[redacted]
2	10.69	0.82		s.a. but slightly elevated temp (30 °C) → medium	3	10.89	0.85	[redacted]	[redacted]	[redacted]
10	10.69	1.65			3	10.89	1.65	[redacted]	[redacted]	[redacted]
Use as solvent in the production of films or hollow fibre spinning										
According to the Dossier Submitter this use is covered by the exposure scenario 'Use as solvent in the production of man-made fibres.										
Manual maintenance (cleaning and repair) of machinery										
28 (indoors, LEV & RPE)	0.36	1.37	<8.66	PROC 8a used as basis 8h full shift, 100 % conc., No elevated temp → low Gloves 90 %, RPE 90 % LEV 90 % or 30 % reduction for outdoors	0.1	0.36	1.37	[redacted]	confidential	
28 (outdoors, RPE)	2.49	1.37			0.7	2.54	1.37			
Use as laboratory chemical										
15	1.78	0.034		8h full shift, 100 % conc., No elevated temp → low Gloves 90 %, LEV 90 %	0.5	1.81	0.034	[redacted]	confidential	
Professional use of DMAC										
Use as laboratory chemical										

Dossier Submitter					RAC					
PROC	Estimated exposure concentrations long-term		8h time weighted inhalation measure-ment results	Used reduction factors, OCs, PPE	Estimated exposure concentrations long-term			8h time weighted inhalation measurement results	Biomonitoring post-shift urine concentrations of NMAC	Remarks
	Inhalation	Dermal			Inhalation		Dermal			
	mg/m^3	mg/kg bw/ day	mg/m^3		ppm	mg/m^3	mg/kg bw/day	mg/m^3	mg/g creatinine (unless otherwise indicated)	
15	3.56	0.068		8h full shift, 100 % conc., No elevated temp → low Gloves 80 %, LEV 80 %	1	3.63	0.068	No air or biomonitoring values are available.		

Table 2: Range of estimated exposure concentrations and measurement results for NEP per exposure scenario - Details

Dossier submitter				RAC					
Exposure Scenario & Process Categories	Estimated exposure concentrations long-term		Used reduction factors, PPE, OC	Estimated exposure concentrations long-term			8h time weighted inhalation measurement results	Biomonitoring	Remarks
	Inhalation	Dermal		Inhalative		Dermal		Post shift urine concentrations of 5-HNEP and 2-HESI	
	mg/m³	mg/kg bw/ day		ppm	mg/m³	mg/kg bw/day	mg/m³	mg/g creatinine	
Industrial use of NEP									
Manufacturing									
Low fugacity category									
1	0.046	0.034	8h full shift, 100 % conc., No elevated temp → low Gloves 90 % (cons. only for PROC 4) LEV 90 % (only for PROC 4)	0.01	0.047	0.03	No air or biomonitoring values are available.		
2	4.63	1.37		1	4.72	1.37			
3	13.88	0.69		3	14.14	0.69			
4	2.31	0.69		0.5	2.36	0.69			
Medium fugacity category									
1	0.046	0.034	8h full shift, 100 % conc., elevated temp (precise temp. not known) → medium Gloves 90 % (cons. only for PROC 4) LEV 90 % (only for PROC 4)	0.01	0.047	0.03	No air or biomonitoring values are available.		
2	23.14	1.37		5	23.58	1.37			
3	46.28	0.69		10	47.15	0.69			
4	9.26	0.69		2	9.43	0.69			
Formulation									
Low fugacity category									
1	0.046	0.034	8h full shift, 100 % conc., elevated temp (precise temp. not known) → medium LEV 90 % (for PROC 4, 5 & 14) Gloves 90 % (for PROC 4, 5 & 14)	0.01	0.047	0.03	No air or biomonitoring values are available.		
2	4.63	1.37		1	4.72	1.37			
3	13.88	0.69		3	14.14	0.69			
4	2.31	0.69		0.5	2.36	0.69			
5	2.31	1.37		0.5	2.36	1.37			
14	2.31	0.34		0.5	2.36	0.34			
Medium fugacity category									
5	23.14	1.37	8h full shift, 100 % conc., elevated temp → medium LEV 90 % and gloves 90 %	5	23.58	1.37	No air or biomonitoring values are available.		

Dossier submitter				RAC					
Exposure Scenario & Process Categories	Estimated exposure concentrations long-term		Used reduction factors, PPE, OC	Estimated exposure concentrations long-term			8h time weighted inhalation measurement results	Biomonitoring	Remarks
	Inhalation	Dermal		Inhalative		Dermal		Post shift urine concentrations of 5-HNEP and 2-HESI	
	mg/m³	mg/kg bw/ day		ppm	mg/m³	mg/kg bw/day	mg/m³	mg/g creatinine	
Charging and discharging									
8a (LEV)	4.63	1.37	8h full shift 100 % conc. No elevated temp → low LEV 90-95 % Gloves 90 %	1	4.72	1.37	**confidential**	No biomonitoring data available	
8a (no LEV)	46.28	1.37		10	47.15	1.37			
8b (LEV)	1.16	1.37		0.25	1.18	1.37			
8b (no LEV)	23.14	1.37		5	23.58	1.37			
9 (LEV)	2.31	0.69		0.5	2,36	0.69			
9 (no LEV)	23.14	0.69		5	23.58	0.69			
Use as solvent in industrial processes									
1	0.046	0.034	8h full shift 100 % conc. No elevated temp → low LEV 90 % and gloves 90 %	0.01	0.047	0.03	No air or biomonitoring values are available.		
2	4.63	1.37		1	4.72	1.37			
3	13.88	0.69		3	14.14	0.69			
4	2.31	0.69		0.5	2.36	0.69			
Use as solvent in coatings									
Low fugacity category									
2	2.78	0.82	8h full shift 5-25 % conc. → 40 % reduction, No elevated temp → low LEV 90-95 % (not for PROC 2) Gloves 90 %	0.6	2.83	0.82	No air monitoring values are available.	[4] **confidential**	
7	13.88	2.57		3	14.14	2.57			
10	2.78	1.65		0.6	2.83	1.64			
13	2.78	0.82		0.6	2.83	0.82			
Medium fugacity category									
2	13.88	0.82	8h full shift, 5-25 % conc. → 40 % reduction, elevated temp (PROC 2 > 30 °C & PROC 13 up to 130 °C) → medium LEV 90 % (not for PROC 2), Gloves 90 %	3	14.14	0.82			
10	13.88	1.65		3	14.14	1.64			
13	13.88	0.82		3	14.14	0.82			
Manual maintenance (cleaning and repair) of machinery									

[4] Information is confidential

Dossier submitter				RAC					
Exposure Scenario & Process Categories	Estimated exposure concentrations long-term		Used reduction factors, PPE, OC	Estimated exposure concentrations long-term			8h time weighted inhalation measurement results	Biomonitoring	Remarks
	Inhalation	Dermal		Inhalative		Dermal		Post shift urine concentrations of 5-HNEP and 2-HESI	
	mg/m³	mg/kg bw/ day		ppm	mg/m³	mg/kg bw/day	mg/m³	mg/g creatinine	
28 (indoors, with RPE)	0.46	1.37	PROC 8a used for calculation 8h full shift, 100 % conc., No elevated temp → low Gloves 90 %, RPE 90 %, LEV 90 % or 30 % reduction for outdoors	0.1	0.47	1.37	No air monitoring values are available.	confidential	
28 (outdoors, with RPE)	3.24	1.37		0.7	3.30	1.37			
Use as laboratory chemical									
15	2.31	0.034	8h full shift, 100 % conc., No elevated temp → low, Gloves 90 %, LEV 90 %	0.5	2.36	0.034	No air or biomonitoring values are available.		8h full shift rather conservative
Binder and release agent									
6	1.39	1.65	8h full shift 5-25 % conc. → 40 % reduction No elevated temp → low Gloves 90 % LEV 90-95 %	0.3	1.41	1.65	No air or biomonitoring values are available.		
7	13.88	2.57		3	14.14	2.57			
10	2.78	1.65		0.6	2.83	1.65			
13	2.78	0.82		0.6	2.83	0.82			
14	1.39	0.21		0.3	1.41	0.20			
Cleaning agents (e.g. paint removers, cleaners, degreasers)									
Low fugacity category									
7	13.88	2.57	8h full shift, 5-25 % conc. → 40 % reduction, No elevated temp → low Gloves 90 %, LEV 90-95 %	3	14.14	2.57	No air or biomonitoring values are available.		
10	2.78	1.65		0.6	2.83	1.65			
13	2.78	0.82		0.6	2.83	0.82			
Medium fugacity category									
13	13.88	0.82	8h full shift 5-25 % conc. → 40 % reduction Temp. up to 130 °C → medium Gloves 90 %, LEV 90-95 %	3	14.14	0.82			
Oil field drilling and production operations (one registrant)									
1	0.046	0.034	8h full shift 100 % conc.	0.01	0.047	0.03	No air or biomonitoring values are available.		
2	4.63	1.37		1	4.72	1.37			

Dossier submitter				RAC					
Exposure Scenario & Process Categories	Estimated exposure concentrations long-term		Used reduction factors, PPE, OC	Estimated exposure concentrations long-term			8h time weighted inhalation measurement results	Biomonitoring	Remarks
	Inhalation	Dermal		Inhalative		Dermal		Post shift urine concentrations of 5-HNEP and 2-HESI	
	mg/m³	mg/kg bw/ day		ppm	mg/m³	mg/kg bw/day	mg/m³	mg/g creatinine	
3	13.88	0.69	No elevated temp → low Gloves 90 % & LEV 90 % only for PROC 4	3	14.14	0.69			
4	2.31	0.69		0.5	2.36	0.69			
Functional fluids									
1	0.046	0.034	8h full shift 100 % conc. No elevated temp → low Gloves 90 % & LEV 90 % only for PROC 4	0.01	0.047	0.03	No air or biomonitoring values are available.		
2	4.63	1.37		1	4.72	1.37			
3	13.88	0.69		3	14.14	0.69			
4	2.31	0.69		0.5	2.36	0.69			
Polymer processing (one registrant)									
1	0.046	0.034	8h full shift 100 % conc. (PROC 1-5) 5-25 % conc. → 40 % reduction (PROC 6, 13, 14) No elevated temp → low Gloves 90 % (PROC 4, 5, 6, 13, 14) LEV 90 % (PROC 4, 5, 6, 13, 14)	0.01	0.047	0.03	No air or biomonitoring values are available.		
2	4.63	1.37		1	4.72	1.37			
3	13.88	0.69		3	14.14	0.69			
4	2.31	0.69		0.5	2.36	0.69			
5	2.31	1.37		0.5	2.36	1.37			
6	1.39	1.65		0.3	1.41	1.65			
13	2.78	0.82		0.6	2.83	0.82			
14	1.39	0.21		0.3	1.41	0.21			
Water treatment (one registrant)									
1	0.046	0.034	8h full shift , 100 % conc. (PROC 1-4) 5-25 % conc. → 40 % reduction (PROC 13) No elevated temp → low Gloves 90 % (PROC 4, 13) LEV 90 % (PROC 4, 13)	0.01	0.047	0.03	No air or biomonitoring values are available.		
2	4.63	1.37		1	4.72	1.37			
3	13.88	0.69		3	14.14	0.69			
4	2.31	0.69		0.5	2.36	0.69			
13	2.78	0.82		0.6	2.83	0.82			
Professional use of NEP									

Dossier submitter				RAC					
Exposure Scenario & Process Categories	Estimated exposure concentrations long-term		Used reduction factors, PPE, OC	Estimated exposure concentrations long-term			8h time weighted inhalation measurement results	Biomonitoring	Remarks
	Inhalation	Dermal		Inhalative		Dermal		Post shift urine concentrations of 5-HNEP and 2-HESI	
	mg/m³	mg/kg bw/ day		ppm	mg/m³	mg/kg bw/day	mg/m³	mg/g creatinine	
Charging and discharging									
8a (LEV)	13.88	1.65	8h full shift 5-25 % conc. → 40 % reduction No elevated temp → low LEV 80-90 % Gloves 80 %	3	14.14	1.65	No air or biomonitoring values are available.		
8a (no LEV)	69.42	1.65		15	70.72	1.65			
8b (LEV)	2.78	1.65		0.6	2.83	1.65			
8b (no LEV)	27.77	1.65		6	28.29	1.65			
9 (LEV)	5.55	0.82		1.2	5.66	0.82			
9 (no LEV)	27.77	0.82		6	28.29	0.82			
Use as solvent in coatings									
10	13.88	3.29	8h full shift, 5-25 % conc. → 40 % reduction No elevated temp → low LEV 80 %, Gloves 80 % RPE 90 % for PROC 11	3	14.14	3.29	No air or biomonitoring values are available.		
11	5.55	12.86		1.2	5.66	12.86			
13	5.55	1.65		1.2	5.66	1.65			
19	13.88	16.97		3	14.14	16.97			
Manual maintenance (cleaning and repair) of machinery									
28 (indoors with RPE)	1.39	1.65	PROC 8a used for calculation, 8h full shift < 25 % conc. → 40 % reduction, No elevated temp → low, Gloves 80 %, RPE 90 %, LEV 80 % (indoors), outdoors 30 % reduction	0.3	1.41	1.65	No air or biomonitoring values are available.		
28 (outdoors with RPE)	4.86	1.65		1.05	4.95	1.65			
Use as laboratory chemical									
15	4.63	0.068	8h full shift, 100 % conc., No elevated temp → low, Gloves 80 %, LEV 80 %	1	4.72	0.068	No air or biomonitoring values are available.		
Binder and release agent									
10	13.88	3.29	8h full shift, 5-25 % conc. → 40 % reduction, No elevated temp → low, Gloves 80 %, LEV 80 %, RPE 90 % for PROC 11	3	14.14	3.29	No air or biomonitoring values are available.		
11	5.55	12.86		1.2	5.66	12.86			
13	5.55	1.65		1.2	5.66	1.65			
Cleaning agents									
10	13.88	3.29		3	14.14	3.29	No air or biomonitoring values are available.		

Dossier submitter				RAC					
Exposure Scenario & Process Categories	Estimated exposure concentrations long-term		Used reduction factors, PPE, OC	Estimated exposure concentrations long-term			8h time weighted inhalation measurement results	Biomonitoring	Remarks
	Inhalation	Dermal		Inhalative		Dermal		Post shift urine concentrations of 5-HNEP and 2-HESI	
	mg/m³	mg/kg bw/ day		ppm	mg/m³	mg/kg bw/day	mg/m³	mg/g creatinine	
11	5.55	12.86	8h full shift, 5-25 % conc. → 40 % reduction, No elevated temp → low, Gloves 80 %, LEV 80 %, RPE 90 % for PROC 11	1.2	5.66	12.86			
13	5.55	1.65		1.2	5.66	1.64			
Use as excipient in agrochemicals (one registrant)									
5	46.28	2.74	8h full shift, 100 % conc. No elevated temp → low Gloves 80 %, RPE 90 % for PROC 11	10	47.15	2.74	No air or biomonitoring values are available.		
11	46.28	21.43		10	47.15	21.43			
13	46.28	2.74		10	47.15	2.74			
Functional fluids (one registrant)									
20	13.88	0.21	8h full shift, 5-25 % conc. → 40 % reduction, No elevated temp → low Gloves 80 %	3	14.14	0.21	No air or biomonitoring values are available.		
Road and construction applications (one registrant)									
10	80.99	5.49	8h full shift, 100 % conc., No elevated temp → low, Gloves 80 %, Outdoors 30 % reduction, RPE 90 % for PROC 11	17.5	82.51	5.49	No air or biomonitoring values are available.		
11	32.40	21.43		7	33.00	21.43			
13	32.40	2.74		7	33.00	2.74			
Polymer processing									
1	0.046	0.034	8h full shift, 100 % conc. (PROC 1 & 2), 5-25 % conc. → 40 % reduction (PROC 14) No elevated temp → low, Gloves 80 % (PROC 14), LEV 80 % (PROC 14)	0.01	0.047	0.03	No air or biomonitoring values are available.		
2	23.14	1.37		5	23.58	1.37			
14	5.55	0.41		1.2	5.66	0.41			

2. RAC interpretation of biological monitoring data for DMAC and NEP – including confidential information

Table 3: RAC interpretation of biological monitoring data for DMAC – post-shift urine concentrations in mg NMAC/g creatinine (unless otherwise indicated); data further considered is highlighted in blue, [redacted]

Sector	Study	Job-title	Geometric mean	arithmetic mean	Range	50th percentile	90th percentile	Remarks	Remarks RAC
			mg NMAC/g creatinine	mg NMAC/g creatinine	mg NMAC/g creatinine	mg NMAC/g creatinine	mg NMAC/g creatinine		
Primary fibre production	(Kennedy Jr & Pruett, 1989)	Operator (n=3)	11.78 (mg/L urine)		7 – 20 (mg/L urine)				Not considered (too few datapoints)
	(Kennedy Jr & Pruett, 1989)	Non-DMAC operator (n=1)	17.75 (mg/L urine)		13 – 26 (mg/L urine)				
	(Spies et al., 1995a)	Operator (n=55)	1.7					First day, before shift	Not considered (only geometric mean, no conclusion possible on the 90th percentile, data rather old)
	(Spies et al., 1995a)	Operator (n=54)	15.4					First day, end of shift	
	(Spies et al., 1995a)	Operator (n=57)	8.9					Second day, before shift	
	(Spies et al., 1995a)	Operator (n=335)	16.1					Second day, end of shift	
	(Spies et al., 1995a)	Operator (n=98)	26.7					High exposure group	
	(Spies et al., 1995a)	Operator (n=295)	13.5					Unspecified exposure group	
	(Spies et al., 1995a)	Operator	35 (80-percentile)						
	(Kawai et al., 1997)	Operator (n=27)			Up to 78 (mg/L urine)				Not considered (not enough contextual information given)

Sector	Study	Job-title	Geometric mean	arithmetic mean	Range	50th percentile	90th percentile	Remarks	Remarks RAC
			mg NMAC/g creatinine	mg NMAC/g creatinine	mg NMAC/g creatinine	mg NMAC/g creatinine	mg NMAC/g creatinine		
	(Perbellini et al., 2003)	All operators (post-shift, n=223).		20.5	1.5 – 173.6	7.7		The task of most workers was to check the automatic production of fibres. Every day, two groups of six workers started up two or three spinning machines (duration about 30 minutes), which would then work continuously for about 15 days except for occasional unscheduled stoppages.	extreme range, values cannot be allocated to a specific function during the work shift. Most samples came from workers engaged in starting up of spinning machines on previous days. 43 workers (about 19%) had urinary NMA levels higher than 30 mg/g creatinine. No conclusion possible on the 90th percentile → not considered
	(Perbellini et al., 2003)	Starting up of machinery (pre-shift, n=35)		7.3	1.5 – 30.6	4.9		During machine startup Operations (duration about 30 minutes), some workers had to immerse their hands (protected by gloves) in a water/DMAC solution (50 %) at a temperature of 50 °C. 17 workers	Values before or during work not representative.
	(Perbellini et al., 2003)	Starting up of machinery (halfway through the shift, n=35)		7.8	1.5 – 26.5	5.0			
	(Perbellini et al., 2003)	Starting up of machinery		14.2	5.6 – 44.6	11.6			Value roughly considered, as kind of worst case: up to 44 mg NMAC/g creatinine

Sector	Study	Job-title	Geometric mean	arithmetic mean	Range	50th percentile	90th percentile	Remarks	Remarks RAC
			mg NMAC/g creatinine	mg NMAC/g creatinine	mg NMAC/g creatinine	mg NMAC/g creatinine	mg NMAC/g creatinine		
		(post-shift, n=35)						(belonging to the 2nd, 4th, and 6th teams) were supplied with an active charcoal mask. Workers in the 1st, 3rd, and 5th teams did not use a mask.	no conclusion possible on the 90th percentile Starting up machine is linked to higher exposures than attending machine, not possible to assign the data to one of these tasks.
	(Perbellini et al., 2003)	Starting up of machinery (n=18)		12.8	6.6 – 24.3	11.9		Post-shift. Without mask	Not considered, only specific evaluation of the summarized values above.
	(Perbellini et al., 2003)	Starting up of machinery (n=17)		15.7	5.6 – 44.6	10.7		Post-shift. With mask	
	(Perbellini et al., 2003)	Starting up of machinery (n=18)		12.6	6.4 – 24-3	11.7		Post-shift. No immersion of hands	
	(Perbellini et al., 2003)	Starting up of machinery (n=16)		14.5	5.6 – 44.6	10.4		Post-shift. Immersion of hands	
	(Perbellini et al., 2003)	Starting up of machinery (n=17)		2.5	1.5 – 10.3	1.5		First day after two days rest, pre-shift.	Not considered, only specific evaluation of the summarized values above.
	(Perbellini et al., 2003)	Starting up of machinery (n=14)		10.8	2.7 – 21.9	10.0		First day, post-shift. With end of shift shower and change of clothing.	

Sector	Study	Job-title	Geometric mean	arithmetic mean	Range	50th percentile	90th percentile	Remarks	Remarks RAC
			mg NMAC/g creatinine	mg NMAC/g creatinine	mg NMAC/g creatinine	mg NMAC/g creatinine	mg NMAC/g creatinine		
	(Perbellini et al., 2003)	Starting up of machinery (n=13)		4.7	1.5 – 11.7	3.5		Second day (16 hours later), pre-shift.	
	(Perbellini et al., 2003)	Starting up of machinery (n=14)		17.6	7.1 – 28.2	17.2		Second day, post-shift. With end of shift shower and change of clothing.	
	(Perbellini et al., 2003)	Starting up of machinery (n=13)		4.9	2.7 – 7.1	4.7		Third day (24 hours later), pre-shift.	
	(Lee et al., 2006)	DMAC induced hepatic injuries group (n = 503)			2.2 – 196.5	19.6			Large number of measurements, however no conclusion possible on the 90th percentile. Large difference between the 50th percentile and the maximum value. → not considered
	(Lee et al., 2006)	Non-DIHI group (n = 464)			0.1 – 79.2	5.2			
	(Jung et al., 2007)	DMAC induced hepatic injury group (packing, exchanging spinneret, visual inspection) (n=21 cases / 228 samples)			4.6 – 196.5	25.1			Large number of measurements, however no conclusion possible on the 90th percentile. Large difference between the 50th percentile and the maximum value. → not considered

Sector	Study	Job-title	Geometric mean	arithmetic mean	Range	50th percentile	90th percentile	Remarks	Remarks RAC
			mg NMAC/g creatinine	mg NMAC/g creatinine	mg NMAC/g creatinine	mg NMAC/g creatinine	mg NMAC/g creatinine		
	(Jung et al., 2007)	Other workers not part of DIHI group (n=1,056)			0.1 – 133.9	11.8			
	(Duarte, 2015)	Group A	<LOQ					Control group (no DMAC exposure)	Not considered (control group)
	(Duarte, 2015)	Group B		2.93 (0.26 mg DMAC/L)				Expected inhalation exposure <7.2 mg/m^3	Grouping done according to inhalation exposure values → not relevant here. Same data is given below again, grouped by activities.
	(Duarte, 2015)	Group C		18.35 (0.60 mg DMAC/L)				Expected inhalation exposure 7.2-36 mg/m^3	
	(Duarte, 2015)	Group D		40.04 (2.91 mg DMAC/L)				Expected inhalation exposure >36 mg/m^3	
	(Duarte, 2015)	Dope preparation (n=5)		69.89			59.2	Dissolve polymer in DMAC	Data available to conclude on the 90th percentile. However, only roughly considered as a kind of worst case value, due to the low number of measurements.
	(Duarte, 2015)	Spinning (n=20)		45.35				Fibre is subjected to: coagulation, extrusion, washing, dyeing, drying and crimping.	
	(Duarte, 2015)	Tow-to-top (n=4) ##		6.60				Continuous filaments from cut and bailing area are subjected to opening, carding,	

Sector	Study	Job-title	Geometric mean	arithmetic mean	Range	50th percentile	90th percentile	Remarks	Remarks RAC
			mg NMAC/g creatinine	mg NMAC/g creatinine	mg NMAC/g creatinine	mg NMAC/g creatinine	mg NMAC/g creatinine		
								spinning and packaging.	
	(Duarte, 2015)	Other		<6.45				All other work areas: solvent recovery, cut and bailing, open-end-spinning, pilot plant and laboratory.	
	(Tutkun et al., 2019)	Control group (n=101)	0.06 (mg DMAC/L urine)						Not considered (control group)
	(Tutkun et al., 2019)	Group 2 (n=71)		2.43 (mg DMAC/L urine)				Polyvinyl chloride workers Operators whose previous urinary DMAC levels were between 1-3 mg/L.	Not considered (not reflecting usual workplaces in this industry, no conclusion possible on the 90th percentile)
	(Tutkun et al., 2019)	Group 3 (n=38)		3.17 (mg DMAC/L urine)				Polyvinyl chloride workers Operators whose previous urinary DMAC levels were between >3 mg/L.	
	confidential								In general, a positive development towards lower values can be recognized, with an outlier for 2017. confidential

Sector	Study	Job-title	Geometric mean	arithmetic mean	Range	50th percentile	90th percentile	Remarks	Remarks RAC
			mg NMAC/g creatinine	mg NMAC/g creatinine	mg NMAC/g creatinine	mg NMAC/g creatinine	mg NMAC/g creatinine		

Sector	Study	Job-title	Geometric mean	arithmetic mean	Range	50th percentile	90th percentile	Remarks	Remarks RAC
			mg NMAC/g creatinine	mg NMAC/g creatinine	mg NMAC/g creatinine	mg NMAC/g creatinine	mg NMAC/g creatinine		
	[redacted]								
	[redacted]								
	[redacted]				**confidential**				
Secondary fibre processing	(Borm et al., 1988)	Operator A (n=3)	41.42		11.69 – 129.5				Not considered (data outdated and low number of managements)
	(Borm et al., 1988)	Cleaner (n=1)	50.21		36.37 – 73.45				
	(Borm et al., 1988)	Operator B (n=2)	54.65		32.24 – 101.6				
	(Borm et al., 1988)	Inspection (n=2)#	8.71		<LOD – 14.6				
	[redacted]								
	[redacted]				**confidential**				
	[redacted]								

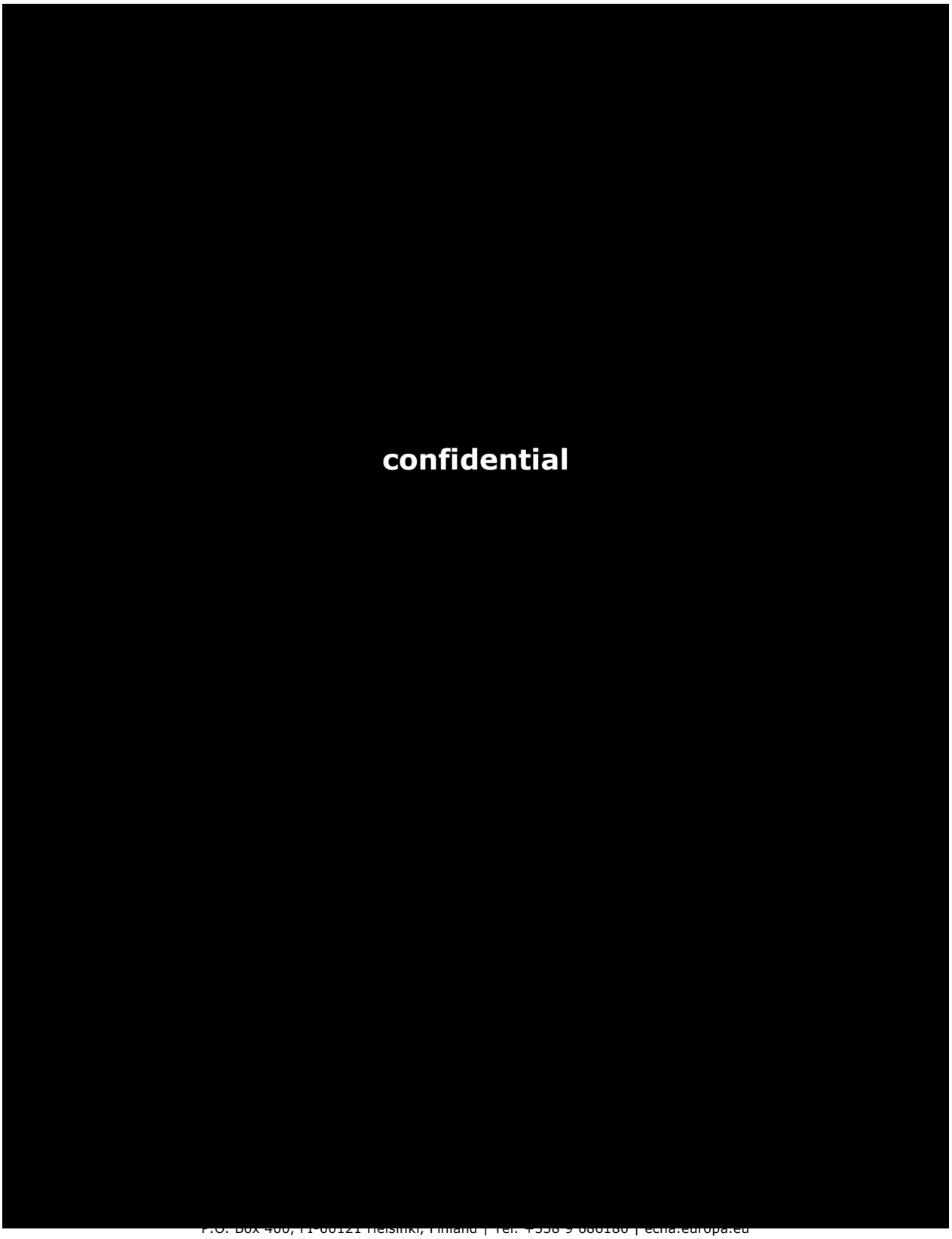
Sector	Study	Job-title	Geometric mean	arithmetic mean	Range	50th percentile	90th percentile	Remarks	Remarks RAC
			mg NMAC/g creatinine	mg NMAC/g creatinine	mg NMAC/g creatinine	mg NMAC/g creatinine	mg NMAC/g creatinine		
Maintenance	(Kennedy Jr & Pruett, 1989)	Machine repairman (n=1)	9.19 (mg/L urine)		8 – 11 (mg/L urine)				
	(Duarte, 2015)	Mechanic Maintenance (n=2)		6.45	0.80 – 12.10			Maintenance of equipment in contact with DMAC	Subset of the data presented above. Only two data points. Therefore the AM is used only for comparison with modelled values.
Laboratory	(Duarte, 2015)	Laboratory (n=7)		1.58	0.29 – 7.26		3.56	Laboratory	Subset of the data presented above. Low number of data points. Therefore only used for comparison with modelled values.

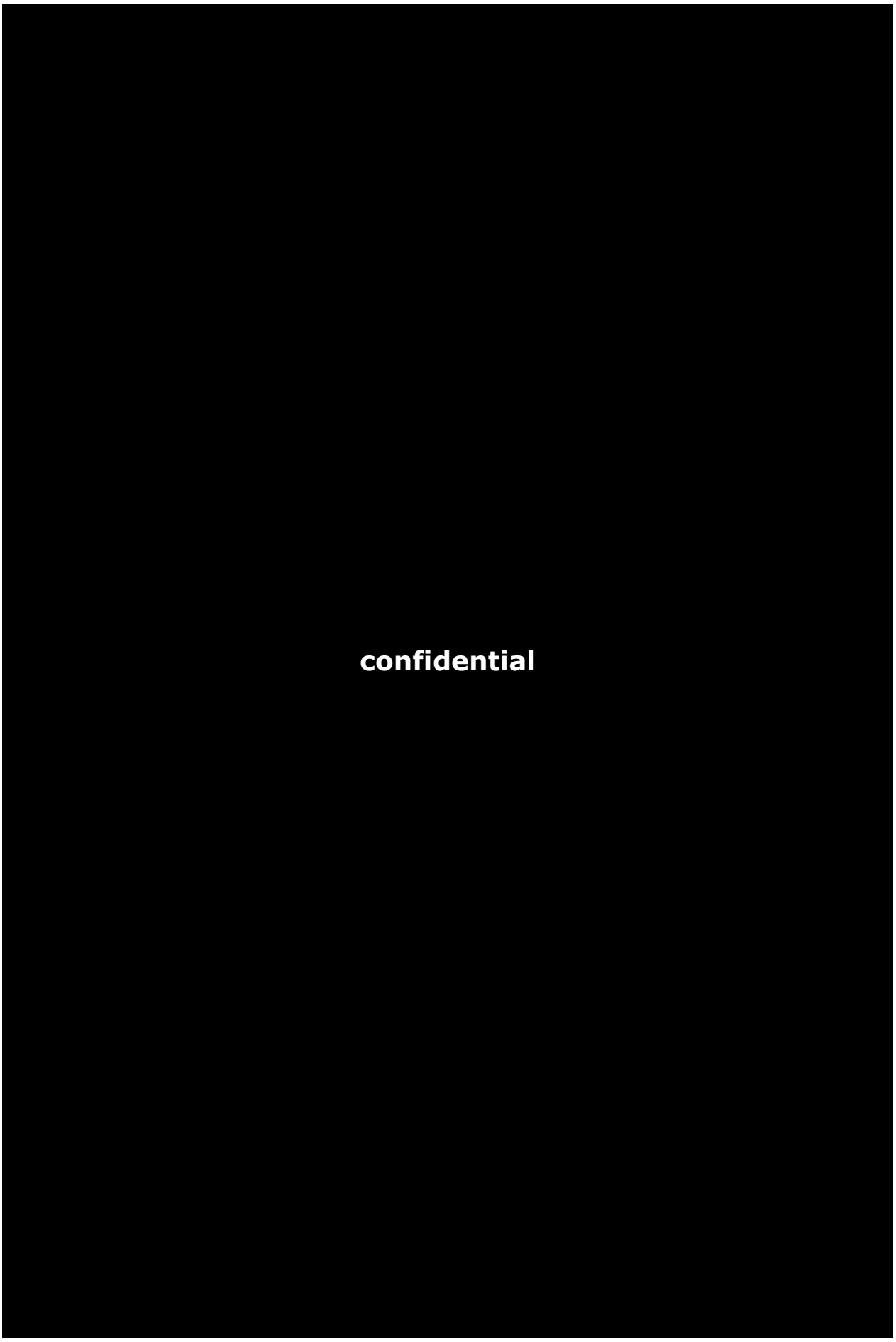
Table 4: RAC interpretation of biological monitoring data for NEP – urine 5-HNEP and 2-HESI concentrations in mg/g creatinine

Sector	Study	Job-title	arithmetic mean		Range		50th percentile		Remarks	Remarks RAC
			5-HNEP mg/L	2-HESI mg/L	mg 5-HNEP/g creatinine	mg 2-HESI/g creatinine	mg 5-HNEP/g creatinine	mg 2-HESI/g creatinine		
automobile varnishers	(Koslitz et al., 2014)	Regular work tasks (n=12)	0.41 0.6	0.62 0.74	0.06 – 2.56 0.01 – 3.47	0.03 – 2.40 0.04 – 4.52	0.18 0.11	0.18 0.17	Post-shift Pre-shift 2	Low number of data points. Therefore only used for comparison with modelled values.
		Special cleaning tasks (n=2)			0.83 – 1.10 2.52 – 17.00	0.84 - 0.98 1.95 – 4.63			Post-shift Pre-shift 2	

3. Use of DMAC in the Man-Made-Fibre Industry

The following information was provided during the Annex XV consultation by CIRFS European Man-Made Fibres Association (TR No: 40197342894048), in agreement with IVC as the Association of the German, Austrian and Swiss Man-Made Fibres Industries (TR No. 49913771894-86). CIRFS considers this confidential CSR information.

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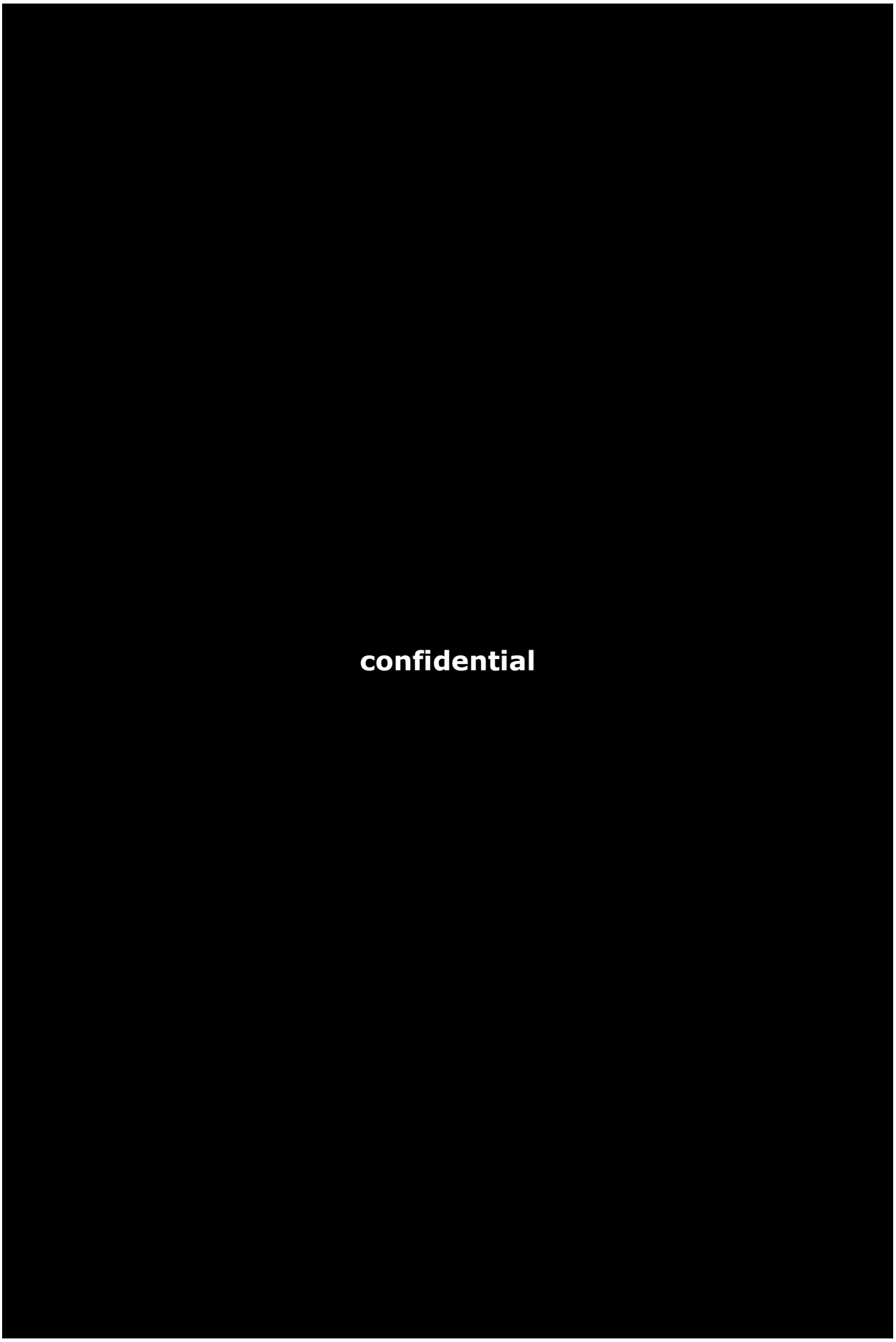
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4. IFA reports on measurements performed between 2012-2021 for NEP and DMAC

4.1. General information

The two reports include current (2012 - 2021) data for DMAC and NEP for inhalation exposure in German workplaces. The two reports are published on the IFA website[5].

Older data (before 2012) for DMAC are available at the IFA homepage (https://www.dguv.de/ifa/gestis/expositionsdatenbank-mega/expositionsdaten-aus-mega-in-publikationen/publikationen-nach-stoffen/index.jsp#D) and are included in the dossier. The IFA MEGA Database on the mentioned homepage does not publish data for NEP.

The RAC conclusions are published in the RAC box in the BD.

4.2. DMAC

The airborne concentration of DMAC is measured by means of a sampling pump with a defined volume of air pumped through a silica gel tube. After extraction with a two-percent potassium hydroxide methanol solution, the quantitative determination of the DMAC is performed by means of gas chromatography. The LOD for DMAC is 0.3 mg/m³ for a two-hour sampling period with a flow rate of 20 L/h (≙ 40 litre sample volume).

Table 16: Data situation for the measurements of DMAC evaluated for this report

General description	Number of measurements
total	119
below LOD	108
Sampling type	
personal	62
stationary:	
• undifferentiated	2
• person-related for exposure assessment	38
• background	17
Limit value reference	
Number of data > DE limit value (18,0 mg/m³)	0
Information about engineering controls	
engineering controls (e.g. LEV) in place and operational	60
engineering controls NOT in place or NOT in operation	41
No information regarding engineering controls	18

[5] DMAC: https://www.dguv.de/medien/ifa/de/gestis/mega/onlinebericht_dmac.pdf

NEP: https://www.dguv.de/medien/ifa/de/gestis/mega/onlinebericht_nep.pdf

Table 17: Exposure data for DMAC from 2012 to 2021

Number of measurements	Number of sites	Values below LOD	Percentage below LOD	Highest LOD in mg/m³	Lowest value above LOD in mg/m³	Highest value in mg/m³
119	69	108	90.8	3	0.3	13

4.3. NEP

For air monitoring of NEP at the workplace, two different methods were used in the period from 2010 to 2021.

2010 to 2017 – **NEP VAPOUR**: Using a sampling pump, a defined volume of air was sucked through a silica gel tube ADS. After extraction with a two percent KOH methanol solution, the quantitative determination of the NEP vapour was carried out using gas chromatography. The LOD for NEP VAPOUR is 0.2 mg/m³ for a two-hour sampling with a volume flow of 20 l/h (≙ 40 litre sample volumes).

2018 to 2021 – **NEP**: Using a sampling pump, a defined volume of air is sucked through a glass fibre filter and a silica gel tube ADS. After extraction with a two-percent KOH methanol solution, the quantitative determination of NEP is carried out by gas chromatography. The LOD for NEP is 0.3 mg/m³ for a two-hour sampling with a volume flow of 20 l/h (≙ 40 litre sample volume).

Table 18: Data situation for the measurements of NEP evaluated for this report

General description	Number of measurements	
	NEP (2018 to 2021)	**NEP VAPOUR** (2010 to 2017)
total	196	171
below LOD	188	114
Sampling type		
personal	110	114
stationary		
• undifferentiated	--	20
• person-related for exposure assessment	79	34
• background	7	3
Limit value reference		
Number of data > DE limit value (23,0 mg/m³)	0	Not available
Information about engineering controls		
engineering controls (e.g. LEV) in place and operational	141	90
engineering controls NOT in place or NOT in operation	47	51
No information regarding engineering controls	8	30

For NEP the situation is more complex compared to DMAC, due to the two different monitoring methods that were used and the fact that the proposed systemic long-term inhalation DNEL of 4.0 mg/m³ was exceeded in several workplaces (marked red in the tables below).

Table 19: Exposure data for NEP von 2018 to 2021 (method NEP)

Number of measurements	Number of sites	Values below LOD	Percentage below LOD	Highest LOD in mg/m³	Lowest value above LOD in mg/m³	Highest value in mg/m³
196	90	188	95.9	2.4	0.3	**8.6**

Table 20: Exposure data for NEP von 2010 to 2017 (method NEP VAPOUR)

Number of measurements	Number of sites	Values below LOD	Percentage below LOD	Highest LOD in mg/m³	90th percentile in mg/m³	95th percentile in mg/m³
Chemical industry						
20	10	18	90	24	0.5019	3.691
Plastics industry						
29	13	10	34.48	0.8	**9.294**	**21.32**
Painting and varnishing						
17	11	12	70.59	0.4	0.7868	1.607
Metalworking, mechanical and vehicle engineering						
20	9	15	75	1.5	0.556	0.9324
Electrical engineering, precision mechanics, optics						
19	14	15	78.95	1.6	1.63	**6.261**
Wood processing						
32	7	22	68.75	1	0.8295	1.327
Leather and textile industry						
12	7	8	66.67	0.2	0.7392	1.356
other sectors						
16	8	14	87.5	0.9	0.2263	0.2672