

# **HANDBOOK OF PROCEDURES FOR SPECIFIC INHALATION CHALLENGE TESTING IN THE DIAGNOSIS OF OCCUPATIONAL ASTHMA**

**European Taskforce on SIC  
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**(to be updated 2018)**

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## **INTRODUCTION**

This handbook is a product of a pan-European taskforce on specific inhalation challenge (SIC) testing in the diagnosis of occupational asthma. It was compiled from information provided by twelve specialist clinical centres under the direction of Katri Suuronen. Our purpose was to provide to others information on the techniques used in each centre for SIC with different occupational agents. The tables below include information on the form and nature of the active and control agents and on methods, quantities and duration of delivery; where appropriate 'comments' and references are provided.

The information here is not intended as a set of full 'recipes' but as a guide; the handbook should be read in concert with the full taskforce report (reference). Readers are reminded that the general safety requirements, contra-indications and precautions described in the full report should be strictly applied in order to minimise the risk of severe adverse events; that the duration and/or concentration of exposure to occupational agents should only be gradually increased under close monitoring of functional parameters; that the starting doses listed here are a guide only and should be adjusted in light of a particular patient's circumstances; and that a control challenge test with a 6-8 hour period of spirometric monitoring on a separate day is required for the interpretation of the SIC results. Further information can be obtained from any of the centres listed and contact details are provided (page 3).

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## List of abbreviations:

EA	Ethanolamines
HDI	Hexamethylene diisocyanate
HMW	High molecular weight
IPDI	Isophorone diisocyanate
LMW	Low molecular weight
MDF	Medium density fibreboard
MDI	Methylenediphenyl diisocyanate
MIG	Metal inert gas
MMA	Methylmethacrylate
MWF	Metalworking fluid
NA	Data not available
NCO	Reactive isocyanate group ( $-N=C=O$ )
NDI	1,5-naphthalene diisocyanate
NM	Not measured
NRL	Natural rubber latex
NSBHR	Nonspecific bronchial hyperresponsiveness
OEL	Occupational exposure limit
PBS	Phosphate buffered saline
PE	Polyethylene
PM	Particle measurement
pMMA	Polymethylmethacrylate
PP	Polypropylene
ppb	Parts per billion
PVC	Polyvinyl chloride
RT	Room temperature
SIC	Specific inhalation challenge
TDI	Toluene diisocyanate
TGIC	Triglycidyl isocyanurate
TIG	Tungsten inert gas
TLV	Threshold limit value
TPU	Thermoplastic urethane
VOC	Volatile organic compounds

## CENTRES: abbreviations and contact details

Abbreviation	Centre	Contact person: name and email
BHH	Birmingham Heartlands Hospital, Occupational Lung Disease Unit, Birmingham, UK	Vicky Moore <a href="mailto:vicky.c.moore@heartofengland.nhs.uk">vicky.c.moore@heartofengland.nhs.uk</a>
CHUM	Department of Chest Medicine, Centre Hospitalier Universitaire de Mont-Godinne; Université Catholique de Louvain, Yvoir, Belgium	Olivier Vandenplas <a href="mailto:olivier.vandenplas@uclouvain.be">olivier.vandenplas@uclouvain.be</a> Geneviève Evrand <a href="mailto:Geneviève.evrard@uclouvain.be">Geneviève.evrard@uclouvain.be</a>
CIOM/ IOMM	Institute for Occupational Medicine, Charité University, Berlin, Germany Institute for Occupational and Maritime Medicine, Hamburg, Germany	Xaver Baur <a href="mailto:xaver.baur@charite.de">xaver.baur@charite.de</a> Lygia Therese Budnik <a href="mailto:L.Budnik@uke.de">L.Budnik@uke.de</a>
FIOH	Occupational Medicine Team, Finnish Institute of Occupational Health, Helsinki, Finland	Katri Suuronen <a href="mailto:katri.suuronen@ttl.fi">katri.suuronen@ttl.fi</a>
FJDM	Allergy Department, Fundacion Jimenez Diaz-Capio, CIBER de Enfermedades Respiratorias (CIBERES), Madrid, Spain	Dominguez Joaquin Sastre <a href="mailto:JSastre@fjd.es">JSastre@fjd.es</a>
FSM	Allergology and Immunology Unit, Fondazione Salvatore Maugeri, Institute of Care and Research, Scientific Institute of Pavia, Pavia, Italy	Gianna Moscato <a href="mailto:gianna.moscato@fsm.it">gianna.moscato@fsm.it</a>
SUH	Division of Asthma and Allergy, Department of Chest Diseases, Strasbourg University Hospital, Strasbourg, France	Frédéric de Blay <a href="mailto:Frederic.DEBLAY@chru-strasbourg.fr">Frederic.DEBLAY@chru-strasbourg.fr</a>
NIOM	Nofer Institute of Occupational Medicine, Department of Occupational Diseases&Clinical Toxicology, Lodz, Poland	Jolanta Walusiak-Skorupa <a href="mailto:jolantaw@imp.lodz.pl">jolantaw@imp.lodz.pl</a>
NMGH	Department of Respiratory Medicine North Manchester General Hospital, Manchester, United Kingdom	Jennifer Hoyle <a href="mailto:Jennifer.hoyle@pat.nhs.uk">Jennifer.hoyle@pat.nhs.uk</a>
RBHT	Department of Occupational and Environmental Medicine, Imperial College, National Heart and Lung Institute, London, United Kingdom	Julie Cannon <a href="mailto:j.cannon@rbht.nhs.uk">j.cannon@rbht.nhs.uk</a>
UNIPD	Department of Cardiologic, Thoracic, and Vascular Sciences,	Piero Maestrelli

	University of Padova, Padova, Italy	<a href="mailto:piero.maestrelli@unipd.it">piero.maestrelli@unipd.it</a>
VHIR	Institut de Recerce, Hospital Vall d'Hebron, Barcelona, Spain	Xavier Muñoz <a href="mailto:xmunoz@vhebron.net">xmunoz@vhebron.net</a>

## HIGH MOLECULAR WEIGHT AGENTS

**Flours: wheat, rye, oats, barley, soy, buckwheat**

**Notes:**

- most centres use a dust-tipping method but nebulisation is an alternative
- particle size and/or particle mass may be measured during active challenges
- flours from the workplace are preferred, because shop-bought flours may lack relevant allergens

Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Comments	Centre
Dust tipping						
Powder	Lactose powder (dusting with pressured air)	Dusting with pressured air (1 blow/minute)	100-300 g as such or diluted in lactose	30 –60 min	If IgE sensitization is strong, dilution to 10-50% in lactose in the first challenge	FIOH
Powder	Lactose or starch powder	Tipping and dusting 30 centimetres away from patient's face	~500- 1000 g	Up to 60 min (1, 15, 30, 60 min)		NIOM
Powder diluted in lactose	Lactose powder	Dust tipping from one tray to another 30 centimetres away from the patients face	10 - 100 g diluted in 150g of lactose	Exposure gradually increasing up to a maximum of 60 min	The quantity of flour mixed with lactose depends on clinical criteria according to patient sensitization and respiratory functional status	VHIR
Powder	Lactose	Tipping and dusting with pressured air	500 g flour used at work	Up to 120 min (1, 4, 10, 15, 30, 60 min)		CHUM

Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Comments	Centre
Powder	Lactose powder	Dust tipping	Up to 1kg	Up to 70 min (10+20+40)		BHH
Powder	Lactose powder, sieved and baked	Mixing with lactose powder, then tipping repeatedly by patient	1% to 10% in 250 g lactose	20 min		RBHT
Powder	Lactose or tapioca flour	Tipping from one tray to another	~500 g	Up to 30 min		IOMM/ CIOM
Powder	Lactose powder	Tipping and dusting with pressured air	100-300 g as such	Up to 120 min (1, 4, 10, 15, 30, 60 min)		FSM
Powder	Lactose powder	Tipping from a small vase through a sieve 30 cm from the patient	250-500 g	Up to 60 min, starting with 1,2,5,10,15,30, etc.	Starting with weak mixture in suspicion of strong sensitization based on clinical history and IgE	NMGH
Powder	Lactose	Close-circuit delivery machine		Up to 30 min		FJDM
<b>Nebulisation</b>						
Homemade /commercial extracts	Saline	Nebulisation by tidal volume method with home-made extracts/commercial extracts		2 min each concentration		FJDM
Commercially available extracts	Saline diluent	Nebulisation in increasing concentrations	Commercial standardized conc.	2 min each concentration	In case of strong sensitization or strong NSBHR initial dilution is 1/10,000 or higher; stepwise increase: 1/1,000, 1/100, 1/10	IOMM/ CIOM



## Grains and animal feed

### Notes:

- seeds or large particles may be ground smaller prior to SIC
- particle size and/or particle mass may be measured
- dust tipping or nebulisation methods may be used

Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Comments and references	Centre
<b><i>Wheat, rye, oats, barley and their mixtures</i></b>						
Powder, rough particles, pellets, etc.	Lactose powder	Dust tipping or dusting with pressurised air (1 blow/minute)	100-300 g as such or diluted in lactose	30 –60 min	If IgE sensitization is strong, dilution to 10-50% in lactose in the first challenge	FIOH
Powder, rough particles, etc.	Lactose powder	Dust tipping	~500- 1000 g	30 –60 min		NIOM
Powder, rough particles, etc.	Lactose powder	Dust tipping	100-300 g as such	1, 4, 10, 15, 30, 60, 120min		FSM
Liquid home-made extracts	Saline	Nebulisation (tidal volume method)	Starting concentration based on skin endpoint titration	2 min each concentration	Starting concentration by end-point skin titration (Vereda et al. Allergy 2007;62:211-2)	FJDM
<b><i>Soy hull</i></b>						
Powder diluted in	Lactose powder,	Dust tipping	1% in 250 g lactose	Exposure gradually		RBHT

Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Comments and references	Centre
lactose	sieved and baked			increasing up to a maximum of 20 min		
Liquid home-made extracts	Saline	Nebulisation using a dosimeter	Increasing concentrations from 1:1000; 1:100; 1:10; 1:1 and no of inhalations up to 40	2 min each concentration.	Starting concentration by end-point skin titration	FSM
Liquid in-house antigen extract	Saline	Nebulisation using a nebulizer	2 ml of each concentration, the starting conc. being based on metacholine PC20 and skin prick test reactivity	-	-Antigen extract made according to Gomez-Olles S et al. Clin Exp Allergy 2006; 36: 1176-83 -The starting conc. is calculated from methacholine PC20 and the smallest antigen conc provoking a positive skin response (Cockcroft DW, et al. Am Rev Respir Dis 1987;135:264-267)	VHIR
<b>Other</b>						
Liquid lima Bean ( <i>P. lunatus</i> ) extract	Saline	Nebulisation using a dosimeter	Dilution 1:100	1, 4, 10, 15, 30, 60 min	Tonini S et al. Letters/Ann Allergy Asthma Immunol 2012;108:60-67	FSM
Mushroom spores, liquid homemade extracts	Saline	Nebulisation using a dosimeter	Increasing concentrations from 1:1000; 1:100; 1:10; 1:1 and n° of inhalations up to 40	2 min each concentration.	Starting concentration by end-point skin titration	FSM
Mushroom spores, liquid homemade	Saline	Nebulisation (tidal volume method)	Starting concentration based on skin endpoint titration	2 min each concentration	Vereda et al. Allergy 2007;62:211-2	FJDM

<b>Physical form</b>	<b>Control agent</b>	<b>Method of delivery</b>	<b>Approximate amount used</b>	<b>Duration</b>	<b>Comments and references</b>	<b>Centre</b>
extracts						

**Enzymes: amylases, lipases, proteases, cellulases, xylanases, enzyme mixtures etc.**

**Notes:**

- enzymes are potent allergens and testing should be started with a low concentration
- while most centres use a dust-tipping method, some use nebulisation

Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Comments	Centre
Dust tipping						
Powder diluted in lactose	Lactose powder	Dusting	0.03 - 3% enzyme in 100 g lactose	30 min	Usually started with the lowest concentration (0.03%).	FIOH
Powder	Lactose powder sieved and baked	Enzyme dust added to 250g lactose powder, then tipped repeatedly by patient	0.1% to 2.5% in lactose	20 min	Can be extremely potent at small doses	RBHT
Powder diluted in lactose	Lactose powder	Dusting	Increasing dilutions in 100 g lactose (1/1.000, 1/100, 1/10, pure powder)	1, 4, and 10 min for each dilution, then pure powder up to 120 min ((1, 4, 10, 15, 30, 60 min)	Starting dilution determined by end-point skin titration	CHUM
Powder	Lactose	Close-circuit delivery machine		Up to 30 min		FJDM
Nebulisation						
Liquid, diluted in saline	Saline	Nebulisation in increasing concentrations	1 ml of each concentration	2 min of each concentration	Starting concentration is usually from 0.00001 mg/ml; stepwise increase to	IOMM/ CIOM

Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Comments	Centre
					0.1 mg/ml; depending on the level of IgE sensitization and NSBHR	
Homemade extracts	Saline	Nebulisation Tidal volume method with extracts		2 min each dilution	Starting concentration by end-point skin titration	FJDM

## Natural rubber latex (NRL): gloves

### Notes:

- most centres use whole, powdered latex gloves but nebulisation of a commercial extract is an alternative

Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Comments and references	Centre
Powdered latex gloves						
Powdered NRL gloves	PVC gloves	Handling gloves	6-10 gloves	30 min	Number of gloves depends on the level of IgE sensitization	FIOH
Powdered NRL gloves	PVC gloves	Handling and shaking gloves	2 gloves per 5 min	1, 4, 10, 15, 30, 60, 120 min		NIOM
Powdered NRL gloves	PVC or nitrile gloves	Handling gloves	Up to 15 gloves	Up to 70 min		BHH
Powdered NRL gloves	PVC gloves	Handling gloves	10 gloves	20 min		RBHT
Powdered NRL gloves	PVC gloves	Handling gloves	1-10 gloves	Up to 30 min	Number of gloves depends on the level of IgE sensitization and NSBHR	IOMM/ CIOM
Powdered NRL gloves	PVC gloves	Handling and shaking gloves	2 gloves per 5 min	Up to 120 min (1, 4, 10, 15, 30, 60 min)	Vandenplas O. Occupational asthma caused by natural rubber latex. Eur Respir J. 1995;8:1957-65.	CHUM
Powdered NRL gloves	PVC or nitrile gloves	Handling gloves	6 – 15 gloves	30 -60 min	Number of gloves depends on the level of IgE sensitization	FSM
Nebulisation						
Commercial NRL extract	Saline	Administered by aerosol using a nebuliser	2 ml of each concentration		The starting concentration is calculated from methacholine PC <sub>20</sub> and the smallest antigen concentration provoking a positive skin response (Cockcroft DW, et al. Am Rev Respir Dis 1987;135:264-267)	VHIR

**Wood dusts: obeche, teak, iroko, western red cedar, ebony; ash, beech, pine; also medium density fibreboard (MDF)**

**Notes:**

- some woods contain HMW (protein) allergens, while in some materials (Western red cedar, MDF) the suspected agent is a LMW compound
- almost all centres use a form of dust-tipping

Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Comments and references	Centre
Dust tipping						
Neat wood dust	Lactose or starch powder	Dust tipping	500- 1000 g	Up to 60 min		NIOM
Neat wood dust/shavings or diluted in lactose	Lactose powder	Dust tipping	10 - 100g diluted in 150g of lactose	Gradually increasing to a maximum of 60 min	The quantity of dust mixed with lactose depends on clinical criteria according to patient sensitisation and respiratory functional status (Munoz X et al. Scand J Work Environ Health 2007;33(2):153–158)	VHIR
Neat wood dust	lactose powder	Dust tipping	100g	30 min		FJDM
Neat wood dust	Lactose powder	Sanding piece of wood using an electric sander		1, 4, 10, 15, 30, 60, 120 min	Malo JL, Cartier A, Desjardins A, Van de Weyer R, Vandenplas O. Occupational asthma caused by oak wood dust. Chest. 1995;108:856-8.	CHUM
Neat wood dust	Pine	Sanding piece of wood using an electric sander		5 – 20 min		RBHT
Neat wood dust	Pine or spruce wood	Manual or electrical sanding		1, 4, 10, 15, 30, 60, 120 min		UNIPD
Neat wood dust	Pine	Sanding piece of wood using an		Up to 60 min		NIOM

Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Comments and references	Centre
		electric sander				
Neat wood dust	Lactose powder	Sanding piece of wood using an electric sander or Dust tipping		5 – 20 min		FSM
Neat wood dust or diluted in lactose	Lactose powder	Dusting with pressurised air (1 blow/minute)	10-50% wood dust in ~100g lactose	30 min	Dilution in lactose in the 1 <sup>st</sup> SIC; the 2 <sup>nd</sup> SIC possibly with 100% wood dust	FIOH
1) Solid wood sanded 2) Powder	Another wood species (sanded or powder depending on the active SIC)	1) Sanding the wood, electric sander 2) Tipping from one tray to another	1) wood block 2) 250-500g	Gradually increasing up to total 60 min	The method depends on the mode of usage at work	NMHG
MDF	Pine	Sanding piece of MDF using an electric sander		5 – 20 min	Burton C et al. Medium density fibreboard and occupational asthma. A case series. Occup Med 2011;61:357-364	RBHT
MDF dust	Formaldehyde painted on to cardboard	Sanding with electric or hand sander		Up to 60 min		BHH
<b>Nebulisation</b>						
Home-made extracts	Saline	Nebulisation (tidal volume method) with home-made extracts		2 min each dilution		FJDM



## Animal derived proteins

### Notes:

- a variety of methods are used: dust-tipping, mimicking work tasks, nebulisation of commercial or home-made extracts, quasi-controlled workplace challenges

Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Comments and references	Centre
<b><i>Animal epithelium and urine (cow, pig, mouse, rat, rabbit, mites, fur animals etc.)</i></b>							
Mouse and rat epithelium and urine	Animal beddings (flakes + powder)	Lactose powder or unused beddings (dusting or tipping)	Tipping used animal beddings containing fresh urine and epithelium beddings from vase to another	500-1000 ml	30-45 min		FIOH
Rat, mouse epithelium an urine	Animal beddings	Unused beddings	Beddings containing fresh urine and epithelium	Approx. 500g	1-60 min		SUH
Laboratory animals (mice)	Live animals as such	Unused beddings	Patient undergoing prolonged exposure inside the animal facilities	Approximately 100 mice are housed	30 and 60 min on successive days	Munoz X et al. Respiration 2007;74(4):467-470	VHIR
Live laboratory mice	Live animals in cage with bedding	Monitoring patient over 1 day without animal exposure	Handling the animals, cleaning them out as in normal working day		10 – 30 min	This is done in the animal research facility, not in the challenge lab	RBHT
Furs (blue fox, mink, etc.)	As such	Lactose powder or	Handling (dusting, brushing etc) of furs	3-7 furs	30-45 min		FIOH
Fur animals and feathers,	As such	Lactose powder or starch powder	Handling (dusting, brushing, pulling,	3-5 furs	Up to 60 min		NIOM

Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Comments and references	Centre
etc.			tousling etc.) of furs				
Homemade or commercial allergen extracts of hair, dander, mites, etc.	Liquid	Saline	Nebulisation of with tidal volume method		2 min each dilution	Starting concentration by end-point skin titration	FJDM
Commercial allergen extracts of cow or dog danders	Liquid	Saline	Through dosimeter	Increasing concentrations from 1:1000; 1:100; 1:10; 1:1 and n° of inhalations up to 40	2 min each concentration		FSM
Commercial extract of sheep wool	Liquid	Saline	Through dosimeter	Increasing concentrations from 1:1000; 1:100; 1:10; 1:1 and n° of inhalations up to 40	2 min each concentration		FSM
Commercial allergen extracts of cow epithelium, storage mites, etc.	Liquid	Commercial allergen diluent	Spira Elektro 2 dosimeter	1-20 breaths	15-60 min	-Allergen dilution 5-50 BU/ml or 10 000-100 w/w -Stepwise increase in the number of inhalations, depending on the level of IgE sensitization and symptoms during the test	FIOH

Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Comments and references	Centre
<b>Other</b>							
Fish	Solid	Other fish with negative IgE	Mimicking the patients job		Up to 60–120 min		FJDM
Carmine	Powder	Lactose powder or in-house control solution	Dusting or mixing or pouring carmine diluted in lactose from a vase to another	~100 g lactose/carmine mixture	15–30 minutes	- carmine colour derived from cochineal insect - if IgE sensitization is strong, dilution to 10-50% in lactose is done	FIOH
Carmine	Liquid	Saline	Nebulizing solutions with increasing concentrations of carmine with a nebulizer	2 ml of each concentration		- method: Cockcroft DW, et al. Am Rev Respir Dis 1987;135:264-267 - protein concentration of carmine determined by the BCA protein assay -The starting concentration is based on metacholine PC <sub>20</sub> and the skin prick test reactivity	VHIR

## Miscellaneous plant derived materials

### Notes:

- a wide variety of methods are used: tipping, dusting, work mimicking, nebulisation of home-made extracts, etc
- processing the material (e.g. boiling) may affect the allergenicity of the proteins

Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Comments and references	Centre
<b><i>Decorative plants and vegetables</i></b>							
Fresh plants/vegetables	Solid	Cutting lettuce or in-house control solution (nebulised)	Handling (cutting, ripping, turning) plants	e.g. 3-15 decorative flowers	30 min		FIOH
Fresh plants/vegetables	Solid	Saline control solution or cutting lettuce	Handling plants (cutting, ripping, turning)	3-15 decorative flowers	Up to 60 min		NIOM
Fresh vegetables	Solid	Saline	Boil fresh vegetable in pot in a chamber	3-5 fresh vegetables	Up to 60 min		NIOM
Fresh vegetables	Solid	Saline	Boil fresh vegetable in glass jar into a chamber		Up to 60 min	- Quirce et al. Allergy 2005; 60: 969-970 - blinding is difficult due to odour	FJDM
<b><i>Foodstuffs and spices</i></b>							
Spices	Powder or flakes	Lactose powder (dusting with pressured air)	Dusting powder or flakes mixed in lactose with pressured air or handling (1 blow/minute)	~100 g lactose mixture	30 min	Cardamom, pepper, oregano, coriander, etc.	FIOH
Spices	Powder	Lactose powder		~100-500 g		Pepper,	NIOM

Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Comments and references	Centre
	or flakes			spice mixture	30 min	oregano, basil, cardamon etc.	
Spices, homemade extracts	Liquid	Saline	Nebulisation by tidal volume method with home-made extracts		2 min each dilution, starting with end-point titration	Starting concentration by end-point skin titration	FJDM
Spices	Liquid	Saline	Nebulisation by tidal volume method with home-made extracts		2 min each dilution	Starting concentration by end-point skin titration	CHUM
Food additives: gum arabicum, carob tree, etc.	Powder	Lactose powder (dusting with pressured air)	Dusting with pressured air (1 blow/minute)	~100 g lactose/additive mixture	30 min	Dilution to 10-50% in lactose in the first challenge	FIOH
Raw coffee	Powder	Lactose powder	Dusting with pressured air (1 blow/minute)	~100 g lactose/coffee mixture	30 min	Dilution to 10-50% in the first challenge	FIOH
Raw coffee	Powder	Lactose or tapioca flour	Shaking the beans	c. 500 g	Up to 30 min		IOMM/CIOM
Raw coffee	Powder	Lactose powder	Dusting tipping	100 g coffee	30 min up to 2 h		FSM
Raw coffee (green coffee bean)	Liquid	Saline	Handling	Increasing concentrations from 1:1000; 1:100; 1:10; 1:1	30 min up to 2 h		FSM
Tea dust, herbal teas	Powder	Lactose powder, sieved and baked	% dust added to 250g lactose powder, then tipped repeatedly by	1% to 10 %	20 min		RBHT

Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Comments and references	Centre
			patient				
Cacao (grained raw cacao beans)		Lactose powder	Dust tipping	100 g cacao	30 min up to 2 h		FSM
Mushroom spores	Powder and pieces	Lactose powder	Tipping from one tray to another		10 – 15 – 30 – 60 min. Up to 2 h		FSM
Mushroom spores, home-made extracts	Liquid	Saline	Nebulisation using a dosimeter with home-made extracts	Increasing concentrations from 1:1000; 1:100; 1:10; 1:1 and n° of inhalations up to 40	2 min each concentration.	Starting concentration by end-point skin titration	FSM
Fungi on salami surface	Solid/ powder	Lactose powder	Mimicking the patients job = brushing of the salami surface		10 – 15 – 30 – 60 min. Up to 2 h		FSM
<i>Ephestia kuehniella</i> (flour moth) in flour	Powder or flakes	Lactose powder	Tipping from one tray to another		10 – 15 – 30 – 60 min. Up to 2 h		FSM
<i>Plantago ovata</i>	Powder	Lactose powder	Dust tipping from one tray to another 30 cm away from the face	10 g diluted in 150g of lactose	15 min	Munoz X et al. Ann Allergy Asthma Immunol 2006;96:494–6.	VHIR
<b>Other</b>							
Black Henna	Powder	Lactose powder	Mimicking the patients job	Diluted powder 1:10	10 – 15 – 30 – 60 min. Up to 2 h	Scibilia E et al. Allergy	FSM

Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Comments and references	Centre
						1997;52:231-232	
Liquid, standardized commercial extracts of appropriate material	Liquid	Diluent of the commercially available extract	Use of a nebuliser	Commercial standardized concentration	2 min each	<ul style="list-style-type: none"> <li>- allergen extracts by Bencard Allergi Gmbh</li> <li>- Stepwise increase of concentration, starting with 1/1,000, higher dilutions if strong degree of IgE sensitization and/or NSBHR</li> </ul>	IOMM/CIOM

## LOW MOLECULAR WEIGHT AGENTS

<b>Diisocyanates</b>								
<b>Notes:</b>								
- either diisocyanate-containing products or in-house solutions of pure diisocyanates may be used								
- for some agents e.g. paint hardeners containing both hexamethylene diisocyanate(HDI) and HDI-prepolymers, the use of relevant workplace products is preferred								

Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Approximate target concentration	Exposure monitoring	Comments and references	Centre
<b><i>Methylenediphenyl diisocyanate (MDI)</i></b>								
Liquid	1,5 ml toluene nebulised	Nebulisation of an in-house MDI solution (in toluene) from a small glass jar with pressured air	1,5 ml	15 min	level I: 0.0035 mg/m <sup>3</sup> NCO (1/10 of the OEL) level II: 0,010 mg/m <sup>3</sup> NCO (1/3 of the OEL)	Filter collection + analysis of NCO (isocyanate groups) in the air : ISO 16702 (2001)	Suojalehto H et al. Am J Ind Med. 2011 Dec;54(12): 906-10	FIOH
Liquid solution with olive oil	Solvent nebulised for 30 min	Heating to 120°C: mimicking the patients job- painting or spraying	5-10ml	1, 15, 30, 60 min		NM		NIOM
Liquid	Solvent	Nebulisation from glass jar (heated)	NA	10 min 20 min 30 min 60 min	15-20 ppb	Continuously. measured by Honeywell SPM monitor	Sastre et al. Chest 2003; 123:1276-1279.	FJDM
Liquid	Solvent nebulised	Heating to 120°C	50 ml or adapted to	1, 4, 10, 15, 30,	~10 ppb (below 20 ppb)	MDA 7100 monitor	Vandenplas O, Malo JL. Eur Respir	CHUM



Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Approximate target concentration	Exposure monitoring	Comments and references	Centre
	for 30 min		generate 10 and 15 ppb	60 min			J. 1997;10:2612-29.	
Solid crystals	Solvent or if a 2-part system, the paint alone	Heating to 120 °C	<1g	Up to 70 min (10+20+40)	< 20ppb	Toxic gas detector		BHH
Liquid	Non-hazardous liquid component	Mimicking work, eg. <ul style="list-style-type: none"> <li>Painting liquid onto surface</li> <li>Adding 2 components to make foam</li> </ul>	Variable, but enough to achieve up to 20 ppb	30 –60 sec	20 ppb max	MDI monitor (TLD-1 toxic gas detector)		RBHT
Solid crystals	120°C heated clean sand	Heating to 120 °C	2 g	60 min	~10 ppb (below 20 ppb)	MDA 7100 monitor Polymetron		UNIPD
Liquid	Atmospheric (pure) air	Evaporation at 80°C	Variable, but enough to achieve up to 10 ppb	10 min 20 min 30 min 60 min	2.5 ppb 5 ppb 5 ppb 5 ppb	Continuously measured by Honeywell SPM monitor		IOMM/ CIOM
Liquid	Isobutylacetate	Evaporation at 60°C	Variable, but enough to achieve up to 10 ppb	10 min 20 min 30 min 60 min	2.5 ppb 5 ppb 5ppb 5 ppb	Continuously measured by Honeywell SPM monitor		FSM

Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Approximate target concentration	Exposure monitoring	Comments and references	Centre
<b>Hexamethylene diisocyanate (HDI) (usually in a paint or glue hardener or a related product)</b>								
Liquid	2 ml butyl acetate nebulised	Nebulisation of HDI-containing paint hardener from a small glass jar with pressured air	2 ml	15 min	HDI monomers < 0.0035 mg/m <sup>3</sup>	Filter collection + analysis of NCO (isocyanate groups) in the air : ISO 16702 (2001)		FIOH
Liquid solution with olive oil	Paint without HDI component	Mimicking the patients job - painting onto cardboard or spraying (depending on work)		Up to 60 min	-	NM		NIOM
Liquid	Saline	Nebulisation from nebuliser	4 ml	10 min 20 min 30 min 60 min	15-20 ppb	Continuously measured by Honeywell SPM monitor	Sastre et al. Chest 2003; 123:1276-1279.	FJDM
Liquid	Solvent nebulised for 30 min	Diluted 1/10 in appropriate solvent and nebulised in the challenge room		1, 4, 10, 15, 30, 60 min	~10 ppb (below 20 ppb)	MDA 7100 monitor		CHUM
Liquid	Solvent or if a 2-part system, the paint alone	Painting onto cardboard or spraying depending on work exposure or levels achieved		Up to 70 min (10+20+40)	< 20ppb	Toxic gas detector		BHH

Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Approximate target concentration	Exposure monitoring	Comments and references	Centre
Liquid	Paint without HDI component	Mimicking work - Spray painting	Enough to achieve up to 20 ppb	15 sec – 3 min	20 ppb max	HDI monitor (model TLD-1 toxic gas detector)		RBHT
Liquid	Water at 80°C	Evaporation at 80°C	5 ml	60 min	10-20 ppb	MDA 7100 monitor Polymetron Sieger		UNIPD
Liquid	Atmospheric (pure) air	Evaporation at 60°C	Variable, but enough to achieve up to 10 ppb	10 min 20 min 30 min 60 min	2.5 ppb 5 ppb 5ppb 5 ppb	Continuously measured by Honeywell SPM monitor	Solution of pure HDI	IOMM/ CIOM
Liquid	Isobutylacetate	Evaporation at 60°C	Variable, but enough to achieve a ppb of up to 10 ppb	10 min 20 min 30 min 60 min	2.5 ppb 5 ppb 5ppb 5 ppb	Continuously measured by Honeywell SPM monitor		FSM
<b><i>Toluene diisocyanate (TDI)</i></b>								
Liquid	1 ml toluene (evaporation)	Evaporation of in-house TDI solution (in toluene) from a small glass cup at 175°C	1 ml	15	< 0.0035 mg/m <sup>3</sup>	Filter collection + analysis of NCO (isocyanate groups) in the air : ISO 16702 (2001)	-Level 1 solution: 0.18 mg/ml in toluene -Level 2 solution: 3.1 mg/ml in toluene	FIOH

Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Approximate target concentration	Exposure monitoring	Comments and references	Centre
Liquid solution with olive oil	Solvent or if a 2-part system, the paint alone	Mimicking the patients job - painting onto cardboard or spraying (depending on work)		Up to 60 min	-	NM		NIOM
Liquid	Water mixed with lactose	Nebulisation in a volumetric flask with pressured air. The flask contains 60 ml of TDI solution (SIGMA, Ref: T39853)	60 ml. After the test it is possible to recover most of the product	5 – 120 min	level of TDI between 10 – 15 ppb	TDI concentration controlled by a MDA 7100monitor (MDA Scientific, Inc, Glenview, Illinois, USA).	Concentration is very temperature dependent. It is necessary to maintain the temperature of the chamber between 22-24°C	VHIR
Liquid	Saline	Nebulisation by an aerosol generator GENASIC° The flask contains 1.5 ml (TDI, SIGMA)	~ 0.1 mL	1 min 2 min 4 min 8 min 15 min 30 min	0 – 20 ppb	Continuously. measured by ppbRAE 3000 by RAE system monitor	Based on our own and the Canadian experience	SUH
Liquid	Solvent nebulised for 30 min	Evaporation at room temperature in a glass flask + airflow		1, 4, 10, 15, 30, 60 min	~10 ppb (below 20 ppb)	MDA 7100 monitor	Vandenplas O et al. Eur Respir J. 1999;13:1144-50.	CHUM
Liquid	Solvent or if a 2-part system, the paint alone	Painting onto cardboard or spraying depending on work exposure or levels	Up to 20ppb	Up to 70 min (10+20+40)	< 20ppb	Toxic gas detector		BHH

Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Approximate target concentration	Exposure monitoring	Comments and references	Centre
		achieved						
Liquid	Water flushed with medical O2	Evaporation of TDI liquid solution from a flask flushed with medical O2.	20 ml	60 min	10-20 ppb	Continuously. measured by Polymetron Sieger monitor		UNIPD
Liquid	Atmospheric (pure) air	Evaporation at 80°C	Variable, but enough to achieve up to 10 ppb	10 min 20 min 30 min 60 min	5 ppb 10 ppb 10 ppb 10 ppb	Continuously. measured by Honeywell SPM monitor		IOMM/ CIOM
Liquid	Isobutylacetate	Evaporation at 60°C	Variable, but enough to achieve up to 10 ppb	10 min 20 min 30 min 60 min	2.5 ppb 5 ppb 5ppb 5 ppb	Continuously. measured by Honeywell SPM monitor		FSM
<b>Other Isophorone diisocyanate (IPDI), 1,5-naphthalene diisocyanate (NDI)</b>								
Liquid	Atmospheric (pure) air	Evaporation of pure IPDI at 60°C	Variable, but enough to achieve up to 10 ppb	10 min 20 min 30 min 60 min	2.5 ppb 5 ppb 5ppb 5 ppb	Continuously. measured by Honeywell SPM monitor		IOMM/ CIOM
NDI Solid (Wax)	Atmospheric (pure) air	Evaporation of wax-like crystals of NDI at 120°C	Variable, but enough to achieve up to 10 ppb	10 min 20 min 30 min 60 min	2.5 ppb 5 ppb 5ppb 5 ppb	Continuously. measured by Honeywell SPM monitor		IOMM/ CIOM

**Other plastic chemicals: epoxy resins, acrylic resins, powder paints, acid anhydrides, etc.**

**Notes:**

- in resin systems containing solvents, the solvent alone may be used as the control agent
- many resin systems contain irritant ingredients
- on heating, PVC may release hydrochloric acid that is irritating to the airways
- cyanoacrylates polymerise with water vapour, monomer exposures are higher on less humid days
- with phthalic acid anhydrides care is needed if heated or nebulised; start with very short exposures

Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Approximate target concentration	Exposure monitoring	Comments and references	Centre
<b>Epoxy resins</b>									
Epoxy paint + hardener	Liquid paint and hardener	2 ml butylacetate (nebulisation)	Mixing the paint and the hardener in a bowl	Paint 100 ml + suitable amount of hardener	30 min	–	NM	The patient may also spread the mixture on a plate Hannu T et al. Int Arch Allergy Immunol. 2009;148(1):41-4	FIOH
Epoxy paint + hardener	Liquid paint and hardener	Saline	Mixing the paint and the hardener in a bowl	Paint 100 ml + suitable amount of hardener	30 min	–	NM	The patient may also spread the mixture on a plate	NIOM

Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Approximate target concentration	Exposure monitoring	Comments and references	Centre
Epoxy resin paints or glues	Liquid	Non-hazardous paint, other workplace product e.g. cleaning agent	Mimicking work – painting or spraying	Strength as used in the workplace	Up to 60 min				NIOM
Epoxy resins	Solid form (lentil form)	Lactose	The resin in solid form is placed in a container in a heated (80 - 90 °C) water bath.	100 mg in a tray	5-30 min or 20-60 min	–	NM	Gases are released with heat	VHIR
Epoxy resins	Liquid	Saline	Liquid	50 to 100 ml	1 min 2 min 4 min 8 min 15 min 30 min	–	NM		SUH
Epoxy resin paints or glues	Liquid	Other workplace product e.g. cleaning agent, body filler (styrene) or other	Painting or spraying	As used in workplace	Up to 70 min	–	NM		BHH

Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Approximate target concentration	Exposure monitoring	Comments and references	Centre
Epoxy resin paints	Liquid	Non-hazardous paint	Mimicking work – painting or spraying	Strength as used in the workplace	15 sec– 2 min	–	NM		RBHT
<b>Acrylic resins: acrylates, methacrylates and products based on them</b>									
Artificial nail (meth)acrylates	Sculpturing gels, glues and nail tips	In-house control solution (nebulised)	Work mimicking preparing nails	Enough materials for 4 -6 nails or	30-45 min	–	VOC method: ISO 16000-6	Sauni R et al. Am J Ind Med. 2008 51(12):968-74.	FIOH
Prosthesis methacrylates	Powder + liquid	In-house control solution (nebulised)	Work mimicking: mixing prosthesis pMMA powder and MMA liquid	5-10 ml liquid and suitable amount of powder	30 min	–	VOC method: ISO 16000-6		FIOH
Dental (meth)acrylates	Liquid	In-house control solution (nebulised)	Evaporation at room temperature	2 x 10-20 drops of a dental adhesive (at 0 and 15 min)	30 min	–	VOC method: ISO 16000-6	Lindström M et al. Allergy. 2002;57(6):543-5.	FIOH
Acrylates	Liquid	Nebulised solvent	Mimicking the patients job	As used in the patients workplace	Up to 60 min	–	NM		NIOM
Acrylates	Liquid	Nebulised solvent	Mimicking the patients job	Strength as used in the	1, 4, 10, 15, 30,	–	NM		CHUM



Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Approximate target concentration	Exposure monitoring	Comments and references	Centre
				patients workplace	60 min				
Acrylates	Liquid	Nebulised solvent	Room temperature, mixing in an open vessel	Strength as used in the patients workplace	20 min Up to 1 h		NM		FSM
Methyl-methacrylate (MMA)	Liquid	Latex gloves, cleaning agents	Adding liquid to powder as performed in the workplace and sitting and breathing fumes afterwards	As workplace	1 –60 min	–	NM	Lozewicz S et al. Occupational asthma due to methyl methacrylate and cyanoacrylates. Thorax 1985;40:836-839	BHH
Methyl-methacrylate (MMA)	Liquid	Non-hazardous liquid component on its own	Adding 2 liquids together and breathing in fumes, mixing or stirring, as used in the workplace	Strength as used in the patients workplace	1 – 5 min	–	NM		RBHT
<b>Cyanoacrylate: instant glues and related products</b>									
Cyanoacrylate-based instant glue	Liquid glue	In-house control solution (nebulised)	Evaporation at room temperature or spreading glue on	3 x 3 drops of eye lash glue (at 0, 15 and 30	45 min	<1 mg/m <sup>3</sup>	VOC method: ISO 16000-6;	Lindström et al. Occup. Med, 2013	FIOH

Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Approximate target concentration	Exposure monitoring	Comments and references	Centre
			a plate	min) or 2-4 ml of industrial glue					
Cyanoacrylate-based instant glue	Liquid glue	Nebulised solvent	Mimicking the patients job	As used in the patients workplace	Up to 60 min	–	NM		NIOM
Cyanoacrylate	Glue	Food gelatine	Mimicking the patients job	–	30 min	–	–	Andujar R et al. Am J Ind Med 2011; 54:714-8.	VHIR
Cyanoacrylate-based instant glue	Glues and gels	Saline	Work mimicking= mixing liquid	1-10 mL	1 min 2 min 4 min 8 min 15 min 30 min	–	NM		SUH
Cyanoacrylate	Glue	Isobutylacetate	Mimicking the patients job	–	30 min	–	–		FSM
<b>Phthalic acid anhydrides</b>									
Phthalic acid anhydrides (in epoxy resin hardeners or as such)	Liquid	In-house control solution (nebulised)	Evaporation at room temperature and if negative, at 40-80 °C on the following day	50 ml of hardener	30 min	< 0.035 mg/m <sup>3</sup>	Collection into Tenax tubes, analysis according to Pfäffli et al. J Environ Monit. 2004 Apr;6(4):295-9	-IgE-mediated allergy - anhydrides evaporate easily upon heating, thus conc. is difficult to control	FIOH

Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Approximate target concentration	Exposure monitoring	Comments and references	Centre
Tetrahydrophthalic anhydride	Powder	Lactose	Tipping 5% in lactose		30 min	< 5 mg/m <sup>3</sup>	PM (Dustrack®)		FJDM
Acid anhydrides	Pure (powder)	Lactose	Tipping powder diluted 1/10 in lactose	~200 g	1, 4, 10, 15, 30, 60 min		NM		CHUM
Tetrahydrophthalic anhydride	Powder	Lactose	Evaporation	Up to 5 mg/m <sup>3</sup>	20 min	< 5 mg/m <sup>3</sup>			FSM
<b><i>Other/miscellaneous plastics and resins</i></b>									
Powder coatings (epoxy and/or polyester)	Powder	50-100 ml lactose powder (dusting)	Heating with a soldering iron at 250°C	50-100 ml	30 min	–	PM		FIOH
Powder coatings, TGIC	Powder	Lactose powder tipped or other powder e.g. TGIC heated	Tipping or heating to 250°C using a boiling tube in a heated block	5g heated, approx. 200g tipped	Up to 70 min	–	PM	Anees W et al. Occupational asthma caused by heated triglycidyl isocyanurate Occupational Medicine 2011;61:65-67	BHH
Triglycidyl isocyanurate	Powder	Lactose	Tipping 4% in lactose		30 min	< 5 mg/m <sup>3</sup>	PM (Dustrack®)	Sastre J et al. Int Arch Occup Environ Health. 2011;84(5):547-9.	FJDM

Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Approximate target concentration	Exposure monitoring	Comments and references	Centre
Resins and paints (not based on isocyanates)	Liquid or semi-solid	Non-hardening part of the resin	Mimicking work (painting or spraying)	Same quantity as at work	1, 4, 10, 15, 30, 60 min	–	NM		CHUM
Phthalate Ester (dioctyl phthalate)	Liquid	Isobutylacetate	Evaporation to boiling point	Variable but no more 5 mg/m <sup>3</sup>	Up to 30 min		NM	Dioctyl phthalate released in polyethylene extrusion process	FSM
<b><i>Finished plastics</i></b>									
Miscellaneous plastic materials (PE, PP, TPU, etc.)	Solid (sheets, pellets, etc.)	In-house control solution (nebulised)	Heating plastic with a soldering iron at ~250°C	50-150 ml of plastic pellets or sheets	30 min	formaldehyde < 0.37 mg/m <sup>3</sup>	- Aldehydes: US Environmental protection agency EPA (1999); method TO11A	Formaldehyde release is often measured; Particle measurement possible but seldom done	FIOH

Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Approximate target concentration	Exposure monitoring	Comments and references	Centre
Shrink wrap (plastic)	Plastic film on a roll with heat seal machine	Using heat seal machine without plastic film	Mimicking the patients job by using the heat seal machine	Wrap as used in the workplace	Gradually increasing up to a maximum of 60 min	–	NM	Gannon PFG et al. Occupational asthma due to polyethylene shrink wrapping (paper wrapper's asthma) Thorax 1992;47:759	RBHT
Shrink wrap (plastic)	Solid	Cleaning agents or other agents used in the workplace	Up to 10 cm <sup>2</sup> heated in a boiling tube to temp used at work		Up to 70 min	–	NM		BHH
PVC; Vacuum packing	Plastic bags	Use of vacuum packaging machine without plastic bags	Simulation of the working conditions in a provocation chamber with a vacuum packaging machine	–	60-180 min	–	NM	Muñoz X, et al. Arch Bronconeumol 2003;39(7):324-6	VHIR
PVC	Plastic drops	Isobutylacetate	Mimicking the patients job	–	60-120 min	–	NM		FSM
Polyurethane mattress foam	Solid blocks of foam	A different type of foam	Cutting the form with an electric kitchen knife	1m x 0,5 m block	1,2,5,10, 30 up to 60	–		Dust difficult to produce enough by cutting	NMGH

## Metals and metal salts: welding fumes, nickel, cobalt, chromium, platinum, etc.

### Notes

- precious metal salts are very potent and very low doses should be used for SIC
- metal dusts and welding fumes are irritating to the airways

Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Approximate target concentration	Exposure monitoring	Comments and references	Centre
<b>Welding fumes</b>									
Welding fumes of stainless steel (containing Ni and Cr)	Welding plate + electrodes (solid metal)	Mild steel (welding 2,5 electrodes)	Welding	7,5 electrodes (4 mm diameter) or MIG/TIG welding	30 min	Particles: < 10 mg/m <sup>3</sup> Ni < 0,1 mg/m <sup>3</sup> Cr < 0,5 mg/m <sup>3</sup>	Filter collection (CEN 481:1993) and gravimetric/metal analysis	Hannu T et al. Eur Respir J. 2007 Jan;29(1):85-90.	FIOH
Welding fumes	-	Mild steel	Work mimicking: welding tasks similar to those carried out in the daily work but carried out within the maintenance service of the hospital	not measured	15-120 min	Environmental levels of Fe, Cd, Cu, Cr, Ni, NO <sub>2</sub> , NO, CO, and O <sub>3</sub> < Spanish TLV	Absorption spectrometry, adsorbent tubes and UV-VIS spectrophotometry	- Muñoz X, et al. Respiration 2009; 78(4):455-459 - Levels of Fe, Cd, Cu, Cr, Ni, NO <sub>2</sub> , NO, CO, and O <sub>3</sub> < Spanish TLV in a pre-test. The highest level was O <sub>3</sub> , 0.04 mg/m <sup>3</sup>	VHIR

Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Approximate target concentration	Exposure monitoring	Comments and references	Centre
								(mean)	
Welding fumes	Fumes	Mild steel	Work mimicking	Work mimicking	30, 30, 60 min	1, 4, 10, 15, 30 on the first day (risk of delayed reactions ) 1, 4, 10, 15, 30, and 60 on the second day	NM	Vandenplas O, Thorax. 1995;50:587-8: Vandenplas O et al. Eur Respir J. 1998;11:1182-4.	CHUM
Welding fumes	Solid	Nebulised metal solution e.g. potassium chloride or welding mild steel if other metals are more likely to be the issue	Patient brings in own metal from work and welds in our estates at the hospital	NM	Up to 120 min		PM		BHH

Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Approximate target concentration	Exposure monitoring	Comments and references	Centre
<b>Nickel</b>									
Nickel sulphate solution	Liquid	1 ml/ 10 breaths of the commercial ALK diluent	Spira Elektro 2 dosimeter	3 x 1 ml (0.1 - 1 - 10 mg/ml NiSO <sub>4</sub> in water)	45 min	-	NM	Done with increasing doses upon 45 minutes	FIOH
Nickel	Nickel chloride, powder	Nebulised solvent	Nebulisation with a de Vilbiss 646 nebuliser	0.1-10 mg/ml	1-5 min	-	NM	Inhalation for 1 min; if the FEV1 fall < 10%, another 2 min inhalation phases up to total 5 min	NIOM
Nickel chloride	Powder	Saline	Nebulisation with a de Vilbiss 646 nebulizer	Between 0.1 to 10 mg/ml	Inhalation for 1 min; if the FEV1 fall < 10%, another 2 min inhalation phases up to total 5 min	-	NM	- Cruz MJ, et al. Arch Bronconeumol 2006; 42(6):305-9.  - Method: Bright P, et al. Thorax 1997; 52:28-32	VHIR



Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Approximate target concentration	Exposure monitoring	Comments and references	Centre
Nickel sulphate	Nickel sulphate	Saline	Tidal volume method	10 mg/ml	2 min each concentration 1/1000-1/1	-	NM	Fernandez et al. Int Arch Occup Environ Health. 2006;79(6):483-6.	FJDM
Nickel chloride	Powder	Normal saline	Nebulisation with a de Vilbiss 646 nebulizer	Between 0.1 to 10 mg/ml	60 min	-	NM		UNIPD
Nickel sulphate solution in water	Liquid	Isobutyl acetate	Nebulisation in exposure chamber	2 ml 1% Nickel sulphate solution	20 min	-	NM		FSM
<b>Cobalt</b>									
Cobalt chloride solution	Liquid	1 ml/ 10 breaths of the commercial ALK diluent	Spira Elektro 2 dosimeter	3 x 1 ml (0.1 - 1 - 10 mg/ml CoCl <sub>2</sub> in water)	45 min	-	NM	Done with increasing doses upon 45 minutes	FIOH
Cobalt	Powder	Lactose powder, sieved and baked	% Dust added to 250g lactose powder, then tipped repeatedly by patient	1% to 5%	20 min	-	NM		RBHT

Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Approximate target concentration	Exposure monitoring	Comments and references	Centre
Cobalt chloride	Liquid	Potassium Chloride or other metal salt nebulised	Nebulising it directly using a Turboneb II and maxineb 90 nebuliser pot and mask	~20 ml total (10mg/ml CoCl <sub>2</sub> in saline)	35 min (5+10+20)	-	NM		BHH
Cobalt (in tungsten carbide)	Powder	Mixture of lactose + charcoal powders	Tipping pure hard metal dust			-			CHUM
Cobalt	Powder	Lactose powder	Cobalt dust diluted in 250g lactose powder, then tipped repeatedly by patient	1% to 5%	60 min	NA	NM		UNIPD
Cobalt nitrate solution in water	Liquid	Isobutyl acetate	Nebulisation in exposure chamber	0.12 ml 1% solution	20 min	-	NM		FSM
<b>Chromium</b>									
Chromium: potassium dichromate solution	Liquid	1 ml/ 10 breaths of the commercial diluent	Spira Elektro 2 dosimeter	3 x 1 ml (0.1 - 1 - 10 mg/ml K <sub>2</sub> Cr <sub>2</sub> O <sub>7</sub> in water)	45 min	-	NM	Done with increasing doses over 45 minutes	FIOH

Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Approximate target concentration	Exposure monitoring	Comments and references	Centre
Chromium	Potassium dichromate solution, Liquid	Nebulised solvent	Nebulisation with a de Vilbiss 646 nebuliser	0.1-10 mg/ml	1-5 min	–	NM	Inhalation for 1 min; if the FEV1 fall < 10%, another 2 min inhalation phases up to total 5 min	NIOM
Chromium (Potassium dichromate).	Powder	Saline	Nebulisation with a de Vilbiss 646 nebulizer	Between 0.1 to 10 mg/ml	Inhalation for 1 min; if the FEV1 fall < 10%, another 2 min inhalation phases up to total 5 min	–	NM	-ref. Cruz MJ, et al. Arch Bronconeumol 2006; 42(6):305-9. -Based on the method described by Bright P, et al. Thorax 1997; 52:28-32	VHIR
Chromium: potassium dichromate	Liquid	Potassium Chloride or other metal salt nebulised	Nebulising directly using a Turboneb II and maxineb 90 nebuliser pot and mask	~20 ml total (2mg/ml K2Cr2O7 dissolved in saline)	35 min(5+10+20)	–	NM	Bright P et al. Occupational asthma due to chrome and nickel electroplating Thorax 1997;52:28-32	BHH

Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Approximate target concentration	Exposure monitoring	Comments and references	Centre
Chromium: potassium dichromate Water solution	Liquid	Isobutyl acetate	Nebulising it directly	(0,01% in 10 ml of water) 10 ml total	20 min				FSM
<b>Other</b>									
Platinum salts	Powder	Lactose powder, sieved and baked	Tipped repeatedly by the patient	0.00004% to 0.0004% dust in 250 g lactose powder	20 min	–	NM	potent	RBHT
Palladium, Iridium	Powder	Lactose powder, sieved and baked	Tipping repeatedly by the patient	0.0002% to 0.002% dust in 250 g lactose powder	20 min	–	NM	potent	RBHT
Zinc Sulphate	Liquid	Other metal salt nebulised	Nebulising it directly using a Turboneb II and maxineb 90 nebuliser pot and mask	~20 ml total (up to 10mg/ml ZnSO <sub>4</sub> in saline)	35 min (5+10+20)		NM		BHH
Aluminium chloride	Liquid	Potassium chloride 10mg/ml	Direct nebulisation	10mg/ml	3 minutes	No	NM	Burge PS et al. Occupational asthma caused by aluminium Allergy	BHH

Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Approximate target concentration	Exposure monitoring	Comments and references	Centre
								2000;555:779-800	
Vanadium	Liquid (Water solutions )	Nebulised solvent	Nebulisation with a de Vilbiss 646 nebuliser	0.1-10 mg/ml	1-5 min	–	NM	Inhalation for 1 min; if the FEV1 fall < 10%, another 2 min inhalation phases up to total 5 min	NIOM

**Other chemicals in metal and electronics industry: metalworking fluids (MWF), soldering fluxes, etc.**

**Notes:**

- used MWF's may contain unknown, microbiological impurities

Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Comments and references	Centre
<b><i>Metalworking fluids (MWF)</i></b>							
MWF, unused	Liquid	In-house control solution (nebulised)	Nebulisation of ~40°C unused MWF from a small glass jar with pressured air	3 x 1,5 ml (5% MWF in water) at 0 min, 10 min and 20 min	30 min	- The target concentrations of EA's and formaldehyde are about 1/10 of the Finnish OEL's -EA: Henriks-Eckerman et al. Ann, Occup. Hyg 2007 - Formaldehyde: US Environmental protection agency EPA (1999); method TO11A - Hannu et al. Int Arch Occup Environ Health. 2013 Feb;86(2):189-97	FIOH
MWF, unused	Liquid	Nebulised theatre smoke	Nebulising into room, then patient sits in room surrounded by mist (not nebulised onto patient directly)	Strength as used in the workplace – enough to cause a visible mist	Up to 10 min		RBHT
Used MWF	Liquid	Solvent	Nebulised	200 ml	1, 4, 10, 15, 30,		CHUM

Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Comments and references	Centre
					60 min		
Used MWF	Liquid	Unused MWF with the same procedure	Nebulising in the breathing zone using a Turboneb II and pari-pot nebuliser	~20 ml total (up to 8% MWF in water, as used in workplace )	70 min (10+20+40)	Robertson AS et al. Occupational asthma due to oil mists. Thorax 1988;43:200-205	BHH
Ethanolamines (in MWF) or unused MWF	Liquids	Olive oil	Heating in glass jar	15 ml	30 min	-Air concentration < 1 mg/m <sup>3</sup> , monitored by (Dustrack®) -Sastre et al. J Invest Allergol Clin Immunol 2013 (in press)	FJDM
<b>Soldering materials &amp; colophony</b>							
Soldering/colophony fumes	Solid	In-house control solution (nebulised)	Soldering with colophony containing wire and/or flux onto a circuit board	30 min	-		FIOH
Colophony, solder	Solid	Non-colophony solder wire	Mimicking the patients job-heating and breathing vapours of melting solution		Up to 30 min		NIOM
Colophony	Solid	Saline	Mimicking the patients job		1-30 min		SUH

Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Comments and references	Centre
Colophony	Solid	Non-colophony solder wire	Mimicking the patients job by melting the multicore solder with a soldering iron	1 inspiration initially, then gradually increasing up to the maximum exposure if necessary	Up to 10 min		RBHT
Colophony or non-colophony solder fluxes (dodecanedioic acid, adipic acid)	Solid or liquids if flux alone	Non-colophony fluxed wire or vice versa	Melting with a soldering iron ~300°C or dipping in the flux every 1-2 min	Up to 6 metres of wire	Up to 70 min	<ul style="list-style-type: none"> <li>- Burge PS et al. Bronchial provocation studies in workers exposed to the fumes of electronic soldering fluxes. <i>Clinical Allergy</i> 1980;10: 137-149</li> <li>- Moore VC et al. Occupational asthma caused by dodecanedioic acid. <i>Allergy</i> 2009;64:1099-1100</li> <li>- Moore VC et al. Occupational asthma to solder wire containing an adipic acid flux <i>Eur Respir J.</i> 2010 ;36 : 962-963</li> </ul>	BHH
Soldering/ colophony fumes	Solid	Soldering with wire without colophony	Soldering with colophony containing wire and/or flux onto a circuit board, or pure colophony	NA	30-60 min		UNIPD
Colophony	Solid	Heated ethanol	Direct heating	770 mg	20 min		FSM



Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Comments and references	Centre

## Hairdressing chemicals

### Notes:

- hair colour oxidants may irritate the airways

Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Comments and references	Centre
<b><i>Bleaching agents containing persulphates</i></b>						
Powder + liquid	50-100 ml lactose powder or oxidant alone (dusting)	Mixing	3 doses of bleaching powder + suitable amount of oxidant	30 min	Liquid oxidant usually ~9% hydrogen peroxide	FIOH
Powder +liquid	Water, saline or phosphate buffered saline solution	Mixing and tipping the mixture from one tray to another ~ 30 cm from the face	30 g bleaching powder + 30 ml oxidant	Up to 60 min		NIOM
Powder	Lactose powder	Mixing persulphate salt with 150 g lactose, tipping the mixture from one tray to another at 30 cm from the face	Between 5 – 30 g	5 - 60 min	-Muñoz X, et al. Occup Environ Med 2004;61:861-6 -The estimated concentration of this substance in the air is between 1 and 6 mg/m <sup>3</sup>	VHIR
Powder +liquid	Water	The persulphate salt (30 g) is mixed with oxidant (30 ml) by the patient and applied on a wig		2 - 20 min		SUH
Powder	Lactose powder	Tipping powder	200g	1, 4, 10, 15, 30, 60 min		CHUM

Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Comments and references	Centre
Powder	50-100 g. lactose powder (dusting)	Tipping persulphate powder diluted in lactose	0.1%, 1%, 10% persulphate in lactose powder	60 min	Alternative method: Persulphate mixed with liquid oxidant, usually ~9% hydrogen peroxide	UNIPD
Powder plus liquid	Lactose plus peroxide oxidant mixed	Mixing	As used in workplace	Up to 70 min		BHH
Powder	Lactose powder, sieved and baked	% dust added to 250g lactose powder, then tipped repeatedly by patient	0.1%	5 min to 20 min		RBHT
Liquid	Ethanol	Nebulisation	8 mg of ammonium persulphate in 3 ml water	30 min	Approximate target concentration 1,1 mg/m <sup>3</sup>	FSM
<b>Other hair dyes: oxidated dark and red hair dyes</b>						
Liquid + liquid	Oxidant alone or in-house control solution (nebulised)	Mixing	80 ml of hair dye + suitable amount of oxidant	30 min	Liquid oxidant usually ~9% hydrogen peroxide	FIOH
Liquid + liquid	Water, saline or phosphate buffered saline solution	Mixing	80 ml of hair dye + suitable amount of oxidant	Up to 60 min		NIOM
Liquid	Water	Mixing		2 - 20 min		SUH
<b>Perm wave solutions</b>						
Liquid	In-house control solution	Evaporation at room temperature	60-80 ml	30 min	May be heated to ~40°C	FIOH

<b>Physical form</b>	<b>Control agent</b>	<b>Method of delivery</b>	<b>Approximate amount used</b>	<b>Duration</b>	<b>Comments and references</b>	<b>Centre</b>
	(nebulised)					
Liquid	Water, saline or phosphate buffered saline solution	Painted onto cardboard	As used at work	Up to 60 min		NIOM
Liquid	Other workplace products painted	Painted onto cardboard	As used at work	Up to 70 min		BHH

## Antimicrobials, disinfectants and detergents

### Notes:

- the irritancy of a cleaning agent is largely dependent on its pH

Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Comments and references	Centre
<b>Formaldehyde</b>						
Powder	In-house control solution (nebulised)	Heating up paraformaldehyde powder in a 65 °C oil-bath	2.5 g	15 min	- target conc. < 0.37 mg/m <sup>3</sup> - monitoring: formaldehyde and other aldehydes: US Environmental protection agency EPA (1999); method TO11A	FIOH
Liquid	Water, saline or PBS	Standing in room while breathing in substance in open tray at RT or mixing substance in a bowl	Strength as used in the workplace (50-100 ml)	Up to 60 min		NIOM
Liquid	Solvent	Evaporation at RT	200 ml	1, 4, 10, 15, 30, 60 min	Vandenplas O et al. Persistent asthma following accidental exposure to formaldehyde. Allergy. 2004;59:115-6.	CHUM
Liquid	Cleaning agent painted onto cardboard	Painting onto cardboard	100 ml 10% solution	Up to 70 minutes	Burge PS et al. Occupational asthma due to formaldehyde. Thorax 1985;40: 255-260	BHH
Liquid	Water	Standing in room while breathing in substance in open tray	Strength as used in the workplace	5 – 15 minutes		RBHT
Liquid	Water	Direct nebulisation	70 µl of formaldehyde 4% in 10 ml water	Up to 1 h		FSM

Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Comments and references	Centre
<b>Glutaraldehyde</b>						
Liquid	In-house control solution (nebulised)	Mixing at 40 °C	2-5 ml 25% glutaraldehyde solution + 500 ml water	30 min	-Target conc. < 0,42 mg/m <sup>3</sup> -Formaldehyde and other aldehydes: US Environmental protection agency EPA (1999); method TO11A	FIOH
Liquid	Water, saline or PBS	Standing in room while breathing in substance in open tray at RT or mixing substance in a bowl	Strength as used in the workplace (50-100 ml)	Up to 60 min		NIOM
Liquid	Saline	Nebulisation in chamber from nebulizer (glutaraldehyde 2%)		30 min	Quirce et al. Allergy 1999; 54; 1121-22	FJDM
Liquid	Water	Mixing at 25 °C		1 - 30 min		SUH
Liquid	Water with yellow food dye	Standing in room while breathing in substance in open tray	2% as used in the workplace	5 – 15 minutes		RBHT
Liquid	Solvent	Evaporation at RT	200 ml	1, 4, 10, 15, 30, 60 min	Vandenplas O et al. Persistent asthma following accidental exposure to formaldehyde. Allergy. 2004;59:115-6.	CHUM
Liquid	Cleaning agent painted onto cardboard	Painting onto cardboard	As used in workplace	Up to 70 min	Gannon PFG et al. Occupational asthma due to glutaraldehyde and formaldehyde in endoscopy and X-ray departments Thorax; 1995;50:156-159	BHH
Liquid	Ethanol	Nebulisation in chamber	0,2 ml 25% glutaraldehyde in 4,9 ml water	Up to 30 min		FSM

Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Comments and references	Centre
<b>Glyoxal</b>						
Liquid	In-house control solution (nebulised)	Spraying	3 x 1.2 ml 1 mg/ml Glyoxal solution (at 0, 15 and 30 min)	30 - 45 min	- Target conc. < 0,2 mg/m <sup>3</sup> - Formaldehyde and other aldehydes: US Environmental protection agency EPA (1999); method TO11A	FIOH
Liquid	Water, saline or PBS	Spraying at RT or mixing substance in a bowl	Strength as used in the workplace (50-100 ml)	Up to 60 min		NIOM
<b>Chloramine T</b>						
Liquid	In-house control solution (nebulised)	Spreading on a plate	50-100 ml	30 min	Mäkelä R et al. Occup Med (Lond). 2011 Mar;61(2):121-6.	FIOH
Liquid	Water, saline or PBS	Spreading on a plate at RT or mixing substance in a bowl	Strength as used in the workplace (50-100 ml)	Up to 60 min		NIOM
Liquid	In-house control solution (nebulised)	Nebulisation in chamber	5 ml 0,5% chloramine T solution	30 min up to 1 h		FSM
<b>Chloramines and nitrogen trichloride</b>						
Vapour	Chlorine c 0.5mg/m <sup>3</sup> from 1:20 sodium hypochlorite	Freshly generated nitrogen trichloride atmosphere	Chamber levels 0.5mg/m <sup>3</sup>	Up to 30 minutes	Thickett KM et al. Occupational asthma caused by chloramines in indoor swimming-pool air Eur Respir J 2002;9:827-832	BHH

Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Comments and references	Centre
<b><i>Quaternary ammonium compounds</i></b>						
Liquid	Solvent	Nebulising commercial dilution of quaternary ammonium compounds "as used"	200 ml	1, 4, 10, 15, 30, 60 min		CHUM
<b><i>Other, various detergents, cleaning agents and preservatives</i></b>						
Liquid detergents	Water, saline or PBS	Mixing the detergent in a bowl at RT	Strength as used in the workplace (50-100 ml)	Up to 60 min		NIOM
Liquid detergents	Water with food coloring to simulate the color of detergent	Mixing the detergent in two vessels	250 ml in a vessel	5 – 120 min		VHIR
Liquid detergents	Another similarly irritant cleaning product without the same active chemical	Spraying	1) 5 sprays 2) Up to 5 sprays, continuing with work simulation (wiping, rubbing as at work)	1-5 minutes, up to 35	Spraying by the hospital personnel beforehand, and taking the patient into the chamber, or if negative, spraying by the patient	NMGH
Liquid detergent	Water, saline or PBS	Evaporating the substance in open tray at RT or mixing substance in a bowl or spraying	Strength as used in the workplace (50-100 ml)	Up to 60 min		NIOM
Liquid preservative: 4,4-	Other metal-working fluid constituents	Nebulised to challenge chamber	0.7%	Up to 50 min	This is a biocide used in metal-working fluids	BHH



Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Comments and references	Centre
methylene-bismorpholine						

### Pharmaceutical agents etc.

#### Notes:

- antibiotics may induce isolated late-phase reactions.

Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Comments and references	Centre
Various solid pharmaceuticals	Tablets, powders etc.	50-100 ml lactose powder (dusting)	Diluted usually < 10% in lactose powder and dusted with pressured air every 1 minute	~100 ml lactose/drug mix	30-45 min	The challenge technique and dose depend on the level of sensitization, symptoms, etc.	FIOH
Antibiotics Erythromycin Penicillin Augmentin Amoxicillin Flucloxacillin	Powder	Lactose powder, sieved and baked	% Dust added to 250g lactose powder, then tipped repeatedly by patient	0.1% to 5%	20 minutes		RBHT
Antibiotics	Powder	Lactose powder	Tipping powder diluted 1/10 in lactose	200 g	1, 4, 10, 15, 30, 60 min		CHUM
Colistin or other pharmaceutical agents	Colistin, powder form	Lactose powder	One gram of colistin is mixed with 50 g lactose and the patient tipped the mixture from one tray to another at a	1 gr	15 min	- Ref. Gómez-Ollés S, et al. Chest 2010; 137 (5): 1200 – 2 -Based on the method	VHIR

Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Comments and references	Centre
			distance of 30 cm from the face			described by Moscato G, et al. Eur Respir J 1995;8:467-9.	
Sodium alendronate	Solid	Lactose powder	Mimicking the patients job	10 mg	60 min	G. Pala, L. Perfetti, I. Cappelli, M. Carminati, G. Moscato. Allergy Net; 2008; 1092	FSM
Piperazine	Powder	Lactose	Close-circuit delivery machine		Up to 30 min	- Target concentration < 2 mg/m <sup>3</sup> , PM with Dustrack® - Quirce et al. J Investig Allergol Clin Immunol 2006; 16: 138-9	FJDM
Denatonium benzoate (1% in ethanol)	Liquid	Ethanol	Painting and rubbing onto hands (wearing nitrile gloves)	100 ml	70 min (10+20+40)		BHH
Sevoflurane and Isoflurane	Gas	Other anaesthetic gas	Gas from anaesthetic machine	0.25-0.5% in air	15 breaths	Vellore AD et al. Occupational asthma and allergy to sevoflurane and isoflurane in anaesthetic staff Allergy 2006;61:1485-6	BHH
Thiamine	Powder or	Lactose (tipped) or	tipped or nebulised	100g	30 min	Drought VI et al. Occupational asthma	BHH

Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration	Comments and references	Centre
	solution	normal saline (nebulised)				induced by thiamine in a vitamin supplement for breakfast cereals Allergy 2005;60:1213-1214	