Specific challenge testing for occupational asthma: revised handbook

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Specific inhalation challenge is considered a reference standard in the diagnosis of occupational asthma. An updated handbook of challenge techniques for a large number of sensitising agents from 11 European centres is now available. http://bit.ly/2XVpW1P

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When undertaken carefully, and in experienced hands, specific inhalation challenge (SIC) testing is widely considered to be the reference standard in the diagnosis of occupational asthma. In 2013 the European Respiratory Society commissioned a pan-European task force to produce standards for the conduct and interpretation of SIC with the aim of sharing expertise among those centres who offer the service and with centres who wish to develop a new service. The findings and recommendations of the taskforce were published in the *European Respiratory Journal* [1].

Alongside the main report, we produced a handbook of challenge techniques for a large number of different sensitising agents, including both those of high and low molecular mass. We committed ourselves to provide an update within 5 years; this has been completed, as planned, and is presented as a supplementary file to this editorial. The techniques are those used in 11 specialist centres and are listed by agent category with contact information for each centre should practitioners require more detailed information; the occupational asthma community in Europe prides itself on being collaborative, and collectively is happy to share its experience and expertise.

Controlled, experimental SIC was first developed – formally, as a diagnostic tool for occupational asthma – around 50 years ago, in a single centre. Its practice has flourished and spread since but it is fair to say that access remains patchy, with some European countries, and many regions within them, having no provision at all. This disadvantages patients who require the highest standard of diagnostic accuracy, employers who need to know which of the agents in their workplaces is giving rise to disease in their workers, and regulators charged with controlling what is essentially a preventable disease. Moreover, it hampers the identification of novel sensitisers and the exploration of the mechanisms behind their sensitising properties; this is, perhaps, especially important in the study of chemical sensitisers and particularly so since, rightly or wrongly, they are now considered Substances of Very High Concern under REACH. For these reasons we encourage respiratory physicians and the commissioners of healthcare to familiarise themselves with the relevant guidelines and to consider the equitable provision of SIC across Europe wherever the resources to perform SIC safely and with high quality can be ensured.

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Reference

1 Vandenplas O, Suojalehto H, Aasen TB, *et al.* Specific inhalation challenge in the diagnosis of occupational asthma: consensus statement. *Eur Respir J* 2014; 43: 1573–1587.

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

European Taskforce on SIC
3/2019 (updated from the original version published in June 2013)

Compiled by Katri Suuronen, Hille Suojalehto and Paul Cullinan, on behalf of the ERS Task Force on Specific Inhalation Challenges with Occupational Agents

INTRODUCTION

This handbook is the updated product of a pan-European taskforce on specific inhalation challenge (SIC) testing in the diagnosis of occupational asthma. It was first compiled from information provided by twelve specialist clinical centres in 2013. The content here was updated in 2019, based on information from eleven centres*; the next update is planned for 2024. We are pleased to learn that the original has been used (and welcomed) by several centres, including a few new ones.

Our purpose is to provide information to others on the SIC techniques used in each centre for 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. This version includes an update on diisocyanate monitoring during SIC and in particular the targeted average and maximimum values used in each centre, where these are available.

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 (Vandenplas O et al. Eur Respir J. 2014;43:1573-8). There are, inevitably, differences in practice beween centres and some of these are reflected in the material below; further information can be obtained from any of the centres listed whose contact details are provided (page 4).

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 and gradually be 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.

*the twelfth centre no longer carries out SIC

8 March 2019

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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
MMA	Metylmethacrylate
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	Polyetylene
PM	Particle measurement
pMMA	Polymetylmethacrylate
PP	Polypropylene
ppb	Parts per billion
PVC	Polyvinyl chloride
RT	Room temperature
SIC	Specific Inhalation Challenge
TDI	Toluene diisocyanate
TGIC	Triglycidyl isocyanurate
TLV	Treshold 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; vicky.c.moore@heartofengland.nhs.uk
CHUM	Department of Chest Medicine, Centre Hospitalier Universitaire de Mont-Godinne; Université Catholique de Louvain, Yvoir, Belgium	Olivier Vandenplas; olivier.vandenplas@uclouvain.be
CIOM/ IOMM	Institute for Occupational Medicine, Charité University, Berlin, Germany Institute for Occupational and Maritime Medicine, Hamburg, Germany	Xaver Baur; xaver.baur@charite.de Lygia Therese Budnik; L.Budnik@uke.de
FIOH	Occupational Medicine Team, Finnish Institute of Occupational Health, Helsinki, Finland	Katri Suuronen; katri.suuronen@ttl.fi Hille Suojalehto; hille.suojalehto@ttl.fi
FJDM	Allergy Department, Fundacion Jimenez Diaz-Capio, CIBER de Enfermedades Respiratorias (CIBERES), Madrid, Spain	Dominguez Joaquin Sastre; JSastre@fjd.es
SUH	Chest Diseases, Strasbourg University Hospital, University of Strasbourg, France	Frédéric de Blay; Frederic.DEBLAY@chru-strasbourg.fr Laura Hurdubaea; laura.hurdubaea@chru-strasbourg.fr Brigitte Sbinne; Brigitte.Sbinne@chru-strasbourg.fr
NIOM	Nofer Institute of Occupational Medicine, Depatrment of Occupational Diseases&Clinical Toxicology, Lodz, Poland	Jolanta Walusiak-Skorupa;jolantaw@imp.lodz.pl
NMGH	Department of Respiratory Medicine North Manchester General Hospital, Manchester, United Kingdom	Jennifer Hoyle; jennifer.hoyle@pat.nhs.uk
RBHT	Department of Occupational and Environmental Medicine, Royal Brompton Hospital, London, United Kingdom	Julie Cannon; j.cannon@rbht.nhs.uk www.lungsatwork.org.uk
UNIPD	Department of Cardiologic, Thoracic, and Vascular Sciences, University of Padova, Padova, Italy	Piero Maestrelli; piero.maestrelli@unipd.it
VHIR	Institut de Recerce, Hospital Vall d'Hebron, Barcelona, Spain	Xavier Muńoz; xmunoz@vhebron.net

HIGH MOLECULAR WEIGHT AGENTS

Flours: wheat, rye, oats, barley, soy, buckwheat, tapioca, etc
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 of one challenge**	**Comments and references**	**Centre**
Dust tipping						
Powder	Lactose powder (dusting with pressurised air)	Dusting with pressurised air (1 blow/minute)	100-1000 g as such or diluted in lactose	30-90 min	If IgE sensitization is strong, dilution to 1-50% in lactose in the first challenge, followed by stepwise increase in concentration	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 patient's 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 diluted in lactose	Lactose powder	Dust tipping from one tray to another 30 centimetres away from the patient's 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	SUH

Physical form	Control agent	Method of delivery	Approximate amount used	Duration of one challenge	Comments and references	Centre
Powder	Lactose powder	Tipping and dusting with pressurised air	500 g flour used at work	Up to 120 min (1, 4, 10, 15, 30, 60 min)		CHUM
Powder	Lactose powder	Dust tipping	Up to 1kg	Up to 70 min (10+20+40)		BHH
Powder	Lactose powder baked and sieved	Mixing with lactose powder, then tipping repeatedly by patient	1% to 10% in 250 g lactose	20 min		RBHT
Powder	Lactose powder or tapioca flour	Tipping from one tray to another	~500 g	Up to 30 min		IOMM/ CIOM
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 if suspicion of strong sensitization based on clinical history and IgE	NMGH
Powder	Lactose powder	Close-circuit delivery machine		Up to 30 min		FJDM
Nebulisation						
Homemade /commercial extracts	Saline	Nebulisation by tidal volume method with home-made extracts/commercial extracts		2 min each concentration, based to prick test end-point titration	Quirce S, Polo F, Figueredo E, Gonzalez R, Sastre J .Occupational asthma caused by soybean flour in bakers-differences with soybean-induced epidemic asthma. Clin Exp Allergy 2000; 30:839-846.	FJDM
Commercially available extracts	Saline	Nebulisation in increasing concentrations	Commercial standardized conc.	2 min each concentration	In case of strong IgE sensitisation 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 of one challenge**	**Comments and references**	**Centre**
Wheat, rye, oats, barley and their mixtures						
Powder, rough particles, pellets, etc.	Lactose powder	Dust tipping or dusting with pressurised air (1 blow/minute)	100-1000 g as such or diluted in lactose	30-90 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, 120 min		SUH
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
Soy hull						
Powder diluted in lactose	Lactose powder, sieved and baked	Dust tipping	1% in 250 g lactose	Exposure gradually increasing up to a maximum of 20 min		RBHT

Physical form	Control agent	Method of delivery	Approximate amount used	Duration of one challenge	Comments and references	Centre
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 concentration 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

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 of one challenge	Comments and references	Centre
Dusting/dust tipping						
Powder diluted in lactose	Lactose powder	Dusting with pressurised air (1 blow/minute)	Increasing dilutions of enzyme in 100 g lactose (0.03-0.3-3%)	30 min	Starting concentration depends on the level of IgE-sensitisation and other clinical findings, but is usually 0.03%.	FIOH
Powder	Lactose powder baked and sieved	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

Physical form	Control agent	Method of delivery	Approximate amount used	Duration of one challenge	Comments and references	Centre
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 powder	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 0.1 mg/ml; depending on the level of IgE sensitisation and NSBHR	IOMM/ CIOM
In-house extracts	Saline	Nebulisation: tidal volume method with extracts		2 min each dilution	Starting concentration by end-point skin titration. Quirce S et al. Soy-bean trypsin inhibitor is an occupational inhalant allergen. J Allergy Clin Immunol 2002; 109:178	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 of one challenge**	**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 and other clinical findings.	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 sensitisation 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
Nebulisation						
Commercial NRL extract	Saline	Administered by aerosol using a nebuliser	2 ml of each concentration		The starting concentration is calculated from methacholine PC_{20} and the smallest antigen concentration provoking a positive skin response (Cockcroft DW, et al. Am Rev Respir Dis 1987;135:264-267)	VHIR
Powdered NRL gloves	Non latex gloves	Handling gloves	5-15 gloves	30-60 min	Sastre et al. Specific immunotherapy with a standardized latex extract in allergic workers. A double blind,	FJDM

Physical form	Control agent	Method of delivery	Approximate amount used	Duration of one challenge	Comments and references	Centre
					placebo-controlled, study. J Allergy Clin Immunol 2003; 111:985-94.	

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 others (Western red cedar, MDF) the suspected agent is a LMW compound - almost all centres use a form of dust-tipping - freshly formed dust appears to be more allergenic

Physical form	Control agent	Method of delivery	Approximate amount used	Duration of one challenge	Comments and references	Centre
Dust tipping						
Neat wood dust or diluted in lactose	Lactose powder	Dusting with pressurised air (1 blow/minute)	100-1000g wood dust	30 -90 min	Dilution to 1-50 % in lactose if needed, depending on the level of sensitisation and other clinical findings.	FIOH
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

Physical form	Control agent	Method of delivery	Approximate amount used	Duration of one challenge	Comments and references	Centre
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 electric sander		Up to 60 min		NIOM
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
Nebulisation						
In-house extracts	Saline	Nebulisation (tidal volume method) with home-made extracts		2 min each dilution	Quirce S et al. Identification of obeche wood (Triplochiton scleroxylon) allergens causing occupational asthma. J Allergy Clin Immunol 2000;106:400-401.	FJDM

Physical form	Control agent	Method of delivery	Approximate amount used	Duration of one challenge	Comments and references	Centre
					Quirce S et al Occupational asthma caused by tali and jatoba wood dusts. J Allergy Clin Immunol 2004; 113: 361-3.	

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 of one challenge	Comments and references	Centre
Decorative plants and vegetables							
Fresh plants/vegetables	Solid	Cutting lettuce	Handling (cutting, ripping, turning) fresh plants	e.g. 3-15 decorative flowers or other plants	30-60 min		FIOH
Fresh plants/vegetables	Solid	Saline	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 in a chamber		Up to 60 min	- Quirce et al. Allergy 2005; 60: 969-970	FJDM

Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration of one challenge	Comments and references	Centre
Foodstuffs and spices							
Spices (cardamom, pepper, oregano, coriander, etc.) etc	Powder or flakes	Lactose powder (dusting with pressured air)	Dusting powder or flakes mixed in lactose with pressured air (1 blow/minute) or handling as at work	~100 g lactose/spice mixture	30-60 min		FIOH
Spices (pepper, oregano, basil, cardamon etc.)	Powder or flakes	Lactose powder		~100-500 g spice mixture	30 min		NIOM
Spices, in-house 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 Sastre J, et al Occupational asthma due to different spices. Allergy 1996: 51: 117-120	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	30-60 min	Dilution to 10-50% in lactose in the first challenge, depending on the level of IgE-sensitisation	FIOH
Raw coffee	Powder	Lactose powder	Dusting with pressured air (1 blow/minute)	~100 g lactose/coffee mixture	30-60 min	Dilution to 10-50% in lactose in the first challenge, depending on the level of IgE sensitisation and other clinical findings	FIOH

Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration of one challenge	Comments and references	Centre
Raw coffee	Powder	Lactose powder 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 baked and sieved	% dust added to 250g lactose powder, then tipped repeatedly by patient	1% to 10 %	20 min		RBHT
Shiitake mushroom (*Lentinula edodes*)	Pieces	Lactose powder	Handling mushroom (cutting, ripping, turning)	3-15 mushrooms	Up to 60 min		NIOM
Mushroom spore, Homemade extracts	liquid	Saline	Nebulization at tidal volume	Incresing concentrations, derived from end-point titration skin prick test	2 min each inhalation	Vereda A, et al. Occupational asthma due to spores of Pleurotus ostreatus. Allergy 2007 Feb;62(2):211-2.	FJDM
Plantago ovata	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
Other							
Liquid, standardized commercial	Liquid	Diluent of the commercially available extract	Use of a nebuliser	Commercial standardized concentration	2 min each	- allergen extracts by Bencard Allergi Gmbh	IOMM/ CIOM

Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration of one challenge	Comments and references	Centre
extracts of appropriate material						- Stepwise increase of concentration, starting with 1/1,000, higher dilutions if strong degree of IgE sensitization and/or NSBHR	

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 of one challenge	Comments and references	Centre
Animal epithelium and urine (cow, pig, mouse, rat, rabbit, mites, fur animals etc.)							
Mouse and rat epithelium and urine	Used animal beddings (flakes + powder)	Lactose powder or unused bedding (dusting or tipping)	Tipping used animal beddings containing fresh urine and epithelium from vase to another or handling dead animals.	500-2000 ml	30 -60 min		FIOH
Rat, mouse epithelium and urine	Animal beddings	Unused bedding	Beddings containing fresh urine and epithelium	Approx. 500g	1-60 min		SUH
Laboratory animals (mice)	Live animals as such	Unused bedding	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

Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration of one challenge	Comments and references	Centre
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	Handling (dusting, brushing etc) of furs	3-7 furs	30–45 min		FIOH
Fur animals and feathers, etc. or live laboratory mice or rabbits	As such, live animals in cage with bedding	Lactose powder or starch powder	Handling (dusting, brushing, pulling, tousling etc.) of furs or handling the animals, cleaning them out as in normal working day	3-5 furs	Up to 60 min		NIOM
In-house 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. de las Heras M et al. Occupational asthma caused by gerbil: purification and partial characterization of a new gerbil allergen. Ann Allergy Asthma Immunol. 2010;104:540-2 Torres JA et al. Molecular and immunological characterization of the first allergenic lipocalin in hamster: the major allergen from Siberian hamster (Phodopus sungorus). J Biol Chem; 2014; 289:23382-8.	FJDM

Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration of one challenge	Comments and references	Centre
In-house allergen extracts of storage mites, cow dander, biological pest control organisms	Liquid	Commercial allergen diluent	Spira Elektro 2 dosimeter	1+10+90 breaths in 15 min intervals, total ~1 ml	45 min	-In-house extracts: protein content 0.2 mg/ml – 10 mg/ml -Stepwise increase in the number of inhalations, depending on the level of IgE sensitization and symptoms during the test. Lindström I et al. J Allergy Clin Immunol Pract. 2018;6:692-694	FIOH
Other							
Fish	Solid	Other fish with negative IgE	Mimicking the patients job		Up to 60–120 min	Uriarte SA, et al. Occupational asthma in seafood manufacturing and food allergy to seafood.J Investig Allergol Clin Immunol. 2015;25(1):59-60.	FJDM
Gammarus (shrimp)	Powder	Lactose powder	Dust tipping	50 gr of shrimp Gammarus dust mixed in 100 gr of lactose	5 min	Sogo A et al. Identification of Pen m 4 as a cause of occupational asthma to Gammarus shrimp. Clin Trans Allergy 2018;9;8:46.	VHIR
Carmine	Powder	Lactose powder	Dusting or mixing or pouring carmine diluted in lactose from a vase to another	~100 g lactose/carmine mixture	15–30 min	- Carmine colour derived from cochineal insect - Dilution to 10-50% in lactose in the first challenge, depending on the level of IgE-	FIOH

Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration of one challenge	Comments and references	Centre
						sensitisation and other clinical findings.	
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_{20} and the skin prick test reactivity	VHIR

LOW MOLECULAR WEIGHT AGENTS

Diisocyanates
Notes: - 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**	**Approxi-mate amount used**	**Duration of one challeng e**	**Approximate target concentration**	**Exposure monitoring**	**Comments and references**	**Centre**
Methylenediphenyl diisocyanate (MDI)								
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: average 0.0035 mg/m^3 NCO or 1 ppb (max 5 ppb) level II: average 0,010 mg/m3 NCO or 3-4 ppb (max 5 ppb)	-filter collection and analysis of NCO groups (mg/m^3): ISO 16702 (2001) -on-line measurement (ppb) with Honeywell SPM Flex	-Suojalehto H et al. Am J Ind Med. 2011 Dec;54(12): 906-10; -Finnish OEL 0.035 mg/m^3 NCO; level I 1/10 and level II 1/3 of the OEL	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	15-20 ppb	Continuously measured by	Sastre et al. Chest 2003; 123:1276-1279.	FJDM

Physical form	Control agent	Method of delivery	Approxi-mate amount used	Duration of one challenge	Approximate target concentration	Exposure monitoring	Comments and references	Centre
				20 min 30 min 60 min		Honeywell SPM monitor		
Liquid	Solvent nebulised for 30 min	Heating to 120°C	50 ml or adapted to generate 10 and 15 ppb	1, 4, 10, 15, 30, 60 min	average ~10 ppb (max 20 ppb)	MDA 7100 monitor	Vandenplas O, Malo JL. Eur Respir J. 1997;10:2612-29.	CHUM
Solid crystals or liquid if using paint	Solvent or if a 2-part system, the paint alone	Heating to 120 °C or 2 parts mixed together and painted/sprayed	<1g; enough to achieve up to 20 ppb	Up to 70 min (10+20+40)	average 7 ppb (max 20 ppb)	Honeywell SPM Flex Monitor		BHH
Liquid	Non-hazardous liquid component	Mimicking work, eg. -Painting liquid onto surface -Adding 2 components to make foam	Variable, but enough to achieve up to 20 ppb	30 –60 sec	max 20 ppb	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 (max 20 ppb)	Continuously measured by MDA 7100 monitor		UNIPD
Liquid	Atmospheric (pure) air	Evaporation at 80°C	Variable, but enough to achieve	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

Physical form	Control agent	Method of delivery	Approxi-mate amount used	Duration of one challenge	Approximate target concentration	Exposure monitoring	Comments and references	Centre
			up to 10 ppb					
Hexamethylene diisocyanate (HDI) (usually in a paint or glue hardener or a related product)								
Liquid	2 ml butyl acetate nebulised	Nebulisation of the patient's own HDI-containing hardener from a glass jar with pressured air; diluted in butyl acetate where needed	2 – 6 ml devided to 1-3 doses	15-45 min	HDI monomers < 0.020 mg/m^3 or average 15 ppb (max 45 ppb isocyanates)	-filter collection and analysis of NCO groups (mg/m^3): ISO 16702 (2001) -on-line measurement (ppb) with Honeywell SPM Flex	-2nd challenge with 2 x 2 ml -3rd challenge with 3 x 2 ml -Finnish OEL 0.035 mg/m^3 NCO -Maximum ppb may be high due to high amount of prepolymers in the product	FIOH
Liquid solution with olive oil	Paint without HDI component	Mimicking the patient's job - painting onto cardboard or spraying (depending on work)		Up to 60 min	–	NM		NIOM
Liquid	Saline	Patient's own or in-house HDI product; 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	Patient's own HDI hardener diluted 1/10 in appropriate solvent		1, 4, 10, 15, 30, 60 min	~10 ppb (below 20 ppb)	MDA 7100 monitor		CHUM

Physical form	Control agent	Method of delivery	Approxi-mate amount used	Duration of one challenge	Approximate target concentration	Exposure monitoring	Comments and references	Centre
		and nebulised in the challenge room						
Liquid	Solvent or if a 2-part system, the paint alone	Painting the patient's own or in-house HDI product onto cardboard or spraying depending on work exposure or levels achieved	Enough to achieve up to 20 ppb	Up to 70 min (10+20+40)	< 20ppb	Honeywell SPM Flex Monitor		BHH
Liquid	Paint without HDI component	Mimicking work - spray painting with the patient's own HDI product	Enough to achieve up to 20 ppb	15 sec – 3 min	20 ppb max	HDI monitor (TLD-1 toxic gas detector)		RBHT
Liquid	Water at 80°C	Evaporation at 80°C	5 ml	Up to 60 min	10-20 ppb	Continuously measured by MDA 7100 monitor		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
Toluene diisocyanate (TDI)								
Liquid	1 ml toluene	Evaporation of in-house TDI solution	1 ml	15	level I: TDI average 0. 0035 mg/m^3	-filter collection and analysis of	-Level I 1/10 and level II 1/3 of OEL	FIOH

Physical form	Control agent	Method of delivery	Approxi-mate amount used	Duration of one challenge	Approximate target concentration	Exposure monitoring	Comments and references	Centre
	(evapora-tion)	(in toluene) from a small glass cup at 175°C			or 1-3 ppb level II: TDI average 0.010 mg/m^3 or 3-10 ppb	NCO groups (mg/m^3): ISO 16702 (2001) -on-line measurement (ppb) with Honeywell SPM Flex	-level I solution: 0.18 mg/ml in toluene -level II solution: 3.1 mg/ml in toluene - Finnish OEL 0.035 mg/m^3 NCO	
Liquid solution with olive oil	Solvent or if a 2-part system, the paint alone	Mimicking the patient's 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

Physical form	Control agent	Method of delivery	Approxi-mate amount used	Duration of one challenge	Approximate target concentration	Exposure monitoring	Comments and references	Centre
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 achieved	Up to Enough to achieve up to 20 ppb	Up to 70 min (10+20+40)	< 20 ppb	Honeywell SPM Flex Monitor		BHH
Liquid	Water flushed with medical O2	Evaporation of TDI liquid solution from a flask flushed with medical O2.	20 ml	Up to 60 min	10-20 ppb	Continuously measured by MDA 7100 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
Other: isophorone diisocyanate (IPDI), 1,5-naphthalene diisocyanate (NDI)								
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	10 min 20 min 30 min	2.5 ppb 5 ppb 5ppb	Continuously. measured by		IOMM/ CIOM

Physical form	Control agent	Method of delivery	Approxi-mate amount used	Duration of one challenge	Approximate target concentration	Exposure monitoring	Comments and references	Centre
			up to 10 ppb	60 min	5 ppb	Honeywell SPM monitor		

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 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 of one challenge	Approximate target concentration	Exposure monitoring	Comments and references	Centre
Epoxy resins									
Epoxy paint + hardener	Liquid paint and hardener	2 ml butylacetate nebulised	Mixing the paint and the hardener in a bowl	Paint 100 ml + suitable amount of hardener	30–45 min	–	NM	The patient may also spread the mixture on a plate -Suojalehto H et al. J Allergy Clin Immunol Pract. 2019;7(1):191-198	FIOH

Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration of one challenge	Approximate target concentration	Exposure monitoring	Comments and references	Centre
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
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 powder	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

Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration of one challenge	Approximate target concentration	Exposure monitoring	Comments and references	Centre
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
Epoxy resin paints	Liquid	Non-hazardous paint	Mimicking work – painting or spraying	Strength as used in the workplace	15 sec– 2 min	–	NM		RBHT
Epoxy resins	liquid	solvent-base paint	Mixing epoxy and hardener in chamber	100-200 ml	30 min	-	-	Suojalehto H et al. J Allergy Clin Immunol Pract. 2019;7(1):191-198	FJDM

Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration of one challenge	Approximate target concentration	Exposure monitoring	Comments and references	Centre
Acrylic resins: acrylates, methacrylates and products based on them									
Artificial nail (meth)acrylates	Gels, liquid glues and solid nail tips	2 ml butylacetate nebulised	-preparing nails on plastic tips by mixing and forming -grinding the newly prepared nails on the following day	Enough material for 4 -6 nails	30 min 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	2-4 ml butylacetate evaporated	Mimicking work: mixing pMMA powder and MMA liquid	5-10 ml liquid and suitable amount of powder	30 min 45 min	–	VOC method: ISO 16000-6		FIOH
Dental (meth)acrylates	Liquid	2 ml butylacetate nebulised	Evaporation at room temperature	2 x 10-20 drops of a dental adhesive (at 0 and 15 min)	30 min 45 min	–	VOC method: ISO 16000-6	Lindström M et al. Allergy. 2002;57(6):543-5.	FIOH
Acrylates	Liquid	Nebulised solvent	Mimicking the patient's job	As used in the patients workplace	Up to 60 min	–	NM		NIOM
Acrylates	Liquid	Nebulised solvent	Mimicking the patient's job	Strength as used in the patients workplace	1, 4, 10, 15, 30, 60 min	–	NM		CHUM

Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration of one challenge	Approximate target concentration	Exposure monitoring	Comments and references	Centre
Methyl-methacrylate (MMA)	Liquid	Latex gloves, cleaning agents, a non-hazardous liquid component, another workplace agent	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
Trimethylolpropane-triacrylate	powder	Thermal printer without ink	Thermal printer		30 min	unknown	NM	Sanchez-García S, et al. N Eng J Med 2009;360(22):2375-6	FJDM
Acrylic polymer	powder	lactose	Handling, tipping	-	30 min	-	Dusttrack	Quirce S et al. J Investig Allergol Clin Immunol 2011; 21:78-79	FJDM

Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration of one challenge	Approximate target concentration	Exposure monitoring	Comments and references	Centre
Cyanoacrylate: instant glues and related products									
Cyanoacrylate-based instant glue	Liquid glue	2 ml butylacetate nebulised	Evaporation at room temperature or spreading glue on a plate	3 x 3 drops of eye lash glue (at 0, 10 and 20 min) or 2-4 ml of industrial glue	30-45 min	<1 mg/m^3	VOC method: ISO 16000-6;	Lindström I et al. Occup. Med, 2013	FIOH
Cyanoacrylate-based instant glue	Liquid glue	Nebulised solvent	Mimicking the patient's job	As used in the patient's workplace	Up to 60 min	–	NM		NIOM
Cyanoacrylate	Glue	Food gelatine	Mimicking the patient's job	–	30 min	–	–	Andujar R et al. Am J Ind Med 2011; 54:714-8.	VHIR
Cyanoacrylate-based instant glue	Glues and gels	Saline	Mimicking work; mixing liquid	1-10 mL	1 min 2 min 4 min 8 min 15 min 30 min 60 min 120 min	–	NM		SUH
Cyanoacrylate	Glue	Glue without cyanoacrylte	Mimicking the patient's job		30 min	-	-	Quirce S, et al Allergy 2001; 56:446-449.	FJDM

Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration of one challenge	Approximate target concentration	Exposure monitoring	Comments and references	Centre
Acid anhydrides									
Phthalic acid anhydrides (in epoxy hardeners or as such)	Liquid	2 ml butylacetate 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^3	Collection into Tenax adsorbent 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
Tetrahydrophthalic anhydride	Powder	Lactose	Tipping 5% in lactose		30 min	< 5 mg/m^3	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
Other/miscellaneous plastics and resins									
Powder coatings (epoxy and/or polyester)	Powder	50-100 ml lactose powder (dusting)	Heating in a disposable aluminium form 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	BHH

Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration of one challenge	Approximate target concentration	Exposure monitoring	Comments and references	Centre
								triglycidyl isocyanurate Occupational Medicine 2011;61:65-67	
TGIC	Powder	Lactose powder	Tipping 4% in lactose		30 min	< 5 mg/m^3	PM (Dustrack®)	Sastre J et al. Int Arch Occup Environ Health. 2011;84(5):547-9.	FJDM
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
Aziridine	Liquid	Water	Mimicking work: painting a plate	30 ml	Up to 60 min	-	NM		UNIPD

Finished plastics									
Shrink wrap (plastic)	Plastic film on a roll with heat seal machine	Using heat seal machine without plastic film	Mimicking the patient's 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^2 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	Solid Plastic blocks	Heating plastic without PVC	Heating PVC	-	60 min	-	-	Uriarte S, et al. Investig Allergol Clin Immunol. 2013;23(6):437-8	FJDM
Polyurethane mattress foam	Solid blocks of foam	A different type of foam	Cutting the foam 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**	**Approxi-mate amount used**	**Duration of one challeng e**	**Approxi-mate target concen-tration**	**Exposure monitoring**	**Comments and references**	**Centre**
Welding fumes									
Welding fumes of stainless steel (containing Ni and Cr)	Welding plate + electrod es (solid metal)	Mild steel (welding 2,5 electrodes)	Welding	7,5 electrodes (4 mm diameter) or MIG/TIG welding	30 min	Particles: < 10 mg/m3 Ni < 0,1 mg/m^3 Cr < 0,5 mg/m^3	Filter collection (CEN 481:1993) and gravimetric/ metal analysis	-Hannu T et al. Eur Respir J. 2007;29(1):85-90. - only seldom done because of the irritancy of the welding fumes	FIOH
Welding fumes		Mild steel	Mimicking work: 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	Environmen tal levels of Fe, Cd, Cu, Cr, Ni, NO_2, NO, CO, and O_3 < Spanish TLV	Absorption spectrometr y, adsorbent tubes and UV-VIS spectrophot ometry	- Muñoz X, et al. Respiration 2009; 78(4):455-459 - Levels of Fe, Cd, Cu, Cr, Ni, NO_2, NO, CO, and O_3 < Spanish TLV in a pre-test. The highest level was O_3, 0.04 mg/m3 (mean)	VHIR

Active agent	Physical form	Control agent	Method of delivery	Approxi-mate amount used	Duration of one challenge	Approxi-mate target concen-tration	Exposure monitoring	Comments and references	Centre
Welding fumes	Fumes	Mild steel	Mimicking work	Mimicking work	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 department at the hospital	NM	Up to 120 min		PM		BHH

Active agent	Physical form	Control agent	Method of delivery	Approxi-mate amount used	Duration of one challenge	Approxi-mate target concen-tration	Exposure monitoring	Comments and references	Centre
Nickel									
Nickel sulphate solution	Liquid	1 ml/ 10 breaths of the commercial diluent	Spira Elektro 2 dosimeter	1+10+90 breaths; 3 x 1 ml (0.1 - 1-10 mg/ml $NiSO_4$ in water)	15-45 min	–	NM	Done with increasing doses in 15 min intervals over 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 or Nickel sulphate	Powder	Saline	Nebulisation with a de Vilbiss 646 nebuliser	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	Approxi-mate amount used	Duration of one challenge	Approxi-mate target concen-tration	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 nebuliser	Between 0.1 to 10 mg/ml	Up to 60 min	–	NM		UNIPD
Cobalt									
Cobalt chloride solution	Liquid	1 ml/ 10 breaths of the commercial ALK diluent	Spira Elektro 2 dosimeter	1+10+90 breaths; 3 x 1 ml (0.1 - 1 - 10 mg/ml $CoCl_2$ in water)	15-45 min	–	NM	Done with increasing doses in 15 min intervals over 45 minutes	FIOH
Cobalt	Powder	Lactose powder baked and sieved	% dust added to 250g lactose powder, then tipped repeatedly by patient	1% to 5%	20 min	–	NM		RBHT
Cobalt chloride	Liquid	Potassium chloride or other metal salt nebulised	Nebulising it directly using a Turboneb II and Maxineb 90	~20 ml total (10mg/ml $CoCl_2$ in saline)	35 min (5+10+20)	–	NM		BHH

Active agent	Physical form	Control agent	Method of delivery	Approxi-mate amount used	Duration of one challenge	Approxi-mate target concen-tration	Exposure monitoring	Comments and references	Centre
			nebuliser pot and mask						
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%	Up to 60 min	NA	NM		UNIPD
Chromium									
Chromium: potassium dichromate solution	Liquid	1 ml/ 10 breaths of the commercial diluent	Spira Elektro 2 dosimeter	1+10+90 breaths; 3 x 1 ml (0.1 - 1-10 mg/ml $K_2Cr_2O_7$ in water)	15-45 min	–	NM	Done with increasing doses in 15 minutes intervals over 45 minutes	FIOH
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

Active agent	Physical form	Control agent	Method of delivery	Approxi-mate amount used	Duration of one challenge	Approxi-mate target concen-tration	Exposure monitoring	Comments and references	Centre
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
Other									
Platinum salts	Powder	Lactose powder, sieved and baked	Tipped repeatedly by the patient	0.000004% to 0.00004% dust in 250	20 min	–	NM	potent	RBHT

Active agent	Physical form	Control agent	Method of delivery	Approxi-mate amount used	Duration of one challenge	Approxi-mate target concen-tration	Exposure monitoring	Comments and references	Centre
				g lactose powder					
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 $ZnSO_4$ 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 2000;555:779-800	BHH
2-pack glue: Zinc sulphate (anhydrous) hardener + Zinc phthalocyanine pigment	Liquid	Solvent	Two trigger sprays hand held and spray together to form a single jet	500 ml	Up to one hour, start at 1 min, 2min, 5min, 10	-	NM	-Inhaled whist spraying for 1 min and then double, FEV1 check and re-expose -Visible glue forms immediately on mixing	NMGH

Active agent	Physical form	Control agent	Method of delivery	Approxi-mate amount used	Duration of one challeng e	Approxi-mate target concen-tration	Exposure monitoring	Comments and references	Centre
					min, 20 min.				
Vanadium	Liquid (water solution)	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	Approxi-mate amount used	Duration of one challeng e	Comments and references	Centre
Metalworking fluids (MWF)							
MWF, unused	Liquid	2 ml butyl acetate, nebulised	Nebulisation of ~40˚C unused MWF from a small glass jar with pressured air	3 x 2ml (5% MWF in water) at 0 min, 10 min and 20 min	30 min 45 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	FIOH

Active agent	Physical form	Control agent	Method of delivery	Approxi-mate amount used	Duration of one challenge	Comments and references	Centre
						- Formaldehyde: US Environmental protection agency EPA (1999); method TO11A - Hannu et al. Int Arch Occup Environ Health. 2013;86(2):189-97	
MWF, unused	Liquid	Nebulised theatre smoke	Nebulising into room, then patient sits in room surrounded by mist (not nebulised into 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, 60 min		CHUM
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/m3, monitored by (Dustrack®) -Sastre J, et al. Allergol Immunopathol (Madr). 2013; 41:354-355	FJDM

Active agent	Physical form	Control agent	Method of delivery	Approxi-mate amount used	Duration of one challenge	Comments and references	Centre
Soldering materials & colophony							
Soldering/ colophony fumes	Solid	2 ml butyl acetate, 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 patient's job-heating and breathing vapours of melting solution		Up to 30 min		NIOM
Colophony	Solid	Saline	Mimicking the patient's job		1-60 min		SUH
Colophony	Solid	Non-colophony solder wire	Mimicking the patient's job by melting the multicore solder with a soldering iron	1 inhalation 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	- Burge PS et al. Bronchial provocation studies in workers exposed to the fumes of electronic soldering fluxes. Clinical Allergy 1980;10: 137-149	BHH

Active agent	Physical form	Control agent	Method of delivery	Approxi-mate amount used	Duration of one challenge	Comments and references	Centre
						- Moore VC et al. Occupational asthma caused by dodecanedioic acid. Allergy 2009;64:1099-1100 - Moore VC et al. Occupational asthma to solder wire containing an adipic acid flux Eur Respir J. 2010 ;36 : 962-963	
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	Up to 60 min		UNIPD
Bow rosin (colophony)	Solid	Lactose	Adding rosing on string instrument bow and playing	1-5 g	30-60 min	Solid rosin added on the bow dusts when played	FIOH

Hairdressing chemicals
Notes: - hair colour oxidants may irritate the airways

Physical form	Control agent	Method of delivery	Approximate amount used	Duration of one challenge	Comments and references	Centre
Bleaching agents containing persulphates						

Physical form	Control agent	Method of delivery	Approximate amount used	Duration of one challenge	Comments and references	Centre
Powder + liquid	100 ml of oxidant alone	Mixing	3 doses of bleaching powder + suitable amount of oxidant	30 -45min	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^3	VHIR
Powder + liquid	Lactose powder + rice milk	The persulphate salt (30 g) is mixed with oxidant (30 ml) by the patient and applied on a wig	200-300 ml	2 - 120 min		SUH
Powder	Lactose powder	Tipping powder	200g	1, 4, 10, 15, 30, 60 min		CHUM
Powder	50-100 g. lactose powder (dusting)	Tipping persulphate powder diluted in lactose	0.1%, 1%, 10% persulphate in lactose powder	Up to 60 min	Alternative method: Persulphate mixed with liquid oxidant, usually ~9% hydrogen peroxide, spread on a wig	UNIPD

Physical form	Control agent	Method of delivery	Approximate amount used	Duration of one challenge	Comments and references	Centre
Powder + liquid	Lactose plus peroxide oxidant mixed	Mixing	As used in workplace	Up to 70 min		BHH
Powder	Lactose powder baked and sieved	% dust added to 250g lactose powder, then tipped repeatedly by patient	0.1%	5 min to 20 min		RBHT
Powder + liquid	Lactose	mixing	As used in the workplace	30-60 min		FJDM
Other hair dyes: oxidated dark and red hair dyes						
Liquid + liquid	100 ml of oxidant alone	Mixing	80 ml of hair dye (2 tubes) + suitable amount of oxidant	30-45 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
Perm wave solutions						
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 of one challenge**	**Comments and references**	**Centre**
Formaldehyde						
Liquid	2 ml butyl acetate, nebulised	Evaporation from a bowl at room temperature	10-100 ml of 10 % formaldehyde solution in water	15 min	- target conc. < 0.37 mg/m^3 - seldom done due to the irritancy of formaldehyde - 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
Glutaraldehyde						
Liquid	2ml butylacetate, nebulised	Mixing at 40 ˚C or nebulised	mixing of 2-5 ml 25% glutaraldehyde	30 min	-Target conc. < 0,42 mg/m^3	FIOH

Physical form	Control agent	Method of delivery	Approximate amount used	Duration of one challenge	Comments and references	Centre
			solution + 500 ml water or nebulising of 1-2 ml 1% glutaraldehyde solution		-Formaldehyde and other aldehydes: US Environmental protection agency EPA (1999); method TO11A	
Liquid	Water, saline or PBS	Standing in room while breathing in substance in open tray at room temperature 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		1-60 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 room temperatureRT	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
Glyoxal						

Physical form	Control agent	Method of delivery	Approximate amount used	Duration of one challenge	Comments and references	Centre
Liquid	2ml butylacetate, 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^3 - 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
Chloramine T						
Liquid	2ml butylacetate, nebulised	Spreading on a plate	50-100 ml of 1-5% dilution, as used at work	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 room temperature or mixing substance in a bowl	Strength as used in the workplace (50-100 ml)	Up to 60 min		NIOM
Chloramines and nitrogen trichloride						
Vapour	Chlorine 0.5mg/m^3 from 1:20 sodium hypochlorite	Freshly generated nitrogen trichloride atmosphere	Chamber levels 0.5mg/m3	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
Quaternary ammonium compounds						
Liquid	Solvent	Nebulising commercial dilution of quaternary ammonium compounds “as used”	200 ml	1, 4, 10, 15, 30, 60 min		CHUM
Liquid	Water	0.0001% dilution of quaternary ammonium compound in water, used	3 l minimum	1, 4, 10, 15, 30, 60, 120 min		SUH

Physical form	Control agent	Method of delivery	Approximate amount used	Duration of one challenge	Comments and references	Centre
		to clean a surface, mimiking work				
Other, various detergents, cleaning agents and preservatives						
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-methlyene-bismorpholine	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
Bleach	Saline	Nebulized in challenge chamber	Commercial bleach	Up 60 min	-Chlorine is monitored , no more than 0.5 ppb	FJDM

Physical form	Control agent	Method of delivery	Approximate amount used	Duration of one challenge	Comments and references	Centre
					-Sastre J, et al. Am J Ind Med2011 ;54(4):293-9	

Pharmaceutical agents etc.
Notes: - antibiotics may induce isolated late-phase reactions.

Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration of SIC	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 penicillins augmentin amoxicillin flucloxacillin	Powder	Lactose powder baked and sieved	% 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 distance of 30 cm from the face	1 gr	15 min	- Ref. Gómez-Ollés S, et al. Chest 2010; 137 (5): 1200 – 2 -Based on the method described by Moscato G, et al. Eur Respir J 1995;8:467-9.	VHIR

Active agent	Physical form	Control agent	Method of delivery	Approximate amount used	Duration of SIC	Comments and references	Centre
Piperazine	Powder	Lactose	Close-circuit delivery machine		Up to 30 min	- Target concentration < 2 mg/m3, PM with Dustrack® - Quirce et al. J Investig Allergol Clin Immunol 2006; 16: 138-9	FJDM
Ferrimanitol, Ovalbumin, Clarithromycin, Glucosamine Hydrochloride (powders)	Powder	Lactose	Tipping for powders	100 g	30-60 min	Valverde-Monge M, et al. Novel causes of drug-induced occupational asthma. J Allergy Clin Immunol in pract. in press 2018	FJDM
Minoxidil (liquid)	liquid	Ethanol	Mimicking patient´s job	50 ml	30-60 min	Valverde-Monge M, et al. Novel causes of drug-induced occupational asthma. J Allergy Clin Immunol in pract. in press 2018	FJDM
Denatonium benzoate (1% in ethanol)	Liquid	Ethanol	Painting and rubbing onto hands (wearing nitrile gloves)	100 ml	70 min (10+20+40)		BHH
Sevofluorane and isofluorane	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 liquid	Lactose powder (tipped) or	Tipped or nebulised	100g	30 min	Drought VI et al. Occupational asthma induced by thiamine in a vitamin	BHH

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

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Specific challenge testing for occupational asthma: revised handbook

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Specific inhalation challenge is considered a reference standard in the diagnosis of occupational asthma. An updated handbook of challenge techniques for a large number of sensitising agents from 11 European centres is now available. http://bit.ly/2XVpW1P

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When undertaken carefully, and in experienced hands, specific inhalation challenge (SIC) testing is widely considered to be the reference standard in the diagnosis of occupational asthma. In 2013 the European Respiratory Society commissioned a pan-European task force to produce standards for the conduct and interpretation of SIC with the aim of sharing expertise among those centres who offer the service and with centres who wish to develop a new service. The findings and recommendations of the taskforce were published in the *European Respiratory Journal* [1].

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