# 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)

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# 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

## LIST OF TABLES

**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<br>Institute for Occupational and Maritime Medicine, Hamburg, Germany | Xaver Baur; xaver.baur@charite.de<br>Lygia Therese Budnik; L.Budnik@uke.de |
| FIOH | Occupational Medicine Team, Finnish Institute of Occupational Health, Helsinki, Finland | Katri Suuronen; katri.suuronen@ttl.fi<br>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<br>Laura Hurdubaea; laura.hurdubaea@chru-strasbourg.fr<br>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<br>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:**<br>- most centres use a dust-tipping method but nebulisation is an alternative<br>- particle size and/or particle mass may be measured during active challenges<br>- 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:**<br>- seeds or large particles may be ground smaller prior to SIC<br>- particle size and/or particle mass may be measured<br>- 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<br>-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.<br>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** |
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| **Notes:**<br>- 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:**<br>- some woods contain HMW (protein) allergens, while in others (Western red cedar, MDF) the suspected agent is a LMW compound<br>- almost all centres use a form of dust-tipping<br>- 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<br>(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<br><br>2) Powder | Another wood species (sanded or powder depending on the active SIC) | 1) Sanding the wood, electric sander<br><br>2) Tipping from one tray to another | 1) wood block<br><br>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:**<br>- a wide variety of methods are used: tipping, dusting, work mimicking, nebulisation of home-made extracts, etc<br>- 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** |
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| **Notes:**<br>- 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.<br>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<br>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<br>-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<br>- 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<br>- protein concentration of carmine determined by the BCA protein assay<br>-The starting concentration is based on metacholine $PC_{20}$ and the skin prick test reactivity | VHIR |

## LOW MOLECULAR WEIGHT AGENTS

| **Diisocyanates** |
|---|
| **Notes:**<br>- either diisocyanate-containing products or in-house solutions of pure diisocyanates may be used<br>- 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)<br><br>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)<br>-on-line measurement (ppb) with Honeywell SPM Flex | -Suojalehto H et al. Am J Ind Med. 2011 Dec;54(12): 906-10;<br>-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<br>30 min<br>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.<br>-Painting liquid onto surface<br>-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<br>20 min<br>30 min<br>60 min | 2.5 ppb<br>5 ppb<br>5 ppb<br>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)<br>-on-line measurement (ppb) with Honeywell SPM Flex | -2$^{nd}$ challenge with 2 x 2 ml<br>-3$^{rd}$ challenge with 3 x 2 ml<br>-Finnish OEL 0.035 mg/m$^3$ NCO<br>-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<br>20 min<br>30 min<br>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<br>20 min<br>30 min<br>60 min | 2.5 ppb<br>5 ppb<br>5ppb<br>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<br><br>level II: TDI average 0.010 mg/$m^3$<br>or 3-10 ppb | NCO groups (mg/$m^3$): ISO 16702 (2001)<br>-on-line measurement (ppb) with Honeywell SPM Flex | -level I solution: 0.18 mg/ml in toluene<br>-level II solution: 3.1 mg/ml in toluene<br>- 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°<br>The flask contains 1.5 ml (TDI, SIGMA) | ~ 0.1 mL | 1 min<br>2 min<br>4 min<br>8 min<br>15 min<br>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<br>20 min<br>30 min<br>60 min | 5 ppb<br>10 ppb<br>10 ppb<br>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<br>20 min<br>30 min<br>60 min | 2.5 ppb<br>5 ppb<br>5ppb<br>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<br>20 min<br>30 min | 2.5 ppb<br>5 ppb<br>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<br>2 min<br>4 min<br>8 min<br>15 min<br>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<br>-grinding the newly prepared nails on the following day | Enough material for 4 -6 nails | 30 min<br>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<br>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<br>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<br>2 min<br>4 min<br>8 min<br>15 min<br>30 min<br>60 min<br>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<br>- 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**<br>- precious metal salts are very potent and very low doses should be used for SIC<br>- 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<br>Ni < 0,1 $mg/m^3$<br>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.<br>- 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<br>- 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.<br><br>- 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<br>-Visible glue forms immediately on mixing | NMGH |

| 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 |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | 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:**<br>- used MWF's may contain unknown, microbiological impurities |

| Active agent | Physical form | Control agent | Method of delivery | Approxi-mate amount used | Duration of one challenge | 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<br>-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<br>- 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®)<br>-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<br>- 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:**<br>- 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<br>-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:**<br>- 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$^3$<br>- seldom done due to the irritancy of formaldehyde<br>- 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<br>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/$m^3$<br>- 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<br>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:**<br>- 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:<br>erythromycin<br>penicillins<br>augmentin<br>amoxicillin<br>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<br>-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®<br>- 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<br>Allergy 2005;60:1213-1214 | |