

Revised Baseline Series of the International Contact Research Group

To the Editor:

To develop international comparative data, the International Contact Dermatitis Research Group (ICDRG) created a standard series in 1997 composed of 20 haptens. This series was expanded to contain 32 haptens in 2011,¹ which serves as a basis for the new revision presented here. When considering haptens for inclusion in a baseline series, a general recommendation is to include a sensitizer if the frequency of contact allergy is at least 0.5% to 1% in all tested individuals.² If its sensitization rate falls below this threshold, the presence of this hapten in the environment should be reassessed: if its presence in the environment is high, despite a low contact allergy frequency, this substance might still be a candidate for a baseline series. One such example is the paraben preservatives present in paraben mix. The frequency of positive reactions to paraben mix is in most clinics less than 0.5%. However, when it occurs, it is often of high clinical relevance.²

In addition, the ICDRG baseline patch test results from 13 centers representing 4 continents of the ICDRG from 2012 to 2016 were collected. The patch test results were discussed, and it was decided, based on consensus, whether a hapten should continue to be included. Factors included in the discussion were low frequency of contact allergy, few cases of clinical relevance, or clinical importance only in a specific geographical area.

Several multicenter patch test studies have been performed within the group to see whether specific haptens should be incorporated into the ICDRG baseline series or not. The haptens that have been investigated are as follows: textile dye mix (TDM) 6.6%,³ a resol resin based on phenol and formaldehyde (PFR-2),⁴ methylchloroisothiazolinone (MCI)/methylisothiazolinone (MI) 0.02%, and MI 0.2%,⁵ and recently also MCI/MI 0.02%, MCI/MI 0.215%, and MI 0.2%, as well as mercaptobenzothiazole (MBT) 2%, mercapto mix 2%, and mercapto mix 3.5%.

Based on the previously mentioned, the following changes to the 2019 ICDRG baseline series (Table 1) were decided:

Deleted haptens:

Hydrocortisone-17-butyrate was deleted from the series because it was shown that the detection rate was very low and because budesonide is a cross-reacting substance that better detects allergy to this group of topical corticosteroids.

Tosylamide/formaldehyde resin was excluded because of the low detection rate and the fact that it is seldom present in nail cosmetics anymore.

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Hydroxyisohexyl 3-cyclohexene carboxaldehyde was excluded based on the results of a retrospective study of contact allergy to fragrance mix II (FM II) and hydroxyisohexyl 3-cyclohexene carboxaldehyde within the ICDRG. The detection rate was low, usage was minimal, and the additional contact sensitization detected, excluding those from FM II tests, was less than 0.5% (to be published).

Changed patch test concentration and/or test preparations of haptens already present in the baseline series:

Formaldehyde: To substantiate the change of formaldehyde from 1% to 2% in 2011, a multicenter study was performed, which demonstrated that a significantly higher number of contact sensitizations is detected with the higher concentration.⁶

Methylchloroisothiazolinone/methylisothiazolinone: One ICDRG study in 9 countries representing South America, Europe, and Asia assessed how many additional contact sensitized individuals were found by testing MI 0.2% aqueous in parallel with MCI/MI 0.02%. Contact sensitization to MI was found in 7.3%, with frequencies ranging from 0.8% to 10.9%. Contact sensitization to MI alone without any simultaneous contact sensitization to MCI/MI 0.02% was diagnosed in 2.4% of all tested patients, and the contact sensitization could explain or contribute to the dermatitis in approximately 30% of the patients.⁵ Results led to several centers testing to MI 0.2% instead of 0.01% as stated in the minimal ICDRG baseline series from 2011.

Recently, another multicenter ICDRG study has been performed in which MCI/MI 0.02% (MCI 0.015% and MI 0.005%) and MI 0.2% were compared with testing with a new mix, namely, MCI/MI 0.215% (MCI 0.015% and MI 0.2%). Results showed that this new mix detects more sensitized individuals than the other two do. Hence, MCI/MI 0.02% and MI 0.2% will be excluded and replaced with MCI/MI 0.215% (to be published). A similar study in Sweden within the Swedish Contact Dermatitis Research Group (SCDRG) showed the same results, and the high mix will also be recommended for inclusion into the Swedish baseline series (to be published).

Mercapto mix: MBT 2% and mercapto mix 2% (4 substances including MBT, morpholinylmercaptobenzothiazole, dibenzothiazyl disulfide, and *N*-cyclohexyl-2-benzothiazolesulfenamide, each at 0.5%) were present in the baseline series from 2011. Both showed prevalence rates just more than 0.5% (0.8% and 0.6%, respectively) in the ICDRG study on baseline patch test results from 13 ICDRG centers representing 4 continents from 2012 to 2016 and were therefore candidates for removal from the baseline series (to be published). These findings were supported by another multicenter ICDRG study in which testing to MBT 2% and mercapto mix 2% has been compared with testing with a new mix, namely, mercapto mix 3.5%, and results have shown that this new mix is a candidate to replace MBT 2% and mercapto

TABLE 1. Updated 2019 Baseline Series of the ICDRG: Selected Haptens and Concentrations in Percent

1	<i>p</i> -Phenylenediamine	1.0
2	4- <i>tert</i> -Butylphenol formaldehyde resin	1.0
3	Budesonide	0.01
4	Carba mix	3.0
5	MCI/MI*	0.215
6	Cobalt chloride	1.0
7	Colophony	20.0
8	Compositae mix	5.0
9	Diazolidinyl urea	2.0
10	Epoxy resin	1.0
11	Formaldehyde*	2.0
12	FM I	8.0
13	FM II	14.0
14	Imidazolidinyl urea	2.0
15	Lanolin alcohol	30.0
16	Mercapto mix	3.5
17	Methyldibromoglutaronitrile	0.3
18	<i>Myroxylon pereirae</i>	25.0
19	<i>N</i> -isopropyl- <i>N</i> -phenyl-4-phenylenediamine	0.1
20	Neomycin sulfate	20.0
21	Nickel sulfate	2.5
22	Paraben mix	16.0
23	PFR-2	1.0
24	Potassium dichromate	0.5
25	Quaternium-15	2.0
26	Sesquiterpene lactone mix	0.1
27	Textile dye mix	6.6
28	Thiuram mix	1.0
29	Tixocortol-21-pivalate	0.1

Vehicle is petrolatum if not stated otherwise. Bold font indicates haptens and/or concentrations that were changed/added.

*Vehicle is aqua.

mix 2% (to be published). The same kind of testing was also performed separately by the SCDRG in Sweden resulting in the new mix 3.5% detecting more allergic individuals than MBT 2% and mercapto mix 2%.⁷ Hence, to save space, it was decided to exclude MBT 2% and mercapto mix 2% and include the new mercapto mix 3.5% instead into the ICDRG baseline series.

New additions to the baseline series:

Textile dye mix: Textile dye mix 6.6% was shown to have contact allergy frequencies ranging from 1.3% to 18.2% in 8 different countries representing Europe, Asia, and North America, and the clinical relevance was reported to be approximately 20%, a figure that renders this preparation suitable for inclusion in the new ICDRG baseline series.³ However, concern within the group was raised about extremely strong patch test reactions in a few patients simultaneously allergic to *p*-phenylenediamine. This problem is attributed to simultaneous contact allergy to *p*-phenylenediamine and one of the constituents of TDM, namely, Disperse Orange 3.^{8,9} Studies have been initiated to elucidate and solve this problem both within the SCDRG and

ICDRG. Nevertheless, contact allergy to textile dyes is considered important, and TDM 6.6% will become one of the 29 haptens of the updated ICDRG baseline series until results are procured from the new textile dye studies.

Phenol and formaldehyde resin: When testing to PFR-2, a resol resin based on PFR-2, in 11 different centers representing North and South America, Europe, Asia, and Oceania, 1.5% of patients reacted positively. Only 20% of patients were simultaneously allergic to *p*-*tert*-butylphenol formaldehyde resin. The contact allergy to PFR-2 was considered clinically relevant in 25% of all cases, either as the explanation to the dermatitis or as an aggravating/contributing factor, results that make this preparation appropriate to be included in the new ICDRG baseline series.⁴

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REFERENCES

1. Alikhan A, Cheng LS, Ale I, et al. Revised minimal baseline series of the International Contact Dermatitis Research Group: evidence-based approach. *Dermatitis* 2011;22:121–122.
2. Bruze M, Condé-Salazar L, Goossens A, et al. Thoughts on sensitizers in a standard patch test series. The European Society of Contact Dermatitis. *Contact Dermatitis* 1999;41:241–250.
3. Isaksson M, Ale I, Andersen KE, et al. Patch testing to a textile dye mix by the International Contact Dermatitis Research Group. *Dermatitis* 2015;26:170–176.
4. Isaksson M, Ale I, Andersen K, et al. International Contact Dermatitis Research Group. Multicenter patch testing with a resol resin based on phenol and formaldehyde within the International Contact Dermatitis Research Group. *Dermatitis* 2015;26:230–234.
5. Isaksson M, Ale I, Andersen KE, et al. Multicenter patch testing with methylisothiazolinone and methylchloroisothiazolinone/methylisothiazolinone within the International Contact Dermatitis Research Group. *Dermatitis* 2017;28:210–214.
6. Isaksson M, Ale I, Andersen KE, et al. Patch testing with formaldehyde 2.0% (0.60 mg/cm²) detects substantially more contact allergy to formaldehyde than 1.0%. *Dermatitis* 2019;30:342–346.
7. Engfeldt M, Isaksson M, Glas B, et al. Patch testing with a new composition of the mercapto mix—a multicentre study by the Swedish Contact Dermatitis Research Group. *Acta Derm Venereol.* 2019;99:960–963.
8. Isaksson M, Bruze M, Dahlin J. Patch testing with two textile dye mixes without Disperse Orange 3—which one should be used? *Contact Dermatitis* 2018;79(S1):91–92.
9. Dahlin J. Patch testing with a textile dye mix with and without Disperse Orange 3. *Contact Dermatitis* 2018;79(S1):35.

Reporting of Patient Global Assessments in Atopic Dermatitis Randomized Controlled Trials

To the Editor:

Standardization of clinical trials improves the integrity and utility of study results and allows for data synthesis, comparison,

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