

Michel CASTELAIN^{1,2}
 Haudrey ASSIER²
 Marie BAECK^{2,4}
 Corina BARA⁵
 Annick BARBAUD^{2,6}
 Florence CASTELAIN⁷
 Brigitte FELIX⁸
 Marie Christine FERRIE LE
 BOUEDEC⁹
 Christian FRICK¹⁰
 Pascal GIRARDIN⁷
 Marie Claude JACOBS¹¹
 Gilbert JELEN^{2,10}
 Isabelle LARTIGAUD¹²
 Nadia RAISON-PEYRON^{2,13}
 Dominique TENNSTEDT³
 Florence TETARD^{2,4}
 Martine VIGAN^{2,7}
 Julie WATON⁶

¹ Department of Dermatology,
 Timone Hospital,
 264 Rue Saint Pierre F- 13385 Marseille
 Cedex

² Groupe d'Etudes et de Recherches en
 Dermato-Allergologie (GERDA)

³ Department of Dermatology,
 Henri Mondor Hospital,
 F-94010 Créteil

⁴ Department of Dermatology - Cliniques
 universitaires Saint Luc,
 B-1200 Brussels Belgium

⁵ Dermatologie,
 le Mans Hospital,
 F-72000 Le Mans

⁶ Department of Dermatology,
 Brabois Hospital,
 University Hospital of Nancy,
 F-54500 Vandœuvre les Nancy

⁷ Department of Dermatology ,
 St Jacques Hospital,
 F-25000 Besançon

⁸ Department of Dermatology,
 Saint André Hospital,
 F-33075 Bordeaux

⁹ Department of Dermatology,
 Estaing Hospital,
 University Hospital of Clermont-Ferrand,
 F-63003 Clermont-Ferrand

¹⁰ Consultation of Dermatology,
 F-67700 Saverne

¹¹ Department of Dermatology, Saint Jean
 Clinic,
 B-1000 Brussels Belgium

¹² Department of Dermatology,
 CHRU University Lille Nord de France,
 F-59000 Lille

¹³ Department of Dermatology,
 Saint Eloi Hospital,
 F-34295 Montpellier Cedex 5

¹⁴ Department of Dermatology,
 Charles Nicolle Hospital,
 F-76053 Rouen Cedex

Reprints: M. Castelain
 <mcastell.mrs@wanadoo.fr>

Article accepted on 9/22/2013

The European Standard Series and its additions: are they of any use in 2013?

This study has two purposes: - to know whether the European standard series is still the key reference when it comes to contact dermatitis, i.e., are its components still the most frequently involved allergens in contact dermatitis nowadays? - to assess the results of the European standard series among French and Belgian dermatologists/allergists as, so far, most of them have failed to provide statistical data within the European community of allergists/dermatologists. 18 participants from 2 dermatology and allergy centres in Belgium and 11 centres in France collected their results from 3,073 patients tested in 2011. They assessed the relevance of some tests as well as that of the standard series and additional series to establish an etiological diagnosis of contact dermatitis. These results, together with the history of the European standard series, have shown that some allergens are obsolete and that others should be included in a new standard series for which we are making a few suggestions.

Key words: contact allergens, contact dermatitis, European standard series, patch tests, relevance

The standard series is a series of allergens supplied by manufacturers in syringes. The list, the concentration and the vehicle of the allergens are known and standardised within a community of allergists, for instance within a continent or country.

The aim of the standard series is to help allergists detect the most frequent contact sensitisations in contact dermatitis. Some are detected as early as in the history-taking procedure, others are more difficult to detect, even with a very thorough history, and the standard series helps us not to forget or lose sight of them, sometimes leading the allergist to ask further retrospective questions following a positive test to a first unsuspected allergen.

The standard series also permits statistics to be gathered among dermatologists-allergists.

Evolution of the European standard series

The standard series first appeared in the early 1980s at the instigation of the ICDRG (International Contact Dermatitis Research Group). There are differences in Europe, North America and Japan as to the number and the composition of allergens included [1, 2]. In Europe, it has been adapted by the European Environmental Contact Dermatitis Research Group (EECDRG) and is monitored and updated by the European Society of Contact Dermatitis (ESCD) [3].

The proportion of positive reactions with the European standard series alone ranges from 37 to 73% depending on the authors [4-7], whereas the proportion with products brought by patients or tested alone ranges from 5 to 23%. This difference confirms the relevance of such standard series as well as the need for them to be regularly updated by groups such as the ESCD. Some allergens which have become less relevant and less frequent are therefore withdrawn, while other more relevant allergens are added. The first European standard series (ESS) included some twenty allergens.

In 1989, para-phenylenediamine hydrochloride (PPD) 0.5% in petrolatum (pet) was replaced by PPD free base 1% (pet); carba mix was removed, mercaptobenzothiazole (MBT) 2% pet was added as a complement to the sometimes faulty MBT mix, as well as Kathon CG (methylisothiazolinone + chloromethylisothiazolinone) 100ppm in water, a compound that caused an epidemic of contact dermatitis from cosmetic products in the late 1980s. The series included 23 allergens at the time.

In 1995, black rubber mix was withdrawn and replaced by N-isopropyl-N'-phenyl-4-phenylenediamine (IPPD), ethylenediamine was removed, quinolone mix was replaced by clioquinol and paraben mix was modified, while benzyl parahydroxybenzoate was removed from the mix. Sesquiterpene lactone mix 0.1% pet was added to the series. At that time, the European standard series still included 23 allergens.

In 2000, markers of contact allergy to topical corticosteroids were added, i.e. budesonide 0.01% and tixocortol pivalate 0.1% pet [8]. The primin patch test became optional. The standard series then included 25 allergens (one of which was optional).

In 2005, dibromodicyanobutane or methyldibromoglutaronitrile 0.5% in petrolatum, a cosmetic preservative and

component of Euxyl 400, was added as it caused a steep increase in the rate of contact sensitisation in Europe, following recommendations on the use of Kathon CG [9]. Thus the ESS increased to 26 allergens, one of which was optional.

Finally, in 2008, the EECDRG added Fragrance mix II 14% pet, a second mix of fragrances [10, 11], and a synthetic fragrance, lyral 5% pet or kovanol [12]. In fact, fragrance mix and its 8 allergens are well-known to perfumers and cosmeticians but the current composition of fragrances has evolved and fragrance mix alone was insufficient as its components are nowadays mainly found in household products, room or cheap fragrances.

The 28 allergens (one of which is optional) of the 2012 standard series are listed in *table 1*. The main sources of the allergens of components of the standard series have been the topic of many publications and websites [13]. In order to reduce the number of substances to be tested, some of them are included in mixes. There are six mixes in the standard series, their composition is given in *table 2*

Table 1. Allergens of the European standard series in 2012. (pet = petrolatum)

	Test Substance	Concentration %
1	Potassium dichromate	0.5 pet
2	4-phenylenediamine base (PPD)	1 pet
3	Thiuram-mix	1 pet
4	Neomycin sulfate	20 pet
5	Cobalt chloride	1 pet
6	Benzocaine	5 pet
7	Nickel sulfate	5 pet
8	Clioquinol	5 pet
9	Colophonium	20 pet
10	Paraben-mix	16 pet
11	N-isopropyl-N'-phenyl-4-paraphenylene diamine (IPPD)	0.1 pet
12	Lanolin alcohol*	30 pet
13	Mercapto mix	2 pet
14	Epoxy resin	1 pet
15	Myroxylon pereirae* (balsam of Peru)	25 pet
16	4-tert-butylphenol formaldehyde resin	1 pet
17	Mercaptobenzothiazole	2 pet
18	Formaldehyde	1 water
19	Fragrance-mix I	8 pet
20	Sesquiterpene lactone-mix	0.1 pet
21	Quaternium 15*	1 pet
22	Primin	0.01 pet
23	Methylchloroisothiazolinone-methylisothiazolinone	0.01 % water
24	Budesonide	0.01 pet
25	Tixocortol pivalate	0.1 pet
26	Methyldibromoglutaronitrile	0.5 pet
27	Fragrance-mix II	14 pet
28	Hydroxyisohexyl 3-cyclohexene carboxaldehyde (lyral)	5 pet

* International Nomenclature of Cosmetic Ingredients (INCI)

Table 2. Composition of the *mixes* of the European standard series.

Thiuram-mix 1% pet
Dipentamethylenethiuram disulfide (0.25%)
Tetramethylthiuram disulfide (0.25%)
Tetraethylthiuram disulfide (0.25%)
Tetramethylthiuram monosulfide (0.25%)
Mercapto-mix 2% pet
N-cyclohexylbenzothiazyl sulfenamide (0.5%)
Dibenzothiazyl disulfide (0.5%)
Mercaptobenzothiazole (0.5%)
Morpholinyl mercaptobenzothiazole (0.5%)
Fragrance-mix I (including 5% sorbitan sesquioleate) 8% pet
α -amylcinnamaldehyde (1%)
Cinnamaldehyde (1%)
Cinnamyl alcohol (1%)
Eugenol (1%)
Geraniol (1%)
Hydroxycitronellal (1%)
Isoeugenol (1%)
Oak moss absolute (Evernia prunastri) (1%)
Paraben-mix (%)16% pet
Butylparaben (4%)
Ethylparaben (4%)
Methylparaben (4%)
Propylparaben (4%)
Sesquiterpene lactone-mix 0.1% pet
Alantolactone (0.033%)
Dehydrocostus lactone (0.033%)
Costunolide (0.033%)
Fragrance-mix II 14% pet
Hydroxyisohexyl 3-cyclohexene carboxaldehyde (2.5%)
Citral (1%)
Farnesol (2.5%)
Coumarin (2.5%)
Citronellol (0.5%)
α -hexyl cinnamaldehyde (5%)

[from 1, 3]: Thiuram mix, mercapto mix, fragrance mix 1 and 2, paraben mix and sesquiterpene lactone mix. Testing only the few allergens that seem obvious when taking a patient's history leads, in about half of cases, to missing contact sensitisation to a product, a piece of information which might prove useful for the patient. Going further into patch testing requires experience and large, expensive allergen databases that quickly become outdated and are therefore uneconomical outside a contact allergy-oriented activity. However, any practitioner can add to his or her own series a few allergens that seem necessary in view of the area in which he or she operates. However, the 27 current basic allergens remain essential for epidemiological reasons, even if testing for primin does not seem as useful in Provence (South Eastern France) as in the Netherlands. Thus, some authors propose minimal standard series as well as additional series [14].

Other series

There are specific series that enable a more thorough investigation: for plastic materials and glues, rubber, clothes dyes, hair products, fragrances, preservatives and medicines [15]. Interesting as they may be, these series cannot be considered to provide a firm guarantee of identification of the culprit allergen.

The most serious risk of contact tests is patch test-induced sensitisation of the patient [16]. This is always a risk but it is extremely rare with the allergens of the standard series as, in such series, the most suitable concentrations have previously been determined, which is not necessarily the case with additional tests.

Finally, in children, particularly before the age of six – i.e. before any occupational exposure and before starting to practise sport or hobbies – this series should be limited and irrelevant allergens should be withdrawn: benzocaine, clioquinol, primin, quaternium 15 or occupational allergens such as, for instance, epoxy resins and, above of all, PPD-free base, the allergen of the standard series most likely to cause active sensitisation [17]. Thus, it seems reasonable to propose a standard series including 16 allergens for children under 6, especially for atopic children [18]:

- nickel sulfate
- potassium dichromate
- lanolin
- neomycin sulfate
- fragrance mix
- colophonium
- Myroxylon Pereirae resin
- paraben mix
- thiuram mix
- 4 ter butylphenol formaldehyde resin
- formaldehyde
- tixocortol pivalate
- budesonide
- chloromethylisothiazolinone / methylisothiazolinone
- sesquiterpene lactone mix
- mercapto mix

Concentrations are the same as for adults, however, before the age of 3, it is recommended to use open tests for metals. Not everybody follows these guidelines, for instance, Dutch authors recommend testing children, especially children over 5, including those with recalcitrant atopic dermatitis [19]. In order to do so, they use True tests[®] to which they add tixocortol, budesonide and three commonly used emollients. They found positive patch tests in 40 of the 79 patch-tested children.

Some Europeans adapt the ESS since, as shown in Cheng's study [2], not all German allergists test for benzocaine, PPD, neomycin, quaternium, lactone mix, the two corticosteroids and primin. The Danes do not test for methylidibromoglutaronitrile, budesonide and tixocortol. The Finns do not test for parabens, IPPD, lactone mix and clioquinol. The Dutch do not test for PPD whereas the Italians do not test for mercapto mix, quaternium 15 and clioquinol. The Portuguese do not test for mercaptobenzothiazole, IPPD, methylidibromoglutaronitrile, lactone mix, budesonide and tixocortol...

Table 3. Common allergens in the Australian, Brazilian and North American standard series

1	Potassium dichromate
2	Thiuram mix
3	Cobalt chloride
4	Nickel sulfate
5	Colophonium
6	Paraben mix
7	Lanolin alcohols*
8	Epoxy resin
9	Myroxylon pereirae
10	4-tert-butylphenol formaldehyde resin
11	Formaldehyde
12	Fragrance mix
13	Kathon CG

The Australian, Brazilian, European and North American standard series have 13 allergens in common (*table 3*) [2].

Test results with the European standard series

Prevalence of allergens

In 2004, 31 ESSCA (European Surveillance System on Contact Allergies) dermatology departments in 11 European countries collected patch test results of patients tested with the European standard series (ESS) or with local standard allergen series, using the multilingual Winall-dat/ESSCA database. Nearly 10,000 patients were tested with the standard series and 44% of them tested positive to one or more substances of the ESS. Nickel sulfate, the fragrance mix, balsams of Peru, cobalt chloride, potassium dichromate, methyldibromoglutaronitrile and paraphenylenediamine were the most frequently detected allergens. Several additional substances systematically tested in a few clinics were also identified. Among these allergens, propolis and compositae mix had a relatively high positivity rate [20]. Results are shown in *table 4*.

Other European countries are beginning to publish their statistics: The patch test results of 12,058 patients (4,416 men and 7,642 women) from 9 clinics in the Czech Republic between January 1997 and December 2001 were evaluated. All patients were tested with the 23-allergen European standard series [21]. 7,661 (63.5%) had one or more positive patch test reaction. On average, there were 2.8 positive reactions per patient. Relevant allergic contact dermatitis was diagnosed in 5,339 of these patients (69.7%). The most frequent allergens were metals (22.9%), especially nickel sulfate (13.8%), followed by balsam of Peru (7.3%), the fragrance mix (5.8%), formaldehyde (4.2%) and lanolin alcohol (3.0%).

Regional differences

The clinical and patch test data of 19,793 patients tested in 2005/2006 in the 31 participating departments from 10 European countries (the European Surveillance System on

Table 4. Results of the ESSCA on approximately 10,000 patients tested (tixocortol : 2,162 patients tested, clioquinol 1,629) from [18] .

1	Nickel sulfate	20.67%
2	Fragrance mix	7.24%
3	Cobalt chloride	6.90%
4	Balsam of Peru	5.70%
5	Potassium dichromate	4.35%
6	Paraphenylenediamine base	4.11%
7	Colophonium	3.70%
8	Thiuram mix	2.57%
9	Methyldibromo glutaronitrile	2.53%
10	Kathon CG	2.22%
11	Lanolin alcohols	2.18%
12	Neomycin	2.07%
13	Formaldehyde	2.01%
14	Budesonide	1.46%
15	4-tert-butylphenol form resin	1.40%
16	Quaternium 15	1.38%
17	Epoxy resin	1.13%
18	Benzocaine	1.10%
19	Paraben mix	0.99%
20	Primin	0.78%
21	Sesquiterpene lactone mix	0.73%
22	IPPD	0.72%
23	Mercapto mix	0.71%
24	Mercaptobenzothiazole	0.69%
25	Tixocortol	0.51%
26	Clioquinol	0.28%

Contact Allergies (ESCA) www.essca-dc.org) were analysed and aggregated to four European regions [22]. France was not among the participants.

Nickel sulfate remains the most common allergen, with a prevalence ranging from 19.7% (Central Europe) to 24.4% (Southern Europe). While a certain number of allergens show limited variations across the four regions, such as balsam of Peru (5.3-6.8%), cobalt chloride (6.2-8.8%) or thiuram mix (1.7-2.4%), the differences observed with other allergens may imply great differences regarding exposure, for example: potassium dichromate 2.4% in the U.K compared with 4.5-5.9% in the remaining European Union regions, methylchloroisothiazolinone / methylisothiazolinone 4.1% in the south compared to 2.1-2.7% in the other regions. As regards contact allergy to chromium, marked differences were noted between two centres focused on occupational diseases: 2.2% in Basel (Switzerland) *versus* 9.5% in Padua (Italy). Such differences most likely reflect the beneficial effect of adding ferrous sulfate to cement in one of the two countries [23]. Such results are obviously affected by methodological differences between the various centres and by the difficulties in collecting the results.

Ethnic differences

English authors have compared patch test results using the European standard series in white Europeans with skin

phototypes I to IV and Indo-Pakistani patients with skin phototype V, between 2004 and 2006. 435 patients were tested, 11.5% of them from the Indian subcontinent. The latter had fewer positive reactions (44%) compared with the European patients (56%), with no significant differences in the culprit contact allergens. This modest difference is probably due to an age difference (average age was slightly lower in the Indian subcontinent population) rather than to a difference in susceptibility to developing sensitisation following equal exposure [24].

Other continents using the ESS

Many papers have mentioned the use of and interest in the European Standard Series beyond Europe. For instance, in Riyadh (Saudi Arabia) before 1995 [25], in Australia in the late 1990s [26], in Chandigarh (India), before 1997 [27], in Hong Kong between 1995 and 1999 [28], in Ankara (Turkey) from 1992 to 2004 [29], in Tel Aviv (Israel) between 1998 and 2004 [30], in Beijing (People's Republic of China) in 2001-2002 with a modified European standard series [31], in Harvard (Boston USA) from 1998 to 2006, with a series of 21 allergens very much like the 1980s version of the ESS [32]. . .

The Revidal-Gerda study

Eleven French centres and two Belgian centres took part in this study. The 18 participants in the study aggregated the patch test results of 3,073 patients tested in 2011 using the full ESS. 68.3% were female and 31.7% male, with a mean age of 43.40 years and ages ranging from 3 to 90. Detailed test results are shown in *table 5*. *Table 6* shows the ESS list of contact allergens in order of frequency in the Revidal Gerda study. 14 allergens are above the once-required 1% for an allergen to still be in the ESS, *versus* 17 in the European study [19].

The top ten allergens are: nickel sulfate (20.21%), fragrance mix (8.53%), balsams of Peru (8.27%), potassium dichromate (7.19%), Cobalt chloride (6.57%), fragrance mix II (5.01%), paraphenylenediamine base (4.36%), Kathon CG (3.74%), colophonium (2.47%) and lanolin alcohols (2.12%). When comparing these results with the ESSCA study [19], it is to be noted that our top 10 allergens are included in their top 12. In their statistics, two allergens slip into our top ten, i.e. methyl dibromoglutaronitrile, whose positivity rate has dropped dramatically since 2005 due to European regulations, as it was banned from cosmetic products, and thiuram mix, ranking 12th in our list (after Lyrall, a recently introduced allergen). Thus the differences are marginally significant.

In our statistics, 5 allergens are below 0.5%: sesquiterpene lactone mix (0.49%), Neomycin sulfate (0.49%), paraben mix (0.46%), clioquinol (0.13%) and primin (0.10%).

Clioquinol has almost disappeared from the French pharmacopoeia, which therefore accounts for such a low percentage and for there being limited interest for this allergen to remain in the ESS. Thus it should be withdrawn.

Primin was already optional in the ESS and its low emergence rate should also lead to its being withdrawn from the ESS. It should be tested only in florists and horticulturists.

Table 5. Results of the ESS patch tests in 2011 (Revidal-Gerda): in 3,073 patients :

1	Potassium dichromate	221	7.19%
2	Paraphenylenediamine base	134	4.36%
3	Thiuram mix	43	1.40%
4	Neomycin sulfate	15	0.49%
5	Cobalt chloride	202	6.57%
6	Benzocaine	25	0.81%
7	Nickel sulfate	621	20.21%
8	Clioquinol	4	0.13%
9	Colophonium	76	2.47%
10	Paraben mix	14	0.46%
11	IPPD	18	0.59%
12	Lanolin alcohols*	65	2.12%
13	Mercapto mix	20	0.65%
14	Epoxy resin	37	1.20%
15	Myroxylon pereirae	254	8.27%
16	4-tert-butylphenol formaldehyde resin	26	0.85%
17	Mercaptobenzothiazole	17	0.55%
18	Formaldehyde	28	0.91%
19	Fragrance mix	262	8.53%
20	Sesquiterpene lactone mix	15	0.49%
21	Quaternium 15*	22	0.72%
22	Primin	3	0.10%
23	Kathon CG	115	3.74%
24	Budesonide	25	0.81%
25	Tixocortol pivalate	19	0.62%
26	Methyldibromo glutaronitrile	30	0.98%
27	Fragrance mix II	154	5.01%
28	Lyrall	45	1.46%

In 2009, the ESS was already the subject of an unpublished statistical study by the Revival GERDA on 1,505 patients. When comparing the figures of 2009 and 2011 (*table 7*), we note that:

- parabens are still decreasing (respectively 0.60% and 0.46%), because they have been banned from most recent cosmetic products.
- Methyldibromo glutaronitrile (MDBGN) has fallen sharply from 2.59% to 1.01% as, here again, it has been banned in European cosmetic products. Thus its relevance is no longer what it used to be unless the fact that it has been banned from cosmetics is counterbalanced by a growing use in other everyday consumer products. Parabens and MDBGN may be withdrawn from the next ESS, due to the evolution of European regulations on cosmetic products.
- Mercaptobenzothiazole has dropped from 1.13% to 0.55%.
- Budesonide has dropped from 1.26% to 0.81%.

Conversely,

- epoxy resin has increased by half, from 0.80% to 1.20%.
- 4-tert-butylphenol formaldehyde resin has increased from 0.47% to 0.85% (while formaldehyde has tended to decrease from 1.26% to 0.91%)

Table 6. Results of the ESS patch tests in 2011 (Revidal-Gerda): in order of frequency

1	Nickel sulfate	20.21%
2	Fragrance mix	8.53%
3	Balsam of Peru	8.27%
4	Potassium dichromate	7.19%
5	Cobalt chloride	6.57%
6	Fragrance mix II	5.01%
7	Paraphenylenediamine base	4.36%
8	Kathon CG	3.74%
9	Colophonium	2.47%
10	Lanolin alcohols	2.12%
11	Lyrar	1.46%
12	Thiuram mix	1.40%
13	Epoxy resin	1.20%
14	Methyldibromo glutaronitrile	1.01%
15	Formaldehyde	0.91%
16	4-tert-butylphenol formaldehyde resin	0.85%
17	Budesonide	0.81%
18	Benzocaine	0.81%
19	Quaternium 15*	0.72%
20	Mercapto mix	0.65%
21	Tixocortol pivalate	0.62%
22	IPPD	0.59%
23	Mercaptobenzothiazole	0.55%
24	Sesquiterpene-lactone mix	0.49%
25	Neomycin sulfate	0.49%
26	Paraben mix	0.46%
27	Clioquinol	0.13%
28	Primin	0.10%

– benzocaine has almost doubled from 0.47% to 0.81%, with no clear explanation. As for PPD, it has remained stable around 4%. Benzocaine, like clioquinol, is decreasingly used in the French pharmacopoeia.

This leads us to mention the patch test reading schedule and the relevance of positive patch tests. Thus, when only one reading was carried out at 48 hours (in 980 patients tested), 18% of positive patch tests were missed, whereas with a single reading at 72 hours, only 1% of positive results were missed.

As regards relevance, in 1,108 tested patients for whom it was possible to assess test relevance, there were 11 positive allergens with a seemingly reliable relevance in over two thirds of the cases (*table 8*). It can be considered that allergens such as budesonide, sesquiterpene lactone mix, and MBT have good relevance and this might be a valid argument for keeping them in the ESS while their positivity rates seem to be decreasing.

On the other hand, 5 allergens have no relevance in over a third or even half of cases (tested in 1,108 patients), these allergens are: IPPD (71.4%), nickel (46.5%), neomycin (40%), fragrance mix (38.5%) and cobalt (35.6%). It is striking to note that 3 among the top 10 allergens have no relevance in over a third of cases, thus their interest and

Table 7. Comparison of the results of the 2009 and 2011 ESS by the Revidal- Gerda: in 1,505 et 3,073 patients, respectively

	ESS allergens	% 2009	% 2011
1	Nickel sulfate	19.80	20.21
2	Fragrance mix	8.04	8.53
3	Balsam of Peru	7.11	8.27
4	Potassium dichromate	7.11	7.19
5	Cobalt chloride	7.97	6.57
6	Fragrance mix II	4.05	5.01
7	Paraphenylenediamine base	3.92	4.36
8	Kathon CG	3.92	3.74
9	Colophonium	2.92	2.47
10	Lanolin alcohols	1.79	2.12
11	LYRAL	1.46	1.46
12	Thiuram mix	1.66	1.40
13	Epoxy resin	0.80	1.20
14	Methyldibromo glutaronitrile	2.59	1.01
15	Formaldehyde	1.26	0.91
16	4-tert-butylphenol formaldehyde resin	0.47	0.85
17	Budesonide	1.26	0.81
18	Benzocaine	0.47	0.81
19	Quaternium 15*	0.66	0.72
20	Mercapto mix	0.73	0.65
21	Tixocortol pivalate	0.73	0.62
22	IPPD	0.73	0.59
23	Mercaptobenzothiazole	1.13	0.55
24	24 Sesquiterpene-lactone mix	0.60	0.49
25	Neomycin sulphate	0.73	0.49
26	Paraben mix	0.60	0.46
27	Clioquinol	0.07	0.13
28	Primin	0.20	0.10

ranking have to be somewhat qualified. The relevance of clioquinol, benzocaine and primin has not been assessed, as their positivity rates were too low.

We may therefore wonder whether IPPD and neomycin should still be tested as not only do they have low positivity rates but their relevance may often be found wanting.

Table 8. Positive tests with good relevance (in 1,108 patients tested): “model allergen”

Budesonide	100%
Lactone mix	83.3%
Lyrar	73.3%
Kathon CG	71%
Fragrance mix 2	70%
Mercaptobenzothiazole	69.7%
Epoxy	69.6%
PPD base	69.5%
Thiuram	68.4%
Colophonium	68%
Tixocortol	66.7%

In light of these results, it can be considered that the allergens that should soon be withdrawn from the ESS are: primin, clioquinol, benzocaine, neomycin, parabens and MDBGN.

To what extent do standard series of patch tests contribute to etiological diagnosis?

In the 2011 Revidal-Gerda study, their relevance was studied in 1,723 patients:

- The ESS identified several allergens responsible for current reactions in 40.1% of cases, which places our study in the lower range in the literature ;
- The Revidal-Gerda additional series contributed to identification of the allergen in 11.38% of cases
- This makes a total of 51.48% of allergens that were identified with the ESS and relevant additions. This result is just above average. Some of the patients who were tested may not even have suffered from any contact allergy. . . Thus these results have to be qualified and relevant series should be compared to the total number of patients who do have proven contact allergy. Nonetheless, there is still room for improvement and the ESS should be updated in order to make it more effective.

Thus, obsolete allergens should be withdrawn while more efficient allergens should be added. Among them are: Amerchol L101, DMAPA (dimethylaminopropylamine), benzalkonium chloride, disperse blue 106 – this has been above the critical mark of 1% for several years – as well as allergens that have only recently been tested but seem relevant, i.e methylisothiazolinone and lauryl glucoside. Some European authors suggest adding compositae mix too, in order to make up for lactone mix's poor sensitivity and they recommend adding propolis [19], which is already part of our additional series.

However, we will have to wait for larger statistical data to be published, at least for the last four allergens, before being able to assess their legitimacy. Moreover, we should also contribute to the ESCD so that Europe can take the advice of French allergists into account in the evolution of the ESS.

Conclusion

The standard series remains the key reference tool for testing patients with contact dermatitis. In the Revidal Gerda study carried out in 3,073 patients, 14 allergens were still above the 1% mark of positive tests whereas 5 allergens were below 0.5% and are likely to be withdrawn in the next versions of the ESS. Some additions might become part of the next ESS, as has already happened with fragrance mix 2, MDBGN and lyral. Thus, we may propose a draft for the next standard series (see *table 9*) which would take these results into account, although our proposal remains a mere suggestion. As a matter of fact, our results will only be of any use on a European level if we once and for all agree

Table 9. Proposal for the next ESS (under the authors' sole responsibility)

	Substances	Concentration %
1	Potassium dichromate	0.5 pet
2	4-p-phenylene diamine base	1 pet
3	Thiuram-mix	1 pet
4	Cobalt chloride	1 pet
5	Nickel sulfate	5 pet
6	Colophonium	20 pet
7	Lanolin alcohol*	30 pet
8	Mercapto-mix	2 pet
9	Epoxy resin	1 pet
10	Myroxylon pereirae* [balsam of Peru]	25 pet
11	4-tert-butylphenol formaldehyde resin	1 pet
12	Mercaptobenzothiazole	2 pet
13	Formaldehyde	1 water
14	Fragrance-mix I	8 pet
15	Sesquiterpene lactone-mix	0.1 pet
16	Quaternium 15*	1 pet
17	Methylchloroisothiazolinone-methylisothiazolinone	0.01 % water
18	Budesonide	0.01 pet
19	Tixocortol pivalate	0.1 pet
20	Fragrance-mix II	14 pet
21	Hydroxyisohexyl3-cyclohexene carboxaldehyde (lyral)	5 pet
22	Amerchol L101	50% pet
23	Benzalkonium chloride	0.1% pet
24	dimethylaminopropylamine	1% water
25	Disperse blue 106	1% pet
26	methylisothiazolinone	0.05% water

to use the computing tools that nearly all dermatologists of the ESCD have agreed to use. Finally, the low relevance of our standard series may also mean that we may too readily test patients who are not really susceptible to contact dermatitis. ■

Disclosure. *Acknowledgments: The GERDA thanks Basilea, Pierre Fabre and Unilever for their institutional support for publication of this article. Financial support: none. Conflict of interest: none.*

This review article is part of a series of papers published by experts from GERDA, the French study and research group on contact dermatitis



1. Lachapelle JM. The standard series of patch tests. In: *Patch testing and prick testing*, 2nd Ed, 1 Vo.l Springer Berlin 2009, pp 71-82.
2. Cheng LS, Alikhan A, Maibach HI. Compilation of international standards for patch testing methodology and allergens. *Dermatitis* 2009; 20: 257-60.
3. Raison-Peyron N. Méthodologie des patch tests: supports et allergènes. *Ann Dermatol Venerol* 2009; 136: 585-91.
4. Doms Goossens A. Evaluation critique du test épicutané. In: *Progress en Dermato-Allergologie* tome II. Médiscript Ed. Viternes 1996 : 103-107.
5. Wahlberg JE. Patch-testing. In *Contact Dermatitis* [textbook of], Rycroft R J G, Menné T, Frosch P J, Benezra C Eds, Berlin 1991, Springer Verlag, 239-268.
6. Ada S, Seckin D. Patch testing in allergic contact dermatitis: is it useful to perform the cosmetic series in addition to the European standard series? *J Eur Acad Dermatol Venerol* 2010; 24: 1192-6.
7. Akasya-Hillenbrand E, Ozkaya-Bayazit E. Patch test results in 542 patients with suspected contact dermatitis in Turkey. *Contact Dermatitis* 2002; 46: 17-23.
8. Isaksson M, Brandao FM, Bruze M, Goossens A. Recommendation to include budesonide and tixocortol pivalate in the European standard series. *Contact Dermatitis* 2000; 43: 41-2.
9. Bruze M, Goossens A, Gruvberger B; ESCD; EECDRG. Recommendation to include methyldibromo glutaronitrile in the European standard patch test series. *Contact Dermatitis* 2005; 52: 24-8.
10. Frosch PJ, Rastogi SC, Pirker C, et al. Patch testing with a new fragrance mix - reactivity to the individual constituents and chemical detection in relevant cosmetic products. *Contact Dermatitis* 2005; 52: 216-25.
11. Bruze M, Andersen KE, Goossens A; ESCD; EECDRG. Recommendation to include fragrance mix 2 and hydroxyisohexyl 3-cyclohexene carboxaldehyde (Lyrall) in the European baseline patch test series. *Contact Dermatitis* 2008; 58: 129-33.
12. Frosch PJ, Johansen JD, Menné T, et al. Lyrall is an important sensitizer in patients sensitive to fragrances. *Br J Dermatol* 1999; 141: 1076-83.
13. Giordano-Labadie F. Listes d'éviction. *Ann Derm Venerol* 2009; 136: 656-8.
14. Lachapelle JM, Ale SI, Freeman S, et al. Proposal for a revised international standard series of patch tests. *Contact Dermatitis* 1997; 36: 121.
15. Cleenewerck MB. Patch-testing methods: Méthodologie des patch-tests: Batteries dites spécialisées, additionnelles. *Ann Derm Venerol* 2009; 136: 593-5.
16. Castelain M. Effets secondaires, complications et contre-indications des patch-tests. *Ann Derm Venerol* 2009; 136: 645-9.
17. Vigan M, Adessi B, Arnoult E, et al. Tests épicutanés chez l'enfant : élaboration d'une batterie standard adaptée. *Ann Derm Venerol* 2000; 127 (suppl. 4): 116-7.
18. Vigan M. Particularités des tests épicutanés chez l'enfant. *Ann Derm Venerol* 2009; 136: 617-20.
19. De Waard-van der Spek FB, Oranje AP. Patch tests in children with suspected allergic contact dermatitis: a prospective study and review of the literature. *Dermatology* 2009; 218: 119-25.
20. The European Surveillance System of Contact Allergies [ESSCA]: results of patch testing the standard series, 2004. *J Eur Acad Dermatol Venerol* 2008 ; 22 :174-81.
21. Machovcova A, Dastychova E, Kostalova D, et al. Common contact sensitizers in the Czech Republic. Patch test results in 12,058 patients with suspected contact dermatitis. *Contact Dermatitis* 2005; 53: 162-6.
22. Uter W, Rämisch C, Aberer W, et al. The European baseline series in 10 European Countries, 2005/2006-results of the European Surveillance System on Contact Allergies [ESSCA]. *Contact Dermatitis* 2009; 61: 31-8.
23. Uter W, Hegewald J, Aberer W, et al. The European standard series in 9 European countries, 2002/2003 - first results of the European Surveillance System on Contact Allergies. *Contact Dermatitis* 2005; 53: 136-45.
24. Fairhurst DA, Shah M. Comparison of patch test results among white Europeans and patients from the Indian subcontinent living within the same community. *J Eur Acad Dermatol Venerol* 2008; 22: 1227-31.
25. El-Rab MO, al-Sheikh OA. Is the European standard series suitable for patch testing in Riyadh, Saudi Arabia? *Contact Dermatitis* 1995; 33: 310-4.
26. Greig JE, Carson CF, Stuckey MS, et al. Prevalence of delayed hypersensitivity to the European standard series in a self-selected population. *Australas J Dermatol* 2000; 41: 86-9.
27. Sharma VK, Chakrabarti A. Common contact sensitizers in Chandigarh, India. A study of 200 patients with the European standard series. *Contact Dermatitis* 1998; 38: 127-31.
28. Lam WS, Chan LY, Ho SC, et al. A retrospective study of 2585 patients patch tested with the European standard series in Hong Kong (1995-99). *Int J Dermatol* 2008; 47: 128-33.
29. Akyol A, Boyvat A, Peksari Y, et al. Contact sensitivity to standard series allergens in 1038 patients with contact dermatitis in Turkey. *Contact Dermatitis* 2005; 52: 333-7.
30. Lazarov A. European Standard Series patch test results from a contact dermatitis clinic in Israel during the 7-year period from 1998 to 2004. *Contact Dermatitis* 2006; 55: 73-6.
31. Li LF, Guo J, Wang J. Environmental contact factors in eczema and the results of patch testing Chinese patients with a modified European standard series of allergens. *Contact Dermatitis* 2004; 51: 22-5.
32. Landeck L, Schalock PC, Baden LA, et al. Patch-testing with the standard series at the Massachusetts General Hospital, 1998 to 2006. *Dermatitis* 2009; 20: 89-94.