

Procedure for determination of patch test concentrations

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Present situation

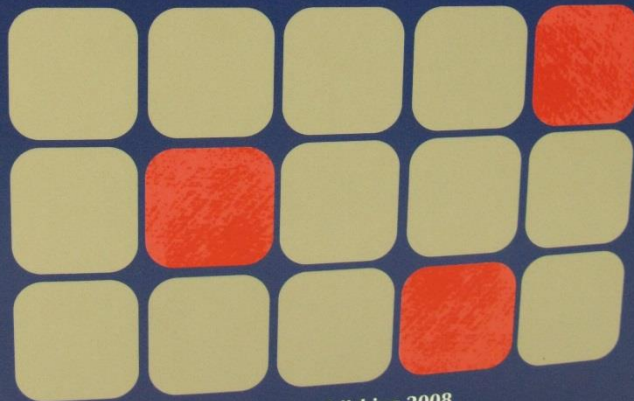
No guidelines/recommendations of universal acceptance concerning how to find the optimal patch test concentration

ANTON C. DE GROOT

Test Concentrations and Vehicles for 4350 Chemicals

PATCH TESTING

THIRD EDITION



acdegroot publishing 2008

Basis for recommended patch test concentrations

Cases

Product ingredients at higher
concentrations than in product

Avoidance of false-negative patch test reactions

Patch test concentrations versus concentrations in daily life products

Higher patch test concentrations

Substance	Patch test conc.	Use conc.	Patch test conc/ use conc.
Chromate	0.5%	0.0056%	90
Formaldehyde	2%	0.05 – 0.2%	10 – 40
Kathon CG	200 ppm	5 – 15 ppm	13 – 40
Neomycin	20%	0.5 – 1%	20 - 40
Parabenes	15%	0.2 – 0.4%	37 - 75

Bruze et al.

In Exogenous dermatoses: environmental dermatitis, page 289, 1991

Patch test concentrations versus concentrations in daily life products

Up to 20 times higher

Formaldehyde

MCI/MI

Neomycin

Chromate

MI (100 ppm x 20 = 2000 ppm)

Why not a higher concentration -
>20 times?

Risk of active sensitization

Example – Kathon CG

Kathon CG

First 2 cases in 1981

Pos reaction to 1000 ppm

Additional cases pos to 300 ppm (20x15) – 4%
pos reactions

Irritant reaction? sharp demarcation and
dose-response curve

Allergic reaction? morphology

Kathon CG – allergy or irritancy?

Simultaneous testing with 300 and 1000 ppm in 40 dermatitis patients

Irritant reactions in 10/40

Active sensitization

Recommended test concentration

200 ppm

Concentration - dose

Number of molecules/cm²

Liquids - 30 μ l/cm²

Petrolatum - 40 mg/cm²

Dose

Test conc.

0.3%

0.5%

Applied
amount



33 mg

20 mg

Dose

0.2 mg/cm²

0.2 mg/cm²

Historical aspects - ICDRG



Darrel Wilkinson, England, Veikko Pirilä, Finland, Carlo Meneghini, Italien, Howard Maibach, USA, Klaus Malten, Holland, Niels Hiorth, Danmark, Bertil Magnusson, Sverige, Sigfrid Prefert, Sverige, Etain Cronin, England, Charles Calnan, England, Hans-Jürgen Bandman, Tyskland

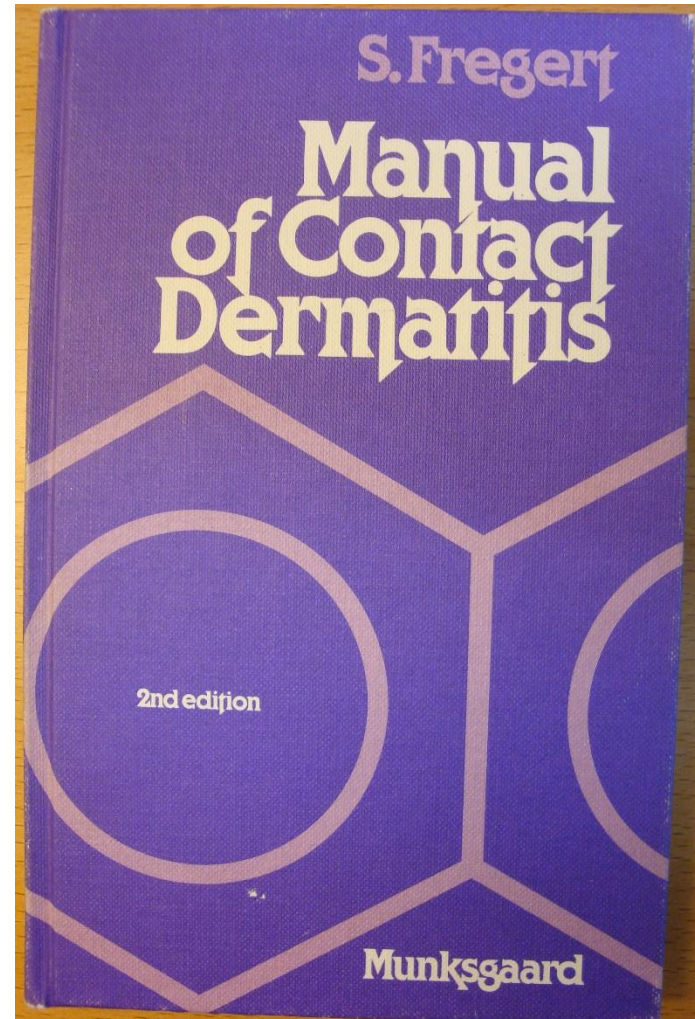
Acta Derm Venereol. 1970;50(4):287-92.

Terminology of contact dermatitis.

Wilkinson DS, Fregert S, Magnusson B, Bandmann HJ, Calnan CD, Cronin E, Hjorth N, Maibach HJ, Malaiten KE, Meneghini CL, Pirilä V.

PMID: 4195865

[Indexed for MEDLINE]



Terminology paper

“...which may lead to further improvements”

“A positive patch test is considered 'relevant' if the allergen is traced.”

Different opinions on use of relevant test concentration

- ICDRG – type IV
 - Allergologists – type I
 - YES
- Magnus Bruze
 - No

Consequences of the old ICDRG view

Pos test reaction + exposure = allergic
contact dermatitis

Use of relevant test concentration –
too many false neg reactions

Confusion

Contact allergy – allergic contact dermatitis

Malmö example

Pos patch test reaction to nickel =
contact allergy to nickel = allergic
contact dermatitis from nickel

Change in Malmö – 2 diagnoses

Contact allergy

Allergic contact dermatitis

Lund example

Contact allergy to nickel and
exposure to nickel = allergic
contact dermatitis from nickel

Confusion

Contact allergy – allergic contact dermatitis

Contact allergy

No disease

Reaction pattern

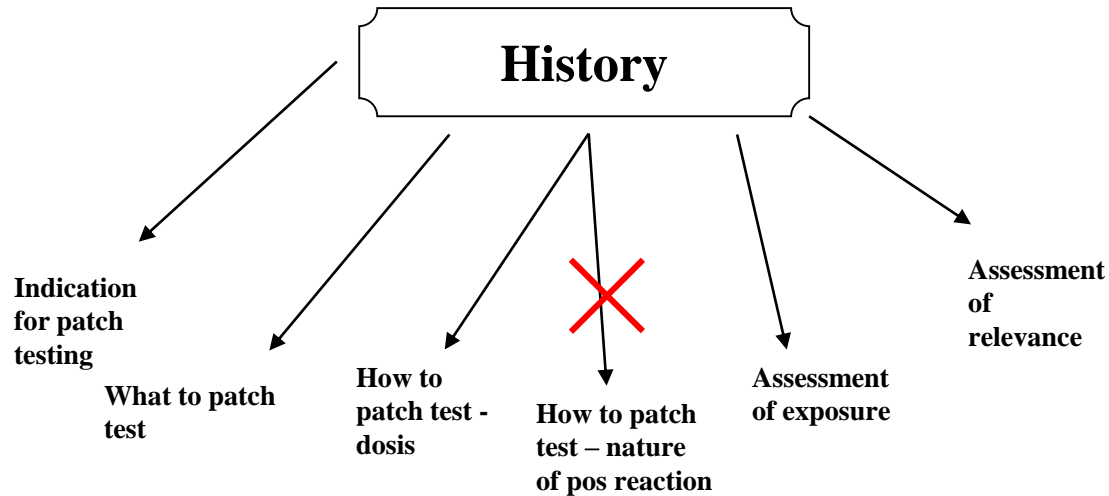
Allergic contact dermatitis

Contact allergy

Exposure

Relevance

Use of history for diagnosis of contact allergy and allergic contact dermatitis



Questioning of paradigm shift

SKDG

EECDRG

ESCD

Rexpan

ICDRG

Eden fragrance group

Journal reviewers – Contact Dermatitis

- Dermatitis

Old view - relevant patch test concentration – 2 examples

Gold

Formaldehyde

Patch testing with the dental series in 1990 in 92 patients

Potassium dicyanoaurate 0.001%/aq. 0% pos

Gold sodium thiosulfate 0.5%/aq. 8.7% pos

False-pos reactions?

Non-comparable entities (non-equimolar concentrations)?

GLDNATRIUMTIOSENFAT

NATRIUMTIOSENFAT

GLDNATRIUMTIOSENFAT 0,25 % AQ

GLDNATRIUMTIOSENFAT 0,5 % AQ

GLDNATRIUMTIOSENFAT 0,05 % AQ

GLDNATRIUMTIOSENFAT 0,16 % AQ

GLDNATRIUMTIOSENFAT 0,075 % AQ

GLDNATRIUMTIOSENFAT 0,05 % AQ

GLDNATRIUMTIOSENFAT 0,125 % AQ

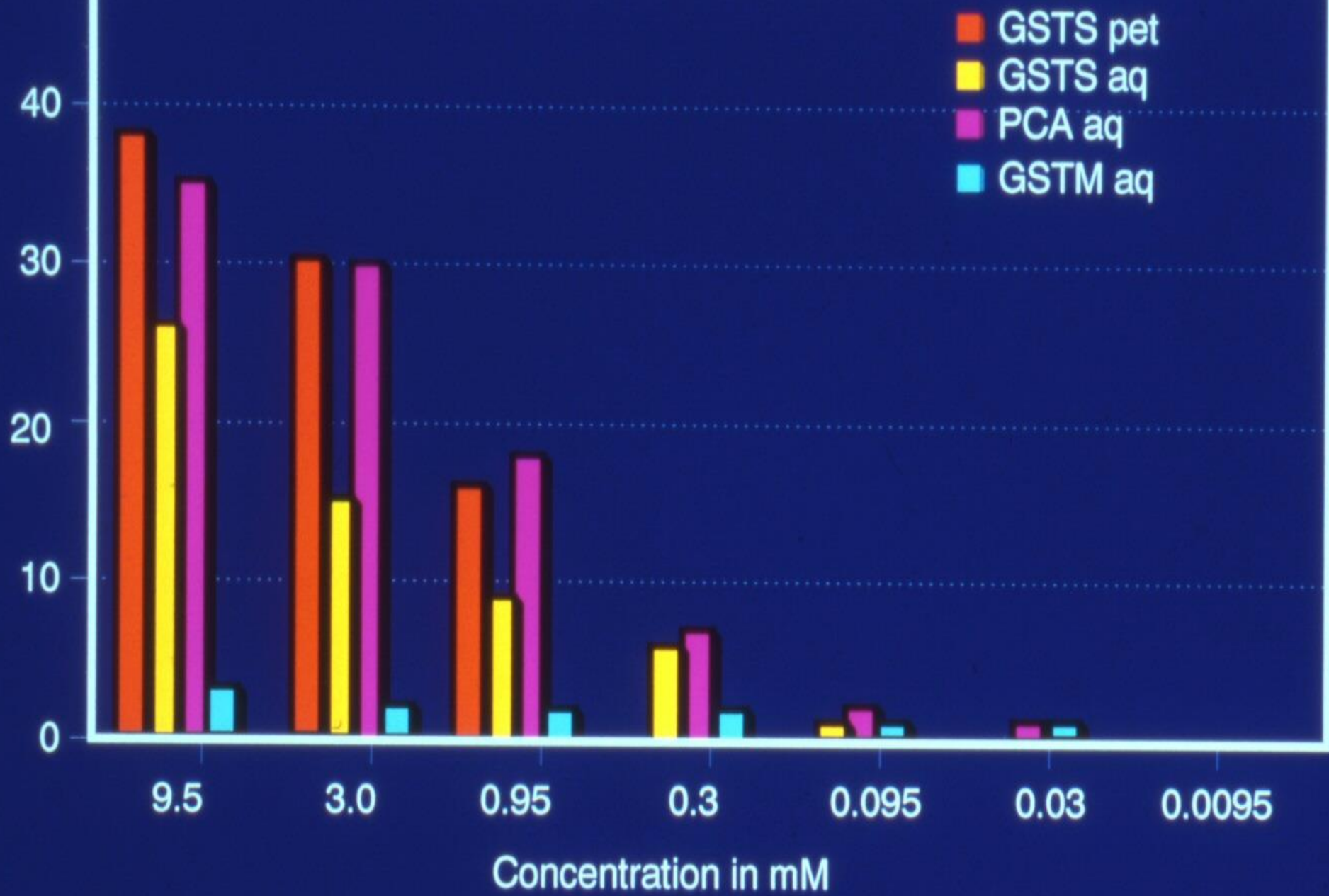
GLDNATRIUMTIOSENFAT 0,016 % AQ

GLDNATRIUMTIOSENFAT 0,5 % VAS
1 HÄND GAMMAL TEST

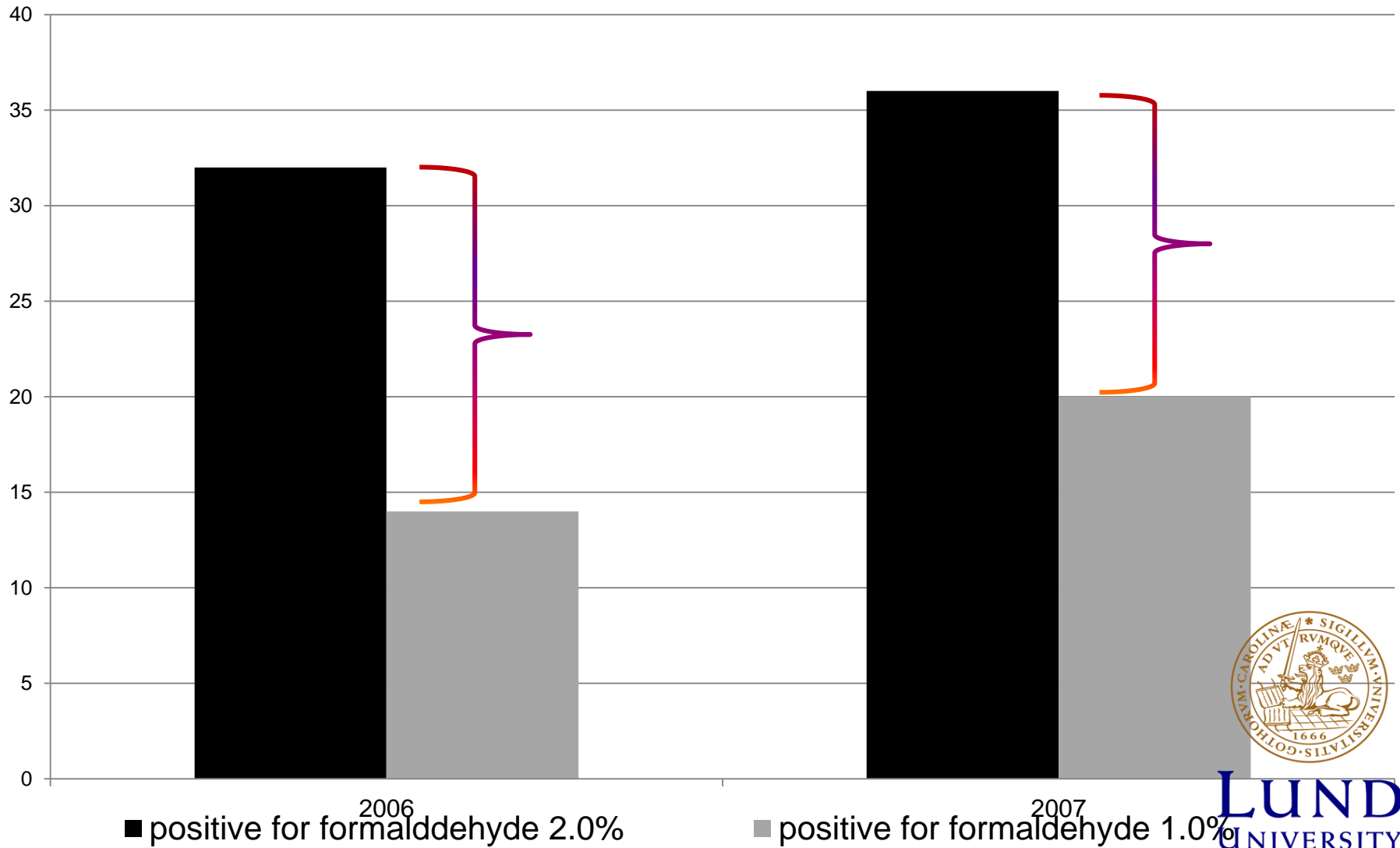
GLDNATRIUMTIOSENFAT

GLDNATRIUMTIOSENFAT

GLDNATRIUMTIOSENFAT



Is contact allergy to formaldehyde 2.0% clinically relevant?



How to choose test concentration?

As high as possible without causing adverse reactions, particularly active sensitization

How to choose test concentration

Exposure conditions

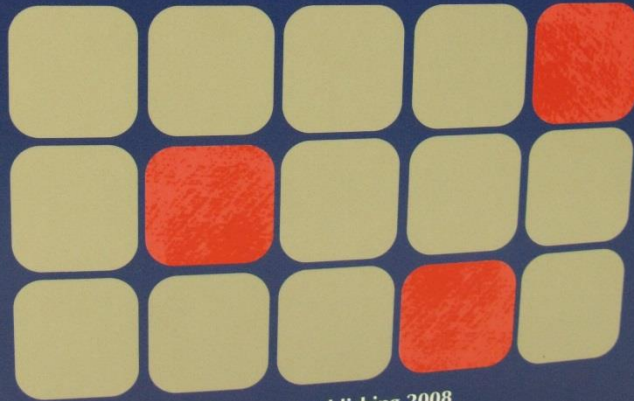
Textbooks

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Fragrances in the baseline patch test series

Fragrance mix I – 16% →

8%

7 ingredients at 2%

Cinnamal at 1%

Contact Dermatitis. 2012;66:131-6.

Patch test concentrations (doses in mg/cm²) for the 12 non-mix fragrance substances regulated by European legislation.

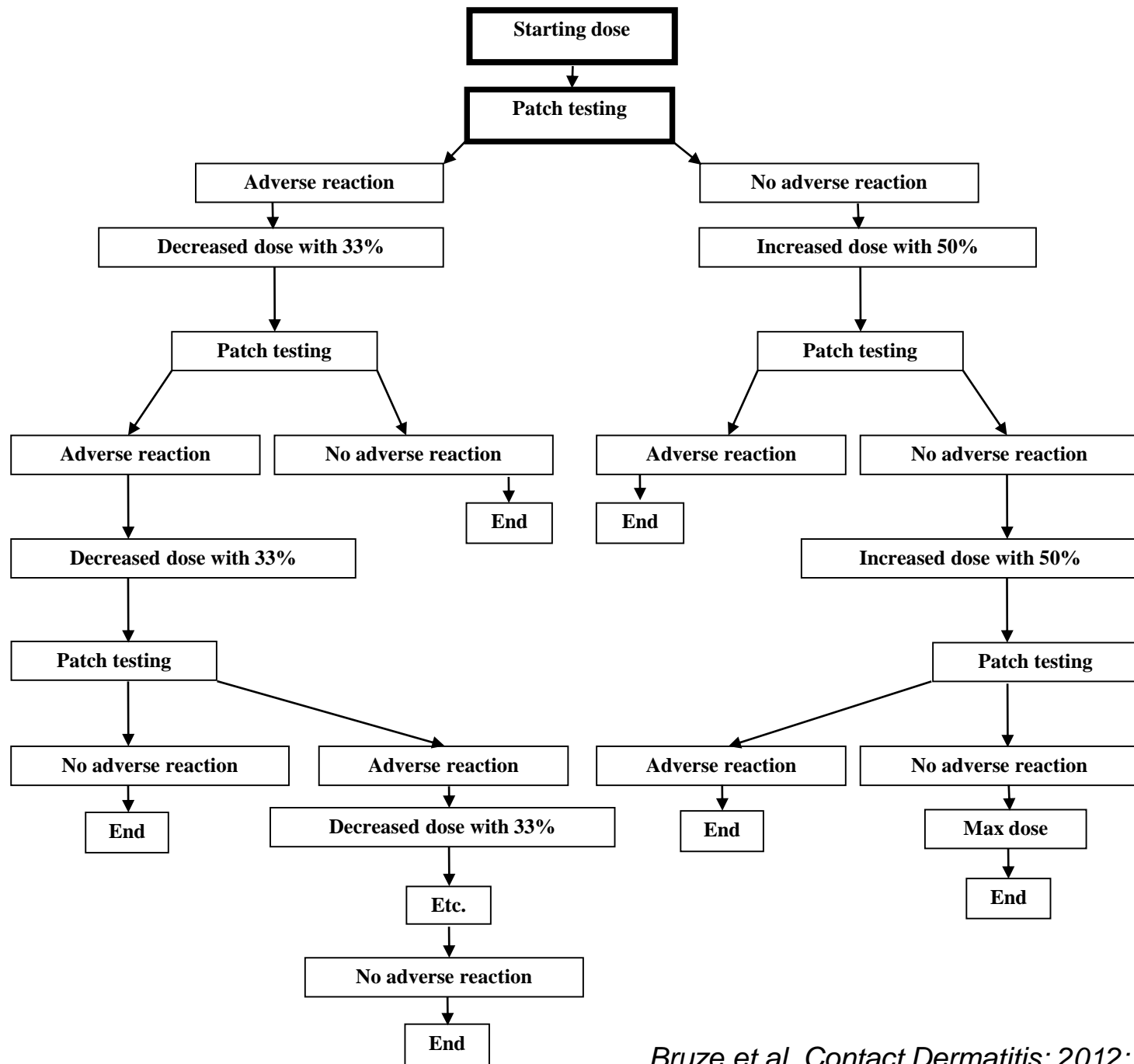
Bruze M¹, Svedman C, Andersen KE, Bruynzeel D, Goossens A, Johansen JD, Matura M, Orton D, Vigan M; ESCD.

Systematically derived patch test concentrations

Maximum patch test concentration – 2 criteria

One practical – 30% in pet

One immunological – 5 times higher
than the maximum concentration
used in scented products



Fragrance	Recommended test dose (mg/cm ²)	Recommended test concentration (% w/w)
Amylcinnamyl alcohol	2.25	5.0
Anise alcohol	3.75	10.0
Benzyl alcohol	4.5	10.0
Benzyl benzoate	4.5	10.0
Benzyl cinnamate	4.5	10.0
Benzyl salicylate	4.5	10.0
Butylphenyl methylpropional	3.38	10.0
Evernia furfuracea	0.45	1.0
Alpha-isomethyl ionone	4.5	10.0
d-Limonene	4.5	10.0
Linalool	4.5	10.0
Methyl-2-octynoate	0.075	0.2

ROAT study

17 Patients

Positive to formaldehyde 2.0% and negative to 1.0%

19 Controls

Without contact allergy to formaldehyde and formaldehyde releasers

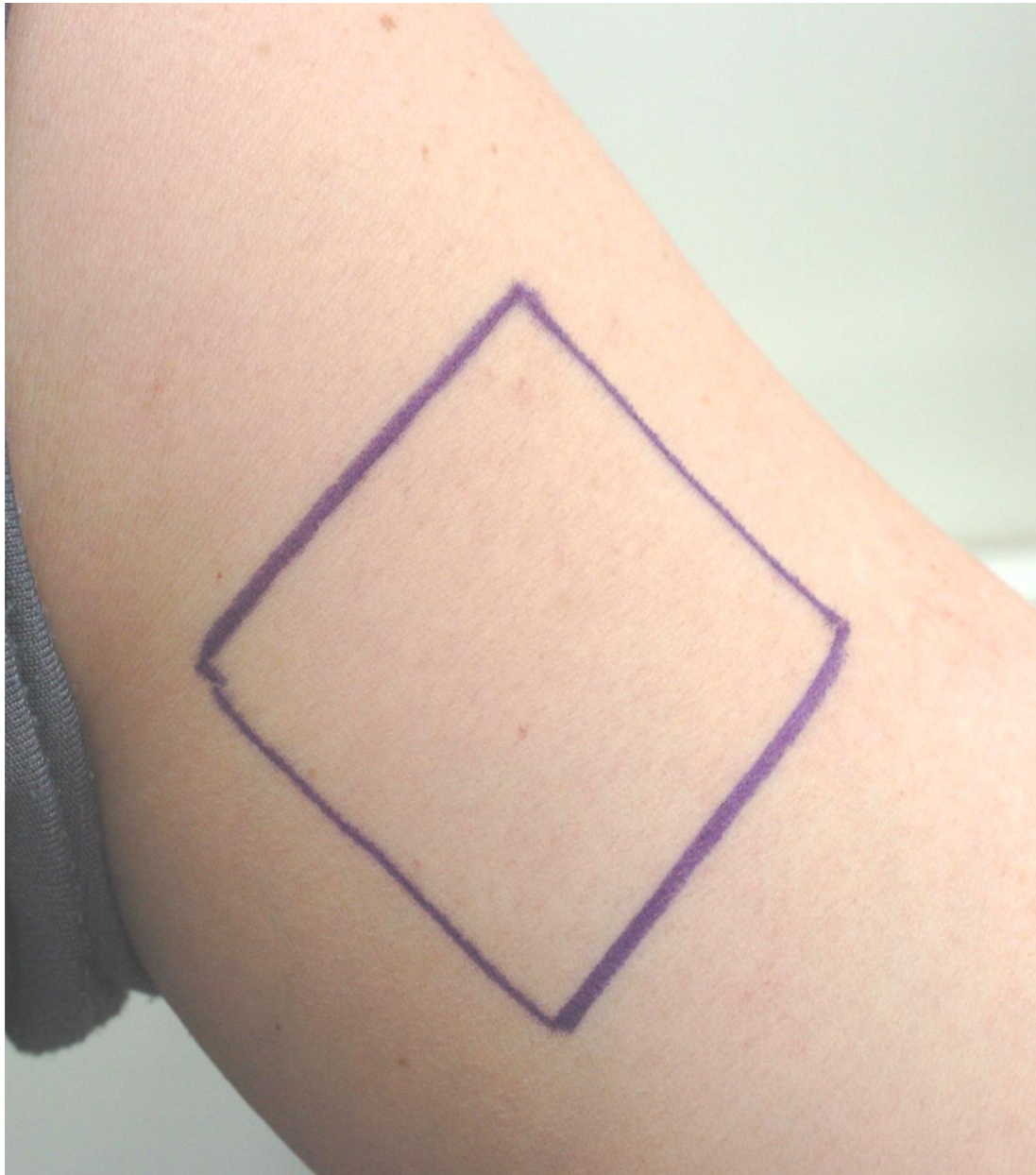
2 moisturisers

1 - the maximum permitted concentration in leave-on cosmetic products 0.2% (2000ppm)

2 – without formaldehyde

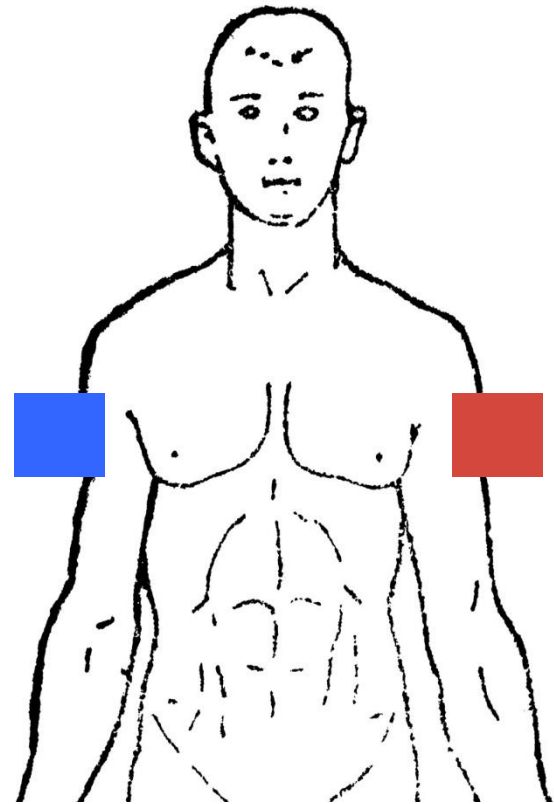
Double-blind and randomized





- on healthy skin
- application 2x daily
- 5x5 cm inside of the upper arm
- maximum 4 weeks
- reading 1x weekly





LUND
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Results

	<i>Patients</i>	<i>Positive reactions</i>	<i>Toxic reactions</i>
Patients	17	9	1*
Controls	19	0	0

Fisher's
Exact Test,
two-sided
p<0.001

* petechiae, slight dryness

