

Sensitivity and specificity of the nickel spot (dimethylglyoxime) test

JACOB P. THYSEN¹, LIZBET SKARE², LENNART LUNDGREN^{2,3}, TORKIL MENNÉ¹, JEANNE D. JOHANSEN¹,
HOWARD I. MAIBACH⁴ AND CAROLA LIDÉN²

¹National Allergy Research Centre, Department of Dermato-Allergology, Copenhagen University Hospital Gentofte, University of Copenhagen, Denmark, ²Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden, ³Department of Applied Environmental Science, Stockholm University, Sweden, and ⁴Department of Dermatology, School of Medicine, University of California San Francisco (UCSF), USA

Background: The accuracy of the dimethylglyoxime (DMG) nickel spot test has been questioned because of false negative and positive test reactions. The EN 1811, a European standard reference method developed by the European Committee for Standardization (CEN), is fine-tuned to estimate nickel release around the limit value of the EU Nickel Directive from products intended to come into direct and prolonged skin contact. Because assessments according to EN 1811 are expensive to perform, time consuming, and may destruct the test item, it should be of great value to know the accuracy of the DMG screening test.

Objectives: To evaluate the sensitivity and specificity of the DMG test.

Methods: DMG spot testing, chemical analysis according to the EN 1811 reference method, and X-ray fluorescence spectroscopy (XRF) were performed concomitantly on 96 metallic components from earrings recently purchased in San Francisco.

Results: The sensitivity of the DMG test was 59.3% and the specificity was 97.5% based on DMG-test results and nickel release concentrations determined by the EN 1811 reference method.

Conclusions: The DMG test has a high specificity but a modest sensitivity. It may serve well for screening purposes. Past exposure studies may have underestimated nickel release from consumer items.

Key words: chemical analyses; dimethylglyoxime test; nickel release; sensitivity; specificity; validation.
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Nickel allergy is prevalent among dermatitis patients and subjects from the general population (1–4) and is typically observed following repeated or prolonged cutaneous exposure to nickel releasing consumer items such as jewellery, clothing fasteners, belts, and mobile phones (5–11). Furthermore, nickel is released from a large proportion of work tools and coins and may result in high nickel concentrations on the skin in some occupations (12–14). Nickel allergic individuals have an increased risk of developing hand eczema (2, 15, 16). Despite the fact that the prevalence of nickel allergy is starting to decrease adult European

women following regulatory intervention on nickel in consumer products (17–19), it remains of utmost importance that excessive nickel release from metallic items can be easily detected to protect consumers, workers, and patients from potentially harmful skin contact with nickel ions.

The dimethylglyoxime (DMG) nickel spot test is an inexpensive and rapid test method that detects nickel release. It is ultimate in simplicity, making it useful for consumers, retailers, and dermatologists (20, 21). The DMG test is typically performed by rubbing a white cotton swab against a metallic item. A bright pink colour is observed when

DMG reacts with nickel salts together with ammonia solution. The detection limit of the DMG test has often been estimated to be close to $0.5 \mu\text{g}/\text{cm}^2/\text{week}$, and thus a clinically relevant and useful screening test (7, 12, 22). The limit therefore indicates the presence of nickel in sufficient concentrations to elicit nickel dermatitis (23, 24). The Danish nickel regulation recommended the DMG test as a method to identify objects that were not in compliance with the regulation (25). Furthermore, the European Committee for Standardization (CEN) developed the CR 12471 screening procedure, which was mainly based on the DMG test for the detection of nickel release (26).

The accuracy of the DMG test has, however, sometimes been questioned because of false negative and positive test reactions (22, 27–30). The EN 1811, a European standard reference method developed by the CEN (31), is fine-tuned to estimate nickel release around the limit value of the EU Nickel Directive from products intended to come into direct and prolonged skin contact and is used to determine whether consumer products comply with the EU Nickel Directive (which is now an integrated part of REACH, the new European Community Regulation on chemicals and their safe use) (32). Because assessments according to EN 1811 are expensive to perform, time consuming, and may destruct the test item, it should be of great value to know the accuracy of the DMG screening test. The current study re-evaluates the sensitivity (i.e. the proportion of true positive reactions correctly identified by the DMG test) and specificity (i.e. the proportion of true negative reactions correctly identified by the DMG test) of the DMG test by concomitantly performing the spot test and the EN 1811 reference method on a sample of metallic components from earrings recently purchased in San Francisco (33). This validation study is of relevance to industries, consumers, physicians, and authorities as the use of advanced chemical analyses may often not be a realistic alternative to the DMG test.

Materials and Methods

Selection of metallic components

Among 277 pairs of earrings previously purchased and DMG tested (33), we selected 73 pairs to ensure a broad variety of metallic components (e.g. rings, discs, posts, and wires) that was still in accordance with overall prevalence estimate (33). Thus, the selection was based on size, shape, colour, surface area, producer, and previous DMG-test outcome (33). Each earring was carefully inspected to identify components in skin contact at normal use. Metallic parts that were not in skin contact as well as non-metallic parts (e.g. plastic, wood, glass,

and stone) were removed from the earrings by a pair of DMG-test negative tongs. For practical reasons, components with a diameter $>21 \text{ mm}$ were excluded as they did not fit in the uniform sample bottles used. As most hoops were larger, these did not fit in the bottles and were excluded. For the above reasons, a large proportion of the metallic components were hooks, posts, and post assemblies. Hooks and posts are long and thin metal pieces that perforate the earlobe. We ended up with 96 sets of metallic parts for this study (73 pairs of posts and hooks and 23 pairs of decorative attachments).

Cleaning procedure

The cleaning procedure was performed in accordance with EN 1811 (31). Thus, all components were gently swirled for 2 min in a degreasing solution containing 5 g dodecylbenzene sulfonate (CAS: 25155-30-0, Sigma-Aldrich Chemie GmbH, Steinheim, Germany) in 1000 ml deionized water at room temperature ($20\text{--}22^\circ\text{C}$) to remove extraneous grease and skin secretions as well as nickel contamination. The components were then rinsed with deionized water and left to dry. From this step, all handling was performed using protective plastic gloves and plastic forceps.

X-ray fluorescence spectrometry

Metallic sample components were individually examined by a handheld X-ray fluorescence analyser (Innov-X, Alpha 4000, Innov-X-Europe, The Netherlands) to determine the composition of the outer layers. X-ray fluorescence spectroscopy (XRF) is a non-destructive analytical technique widely used for elemental and chemical analysis. Briefly, high-energy X-rays bombard the metal and lead to emission of characteristic fluorescent X-rays that are registered. The detected X-ray intensities were evaluated with the use of the instruments own standard module for alloy analysis.

DMG testing

The DMG test (Chemo Nickel TestTM, Chemotechnique Diagnostics®, Vellinge, Sweden) [DMG 1%, ethanol and ammonium hydroxide (9.9%) solution; in one bottle together] was administered by placing two drops of the test solution on a white cotton swab that was rubbed for up to 30 seconds against the metallic component. A positive reaction was indicated by a pink colour on the cotton swab when viewed against a white background. A negative reaction was registered when no colour change was observed against a white background. Doubtful reactions were defined as reactions where

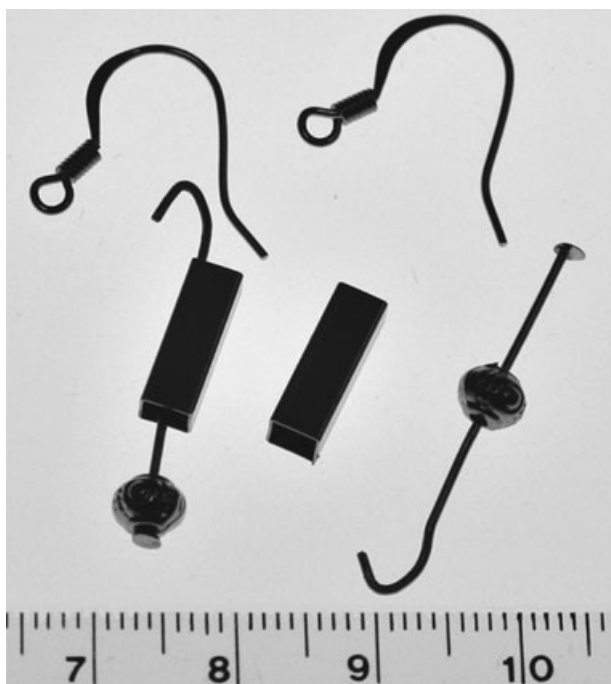


Fig. 1. A pair of earrings has been dismantled before area measurement. Both the interior as well as the exterior of the square tubes in the lower part of the figure were included in the total area as these will become exposed to artificial sweat during chemical analysis.

the investigator could not convincingly classify the test outcome as either negative or positive, typically because of discoloration possibly masking pink colour. The DMG test was performed on all components before they were put into the artificial sweat, and it was also performed on a large proportion of components after being immersed in artificial sweat.

Area measurement

Area measurement was performed using computerized image analysis, instead of the rough area assessment described in EN 1811. Individual components were digitally photographed together with a ruler (Fig. 1). The pictures were then viewed and evaluated with image analysis software, ImageJ®; a software program available for different platforms and freely downloaded from the internet (<http://rsbweb.nih.gov/ij/>). This program allows the user to measure the size after calibration with the ruler of different parts of the metallic components. Using basic measurement formulas, areas of these components were calculated. All areas expected to become exposed to artificial sweat during analysis were measured and calculated, for example, the interior of a square tube shaped component was included in the total sample area of that component (Fig. 1).

Nickel release and chemical analysis according to EN 1811

To determine nickel release, the European Standard EN 1811 developed by CEN/TC 283/WG4 was followed (31). All 96 pairs of earring components were simultaneously investigated for nickel release by immersion in artificial sweat consisting of deionized and aerated water containing sodium chloride 0.5%, lactic acid 0.1%, and urea 0.1%. pH was adjusted to 6.5 with ammonia. The solution was used within 3 hr of preparation. Furthermore, nickel free acid prewashed plastic vessels with lid (Nalgene polypropylene) in 30 and 60 ml were prepared according to the EN 1811. Each pair of earring components was totally immersed in approximately 1 ml artificial sweat per cm² sample area. The minimum volume of artificial sweat required by the analytical laboratory for this chemical analysis was 6 ml. The vessels were left untouched in an oven for nickel extraction at 30°C for 1 week. The earring components were then removed by plastic forceps, which were rinsed between samples. To obtain 1% nitric acid concentration, 400 µl of 25% nitric acid was added to the vessels. Finally, the solutions were stored at 8°C until analysed, which was performed within 4 weeks by the SP Technical Research Institute of Sweden, Borås, Sweden. Inductively coupled plasma optical emission spectroscopy (ICP-OES by Perkin Elmer Optima 5300DV) was used for the analysis of nickel in the artificial sweat extracts. The detection limit of nickel was 0.01 µg/l. The final results were expressed in µg/cm²/week. We reported the analytical values of nickel release, and did not multiply the values by the adjustment factor of 0.1 described in the current version of EN 1811.

Calculation of specificity and sensitivity

A positive DMG-test result (i.e. a pink coloration) indicates that nickel release exceeds approximately 0.5 µg nickel/cm²/week (23), whereas the chemical analysis used in the EN 1811 can express nickel release in various concentrations. The ability of the DMG test to detect release of nickel ions in concentrations that can elicit nickel dermatitis (in nickel allergic patients) was first estimated by Menné et al. (22, 23). They submitted 15 alloys of known composition to the DMG test as well as a 1-week corrosion test (22, 23). Furthermore, they used discs with identical composition for patch testing in nickel allergic dermatitis patients (22, 23). They found that those discs that released nickel in concentrations >0.5 µg/cm²/week also gave positive DMG-test reactions and positive patch test reactions in the majority of cases (22, 23). Thus, the 0.5 µg nickel/cm²/week limit that is commonly used to describe the transition point of the DMG test

is an estimate based on past experience. When the sensitivity and specificity of a test is assessed, one needs to correlate test results from the test that is under validation against test results from a gold standard. In this study, the DMG test was validated against the chemical analysis described in the EN 1811. It should be noted that the corrosion test in rare cases may give misleading results. Menné et al. showed that an alloy with a high nickel (77%) and chromium content (15%) resulted in positive patch test reactions in the majority of nickel allergic patients when used for patch testing but corrosion and DMG testing showed nickel release below $0.5 \mu\text{g}/\text{cm}^2/\text{week}$ (23). The discordance was explained by the formation of chromium oxides on the surface during corrosion (23).

Sensitivity and specificity were defined as observed below and given with 95% confidence intervals (CIs) (34):

$$\text{Sensitivity} = \frac{\text{Number of true positives}}{(\text{Number of true positives} + \text{Number of false negatives})}$$

$$\text{Specificity} = \frac{\text{Number of true negatives}}{(\text{Number of true negatives} + \text{Number of false positives})}$$

True positive reactions were defined as 'positive DMG-test reactions that were confirmed by nickel release $>0.5 \mu\text{g}/\text{cm}^2/\text{week}$ '. False positive reactions were defined as 'positive DMG-test reactions but with a nickel release concentration below $0.5 \mu\text{g}/\text{cm}^2/\text{week}$ '. True negative reactions were defined as 'negative DMG test confirmed by a nickel release below $0.5 \mu\text{g}/\text{cm}^2/\text{week}$ '. Finally, false negative reactions were defined as 'negative DMG-test reactions but where nickel release was $>0.5 \mu\text{g}/\text{cm}^2/\text{week}$ '.

Results

Tables 1 and 2 show test results obtained by concomitantly performing the DMG spot test as well as the chemical analysis described in EN 1811 on 96 pairs of metallic components. DMG testing showed that 33 (34.4%) pairs of components were positive, 61 (63.5%) were negative, and 2 (2.1%) were doubtful. The median area of metallic components was 2.61 cm^2 (range $0.63\text{--}28.34 \text{ cm}^2$) and chemical analysis showed that 55 (57.3%) pairs of components released $>0.5 \mu\text{g}$ nickel/ cm^2/week and that 41 (42.3%) pairs released $<0.5 \mu\text{g}$ nickel/ cm^2/week . Median nickel release after 1 week in artificial sweat was $18.9 \mu\text{g}$ nickel/ cm^2/week (range $0.1\text{--}598.4$) among DMG positive metallic components and $0.11 \mu\text{g}$ nickel/ cm^2/week (range $0.01\text{--}88.1$) among

DMG negative metallic components (Tables 1 and 2). A calculation excluding the two doubtful DMG-test results showed that the sensitivity of the DMG test was 59.3% (CI 95% = 13.1–46.2%) and that the specificity was 97.5% (CI 95% = 92.7–100%) (Table 3).

When the DMG test was repeated after immersion in artificial sweat, 8 (24.2%) of 33 initially DMG-test positive components had a negative DMG-test result (Table 1). Of the 63 initially DMG-test negative or doubtful components, 28 were retested, excluding those with a negative XRF-result and the lowest nickel release values. It was showed that 5 (17.9%) of the initially DMG-test negative components had a positive DMG test (Table 2). When the surface of all components was visually inspected after immersion for 1 week in artificial sweat, by comparison with photos taken for the area measurement, the appearance had often changed (Tables 1 and 2). Only qualitative assessment was performed, with no attempt to quantify or describe the changes which varied from small to large.

Metallic components were examined for their metal content by XRF spectrometer (Tables 1 and 2). We found that all components releasing $>0.5 \mu\text{g}$ nickel/ cm^2/week also contained nickel. Furthermore, few components with high nickel content did not release nickel or released nickel in amounts that were $<0.5 \mu\text{g}$ nickel/ cm^2/week .

Discussion

The sensitivity of the DMG test was 59.3% and the specificity was 97.5%. The sensitivity describes the proportion of true positive reactions correctly identified by the DMG test, that is, the probability that the DMG test is positive given that the metal object under investigation releases $>0.5 \mu\text{g}$ nickel/ cm^2/week . Thus, the true prevalence of materials that release too much nickel will be underestimated if one relies only on positive DMG test results. The specificity describes the proportion of true negative test reactions that were correctly identified by the DMG test, that is, the probability that the DMG test is negative given that the metal objects under investigation release $<0.5 \mu\text{g}$ nickel/ cm^2/week . As described, the $0.5 \mu\text{g}$ nickel/ cm^2/week limit which is commonly used to describe the transition point of the DMG test is only an estimate based on past experience rather than an accurate measure (22, 23).

Our calculation had weaknesses that should be mentioned. Firstly, we did not examine the reproducibility of the DMG test. It is possible that weak DMG-test reactions would be interpreted differently by various investigators. However, we assume

Table 1. Results from testing in total 96 pairs of earring components by the dimethylglyoxime (DMG) screening test for nickel release, by immersion in artificial sweat and chemical analysis according to EN 1811 for assessment of the amount of nickel release, and by X-ray fluorescence spectrometry (XRF) for nickel in the outer layers. This table shows the results of the 33 initially DMG-test positives (the DMG-test negatives are shown in Table 2)

Sample numbers	DMG-test result before artificial sweat ^a	DMG-test result after artificial sweat ^b	Chemical analysis ($\mu\text{g nickel}/\text{cm}^2/\text{week}$)	XRF ^c (% nickel)	Visible surface change after artificial sweat ^d
1	+	–	0.11 ^e	2.6	–
2	+	+	0.88	28	–
3	+	+	1.43	26	–
4	+	+	1.54	45	–
5	+	+	1.74	36	–
6	+	–	1.91	4.7	+
7	+	+	2.07	1.7	+
8	+	–	2.19	17	–
9	+	–	2.24	63	–
10	+	+	2.42	36	–
11	+	+	2.83	7.7	+
12	+	+	3.67	11	+
13	+	+	3.94	3.5	+
14	+	–	4.01	65	–
15	+	+	5.05	31	+
16	+	+	18.9	13	+
17	+	–	18.9	6.3	+
18	+	–	26.1	1.2	+
19	+	+	36.3	13	+
20	+	–	38.4	44	–
21	+	+	45.9	8.2	+
22	+	+	49.0	20	+
23	+	+	59.8	28	+
24	+	+	67.1	43	–
25	+	+	68.3	13	+
26	+	+	80.8	24	+
27	+	+	129	25	+
28	+	+	145	22	+
29	+	+	155	25	+
30	+	+	200	27	+
31	+	+	204	38	+
32	+	+	410	42	+
33	+	+	598	18	+
All samples (<i>n</i> = 33)	33 positive	8 negative 25 positive	1 < 0.5 $\mu\text{g}/\text{cm}^2/\text{week}$ 32 $\geq$ 0.5 $\mu\text{g}/\text{cm}^2/\text{week}$	33 positive	11 no visible change 22 visible change

+, positive DMG-test result; or visible surface change; –, negative DMG-test result; or no visible surface change.

^aDMG test before immersion for 1 week in artificial sweat.

^bDMG test after immersion for 1 week in artificial sweat according to EN 1811.

^cXRF performed before immersion for 1 week in artificial sweat.

^dAssessed by visual inspection after immersion in artificial sweat and comparing with photos for area measurement before immersion.

^eDiscrepancy.

that interpretation of DMG-test results is generally straightforward, considering the need of normal colour vision, and therefore highly reproducible. Thus, positive DMG-test reactions typically leave a clear pink or cerise coloration of the white cotton stick whereas negative reactions leave the cotton stick white or slightly grey. In our and others experience, doubtful reactions are uncommon. Lidén et al. found that 21 of 725 (3%) (35) and 69 of 786 (9%) (7) of tested items in 1999 and 2002/2003, respectively, gave doubtful test result because of discoloration. Heim et al. found that 1 of 173 samples showed a doubtful DMG-test reaction (10). In

the San Francisco earring study, we only found 2 doubtful DMG-test reactions among 277 items (33). Doubtful reactions are therefore not expected to affect the reproducibility to a high extent. However, we acknowledge that a separate validation study using kappa statistics is needed to clarify the reproducibility of the DMG test. Secondly, surface coatings may be affected when items are exposed to artificial sweat and heat, which may result in increased nickel release. Based on this knowledge, CEN developed a screening test suitable for indicative assessment of compliance with the EU Nickel Directive (26). The CEN screening test is based on

Table 2. Results from testing in total 96 pairs of earring components by the dimethylglyoxime (DMG) screening test for nickel release, by immersion in artificial sweat and chemical analysis according to EN 1811 for assessment of the amount of nickel release, and by X-ray fluorescence spectrometry (XRF) for nickel in the outer layers. This table presents results of the 61 initially DMG-test negatives and 2 DMG-test doubtful results (the DMG-test positives are shown in Table 1)

Sample numbers	DMG-test result before artificial sweat ^a	DMG-test result after artificial sweat ^b	Chemical analysis (µg nickel/cm ² /week)	XRF ^c (% nickel)	Visible surface change after artificial sweat ^d
34	—	NT	< 0.01	—	+
35	—	NT	< 0.02	—	+
36	—	NT	< 0.02	—	+
37	—	NT	< 0.02	—	+
38	—	NT	< 0.03	—	+
39	—	NT	< 0.03	—	+
40	—	NT	< 0.03	—	+
41	—	NT	< 0.03	—	+
42	—	NT	< 0.04	12	+
43	—	NT	< 0.04	—	+
44	—	NT	< 0.05	—	+
45	—	NT	< 0.05	—	+
46	—	NT	< 0.05	—	+
47	—	NT	< 0.05	—	+
48	—	NT	< 0.06	—	+
49	—	NT	< 0.10	—	—
50	—	NT	< 0.26	0.2	+
51	—	NT	0.01	—	+
52	—	NT	0.04	—	+
53	—	NT	0.04	—	—
54	—	NT	0.05	—	—
55	—	NT	0.05	—	+
56	—	NT	0.05	—	—
57	—	NT	0.06	—	+
58	—	NT	0.06	—	+
59	—	NT	0.06	—	+
60	—	NT	0.06	—	+
61	—	NT	0.06	—	+
62	—	NT	0.06	—	+
63	—	NT	0.10	—	+
64	—	NT	0.11	—	+
65	—	NT	0.12	—	+
66	—	NT	0.13	—	+
67	—	NT	0.14	3.1	+
68	—	—	0.16	—	+
69	—	—	0.20	—	+
70	—	—	0.20	0.2	+
71	—	—	0.20	0.06	+
72	—	—	0.33	25	+
73	—	—	0.51	—	+
74	—	—	0.55	2.9	+
75	—	—	0.71	2.3	—
76	—	—	0.75	9.3	+
77	—	—	0.79	19	—
78	—	—	0.81	43	+
79	—	—	1.08	1.8	+
80	—	—	1.63	53	+
81	—	—	2.47	7.6	+
82	—	—	2.80	6.5	+
83	—	—	3.50	4.7	+
84	—	—	3.59	0.3	+
85	—	—	3.75	5.1	+
86	—	—	4.38	9.7	+
87	—	—	4.56	13	+
88	—	—	4.73	40	+
89	—	—	5.73	4.8	—
90	—	+	11.5	13	+

Table 2. Continued

Sample numbers	DMG-test result before artificial sweat ^a	DMG-test result after artificial sweat ^b	Chemical analysis (μg nickel/ cm^2/week)	XRF ^c (% nickel)	Visible surface change after artificial sweat ^d
91	—	+	19.2	25	+
92	—	+	20.4	13	+
93	—	+	22.9	8.6	+
94	—	+	88.1	8.5	+
95	?	NT	0.06	—	+
96	?	—	5.95	15	—
All samples ($n = 63$)	61 negative 2 doubtful	35 not tested 23 negative 5 positive	$40 < 0.5 \mu\text{g}/\text{cm}^2/\text{week}$ $23 \geq 0.5 \mu\text{g}/\text{cm}^2/\text{week}$	35 negative 28 positive	8 no visible change 55 visible change

+, positive DMG-test result; or visible surface change; —, negative DMG-test result; or no nickel detected by XRF; or no visible surface change; ?, doubtful DMG-test result; NT, not tested by DMG test.

^aDMG test before immersion for 1 week in artificial sweat.

^bDMG test after immersion for 1 week in artificial sweat according to EN 1811.

^cXRF performed before immersion for 1 week in artificial sweat.

^dAssessed by visual inspection after immersion in artificial sweat and comparing with photos for area measurement before immersion.

Table 3. Comparison of test results obtained using the dimethylglyoxime (DMG) test and assessment of nickel release by immersion in artificial sweat and chemical analysis according to EN 1811 (gold standard) in 94 pairs of earring components. Data based on results in Tables 1 and 2 (two samples with doubtful DMG-test results in Table 2 were excluded from this table)

		Chemical analysis		Total
		+	—	
DMG-test result ^a	+	32	1	33
	—	22	39	61
Total		54	40	94

+, positive DMG test; or nickel release $\geq 0.5 \mu\text{g}/\text{cm}^2/\text{week}$ according to chemical analysis; —, negative DMG test; or nickel release $< 0.5 \mu\text{g}/\text{cm}^2/\text{week}$ according to chemical analysis.

^aDMG test before immersion in artificial sweat.

the simple DMG test and pretreatment with a drop of artificial sweat and heat by a hairdryer or lamp for field application, or in an oven for laboratory use. Pönkä et al. showed that 9 (14%) of 66 DMG negative earrings became DMG positive after 1 week in artificial sweat (29). In the present study, we repeated the DMG test after the immersion for 1 week in artificial sweat. Both new DMG-test negatives (24.2%) and positives (17.9%) were recorded, and the surface of a large proportion of items had been visibly affected.

We performed a literature review to identify past studies that validated the DMG test. Table 4 shows that different methods were used and that the DMG test was applied on various metallic items. When data from past studies were analysed together, we found that the sensitivity was 68.2% and the specificity was 87.1%. Like ours, these data support the notion that the DMG test may be a valuable screening tool. However, we believe that our study findings may be of particular value for several reasons. First, our sample size was markedly larger

that the sample size in each single study. Second, we followed carefully the EN 1811 reference test method, developed by CEN under mandate by the European Commission for testing compliance with the EU Nickel Directive (31). We performed the required separation of components made of different materials, for separate analysis. This is seldom performed by others. Third, the novel image analysis method used here to calculate area size must be regarded more accurate than the rough area calculation methods, for example, Vernier callipers, in EN 1811. According to the current version of EN 1811, the measured and calculated nickel release shall be reported, and this value may be multiplied by an adjustment factor of 0.1 for interpretation of compliance with the EU Nickel Directive. This adjustment factor was introduced into EN 1811 reference method to compensate for difficulties when calculating complicated area sizes (e.g. of chains), and for the lack of experience from applying the test method on analysis of real objects. The current adjustment factor has a great impact on the interpretation of test data. Thus, a metallic chain that release $4.9 \mu\text{g}$ nickel/ cm^2/week in the EN 1811 reference method will comply with the EU Nickel Directive when it is multiplied by 0.1 (as $0.49 \mu\text{g}$ nickel/ cm^2/week is below the limit). Heim et al. performed the EN 1811 reference method on 10 children's clothing fasteners that were positive upon DMG testing (10). Chemical analysis showed that all 10 samples released $> 0.5 \mu\text{g}$ nickel/ cm^2/week before adjustment but only 7 of 10 samples released an excessive nickel amount after multiplication with the adjustment factor. In the revision of the EU Nickel Directive 2004 (36), the Commission invited CEN to review EN 1811, in particular regarding the adjustment factor and to prepare a revised standard without adjustment factor, or with a smaller

Table 4. Studies that have performed both dimethylglyoxime testing (DMG) as well as confirmatory testing for assessment of nickel release

Author	Examined items	DMG-test result (no. of items)		Analytical method	Confirmatory test			Validity	
		n	+		Nickel release >0.5 µg/cm ² /week (no. of items)	Nickel release <0.5 µg/cm ² /week (no. of items)	Nickel present in base alloy or surface (no. of items)	Sensitivity (%)	Specificity (%)
Fischer (37)	Unplated white gold discs ^a	8	0	8	Graphite furnace AAS after 1 week in artificial sweat	b	—	—	—
Fischer (37)	Rhodium-plated white gold discs ^a	8	0	8	Graphite furnace AAS after 1 week in artificial sweat	c	—	—	—
Fischer (6)	Earrings, piercing studs, clasps, and instruments	38	d	d	Graphite furnace AAS after 1 week in artificial sweat	d	—	—	—
Cavelier (38)	Not-tolerated clothing objects	37	33	4	X-ray energy dispersion in electron microscopy	—	33	—	—
Cavelier (38)	Well tolerated clothing objects	20	5	15	X-ray energy dispersion in electron microscopy	—	5	—	—
Menné (22)	Purchased metal objects (ear-clips, buttons, jewellery, eyeglasses)	54	36	18	X-ray dispersive analysis (EDAX)	—	36	—	—
Menné (22, 23)	Metal and alloy discs ^a	15	8	7 ^e	Zeeman AAS after 1, 3, and 6 weeks in artificial sweat	8	—	87.5	85.7
Räsänen (30)	Ear piercing kits	9	2	7 ^f	Graphite furnace AAS after 1 week in distilled water and then 1 week in human plasma	2 (in water) and 6 (in plasma)	7 (in water) and 3 (in plasma)	50 (plasma)	100 (plasma)
Haudrechy (39)	Nickel-plated metal samples	2	2	0	AAS after 1 week in artificial sweat	2	—	—	—
Haudrechy (39)	Stainless steel grades	4	0	4 ^g	AAS after 1 week in artificial sweat	1	—	—	—
Kanerva (27)	Metallic samples (earrings, necklace, bracelet, ring, and rivets)	10	5	5 ^h	Flame AAS after 1, 3, and 6 weeks in artificial sweat	8	—	62.5	100
Lidén (12)	Samples from work tools	30	22	4 ⁱ	ICP detection after 1 week in artificial sweat and EDAX	23	7/7	90.9	50
Haudrechy (40)	Stainless steel grades	5	0	5 ^j	AAS after 1 week in artificial sweat	1	—	—	100
Pönkä (29)	Piercing earrings (n = 30) and back pieces (n = 36)	66	0 ^k	66	Graphite furnace and flame technique AAS after 1 week in artificial sweat or hydrofluoric acid	11 (in sweat) and 25 (in hydrofluoric acid)	55 (in sweat) and 41 (in hydrofluoric acid)	36.4	90.1

Table 4. Continued

Author	Type	Examined items	DMG-test result (no. of items)	Confirmatory test			Validity	
				Analytical method	Nickel release >0.5 µg/cm ² /week (no. of items)	Nickel release <0.5 µg/cm ² /week (no. of items)	Nickel present in base alloy or surface (no. of items)	Specificity (%)
Heim (10)	Children's clothing fasteners		20	En 1811 test protocol (31)	7	7	–	70
–, not calculated or stated; AAS, atomic absorption spectrophotometry; ICP, inductively coupled plasma.								
^a Discs of known composition.								
^b Unplated discs released 0.09–0.82 µg nickel/cm ² /week.								
^c Rhodium-plated discs released 0.04–0.54 µg nickel/cm ² /week.								
^d According to Fischer et al., the detection limit for the DMG test was 10 µg nickel/cm ² /week. Seven earrings 6–25 µg nickel/cm ² /week (6).								
^e Menné et al. identified one false positive DMG reaction and one false negative reaction.								
^f Räsänen et al. identified one false negative DMG reaction when assessed in distilled water and four false negative DMG reactions when assessed in plasma.								
^g Haudrechy et al. identified one false negative DMG reaction.								
^h Kanerva et al. identified three false negative DMG reactions.								
ⁱ Three doubtful DMG reactions. Lidén et al. identified two false negative DMG reactions and two false positive DMG reactions.								
^j Haudrechy et al. identified one false negative DMG reaction.								
^k Pönkä et al. identified further nine positive DMG-test reactions after earring exposure to artificial sweat.								

adjustment factor than the current 0.1. A revised version will supersede the present EN 1811:1998, and the Draft prEN 1811:July 2009 is currently in the CEN voting procedure.

XRF was used in the present study to assess presence (not release) of nickel and other metals of concern for health and environment. The technique is useful for quick screening concerning the potential of release of different metals of interest from large numbers of items. It is however important to recall that XRF cannot replace testing with the DMG test or by EN 1811 reference method for assessment of nickel release and compliance with the EU Nickel Directive.

Based on our data, it is interesting to re-evaluate the results from past nickel exposure assessment studies using the DMG test (5, 7–12, 33). As the sensitivity of the DMG test was only around 60%, it is possible that the prevalence estimates of consumer items that release an excessive amount of nickel (0.5 µg nickel/cm²/week) may be even higher.

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Address:

Jacob Pontoppidan Thyssen, MD
 National Allergy Research Centre
 Department of Dermato-Allergology
 Copenhagen University Hospital Gentofte
 University of Copenhagen
 Ledreborg Allé 40
 I. 2820 Gentofte
 Denmark
 Tel: +45 3977 7307
 Fax: +45 3977 7118
 e-mail: jacph01@geh.regionh.dk