Nickel allergy and EU nickel restriction

ECHA draft Guideline - list of articles in direct and prolonged contact with skin

Position Paper

MARCH 2018
CONTENTS

Summary .......................................................................................................................................................... 4

Background ..................................................................................................................................................... 6

What is nickel? .............................................................................................................................................. 6

What is nickel allergic contact dermatitis? ................................................................................................. 6

Nickel allergy and EU restriction (REACH, Entry 27, Annex XVII) .............................................. 9

ECHA draft Guideline and list of articles within the restriction scope ........................................ 11

Nickel Institute's comments on ECHA draft Guideline list ................................................................. 12

Nickel Institute's position: How to address the problem ................................................................. 17

Nickel Institute and NiPERA activities .................................................................................................... 19

Industry views and experience ...................................................................................................................... 21

The way forward: appropriate materials in appropriate applications ............................................. 22

Summary conclusions ................................................................................................................................. 23

References ..................................................................................................................................................... 24

Annexes ............................................................................................................................................................ 25
This paper outlines the position of the Nickel Institute (NI) on nickel allergy, the implementation of the EU nickel restriction (REACH Annex XVII, Entry 27) and ongoing regulatory activities by the European Chemicals Agency (ECHA) to develop a guideline list of articles to be considered within the scope of the restriction.

The paper also provides background information about nickel, nickel allergic contact dermatitis (NACD) as well as an update on the research activities from NiPERA, the NI’s scientific division, to understand nickel allergy and the causes of its prevalence.

Nickel is a well-known allergen and studies have shown that between 12-15% of women and 1-2% of men in the general population are allergic to nickel. NI fully supports the need to protect people from becoming allergic (i.e. sensitized) to nickel and to prevent NACD in already nickel-allergic individuals. It is essential to use appropriate materials in applications where the use involves direct and prolonged contact with the skin. In such applications, only low nickel-releasing materials should be used to avoid sensitization or NACD. The NI does not support the use of nickel in applications and materials that cause these reactions. First and foremost, because of the need to protect public health, but also because nickel allergy contributes to nickel stigmatization and can lead to disproportionate regulatory measures unnecessarily affecting the use of nickel in other safe materials and applications.

Nickel allergy is an issue important to both human health and socio-economics in the EU since nickel-containing materials are so widely and safely used in industrial and consumer applications and given that the EU accounts for about 20% of global nickel use.

The draft ECHA Guideline list of articles extends the scope of the existing nickel restriction without justification.

NI supports the objectives of the EU nickel restriction (i.e. preventing nickel allergy and NACD). Unfortunately, in its current form, the draft ECHA Guideline list would not bring significant added value to the prevention of nickel allergy as it includes many articles that are either:

- not clinically relevant causes of NACD;
- nor expected to come into sufficient prolonged and direct skin contact to cause nickel allergy or NACD.
This draft ECHA Guideline list, if implemented, may lead to needless testing and product changes, without producing any real health benefits, while diverting enforcement resources away from the five, well documented, primary causes of nickel sensitization. If, instead, the focus was on eliminating exposure to the most significant sources of sensitization and NACD, which are already listed in the EU nickel restriction as examples, then nickel allergy would be substantially reduced.

**NiPERA scientific research on “prolonged skin contact”**.

To determine the clinically relevant definition of prolonged skin contact, beginning in 2015 NiPERA has sponsored a human patch testing study in nickel-sensitized individuals. Results of testing thus far (Phase 1 and Phase 2) indicate that the amount of prolonged skin contact needed to elicit a reaction in nickel-allergic individuals is more than 2 hours for one occurrence or more than 30 minutes for 3 occurrences within two-weeks. The findings of this research, recently submitted to a peer reviewed journal, are consistent with those of previous research and indicate that reactivity to nickel patch tests requires exposure in hours, not just minutes. These findings are very relevant to what types of items are responsible for nickel sensitization and NACD. These scientific results should be taken into account in the ongoing discussions concerning the interpretation of the existing nickel restriction and refinement of the draft ECHA Guideline list.

**The existing legislation is protective, if complied with and enforced.**

The way forward is to prevent nickel sensitization in the first place. Issuing the ECHA Guideline list which extends the nickel restriction to articles that are not demonstrated or likely to cause nickel sensitization or NACD will be ineffective. Overall, more education and awareness, eliminating the leading causes of nickel sensitization and better enforcement of existing legislation to improve compliance will achieve the public health objective of preventing nickel sensitization.
Background

What is nickel?

Nickel is a naturally occurring, silvery-white metallic element. It is the fifth most common element on earth. For many decades, nickel has been mined, refined and produced for end use in thousands of applications. Although it is “invisible” in our daily lives, nickel plays an essential role in many critical applications important for our modern economy and lifestyles.

Nickel is an essential micro-nutrient for plant growth. It is therefore naturally present in a wide range of crops, animals and foodstuffs. As such, it is a natural component of the human diet. For example, low amounts of nickel are present in oats, nuts, chocolate, coffee, and other foods.

Nickel is used in a wide range of applications because of its unique combination of outstanding physico-chemical properties. It is resistant to very high temperatures, corrosion and oxidation; it has catalytic and magnetic properties. It is very ductile, it alloys readily and it is fully recyclable. Because of these properties, nickel is used in critical applications throughout modern society and assists in virtually every aspect of modern life. It is used in over 300,000 products including for consumer, industrial, military, transport, aerospace, marine and architectural applications.

More specifically, nickel, after extraction, processing and refining, may be used as metallic nickel, as an element in nickel-containing alloys such as stainless steel, or as nickel compounds, such as nickel sulphate and nickel chloride. Nickel metal, nickel-containing alloys and nickel compounds each have different physico-chemical, toxicological properties and hazard classifications.

Nickel compounds are specialty chemicals used in industrial settings and consumers are not exposed to nickel compounds. On the other hand, consumers come into contact with metallic nickel (less so) and nickel-containing alloys, especially stainless steel (more so), because they are used in so many applications and consumer goods.

The most significant use of produced nickel is in nickel-containing alloys. About 66% of the global nickel production is used to manufacture stainless steel. Another 20% of produced nickel is used in the production of other alloys - often for highly specialized and demanding applications in industry, aerospace and the military. Other important uses of nickel include electroplating (9%) and other applications (6%) including battery technologies and catalysts. In many applications, there is either no substitute for nickel or no substitute for nickel without reducing performance or increasing cost.

Europe accounts for around 20% of global nickel use. Nickel and nickel-containing materials are very important for the EU economy and industrial value chains. They play a vital role in many applications that bring widespread societal benefits, contributing to innovation (development of green technologies, etc.) and virtually all manufacturing industries.

2. About 66% of all stainless steel is nickel-containing stainless steel. Each grade of stainless steel, whether nickel-containing or not, has different physico-chemical properties.
What is nickel allergic contact dermatitis?

Nickel is a well-known skin allergen and a common cause of allergic contact dermatitis. Nickel sensitization is the process of becoming allergic to nickel, or nickel-sensitized, which can be diagnosed by a dermatologist using patch testing with water-soluble nickel sulphate. Nickel allergic contact dermatitis (NACD) is the allergic reaction in nickel-sensitized (i.e. nickel-allergic) individuals. People who are allergic to nickel may experience a skin reaction, usually inflammation and itching, when they come in direct and prolonged contact with items releasing a sufficiently high amount of nickel.

While NACD may cause discomfort (for example itching and inflammation), it is not life threatening. Nickel allergy is a delayed-type allergy (type 4), which does not trigger anaphylactic shock unlike some other types of allergies (type 1, 2, or 3). The allergic reaction begins to disappear when direct skin contact with the nickel-releasing article stops. Therefore, with care, education, awareness and appropriate actions, NACD is avoidable and the risks can be managed.

What is the nickel allergy mechanism? Nickel sensitization and elicitation

Nickel sensitization is not an inherited condition. Individuals become sensitized to nickel through direct and continuous prolonged skin contact with articles, such as earrings or clothing buttons if these articles release an amount of nickel sufficiently high to cause nickel sensitization. Once an individual has become nickel-sensitized, direct and continuous prolonged exposure to articles releasing sufficient nickel can cause elicitation, known as NACD. The threshold (i.e. amount needed to cause a reaction) to elicit an allergic reaction is lower than the threshold for nickel sensitization. This means that preventing nickel dermatitis reactions in allergic individuals will also protect non-nickel allergic individuals from becoming nickel-sensitized in the first place.

Nickel sensitization is preventable and NACD is avoidable. Both can be forestalled by avoiding direct and continuous prolonged skin contact with articles that could potentially release a sufficient amount of nickel to cause sensitization or NACD (elicitation).

Three conditions are needed and must be met simultaneously for sensitization or NACD reactions to occur:

1. The contact with the skin must be direct;

2. The direct skin contact must be continuous prolonged on the same part of the skin;

3. A sufficiently high amount of nickel ions must be released and absorbed into the skin.
Nickel release is the key factor

The release of nickel ions from articles is responsible for causing sensitization and NACD reactions. Sensitization and NACD are “threshold effects”, meaning they require release of ions above a specific amount to cause an immune reaction. Nickel release does not necessarily correlate with nickel content. Many nickel-containing alloys, including nickel-containing stainless steels, which are very resistant to corrosion, do not release a sufficient amount of nickel (i.e. above the threshold) to cause sensitization or NACD in most sensitized individuals. A standardized methodology (EN 18113) exists to measure nickel release in synthetic sweat to mimic the conditions on the skin.

The prevalence of nickel allergy

Studies of nickel allergy prevalence have shown that in the general population between 12-15% of females and 1-2% of males are nickel-sensitized. The significant differences in prevalence between females and males is sometimes correlated with the much higher prevalence of ear-piercing among females. High nickel-releasing ear-piercing studs are generally viewed as one of the primary causes of nickel sensitization and NACD. Since the implementation of the EU nickel restriction (previously referred to as the Nickel Directive and now included as Annex XVII, Entry 27 under REACH), prevalence of nickel sensitization has decreased in the younger population although it has not disappeared. Based on market surveys, it appears that lack of compliance with the existing nickel restriction is responsible for the remaining prevalence of nickel sensitization among the younger population.

Nickel is a weak to moderate sensitizer. Accordingly, the prevalence of nickel allergy in the general population is best explained by the frequency of direct and continuous and prolonged contact with nickel-releasing articles, rather than the potency of nickel as an allergen.

For a sufficiently high amount of nickel ions to be released and absorbed into the skin, corrosion must occur. Direct and continuous prolonged contact is needed for corrosion of the nickel metal or alloy so that a sufficient amount of nickel ions are released which can then be absorbed through the skin. In addition, time, i.e. prolonged contact, is needed for a sufficient amount of nickel ions to be released and absorbed through the skin.

Furthermore, the direct and continuous prolonged contact must be with the same area of the article and patch of the skin. It is this direct and continuous prolonged contact with the same area of the article and patch of the skin that creates the conditions for corrosion and the subsequent release of nickel ions, which over time can result in sufficient nickel ion release and absorption into the skin in that area to cause sensitization or NACD.

3. EN 1811:2011+A1:2015: Reference test method for release of nickel from all post assemblies which are inserted into pierced parts of the human body and articles intended to come into direct and prolonged contact with the skin.
Nickel allergy and hypersensitivity

A very small fraction of the nickel-sensitized population is hypersensitized to nickel. Hypersensitized individuals react to lower concentrations of nickel than most nickel-sensitized individuals. Prevention of elicitation in hypersensitive individuals, i.e. NACD, is important and can only be done on a case-by-case basis. Because there may be a much lower threshold for hypersensitized individuals, individualized counselling and tailored advice from dermatologists is needed. In these cases, regardless of any regulatory restriction, education and awareness are the best approach because special care and appropriate precautions (e.g. using protective cases, wearing gloves, using specific products) are necessary to avoid exposure to nickel-releasing articles.

Appropriate materials in appropriate applications

Because the NI’s philosophy is “appropriate materials in appropriate applications”, NI shares the concern about the need to protect people by preventing nickel sensitization and avoiding NACD. If the use involves direct and continuous prolonged skin contact, then only low nickel-releasing materials should be used to avoid nickel sensitization and NACD. Because it is the rate of nickel release (and not nickel content itself) that is the relevant factor, articles may contain nickel but not cause a nickel-allergic reaction. For example, nickel-containing stainless steels are used in the manufacture of high quality watches that do not cause nickel allergy. These stainless steels contain between 9% to 28% nickel and are very resistant to corrosion, so do not release nickel in amounts that cause nickel sensitization or NACD.

Nickel allergy and EU restriction (REACH, Entry 27, Annex XVII)

Since 1994, the EU has established legislation to restrict the use of nickel in articles intended for direct and prolonged skin contact. The restriction was first established by Directive 94/27/EC (the so called Nickel Directive) and subsequently incorporated into REACH (Annex XVII, Entry 27). The aim was to prevent the general population from becoming sensitized to nickel and to reduce NACD reactions in most nickel-sensitized individuals. To this purpose, the Regulation provides that “Nickel and Nickel compounds shall not be used:

a. in any post assemblies which are inserted into pierced ears and other pierced parts of the human body [body piercings] unless the nickel release […] is less than 0.2 μg/cm²/week

b. in articles intended to come into direct and prolonged contact with the skin such as: earrings, necklaces, bracelets and chains, anklets, finger rings, wrist-watch cases, watch straps and tighteners, rivet buttons, tighteners, rivets, zippers and metal marks, when these are used in garments, if the Nickel release rate from the parts of these articles coming into direct and prolonged contact with the skin is greater than 0.5 μg/cm²/week”.

Articles cannot be placed on the EU market unless they comply with this requirement, in accordance with the relevant CEN standards on nickel release testing (e.g. EN 1811; EN 12472; EN 16128).
The interpretation of “prolonged skin contact” – ECHA definition

The text of the Regulation does not provide an explicit definition of “prolonged contact with the skin”. Over the years, the issue of its interpretation has been raised by some stakeholders. In April 2014, REACH Competent Authorities (CARACAL) endorsed a first guidance definition of “prolonged contact with the skin” developed by the European Chemicals Agency (ECHA). This guidance definition was based on a literature review of limited available relevant information. According to this ECHA definition, prolonged contact is defined as contact with the skin of potentially more than:

- 10 minutes on three or more occasions within two weeks, or
- 30 minutes on one or more occasions within two weeks.

Before and at the CARACAL meeting in April 2014, NiPERA (NI’s scientific division) provided detailed comments on the proposed ECHA guidance definition highlighting that the definition was derived from limited existing data and based on conservative assumptions not substantiated by clinical data.

NiPERA “prolonged skin contact” study results

To address the lack of clinical data for time of exposure, NiPERA sponsored a human patch testing study. The study protocol used patch testing in nickel-sensitized individuals to determine the time it takes a significant number of these patients to elicit NACD. From this scientific data it is possible to derive a clinically meaningful definition of prolonged skin contact. As discussed in greater detail below (see page 19), the results of the first phases of this study demonstrate that the ECHA guidance definition of “prolonged contact” is not consistent with clinical reactivity for nickel metal. Furthermore, as a result of this research thus far, “prolonged contact” should be defined as:

- more than 2 hours for one occurrence within two-weeks; or
- more than 30 minutes for three occurrences within two-weeks.
Following the adoption of the ECHA guidance definition of “prolonged contact” by CARACAL and a request from them, the European Commission mandated ECHA to provide further practical guidance on the application of the nickel restriction and the interpretation of “prolonged skin contact”, including development of a non-exhaustive list of articles to be considered as falling in the scope of the restriction as well as a list of articles to be considered as outside of the scope. The draft Guideline list was published by ECHA in January 2017 and was subject to a call for comments until April 2017. A new version (October 2017) was presented by ECHA for discussion at the CARACAL meeting in November 2017. The draft Guideline list of items in the scope is very long and contains a wide range of articles (Annex 1 Table 2) and parts of articles (Annex 1 Table 1) which, so far, were not considered within the scope of the restriction.

EXAMPLES OF ARTICLES PROPOSED TO BE WITHIN THE SCOPE OF RESTRICTION

**GRIPS:** umbrellas, scissors, garden (e.g. spades, shovels, rakes) and gym (e.g. dumbbell/kettlebell) tools and equipment, bikes and kick scooters.

**HANDLES:** prams, golf clubs, garden equipment (e.g. lawnmower, trimmer) handles of home equipment (e.g. vacuum cleaner).

**SEATS/ BACKS/ ARM RESTS:** of chairs or similar furniture.

**RUDDER TILLERS, STEERING WHEELS:** for boats, ships, cars and other vehicles.

**TOOLS AND UTENSILS USED BY HAND:**

**ARTICLES:** needles, pins, thimbles, knitting needles, crochet hooks, manicure/pedicure tools (e.g. nail files), tweezers, pencil sharpeners, keychains, key rings, key fobs, trays, mugs (including thermos mugs).

**HOLDING AREA:** writing instruments/mechanical pencil/ball point pens; mugs (including thermos mugs), tools (e.g. pocket knives, knives, hammers, spanners, pliers, screwdrivers, chisels, wrenches).

**HAND HELD EQUIPMENT AND DEVICES:**

**OUTER CASE OR HOLDING AREA:** cameras, calculators, dictation machines, electric razors, electronic cigarettes, cigarette mouthpieces, whistles, flashlights, compasses, hair dryers, straighteners, curlers, other handheld equipment.

**HOLDING AREA:** Fishing and hunting equipment (including sports weapons).

---

4. CARACAL is an expert group of the European Commission composed by representatives of national REACH and CLP Competent Authorities.
Nickel Institute’s comments on ECHA draft Guideline list

With a view to constructively contributing to the efforts to find effective, and evidence-based solutions to reduce NACD, NI submitted general and specific comments on the draft Guideline to the ECHA public consultation and on the revised version presented at the CARACAL meeting. Below is a summary of the NI views and position, with suggestions for a possible way forward.

1. ECHA draft Guideline list is well intended but misses the focus

While NI fully supports the existing nickel restriction and understands the need to provide practical guidelines to stakeholders and competent authorities for compliance and enforcement, there are remaining concerns about the approach of ECHA draft Guideline list (as of October 2017).

As it stands, the ECHA draft Guideline list of articles will lead to legal uncertainty (because of the use of undefined terms and the listing of general categories), may result in unnecessary product changes and nickel stigmatisation, and most importantly, are unlikely to deliver any meaningful reduction of nickel sensitization or prevention of NACD.

2. Extension of the Regulation’s scope without justification

While the nickel restriction itself does not provide an explicit definition of “prolonged skin contact”, the non-exhaustive original list of articles included in Entry 27 (REACH Annex XVII) provides a clear pattern of exposure. The examples given in the original list within the EU nickel restriction are clearly intended to come into prolonged contact with the skin for several consecutive hours. As such, the original list provides an insight and understanding of what the legislator considered to be “prolonged skin contact” to prevent nickel allergy when the restriction was adopted in 1994. In this regard, they were scientifically correct.

The draft ECHA Guideline list contains many articles which go beyond the scope of the restriction as originally intended and properly framed. Indeed, the draft Guideline list goes beyond even the ECHA guidance definition of “prolonged contact” endorsed by CARACAL in 2014. It includes articles that are not expected to be in continuous prolonged skin contact for the relatively short time of 10 minutes (on 3 or more occasions within 2 weeks) or 30 minutes (on 1 or more occasions within 2 weeks). As stated in Section 2.3 of the draft Guideline list, the skin contact “needs to be continuous and not consisting of several discontinuous short periods of contacts”. The list includes many items that clearly do not fulfil these criteria under their intended use. The Guideline list does not represent a proper legal interpretation of the existing nickel restriction.

Furthermore, and even more important than the proper legal interpretation of the nickel restriction, the draft ECHA Guideline list contains many articles for which there is no scientific justification. The lengthy list of articles, including items that are inappropriate and irrelevant to nickel allergy (e.g. handles of golf clubs, pencil sharpeners) will undermine the credibility and the quality of the list as a whole. Indeed, it will divert the focus from the items (earrings, buttons on clothing, other jewellery, wrist watches, zips) which are understood to be the primary causes of nickel sensitization and NACD when non-compliant with the existing nickel restriction.
3. The draft Guideline includes items that are not clinically relevant per DEPA study

The draft ECHA list does not consider the findings of a 2016 independent survey carried out by the Danish Environmental Protection Agency (DEPA) to better understand possible causes and exposures leading to nickel allergy.5.

The results of the DEPA survey indicate that most reported as causes of sensitization and first-time NACD are the following five articles categories:

- earrings
- buttons on clothing
- wrist watches
- “other jewellery”
- zips

The DEPA survey notes that “earrings still seem to play a major role” and on page 9 notes “random samples have shown that 15-20% of investigated earrings” do not seem to be compliant as they “released larger amounts of nickel than permitted”.

These articles are all items which are already explicitly listed in Entry 27. On the other hand, other articles that are not listed in Entry 27 and are included in the draft ECHA Guideline list, are not reported in the DEPA survey as causing NACD. These other articles are considered as “relatively rare causes”.

---

<table>
<thead>
<tr>
<th>Item</th>
<th>Woman (N=276)</th>
<th>Men (N=18)</th>
<th>Total (N=294)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at first rash</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median; 25/75</td>
<td>16 years 12-25</td>
<td>18 years 25-50</td>
<td>16 years 13-25</td>
<td></td>
</tr>
<tr>
<td>Items causing first-time rash</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Earrings</td>
<td>187 (67.8%)</td>
<td>3 (16.7%)</td>
<td>190 (64.6%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Buttons on clothing</td>
<td>153 (55.4%)</td>
<td>3 (16.7%)</td>
<td>156 (53.1%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Wrist watches</td>
<td>142 (51.4%)</td>
<td>10 (55.6%)</td>
<td>152 (51.7%)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Jewellery</td>
<td>138 (50%)</td>
<td>4 (22.2%)</td>
<td>142 (48.3%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Zips</td>
<td>65 (23.6%)</td>
<td>1 (5.6%)</td>
<td>66 (22.4%)</td>
<td>n.s.</td>
</tr>
</tbody>
</table>


---

4. Non-compliance in articles already explicitly listed in Entry 27

These DEPA findings confirm that non-compliant body piercings, earrings, buttons on clothing, wrist watches, jewellery, zips and, i.e., low-quality/high-nickel releasing items are still the primary cause of nickel sensitization and first time NACD.

Other studies also find lack of compliance in different countries6. Below are outlined a few examples taken from peer-reviewed publications, some recent market surveillance investigations and studies:

4.1. Peer-reviewed publications

- **Biesterbos et al., 2010**
  Nickel release was assessed from 659 items covered by the EU nickel restriction using the dimethylglyoxime (DMG) test. Results showed that 9% of the tested items released nickel according to the DMG test. A high proportion of these nickel-releasing items were purchased at haberdashery shops (34%) and street markets (61%).

- **Biesterbos et al., 2011**
  This study tested a broad selection of items in The Netherlands which are covered by the Nickel Directive. In total 505 items were tested, with 12% of the items being DMG-positive. Items from street markets (16 positive/28 tested) and haberdashery shops (11 positive/23 tested) tested positive with the DMG.

- **Schnuch et al., 2011**
  Different parts of 609 items of costume jewellery purchased in Germany were analyzed for nickel release using EN 1811:1998+Al:2008 in five official German laboratories of food and non-food investigation. Of the post-assemblies, 14.4% exceeded the migration limit of ≥0.2 µg Ni/cm² per week. In other articles with direct and prolonged skin contact, 5.6% of decorative parts and 9% of clasps exceeded the migration limit of ≥0.5 µg Ni/cm² per week. These values include the application of the adjustment factor of 0.1 included in the methodology of EN1811 at the time of testing.

- **Thyssen et al., 2011**
  Random inexpensive metallic earrings were purchased from stores and vendors in London and Warsaw. DMG testing of earrings in London and Warsaw revealed 15.1% (n = 205) and 18.4% (n = 206) of earrings were DMG-positive. DMG test-positive jewellery were mainly purchased from street markets and from stores that were not part of national or international chains.

- **Krecisz et al., 2012**
  DMG testing was done on 399 metal accessories. Of these metal items, 26.1% were DMG positive, including 10.0% of earrings, 11.4% of snaps, and 56.2% of belt buckles.

It should be noted that most testing in the above-mentioned peer-review studies were performed using the DMG screening test. It is acknowledged that the DMG test is not definitive (as it can give a significant rate of false positive and false negative results). However, it can give an indication of lack of compliance.

---

6. Biesterbos et al., 2010; Schnuch et al., 2011; Biesterbos et al., 2011; Thyssen et al., 2011; Krecisz et al., 2012.
4.2. RAPEX Notifications involving nickel

According to the EU RAPEX system, for the years 2014-2016, most products notified for non-compliance with the EU nickel restriction were low cost, costume jewellery items imported from non-EU countries.

4.3. Results of Dutch market surveillance investigation

A recent market surveillance research undertaken by the Dutch Consumer and Product Safety Authority on metals in jewellery (necklaces and earrings) found that 4 out of 52 earrings were non-compliant with the restriction on nickel release according to the EN 1811 release test.

4.4. Danish EPA Report

As mentioned earlier, the 2016 Danish EPA study (see Introduction, page 9) notes that “random samples have shown that 15-20% of investigated earrings” do not seem to be compliant as they “released larger amounts of nickel than permitted”. Given this level of non-compliance, earrings alone (not including other jewellery items) could account for the majority of the persistence of nickel allergy prevalence amongst the young female population, as piercings are known to be a primary cause of nickel allergy.

5. Compliance and enforcement

Overall, the weight of evidence shows a notable lack of compliance with the existing nickel restriction. It is difficult to understand how extending the articles subject to the nickel restriction as set out in the draft Guideline list will improve compliance when these articles only give rise to relatively rare occurrences of sensitization and NACD. The critical articles (Entry 27) that do give rise to significant occurrences of sensitization and NACD are already listed in the nickel restriction. For this reason, NI supports the DEPA survey’s recommendation that focus should be put on “market-place inspections” on those items, such as earrings and other significant known causes of nickel allergy.

Rather than extending the list of articles, it seems the existing nickel restriction needs to be enforced more effectively. In fact, extending the list of articles, may result in existing enforcement becoming less effective. Enforcement authorities will be applying scarce resources for market-place inspections of articles which are not significant sources of nickel sensitization or NACD. This will result in fewer resources available for market-place inspections focused on the already well-known articles primarily responsible for nickel sensitization and NACD and which are those already explicitly mentioned in the nickel EU restriction (Entry 27).
6. Inclusion of articles in the ECHA Guideline should not be based only on few case studies

The nickel restriction is aimed at the total population rather than the hypersensitized. The objective of the nickel restriction is to prevent individuals from becoming sensitized to nickel and to avoid NACD to the extent possible. This is supported by the fact that the nickel release limit of 0.5 µg Ni/cm²/week, derived from Menné et al. (1987) corresponded to no patch test reactivity in most nickel-sensitized individuals. Therefore, when considering what items should be included on any Guideline list of articles for restriction, the number of case reports in the context of the intended use of the article and the number of exposed individuals should be considered. If there are only one or two case reports for an article commonly used in its intended use, then it is unlikely that this use/article is a cause of nickel sensitization or NACD in a significant part of the population and it should therefore not fall into the scope of the restriction. For example, it does not seem reasonable to restrict nickel in items such e.g. keys, which have been safely used by hundreds of millions of people for decades in Europe, on the basis of potential inappropriate uses of the article.

Of course, some cases are published in scientific journals precisely because they are rare. Typically, such rare cases involve individuals who, unfortunately, are hyper-sensitized. These individuals represent a very small portion of the total population and those who are sensitized to nickel. While nickel hypersensitivity can be a significant health problem for those individuals who suffer it, these individuals are normally aware of their condition and of the need to take specific precautions (e.g. using protective cases, wearing gloves, or using specific products) to avoid exposure to nickel-releasing items and, in many cases, to other allergens as well.

7. Correlation of exposure with clinical reactions to an article

While the rate of nickel release is certainly of interest under the correct exposure scenarios, the ultimate measure to assess if an article can be a cause of nickel sensitization or NACD is the correlation between exposure and clinical experience. A significant number of nickel allergic reactions should be evident from high nickel-releasing articles in order to demonstrate that these articles are a substantial source of nickel allergy or NACD.

8. DMG test results alone should not be used to support inclusion of articles in the ECHA guideline list

Without knowing the pattern of exposure, nickel release alone is not definitive in determining if an item will cause nickel allergy or NACD. Before concluding that an article is a significant source of nickel sensitization or NACD, an appropriate pattern of use involving direct and continuous prolonged contact with a substantial number of nickel allergic reactions should be observed.

The DMG test for nickel release has a significant rate of false positives and false negatives. The DMG test is not a reliable test for predicting nickel allergy. For this reason, it has not been approved for use in testing of articles for compliance with the existing nickel restriction. It logically follows that results from any DMG testing should not be used as definitive evidence of nickel release rates or form the basis for including articles on the draft ECHA Guideline list.

7. The DMG (dimethylglyoxime) is a screening method to test for nickel release from alloys and coating.
Nickel Institute’s position: How to address the problem?

1. More education and awareness

Firstly, education and awareness play an important role. Sharing information which leads to informed decisions is key to better understanding and preventing nickel sensitization and NACD. It is essential to avoid nickel sensitization in first instance. This can be done by focusing on the main causes of nickel sensitization, i.e. those five article categories that are in direct and continuous prolonged skin contact for hours. In some cases, (e.g. people hypersensitive to nickel) extra measures may be required. In all cases, more education and awareness will assist everyone to avoid sensitization and NACD.

2. Eliminating leading causes of nickel sensitization

Five main article categories:
- Earrings
- Clothing buttons
- Wrist watches
- “Other jewellery”
- Zips

Given the limited resources available to regulators, which must enforce many restrictions on many materials, and given the complexity and time needed for nickel release testing (EN 1811 standard, etc.), it is crucial that enforcement focuses on those article categories that are clinically relevant and are primarily associated with nickel sensitization. Focusing on the main article categories causing nickel sensitization – rather than extending the Guideline list to articles which are not clinically significant - will lead to further decreases in nickel allergy and NACD.

Putting this another way, extending the interpretation of the existing nickel restriction to other articles which are not clinically relevant to nickel allergy will not bring any health benefit. In fact, this will likely be counterproductive by diverting enforcement resources to articles which are not clinically relevant causes of nickel sensitization.

3. Better enforcement of existing legislation to improve compliance

The main categories of potentially non-compliant articles are well documented. To further reduce nickel sensitization and allergy prevalence robust and proper enforcement of the existing EU nickel restriction is needed. This will lead to improved compliance preventing articles from being placed on the market.
**REF-4 Enforcement project**

In this context, it is important to look carefully at the outcome of the coordinated REACH enforcement project (REF-4) launched in 2016 at the EU level, in cooperation with Member States, to check compliance with a number of REACH restrictions, including on nickel release in articles in prolonged skin contact. The findings of the 2016 compliance checks, published in February 2018, show that 8% of tested jewellery items and 11% of metallic parts of clothes were not compliant with the nickel release limits.

Nickel Institute welcomes similar efforts to further improve enforcement and compliance with the existing EU nickel restriction. To better understand the current situation, NI has launched a research project to investigate compliance of articles in the scope of the existing nickel restriction and available in the EU market. Results are expected in the first half 2018.

**Nickel Institute's recommendations:**

1. More education and awareness
2. Eliminating the leading causes of nickel sensitization
3. Better enforcement of existing legislation to improve compliance
NiPERA research project on “prolonged skin contact”

Over the last years, NiPERA supported further research to understand remaining uncertainties around NACD. A study launched by NiPERA in 2015 was designed to determine what time is needed to elicit a nickel allergic reaction and better define the meaning of “prolonged contact” in the context of the nickel restriction. This is essential, as the ECHA 2014 guidance definition of “prolonged contact” was based on available information at that time, which was not aimed at defining prolonged contact for NACD and, therefore, made several overly conservative assumptions.

This study is being carried out on behalf of NiPERA by an independent dermatologist, Dr. Rosemary Nixon⁸. Results of the Phase 1 and 2 testing have been summarized in a scientific paper and were submitted to a peer-reviewed journal in November 2017.

Phase 1 results

The aim of the first phase of the project was to explore the definition of prolonged contact by testing nickel metal on nickel sensitive individuals for varying times, including those of ECHA guidance definition of prolonged contact. The results of the first phase of the project were presented at the meeting of the European Society of Contact Dermatitis in Manchester (September 2016).

The research found that 15 out of 19 nickel allergic patients reacted to nickel metal discs after a 48-hour patch testing. At the same time, only one out of 20 nickel-sensitive patients reacted to a 30-minute contact time (but not to the 10-minute application of the discs). According to the study, it would appear that the vast majority of nickel-allergic subjects do not react to repetitive exposure to nickel of 10 minutes on 3 occasions over 2 weeks. The outcome, therefore, indicates that the ECHA guidance definition of “prolonged contact” is not consistent with clinical reactivity for nickel metal.

Phase 2 results

A second phase of the project was launched at the end of 2016, using nickel-plated brass discs for patch testing of nickel-sensitized individuals. The aim was to generate additional data, testing the patients with a material (nickel-plated brass discs), which is considered as more representative of those items on the market which can cause NACD. The results showed that 22 out of 25 patients (88%) were positive to a 48-hour patch testing with the Ni-plated brass discs. However, there was no consistent reaction of any tested individuals at any of the shorter contact times.

The study findings highlight, once again, that the 2014 ECHA guidance definition of “prolonged contact” is not supported by clinical data and is therefore not scientifically accurate. As a result of the research thus far, prolonged contact should be defined as contact with the skin for:

- more than 2 hours for one occurrence within two-weeks, or
- more than 30 minutes for three occurrences within two-weeks.

⁸. Associate Professor, Occupational Dermatology Research and Education Centre, Skin and Cancer Foundation, Carlton, Melbourne, Australia.
Next steps – phase 3

It is desirable to perform further testing for longer time periods to determine a clinically relevant definition of “prolonged contact” for NACD reactions. NiPERA intends to pursue the research and share the final results, with ECHA, the European Commission, competent authorities and stakeholders.

The outcome of this project will deliver useful data to increase the knowledge around NACD and contribute to the adoption of a more scientifically robust and clinically relevant definition of prolonged contact.

NiPERA research on sources of nickel allergy and NACD in North America

To better understand the sources of nickel allergy and NACD, a clinical database study was initiated to find out the prevalence of nickel allergy, incidence of NACD, and types of articles causing NACD as correlated with a number of different factors. These include age, gender, race, body site of dermatitis, atopic dermatitis, hay fever, asthma, and occupational related dermatitis.

NiPERA compliance survey

In order to better understand the causes of nickel sensitization and the persisting prevalence of nickel allergy in Europe, particularly in female children, in 2018 NiPERA is carrying out a research project to investigate the degree of compliance with the nickel restriction of articles on the EU market. The focus of the survey will be on: those articles that are understood to be amongst the main causes of nickel sensitization, are aimed at children and are already listed in the existing EU restriction (Entry 27). The results will be a further useful piece of information to better understand the extent of compliance with the existing EU nickel restriction.

Education, dialogue and awareness raising

Education, awareness-raising and further scientific research are all very important parts of the way forward. NI supports the communication of accurate information about nickel allergy and, via our scientific department (NiPERA), it is committed to develop new scientific research. In this context, NI has recently conducted three nickel dermatitis workshops, in Brussels (June 2015 and June 2017) and Chicago (June 2016), to improve knowledge and communication between stakeholders. (Reports on these workshops as well as other communication materials, including our NACD infographic, fact sheet, etc. can be found in the Annex to this Position Paper).
Industry views and experience

A reality check is needed

In our view, the ECHA draft list of articles (as of October 2017) is “speculative”, based on many assumptions, and not scientifically justified. A reality check is needed. If all the articles listed in the ECHA draft guideline list, some of which are used every day by millions of people, were real causes of nickel allergy, how is it then possible that only between 1-2% of men are sensitized to nickel? Most articles included in the ECHA draft list are used by both men and woman (e.g. pencil sharpeners, key fobs, gym tools, pencils) and some (e.g. hand tools) may even be used more by men than women. However, the prevalence of nickel allergy is substantially higher in the female population (around 12%-15%). This seems to indicate that items generally more used by women than by men, such as pierced earrings and other jewellery, are likely to be the primary causes of nickel sensitization.
NI and the nickel industry fully support the need to protect people from becoming sensitized to nickel and prevent NACD in already nickel-sensitive individuals. Nickel allergy prevalence can be further reduced by better education, enforcement and compliance as well as improved knowledge about NACD and - what is crucial - by the use of appropriate materials in appropriate applications. If the use involves direct and continuous prolonged contact with the skin, then only low nickel-releasing materials should be used.

The nickel industry does not support the use of nickel in applications and materials that cause nickel sensitization. This is the case, first and foremost, for ethical reasons and the need to protect public health. In addition, it also makes good sense for commercial reasons. The amount of nickel which may be present in non-compliant and poor-quality articles that are the main problem for nickel allergy (e.g. pierced earrings) is minuscule compared to overall global nickel production and use. It is certainly not in the interest of the nickel industry to have a small amount of nickel creating a public health problem such as nickel allergy, which significantly contributes to nickel stigmatization and can lead to disproportionate regulatory measures unnecessarily affecting the use of nickel in safe materials and applications.

What materials are appropriate?

When it comes to direct and continuous prolonged skin contact, there are many options available, depending on the application, the type of articles and their use as well as other factors such as performance required, cost, material availability, market preference and regulatory requirements (other restrictions, etc.).

Because it is the rate of release of nickel (and not nickel content itself) that is relevant in determining whether there is a risk for NACD, articles may contain nickel but not cause an allergic reaction.

Whatever materials are used, the key principle to prevent nickel sensitization and NACD is that articles in the following categories must not release nickel at a higher rate than that indicated (when tested in accordance with EN 1811 and other relevant EN standards):

- Items with piercing posts such as those used for earrings must not release more nickel than 0.2 µg Ni/cm²/week; and
- Items in direct and continuous prolonged contact must not release more nickel than 0.5 µg Ni/cm²/week.

For example, “surgical” stainless steel (SS 316L) contains 10-15% nickel and does not release nickel at a rate of more than 0.2 µg Ni/cm²/week. Surgical stainless steel is therefore regarded as appropriate for use in articles in either category. For example, the ASTM Standard Consumer Safety Specification for Adult Jewelry (Designation: F2999-13) and Children’s Jewelry (F2923 – 14) list surgical stainless steel as one of the approved materials for adult and children’s body-piercing jewelry, respectively.
Summary conclusions

The ECHA draft Guideline list of articles (as of October 2017) is not scientifically justified and should be significantly amended to be more relevant, proportionate and effective. If adopted in its current form, it would result in an unnecessary and unjustified extension of the scope of the restriction to articles which are not clinically significant, without bringing much (if any) public health benefit, while diverting enforcement resources away from the primary causes of nickel sensitization and NACD.

The trends of nickel allergy prevalence over the last decade in Europe support the understanding that the existing EU restriction can be effective if the legislation is complied with and enforced. From a public health and public policy point of view, it is crucial to prevent the general population from becoming sensitized in the first place.

What remains paramount are more education and awareness of all stakeholders. To protect people and further reduce nickel allergy prevalence, the focus should be on prevention, eliminating the leading causes of nickel sensitization and improving compliance and enforcement of the existing restriction, to prevent potentially harmful articles from being placed on the market. This can be achieved by focusing on the five article categories reported to be the main causes of nickel sensitization.

To prevent nickel sensitization and to avoid NACD, education, awareness and the use of appropriate materials in appropriate application are crucial.
References


Danish EPA, 2016. An investigation of causes of nickel allergy. (link)

European Chemicals Agency, 2018. FORUM REF-4 PROJECT REPORT Harmonised Enforcement Project on Restrictions. (link)

EN 1811:2011+A1:2015: Reference test method for release of nickel from all post assemblies which are inserted into pierced parts of the human body and articles intended to come into direct and prolonged contact with the skin.


EN 16128:2015: Ophthalmic optics - Reference method for the testing of spectacle frames and sunglasses for nickel release.


Annexes

Nickel Institute’s meeting Report, “Workshop on EU nickel restriction, Brussels, June 2017” - link
Presentation on Nickel dermatitis and NiPERA scientific research on “prolonged contact” - link
Nickel Institute’s meeting Report, “Workshop on EU nickel restriction, Brussels, June 2015” - link
Nickel Institute’s meeting Report, “Workshop on nickel dermatitis, Chicago, June 2016” - link
Nickel Institute’s infographic on Nickel Allergic Contact Dermatitis - link
Nickel Institute’s position statement on piercing materials - link
NiPERA Fact Sheet on Nickel Allergic Contact Dermatitis - link
The Nickel Institute is the global association of leading primary nickel producers. Its mission is to promote and support the use of nickel in appropriate applications. NI grows and supports markets for new and existing nickel applications including stainless steel; and promotes sound science, risk management, and socio-economic benefit as the basis for public policy and regulation.

Through its science division NiPERA Inc. (www.nipera.org), we also undertake leading edge scientific research relevant to human health and the environment.

NI is the centre of excellence for information on nickel and nickel-containing materials and has offices in Asia, Europe and North America.