WORKSHOP ON NICKEL DERMATITIS

Chicago, Illinois, June 2016
Meeting report

Nickel INSTITUTE
knowledge for a brighter future

Contents

Executive summary

The Workshop on Nickel Dermatitis was the first event of its kind in North America, bringing together a wide range of stakeholders with the common goal of reducing the prevalence of nickel allergy and incidence of nickel allergic contact dermatitis (NACD). Hosted by the Nickel Institute, the workshop provided a forum for a free exchange of information and views on the causes and pathways for prevention of nickel allergy and NACD.

Although nickel is a weak sensitizer, the sheer number of nickel-releasing items which are available -principally jewelry- mean that a significant proportion of the general population (10-15% of women and 1-3% of men) is sensitized (allergic) to nickel. However, the condition is preventable.

During the workshop, there was consensus among the toxicologists and clinicians present that there is a strong association between body piercings and nickel sensitization. It is unknown whether it is the piercing itself or direct and prolonged contact with jewelry that induces sensitization. When items that release nickel are in direct and prolonged contact with the skin, and enough nickel ions (above the threshold) are able to penetrate the skin, individuals can become sensitized. Once sensitized, a lower amount of nickel is required to trigger an allergic reaction (lower threshold) than that required for the original sensitization to occur.

The mechanism of nickel allergy and the key role nickel plays in so many applications essential for everyday life was explained. Stainless steels were highlighted as materials used for many important items of everyday use that contain nickel but do not release a sufficient amount of nickel to cause nickel allergy or NACD reactions. Inappropriate uses of nickel were also discussed, and the Nickel Institute expressed the view that nickel is not an appropriate material for use in jewelry and other prolonged skin contact applications unless it is contained in a low nickel-releasing material such as surgical stainless steel.

Three potential pathways were identified to reach the common goal of prevention of nickel allergy:

- Communication by clinicians
- Communication by industry
- Regulatory interaction

Valuable lessons were drawn from the European experience where regulation has been in place for over 20 years. While there is evidence of a decrease in the prevalence of nickel allergy in some countries, the process of development and implementation of the regulation and its associated test methods has often been difficult and frustrating for those involved. Participants at the workshop were urged to consider the unintended consequences as well as benefits of the EU regulation in the context of any potential regulation in North America, as well as the effectiveness of voluntary versus mandatory standards.

Throughout the day there was an emphasis on preventing nickel sensitization and NACD in children. There is some evidence from countries in Europe that there is less prevalence of nickel sensitization in younger portions of the population since the nickel restriction was implemented but concern remains that the decrease was not enough.

There was agreement among the participants that the sharing of knowledge about nickel and nickel allergy is in itself useful and that the workshop had brought together a wide range of stakeholders who do not usually have a chance to meet and share ideas. Relationships were established for further communication and collaboration.

Nickel and nickel allergic contact dermatitis (NACD)

It is nickel release, not nickel content, which influences the potential to cause nickel allergy and NACD

====

NACD is caused by corrosion of an article releasing sufficient amount of nickel ions onto the skin

====

Nickel-containing articles can safely come into direct and prolonged contact with the skin as long as they are highly corrosion resistant, thereby not releasing sufficient nickel for a nickel-allergic reaction

Source: Nickel Institute

Goals

Facts, understanding and prevention of nickel dermatitis

The workshop provided a unique occasion for a wide range of stakeholders to gather to discuss, in an open forum, their views and experiences, as well as their concerns and expectations regarding communication and prevention strategies to decrease prevalence of nickel allergy and incidence of nickel dermatitis in North America.

The workshop provided a:

- Historical overview of nickel allergy in North America and Europe
- Outline of how and why nickel is used
- Description of the science of nickel allergy
- Forum for cooperative and constructive communication between stakeholders to share their perspectives
- Briefing on Nickel Institute's ongoing scientific research

Introduction & overview

SETTING THE SCENE & AIM OF THE WORKSHOP

Dr. Kate. Heim, NiPERA Inc.

NiPERA's Dr. Kate Heim, host of the event, welcomed participants and explained that during the day they would hear a lot about the appropriate use of nickel. "Nickel allergy is a concern for the nickel industry. We are interested because it is causing a consumer problem for a material that is a very good material in appropriate applications." She added that the day would provide the opportunity for the participants to update each other on their respective fields, share expertise and discuss paths to achieving a common goal to decrease this "unnecessary problem" of nickel allergy and NACD.

The occasion was all about bringing together people who don't traditionally get a chance to meet: scientists, dermatologists, manufacturers. The aims were to embrace the different views and see how we can move forward to achieve a common goal of decreasing the prevalence of nickel allergy and instances of NACD in North America.

The meeting was chaired by Dr. David Basketter, DABMEB

History of nickel allergy in North America

1889

First occupational cases 'galvanization eczema' in the plating industry (Blaschko Germany)

Early 20th Century

Workers in the plating industry and miners

1931

First non-occupational cases - spectacles frames

Overview of the issue

HISTORY AND PRESENT NACD PREVALENCE, NORTH AMERICA

Dr. Jennifer Chen, Stanford University

For the last 70 years, nickel has been the most common confirmed allergen worldwide. Risk factors include female gender, young age, smoking, and ear piercing. The most common manifestation of nickel allergy is allergic contact dermatitis, which impacts quality of life and carries an enormous economic burden. Although the original cases of nickel dermatitis were primarily occupational, currently sources of nickel exposure and/or sensitization range from jewelry and clothing items, to electronics, toys, coins, tools, medical implants, and diet.

Currently, nickel sensitization is a major cause of contact dermatitis in the North American population, and no nickel regulations exist. The prevalence of nickel allergy has significantly increased over recent decades, and interest in nickel allergy has been growing in the medical community and in consumers alike. Reasons for the rising prevalence of nickel allergy include ready availability of nickel-releasing items used in direct and prolonged contact, lack of awareness of nickel allergy, import of items from other countries such as China, continued introduction of new consumer sources of nickel exposure, and lack of regulation of nickel release.

> “10-30% of inexpensive jewelry releases nickel in concentrations that may result in dermatitis”
>
> Dr. J. Chen

1930s-60s

nickel plated stocking suspenders

1970s-Today

Jewelry: earrings, necklaces, and spectacles

Clothing Items: belt buckles, buttons, clasps

Electronics: excessive nickel release identified in 18-45% of early mobile phones

Diet: 1% of nickel allergic patients may have a reaction to the lower nickel limit of a typical diet

Implants: some sensitizing related to medical implant failure

HISTORY AND PRESENT NACD PREVALENCE, EUROPE

Dr. David. Basketter, DABMED Consultancy Ltd

Nickel dermatitis in Europe was first recognized as a problem in occupational settings, such as nickel plating, but decreased after risk management practices were put in place. Recognition of nickel dermatitis as a significant problem in the European general public, primarily females through jewelry, led to regulation in Denmark (1990) and Sweden (1991), followed by the European Union (EU) in 1994.

The EU "Nickel Directive" was based on the Danish and Swedish regulations to restrict objects intended to come into direct and prolonged skin contact. As the regulation evolved, it was updated with testing and restriction based on nickel release (not nickel content).

The Nickel Directive was subsumed as a restriction under the EU REACH Regulation. It was complemented by an update of the methodology for release testing as well as a by a specific standard for testing spectacles and, more recently, by a guidance definition of "prolonged skin contact".

An indicative list of the types of items that fall under the regulation is being developed to help with enforcement.

Nickel is still a major cause of contact dermatitis amongst the EU population. However, there is evidence that in parts of Europe (Denmark, Sweden, Germany, UK) the prevalence of nickel sensitization for the youngest age group has decreased. Despite the appearance of new sources of exposure such as mobile phones, laptops and toys, piercings remain responsible for much of the nickel allergy.

REGULATORY EFFORTS IN EUROPE

1990	Denmark	Objects intended for prolonged skin contact restricted to release of <0.5µg nickel/cm²/week
1991	Sweden	Ear piercing with nickel-containing piercers or studs was banned if the article contained >0.05% nickel
1994	EU Nickel Directive	Objects intended to come into direct and prolonged contact should not release >0.5µg nickel/cm²/week. Items inserted into piercings may not contain >0,05% nickel
2004	EU Nickel Directive	All items inserted into piercings limited to <0.2µg nickel/cm²/week
2009	REACH Regulation	Mobile phones considered as covered by the nickel restriction (ECHA guidelines)

Current European situation

- Nickel remains a major cause of contact dermatitis amongst EU population
- 10 - 15% of women, 1 - 3% men nickel sensitized in the general population - depending on the country and age group
- Nickel metal has a harmonized EU classification as Category 1 skin sensitizer
- Alloys containing nickel are classified for skin sensitization when the release rate of 0.5 µg Ni/cm²/week, as measured by the European Standard reference test method EN1811, is exceeded
- Evidence that in parts of Europe (Denmark, Sweden, Germany, UK) the prevalence of nickel sensitization for youngest age group has decreased

> “Piercings remain responsible for much of the nickel allergy.
>
> Dr. D. Basketter”

Properties & applications

> Certain nickel-containing materials which are corrosion resistant can be safely used in contact with skin
>
> G. Coates

PHYSICO-CHEMICAL PROPERTIES OF NICKEL, USES, CORROSION PROCESS

Gary Coates, Nickel Institute

Nickel is used extensively in our modern world. It is a cost-effective material used mostly as a component in alloys, although sometimes used as essentially pure nickel or as chemical compounds. The properties that nickel provides (corrosion resistance, ductility, ability to withstand extreme temperatures) explains why it is so commonly found in goods we use every day as well as in many other essential applications. We most commonly find nickel in stainless steels, a family of alloys that is used primarily for their corrosion resistance. In consumer goods it is frequently found in the materials used for surface finishing (plating) and in batteries. The degree of corrosion resistance of nickel-containing materials varies considerably. This correlates with nickel release which is an important contributor to NACD.

Nickel, corrosion and NACD

An NACD response is caused by sufficient nickel ions being released from the metal and then being absorbed into the dermal layer

====

The corrosion resistance of various materials and different alloys (e.g. SS alloys) to sweat varies considerably

====

Nickel-containing stainless steels generally have low metal release rates in sweat, but some are not low enough to pass the acceptance test (EN1811), caused by high impurity levels or poor surface condition

====

Nickel-plating normally has a higher rate of nickel release, but it is possible to lower the metal release rate through the use of various coatings on top, e.g. chromium plating. Certain coatings however may accelerate the rate of nickel release

Sensitization process

NICKEL SENSITIZATION MECHANISMS, EXISTING DATA, RESEARCH

Dr. Kate Heim, NiPERA Inc.

Nickel sensitization is a threshold reaction requiring skin exposure to a sufficient amount of nickel ions (solubilized nickel) to interact with the immune system. This is called induction. Once sensitized to nickel, sufficient amount of skin exposure to nickel ions (above threshold) can cause a nickel allergic contact dermatitis (NACD) reaction. Nickel sensitization is the condition of being allergic to nickel, which can be detected by patch testing. NACD reactions occur in nickel-sensitized (or nickel allergic) individuals, and are determined by relevance data taken at the time of patch testing to assess if the reaction is due to nickel. Nickel release (not content) is the relevant parameter for assessing potential to cause nickel allergy or NACD since it is the availability of the nickel ions released that is necessary for an immune reaction. Therefore, some nickel-containing materials are safe for use in direct and prolonged contact with the skin, such as surgical stainless steel, which contains up to 15% nickel but releases very little nickel, if any.

Nickel is a weak to moderate sensitizer, with prevalence of nickel allergy in the general population being due to frequency and type of exposure to nickel-releasing materials (e.g. jewelry), rather than a high potency of nickel as an allergen. Nickel sensitization and NACD can be prevented by avoiding direct and prolonged contact with items that could potentially release a sufficient amount of nickel to cause sensitization or a NACD reaction. Three simultaneous conditions must be true for NACD to occur: 1) direct contact with the skin, 2) prolonged contact with the skin and corrosive conditions, 3) a sufficient amount of nickel ions released above the threshold to cause an immune reaction.

> “Nickel is a weak to moderate sensitizer, with prevalence of nickel allergy in the general population being due to frequency and type of exposure to nickel-releasing materials (e.g. jewelry), rather than a high potency of nickel as an allergen.
>
> Dr. K. Heim”

Key points on nickel allergy

- Type 4 allergy is a delayed reaction which is not life threatening
- Communication of good information is important for understanding and prevention
- Prevention is the end goal: to decrease the numbers of people who are allergic to nickel and the number of NACD reactions in people who are already nickel-allergic
- Three simultaneous conditions are needed: Direct contact, prolonged contact and sufficient nickel ions must be released
- Released nickel ions must cross through the skin
- Threshold reaction – a certain amount of nickel is needed to elicit a reaction
- Amount needed to become allergic is higher than the amount needed to have an allergic reaction (e.g. NACD) once you have an allergy
- Nickel is a moderate to weak sensitizer - the numbers of people allergic to it is due to frequency and type of exposure to nickel-releasing materials (e.g. jewelry), rather than a high potency of nickel as an allergen.
- Release (not the content) of nickel is the key factor in nickel allergy and NACD
- We know a lot about nickel as an allergen – compared with some other allergens

Source: Nickel Institute

NiPERA research – what length of time does it take to elicit a reaction to nickel?

The amount of prolonged contact needed to result in nickel allergy or NACD is a question that requires more data. NiPERA is funding a research project to address this issue. Phase 1 of the research used nickel metal discs. The outcome produced results that are not conclusive and highlighted the need to generate additional data. This has led to Phase 2 of the testing where nickel-plated discs are used. This material is considered as more realistic for consumer exposure. Results will be published in a peer-reviewed journal and shared with regulatory authorities and stakeholders.

Clinician perspective

NACD IN THE CLINICAL POPULATION

Dr. Erin Warshaw, University of Minnesota

As a group, metals are among the most common contact allergens detected by patch testing in both adults and children. Of these metals, nickel has been the most widely studied. A recent review of published research found the median nickel allergy prevalence in a general European population was 8.6% (range 0.7-27.8%) and this rate was higher in patients with dermatitis. In North America, nickel is the most common contact allergen detected in patients undergoing patch testing (15.5-19.5%). Nickel allergy is considerably higher in females compared to males. This difference has been largely attributed to females' higher prevalence of piercings as nickel-containing jewelry, especially earrings, has long since been proposed as a route for nickel sensitization.

In a retrospective analysis of 9334 patients tested by the North American Contact Dermatitis Group, nickel sensitivity was statistically associated with at least one piercing (RR 2.52, 95% CI 2.26, 2.81;p<.0001) and nickel sensitivity rates increased with number of piercings (16% for 1 piercing to 32% for >5 piercings). Prevalence of nickel sensitivity was higher in females (23.2%) than males (7.1%), but the association with piercing appeared to be stronger in males (RR 2.38, 95% CI 1.72, 3.30;p<.0001) than females (RR 1.30, CI 1.13, 1.49;p=.0002). Crude analysis indicated that cobalt sensitivity was statistically associated with piercing (RR 1.63, 95% CI 1.40, 1.91;p<0.0001); however stratified analysis showed that this relationship was confounded by nickel. After adjusting for nickel sensitivity, the adjusted risk ratio for piercing and cobalt was 0.78 (NS). Chromium sensitivity was negatively associated with piercing (RR 0.60, 95% CI 0.48, 0.75;p<.0001).

> "Patients panic when they get a diagnosis. The Nickel spot kit gives some sort of guide. There are fewer positive reactions from cell phones now that we have smart phones – old flip phones were a problem.
>
> Dr. E. Warshaw"

> We know that piercings are statistically associated. This should be one of our main targets. We can prevent kids becoming sensitized.
>
> Dr. S. Jacob"

NACD IN CHILDREN

Dr. Sharon Jacob, Loma Linda University

Over the last decade, nickel allergic contact dermatitis (NACD) has been increasingly recognized in the United States. In 1986, Weston et al. reported a contact sensitization (CS) rate of 20.3% in 314 unaffected children, with 7.6% demonstrating sensitization to nickel. A smaller pilot study by Bruckner et al. (2000) demonstrated a 24.5% CS rate in unaffected children aged 6 months to 5 years with a nickel sensitization rate of 12.9% (Study limitations-small size, higher nickel rate could have reflected selection bias, increasing prevalence or difference in patch test systems). In 2008, Zug et al. and Jacob et al. published studies by two collaborative groups which reported CS rates in affected US children 56.7% and 83%, with Ni-CS rates of 28.3% and 17.5% respectively. (Study limitations size, extended 5-year time course (not point prevalence), potential selection/referral bias, and geographic limitations). Nevertheless, these are high rates, notably comparable to the rates seen in Europe prior to regulation. A more recent study by the North American Contact Dermatitis Group (Zug et al.) demonstrated CS rate of 62.3%, with Ni-CS of 28.1% (Study limitations: size, extended 8-year time course [2005-2012] (not point prevalence), potential selection/referral bias, geographic limitations). Recently, the Pediatric Contact Dermatitis Registry (PCDR) published that PCDR providers from 34 states reported 1142 cases into the database in 2015. (Goldenberg et al.) The CS rate was 65%, with a Ni-CS rate of 22%. (Study limitations: size; ~2yr time course; inter-investigator variability and training; and variability of allergen substrate (TRUE test, Chemotechnique and Allergeaze antigens utilized at the discretion of the practitioner). There was minimal referral bias, as the majority of providers tested their own patients, and minimal geographic limitations as 34 states were included.

Based on the adult general population data estimating that 11% are sensitized to nickel, it is estimated that of the 74 million children in the US, approximately 8 million children are sensitized to nickel. Not all that are sensitized will develop NACD. Piercing presents the greatest risk factor, while belts, electronics, toys, coins, and instruments are reported to be other potential exposure sources.

Several areas need further investigation. Systemic reactions to nickel in children with atopic dermatitis are likely underreported. The role of staph and filaggrin in dermal reactions remains to be fully elucidated. Patients with atopic dermatitis have increased penetration of the epidermis by allergens, which increases their risk of contracting contact dermatitis.

NACD & IMPLANTS

Dr. Kalman L. Watsky, Yale School of Medicine/Yale-New Haven Hospitals

In recent years, numerous case reports have reported metal allergy associated with failure of primarily orthopedic implants. In the US, there are many fewer patients with symptoms following joint replacement than would be expected from the known prevalence rates of 18.5% for nickel allergy, though patients with failed implants have higher metal sensitivity rates. Orthopedic implants and other implanted devices are most commonly composed of metal alloys including stainless steel (primarily 316L which contains nickel, cobalt, and chromium), titanium alloys, including nitinol (55% nickel and 45% titanium), and oxidized zirconium. The exact constituents will vary by device and manufacturer.

Changes consistent with a Type IV immunologic response have been documented in peri-implant reactions. Epicutaneous patch testing appears to be the best test for evaluation of potential metal or other reactions both pre- and post-implantation. A recommended protocol for patch testing using a baseline series and additional metal allergens based on implant composition was recently published. Testing with components of bone cement is also recommended; metal discs provided by manufacturers are not considered reliable for testing. The lymphocyte transformation test (LTT) is rarely endorsed as an alternative or supplement to patch testing by dermatologists, though it may have a future role.

In the US, pre-implant testing is only recommended for patients who give a history of reactions to metals, though screening for nickel allergy is recommended for all patients undergoing Nuss bar surgery for pes excavatum (a congenital disorder which causes the chest to have a sunken appearance). Use of titanium or oxidized zirconium is recommended for patients with a question of metal sensitivity who do not undergo pre-implant testing.

Post-implant testing should be considered for patients who present with chronic pain, skin reactions, and aseptic joint loosening or implant failure. There are outcome studies examining post-implant testing that show some benefit, though they are of small size and poorly controlled. Published guidelines exist classifying those patients who may benefit from post-implant testing using major and minor criteria. No testing is indicated for patients who are symptom-free after implantation.

“There is no reason to remove implants if there is no reaction - even if you are nickel-sensitive.

- Dr. K. L. Watsky”

Market perspective

BEST PRACTICES, HOW AND WHY NICKEL IS USED IN PRODUCTS, IMPORTANCE OF NICKEL, ACHIEVEMENTS, CHALLENGES & CONCERNS OF BUSINESSES

Marion Wilson, Assay Office Birmingham

Nickel legislation was adopted by the EU in 1995 and enforced from 2000. This was the first consumer product safety legislation applicable to jewelry and accessories. Initial testing requirements have been altered several times over 16 years and have sometimes seemed illogical commercially. The EU was initially the only territory concerned with regulating nickel. Enforcing these requirements within the Far Eastern supply chain proved extremely difficult particularly as implementation expectations across the EU were variable. There were challenges of implementation in these circumstances and AnchorCert Analytical worked hard to communicate with and educate their customers.

Initial reluctance to comply was compounded by confusion over test results. The extensive research carried out by AnchorCert Analytical, which is still ongoing, has explained many of the issues by delivering a significantly deeper understanding of factors impacting nickel release. Prescribed test standards have been informed by research and experience and modified accordingly and the EU now has a relatively robust system. The experience of the EU with regard to implementation, test methods, factors affecting nickel release and enforcement can be a valuable guide for North America.

> “The more we understand the EN1811 test the more we understand the DMG test. The DMG test is a good starting point but not as accurate as the EN1811.
>
> M. Wilson”

Learning points from the EU experience

- Know where you are going before proposing legislation
- Have a defined and proven test method. EN1811 is a sound test. There are doubts about the accuracy of the DMG test. Its limitations have to be understood
- Ensure good communications in the trade you are trying to influence – well in advance
- Be realistic about your ambitions and how fast you can influence the supply chain
- The retailer's leverage over the supplier is key – they give the message to the supplier if they get protest from the customer
- Visible enforcement or accreditation is needed
- Ongoing research and consultancy is available from organizations such as the Assay Office both on market and technical side to help define the way forward

The path forward

CLINICIAN COMMUNICATION ROLE

Dr. Bruce Brod, American Contact Dermatitis Society

Developing sound evidence-based health policy requires the input of expert stakeholders. Strategies on developing and communicating policy designed to reduce the incidence of both sensitization and elicitation of nickel allergic contact dermatitis was the focus of this discussion. Participants were reminded that children's health is largely impacted by nickel allergy and this particular group is unable to advocate on its own behalf. There is precedent for advocacy initiatives based on sound policy to protect children.

The discussion also focused on strategies involved in developing and communicating a message after developing a consensus health policy. Key points included developing a message based on evidence, developing a simple straightforward sound bite, recruiting the assistance of many credible stakeholders, and speaking with a unified voice. Because there were many physicians and scientists in the audience the discussion closed with an emphasis on the unique challenges and opportunities faced by these groups when advocating a message to policymakers.

Presented by Sharon Jacobs & Kalman Watsky (on behalf of Bruce Brod who was prevented from travelling to Chicago by severe weather conditions)

> "We must…take on a leadership role – we have the credibility
>
> Dr. B. Brod"

The unique capacity of clinicians for leadership in advocacy

We are the best at understanding the medical issues

====

We know the link between social factors and health

====

We are credible in the eyes of the public

====

We have access to policy makers, leaders, and citizens (our patients)

INDUSTRY COMMUNICATION ROLE

Dr. Kate Heim, NiPERA Inc.

Industry has an important role in communicating knowledge on nickel allergy. First, the target audiences need to be identified. Stakeholders include consumers, the general public, workers, medical doctors (including dermatologists, family practice physicians, orthopedists, orthodontists, dentists, surgeons, allergists), toxicologists, metallurgists, manufacturers, producers, retailers, testing firms, standardization experts, regulatory authorities and others. What information and the level of technical information provided will depend on the target audience.

What to communicate?

- Research results, scientific knowledge
- Appropriate uses of nickel
- Appropriate materials for items in direct and prolonged contact
- Risks, exposures, risk management measures
- Regulatory updates

How to communicate?

- Infographics & fact sheets
- Workshops, workshop reports
- Social media, websites (Nickel Institute and NiPERA)
- Nickel Institute documents (e.g. Nickel Magazine)
- Position statements
- Peer-reviewed publications
- Personal interaction, conference attendance and participation, stakeholders dialogue
- Cooperation with other stakeholders to ensure the correct target audiences are included, the type of information is appropriate, the information is accurate, and the way it is communicated is sufficient are all important considerations

ASTM voluntary standard for adult jewelry

(ASTM F2999-14) - ASTM Section 6.1 - Body-piercing jewelry shall be made exclusively of the materials listed:

- Surgical implant stainless steel
- Surgical implant grade titanium
- Niobium (Nb)
- Solid 14 karat or higher white or nickel-free gold
- Solid platinum
- A dense, low porosity plastic, including, but not limited to, Tygon or Polytetrafluoroethylene (PTFE) if the plastic contains no intentionally added lead

ASTM section 10.1 - *"Representations regarding the safety of adult jewelry for adults sensitive to nickel... shall be based on reasonable and representative tests... Precious metals listed in Table 2, and stainless or surgical steel grades 304, 316 or 430, are expected to meet these requirements and do not require testing."*

What are the regulatory options?

- Do nothing
- Voluntary public awareness initiatives
- Market based approaches
- Self-regulation & voluntary codes of practice
- Prescriptive regulation

REGULATORY PERSPECTIVE

Christian Richter, Nickel Institute

The U.S. has not followed Europe in addressing NACD through an EU-style nickel directive, and there are currently no formal plans to do so at the national level. The Consumer Product Safety Improvement Act (CPSIA), which Congress passed in 2008, was the most recent opportunity for stakeholders to formulate and advance a federal regulatory response, but nickel was neither included nor prioritized explicitly in the measure. Since passage of the CPSIA, the Consumer Product Safety Commission (CPSC) has taken steps to adopt a combination of voluntary and mandatory ASTM standards for jewelry and toys, with cadmium and lead addressed as the primary concerns in consumer products. With no realistic legislative or regulatory opportunities ahead, stakeholders can consider voluntary approaches using the principles of "best practice" from the regulatory design literature. Lessons from sound regulatory design include: (1) independent, unbiased assessment of relevant information; (2) openness in communication with the public on hazards and remedies; (3) clarity in any new guidance for the public to easily understand and apply; (4) reliability in capturing and updating the best knowledge and new findings over time; (5) efficiency by ensuring technical competence, consistency and burden minimization; and (6) targeting appropriately those populations and communities most affected. These principles in the near term can inform collaboration among industry, clinicians, researchers, consumer organizations and regulatory decision makers. Finally, any approach applied to address the issue under a voluntary or mandatory model should align with the principle of proportionality, in which measures taken are proportionate to the problem and to the desired outcome. So, what is success? In terms of options for collaboration, there is indeed an immediate productive path between "doing nothing" and "prescriptive regulation", including robust, evidence-based public awareness initiatives and outreach as well as voluntary codes of practice, among others.

> "With no realistic legislative or regulatory opportunities ahead, stakeholders can consider voluntary approaches"
>
> C. Richter

Panel discussion

The panel discussion brought up a number of interesting points from all perspectives. There was general consensus that success would be a “significant reduction in contact dermatitis”.

Clinician perspective

There was a general consensus that the main cause of nickel sensitization is body piercings and that this is an area to focus on. Preventing sensitization in children is a priority. There were calls for increased information and education as well as collaboration with manufacturers.

“If you could stop body piercings with nickel-releasing items would you solve the problem?”

“Is there a way to make piercing items standardized and safer? There are advisories available for other items.”

“Putting pressure on the retailers as well as educating consumers may be more effective and quicker than going the regulatory route. For example, ‘mums’ blogs’ can be very powerful.”

“Under 12s would be a good place to start. Implementing a voluntary code for them would be a really good first step. Build on this in the long term.”

“We [clinicians] recognize our limitations. We are downstream seeing the problems. We can’t do it alone – we are looking for help from industry. Perhaps a voluntary industry standard that reputable manufacturers use?”

“People want to know what materials are safe for piercing.”

Industry perspective

Representatives from manufacturing companies called for more information on materials to be made available. However, they cautioned against wholesale substitution of materials which could result in unintended consequences. In the case of nickel, much is known about it and there is a risk that it could be substituted by materials for which we have less scientific knowledge. The introduction of voluntary codes could be a way forward for reputable brands who could leverage their buying power with their suppliers to ensure appropriate materials are used for fabrication of items intended for direct and prolonged skin contact.

"If we have a list of sensitizing products, I'm going to avoid them [in the manufacture of my products]."

"Retailers will be much more receptive to adhering to a voluntary code. Reputable brands will be compliant."

"We need to think about testing. We need to better understand the nickel release curve over different times."

"Companies want to make globally compliant products but we don't have enough information available to us on materials."

"Nickel-containing materials are already replacing other hazardous materials (e.g. zinc nickel coatings are a key replacement for cadmium coatings)."

"We need to be careful we don't push people over to another item or material and everyone gets sensitized to that."

Regulatory perspective

The regulatory discussion centered around taking a focused approach to ensure that we are clear what the issue is we wish to address and what success would look like.

"More time needs to be spent on what exactly is the problem we are trying to address. If it's piercing, focus on the piercing. Is it informing (non-regulatory)? Or do we need a state or local entity to dictate?"

"Unless you have a relative standardized way of measuring the disease you won't see anything. This is one of the big problems with the regulations in Europe."

"Consider the unintended consequences of anything you do."

"In the United States, ASTM standards exist for use of metals in adult's and children's jewelry. They were originally put in place for cadmium but include other metals such as lead and nickel. These standards mirror the nickel regulation in Europe but are guidelines, not regulations. The ASTM standards for children's and adult's jewelry specifically note that, and "stainless or surgical steel grades 304, 316 and 430, are expected to comply with the requirements … and do not require further testing for nickel migration." However, it is not known how often these guidelines are used in the United States."

Conclusions

Chairperson – Dr. David Basketter, DABMEB Consultancy Ltd

Summing up the day's discussion, David Basketter said: "it is very obvious that despite some regulations in Europe, Nickel allergy remains a significant issue. Although EU regulations have been in place for some time, they are clearly not ideal, but do provide learning into the direction we should go in North America."

1. We need to have a clear target – do we want to solve all nickel allergy or avoid piercings?
2. Whatever the regulations - voluntary or mandatory regulations must have clarity
3. Be careful of unintended consequences. For example, in Spain the practice of babies being ear pierced just after they are born, may induce tolerance.
4. Nickel does not necessarily have to be avoided. The important concept is that of nickel release versus nickel content.

There was general consensus that the day had provided a unique forum for collaboration between a diverse group of participants. It had been a valuable opportunity to share perspectives and knowledge as well as forge contacts as part of a common drive to reduce the incidence of nickel allergic contact dermatitis, a preventable condition.

Program of the day

8:30-9:00	*Registration and Coffee*	
9:00-9:15	**Welcome and introduction** Setting the scene & aim of the workshop Introduction of speaker	Dr. K. Heim, NiPERA Inc. Chairperson – Dr. D. Basketter, DABMEB Consultancy Ltd
9:15-10:00	**Overview of the issue** History & present NACD prevalence, North America History & present NACD prevalence, Europe	Dr. J. Chen, Stanford University Dr. D. Basketter, DABMEB Consultancy Ltd.
10:00-10:30	**Properties and applications of nickel** Physico-chemical properties, uses, corrosion process	Mr. G. Coates, Nickel Institute
10:30-11:00	**Nickel sensitization process** Nickel sensitization mechanism, existing data, research	Dr. K. Heim, NiPERA Inc.
11:00-11:15	*Coffee Break*	
11:15 -12:30	**Clinician perspective** NACD in in the clinical population NACD in children NACD & implants	Dr. E. Warshaw, University of Minnesota Dr. S. Jacob, Loma Linda University Dr. K. Watsky, Yale School of Medicine/Yale-New Haven Hospital
12:30-1:30	*Lunch*	
1:30-2:00	**Market perspective** How & why nickel is used in products Importance of nickel Achievements, challenges & concerns of businesses Effects of European nickel restriction Best practices	Ms. M. Wilson, Assay Office Birmingham
2:00-3:15	**Path forward** Clinician communication role Industry communication role Regulatory perspective	Dr. B. Brod, American Contact Dermatitis Society President Dr. K. Heim, NiPERA Inc. Mr. C. Richter, Nickel Institute Consultant
3:15-3:45	**Panel discussion—Q&A** - What information or help is needed from different stakeholder groups to assist in resolving the issue? - What can be learned from the European experience? - Questions for panel members - Next steps	All Speakers & Attendees
3:45-4:00	**Conclusions**	Chairperson – Dr. D. Basketter, DABMEB Consultancy Ltd
4:00 - 5:00	*Networking, Coffee, and Drinks*	

List of participants

American Chemistry Council	David Fischer
American Contact Dermatitis Society	Cindy Froehlich
Assay Office Birmingham	Marion Wilson
DABMEB Consultancy Ltd	David Basketter
Dekra	Joe Langton
Dermatologist	Katherine Wier
Eastern Maine Medical Center	Jan Pelletier
Kohler Company	Chris Wagner
Kohler Company	Samantha Leibham
Loma Linda University	Sharon Jacob
Microsoft	Corinne Holmes
Motorola Mobility LLC	Heather Dowdy
Motorola Mobility LLC	Martin Pais
Mt Sinai West	Nanette Silverberg
National Association for Surface Finishing (NASF)	Jeff Hannapel
Nickel Institute	Clare Richardson
Nickel Institute	Gary Coates
Nickel Institute	Gerry Schuetz
Nickel Institute	Christian Richter
NiPERA Inc.	Connie Lawson
NiPERA Inc.	Kate Heim
Northwestern University	Andrew Scheman
Northwestern University Feinberg School of Medicine	Jonathan Silverberg
Research Institute for Tropical Medicine	Ricky Hipolito
SmartPractice	Kaylee Hamann
Stanford University	Jennifer Chen
U.S. Consumer Product Safety Commission	John W. Boja
U.S. Consumer Product Safety Commission	Stephanee Synnott
University of Minnesota	Erin Warshaw
Yale School of Medicine/Yale-New Haven Hospital	Kalman Watsky






Nickel
Essential Today
ntial Tomorrow






Essential Tomorr

Nickel
Essential Today
Essential Tomorrow


ABOUT THE NICKEL INSTITUTE

Nickel Institute is the global association of the world's primary nickel producers who together account for approximately 85% of worldwide annual nickel production outside China. Our 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 our 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.

communications@nickelinstitute.org
www.nickelinstitute.org
@NickelInstitute

Nickel INSTITUTE
knowledge for a brighter future