

NIA Comment on

SCCP

***Preliminary Opinion on
Safety of Nanomaterials in Cosmetic Products***

September 2007

Introduction to the NIA

Formed in 2005, the Nanotechnology Industries Association (NIA) creates a clear single voice to represent the diverse industries' views in the multi-stakeholder debate on nanotechnology, by providing an interface with government, acting as a source for consultation on regulation and standards, communicating the benefits of nanotechnologies and interacting with the media to ensure an ongoing advancement and commercialisation of nanotechnologies.

The unique feature of the NIA is that it provides a purely industry-led perspective derived from the views of the collective membership, which is made up of many varied companies all at different stages of their life cycle and with a variety of interests in the huge range of technologies that derive their benefit from the nanoscale. This enables those seeking comment from industry to have a single point of entry to the industry and avoids the need to approach individual companies for statements on specific issues. In addition the breadth of the membership enables the NIA to put forward strong proposals to government and regulatory authorities to promote an environment that supports the application and utilisation of nanotechnologies. Initial aims of the association are:

- Establishing a framework of shared principles for the safe, sustainable and socially supportive development and use of nanotechnologies,
- Working closely with regulators and policy makers to realise the full potential of nanotechnology and secure the full economic and societal benefits,
- Developing timely industry perspectives for government and assisting policy development on nanotechnologies,
- Clarifying and demystifying nanotechnologies and raising awareness of their applications in a balanced way amongst key audiences,
- Generating position statements and papers in areas relevant to its members and providing responses to consultation exercises and publishing position papers and statements,
- Identifying, forecasting and roadmapping unique areas of potential competitive advantage using nanotechnology, and
- Interacting with the media to ensure an ongoing advancement and commercialisation of nanotechnologies.
- Encouraging and stimulating industry participation and support for nanotechnology, and
- Providing a forum for discussing topics of relevance to its members.

For further information visit <http://www.nanotechia.co.uk>.

The NIA welcomes the possibility to comment on the SCCP's Preliminary Opinion on *Safety of Nanomaterials in Cosmetic Products*.

The NIA acknowledges the SCCP's effort to provide opinion on the use of nanomaterials in cosmetic products, with a view to advising the European Community, including its governing bodies, as well as other organisations and initiatives. However, the NIA does not fully agree with the opinion outlined in the SCCP's Preliminary Opinion on *Safety of Nanomaterials in Cosmetic Products*. In particular, we would like to comment in detail on the following points:

1. Points contained in the Abstract and Executive Summary

(a) Definition of a nanoparticle as having at least one dimension <100 nm.

The SCCP opinion correctly distinguishes between "labile" and "insoluble" particles. NIA agrees with this distinction and agrees that the definition of "nanoparticle" does not apply to materials that dissolve or otherwise lose their solid structure. The definition in the Opinion of a nanoparticle as "a particle with one or more dimensions at the nanoscale" is inconsistent with other European and international definitions (BfR 2000, ASTM 2006). The definition appears to apply more to "nanomaterials" rather than nanoparticles. For example, according to this definition membranes with a thickness of <100 nm, films, or coatings would be nanoparticles.

Although in its recent Opinion, the SCENIHR described nanoparticles as a "particle with one or more dimensions at the nanoscale", it then characterised "nanoparticles to have two or more dimensions at the nanoscale" (SCENIHR, 2007). This view is comparable with the definition of the US EPA, which defines "nanomaterials" as having a length scale of approximately 1 to 100 nm in any dimension (US EPA, 2005), whereas nanoparticles are considered to have 1 to 100 nm in diameter. This is consistent with other international definitions, such as ILSI defining a nanoparticle as a "particle with a physicochemical structure on a scale greater than atomic/molecular dimensions but less than 100 nm" (Oberdörster et al., 2005). The German Federal Environmental Office defined nanoparticles as "particles smaller than 100 nm" (IKU, 2005). The ASTM standard E56-03 that is currently under evaluation by ISO defines nanoparticles as "a sub-classification of ultra-fine particles with lengths in 2 or 3 dimensions greater than 1 nm and smaller than 100 nm".

(b) Conclusion that the traditional risk assessments methods may not always be suitable for nanomaterials, particularly for insoluble nanoparticles, in cosmetics and new methods should be developed and/or the existing methodologies should be validated.

We disagree with the SCCP's preliminary and believe that currently existing safety methods are suitable and sufficient for the evaluation of nanomaterials, and specifically for the insoluble nanoparticles used as cosmetic ingredients.

Further, the current opinion by the SCCP is inconsistent with the recent SCENIHR opinion on "The appropriateness of the risk assessment methodology in accordance with the technical guidance documents for new and existing substances for assessing the risks of nanomaterials" that concluded that methodologies described in the Technical Guidance Document are generally likely to be able to identify the hazards associated with the use of nanoparticles.

We reiterate our comments provided on the SCENIHR consultation document as they are equally relevant to the SCCP opinion:

- There are many different attributes of nanoparticles that may influence their human toxicological and ecotoxicological properties. Whole organism (*in vivo*) studies are a way of integrating all potential effects, as compared to *in vitro* studies that may be better suited to identifying mechanisms.
- Nanoparticles have complex physiochemical properties that can modulate their biological activity. There are considerable mechanistic and dose discrepancies that exist between *in vitro*, *in vivo* and *ex vivo* testing, and even between different routes of exposure *in vivo* in test species.

Further, we do not agree with the statement that it is "...unknown whether current regulatory tests are adequate or relevant for testing of nanomaterials". A workshop on toxicological approaches to the safety of nanomaterials held in 2004 by the US National Toxicology Program and National Institute of Environmental Health Sciences concluded that "Evaluation of the safety of nanomaterials should be primarily based on traditional *in vivo* toxicity models" (NTP/NIEHS, 2004). The same or a similar view was also expressed by the recent reviews of the US Food and Drug Administration (FDA, 2007), the SCENIHR (2007) and Australia (TGA 2006).

(c) The SCCP considers that the risk assessment of nanoparticles in cosmetics should be carried out on a case-by-case basis taking into account the specific physical, chemical and surface area characteristics of nanomaterials.

We agree that nanoparticles need to be evaluated on a case-by-case basis. The recognition that nanomaterials should not be treated as a class of materials, but instead be "evaluated on a case-by-case basis," appears to be supported by the toxicity data in the scientific literature.

(d) The SCCP concludes that previous safety evaluations on nanomaterials used in cosmetics would also need to be revised.

The wording of the SCCP preliminary opinion can be (mis)interpreted as questioning the safety of nanoparticles in cosmetics, including titanium dioxide or zinc oxide used in sunscreens. The extensive body of scientific evidence indicates that the use of nanoparticles in sunscreens poses no risk to human health. The SCCP (formerly the SCCNFP) concluded in 2000 that titanium dioxide, including nanoparticles "is safe for use in cosmetic products...in order to protect the skin from certain harmful effects of UV radiation" (SCCNFP 2000). Recent publications on the safety of titanium dioxide and zinc oxide confirm that these materials do

not pose a health risk and do not penetrate through human skin. See included references for information not reviewed in the consultation document.

(e) The SCCP considers it necessary to consider the influence of physiologically abnormal skin in the assessment of dermal penetration of nanoparticles.

“Abnormal” skin can range from transient, self-resolving conditions, such as sunburn, to the chronic diseases of eczema and psoriasis. No suitable models have been developed; recent literature reports have used severely abraded skin and the relevance of (minimal) findings from these studies to the human condition is questionable. [A large number of papers are relevant to evaluating this endpoint that were not reviewed in the consultation document. A list of these is provided in the references section of this response.]

2. Further comments:

We would furthermore like to provide some additional comments and reference to scientific evidence, which we consider necessary to fully evaluate the use of nanomaterials in cosmetic products:

1. Many studies show that the use of sunscreens reduces the occurrence and the development of skin and lips cancers, and herpes labial (Pogoda 1996; Rooney 1991; Nohynek 2001)
2. Sunscreens protect DNA from deteriorations induced by ultra-violet radiations, reduce the appearance of modified squamous cells and the development of certain indices of the melanoma (Young 2000; Gallagher 2005; Mahroos 2002; Lee 2005).
3. Today, one cancer in three is skin cancer. Each year 2 to 3 million skin cancers (carcinoma type) and over 130,000 melanomas are diagnosed. One American in five will develop a skin cancer in his life.
4. The incidence of skin cancer has increased considerably over the last decade. The popularity of outdoor activities, including “sun bathing” is the leading cause of this increase. The reduction of the level of protection from the ozone layer, if continued, will worsen this tendency: it is estimated that a decrease of 10% of stratospheric ozone would be responsible for 300,000 carcinoma and 4,500 additional melanomas each year (WHO 2007).
5. In many countries dermatologists' associations (such as The Cancer Council Australia) and national sanitary authorities regularly launch information campaigns inviting people to apply sun products before exposing themselves to the sun. For example, in 2006 this public health strategy was re-confirmed by The American Academy of Dermatology (AAD 2007).
6. According to the IARC (International Agency for Research on Cancer), the regular use of sun creams is essential in the prevention of the skin cancers and those that contain nano titanium dioxide or zinc oxide are the most effective (IAR 2001).
7. A large number of studies have demonstrated the titanium dioxide nanopigments do not cross the skin barrier after topical application. Studies carried out within the framework of the European research program NANODERM showed that nanopigments do not cross the skin barrier in the case of both healthy skin or

- compromised skin (acne, psoriasis) (Lademann 1999; Dussert 1997; Pflucker 1999; Gamer 2006; Roberts 2006; Nohynek 2007; Mavon 2007; Butz 2005).
8. Indeed, M. Kraeling and R. Bronaugh of the FDA recently reported that even quantum dots — nanoparticles not used in cosmetics, but used as cell markers and designed to penetrate into cells — do not cross the skin barrier when applied topically (Kraeling 2007).
 9. Other studies by the FDA showed that, in mice, subcutaneously injected TiO₂ nanoparticles were not systemically available, but remained at the injection site; intravenously injected TiO₂ nanoparticles were rapidly cleared from the circulation and were found inside macrophages in the liver, spleen and the lungs, suggesting normal clearance by the phagocytic barrier (Umbreit 2007; Wiebert 2006).
 10. It is worth mentioning that the IARC classification of TiO₂ as possibly carcinogenic to humans was made on the basis of animal inhalation studies that were conducted with micro-sized and not with nano-sized particles. It has recently been suggested that all respirable, inert and non-toxic particles may produce carcinogenic effects identical to those of TiO₂. Therefore, the inhalation carcinogenicity of (micro-sized) TiO₂ is not due a specific carcinogenic activity of the material, but represents a general biological activity of all investigated bio-durable particles without significant specific toxicity, such as carbon black, aluminium oxide, aluminium silicate, kaolin, titanium dioxide, zirconium dioxide or amorphous silica all of which produce lung overload at high concentrations and all of which were shown to be similarly carcinogenic in rats (Mohr 2006).
 11. It is suggested by the SCCP that cosmetics may produce human systemic exposure via inhalation. Hairsprays are listed as cosmetic products producing human systemic exposure to nanoparticles. However, to our knowledge, current hairsprays do not contain nanoparticles and therefore do not produce human systemic exposure to nanoparticles.
 12. In conclusion, the non-penetration of TiO₂ or ZnO nanoparticles used in sunscreens into or through human skin as well as absence of a health risk has been acknowledged by the German and Australian health authorities, and the recent international expert group assembled by ECETOC. This is hardly surprising given that sunscreen pigments must be present on the surface of the skin in order to protect from UV light (BfR 2006; TGA 2006; Borm 2006).
 13. The guidelines set out recently by the US federal government within the context of the TSCA (TSCA Inventory Status of Nanoscale Substances -- General Approach) do “not consider particle size to distinguish for Inventory purposes two substances that are known to have the same molecular identity. Under principles of traditional chemistry different forms of such substances would not be considered different chemicals”. This interesting approach is also being discussed within the FDA Task force on Nanotechnology.

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Thank you very much for taking our comments into consideration.

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