Submission regarding SCCS Opinion on Zinc oxide (nano form), October 2012

Introduction

A close inspection of the scientific research to date clearly requires a precautionary approach to managing nanomaterial risks. The scientific justification for requiring proponents to demonstrate the safety of nano-products before they can be sold was accepted in 2004 by the United Kingdom's Royal Society and Royal Academy of Engineering. In their seminal report they recommended that nanomaterials be treated as new chemicals and nano-ingredients in products be required to pass rigorous safety assessment before commercial use is permitted.

Friends of the Earth Australia (FoEA) shares the SCCS's conclusion that clear positive toxic responses in some of these tests clearly indicate a potential for risk to humans. We also share the SCCS's concerns regarding the use of zinc oxide (ZnO) in cosmetic products which may result in inhalation.

However, FoEA does not agree with the SCCS's conclusion that the forms of nano-zinc oxide outlined in the document are safe for use in sunscreens. This conclusion is based on the assumption that skin penetration is only likely to occur in ionic form.

We believe there is insufficient evidence to make such an assumption and are concerned about:

1. **The SCCS's reliance on unrealistic ZnO skin penetration research data provided by industry groups with a vested interest in negating such concerns**
   The majority of the skin penetration studies evaluated by the SCCS are short term, *in vitro* and don't consider the role of flexing, skin condition and the widespread use of penetration enhancers in cosmetics.

2. **The high degree of uncertainty regarding the extent of skin penetration by nano zinc oxide**
   There are still no long-term human *in vivo* studies looking at the extent of penetration into the basal skin layer. In formulating its opinion we believe the SCCS failed to adequately consider evidence of skin penetration by other nanomaterials. The SCCS also appears to have failed to consider the strong affinity nanoparticles have with proteins and how this might impact the extent of ionisation and skin penetration.

3. **The numerous data gaps regarding certain aspects of the toxicity and fate of nano ZnO**
   The SCCS noted numerous data gaps regarding certain aspects of the toxicity and fate of nano ZnO, including information regarding long term toxicity, solubility, phototoxicity and carcinogenicity.

4. **The high demonstrated levels of toxicity of nano zinc oxide**
   Various aspects of nano-zinc oxide toxicity are clearly demonstrated and acknowledged in the SCCS Opinion. Moreover, nano-zinc oxide has been demonstrated to have greater potential for toxicity and skin penetration than bulk zinc oxide.

5. **Methodological problems in the existing research which prevent reliable conclusions from being drawn**
   Many of the studies cited by the SCCS have methodological flaws which limit their value in assessing the extent of toxicity and skin penetration.

More detailed comments on specific sections follow.

3.3. Toxicological evaluation

The toxicity of nano-zinc oxide is clearly demonstrated and acknowledged in the SCCS Opinion. Moreover, nano-zinc oxide has been demonstrated to pose higher potential for toxicity and skin penetration.

Examples of the toxicity of ZnO include:

- Acute oral toxicity (p. 30)
    - alarmingly, it was found *"The incidences of microscopic lesions in the liver, pancreas, heart and stomach were higher at lower doses of nano-size zinc oxide compared to higher doses,"* and that *"The nano-sized ZnO induced toxicity at the lowest dose investigated (5 mg/kg body weight)."*
- Local effects in the lung (p. 57)
- Human cell genotoxicity (p. 62)
- Cytotoxicity (p.87)
    - Oxidative stress markers were increased at a dose of 0.008 µg/mL exposure.
- Liver toxicity (p. 93)
    - *"it can be concluded that based on the observations on serum liver enzyme levels and histopathology, the systemic availability of either ZnO nanoparticles or Zn ions has the potential to induce liver toxicity."*

It appears from the evidence presented that micro-scale ZnO, whilst demonstrating some similar toxic effects to nano ZnO, has lower overall toxicity than nano-ZnO:

> *"As far as evaluated in the toxicity testing, micro-sized ZnO has been shown to induce either similar toxic effects (in terms of general toxicity, lung toxicity after inhalation, uptake from gastroIntestinal-tract, serum liver enzyme presence) or lower toxic effects (in terms of genotoxicity, liver histopathology) when compared to nano-sized ZnO."* (p. 98)

Free radical production

The capacity for nanomaterials to create free radicals (reactive oxygen species) is well recognised.[1] As we reduce the size of particles, the larger relative surface area increases the potential for free radical production which can damage proteins and DNA. A study cited in the SCCS Opinion found that when zinc oxide was applied topically to rats over a 28 day period there was:

> *"a significant decrease in the collagen content of the skin and the tail in all the nano ZnO treated groups of rats compared to the control, as well as with the micro-sized zinc oxide treated groups."* (p.59)

It was suggested that this effect was due to:

> *"potential skin penetration of ZnO nanoparticles due to partial dissolution, followed by induction of reactive oxygen species"* (p.59)

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[1] Tran D and Salmon R. (2010) Potential photocarcinogenic effects of nanoparticle sunscreens. *Austral J Dermatol* **52**(1):1-6; Newman M, Stotland M, EllisJ. 2009. The safety of nanosized particles in titanium dioxide and zinc oxide based sunscreens. *J Am Acad Dermatol* **61**: 685-92, http://www.idlc.com.au/pdf/IDLC-Final-nanoparticle-sunblock-lecture.pdf

Nano ZnO was also found to induce DNA damage in human epidermal cells.[2] Another study found that nano zinc oxide induced DNA damage in human nasal mucosal cells whilst bulk zinc oxide didn't.[3] Another study concluded that:

> *"repetitive exposure to low concentrations of ZnO nanoparticles results in persistent or ongoing DNA damage."*[4]

Phototoxicity/photoirritation and photosensitisation

The SCCS Opinion notes that a 2006 study using Chinese Hamster lung cells found that treatment with UV light resulted in an increased susceptibility of the cells to DNA damage by nano zinc oxide.[5] Similar results were observed using Chinese Hamster ovary cells (p. 75). FoEA is therefore concerned that no further studies on phototoxicity/photoirritation and photosensitisation have been submitted since (p. 69).

Carcinogenicity

The leader of CSIRO's Nanosafety group warned in 2008 that in a worst-case scenario, nano-ingredients in sunscreens could cause skin cancer.[6] It is therefore deeply concerning that no data was available regarding the carcinogenicity of ZnO, given the known capacity of nanomaterials to damage DNA.[7]

3.3.4 Dermal/percutaneous absorption

This section relies almost exclusively on *in vitro* human and non-human skin studies. There have still been no long-term studies examining the extent to which nano zinc oxide penetrates the skin and remains in the particle form. A precautionary approach should dictate that until these studies are performed, nano zinc oxide should not be deemed 'safe'. Data gaps should not be used as an excuse for regulatory inaction.

Existing skin penetration studies are inadequate

FoEA is concerned about the SCCS's over-reliance on ZnO skin penetration research data provided by industry groups with a vested interest in negating concerns. A literature review by the Australian Therapeutic Goods Administration in 2009 found that most studies to date have found no or limited skin penetration by nano-ingredients. However, serious limitations in these studies prevent us concluding that skin absorption does not occur. The European Union's Scientific Committee on Consumer Products has warned that existing research into skin penetration by nano-ingredients is

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[2] Sharma *et al* (2009) cited in SCCS (2012) Opinion on zinc oxide (nano form) p.62; SCCS (2012) p. 94.

[3] Hackenberg et al (2011a) cited in SCCS (2012) p.64.

[4] Hackenberg et al (2011b) cited in SCCS (2012) p.66.

[5] Shiseido (2006). Photo-chromosomal aberration test of FINEX-50 ZnO with cultured mammalian cells. Safety Assessment Group, Quality Assessment Center, Shiseido Co. Ltd., Japan, 31 August 2006, cited in SCCS (2012)

[6] Safety concerns over high-tech sunscreens, http://www.abc.net.au/7.30/content/2008/s2449409.htm

7 Tran D and Salmon R. (2010)

inadequate and that further studies "taking into account abnormal skin conditions and the possible impact of mechanical effects on skin penetration need to be undertaken"[8], yet no research data addressing the role of abnormal skin condition in potential ZnO penetration is presented in this opinion.

Many existing skin penetration studies are deficient because they:

- **Are overwhelmingly short term, often 24 hours**
- **Mostly based on excised skin *in vitro***, where there is no movement or blood circulation
- **Fail to consider the role of skin condition** (e.g. eczema, acne, sunburn, children with thinner skin) and,
- **Do not assess the role of penetration enhancers**, despite the prevalence of these substances in sunscreens, cosmetics and workplaces

Recent peer-reviewed literature reviews have emphasised that these deficiencies limit the relevance of earlier skin penetration studies to 'real life' scenarios and prevent any reliable conclusion about skin penetration by nano-ingredients.[9] These shortcomings were present in most of the skin penetration studies presented in the Opinion. Only three *in vivo* studies were included:

- Filipe, 2009
  - 2 - 48 hr exposure
  - ZnO nanoparticles observed in the pilosebaceous follicles, but no penetration detected into viable skin tissue
- Zvyagin, 2008
  - 2 - 24 hr exposure
  - nano-ZnO remained either on the skin surface or stratum corneum
- Gulson, 2010
  - Sampling each 24 hrs for 5 days
  - Radiolabelled ^{68}Zn not detected in blood of volunteers until the end of day 2, after 4 applications of sunscreen.
  - Levels of Zn were still increasing at the final (day 5) sampling point

Gulson *et al* emphasise that they first identified radio isotope labelled zinc in blood samples at the end of the second day of their longer term study, after 4 applications of sunscreen.[10] This study therefore raises serious questions regarding the validity of all the other dermal penetration studies relied on by the SCCS in formulating its Opinion –since these all concluded within a 48 hour period. More long-term studies are clearly needed to assess the extent to which nano-ingredients penetrate the skin and to determine their fate if they do.

In a subsequent publication Gulson *et al* explain "The unexpected increase in ^{68}Zn after ceasing sunscreen application [Day 5] may be attributed to:

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8 SCCP (2007) Opinion on safety of nanomaterials in cosmetic products. European Commission. Available at: http://ec.europa.eu/health/ph_risk/committees/04_sccp/docs/sccp_o_123.pdf

9 Tran D &Salmon R. (2010); Newman M, Stotland M, EllisJ. (2009) The safety of nanosized particles in titanium dioxide and zinc oxide based sunscreens. *J Am Acad Dermatol* **61**: 685-92.

10 Gulson B, McCall M, Korsch M, Gomez L, Casey P, Oytam Y, Taylor A, Kinsley L and G Greenoak (2010) Small amounts of zinc from zinc oxide particles in sunscreens applied outdoors are absorbed through human skin. *Toxicol Sci* **118** (1): 140-149.

- substantivity (the binding and retention of residues in the lower epidermis or dermis potentially acting as a long-term chemical reservoir;
- the accumulation of the formulation in hair follicles, skin folds or sweat glands; or
- sequestration into, and later release from, bodily compartments such as the liver or muscle.[11]

Peer-reviewed studies now demonstrate that skin penetration can occur

The Gulson 2010 study found small amounts of zinc from sunscreen in the blood and urine of human trial participants[12]. The study used live human volunteers and was carried out over 5 days, with follow up testing for at least six days. The study was not able to show whether the zinc was absorbed in particle or ionic form, so this requires further research. Another limitation of the study was the poor control used (the 'bulk' zinc control had an average particle size of 110 nm and many particles smaller than 100 nm, meaning that there could not be effective comparison between nano and 'non-nano' zinc uptake). Nonetheless, this study shows that skin uptake of ingredients from sunscreen applied to intact skin does occur in some form. The results of a separate pilot study conducted as a prelude to this study have since been published. This new publication also showed that small amounts of zinc from sunscreen were detectable in blood and urine[13]. It is uncertain why the SCCS opinion did not include this research publication, since it has been available online from 7 February, 2012.

Several other peer-reviewed studies have shown skin penetration by other types of nanomaterials. Quantum dots and fullerenes can penetrate skin[14], especially if skin is flexed[15] (as during exercise) or exposed to 'penetration enhancers' which can be found in some cosmetics.[16]. A 2003 study by the United States National Institute for Occupational Safety and Health[17] found that when accompanied by repetitive skin flexing, inert fluorospheres 1000 nm in size could reach living cells in the dermis. Particles were also found to be concentrated under torn skin, suggesting that compromised skin is more vulnerable to penetration. Despite the relevance of these studies, and the SCCS's claims that "the applicants have performed and provided a comprehensive review and assessment of the available *in vivo* and *in vitro* dermal penetration studies," (p. 92) none of these studies are referred to in the SCCS Opinion.

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[11] Gulson B, Wong H, Korsch M, Gomez L, Casey P, McCall M, McCulloch M, Trotter J, Staubert J, Greenoak G. 2012. Comparison of dermal absorption of zinc from different sunscreen formulations and differing UV exposure based on stable isotope tracing. *Sci Total Env* **420**: 313-318

12 Gulson B *et al* (2010)

13 Gulson B *et al* (2012)

14 Ryman-Rasmussen J, Riviere J, Monteiro-Riviere N. 2006. Penetration of intact skin by quantum dots with diverse physicochemical properties. *Toxicol Sci* **91**(1):159-165.

15 Rouse J, Yang J, Ryman-Rasmussen J, Barron A, Monteiro-Riviere N. 2007. Effects of mechanical flexion on the penetration of fullerene amino acid derivatized peptide nanoparticles through skin. *Nano Lett* **7**(1):155-160.

16 Monteiro-Riviere N, Yang J, Inman A, Ryman-Rasmussen J, Barron A, Riviere J. 2006. Skin penetration of fullerene substituted amino acids and their interactions with human epidermal keratinocytes. *Toxicol* **168** (#827).

17 Tinkle S, Antonini J, Rich B, Roberts J, Salmen R, DePree K, et al. 2003. Skin as a Route of Exposure and Sensitization in Chronic Beryllium Disease. *Environ Health Perspect* **111**:1202-1208.

Nanomaterials may react with other sunscreen ingredients

The SCCS notes that:

> *"a re-evaluation may be needed in the case of use of other specific coatings, which can promote the dermal penetration of ZnO particles (nano or non-nano)."*(p. 98)

Commentators have suggested that since nanomaterials are highly reactive, they may react with other sunscreen ingredients and become coated with proteins or lipids. For example, the rapid formation of a 'protein corona' is well recognised.[18] A number of papers have demonstrated the strong affinity that nanomaterials have with proteins.[19] It is therefore possible that nanomaterials in sunscreens will be coated in proteins (picked up either in sunscreens or from the skin surface). This could make it less likely that zinc oxide in nanoparticle form will ionise when in contact with the skin. A protein coating may also affect the extent of skin penetration[20], as well as the toxicity of individual nanoparticles.[21] However, the key implication is that if skin penetration does occur, it could be in nanoparticle form, rather than as ions.

Studies do not consider the role of penetration enhancers

The SCCS notes that:

> *"Any cosmetic products containing ZnO particles (nano or non-nano) with coatings that can promote dermal penetration will also be of concern."* (p. 98)

The use of penetration enhancers is extremely widespread in the cosmetics industry. A 2009 survey by FoEA found penetration enhancers in seven out of ten of the products assessed.[22] 'Penetration enhancers' are chemicals that alter skin structure, allowing other chemicals to penetrate deeper into

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[18] Turney, J. (2009) Nanomaterials, Section 4.1: How do nanoparticles interact with proteins? http://ec.europa.eu/health/scientific_committees/opinions_layman/nanomaterials/en/l-2/4.htm

[19] Linse, S. e*t al* (2007) Nucleation of protein fibrillation by nanoparticles, *PNAS*, **104**(21):8691-8696, http://www.pnas.org/content/104/21/8691; Cedervall, T. e*t al* (2007) Understanding the nanoparticle–protein corona using methods to quantify exchange rates and affinities of proteins for nanoparticles, *PNAS*, **104** (7):2050-2055, http://www.pnas.org/content/104/7/2050

[20] See for example Zheng, D. *et al* (2012) Topical delivery of siRNA-based spherical nucleic acid nanoparticle conjugates for gene regulation, *PNAS,* July 6, 2012 http://www.pnas.org/content/early/2012/07/03/1118425109.abstract

[21] Webb, S. (2012) Coatings Influence Nanoparticle Toxicity, *Chemical & Engineering* News, January 18, 2012, http://cen.acs.org/articles/90/web/2012/01/Coatings-Influence-Nanoparticle-Toxicity.html

[22] FoE (2009) Beauty industry backs high risk small particles: Controversial nano-ingredients found in big name brands, http://nano.foe.org.au/sites/default/files/Background%20briefing%20nanoparticles%20in%20cosmetics%20November%202009.pdf

the skin, and increasing the amounts of chemicals that reach the bloodstream.[23] Some chemicals that act as penetration enhancers are included in products to increase skin uptake of moisturisers or other active ingredients, whereas for other chemicals their ability to promote skin penetration is incidental. US researchers have found that penetration enhancers "greatly enhance" the uptake of carbon fullerene nanoparticles through skin.[24] However, to the best of our knowledge the influence of penetration enhancers hasn't been explored in relation to the vast majority of nano-ingredients now used in cosmetics.

Given the prevalence of penetration enhancers in the cosmetics industry, FoEA believe that is premature for the SCCS to conclude that skin penetration by nano zinc oxide does not occur, before the impact of these chemicals on skin penetration has been properly assessed.

There are no long-term *in vivo* studies looking at the extent of penetration into the basal skin layer

While the 2010 Gulson study examined the presence of zinc isotope in blood and urine, it didn't examine how much of the zinc (present as either zinc oxide nanoparticles or ions) was absorbed into the basal skin layer.[25] This is important, because if zinc oxide nanoparticles are absorbed into the basal skin layer, the photocatalytic potential of ZnO to generate free radicals and damage active proteins and DNA will be dramatically increased.

Given the limitations of the data regarding skin penetration FoEA believes that it is premature for the SCCS to conclude that:

> *"It is worth highlighting that this opinion has considered the small proportion of the absorbed Zn following dermal application of nano ZnO to most likely be a solubilised ionic form. This is in consideration of the solubility and dissolution aspects of ZnO described in section 3.1.6. However, if any new evidence emerges in the future to show that the translocating species were in the form of insoluble and potentially persistent nanoparticles, then the SCCS may consider revising the safety assessment of nano ZnO."* (p. 97)

FoEA believes that there is sufficient evidence to warrant a precautionary approach and that the SCCS should revisit this issue immediately.

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[23] e.g. Pont, A.R., Charron, A.R., & Brand, R.M. (2004) Active ingredients in sunscreens act as topical penetration enhancers for the herbicide 2,4- dichlorophenoxyacetic acid, *Toxicol Appl Pharmacol* **195**(3): 348-354.

[24] Monteiro-Riviere N, Yang J, Inman A, Ryman-Rasmussen J, Barron A, Riviere J. (2006) Skin penetration of fullerene substituted amino acids and their interactions with human epidermal keratinocytes. *Toxicol* **168** (#827).

[25] Gulson B *et al* (2010)

3.3.13 Safety evaluation

FoEA shares the SCCS's conclusion that:

> *"the data provided on solubility are inadequate to draw conclusions on the dissolution of ZnO nanoparticles. It is the view of the SCCS that the solubility data as presented are insufficient. Furthermore, to enable proper estimation of consumer exposure to any partially dissolved and/or insoluble fractions, the information for nanomaterials to be used as cosmetic ingredients should be provided not only on solubility, but also on the dissolution rate since equilibrium solubility is normally not achieved in the body"* (p. 10)

Elsewhere in the document the SCCS states that:

> *"The literature data and the data which were provided for this submission suggest that there is only minimal absorption and resulting systemic availability of zinc from application of ZnO nanoparticles containing sunscreens on the skin. Whether this zinc is available as zinc oxide nanoparticles or zinc ions has not been determined."* (p. 92)

Given the lack of supporting evidence, we believe it is irresponsible for the SCCS to conclude that:

> *"until proven otherwise, it is assumed that any transdermal penetration following application the nano-ZnO containing cosmetic product is that of Zn ions released from the ZnO nanoparticles."* (p. 88)

3.3.14 Discussion

Inhalation

FoEA shares the SCCS's concerns about the use of ZnO nanoparticles in spray application (p.93).

Mutagenicity

FoEA strongly disagrees with the SCCS's conclusion that:

> *"where ZnO nanoparticles are applied on the skin in a sunscreen formulation, there is sufficient evidence to conclude that due to the very low if any systemic exposure, the risk to the consumer is negligible."* (p. 95)

As mentioned above, the vast majority of skin penetration studies have been extremely short term and *in vitro* -including the Nanoderm Project cited by the SCCS, where the maximum exposure time was 48 hours.[26] Furthermore, in their 2010 study Gulson *et al* observed that:

> *"there are grounds which suggest that the amount of Zn absorbed from sunscreens may be somewhat larger than indicated by the blood results. A strong empirical support provided within the confines of this study for the possibility of additional Zn being deposited elsewhere in the body is that the amount of ^{68}Zn detected in blood continued to increase 6 days after*

[26] Butz, T. et al (2007) NANODERM: Quality of Skin as a Barrier to ultra-fine Particles Final Report, http://www.uni-leipzig.de/~nanoderm/Downloads/Nanoderm_Final_Report.pdf

the last sunscreen application. ^{68}Zn may have concentrated in particular tissues (e.g., epidermis, liver, muscle) with subsequent slow rerelease into the blood."[27]

This hypothesis is further supported by Gulson *et al*'s revelation in their 2012 research publication that levels of ^{68}Zn detected in blood was still increasing on the last day of monitoring at 14 days, rather than at the end of the 5-day exposure.[28]

FoEA believes that there is insufficient evidence regarding the fate of absorbed nano zinc oxide in the body to warrant the SCCS's conclusion that nano zinc oxide in sunscreens is safe.

Carcinogenicity

FoEA is deeply concerned about the data gap regarding the carcinogenicity of nano ZnO and believes there is inadequate evidence to support the SCCS's conclusion that:

> *"In view of the occurring dissolution of the ZnO nanoparticles it can be assumed that the carcinogenic risk is similar to the conventionally manufactured ZnO preparations."*(p. 95)

4. Conclusion

FoEA shares the SCCS's conclusion that:

> "*clear positive toxic responses in some of these tests clearly indicate a potential for risk to humans."* (p. 96)

Dermal exposure

FoEA strongly disagrees with the assertion that "*from the available information, there is no indication for penetration of ZnO nanoparticles through the skin*" (p. 96) because of the limitations in skin penetration studies already outlined.

Inhalation exposure

FoEA shares the SCCS's conclusion that:

> *"on the basis of available information, the use of ZnO nanoparticles in spray products cannot be considered safe."* (p. 96)

Overall conclusions

1. Does the SCCS consider zinc oxide in its nano-form safe for use as a UV-filter with a concentration up to 25% in cosmetic products taking into account the scientific data provided?

[27] Gulson, B. *et al* (2010)

[28] Gulson, B. *et al* (2012)

The SCCS concluded that:

> *"There is no evidence for the absorption of ZnO nanoparticles through skin and via the oral route. Even if there was any dermal and/or oral absorption of ZnO nanoparticles, continuous dissolution of zinc ions would lead to complete solubilization of the particles in the biological environment."* (p. 96)

FoEA believes that there is insufficient evidence to warrant these assumptions for the reasons outlined earlier. It is refreshing to see the SCCS acknowledge the wide gaps in certainty around many aspects of nano zinc oxide in this published opinion. However, FoEAis deeply concerned by the SCCS's conclusion that zinc oxide nanoparticles *"can be considered not to pose a risk of adverse effects in humans after dermal application"* (p. 97), given these acknowledged massive uncertainties.

Data gaps acknowledged in the Opinion include:

- *"the data provided on solubility are inadequate to draw conclusions on the dissolution of ZnO nanoparticles."*(p.10)
- *"no data available on*
    - *repeated dose (30 day) oral toxicity study*
    - *sub-chronic (90 day) toxicity (oral,dermal)*
    - *chronic (>12 months) toxicity"* (p.59)
- *"No data available on carcinogenicity"* (p. 68)
- *"No data specific for ZnO nanoparticles are available on reproductive toxicity"* (p. 68)
- *Phototoxicity/photoirritation and photosensitisation*

The SCCS notes that:

> *"the risk assessment of nanomaterials is currently evolving. In particular, the toxicokinetics aspects have not yet been fully explored in the context of nanoparticles (e.g. the size dependency)."* (p. 97)

Given the acknowledged uncertainty, it is therefore difficult to draw broad conclusions about the safety of nano zinc oxide from the studies detailed in the opinion.

The SCCS also notes that:

"long term stability of the coatings remains unclear" (p. 97)

This is highlighted by a recent study which found that chlorine in swimming pools can strip the coating off titanium dioxide nanoparticles in sunscreens that protect against UV radiation, leaving them able to react with water to form free radicals. Free radicals are known to damage DNA, causing

aging and potentially leading to cancer. [29] This study demonstrates the need for further research on the stability of coated forms of nano zinc oxide before they can be declared 'safe'.

2. Does the SCCS confirm that zinc oxide in its non-nano form is safe for use as a UV- filter with a concentration up to 25% as stated in the SCCP clarification (SCCP/1215/09)?

FoEA disagrees with the SCCS's conclusion that nano particulate forms of ZnO are not absorbed through the skin (p.98) for the reasons previously outlined.

The SCCS have stated that:

"a re-evaluation may be needed in the case of use of other specific coatings, which can promote the dermal penetration of ZnO particles (nano or non-nano)."(p.98)

FoEA believes that the SCCS urgently needs to evaluate:

- the extent to which nano ZnO reacts with other sunscreen ingredients and becomes coated with proteins or lipids
- the widespread use of penetration enhancers in the cosmetics industry has on the extent of skin penetration.

and the impact that these factors may have on skin penetration.

3. And/or does the SCCS have any further scientific concern with regard to the use of zinc oxide in cosmetic products?

FoEA supports the SCCS's conclusion that:

""In view of the lung inflammation induced by ZnO particles after inhalation exposure, the use of ZnO in cosmetic products which may result in inhalation is of concern." (p. 98)

- Moreover, given the recent publication of Nazarenko *et al.* (2012)[30], revealing unexpected routes of exposure of nanomaterials in human airways, FoEAbelieve that all cosmetic powder applications containing nano-forms of zinc oxide should be removed from the market.
- FoEA also supports the SCCS's conclusion that:

  "Any cosmetic products containing ZnO particles (nano or non-nano) with coatings that can promote dermal penetration will also be of concern." (p. 98)

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[29] Virkutyte J., Al-Abed S.R., & Dionysiou D.D. (2012) Depletion of the protective aluminum hydroxide coating in TiO2-based sunscreens by swimming pool water ingredients. *Chemical Engineering Journal,* **191**: 95-103, http://dx.doi.org/10.1016/j.cej.2012.02.074.

[30] Nazarenko Y., Zhen H., Han T., Lioy P.J. & Mainelis G. (2012) Potential for Inhalation Exposure to Engineered Nanoparticles from Nanotechnology-Based Cosmetic Powders. *Environ Health Perspect*. 120(6): 885–892. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3385434/