FoE concerns regarding removal of a webpage

- The 2016 webpage was a statement in response to the 2016 FoE report on US analytical results. It was removed in order to update it to reflect our current view in response to the current media enquiry on the 2017 FoE report.
- The updated statement was published to our website on 2 July 2017 (the date of the SMH article).
- The removal of the 2016 webpage does not change the requirements for infant formula set out in the Food Standards Code.
- Any change to the Code must undergo a comprehensive assessment and public consultation process. The ultimate decision makers are the Ministerial Forum on Food Regulation who decide whether to accept or not the work on standards produced by FSANZ.

Status of hydroxyapatite

- Nanoparticles can occur naturally in foods and may not be the result of intentional addition (e.g. as an additive). Some are naturally occurring and others occur as a result of processing.
- Experiments with dried milk have found that nano-sized particles of calcium phosphate form naturally.
- The presence of something, whether on the nanoscale or not, in a food that does not have a permission in the Code does not mean a food is unsafe.
- Hydroxyapatite is a naturally occurring chemical form of calcium phosphate. Infant formula is based on milk, which naturally contains calcium phosphates in different forms.
- In our 2016 statement in response to the Fo~~e~~E report we noted that hydroxyapatite wasn't a permitted form in the Code – it is not named specifically.
- Further investigation by FSANZ on this matter has shown that hydroxyapatite is a synonym for a range of calcium phosphate compounds which are permitted forms for infant formula
- The physical chemistry of the calcium phosphates is complex because they can have many compositions (different Ca/P ratio), exist in different forms (amorphous or differently crystallised).
- There are several chemical forms of calcium and phosphorus permitted to be used in infant formula. These are listed in Schedule 29 of the Food Standards Code.
- Schedule 3 of the Code lists the specification reference for the permitted forms of minerals.
- Although FSANZ develops food standards, r~~esponsibility~~esponsibility for ensuring foods (including infant formula) ~~compliance with~~meet the standards set out in the Code ~~food standards for both domestically produced food and imported food rests~~ sits with local government, States and Territory Governments in Australia and the New Zealand Government, public health units or local governments.

- They also have the power to recall food deemed to be unsafe, FSANZ does not.

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BACKGROUND

2016 webpage

- In response to a public campaign from FoE in May 2016 FSANZ reviewed the publically available information and determined that the infant formulas in the survey were not formulas available to consumers in Australia.

- To allay concern we published a statement that the infant formulas tested in the USA are not available for retail sale in Australia and New Zealand. We also noted that substances identified in the FoE report were not permitted food additives, or permitted forms of the minerals, in infant formula in Australia and New Zealand ~~as the FoE messaging implied that the substances were being deliberately added to infant formula~~.

- The webpage also stated that FSANZ considered that the detection of small amounts of these substances in infant formula is unlikely to pose a health concern. Titanium dioxide and silicon dioxide have been used safely as food additives in other foods in Australia, and internationally, for many years. Hydroxyapatite is a natural component of bone and teeth, and small amounts in food are likely to readily dissolve in the stomach to release calcium when ingested.

Safety concerns and the EC SCCS report

- Calcium and phosphorus are essential minerals and are required in infant formula. Several chemical forms of these two minerals are permitted additives to infant formula.

- Hydroxyapatite is soluble in acidic environments such as the stomach, so it can be reasoned that small amounts in food will likely dissolve and release its calcium.

- The researchers from the University of Arizona who detected the hydroxyapatite nanoparticles in infant formula also conducted dissolution experiments with hydroxyapatite in both shapes that were detected. This showed rapid dissolution of the needle-shaped hydroxyapatite in simulated acidic gastric fluids (pH 5 –reported to be similar to infant stomach pH).

- The health effects of hydroxyapatite nanoparticles have been studied in animals with no toxicity at levels well above those present in milk.

- Hydroxyapatite nanoparticles have been widely developed to aid bone repair, deliver drugs and have been extensively tested. All results suggest that even levels required to be drug delivery agents, have no significant adverse effects.

- Researchers have studied the safety of consuming hydroxyapatite nanoparticles. Animals who have consumed hydroxyapatite nanoparticles in their food (not injected) showed no toxicity at levels well above those present in milk (up to 100 milligrams per kilogram of body weight a day for a year).

- Studies where animals have been injected (into veins or into body cavities), have found that levels well above those found in infant formulas to cause damage (50 milligrams nano-hydroxyapatite per kilogram body weight in rats) – the equivalent of 200 litres of formula per day for an infant. ~~.~~

- The EC Scientific Committee on Consumer Safety (SCCS) opinion on hydroxyapatite was based on a request from the EC to assess the use of a hydroxyapatite

"nanomaterial" (defined as an insoluble or biopersistent and intentionally manufactured material with one or more external dimensions, or an internal structure, on the scale from 1 to 100 nm). This definition does not cover nano-size materials that are soluble or degradable/non-persistent in biological systems – i.e **hydroxyapatite.**

- ~~(e.g. liposomes, emulsions, etc).~~

- The SCCS Consumer safety study considered that the information provided by the applicants was insufficient to draw a conclusion on safety when used in oral cosmetic products (eg toothpaste, whiteners, mouth washes) at levels of up to 10%.

- In reaching this conclusion, the SCCS noted that the hydroxyapatite materials under consideration could not clearly be related to the data submitted.

- The report is considered of limited relevance to the detection of trace amounts of hydroxyapatite in the FoE-commissioned study.

The conclusion from the EC SCCS report is copied below

Only a limited amount of data was provided by the Applicants that corresponded to the SCCS Guidance on Safety Assessment of Nanomaterials in Cosmetics (SCCS 1484/12). The provided data were also not in line with the SCCS Memorandum on Relevance, Adequacy and Quality of Data in Safety Dossiers on Nanomaterials (SCCS/1524/13). To facilitate the assessment, the SCCS therefore also considered additional information gathered through a search of the published scientific literature. However, after detailed evaluation, the SCCS has concluded that the evidence, both that provided in the submission and that available in the scientific literature, is insufficient to allow drawing a conclusion on the safety of nano-hydroxyapatite when used in oral cosmetic products. This is because:

- The test materials used in toxicological studies mostly lacked information on characterisation, were poorly described, or were different from those under evaluation (Materials 1 and 2). It is not clear in most cases whether and to what extent the investigated materials correspond to the materials under evaluation.
- Almost all of the toxicological studies provided were not compliant with relevant test guidelines in terms of study design. In most cases, study reports included in the submission provided only a poor description of the studies. The quality of the information from scientific publications could not be assessed because detailed study reports were not available.
- No study, either from those provided by the Applicants or obtained from the scientific literature, could be identified that would allow the identification of a point of departure for use in risk assessment.
- Some studies published in the open literature for hydroxyapatite materials, which are different from the materials under evaluation, point to the possibility that nano-hydroxyapatite might be taken up locally (e.g. into buccal cells), and that it might exert systemic effects after oral exposure. Since no information on long-term exposure is available, it is not possible to draw any conclusion on whether repeated, long-term oral exposure to nano-hydroxyapatite would manifest in adverse effects as indicated in the scientific literature (e.g. expressed in Fox *et al.*, 2012).

Based on the information available, SCCS considers that the safety of nano-hydroxyapatite materials included in the submission to the consumer, when used up to a concentration of 10% in oral cosmetic products, cannot be decided on the basis of the data submitted by the applicants and that retrieved from literature search. Since the available data/ information could not be related to the hydroxyapatite materials under evaluation, the SCCS will need toxicological data specific for the materials included in the submission for safety assessment, unless a close similarity with the materials used in the available studies can be demonstrated to allow data read-across.

Guidance on the types of data important for safety evaluation of nanomaterials in cosmetic products is detailed in the SCCS Nano-Guidance (SCCS/1484/12). Further clarification on certain aspects relating to relevance, adequacy and quality of the data required for safety assessment of nanomaterials is provided in the SCCS Memorandum (SCCS/1524/13).

2. SCCS is requested to address any further scientific concerns with regard to the use of Hydroxyapatite in nano form in cosmetic products.

The available information indicates that nano-hydroxyapatite in needle-shaped form is of concern in relation to potential toxicity. Therefore, needle-shaped nano-hydroxyapatite should not be used in cosmetic products. It is of note that Material 2 of the submission also includes nanofibres of needle-like structure.