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SCIENTIFIC COMMITTEE ON CONSUMER PRODUCTS
SCCP

Opinion on

**THE SAFETY OF FLUORINE COMPOUNDS IN ORAL HYGIENE PRODUCTS
FOR CHILDREN UNDER THE AGE OF 6 YEARS**

Adopted by the SCCP during the 5th plenary meeting
of 20 September 2005

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BACKGROUND

In October 2002 the Scientific Committee on Cosmetic Products and Non-Food Products intended for the Consumer (SCCNFP) was requested to make a safety assessment of the fluoride concentration in oral hygiene products used by children under the age of 6 years.

In May 2003 a submission from COLIPA (The European Cosmetic Toiletry and Perfumery Association) with information on “Fluoride Safety and Dental Fluorosis” was presented to the SCCNFP.

In its opinion SCCNFP/0653/03, on “The Safety of Fluorine Compounds in Oral Hygiene Products for Children under the age of 6 years”, adopted 24/25 June 2003 stated, that *“it is of the opinion that the maximum permitted concentration of 0.15% (1500 ppm) fluorine does not pose a safety concern when used by children under the age of 6 years... If the sole source of fluoride exposure is toothpaste containing fluoride between 1000-1500 F ppm, used as recommended, there is minimal risk that children under the age of 6 will develop fluorosis. It is recommended that children under the age of 6 use a pea size amount of toothpaste with supervised brushing”*.

At the meeting of the Working Group of Member States, stakeholders and the European Commission services on Cosmetics in February 2004, a Member State explained that, according to the German Federal Institute for Risk Assessment, for children under 6 years 500 – 700 ppm fluoride would be more appropriate and submitted data concerning its safety calculation.

1. TERMS OF REFERENCE

The SCCP is requested to answer the following questions:

- *Does the data provided change the opinion of the SCCP on the safety of fluorine compounds in oral hygiene products for children under the age of 6 years, as stated in its opinion SCCNFP/0653/03?*
- *If yes, does the SCCP propose any further restrictions or conditions for the use of fluorine compounds in oral hygiene products for children under the age of 6 years?*

2. OPINION

In the opinion of the SCCP, most of the points raised by the Member State had already been discussed in the previous opinion of SCCNFP, (SCCNFP/0653/03), on the safety of fluorine compounds in oral hygiene products for children under the age of 6 years, adopted on its 24th plenary meeting.

Historically, it was the observation that in areas with high natural fluoride levels in water, there was reduced caries in the population. This led to the concept of water fluoridation and fluoride supplementation. Oral dosing was believed to permit fluoride uptake and as partially fluoridated hydroxyapatite, into the enamel. It was thought that the fluoridated hydroxyapatite was

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incorporated into the crystal lattice, improving lattice stability and rendering it less soluble to acid demineralization. Concomitantly, fluorosis was also noted in some of the population.

Fluoride toothpaste was also developed over this period to improve oral hygiene by preventing the development of caries and, as a result, a reduction in the number of decaying or missing teeth. The quality of research on the efficacy of fluoride toothpaste is good, but it has mostly carried out been in isolation from the systemic intake of fluoride. There are few adequate epidemiological studies of the impact of fluoride toothpaste compared with systemic fluoride intake. The quality of the epidemiological studies on the systemic fluoride exposure is very varied.

In young children, there is concern that there is an overlap between the beneficial effects of topical fluoride associated with caries reduction and fluoride ingestion from all exposure sources that might lead to an increased possibility of dental fluorosis (See Appendix1).

The risk of fluorosis

Development of enamel in the pre-eruptive tooth may be disturbed by many factors, e.g., disease, infection and nutrition, including excess fluoride. Systemically absorbed fluoride, in excess, may impair normal development of enamel in the pre-eruptive tooth, causing fluorosis. Amelogenesis of primary teeth occurs *in utero* and the enamel formation is completed before eruption. Toothpaste would not be the main source for fluoride ingestion of a child under 2 years old since it would only be used after tooth eruption. Tooth eruption may occur from 6 months but excessive toothpaste use before the child is 2 years old is unlikely during this period. However the chance of ingestion would be higher since the swallowing reflex is well developed but control to prevent inadvertent swallowing and the spitting response are not well developed at that age. The risk of fluorosis would be by ingestion from other sources at this age.

Amelogenesis of permanent teeth starts approximately 3 months after a full-term birth and continues slowly for years before eruption. From an aesthetic view, the critical phase is from 20 months to 5 years during the development of the most visible teeth, the incisors and canines. The problem of development of fluorosis in the pre-erupted teeth will not be apparent until tooth eruption. For permanent teeth, this will not be seen for 4-5 years after fluoride exposure.

Efficacy of the toothpaste containing fluoride

There is increasing evidence that the cariostatic activity of fluoride is mainly due to its topical effects on erupted teeth. This effect is a direct interaction due to the continual presence of fluoride in the saliva and in the fluid phase of dental plaque that inhibits the demineralization and promotes re-mineralization on the tooth surface.

Ref.: S28, S22

The frequency of use and concentration of fluoride in toothpaste is critical. The meta-analyses reported in the previous opinion showed that daily use of toothpaste with fluoride is effective in preventing caries in permanent teeth of children and adolescents. The effectiveness is influenced by the concentration, i.e., toothpastes with a higher concentration of fluoride, 1500 ppm (0.15 % F) have a greater cariostatic effect than toothpastes with 1000 ppm (0.1 % F).

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The efficacy of toothpastes with fluoride concentration reduced to below 1000 ppm has not been proven since convincing data on efficacy is lacking. Toothpaste, containing 400 ppm fluoride (F^-) have been available in Australia and New Zealand for approximately 20 years, but there have been no clinical trials. No data are available either to assess whether toothpaste at this concentration has reduced the prevalence of enamel fluorosis in those countries. In a British study, free toothpaste containing either 440 or 1450 ppm F^- was supplied regularly to children aged 12 months. The results were assessed in 7,422 children when they were between 5-6 years old. In the group that received the 1450 ppm F^- toothpaste there was significantly less caries compared with the low fluoride paste and controls. There was no difference between the group of children using the low fluoride containing toothpaste (440 ppm F^-) and the control group.

Ref.: S26

The risk of systemic exposure from fluoride toothpastes

Children, under 6 years, are considered at risk

- as cosmetically objectionable fluorosis of front teeth may occur from excessive systemic absorption of fluoride. Posterior teeth are still at a susceptible stage of enamel development but are not readily visible;
- because the swallowing reflex may not be developed sufficiently to control inadvertent swallowing of toothpaste.

Swallowed toothpaste could contribute to the amount of ingested fluoride if parental supervision is inadequate. The amount of toothpaste applied ranges from 0.05 to up to 0.8 gram, depending whether the toothpaste is applied by the parent or child. The recommended ‘pea size’ amount of toothpaste is taken as 0.25 gram. Most studies find oral retention figures in young children to be around 30%. Intake from 0.3 mg toothpaste would be 0.015 mg/kg bw, calculated on 40% oral retention. This is already an overestimate.

However using this data, the contribution from toothpaste to the Adequate Intake is calculated (Table 1). The Adequate Intake (AI) is based on estimated intakes that have been shown to reduce the occurrence of dental caries maximally in a population without causing unwanted side effects including moderate dental fluorosis.

Ref.: 5

Table 1: Fluoride AI for Children

Age	Fluoride AI (mg/day)	Reference Weight	Toothpaste (mg/day bw)	Other sources ^a (mg/day bw)
7 - 12 months	0.5	9 kg	0.135	0.75
1 - 3 years	0.7	13 kg	0.2	1.2
4 - 8 years	1.0	22 kg	0.3	2.07

a Assuming with 100% absorption, water consumption 1.4 l/day (likely to be an overestimate for the present day MRC 2002) and fluoridated 1.2mg/l and diet 0.2-0.4mg/kg (derived from Hamilton, 1992).

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The MRC suggest that the daily exposure/consumption of fluoride used to calculate total intakes of fluoride mg/kg/bw by Hamilton overestimate exposure. The MRC report also highlights the paucity of data on exposure and bioavailability of fluoride from all dietary sources.

Ref.: 9

Since the current scientific thought is that the cariostatic activity of fluoride is mainly due to its topical effects, the need to provide systemic fluoride supplementation for caries prevention is questionable. This is beyond the scope of this mandate but awareness of the possible potential intake from other sources should be borne in mind. Currently, as public health measures, systemic fluoride supplementation in diet, by water fluoridation, salt fluoridation or as prescribed medicines also occurs within the European Union. These measures vary across the Union.

Ref.: EFSA

CONCLUSION

The SCCP reiterates the opinion that the maximum permitted concentration of 0.15% (1500 F ppm) fluoride does not pose a safety concern when used by children under the age of 6 years, based on the available scientific evidence.

It must be emphasised that the data used were generated from studies primarily on sodium fluoride. Extrapolation of this to the other fluoride compounds presently listed in Annex III of the Cosmetics Directive 76/768/EEC can only be made with respect to fluorosis.

There is strong evidence that toothpaste containing 0.15 % (1500 ppm) fluoride is effective at preventing dental caries in all age groups, including children under the age of 6. This cariostatic effect decreases as the fluoride concentration is reduced. Below 1000 ppm, the cariostatic effect of fluoride is not established. Further research is recommended in order to assess the effect under 1000 ppm fluoride.

If the sole source of fluoride exposure is toothpaste containing fluoride between 1000-1500 F ppm, used as recommended, there is a minimal concern that children under the age of 6 will develop fluorosis since the amount absorbed would be less than half the accepted adequate intake of 0.7 mg/day fluoride intake for children between the ages of 1 and 3, that maximally reduces dental caries without causing unwanted side effects.

In this document, the only oral health product considered is toothpaste. No data for other products were considered. It is known that mouthwashes specifically for children have been developed and are available in some EU members.

Although it is beyond the scope of the mandate, there is exposure to fluoride from other sources. This is not addressed in detail here by the SCCP. The present opinion clearly has implications for the efficacy and safety of systemic fluoride supplementation for caries prevention.

3. MINORITY OPINION

Not applicable

4. REFERENCES

1. W. E. Barnhart, L. K. Hiller, G. J. Leonard, and S. E. Michaels. Dentifrice usage and ingestion among four age groups. *Journal Dental Research* 53 (6):1317-1322, 1974.
2. Centre for Disease Control. Recommendations for Using Fluoride to Prevent and Control Dental Cries in the United States. 2001. www.cdc.gov/mmwr
3. Department of Health and Human Services. U.S. Public Health Service. Review of Fluoride: Benefits and Risks. 1991. www.hhs.gov
4. Fluoride Action Network. Facts about Fluoridation, 2002. www.fluoridealert.org/govt-statements.htm
5. Institute of Medicine. Dietary Reference Intakes for Calcium, Phosphorous, Magnesium, Vitamin D, and Fluoride. 1997 . www.nap.edu/0309063507
6. Levy SM. 1994. Review of fluoride exposures and ingestion. *Community Dent Oral Epidemiol* 22:173-180.
7. Levy SM, McGrady JA, Bhuridej P, Warren JJ, Heilman JR, Wefel JS. 2000. Factors affecting dentifrice use and ingestion among a sample of U.S. preschoolers. *Pediatr Dent* 22:389-394.
8. McDonagh MS, Whiting PF, Wilson PM, Sutton AJ, Chestnutt I, Cooper J, Misso K, Bradley M, Treasure E, Kleijnen J. 2000. Systematic review of water fluoridation. *BMJ* 321:855-859.
9. Medical Research Council. Water Fluoridation and Health. 2002. www.mrc.ac.uk
10. World Health Organisation. Fluorides (Environmental Health Criteria Monograph 36). 1984. <http://www.inchem.org/pages/ehc.html>
11. World Health Organisation. Fluorides (Environmental Health Criteria Monograph 227). 2002. <http://www.inchem.org/pages/ehc.html>

Additional Reference

EFSA, opinion of the Scientific Panel on Dietetic Products, Nutrition and Allergies on a request from the Commission related to the Tolerable Upper Intake Level of Fluoride (Request N° EFSA-Q-2003-018) (adopted on 22 February 2005).

5. ACKNOWLEDGEMENTS

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Appendix 1

The dictionary definition of fluorosis is ‘an abnormal condition (as mottled enamel of human teeth) caused by fluorine or its compounds’ or ‘a pathological condition resulting from an excessive intake of fluorine (usually from drinking water)’. This is very simplistic, since mottling of the enamel of teeth is common and may have many aetiologies, including caries, childhood infections, developmental abnormalities and trauma (Table 1). For example, in the early stages of dental caries that are confined to the enamel, the demineralisation of the enamel may be halted. Re-mineralization of the damaged area would occur but leaving a white or brownish mark appearing similar to mottling.

Table 1: Differential diagnosis: milder forms of dental fluorosis (questionable, very mild and mild) and non-fluoride opacities of enamel (From Russell, 1961)

Characteristic	Milder forms of fluorosis	Non-fluoride enamel opacities
Area affected	Usually seen on or near tips of cusps or incisal edges	Usually centred in smooth surface; may affect entire crown
Shape of lesions	Resembles line shading in pencil sketch; lines follow incremental lines in enamel, form irregular caps on cusps	Often round or oval
Demarcation	Shades off imperceptibly into surrounding normal enamel	Clearly differentiated from adjacent normal enamel
Colour	Slightly more opaque than normal enamel; “paper white”. Incisal edges, tips of cusps may have frosted appearance. Does not show stain at time of eruptions (in these milder degrees, rarely at any time)	Usually pigmented at time of eruption; often creamy-yellow to dark reddish-orange
Teeth affected	Most frequent on teeth that calcify slowly (cuspid, bicuspids, second and third molars). Rare on lower incisors. Usually seen on six or eight homologous teeth. Extremely rare in deciduous teeth	Any tooth may be affected. Frequent on labial surfaces of lower incisors. May occur singly. Usually 1-3 teeth affected. Common in deciduous teeth
Gross hypoplasia	None. Pitting of teeth does not occur in the milder forms. Enamel surface has glazed appearance, is smooth to point of explorer	Absent to severe. Enamel surface may seem etched, be rough to explorer
Detection	Often invisible under strong light; most easily detected by line of sight tangential to tooth crown	Seen most easily under strong light on line of sight perpendicular to tooth surface

Fluorosis is considered to range from scarcely visible white striations to mottling and discolouration evidenced by defects in the tooth enamel. There are several scoring systems to assess the range of severity of fluorosis (Table 2 –4).

Table 2: Classification of the clinical appearance of fluorotic enamel changes characterising the single tooth surface (From Thylstrup and Fejerskov, 1978).

Score	Clinical appearance
0	Normal translucency of enamel remains after prolonged air drying
1	Narrow white lines located corresponding to the perichymata
2	Smooth surfaces: More pronounced lines of opacity which follow the perichymata. Occasionally confluence of adjacent lines. Occlusal surfaces: Scattered areas of opacity <2mm in diameter and pronounced opacity of cuspal ridges
3	Smooth surfaces: Merging and irregular cloudy areas of opacity. Accentuated drawing of perichymata often visible between opacities Occlusal surfaces: Confluent areas of marked opacity. Worn areas appear almost normal but usually circumscribed by a rim of opaque enamel
4	Smooth surfaces: The entire surface exhibits marked opacity or appears chalky white. Parts of surface exposed to attrition appear less affected Occlusal surfaces: Entire surface exhibits marked opacity. Attrition is often pronounced shortly after eruption
5	Smooth and occlusal surfaces: Entire surface displays marked opacity with focal loss of outermost enamel (pits) <2mm in diameter
6	Smooth surfaces: Pits are regularly arranged in horizontal bands <2mm in vertical extension Occlusal surfaces: Confluent areas <3mm in diameter exhibit loss of enamel. Marked attrition
7	Smooth surfaces: Loss of outermost enamel in irregular areas involving less than one-half of entire surface Occlusal surfaces: Changes in the morphology caused by merging pits and marked attrition
8	Smooth and occlusal surfaces: Loss of outermost enamel involving $>1^{1/2}$ of surface
9	Smooth and occlusal surfaces: Loss of main part of enamel with change in anatomic appearance of surface. Cervical rim of almost unaffected enamel is often noted

Table 3: Descriptive criteria and scoring system for the Tooth Surface of Fluorosis (TSIF) (after Horowitz, 1986)

Numerical score	Descriptive criteria
0	Enamel shows no evidence of fluorosis
1	Enamel shows definite evidence of fluorosis, namely areas with parchment-white colour that total less than one-third of the visible enamel surface. This category includes fluorosis confined only to incisal edges of anterior teeth and cusp tips of posterior teeth (“snowcapping”)
2	Parchment-white fluorosis totals at least one-third of the visible surface, but less than two-thirds
3	Parchment-white fluorosis totals at least two-thirds of the visible surface
4	Enamel shows staining in conjunction with any of the preceding levels of fluorosis. Staining is defined as an area of definite discolouration that may range from light to very dark brown.
5	Discrete pitting of the enamel exists, unaccompanied by evidence of staining of intact enamel. A pit is defined as a definite physical defect in the enamel surface with a rough floor that is surrounded by a wall of intact enamel. The pitted area is usually stained or differs in colour from the surrounding enamel
6	Both discrete pitting and staining of the intact enamel exist
7	Confluent pitting of the enamel surface exists. Large areas of enamel may be missing and the anatomy of the tooth may be altered. Dark-brown stain is usually present

Table 4: Dental fluorosis index as described by Moller (1965)

Weighting	Diagnosis	Clinical criteria
0	Normal	The enamel shows the usual translucency. The surface is smooth, shiny and usually of a pale, creamy white to grey white colour. In this group are also opacities, which are not considered to be of fluorotic character.
0	Optimal	The enamel is on clinical inspection completely homogeneously mineralised without hypomineralisation of any sort. The enamel is smooth and mirror-like, and has a shiny, "varnished" look. The colour is creamy white to yellowish white.
0.25	Questionable	In areas with relatively low fluoride content in drinking water, there are cases which even the most experienced researchers cannot classify as either Normal or very mild. These cases show mainly labially in the upper front teeth as very narrow, opaque, paper-white, horizontal lines in the tooth's incisal third especially. In back teeth are now and then seen small, opaque spots (about 0.5mm in diameter) directly on the cusp tips, while the rest of the tooth is completely normally mineralised. The features of these opaque lines and spots are so fine that they are often confused with perichymata. This fine feature shows more clearly with drying the tooth, a procedure which should always be done while diagnosing.
0.25-1	Very Mild	Clearer opaque, paper-white, transversely oriented striations or spots, found spread especially on the upper incisors' labial surfaces and most concentrated in the incisal third. In the back teeth are seen opaque regions (<1mm in diameter) directly on the cusp tips. Opaque, paper-white, narrow, transversely running lines reach down over the cusp, while the rest of the tooth is normal. The opaque regions cover at most a fourth of the surface of the tooth. When viewed from a distance, the tooth seems to have a slightly mother-of-pearl sheen. The lower grades of very mild dental fluorosis are rated 0.5 and the worst 1.0.

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Weighting	Diagnosis	Clinical criteria
1.5 -2	Mild	The mainly transversely running opaque lines and spots are more clear and stretch further down over the tooth's surface towards the outer circumference. One can detect that the opaque lines begin to merge together into diffuse regions, so that the tooth seen at a distance (40-50cm) seems whiter – more opaque – than a normally mineralised tooth. Seen close to, these opaque areas take up, however, at most half of the tooth's surface. Changes in the front teeth's lingual surfaces are considerably less obvious than on the labial. As far as the back teeth are concerned, the changes in labial and lingual surfaces are of more or less the same degree. On the cusps of canines, premolars and molars there are cases where the cusp tips are worn, so that the wear facets peripherally are bordered by a narrow, opaque ring (an expression of the fluorotic surface layer) surrounded by the clearer underlying enamel. In pronounced cases the development of pigment can be seen, especially in the upper incisors. Lower grades of mild dental fluorosis are scored 1.5 and the worst 2.0.
2.5 – 3	Moderate	The opaque regions take up practically all the tooth's surface. Tooth shape is normal, but a weak “pit” development can be found, especially on premolar buccal and palatal surfaces, as well as upper incisor labial surfaces. Pigment where present can vary in colour from yellow to brown. The lower grades of moderate dental fluorosis are rated 2.5 and the worst 3.0.
3.5 - 4	Severe	The shape of the tooth can be changed. The development of pits is pronounced. Merging of pits is often seen. Sometimes the outer layer of enamel is partly or completely missing, and the tooth has a corroded look. Pigmentation varies in colour from brown, to dark brown, to black. Lower degrees of severe dental fluorosis score 3.5 and the worst 4.0.