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Public Comment Submission on draft discussion paper "Review of the regulation of products at the interface between cosmetics and therapeutic goods"

Colgate-Palmolive acknowledges the release of the draft Newgreen report, and is pleased to take the opportunity to provide comment on the recommendations contained within the report.

Colgate-Palmolive understands that the guiding principles for this review of regulation includes not only the primary objective of maintaining and enhancing public health and safety, but also any resulting reforms must be in accord with the COAG principles for effective minimal regulation.

Colgate-Palmolive is concerned that a number of the recommendations of the draft report do not appear to be consistent with these guiding principles. It appears that the report has been drafted with a viewpoint that if a product is recommended to be moved outside the jurisdiction of the Therapeutic Goods Act, there can be no confidence in the products safety thereafter. This is of concern, as the regulatory framework that supports the supply of safe and well controlled cosmetic products in Australia through the NICNAS and ACCC legislations provides alternative regulatory sources adequate to ensure consumer confidence.

Recommendations

1 Cosmetics

Cosmetics Claims guidelines should be established by the Joint Agency, in consultation with stakeholders and other regulators, to clarify the distinction between cosmetics and therapeutic products. These guidelines should be underpinned by legislation if necessary.

Colgate-Palmolive supports the need for a guideline that provides clarity to Industry on the distinction between cosmetic and therapeutic products, and their legitimate claims.
Colgate-Palmolive supports the need for such a guideline to be issued by the partnership of industry and regulators. Colgate-Palmolive notes that the existing cosmetic claims guidelines document was produced with the involvement of industry, ACCC & TGA. It would seem appropriate that in moving forward, the new guidelines should be developed by the regulatory agencies ACCC, NICNAS and TGA in collaboration with industry.

2. Antiperspirants

Antiperspirant preparations that derive their antiperspirant properties from inorganic salts [or their organic complexes] of aluminium, zinc or

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zirconium only should not be classified as therapeutic products under the Joint Agency. Antiperspirants other than these should be regulated as Class II medicines.

Colgate-Palmolive supports the recommendation in principle, but is concerned that new product innovations should not default to Class II medicines simply because they do not contain one of the historical, listed active ingredients. Colgate-Palmolive would seek consideration of a revised recommendation that proposes that any topical antiperspirant product should not be classified as a therapeutic product if the ingredients that provide the antiperspirant properties are listed on the AICS, and the products were not scheduled in any schedule to the SUSDP. There should be no impediment to these low risk antiperspirant products being considered suitable for cosmetic product status.

3. Antidandruff Preparations

Antidandruff shampoos, hairdressings and lotions should be classified as therapeutic products by the joint agency.

If the antidandruff product is not scheduled in any schedule to the SUSDP,

(a) the product should be exempted from licensing; and

(b) the premises where the product is manufactured should be exempt from licensing.

The recommendation does not seem to be in accord with the guiding principles 1 & 2. As there seems to be an absence of any identified public health or safety concerns with this category of products, Colgate-Palmolive does not support the draft recommendation.

Colgate-Palmolive understands that if antidandruff preparations not scheduled in any schedule to the SUSDP were classified as excluded goods, they would be subject to the full provisions of the ACCC cosmetics labelling requirements, providing full ingredient disclosure. Public safety would be assured as ingredients would be required to be included on the AICS.

4. Sunscreens

*A. **Primary sunscreens where SPF is ≥ 4** should be classed as therapeutic products and described as Class I medicines. As a condition of licensing, the SPF of each product must be determined by the method prescribed by AS/NZS 2604:1998 for the particular product. The Joint Agency should consider moving to an acceptable international standard when one becomes available. The Joint Agency Rules should specify that all performance statements and markings on the product label (both .mandatory. and .optional.) are expressed in the manner prescribed by AS/NZS 2604:1998 and no other*

*B. **Primary sunscreen products where the SPF is <4** should not be classified as therapeutic products.*

C. ***Moisturisers that contain a sunscreen as and for a secondary purpose where the SPF ≥4*** *should not be classified as therapeutic products provided:*

(a) they meet the definition of secondary sunscreen product. as defined in AS/NZS 2604:1998; and

(b) Any SPF or equivalent category description is disclosed on the label;

(c) the SPF or equivalent category description disclosed on the label is determined by the method prescribed by AS/NZS 2604:1998 for the precise formulation; and

(d) the SPF as disclosed on the label does not exceed 20; and

(e) the formulation is not water-resistant; and

(f) there is an expiry date or use by date on the label if the product is not stable for at least 36 months; and

(g) no therapeutic claims, including any representation about skin cancer, are made; and

(h) any representation about anti-ageing can be made only if the product is defined as a .broad-spectrum product. within the meaning of AS/NZS 2604:1998; and

(i) the pack size does not exceed 300 mL or 300 g; and

(j) all performance statements and markings (both .mandatory. and .optional.) are expressed on the product label in the manner prescribed by AS/NZS2604:1998 and no other.

An Australia- or New Zealand- specific disclaimer or advisory statement to the effect that the product is only for use as a cosmetic should not be compulsory on moisturizers that are secondary sunscreens.

Colgate-Palmolive supports the three recommendations for sunscreening products, and suggests that the AS/NZS standard for secondary sunscreens be included into the Trade Practices (Consumer Product Information Standard) Cosmetics Regulations 1991. The inclusion of these requirements will ensure Industry's compliance with the AS/NZS.

5. Antibacterial skin washes

A. Antibacterial skin washes *(including antibacterial hand wipes) should be classified as therapeutic products and described as Class II medicines.*

B. *The Joint Agency, in conjunction with NICNAS, ERMA and other regulators and in consultation with stakeholders and experts in public*

health and microbiology determine whether the routine domestic use of hand washes containing an antibacterial agent (irrespective of the stated purposes of the product):
(a) gives rise to the development of resistant strains of bacteria;
(b) has a deleterious effect on micro-organisms that are harmless or whose presence has, in some way, a beneficial effect in humans.
If the decision is that there is no risk to public health from the routine domestic use of hand washes containing an antibacterial agent, further consideration should be given to the appropriate classification of these products across the therapeutic / cosmetic interface.

Colgate-Palmolive is very concerned that this recommendation has placed a caveat on consideration of Industry's pragmatic stratified approach to regulation of this diverse product category, due to a perception of public health detriment caused by products in this category.

Colgate-Palmolive does not support the proposal to retain the current level of regulation for these products as Class II products. Colgate-Palmolive supports the Industry position as proposed by ACCORD, and does not consider there is sufficient need to warrant the establishment of a TGA Expert Committee to consider Part B of this recommendation.

Colgate-Palmolive believes that an appropriately constituted working party of relevant industry and regulatory agency stakeholders would be able to access the data held by Industry to facilitate the resolution of this issue, and allow Industry's proposal to be appropriately considered.

6. Antibacterial skin cleansers (anti-acne products)
Antibacterial washes that are represented to prevent or treat acne or pimples should be classified as therapeutic products and described as Class II medicines.

Colgate-Palmolive does not have products in this category and is unable to provide comment on the recommendation.

7. Toothpastes and mouthwashes

A. Desensitising toothpastes and gels *should be classified as therapeutic products and described as Class II medicines.*

B. Toothpastes and gels that contain 1000 mg/kg or less of fluoride ion *and that do not make any claim (except cosmetic claims) other than preventing caries or preventing or removing plaque should not be classified as therapeutic products.*

C. Mouthwashes that contain an antibacterial substance *for freshening the breath or for fighting plaque and where no therapeutic claims are made should not be classified as therapeutic products.*

D. Mouthwashes that contain 220 mg/L or less of fluoride ion *and that do not make any claim (except cosmetic claims) other then*

preventing caries or preventing or removing plaque should not be classified as therapeutic products.

Colgate-Palmolive does not support draft recommendation A, as the draft report does not appear to have demonstrated that public health and safety would be adversely impacted if desensitising toothpastes were not classified as therapeutic products.

The draft report acknowledges that this category of goods are of low regulatory risk, but proposes the retention of a high level of regulatory control over these products. This recommendation appears inconsistent with the guiding principles 1 & 2 of the review.

With regard to public health and safety, it is worthwhile noting that the dental profession regard the risk of dental decay as having significantly greater public health risk than tooth sensitivity. This is confirmed by the literature, and the attached report from a local expert in this field Professor L Walsh, Professor of Dental Science, University of Queensland School of Dentistry.

Fluoride containing toothpastes that prevent dental decay, which are used continuously, have always been appropriately classified in Australia as cosmetics. By comparison toothpastes that relieves sensitive teeth, which are acknowledged within the draft report to "pose little risk... (and are) used episodically, rather than continuously", are highly regulated. The recommendation appears to be inconsistent with the objectives of the review.

As stated above in the opening comments, Colgate-Palmolive is concerned by the statements in the report that propose that if desensitising toothpastes were removed from therapeutic products classification, manufacturers "would no longer have to provide efficacy and could incorporate untested chemicals into the formulations." This statement seems to completely dismiss or ignore the existing, effective regulatory structure that supports all cosmetics supplied in Australia.

Colgate-Palmolive proposes an alternate recommendation, in which desensitising toothpastes which contain active ingredients which are accepted as desensitising agents for self application by the FDA or EU, and which are included in the AICS, should not be classified as therapeutic products. This classification proposal would provide adequate consumer protection for this category of low risk products.

Public safety would be assured as ingredients would be required to be included in the AICS, and the products would be subject to the full provisions of the ACCC cosmetics labelling requirements, providing full ingredient disclosure.

Proposed Recommendation 7A: ***Desensitising toothpastes and gels*** *that are not scheduled in any schedule to the SUSDP, and which derive their desensitising properties from ingredients accepted by the FDA and/or EU for this specified use, should not be classified as therapeutic products.*

Colgate-Palmolive notes that recommendations 7 B & D reflect the current regulatory status quo. Consideration should be given to expanding recommendation 7C to provide clarity that other oral hygiene products that contain an antibacterial substance for freshening the breath or for fighting plaque should also not be classified as therapeutic products. This would provide clarity for Industry and a consistent approach for the oral hygiene category.

*Proposed Recommendation 7C.**Oral hygiene products (including toothpastes that contain 1000mg/kg oror less of fluoride ion**) that contain an antibacterial substance for freshening the breath or for fighting plaque and where no therapeutic claims are made for the antibacterial substance, should not be classified as therapeutic products.*

8. Other product categories that may be candidates for reform

Medicated soaps have been overlooked in this review. Currently medicated soaps are registered therapeutic goods, with an exemption from GMP. Given the scope of the review, there would seem to be a strong justification for considering this category of products in the review. The report states in its discussion on antiperspirants "deodorants that are not antiperspirants rely on the presence of alcohol .. as a masking agent, or an antibacterial agent such as triclosan .." This approach, along with recommendation 7C confirms that the simple presence of an antibacterial agent in the formula does not preclude the product from being used for cosmetic purposes.

Colgate-Palmolive would propose that medicated soaps that behave in the marketplace as cosmetics or toiletries and make no claims in relation to acne or pimples should be regulated as cosmetics. Medicated soaps that make claims in relation to acne, pimples or other skin problems, whilst still considered low risk products with minimal potential for issues of public health and safety could be classified as low level, exempt therapeutic products, exempt from licensing, and exempt from GMP.

Yours sincerely

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Dentine Hypersensitivity:
Current concepts and treatments

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Introduction

Dentine hypersensitivity (DH) may be defined as transient short, sharp, tooth-related pain arising from exposed dentine, typically in response to external tactile, osmotic (evaporative), chemical or thermal stimuli, that is not due to other forms of dental pathology such as dental caries, or dental treatments such as restorative dentistry or bleaching.

There is substantial variation in the response to such stimuli from one person to another (Addy & Dowell, 1983). DH must be differentiated from other conditions that may cause sensitive teeth, and attention must be paid to antecedent conditions such as dental erosion.

Dentine hypersensitivity is a distinct clinical entity, and requires particular management strategies to be used to gain long-term relief. DH manifests a relatively simple cause-and-effect relationship in that there is an obvious association between the location of the exposed dentine with patient dentine tubules and the response to a topically acting stimulus (such as a cold beverage or acidic foods). This is in contrast to dental caries, where dental pain typically develops many months after the destructive process has been underway; the actual carious lesions are frequently in locations where they cannot be seen easily by the patient, and consequently both clinical and radiographic examination by a dental professional is required to chart the location of all carious lesions.

Measures which have been proven to prevent dental caries (such as fluoride dentifrices) do not treat the terminal event (such as the open cavitation of tooth structure); in contrast, with desensitizing dentifrices the patency of the dentine tubules and the hyper-reactivity of the dental pulp nerves which cause the clinical problem of DH are addressed directly by the dentifrice.

DH is a common complaint but does not have serious consequences for the long term health of the dentition, unlike dental caries which is the major cause of tooth loss of adults in Australia. Key important points of difference between dental caries and DH are summarized in Table 1 below.

Dentist

Table 1. Comparison of dental caries and dentinal hypersensitivity

Parameter	Dental caries	Dentinal hypersensitivity
Aetiology	Bacterial plaque; transmissible infectious disease	Exposure of tooth surface from abrasion, erosion, or recession
Symptoms	Short duration discomfort, progressing to unstimulated prolonged throbbing pain	Short duration (transient) discomfort
Prevalence	Relatively low	Relatively high
Sequelae	Reversible pulpitis, irreversible pulpitis, pulp death, periapical infection, tooth loss	Reversible pulpitis; Avoidance of stimuli
Prevention	Dietary modification (sugar restriction), Fluoride, Anti-bacterial agents (chlorhexidine)	Avoidance of erosive foods; correct oral hygiene
Treatment	Caries removal and placement of a restoration into the cavitation	Sealing of patent dentine tubules, measures to reduce reactivity of dental pulp nerves
Role of dentifrices	Sodium fluoride or sodium monofluorophosphate prevents dental caries and enhances remineralization	Potassium citrate/nitrate desensitizes pulpal nerves; stannous fluoride seals exposed dentine tubules
Regulation of therapeutic agents	Fluoride-containing agents have claims of therapeutic efficacy; high fluoride products are restricted for use in adults because of issues with ingestion; conventional adult-strength dentifrices are currently NOT regulated; fluoride mouthrinses of 200 ppm and less are NOT regulated.	Desensitizing dentifrices have similar fluoride levels to conventional adult-strength dentifrices; Issues with toxicity from ingestion are not significant; thus these products should NOT be regulated.

Epidemiology

DH has been described in the dental literature for more than 100 years (Rosenthal, 1990). There is considerable interest in the condition today, which could be due to improvements in oral health, reduced dental caries and greater retention of teeth into the adult years. In parallel with this, there may be greater exposure of root surface dentine

because of gingival recession. Estimates of the prevalence of DH range from 40% of the adult population (Banoczy, 2002). With teeth being maintained longer, there has been an increased demand placed upon the dentist to manage the sensitivity of cervically exposed dentine (Berman, 1985). Reports of the prevalence of dentinal hypersensitivity in the literature vary from 4 to 74%, with many studies in the range of 20 to 30% (Figure 1). This wide variation in prevalence may be because of a number of factors, including different methods used to diagnose the condition, variation in the consumption of erosive foods and drinks and the type of setting where the study was carried out (Rees *et al.* 2003)

In general, a slightly higher incidence of DH is reported in females than in males, which may reflect their overall healthcare and better oral hygiene awareness. Most sufferers from dentine hypersensitivity range in age from 20 to 40 years, however the peak occurrence is found at the end of third decade. In terms of the intra-oral distribution, DH is most commonly reported from the buccal cervical zones of permanent teeth. Sites of predilection in descending order are canines and first premolars, incisors and second premolars and molars (Dababneh *et al.* 1999). The most common sites are easily visible to a patient under normal lighting conditions.

DH affects the eating, brushing, drinking, and breathing habits of patients (Scherman & Jacobsen 1992; Richmond, 1993). Patients who suffer from dentine sensitivity may have endured the condition for several months. This may be explained by acidic components within the diet that are capable of removing the smear layer formed on exposed cervical surfaces by brushing.

Hypersensitive teeth are common temporary annoyances, and dental patients need simple solutions to their dentine hypersensitivity problems. In most studies of DH, response to cold and the movement of air are cited as the most prevalent stimuli. The characteristic nature of the pain associated with DH and its physical association with visibly exposed dentine (typically on the buccal surfaces of teeth) means that patients can identify readily a clear cause-and-effect relationship. This is important, since as already noted other forms of dental pain (such as from dental caries) can also occur in patients, albeit with a lesser frequency – however these may not be detected by the untrained observer.

The clear association between the location of the exposed dentine and how the stimulus is applied (such as a cold or acidic drink) **makes DH eminently suitable to self-applied measures, such as desensitizing dentifrices.** Nevertheless, patients affected by this condition should be made aware of the need to contact their dentist should the problem of DH persist despite their at-home use of dental products. This information would normally be provided on the packaging materials used for such products.

Authors	Country	Setting	Study type	*n*	Prevalence (%)
Jensen, 1964	USA	University	Clinical	3000	30
Graf and Glase, 1977	Switzerland	Practice	Clinical	351	15
Flynn et al., 1985	UK	University	Clinical	369	18
Orchardson and Collins, 1987	UK	University	Clinical	109	74
Fischer et al., 1992	Brazil	University	Clinical	635	17
Murray and Roberts, 1994	Indonesia	Not stated	Questionnaire	1000	27
Murray and Roberts, 1994	USA	Not stated	Questionnaire	1000	18
Murray and Roberts, 1994	Japan	Not stated	Questionnaire	1000	16
Murray and Roberts, 1994	France	Not stated	Questionnaire	1000	14
Murray and Roberts, 1994	Germany	Not stated	Questionnaire	1000	13
Murray and Roberts, 1994	Australia	Not stated	Questionnaire	1000	13
Chabanski et al., 1997	UK	University	Clinical	51	73
Irwin and McCusker, 1997	UK	Practice	Questionnaire	250	57
Liu et al., 1998	Taiwan	University	Clinical	780	32
Rees, 2000	UK	Practice	Clinical	3593	4
Taani and Awartani, 2002	Saudi Arabia	University	Clinical	295	42–60
McCarthy et al., 2002	UK	Air force	Questionnaire	228	50

Figure 1. Summary of prevalence studies on dentine hypersensitivity (From Rees *et al.* 2003).

There is a need for greater professional and thereby public health awareness, through education, of the causes, effects and prevention of tooth wear and gingival recession. When patients have used home care measures and found that their problems of DH persist, the clinical management of the patient by the dentist should account for other clinical conditions can produce symptoms mimicking those of dentine hypersensitivity, such as cracked tooth syndrome, fractured restorations, chipped teeth, dental caries, post-restorative sensitivity, and teeth in acute hyperfunction. Patients generally complain that pain arising from dentine hypersensitivity is usually rapid in onset, sharp in character, and short in duration. More rapid response to stimuli or the persistence of pain after removal of the stimuli have been ascribed to inflammatory changes in the pulp. In such cases conventional approaches to the treatment of dentine hypersensitivity are unlikely to be successful and recourse to endodontics even exodontia may be necessary (Dababneh *et al.* 1999).

Aetiology

The most widely accepted theory of how the pain occurs on DH is Brannstrom's hydrodynamic theory (Jacobsen & Bruce, 2001). Experimental evidence indicates that stimuli, such as probing the dentine surface and air blasts, induce fluid movements in the dentinal tubules. These fluid movements, in turn, activate the intra-dental nerves. The condition of the dentine surface is critically important in allowing this process, with a strong correlation between symptomatic DH and patient dentine tubules (Addy, 2002). In addition, the internal environment of the pulp may influence nerve excitability, and in this provides the biological rationale for the use of potassium ions (Markowitz, 1993). For DH to occur, it is necessary to have exposure of dentine. Periodontal diseases and their treatment by debridement, periodontal surgery, dental erosion, toothbrush abrasion,

and over-eruption due to tooth loss, can all contribute to dentine exposure. Avoidance of painful areas when brushing allows dental plaque to accumulate, and this can trigger a cycle of demineralization of the exposed dentine tubules, leading to more sensitivity and continued ineffective cleaning.

In-office treatments

Usually a hierarchy of treatment methods are used, based on using the most conservative first and saving the most aggressive treatment options until after others have been given time to be effective (Table 2). Three principal treatment strategies are used in the dental office (Brookfield *et al.* 2003). Dentinal tubules can be covered by gingival grafts, bonding agents, or adhesive dental restorations. The tubules can be plugged to reduce the effective diameter and thus the fluid flow along the tubules. This can be done using compounds (such as fluorides, oxalates, and calcium phosphates) that can precipitate together into a large enough mass to occlude the tubules, precipitating and coagulating proteins using glutaraldehyde, or by using infrared lasers, which can cause partial or complete closure of dentine tubules by melting the outer surface of the dentine (Forrest-Winchester & Walsh, 1992; Shakabiae *et al.* 2002). In-office agents that obliterate the dentinal tubules may provide initial relief of pain, but they can impede the flow of potassium and nitrate ions toward the pulp and diminish the long-term beneficial effects seen with the routine use of potassium nitrate dentifrices (Hodosh *et al.* 1994).

The third strategy is to desensitize nerves within the sub-odontoblastic plexus. This can be done using potassium compounds applied topically (Hodosh, 1974), or by low level laser therapy (Sandford & Walsh, 1994). Several over-the-counter products are available to patients to treat this condition.

In terms of complexity and cost-benefit, topical application of fluoride, potassium and oxalate products is technically straightforward, while iontophoresis of fluoride ions is more complex. Application of laser energy is more complex again, as is the application of adhesive restorative materials, such as glass-ionomer cements and dentine bonding agents, to the sensitive tooth region. Coverage of root surfaces using soft tissue surgery is perhaps the most complex in-office therapy (Gangarosa 1994). This type of surgery is delicate and technique sensitive. As a last resort for intractable DH that has not responded to any of the usual treatment modalities over time, endodontic (root canal) therapy is another option. This is costly and may necessitate yet further further treatment such as the placement of crowns.

Home care products

Simple daily plaque removal using a conventional toothpaste can reduce plaque acidogenesis and allow saliva to contact the exposed dentinal tubules and thus achieve some level of remineralization. This process can be enhanced by using mineral delivery systems such as casein phosphopeptides combined with nanoclusters of amorphous calcium phosphate. The limitation of toothbrushing with a conventional toothpaste as a strategy for dealing with DH is that the effect of treatment is relatively slow, whereas

patients demand rapid relief. It is impractical in many patients to expect a sustained level of immaculate oral hygiene.

The dental literature supports the efficacy of potassium, fluoride and strontium-containing toothpastes in the treatment of DH (West *et al.* 1997). Considerable recent attention has been directed to dentifrices containing soluble potassium salts, particularly potassium nitrate and potassium citrate. Other potassium salts which have been examined for this application include potassium chloride and potassium oxalate. Potassium nitrate- and citrate-containing fluoride dentifrices are significantly more effective than conventional fluoride dentifrices at reducing sensitivity (Chesters *et al.*1992).

Colgate Sensitive Tartar Control, which contains 5.0% potassium nitrate, 1.3% soluble pyrophosphate, 1.5% PVM/MA copolymer, and 0.243% sodium fluoride in a silica base when used twice daily (morning and evening) for one minute, has been shown to reduce symptoms of DH, assessed using tactile sensitivity, cold air blast, and a visual analogue pain score. Over 6 weeks, the effect was comparable to a dentifrice containing 5% potassium nitrate and 0.76% sodium monofluorophosphate in a dicalcium phosphate dihydrate base (Sensodyne-F) (Ayad *et al.* 1994). After 6 weeks of use, Colgate Sensitive Tartar Control was shown to provide significant improvements in tactile, thermal (threshold and pain) and air blast sensitivity, as compared to a placebo dentifrice without potassium nitrate (Schiff *et al.* 1994).

The availability of potassium and fluoride from Colgate Sensitive Tartar Control dentifrice was tested by Crawford *et al.* (1994), and found to be acceptable in both freshly prepared and aged samples. Fluoride and potassium availability were also tested at dilutions similar to *in vivo* brushing levels, and the ability of the Sensitive Tartar Control dentifrice to provide fluoride to enamel and reduce enamel solubility was measured. In these tests the Sensitive/Tartar Control dentifrice performed similarly to commercial fluoride dentifrices. Potassium availability was equal to Crest Sensitivity Protection, a product shown to be clinically effective against tooth sensitivity, while fluoride availability and activity was shown to be equal to Crest Tartar Control, a product with published clinical anti-caries effectiveness (Crawford *et al.* 1994).

In vitro and animal studies have shown that the fluoride in Colgate Sensitive/Tartar Control effectively inhibits formation of enamel and dentine caries. *In vitro* studies have also demonstrated that this dentifrice effectively reduces hydraulic conductance by occluding dentine tubules with a mixed surface deposit of copolymer and silica. Using an *in vitro* model that simulates *in vivo* conditions, this dentifrice has been shown to permit rapid penetration of potassium nitrate through the dentine matrix. These findings demonstrate a correlation under *in vivo* conditions between the occlusion of dentine and the ability to deliver topically applied potassium ions to target sites within or below dentine. (Miller *et al.* 1994).

Colgate Sensitive Maximum Strength Toothpaste is a dentifrice which contains 5.0% potassium nitrate and 0.454% stannous fluoride in a silica base, while Sensodyne Fresh Mint Toothpaste contains 5.0% potassium nitrate and 0.243% sodium fluoride, also in a

silica base. Stannous fluoride (and other compounds such as strontium chloride) contribute an additional therapeutic effect on DH by achieving partial occlusion of exposed dentinal tubules. Numerous double-blinded randomized clinical trials have reported that after 2-, 4-, and 8-weeks' use of these products, subjects using Colgate Sensitive Maximum Strength Toothpaste showed greater improvements in tactile and air blast sensitivity, as compared to those using Sensodyne Fresh Mint Toothpaste, Sensodyne F, or a conventional control toothpaste (Colgate Winterfresh Gel) (Conforti *et al.* 2000; Sowinski *et al.* 2000A and 2000B; Sowinski *et al.* 2001; Schiff *et al.* 2000). Similarly positive results have been reported for a dentifrice containing 5.0% potassium nitrate and 1500 ppm sodium monofluorophosphate in a precipitated calcium carbonate (PCC) base for the treatment of DH (Schiff *et al.* 1998).

There is laboratory evidence that potassium nitrate does not reduce dentinal hypersensitivity by occlusion of dentine tubules (Pereira & Chava, 2002). Rather, the postulated mechanism of action is that potassium ions released from toothpastes diffuse along the patent and exposed dentinal tubules to reach the dental pulp, to there inactivate intra-dental nerves by elevating the concentration of potassium ions in the extracellular fluid (Orchardson & Gillam, 2000). For the same reason, potassium nitrate has been incorporated into a range of home bleaching products such as carbamide peroxide gels (Haywood 2000; Tam 2001), and mouthrinses, to alleviate the symptoms of DH (Jerome, 1995; Gillam *et al.* 1996; Pereira & Chava, 2001 & 2002).

Numerous randomized controlled clinical trials (RCTs) have been conducted to assess the effectiveness of dentifrices containing potassium compounds. There have been more than 16 double-blind randomized trials of toothpastes containing potassium nitrate, chloride, or citrate. These toothpaste studies have provided quantitative data on treatment effects, such as percentage reductions in sensitivity to cold air and mechanical stimulation, as well as patients' subjective reports. All such trials of potassium-containing toothpastes have shown a significant reduction in sensitivity to tactile and air stimuli, as well as subjectively reported sensitivity, comparing the active agent (potassium) to minus-active controls as placebos (Chesters *et al.* 1992 ;Orchardson & Gillam, 2000). A recent meta-analysis of four RCTs by the Cochrane group showed a statistically significant effect of potassium nitrate dentifrices on sensitivity to air blast and tactile stimuli, with a standardized mean difference in sensitivity scores of -1.51 (95% CI: -2.09 to -0.94) in favour of treatment, compared with non-potassium nitrate containing placebo control toothpastes (Poulsen *et al.* 2004).

Of importance, the anti-caries efficacy of fluoride dentifrices containing potassium nitrate as the anti-hypersensitivity agent is not significantly different from conventional dentifrices containing fluoride compounds alone. This has been established using a range of laboratory models of dental caries as well as animal studies. For example, in the recent report of Fisher *et al.* (2003), four surrogate studies were performed including fluoride uptake in sound enamel, enamel solubility reduction, fluoride bioavailability and dental caries in animals. Each of these studies indicated the potassium nitrate dentifrice (Colgate Sensitive Maximum Strength) was effective in inhibiting the caries process. Other clinical trials have shown that the level of extrinsic stain removal with Colgate Sensitive

Maximum Strength Toothpaste is identical to that of conventional fluoride dentifrices such as Colgate Winterfresh Gel (Schiff *et al.* 2000).

Safety issues with ingestion of potassium-containing dentifrices

Potassium is a major regulator of key physiological functions including blood pressure, normal muscle contraction, heartbeat, and water balance. A typical diet includes substantial qualities of potassium. Major food sources are potatoes, fresh fruit, fish, citrus and tomato juices, milk, nuts, raisins, canned sardines, and whole grain cereals. The recommended daily allowance for potassium is 3500 mg. Desensitizing dentifrices typically contain 5.0% potassium nitrate by weight. Typical amounts of toothpaste used are in the order of one gram per brushing cycle, and under normal situations only a small quantity of toothpaste is ingested accidentally. Assuming complete ingestion occurs, this would result in an intake of 50 mg of potassium nitrate, which is less than one percent of the normal daily potassium intake.

Ingestion of large quantities of potassium nitrate as a bolus can be harmful, eliciting methemoglobinemia and causing kidney damage. The LD50 has been determined to be 1901 mg kg-1 in the rabbit, and 3750 mg kg-1 in the rat (MSDS, January 2004 from Oxford University; MSDS August 1998 from Fisher Scientific). For an adult human of typical body weight (70 kg), this equates to 133 grams (38 times the recommended daily dietary allowance), using the rabbit LD50 value.

LD50 values for potassium nitrate have not been established. The substance does not pose significant concerns regarding toxic effects with ingestion. In fact, potassium citrate has been used therapeutically by deliberate ingestion in children to treat idiopathic hypocitruria and calcium stones in the kidney. Clinical trials of this therapy demonstrate the safety and efficacy of oral potassium citrate treatment, when used to restore normal urinary citrate levels and to prevent recurrent calcium kidney stone disease in children (Tekin *et al.* 2002). Prior to this, potassium citrate had been used in the 1950's and thereafter for elective cardiac arrest (potassium-based cardioplegia). Today, potassium citrate forms the core of the cardiac surgeon's myocardial protective armamentarium and has contributed towards lowering operative mortality rates for open heart surgery (Shiroishi, 1999). This again attests to the safety of potassium citrate.

Conclusions

The dental literature supports the efficacy of potassium, fluoride and strontium-containing toothpastes in the treatment of DH. Such agents can give long term reductions in the severity of sensitivity to tactile, thermal and air stimuli, as demonstrated in numerous double-blind randomized controlled clinical trials. Given the large normal dietary intake of potassium, there are not significant concerns regarding ingestion of potassium compounds from these toothpastes. Desensitizing toothpastes typically contain levels of fluoride identical to conventional dentifrices used for caries prevention (which are not regulated). **Thus, it is sensible to conclude that because of their low risk-high benefit, desensitizing dentifrices should NOT be regulated.**

Table 2. Treatments for dentinal hypersensitivity

IN OFFICE TREATMENTS

Gels and liquids
- Potassium oxalate
- Ferric oxalates
- Neutral sodium fluoride gels
- Iontophoresis with 2% sodium fluoride
- Casein phosphopeptides-ACP
- Corticosteroids
- Calcium hydroxide

Varnishes
- Copal varnishes
- Fluoride varnishes
- Methacrylate and glutaraldehyde

Resins
- Dentine bonding agents
- Sealants

Glass ionomer cements
- Conventional restorative GIC
- Resin-modified GIC
- High fluoride release materials

Laser therapies
- Laser sealing of tubules
- Laser-enhanced fluoride
- Low level laser therapy

Surgical procedures
- Free gingival grafts
- Connective tissue grafts

HOME CARE TREATMENTS

Dentifrices or gels
- potassium nitrate
- potassium citrate
- stannous fluoride
- strontium chloride
- sodium fluoride
- sodium monofluorophosphate
- casein phosphopeptides-ACP

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