



Tooth Whiteners & Oral Hygiene Products

containing hydrogen peroxide

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Level 2 - Details on Tooth Whiteners & Oral Hygiene Products

Hydrogen Peroxide

1. **What is hydrogen peroxide and what is it used for?3**
2. **What health effects of hydrogen peroxide have been observed?.....3**
 - 2.1 At what levels can swallowing a single dose of hydrogen peroxide be poisonous?.....3
 - 2.2 Can hydrogen peroxide affect skin, eyes, or mucous membranes?.....3
 - 2.3 At what levels can repeated exposure to hydrogen peroxide harm health?5
 - 2.4 Can hydrogen peroxide cause cancer or harm reproduction?.....5
 - 2.5 What genetic disorders make some individuals more vulnerable to hydrogen peroxide?6


Oral hygiene products & tooth whiteners

3. **How is hydrogen peroxide used to whiten teeth?.....7**
4. **How much hydrogen peroxide is an individual exposed to when using dental products?.....7**
 - 4.1 What is the level of exposure when using toothpastes and mouth-rinses containing hydrogen peroxide?.....7
 - 4.2 What is the level of exposure during a tooth whitening treatment?.....8
5. **Can tooth whitening products containing hydrogen peroxide harm teeth? ...9**
 - 5.1 What have clinical safety trials revealed about potential effects on teeth?.....9
 - 5.2 Can tooth whitening affect enamel and dentin?.....9
 - 5.3 Can tooth whitening affect dental pulp?.....10
 - 5.4 Can tooth whitening affect fillings and other dental restorative materials?.....10
6. **How safe are products containing hydrogen peroxide?.....11**
 - 6.1 How are hydrogen peroxide solutions classified and labelled?11
 - 6.2 How safe are oral hygiene products and toothwhiteners?.....11
7. **What should be considered before a tooth whitening treatment?.....12**
8. **Conclusion – Are oral hygiene products and tooth whiteners containing hydrogen peroxide safe and should they be freely available to consumers?.13**

The answers to these questions are a faithful summary of the scientific opinion produced in 2007 by the Scientific Committee on Consumer Products (SCCP):

"Opinion on Hydrogen peroxide, in its free form or when released, in oral hygiene products and tooth whitening products"

The full publication is available at: <http://copublications.greenfacts.org/en/tooth-whiteners/>
and at: <http://ec.europa.eu/health/opinions/en/tooth-whiteners/>

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- Level 3 consists of the Source document, the internationally recognised scientific opinion which is faithfully summarised in Level 2 and further in Level 1.

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1. What is hydrogen peroxide and what is it used for?

Hydrogen peroxide is a highly reactive chemical containing the elements hydrogen and oxygen (H_2O_2). Pure hydrogen peroxide is a colourless liquid, but it is sold on the market as solutions in water, containing up to 33 – 37% pure hydrogen peroxide and other additives to prevent product decomposition. In industry, it is mainly used in the production of chemicals and in bleaching of cellulose pulp and textiles. In Europe, 750 000 tonnes of hydrogen peroxide were produced in 1995.



Carbamide peroxide ($CO(NH_2)_2 \cdot H_2O_2$) is a chemical that contains hydrogen peroxide and urea – an organic compound. Pure carbamide peroxide has the form of white crystals or crystal powder, is soluble in water, and contains approximately 35% hydrogen peroxide. In Europe, about 300 tonnes of carbamide peroxide were used in 1995.

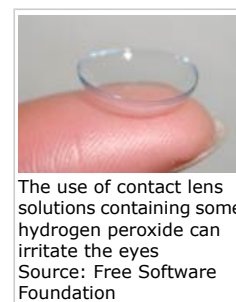
Both hydrogen peroxide and carbamide peroxide have cosmetic uses, mainly as bleaches in consumer products such as hair bleaches, hair perming products, hair relaxers, tooth whiteners. Low concentrations may also be used in oral hygiene products such as mouth rinses and toothpastes as a disinfectant to prevent plaque and inflammation of the gums.

In the European Union, cosmetics are regulated by the Cosmetics Directive

2. What health effects of hydrogen peroxide have been observed?

2.1 At what levels can swallowing a single dose of hydrogen peroxide be poisonous?

In **laboratory tests**, animals were fed a single dose of hydrogen peroxide. Those tests determined doses at which hydrogen peroxide would cause the death of half of the animals (oral LD_{50}). This occurred in rats with a single dose ranging between 600 -1617 mg/kg body weight. For tooth whiteners containing 10 to 22% carbamide peroxide, the values of oral LD_{50} for mice vary between 87.2 - 143.8 mg/kg body weight.



Individual **human poisoning cases** also provide information on the toxicity of hydrogen peroxide. A 16-month-old boy died after accidentally swallowing a single dose of 600 mg/kg body weight hydrogen peroxide. A man briefly fell into a coma after absorbing an estimated dose of 15 mg/kg body weight before quickly recovering. Discontinued oxygen circulation in the veins and arteries was reported in several infants following exposure to hydrogen peroxide as a result of a medical procedure for cleansing the inner wall of the intestine.

2.2 Can hydrogen peroxide affect skin, eyes, or mucous membranes?

Diluted hydrogen peroxide solutions are non-irritant or mildly irritant. However, animal tests have shown that hydrogen peroxide above certain concentrations can cause irritation of the eyes, the skin, and the inside of the mouth, stomach, and intestine.

Skin irritation test on rabbits found no sign that tooth whiteners containing 10-22% carbamide peroxide could irritate the skin. Solutions containing up to 8% hydrogen peroxide were shown to be non-irritant when kept on the skin for 24 hours. Solutions containing 10% and 35% hydrogen peroxide respectively caused a slight and a mild irritation of the skin. In two rabbits out of six, a longer continuous exposure of 14 days caused their skin to peel off.

Skin sensitization tests on guinea pigs did not indicate that solutions containing 3 or 6 % hydrogen peroxide induce skin sensitization when applied on the skin or when injected in the skin. In general, data from studies involving women using or working with hair dyes containing hydrogen peroxide does not provide evidence that hydrogen peroxide is a skin sensitiser in humans.

The dose at which half of the animals tested died following application of hydrogen peroxide on the skin was 700 to 7500 mg/kg body weight for rats and 630 mg/kg body weight for rabbits.

Eye irritation studies on human volunteers show that eye drops containing as little as 0.1% hydrogen peroxide, and contact lenses soaked in solutions containing less than 0.03% hydrogen peroxide, can cause eye irritation. Studies on rabbits indicate that a solution containing 5% hydrogen peroxide is non-irritant to mild-irritant. The larger the amount of hydrogen peroxide in a solution, the more irritation it causes, and solutions with more than 10% hydrogen peroxide present a risk of serious damage to eyes. Moreover, a different type of test has shown that several drops of a 2 to 5% solution or repeated application of a 1% solution can induce clouding of the cornea and inflammation of the conjunctiva of rabbit eyes.

Tests to assess the effect of hydrogen peroxide on **mucous membranes in the mouth** revealed that solutions containing about 1% hydrogen peroxide dripped continuously onto the gums and tongue of anaesthetised dogs caused the gums to swell and the outer layer of the gums to thicken and come off. As far as tooth whiteners are concerned, those containing 10-22% carbamide peroxide do not appear to irritate the mouth or gums of rats, mice or rabbits.

Solutions of 15 mg/kg body weight carbamide peroxide given to rats directly into their **stomachs** caused ulceration, but these appeared to be healing after 24 hours. Hamsters given doses up to 2 000 mg/kg body weight of tooth whiteners containing 10% carbamide peroxide or 70 mg hydrogen peroxide showed no changes in the lining of the stomach or first part of the small intestine.

Biological membranes are highly permeable to hydrogen peroxide, thus hydrogen peroxide could readily enter cells. However, hydrogen peroxide is also effectively transformed by the body, and it is uncertain to what extent the unchanged substance may enter into blood circulation. Moreover, red blood cells are very effective in breaking down hydrogen peroxide and will remove it if it enters the blood stream.

2.3 At what levels can repeated exposure to hydrogen peroxide harm health?

To test whether repeated exposure to hydrogen peroxide can harm health, mice and rats were given hydrogen peroxide solutions either with their drinking water, directly into their stomachs through a tube, or through inhalation of hydrogen peroxide vapours.



Tooth whiteners can be applied to teeth using custom made mouthguards
Source: GreenFacts

Mice that were given about 150 mg/kg body weight through their drinking water every day during a 35-week test period grew normally and developed no visible abnormalities, but an examination of these mice after they died showed changes in the liver, kidney, stomach and small intestine. At doses larger than 1000 mg/kg body weight per day of hydrogen peroxide, they lost a lot of weight and died within 2 weeks. The dose below which no harmful effects were observed in mice that are genetically more vulnerable to hydrogen peroxide was 26 and 37 mg/kg body weight per day for males and females respectively.

Rats that were given 506 mg/kg body weight per day of hydrogen peroxide through a tube (directly into the stomach) 6 days a week for 90 days had less appetite, stopped putting on weight and showed changes in their blood and in some organs, particularly the stomach lining. The level of hydrogen peroxide exposure at which no harmful health effect has been observed (No Observed Adverse Effect Level or NOAEL) was 56.2 mg/kg body weight per day. In a similar study where rats were given hydrogen peroxide daily through a tube (directly into the stomach) for 100 days, the NOAEL was 20 mg/kg body weight per day. In another study, rats were exposed to hydrogen peroxide vapors 5 days per week, for a period of 28 days. Cases of irritation and inflammation of the respiratory tract were observed at exposure levels of 14.6 mg/m³ and more, but not at 2.9 mg/m³ (NOAEL).

Based on the various available studies, a lowest observed adverse effect level (LOAEL) of 75 and 86 mg/kg per day was determined for female and male rats respectively. Risks to humans can be assessed by comparing human exposures to the highest exposure at which no harmful effects were observed in any animal studies: 20 mg/kg body weight per day (NOAEL). The ratio between the two is the margin of safety (see question 6.2).

2.4 Can hydrogen peroxyde cause cancer or harm reproduction?

2.4.1 In *in vitro* studies (studies performed on cell cultures grown in laboratory), there is some evidence that hydrogen peroxide may hinder the natural repair of DNA if the DNA has previously been damaged by other reactive chemicals. In other *in vitro* studies, it was shown that hydrogen peroxide can change and **damage the DNA**. However, available *in vivo* studies (studies performed on living animals) do not suggest that it can cause significant changes to the DNA in the examined tissues of test animals such as rats and mice. In similar tests focusing on a limited number of target cells, tooth whiteners containing 10% carbamide peroxide did not seem to change or damage DNA, even in long-term studies on animals. Data on the possible DNA damaging effects of hydrogen peroxide on relevant animal tissues should be gathered.

Regarding **cancer**, a study on mice, which were given hydrogen peroxide in their drinking water, showed that this can cause an abnormal increase in the number of cells that form the first part of the small intestine, and in a few cases caused localised tumours.

In another study, rats that were given water to drink containing 1% hydrogen peroxide showed benign tumours in their forestomachs more frequently than rats that were not. Even though humans do not have a forestomach, these studies are, in principle, relevant to them since they have comparable tissues in the mouth and the upper part of the

oesophagus. Moreover, a substance that causes cancer in the forestomach of rats may cause such effects in other tissues in humans.

Hydrogen peroxide has a weak potential to cause or promote cancers. The way it acts is unclear, but could involve direct damage to DNA, impairment of DNA repair, or chronic inflammation.

For instance, in a study on 19 patients with cancers that had begun in the oral cavity, the 3 patients who had used tooth whiteners in the past were more likely to have diseased lymph nodes than those who did not. This does not necessarily mean that tooth whiteners cause cancer. However, free radicals released by the whitening process have the potential to cause cancer, and therefore the use of these products in this patient population should be studied further.

2.4.2 Studies available do not allow a complete evaluation of the potential impact of hydrogen peroxide on **reproduction and development**.

Limited studies with mice, rats and rabbits which were given hydrogen peroxide in their drinking water suggest that this does not seriously disturb the male or female reproductive functions.

One study on rats showed that powdered feed mixed with hydrogen peroxide was toxic to the foetus. However, this study has major uncertainties and, although it raises some further questions, cannot be used for an assessment.

2.5 What genetic disorders make some individuals more vulnerable to hydrogen peroxide?

In cells of the body, hydrogen peroxide can be present at very low concentrations as a result of normal biological processes. It passes easily across biological membranes.

Hydrogen peroxide can lead to the production of hydroxyl radicals (OH.), which are highly reactive and attack most molecules in living cells. However, the body has enzymes that limit the amount of hydrogen peroxide by speeding up the break-down of hydrogen peroxide into water and oxygen. In mammals, these enzymes are present in nearly all cells. For instance, enzymes in the saliva process hydrogen peroxide very efficiently and are the primary defences against peroxide produced by bacteria in the mouth.

Individuals with certain inherited genetic disorder, such as acatalasemia, G6PD deficiency, and xerostomia, are more vulnerable to hydrogen peroxide than others.

Acatlasemia is a genetic disorder in which the activity of the enzymes responsible for the break down of hydrogen peroxide is lower than normal.

G6PD deficiency is a genetic disorder in which red blood cells lack an enzyme - G6PD - which causes them to be destroyed prematurely. People with such disorder cannot break down hydrogen peroxide adequately.

Xerostomia, or dry mouth, is a genetic disorder in which the salivary glands are less active than normal. This may affect the break down of hydrogen peroxide in the mouth. However, some studies do not support this theory and suggest that these individuals could still use tooth whiteners without ill effects.

3. How is hydrogen peroxide used to whiten teeth?

Teeth contain organic molecules in their enamel and the dentin. These molecules reflect light and are responsible for their coloration. The more complex these molecules, the more light they reflect and the more teeth appear stained or discoloured.



Tooth whiteners can be applied to teeth using custom made mouthguards
Source: GreenFacts

Tooth colour can be improved by a number of methods and approaches including whitening toothpastes, professional cleaning by scaling and polishing to remove stain and tartar, internal bleaching of non-vital teeth, external bleaching of vital teeth, microabrasion of enamel with abrasives and acid, and placement of tooth-coloured restorations.

Hydrogen peroxide has a whitening effect because it can pass easily into the tooth and break down complex molecules. Less complex molecules that reflect less light lead to a reduction or elimination of the discoloration of both the enamel and the dentin.

Depending on the concentration of peroxide they contain, tooth whiteners and oral hygiene products are either freely sold over the counter for home use, dispensed by dentists for home use, or exclusively applied by dentists in their offices. In the European Union, the free sale of oral hygiene products to consumers is only authorised if they contain no more than 0.1% hydrogen peroxide whereas in the USA, whitening products with considerably higher concentrations are sold. In-office bleaching generally uses relatively high levels of whitening agents, for example 25–35% hydrogen peroxide containing products, for rapid treatments.

Several different techniques are used for bleaching teeth at home. The whitening product may be placed in a mouthguard (or tray) that fits over the teeth, applied through adhesive hydrogen peroxide-containing strips that stick to the surface of the teeth, or “painted” on the teeth in the form of a gel.

The length of treatment depends on the level of discoloration and on the whitening product used. It ranges from short interventions in the dental office to applications at home lasting minutes/hours per day and repeated over a number of days. Single dark teeth can also be bleached successfully. Heavy tobacco stains may need as much as three months of treatment. Whitened teeth generally do not darken after treatment or darken only slightly, and when they do, retreating the teeth can easily be done.

4. How much hydrogen peroxide is an individual exposed to when using dental products?

4.1 What is the level of exposure when using toothpastes and mouth-rinses containing hydrogen peroxide?

Toothpastes and mouth rinses may also contain low concentrations of hydrogen peroxide as a disinfectant to prevent plaque and inflammation of the gums.

Studies have shown that hydrogen peroxide present in toothpaste is rapidly broken down by the saliva and that other toothpaste ingredients, such as fluoride or sodium bicarbonate do not interfere with this process. One study found that 70% of the hydrogen peroxide was broken down during the first minute of brushing.

Some of the toothpaste and mouth rinse used is swallowed:

- It is estimated that on average, the total amount of **toothpaste** a person ingests per day is 0.48 g, Assuming that the toothpaste used contains 0.1% hydrogen peroxide, the amount of hydrogen peroxide swallowed would be 0.48 mg.
- The estimated average amount of **mouth rinses** ingested daily is 3 g. If the mouth rinse contains 0.1% hydrogen peroxide, the resulting amount of hydrogen peroxide ingested per day will be 3 mg.

Summary table of clinical studies using hydrogen peroxide toothpastes [[see Annex 2, p. 16](#)]

Summary table of human safety data of hydrogen peroxide in mouth-rinses
[[see Annex 1, p. 15](#)]

Several clinical trials were conducted with toothpastes and mouth rinses containing hydrogen peroxide over several weeks and months. All these studies seem to have been conducted or sponsored by manufactures of oral hygiene products.

Studies on **humans** repeatedly using oral health products containing hydrogen peroxide have shown that:

- using toothpastes containing up to 1.5% of hydrogen peroxide twice a day for up to six months did not lead to adverse health effects related to hydrogen peroxide.
- using mouth rinses that contain up to 1.5% hydrogen peroxide once or twice daily for up to 2 years had no adverse effects on the inside of the mouth, gums or tongue. However, one study reported discoloration of the inner lining of the mouth and the tongue when used 4 times daily for 5 weeks.
- rinses containing 3% hydrogen peroxide used 3 to 5 times per day can cause irritation in people with a previous mouth injury; and
- rinsing and brushing 2 to 3 times daily with products containing more than 6% hydrogen peroxide did affect the tongue and gums in some healthy people.

During the 1990s millions of units of toothpastes containing 0.75% hydrogen peroxide were sold in the USA. This market experience indicates that toothpastes containing 0.75% hydrogen peroxide are well tolerated, with one adverse effect reported for 100 000 sold products (between 1991 and 1994). This rate of reporting and the nature of the reports were similar to that for other toothpastes marketed in the USA.

4.2 What is the level of exposure during a tooth whitening treatment?

It is difficult to estimate the exposure to hydrogen peroxide during tooth whitening treatment, which may vary with the product and the concentration used.

When people undergo tooth whitening treatment, the amount of hydrogen peroxide that is released into the saliva depends mostly on the bleaching system used and depends only partially on the amount of saliva produced by the individual.

During the first 30 to 60 minutes of tooth whitening treatment, the concentration of hydrogen peroxide at the gums and in the saliva falls very quickly, because hydrogen peroxide is rapidly broken down.

A tooth whitening strip with 6% hydrogen peroxide contains about 12 mg of hydrogen peroxide. A study estimated that people using **4 such tooth whitening strips** per day, swallow about 4.8 to 11.4 mg hydrogen peroxide per day. However, since the flow of saliva – which affects the calculations – is likely to be greater when the strips are applied, actual

exposure may be greater. Swallowing an entire strip – which can occasionally happen – results in an exposure of about 12 mg hydrogen peroxide.

The estimated exposure to hydrogen peroxide through tooth whitening mouthguards containing 10% carbamide peroxide is about 1.68 to 4.2 mg per day considering that a person swallows 10 to 25% of the whitening gel in the mouthguard during application. The techniques used to make custom-fitted mouthguards and the tooth whiteners themselves have improved recently. Hence, modern treatments use a smaller amount of whitener than older methods.

Total amount of hydrogen peroxide swallowed appears to be similar for tooth whitening strips and mouthguards.

5. Can tooth whitening products containing hydrogen peroxide harm teeth?

5.1 What have clinical safety trials revealed about potential effects on teeth?

The two most commonly observed clinical effects of treatments with tooth whiteners include mild tooth over-sensitivity to temperature changes and irritation of the inside of the mouth in some patients. Increased tooth sensitivity, which often occurs at the beginning of the treatment and usually does not last more than a few days, was observed in up to two thirds of patients in various studies. Regarding irritation of the inside of the mouth, the mouthguard rather than the tooth whitening product may be the cause.

Some patients have also reported burning palate, throat, and gums and some of those who inadvertently swallowed whole tooth whitening strips reported minor upsets in their stomach or intestine.

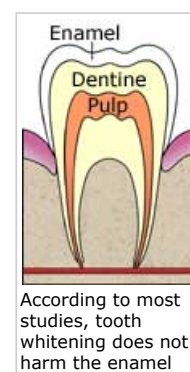
In general, side effects can occur during treatment, but seem to disappear quickly afterwards.

The SCCP noted that the numbers of patients enrolled in the studies are too small to detect undesirable effects that occur very rarely. In addition, many studies do not include a control group to enable comparisons. No studies are available that would allow assessment of possible long-term effects connected with the use of tooth whitening products and of the effects of repeated use of such products.

5.2 Can tooth whitening affect enamel and dentin?

Hydrogen peroxide applied on the tooth surface passes easily and quickly through tooth enamel. The majority of existing studies performed on enamel and dentin in the laboratory (*in vitro*) confirm that bleaching systems are safe.

However, a few studies focussing on effect on surface structure and chemistry have shown a degradation of the tooth surface associated with the whitening process. Indeed, some studies have reported alterations of enamel surfaces, including shallow depression, increased porosity and slight erosion, which is why some authors concluded that patients should be warned of the potential for enamel alteration and its detrimental effect on tooth structure even if long-term consequences are not yet conclusively determined. It should also be noted that soft drinks (e.g., Coca-Cola, Pepsi Cola) and fruit



juices also cause demineralisation and alteration of enamel comparable to those reported for whitening products.

Some studies showed that saliva and fluoride have a remineralizing effect on the softened bleached surfaces of the teeth. The results of the numerous studies on the effects of peroxide-containing tooth whitening products on enamel and dentin depend on the methodology used and the materials tested.

Two clinical cases of serious adverse effects on enamel associated with the use of "over-the-counter" tooth whitening products were reported.

Studies measuring potential effects of toothwhiteners at the microscopic scale have shown no or very little effects on hardness and structure of dentin or enamel.

5.3 Can tooth whitening affect dental pulp?

After crossing the enamel, hydrogen peroxide passes into dentin and pulp. The larger the dose of hydrogen peroxide, the greater the amount of peroxide that reaches the pulp. Products containing hydrogen peroxide lead to a greater penetration than those containing carbamide peroxide.

Despite this penetration, tooth whitening seems to do very little harm to the dental pulp of living teeth, possibly because the levels of hydrogen peroxide are too small to cause damage (by inhibiting enzymes in dental pulp).

However, studies show that whiteners can cause minor inflammation of the upper layers of pulp, where the pulp meets the dentin. It is noteworthy that such minor inflammation of the pulp occurs in parallel with increased tooth sensitivity, which is a well established common adverse effect of tooth whitening.

5.4 Can tooth whitening affect fillings and other dental restorative materials?

Tooth whitening does not usually change the colour of fillings and other restorative materials. Restorations made with composite materials (plastics) may lighten a little, but this is not noticeable to the human eye.

Tooth whitening has no effect on the chemistry or on the texture of porcelain, other ceramics, and dental gold.

However, tooth whitening products can slightly affect restorations made with composite materials, cements, and dental amalgams:

- The surface of composite restoration materials (plastics) can undergo minor etching or softening.
- Some cements used in restorations can become more soluble.
- Dental amalgams can react slightly with the whitening product, which can cause minor localised spotting and colour changes of the surface. Under extreme conditions, dental amalgams could potentially release small amounts of mercury. However, the amount released would be well below the mercury exposure limits set in WHO guidelines.

6. How safe are products containing hydrogen peroxide?

6.1 How are hydrogen peroxide solutions classified and labelled?

Solutions containing more than 5% hydrogen peroxide are labelled "harmful".

In addition solutions containing:

- 5 – 8% hydrogen peroxide are labelled "Irritating to eyes",
- more than 8% are labelled "Harmful if swallowed" and "Risk of serious damage to eyes",
- more than 35% have an additional label "Irritating to respiratory system and skin",
- higher concentrations are in addition labelled "Causes burn".

No labelling is required in EU for hydrogen peroxide solutions of less than 5%.

The International Agency for Research on Cancer (IARC) has concluded that there is only "limited" evidence of carcinogenicity of hydrogen peroxide in experimental animals.

It has therefore classified hydrogen peroxide as "unclassifiable as to carcinogenicity in humans".

6.2 How safe are oral hygiene products and toothwhiteners?

The risk of effects of oral hygiene products and toothwhiteners containing hydrogen peroxide on the body as a whole is low, because the substance is rapidly broken down. However, in animals repeatedly exposed to higher doses adverse effects have been observed. In addition, there are concerns about direct, more localised, effects like irritation in the mouth and in the gastrointestinal system after swallowing.

In the European Union, oral hygiene products are regulated by the Cosmetics Directive and they may only be sold freely to consumers if they contain no more than 0.1% hydrogen peroxide.

In the case of **toothpastes and mouth rinses** the exposure times are short and risks to humans can be assessed by comparing human exposures to the highest exposure at which no harmful effects were observed in any animal studies: 20 mg/kg body weight per day (NOAEL). The ratio between the two is the **margin of safety** for general effects on the body.

- For **toothpastes and mouthrinses** containing 0.1% of hydrogen peroxide, the calculated margin of safety of repeated dose toxicity (2500 and 400 respectively) is considered to give **sufficient protection**. A margin of safety of 2500 means that the calculated exposure of humans using the product is 2500 times lower than the exposure level at which no harmful effects were observed in any animal study.

In the case of tooth whitening products the exposure times are longer. The assessment of the safety of tooth whitening products is based both on calculations of a margin of safety as well as consideration of possible immediate and long-term effects.

- For **tooth whitening products** containing 6% of hydrogen peroxide, the calculated margin of safety for repeated dose toxicity (100) is on the **borderline** of that considered to give sufficient protection.

- For **tooth whitening products** containing more than 6% of hydrogen peroxide, the margin of safety will be below 100, and they are thus **not considered safe**.

In order to carry out a robust risk assessment there is a need for long-term and independent clinical data and long-term epidemiological studies in order to evaluate possible adverse effects in the mouth linked to the use of tooth whitening products.

Although the majority of the products contain hydrogen peroxide or carbamide peroxide, other chemicals such as sodium percarbonate, sodium perborate, and potassium peroxymonosulphate may be used. The later chemicals are should be assessed and regulated in a similar way as hydrogen peroxide on the basis of hydrogen peroxide or reactive oxygen products released.

SCCP's "Guidance document on Epidemiological and clinical studies on Tooth Whitening Products" [see http://ec.europa.eu/health/ph_risk/committees/04_sccp/docs/sccp_o_057.pdf]

7. What should be considered before a tooth whitening treatment?

Above 0.1% hydrogen peroxide, tooth bleaching is not just a simple cosmetic procedure. It is important that the dentists diagnose the cause of the staining, predict whether the stains can be removed or not, check whether patients have any other oral health problems, and counsel patients about the best way of dealing with this esthetical problem.



Before engaging in tooth whitening treatment, a dentist should be consulted
Source: StockXpert

As mentioned in question 5, the **most common undesirable side effects** of tooth whitening treatments are irritations inside the mouth and teeth becoming over-sensitive to temperature changes. These effects usually disappear immediately or a few days after stopping treatment but can sometimes last for over a month. Moreover, consumers may occasionally swallow entire tooth whitening strips and, as a result, suffer from minor upsets of their digestive tract.

Hydrogen peroxide passes through dentin into pulp, but there are few studies on the long-term effects of bleaching products on pulp. Dental pulp is particularly vulnerable in people with conditions such as gum retraction that expose the dentin.

Health conditions such as **pre-existing tissue injury** or the concurrent **use of alcohol and/or tobacco** while using tooth whiteners may also exacerbate their toxic effects. Hydrogen peroxide, even at concentrations as low as 3%, may be especially harmful to oral tissues if they have been previously injured. Therefore, particular care should be taken in administering bleaching agents to patients with mouth diseases or lesions, and to those using alcohol and tobacco. This mixed exposure may be of concern since smokers are likely candidates for tooth bleaching.

Hydrogen peroxide can contribute to the development of existing tumours and therefore increase the risk of oral cancer in persons that already have an increased risk due to tobacco use, alcohol abuse, or genetic predisposition, especially when treatment is repeated. However, since hydrogen peroxide degrades quickly in the mouth, tooth whiteners are unlikely to be a cancer risk in all other population groups.

Hydrogen peroxide has not been shown to be a **skin sensitiser**.

As far as **dental restorative materials** are concerned, prolonged treatment with bleaching agents might cause small changes in amalgam surfaces and may possibly release some mercury. Hence, bleaching of teeth containing amalgam fillings should be approached with caution.

8. Conclusion – Are oral hygiene products and tooth whiteners containing hydrogen peroxide safe and should they be freely available to consumers?

- The use of **toothpastes, mouth-rinses or tooth whitening products containing up to 0.1% hydrogen peroxide** does not pose a risk to the health of the consumer under normal or reasonable foreseeable conditions of use. Toothpastes and mouthrinses should not contain more than 0.1% hydrogen peroxide.

The use of **tooth whitening products containing 0.1 to 6 % hydrogen peroxide** entails potential risks.

With increasing concentration of hydrogen peroxide and frequency of application there will be an increasing risk linked to the use of these products and it cannot be anticipated what the exposure would be if the products were to be freely and directly available to the consumer.

Available data does not allow determining a level of hydrogen peroxide and a frequency of application that would result in exposure which would be considered safe for the consumer. Independent long-term safety evaluations are needed.

The potential risk can be reduced if the absence of risk factors and the proper use are ensured by a dentist:

- If products containing 0.1 to 6 % hydrogen peroxide are only used after consultation with and approval of the consumer's dentist to ensure the absence of risk factors.
 - Some population groups need to be particularly careful when using tooth whitening products: persons with damaged fillings or other restorations, with pre-existing mouth diseases or injuries, or who use tobacco and/or alcohol.
 - The use of tooth whitening products is not recommended before or immediately after dental restoration.
- If the products are used only as intended in terms of frequency and duration of application to avoid reasonably foreseeable misuse.

Independent long-term safety evaluations should be performed, because good clinical data and long-term epidemiological studies that assess the possible adverse effects within the mouth are lacking.¹

Potential health risks of tooth whitening products to children and adolescents could not be assessed due to the absence of specific data.

Tooth whitening products containing more than 6% hydrogen peroxide are not considered safe for use by the consumer.

¹ Read the SCCP's "Guidance document on Epidemiological and clinical studies on Tooth Whitening Products" [see http://ec.europa.eu/health/ph_risk/committees/04_sccp/docs/sccp_o_057.pdf]

Annex

Annex 1:

Table 3.10: Summary of human safety data of hydrogen peroxide in mouth-rinses

Peroxide formulation	n	Dosage regimen	Safety findings	Reference
1.5% Hydrogen peroxide rinse	30 subjects	rinsed 4 times a day for 7 days	No treatment-related effects reported	Winer et al., 1991
1.5% Hydrogen peroxide rinse	93 test 85 control	rinsed 3 times a day for 7 days	No treatment-related effects reported	Gomes et al., 1984
1.5% Hydrogen peroxide rinse	30 children	rinsed once a day for 18 months	No generalized mucosal irritation was noted	Boyd, 1989
6-12.5% Hydrogen peroxide rinse	88 dental students	2-3 times a day for 1-2.5 months	Some gingival changes. 6.4% showed "redder" gums and 3.4 paler gums. 6.6% developed hyperkeratinised filiform papillae of the tongue	Müller et al, 1938
Hydrogen peroxide/sodium bicarbonate system	(not stated)	21 days	No adverse effects reported	Purdue University, 1990
3% Hydrogen peroxide rinse	(not stated)	rinsed 3 to 5 times a day	Mucosal irritation in 2 individuals with prior tissue injury	Rees and Orth, 1986
3% Hydrogen peroxide with sodium bicarbonate	(not stated)		No adverse effects reported	Herrin et al., 1987
1.5% Hydrogen peroxide rinse	(not stated)	18 months	No adverse effects reported	Fischman et al., 1992
1.5% Hydrogen peroxide rinse	(not stated)	Twice daily for 24 months	Improved gingival health	Gangler and Staab, 1985
0.75 or 1.5% Hydrogen peroxide rinse	(not stated)	4 times daily for 5 weeks	Discoloration of mucosal surfaces	Tombes and Gallucci, 1993
1.5% Hydrogen peroxide rinse	(not stated)	2 months	No adverse effects reported	Shibly et al., 1997

Source: SCCP Opinion on Hydrogen peroxide, in its free form or when released, in oral hygiene products (2007) [see http://ec.europa.eu/health/ph_risk/committees/04_sccp/docs/sccp_o_022.pdf], p.44

Annex 2:**Table 3.7: Summary of clinical studies using hydrogen peroxide toothpastes**

Formulation	n	Dosage	Safety findings
0.5% Calcium peroxide toothpaste	25 subjects	applied 4 times a day for 10 days, then 14 days rest and then applied twice on day 25	No adverse events in treatment group*
0.5% Calcium peroxide toothpaste	232 subjects	daily brushing for 7 weeks	Examination at 2, 5 and 7 weeks showed no treatment-related effects*
Sodium percarbonate toothpaste (0.75% H ₂ O ₂)	74 subjects	6 months	Transient angular cheilitis in one subject*
toothpaste (0.75% H ₂ O ₂)	100 subjects	3 months	No product-related findings*
0.75% H ₂ O ₂ with 5% NaHCO ₃ toothpaste	25 patients	twice daily brushing for 28 days after maxillary flap Gingival surgery (bilateral- double-blind cross over study)	No unwanted effects reported. 75% of patients preferred test product to control (Dentino et al., 1995)
0.75% H ₂ O ₂ with 5% NaHCO ₃ toothpaste	62 subjects + 21 controls	twice daily brushing for 6 months	Oral lesions reported in 3 treated patients and 4 controls (Fischman et al., 1992)
0.75% H ₂ O ₂ toothpaste	71 subjects	3 weeks	An adverse effect was reported by one subject in the treatment group and one control*
0.75% and 1.5% H ₂ O ₂ toothpaste	293 subjects	3 weeks	24 reports of oral lesions in the active treatment groups; 46 reports in the control group* 5 reports in each of the treated and control groups* No soft tissue changes associated with either test or control product (Fischman et al. [Abstract], 1992b)
0.75% H ₂ O ₂ toothpaste	279 subjects		
1.5% H ₂ O ₂ with 10% NaHCO ₃ toothpaste	60 subjects + 20 controls	twice daily brushing for 6 months	
* unpublished company data			

Source: SCCP Opinion on Hydrogen peroxide, in its free form or when released, in oral hygiene products (2007) [see http://ec.europa.eu/health/ph_risk/committees/04_sccp/docs/sccp_o_022.pdf], p.41-42

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