LABELLING STANDARD

PEROXIDE ORAL CARE PRODUCTS

I) **Description:**

This labelling standard applies to those single ingredient peroxide products in the form of a liquid or gel intended to cleanse minor wounds and canker sores in the oral cavity or for use as an antiseptic mouthwash.

II) **Pharmaceutical Quality:**

a) All ingredient (medicinal and nonmedicinal) and finished product specifications should, as a minimum, meet the standards described in the publications referred to in Schedule B to the Food and Drugs Act, or equivalent standards. Where no Schedule B monograph exists for the dosage form, specifications should be similar to those of a comparable compendial dosage form. In the absence of a Schedule B standard for any dosage form, testing must be adequate to demonstrate the product's identity, potency, purity and quality.

b) **Special Notes:**

i) Pharmacopoeial standards (Schedule B) for formulated single ingredient peroxide preparations are shown in Appendix I. Note that this list is intended only as a guide and is not necessarily current or all inclusive.

ii) Finished product specifications should include tests for identification and an assay with suitable limits for the medicinal ingredient(s) including its components. The specifications for all dosage forms should include a description of the dosage form including organoleptic properties as well as physico-chemical testing e.g., pH, specific gravity, viscosity, appropriate to the dosage form. Where antimicrobial preservatives are added, an assay with suitable limits should be included. It is recommended that antimicrobial preservative effectiveness be determined in order to establish that the product is capable of resisting microbial contamination.

iii) Products containing amounts of peroxides in excess of those outlined in this standard or for use for more than 2 weeks will be subject to a product specific safety assessment. For details, see Appendix II.

iv) Due to safety concerns the above peroxides will not be permitted as nonmedicinal ingredients in drug products. Also, peroxides will not be permitted as a therapeutic ingredient in dentifrices (ie antiseptic function), products normally intended for long term use, unless a product specific safety assessment supports product safety (Appendix II).

III) **Ingredients:**

a) **Single Medicinal ingredients:**

Ingredient	**Unit**
Hydrogen peroxide	1.5 -6%
Carbamide peroxide*	10%

***Accepted name (USAN)- also known by secondary names as hydrogen urea peroxide, urea peroxide, hydrogen peroxide carbamide

b) **Nonmedicinal Ingredients:**

Nonmedicinal ingredients should be restricted to those substances, necessary for the formulation of the dosage form. Their concentration must not exceed the minimum required to provide their intended effect. They must be harmless in the amounts used, their presence must not affect the bioavailability, therapeutic efficacy or safety of the medicinal ingredients and they must not interfere with assays and tests for the medicinal ingredients and, if present, antimicrobial preservatives.

IV) **Labelling:**

A) This labelling standard describes those requirements that are specific to this class of drugs. Other requirements described in the *Regulations to the Food and Drugs Act* and in the *Guide for the Labelling of Drugs for Human Use* must also be met.

B) **Adequate Directions for Use:**

i) **Indications**

a) Oral use to cleanse (remove foreign material) (debris) (from) minor wounds, canker sores.

b) Oral use to cleanse minor wounds or minor gum inflammation resulting from minor dental procedures, dentures, orthopedic appliances, accidental injury or other minor irritations of the mouth or gums

c) Antiseptic mouthwash

ii) **Alternative acceptable claims:**

Gentle foaming action releases oxygen on contact, helping cleanse oral wounds to aid healing

iii) **Unacceptable Claims:**

Any reference to any other disease or condition

iv) **Dosage Directions:**

a) **For canker sores, minor oral wounds:**

i) Use undiluted (3%) product or

ii) Dilute (6%) solution with equal parts of water.

iii) Apply several drops directly to affected area up to 4 times per day and up to 1 minute each time then spit out (expectorate) **or** use as directed by a dentist or a doctor.

iv) Use should be limited to 14 days unless otherwise directed by a dentist or a doctor.

v) An adult should supervise the use of this product for children under 12 years of age.

b) **As an antiseptic mouthwash:**

i) Swish 10 ml solution (1.5%) in mouth for up to 1 minute, then spit out (expectorate) or

ii) Dilute (3% solution) with equal parts of water, then swish 10 ml of diluted solution in mouth for up to 1 minute, then spit out (expectorate) or

iii) Dilute one part solution (6%) with 3 parts of water, swish 10 ml of diluted solution in mouth for up to 1 minute, then spit out (expectorate).

iv) Use should be limited to 14 days.

v) An adult should supervise the use of this product for children under 12 years of age.

C) **Warnings:**

a) For canker sores, minor oral wounds:

If irritation, pain or redness persists or worsens, or if swelling, rash or fever develops, see your dentist or doctor promptly

b) For use as antiseptic mouthwash:

Do not use for children under 6 years of age, unless directed by a doctor or dentist.

Bureau of Nonprescription Drugs
September 29, 1995

REFERENCES

1. **United States Federal Register,** Vol. 56, No. 185, 1991 Oral Health Care Drug Products for Over-the-Counter Human Use Tentative Final Monograph, September 24, 1991 DHSS, (U.S.) Food and Drug Administration

2. **United States Federal Register**, Vol. 53, No. 17, 1988. Oral Health Care Drug Products for Over-the-Counter Human Use Tentative Final Monograph, January 27, 1988 DHSS, (U.S.) Food and Drug Administration

3. **American Hospital Formulary Service**, Drug Information 1992

4. **Martindale, The Extra Pharmacopoeia**, 29th Edition, Philadelphia College of Pharmaceutical Sciences, 1990.

5. **American Handbook of Nonprescription Drugs**, 9th Edition, American Pharmaceutical Association, 1990.

6. **Self Medication**, 4th Edition, Canadian Pharmaceutical Association, 1992.

7. **Remington's Pharmaceutical Sciences**, 17th Edition, Mack Publishing Co., 1985.

8. **Accepted Dental Therapeutics**, 40th Edition, 1984 American Dental Association

Appendix I

Single Ingredient Preparations

PROPER NAME	U.S.P. 1995	B.P. 1993	B.P.C. 1973*	Ph.f. 1988
Carbamide Peroxide Topical Solution	X			
Hydrogen Peroxide Topical Solution[1]	X			
Hydrogen Peroxide Concentrate[2]	X			
Hydrogen Peroxide Solution (3%)		X		
Hydrogen Peroxide Solution (6%)		X		
Hydrogen Peroxide Solution (20 volumes)[3]			X	
Strong Hydrogen Peroxide Solution[4]			X	
Solution diluée de peroxyde d'hydrogène[5]				X
Solution concentrée de peroxyde d'hydrogène[6]				X

* Presently called "The Pharmaceutical Codex" (11th edition, 1979, 12th edition, 1994)

[1] 2.5 - 3.5 % solution
[2] 29 - 32% solution
[3] 6% solution
[4] 29 - 31% solution
[5] 3% solution
[6] 30% solution

APPENDIX II

Safety Assessment:

Hydrogen peroxide is known to be genotoxic in a variety of *in vitro* and *in vivo* systems. There is also evidence of carcinogenicity in cancer bioassays in rodent models. The safety of hydrogen peroxide, when used in the oral cavity for extended periods, is not known. Therefore, manufacturers wishing to market products with higher concentrations, or with use longer than that specified in the labelling standard, must submit evidence to support the safety of their product.

Studies using suitable animal models, conducted according to current scientific standards, are required (e.g. the National Toxicology Program (NTP) criteria for the technical adequacy of carcinogenicity studies). Ideally, the long-term exposure of the oral cavity to the proposed product containing the peroxide should be studied. Studies of the mechanistic nature in support of the safety of the product are of interest, but they cannot replace cancer bioassays using suitable models.

Epidemiological studies on humans exposed to peroxide for extended periods would also be of value, if available.

If therapeutic claims outside the labelling standard are made for the product, then such claims must be supported by adequate studies conducted to current scientific standards. A risk\benefit analysis of the potential benefits versus the risks would be required.