MEDICINES CONTROL COUNCIL

DEPARTMENT OF HEALTH
Republic of South Africa

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ALCOHOL CONTENT OF MEDICINES

This guideline is intended to provide recommendations to applicants wishing to submit applications for the registration of medicines. It represents the Medicines Control Council's current thinking on the safety, quality and efficacy of medicines. It is not intended as an exclusive approach. Council reserves the right to request any additional information to establish the safety, quality and efficacy of a medicine in keeping with the knowledge current at the time of evaluation. Alternative approaches may be used but these should be scientifically and technically justified. The MCC is committed to ensure that all registered medicines will be of the required quality, safety and efficacy. It is important that applicants adhere to the administrative requirements to avoid delays in the processing and evaluation of applications.

Guidelines and application forms are available from the office of the Registrar of Medicines and the website.

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REGISTRAR OF MEDICINES
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ALCOHOL CONTENT OF MEDICINES INTENDED FOR ORAL ADMINISTRATION

1 The following maximum concentration limits will be allowed for ethyl alcohol as inactive ingredient:

0,5 % *(v/v)* ethyl alcohol for children under 6 years of age;

5,0 % *(v/v)* ethyl alcohol for children 6 to 12 years of age; and

10,0 % (*v/v)* ethyl alcohol for adults and adolescents over 12 years of age.

2 Minute dose preparations are exempted from this requirement.

3 For products where higher concentrations of alcohol are required, (e.g. plant extracts or where solubility or preservation might be problematic), exemption from ethanol concentration limits will be considered individually, provided that justification and motivation is submitted together with proof that the proposed dosage will not result in blood alcohol levels of 25 mg/dl or higher. (Table I is attached for reference purposes only).

4 In all instances, the alcohol content of a mixture must be stated prominently on the immediate container label, the outer label (carton), as well as in the package insert and patient information leaflet.

5 All medicines (registered products, "old medicines" and new applications) must comply with the alcohol levels stated in this policy.

Table I: Volume (millilitres) of ethanol-containing preparation predicted to produce a plasma ethanol concentration of 25 mg/100 ml* (100 ml = 1 dl).

Age in years & mass (kg) / % ethanol *(v/v)* in Product	2 yrs (12 kg)	4 yrs (16 kg)	6 yrs (21 kg)	8 yrs 27 kg)	19 yrs (32 kg)	12 yrs (38 kg)
2,5 %	91 ml	122 ml	160 ml	205 ml	243 ml	289 ml
5,0	46	61	80	103	122	144
7,5	30	41	53	68	81	96
10,0	23	30	40	51	61	72
12,5	18	24	32	41	49	58
20,0	11	15	20	26	30	36
25,0	9	12	16	21	24	29

*Values were calculated from data contained in McCoy et al,1979 by use of the formula:

[dose (mg) = plasma concentration (*Cp*) x volume distributed (*Vd*)] and assuming that absorption is complete.

For example, the calculation to obtain the value of 40 ml for a 6-year-old ingesting a product containing 10 % alcohol would be made as follows:

Cp = 250 mg/ℓ and *Vd* = 0,6 /kg x 21 kg; therefore, dose = 250 mg/l x (0,6 l/kg x 21kg) = 3,150 mg. Because for absolute ethanol (specific gravity 0,789), 1 g = 1,27 ml, 31,5 g = 40 ml; thus, for 10 % ethanol, the calculated volume is 40 ml.

TABLE I is an abstract from an article entitled "Ethanol in liquid preparations intended for children", by the American Academy of Pediatrics, published in *PEDIATRICS*, Vol. 73 (3) March 1984, page 406.