

Generic Medicine Section
Centre of Product & Cosmetic Evaluation (PPPK)
National Pharmaceutical Regulatory Agency (NPRA)
Lot 36, Jalan Universiti,
46200 Petaling Jaya,
Selangor, Malaysia.

Dear Sir/Madam,

ETHANOL 96% CONTENT AS A SOLVENT IN ALLER SYRUP 2.5MG/5ML

Subject mentioned is referred.

2. Chloroform spirit is used as flavour enhancement in this product. It is composed of approximately 95% ethanol 90% and 5% chloroform. The functional role of chloroform spirit in the formulation was predominantly attributed to its ethanol content, which contributes significantly to the solubilization of active pharmaceutical ingredients (APIs) and excipients, particularly those with limited aqueous solubility and the organoleptic properties of the final product, providing mild flavor enhancement. Hence, the functional contribution of chloroform spirit as a flavour enhancer is largely supported by its ethanol content, which provides both solubilizing and organoleptic properties.

3. We have taken note on the directive issued by NPRA regarding “Larangan Penggunaan Chloroform / Chloroform Spirit sebagai Pengawet dalam Produk Farmaseutikal, Produk Semula Jadi dan Produk Suplemen Kesihatan [NPRA.600-1/9/13(47) Jld.1, dated 19-Nov-2024]. Thus, the removal of chloroform spirit in this product is in direct response to the NPRA’s ban on the use of chloroform in pharmaceutical products.

4. Ethanol 96% has been selected as replacement for chloroform spirit as the concentration of ethanol 96% used in the reformulated product is identical to the percentage of chloroform spirit adopted earlier. Ethanol 96% is a pharmaceutically recognized and widely utilized solvent and co-solvent, and we used it to dissolve the parabens in this product. The reformulation involving the removal of chloroform spirit and substitution with ethanol 96% at the same percentage ensures that there is no significant impact on the product’s safety, efficacy, or quality.

5. Below shows our calculation of ethanol content in this product.

Ethanol Content Calculation

1) Approved Batch size (2000 L)

In 2000L of Aller Syrup, it contains 11.11 L of Chloroform Spirit.

Chloroform Spirit is make-up of Ethanol 90% and Chloroform.



Chloroform Spirit composition based:

(based on 100L)

Ethanol 90% : 95 L

Chloroform : 5 L

100 L Chloroform Spirit contains 95 L Ethanol 90%, which is equivalent to 85.5 L Ethanol 100%, so
100 L Chloroform Spirit contains 85.5 L Ethanol 100%

$$\begin{aligned} \text{Ethanol composition} &= \frac{11.11 \text{ L}}{2000 \text{ L}} = \frac{11.11 \text{ L} \times 85.5\% \text{ Ethanol}}{2000 \text{ L}} = \frac{9.499 \text{ L Ethanol}}{2000 \text{ L}} = \frac{0.475 \text{ L Ethanol}}{100 \text{ L}} \\ &= \frac{0.475 \text{ ml Ethanol}}{100 \text{ ml}} \times 100\% \\ &= 0.475\% \text{ v/v Ethanol} \\ &= \mathbf{0.48\% \text{ v/v Ethanol}} \end{aligned}$$

2) Proposed Batch Size (600 L)

In 600L of Aller Syrup, it contains 2.97 L of Ethanol 96%.

Ethanol 96% is make-up of pure ethanol 96% and water 4%.

$$\text{Ethanol} = \frac{96}{100} = 0.96$$

$$\begin{aligned} \text{Ethanol composition} &= \frac{2.97}{600} \times 100 = 0.495\% \times 0.96 = 0.475\% \text{ v/v Ethanol} \\ &= \mathbf{0.48\% \text{ v/v Ethanol}} \end{aligned}$$

We hope the above justification will support our application for the variation. Thank you in advance for your kind attention.

Thank you,

Yours sincerely

Heng

(LEONG SOON HENG)
Regulatory Affairs Senior Manager
KCK Pharmaceutical Industries Sdn. Bhd.

