

Residual Solvents - Statement

Product group: Superdisintegrants

Brand name: Primojel® and Primellose®

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Dear Customer,

Herewith we certify the following:

For manufacturing of our products Primojel® and Primellose® (Sodium Starch Glycolate and Croscarmellose Sodium) no other solvents than potable water and ethanol are used.

This is certified with reference to the solvents listed in ICH guidance Q3C <Residual Solvent>, USP general chapter <467> as well as any other non-ICH solvents in the raw materials, manufacturing process and product. General test 5.4 of the European Pharmacopoeia is also applicable.

Ethanol is classified as a solvent with low toxic potential (Class 3).

Primojel® and Primellose® contain a maximum of 6 % w/w of residual ethanol.

The actual content of ethanol is measured in each batch and the result is printed on the Certificate of Analyses. Ethanol is measured according to validated methods (PD-0094 and PD-0095).

The toxicology of ethanol is very well known and long-term toxicity studies and carcinogenicity studies are commonly available.

No other Class 1, Class 2 and Class 3 (other than Ethanol) solvents are likely to be present in Primojel® and Primellose®.

Class 3 solvents: Solvents with low toxic potential

Solvents with low toxic potential to Human; no health-based exposure limit is needed. Class 3 solvents have PDEs of 50 mg or less per day. PDE: permitted daily exposure

Source: NOTE FOR GUIDANCE ON IMPURITIES: RESIDUAL SOLVENTS (CPMP/ICH/283/95)

As per the guideline, please see below the provided theoretical calculation to demonstrate with a worst case scenario of 10g daily dose of drug product that our products comply with the ICH Q3C guidelines.

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Example:


The permissible daily intake (PDI) of Ethanol shall not exceed 50 mg/day in a drug product of 10 g, i.e. 5000 ppm. The maximum level of ethanol content in our superdisintegrants does not exceed 6% w/w as stated above. Generally our superdisintegrants are added at 3 to 6% w/w into a drug formulation. Considering the worst case scenario of a 10g/day of pharmaceutical product intake, the maximum quantity of ingested per day is: $10g \times 6\% \text{ max} = 0.6g = 600 \text{ mg max}$. The maximum content of residual ethanol will be $600mg \times 6\% \text{ max} = 36 \text{ mg max} = 0.36\% = \mathbf{3600 \text{ ppm}}$

As a conclusion of the above estimations, solvents available into our superdisintegrants (Sodium Starch Glycolate and Croscarmellose Sodium) are below 5000 ppm and therefore pass the Residual solvents recommendation of the ICH Q3C guidelines and associated pharmacopoeias.

This statement substitutes all previous versions issued for the brand names mentioned above. We trust this information, which is made up to the best of our knowledge, will be helpful to you.

Name : Wilbert van de Rakt

Job title : Quality Director

Signature : 

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The above facsimile signature is only for display.