Glycols

Testing active ingredients and excipients for the presence of diethylene glycol or ethylene glycol

Background

Contamination with diethylene glycol or ethylene glycol has been detected in an increasing number of pharmaceuticals in recent years. These substances, or more precisely, their metabolites glycolaldehyde, glyoxal and glyoxylic acid, are all toxic. In 2002, a group tolerable daily intake (TDI) of 0.5 mg/kg body weight was set for ethylene glycol and diethylene glycol by the Scientific Committee on Food (SCF), and this was confirmed by the WHO in 2016.

Strategic evaluation

Glycerol and propylene glycol are used as excipients in pharmaceuticals, medical devices, foodstuffs and cosmetics. Versatile by virtue of their technological properties and sweet flavour, these excipients are used in a broad spectrum of solid, semi-solid and liquid pharmaceuticals, extending through to medicinal products that are particularly sensitive by nature, such as parenteral drugs or syrups for children. While glycerol (E422) is used in food as a humectant and sweetener, propylene glycol has been approved as a food additive (E 1520) for the production of flavourings and chewing gum. Apart from mistaken identity and adulteration of glycerol and propylene glycol, even small amounts of diethylene glycol or ethylene glycol contamination can also be potentially harmful to health and must be precluded with certainty.

Limit values and analytics

Limit values for glycols are prescribed in various pharmacopoeia monographs. Maximum ethylene glycol and diethylene glycol levels in propylene glycol are specified in the United States Pharmacopoeia (USP) monograph "Propylene Glycol (Official as of 01-May-2020)" and in the revised monograph "Propylene Glycol 01/2025:0430", pre-published in the 11th edition of the European Pharmacopoeia (supplement 11.6). The European Pharmacopoeia monograph on glycerol (07/2022:0496) specifies limits for contamination with diethylene glycol and related substances (ethylene glycol and propylene glycol). A limit has been set for the content of diethylene glycol content as a synthesis impurity in the active ingredient etofenamate (Ph. Eur. 01/2017:1513).

In accordance with pharmacopoeial requirements, PhytoLab uses gas chromatography (GC-FID) to determine ethylene glycol and diethylene glycol in propylene glycol (USP) and for the analysis of glycerol and etofenamate.

Apart from conducting analyses on active ingredients, excipients or additives, it may also be necessary to determine glycol in finished products. PhytoLab develops and validates customised procedures specifically for your products, e.g. cough syrup.

We would be delighted to advise you. Your contacts at PhytoLab

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Sources

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https://www.who.int/docs/default-source/food-safety/food-genetically-modified/9789240695405-eng.pdf

https://eur-lex.europa.eu/legal-content/DE/TXT/PDF/?uri=CELEX:02009R1223-20231201

9 October 2017 EMA/CHMP/704195/2013 Committee for Human Medicinal Products (CHMP) Questions and answers on propylene glycol used as an excipient in medicinal products for human use

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