SCIENTIFIC ADVISORY GROUP ON CHEMICAL SAFETY OF NON-FOOD AND NON-MEDICINAL CONSUMER PRODUCTS (SAG-CS)

Opinion on Deoxyarbutin Prohibition in Cosmetic Products.

1. Summary

1.1. 4-[(tetrahydro-2H-pyran-2-yl)oxy]phenol (CAS 53936-56-4) (INCI Name: Tetrahydropyranyloxy Phenol; Common Name: Deoxyarbutin) is not currently regulated under the UK Cosmetic Products Regulation No 1223/2009 (as amended).[1]

1.2. Deoxyarbutin is able to release 1,4-dihydroxybenzene (CAS 123-31-9) (INCI name: Hydroquinone) under normal conditions of use. Hydroquinone is included among the substances prohibited for use in cosmetic products, listed under entry 1339 of Annex II to UK Regulation No 1223/2009 (as amended), with the exception of entry 14 of Annex III to that Regulation where hydroquinone is permitted solely for professional use in artificial nail systems in a concentration in the final product of up to 0.02%.

1.3. Deoxyarbutin and its degradation product, hydroquinone, have been used in some cosmetics products to lighten skin and have been marketed specifically at certain ethnic groups.

1.4. Under UK CLP Regulation No 1272/2008 (as amended)[2] - classification, labelling and packaging of substances and mixtures (CLP), hydroquinone has a harmonised classification as a Category 2 carcinogen with hazard statement

[1] The UK Regulation currently consists of the Regulation UK No 1223/2009 as amended by SI 696/2019 Product Safety and Metrology (EU Exit) Regulations. The full consolidated UK text will be available soon.

[2] The UK CLP Regulation No 1272/2008 as amended by The Chemicals (Health and Safety) and Genetically Modified Organisms (Contained Use) (Amendment etc.) (EU Exit) Regulations 2019. The full consolidated UK text will be available soon.

H351 (suspected of causing cancer) based on Regulation No 1272/2008 Classification, Labelling and Packaging (CLP) Regulation, Annex VI. A Category 2 substance is a suspected human carcinogen based on human and animal evidence, but which is not sufficiently convincing to place the substance in Category 1.

1.5. The use of deoxyarbutin in cosmetic products was assessed by the Scientific Committee on Consumer Safety (SCCS). In its opinion adopted on 25 June 2015 (SCCS/1554/15), the SCCS concluded that due to safety concerns raised with regard to the life cycle and degradation of products containing deoxyarbutin, the use of deoxyarbutin up to 3% in face creams cannot be considered as safe.

1.6. The SCCS performed a calculation within SCCS/1554/15 to assess the lifetime cancer risk from systemic exposure to hydroquinone resulting from deoxyarbutin in cosmetic products. This calculation used data from an outdated T25 study. Assuming a systemic exposure dose of 0.0218 mg/kg bw/day, the lifetime cancer risk was calculated to be around 3 x 10^{-4}. The SCCS noted that although renal tubular cell adenomas are rodent specific and may be of little relevance for human risk assessment, the lifetime risk calculated by a conservative linear extrapolation approach would still exceed the usually accepted risk limits.

1.7. Based on that opinion, Commission Regulation (EU) 2021/1099 of 5th July 2021 accepted the SCCS recommendation, regarding safety of deoxyarbutin up to 3% in face creams, and amended the list of prohibited substances in cosmetics products within Annex II to Regulation (EC) No 1223/2009 to include deoxyarbutin under Entry 1657. This regulation entered force on the 26th July 2021.

1.8. The SAG-CS have been asked for their opinion on the risk posed to health by deoxyarbutin and its degradation product, hydroquinone.

2. Presentation and Discussion by The Scientific Advisory Group on Chemical Safety of Non-Food and Non-Medicinal Consumer Products (SAG-CS)

2.1. At their July 2021 meeting, the SAG-CS discussed a paper which focussed on risks posed by deoxyarbutin owing to its ability to degrade into hydroquinone.

2.2. Members agreed that there are safety risks associated with the use of deoxyarbutin due to its instability under common storage conditions and subsequent degradation to hydroquinone.

2.3. Members agreed that the analytical methods for deoxyarbutin and hydroquinone detection should be further developed to make any limits enforceable. Members wished to flag that OPSS could still set limits for deoxyarbutin based upon the As Low As Reasonably Practicable (ALARP) approach through selection of an appropriate limit of detection (LOD) or limit of quantification (LOQ).

2.4. Members discussed that the use of a T_{25} dose descriptor for calculation of a lifetime cancer risk was no longer appropriate, and that use of a benchmark dose assessment to assess the carcinogenic endpoint of hydroquinone would be more suitable. This approach would require a re-evaluation of the data from the National Toxicology Program, 1989.

2.5. Members considered different endpoints for the carcinogenicity of hydroquinone and suggested that they required more detail from studies. Members further discussed the human specificity of carcinogenic endpoints. Members agreed that it would add confidence to their recommendations to. generate and evaluate additional data which relates breakdown of hydroquinone to a marked effect (DNA damage).

2.6. Members acknowledged, that whilst stability of deoxyarbutin was an issue, its life cycle (use, application, disposal) must also be considered in the risk assessment.

2.7. Members considered that further evidence from a quantitative evaluation for dermal sensitisation is needed to fully quantify the risk.

3. Conclusions

Members were satisfied that there was sufficient evidence to form an opinion at this stage.

Members agreed that there are safety risks associated with the use of deoxyarbutin in cosmetic products due to its instability under common storage conditions and subsequent degradation to hydroquinone.

Due to the status of hydroquinone as a Category 2 carcinogen, a Category 2 mutagen and a strong skin sensitising agent, members concluded that deoxyarbutin and its degradation product, hydroquinone, present a hazard to human health.

Members were unable to perform a risk assessment in order to set a safe level for these compounds in cosmetics with the evidence available to them.

Members considered that to fully quantify the risk of hydroxyquinone it would recommend OPSS to consider further evidence from a quantitative evaluation for dermal sensitisation.

Scientific Advisory Group on Chemical Safety of Non-Food and Non-Medicinal Consumer Products

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References

Commission Regulation (EU) 2021/1099 of 5 July 2021 amending Annexes II and III to Regulation (EC) No 1223/2009 of the European Parliament and of the Council on cosmetic products - https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32021R1099

National Toxicology Program. NTP Toxicology and Carcinogenesis Studies of Hydroquinone (CAS No. 123-31-9) in F344/N Rats and B6C3F1 Mice (Gavage Studies). Natl Toxicol Program Tech Rep Ser. 1989 Oct;366:1-248

SCCS (Scientific Committee on Consumer Safety), Opinion on deoxyarbutin - Tetrahydropyranyloxy Phenol, 25 June 2015, SCCS/1554/15 - https://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_o_183.pdf