DSM Astaxanthin

Short Safety Summary

Dietary Supplement Use

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1. Introduction and Regulatory Status

This summary highlights the comprehensive battery of safety studies undertaken with nature-identical astaxanthin manufactured by DSM Nutritional Products.

DSM markets astaxanthin in the USA based on the existing food color additive regulation at 21 CFR 73.35 obtained in 1995. Additional long term toxicity studies have subsequently been submitted by DSM to the FDA (CFSAN) in 2005, and reviewed by the FDA. The FFDC Act at 413 (a) (1) allows the lawful marketing of DSM's astaxanthin as a dietary ingredient in dietary supplements in the USA

AstaSana™ for human Dietary Supplement use is manufactured in accord with Good Manufacturing Practice (GMP), Food GMP 21CFR110.

2. Animal Safety Studies

A comprehensive range of studies has been performed with DSM-manufactured astaxanthin. The study reference numbers are given in parenthesis:

Short term safety toxicity studies

Acute studies in rats and mice (B-0008756)

Skin and eye irritation studies in rabbits (2500334, 2500335)

Subacute and Subchronic toxicity studies

Studies up to 4 weeks in mice, rats and the dog (individual studies not listed)

13-Week oral (dietary admix) tolerance study in rats (B-0096700)

13-Week oral toxicity study in dogs (B-0046210)

Carcinogenicity and chronic toxicity studies

52-Week chronic toxicity study in rats (B-1007904)

104-Week carcinogenicity study in rats (B-1007905)

52-Week chronic toxicity study in dogs (B-0164930)

80-Week carcinogenicity study in mice (B-1007906)

Genotoxicity studies

Ames test (B-0095579)

In-vitro cytogenetic assay (HLA) (B-0105604)

In-vivo micronucleus assay in the mouse (B-0090162)

Reproductive toxicity studies

Fertility and general reproductive performance study in rats (Segment I) (B-0153176)

Embryotoxicity and teratology study in rats (B-0094689)

Embryotoxicity and teratology study in rabbits (B-0046303)

Two-generation reproduction toxicity study in rats (B-0153197)

Metabolism

ADME, Metabolism and CYP-induction studies including:

Mass balance studies in rats (B-0106698, B-0106731)

Distribution studies in humans, rats, mice (B-0106698)

Metabolism in- vitro studies in humans, rats (B-0106750, B-0106827)

3. Acceptable Daily Intake (ADI)

The package of safety studies undertaken with DSM manufactured astaxanthin is very comprehensive. The package included general toxicity studies in rodent and non-rodent species, developmental reproductive toxicity studies and carcinogenicity studies in the rat and mouse. In these studies, the lowest No Observed Adverse Effect Level (NOAEL) was 40 mg/kg bw/day.

An ADI is conventionally derived using a 100 fold safety factor applied to the lowest NOAEL in the longest and/or more sensitive toxicity study. In the case of DSM astaxanthin (using 40 mg/kg bw/day) this provides an ADI intake of 0.4 mg/kg bw/day for man. For a 60 or 70 kg person this equates to 24 or 28 mg/day, respectively. The DSM proposed supplement dosage is well below the calculated safe ADI dosage.

4. Human Data

Published human data for astaxanthin (from all sources) has been reviewed by DSM. This data is insufficient to be the main basis for the safety evaluation of astaxanthin but supports the toxicological data, therefore further confirming the safety of DSM astaxanthin.

5. Safety Conclusion

It is concluded based on the available data that astaxanthin, as manufactured by DSM, is safe for the intended use as a dietary ingredient in dietary supplements.

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