

Opinion On Use Of Cross-Linked Sodium Carboxymethyl Cellulose In Solid Dietary Supplements

Expressed on 15 January 1998

REQUEST FOR USE OF CROSS-LINKED SODIUM CARBOXYMETHYL CELLULOSE IN SOLID DIETARY SUPPLEMENTS

Terms of reference

To advise the Commission in relation to the request to extend the use of cross-linked sodium carboxymethyl cellulose as a disintegrant in solid dietary supplements taking account of the additional toxicological and exposure data information submitted by the petitioner.

Background

Cross-linked sodium carboxymethyl cellulose is also known as croscarmellose sodium or modified cellulose gum. The Committee has previously recommended that the use of cross-linked sodium carboxymethyl cellulose was acceptable as a disintegrant for sweetener tablets.¹ This opinion was based on toxicity data on the non-cross-linked parent material (sodium carboxymethyl cellulose), limited toxicity data on cross-linked sodium carboxymethyl cellulose itself, the expectation that cross-linking would lead to a reduction in any potential toxicity, information on the nature of the cross links, the identity and magnitude of residues of reactants and solvents, and the specification of the final finished product.² At that time the Committee utilised an estimate of extreme intake of 2.7 mg/kg bodyweight/day if it were used in sweetener tablets at the maximum requested level of 60g/kg. Although the toxicological information was not sufficient to set an Acceptable Daily Intake, the Committee considered, for the reasons set out above, that the use of cross-linked sodium carboxymethyl cellulose as a disintegrant in table-top sweetener tablets was acceptable.

Cross-linked sodium carboxymethyl cellulose was originally developed as a tablet disintegrant for medicinal products and dietary food supplements, allowing dissolution at low use levels (0.25-3.0%). It has an official monograph in the European Pharmacopoeia. In the USA, it is used as a disintegrant in prescription drugs and has generally recognised as safe (GRAS) status for use in dietary supplements. A request for the use of cross-linked sodium carboxymethyl cellulose as a disintegrant in solid dietary supplements has now been submitted to the European Commission. In considering this request, the Committee was provided with information on technical justification, intake estimates, and a new 90-day rat oral feeding study on cross-linked sodium carboxymethyl cellulose.^{3,4}

Projected intakes

While the original submission on sweetener tablets requested use up to a maximum level of 60g/kg, the Committee has been informed that, since 1991, it has been used in sweetener tablets at a maximum level of 30g/kg. The same level of 30g/kg has been requested for use in dietary supplement tablets. Assuming a "worst case" intake of 30 sweetener tablets a day, each weighing 90 mg, and 12 dietary supplement tablets a day, each weighing 1200 mg, and a cross-linked sodium carboxymethyl cellulose content of 30g/kg, the estimate of extreme intake of cross-linked sodium carboxymethyl cellulose from both uses is 8.5 mg/kg bodyweight/day. This represents just over a 3-fold increase in extreme intake from the two uses, if both uses are at a level of 30g/kg, compared with the previous estimate of extreme intake of 2.7 mg/kg bodyweight/day from use only in sweetener tablets at a level of 60g/kg.

Additional toxicity data

A new 90-day oral feeding study⁴ was conducted in which groups of rats were fed diets containing 0, 10,000 or 50,000ppm cross-linked sodium carboxymethyl cellulose or 50,000ppm of a similar modified cellulose gum. There were no treatment-related effects, except for reduced bodyweight in males and increased food consumption and mineralisation of the kidney in females in the group given 50,000ppm cross-linked sodium carboxymethyl cellulose. Similar effects were seen in the group given 50,000ppm modified cellulose gum. Nephrocalcinosis is not uncommonly observed in studies feeding high levels of non-nutrients in the diet. Reduced bodyweight and increased food consumption were also seen in all treatment groups in a previous 13-week oral feeding study,² which compared 10,000 and 50,000ppm cross-linked sodium carboxymethyl cellulose with the parent compound, sodium carboxymethyl cellulose.

Taking into account the adverse effects observed at 50,000ppm, the no-observed-effect level (NOEL) for cross-linked sodium carboxymethyl cellulose is 10,000ppm, equivalent to 757mg/kg bodyweight/day and 893 mg/kg bodyweight/day for males and females respectively. This gives a margin of safety of around 100 between the NOEL and the predicted extreme intake of 8.5mg/kg bodyweight/day for man.

Conclusion

The Committee has taken account of the previous and newly provided technical and toxicological information on cross-linked sodium carboxymethyl cellulose. It notes the lack of toxicity and long history of safe use of the parent compound, sodium carboxymethyl cellulose. The parent compound is known to be poorly absorbed, if at all, in animals and man, and it is likely that cross-linking reduces absorption even further. The Committee therefore recommends that the extension of use of cross-linked sodium carboxymethyl cellulose as a disintegrant in dietary supplements at a level not exceeding 30g/kg is acceptable.

References

1. Minutes of the 94th meeting of the Scientific Committee for Food held on 22-23 September 1994 in Brussels. DG III, Commission of the European Communities, III/5487/94-EN, Brussels.
2. FMC Corporation (1991). Submission of a request for approval of a food additive: Ac-Di-Sol. Submitted to the Scientific Committee for Food of the EC Commission, FMC Corporation NV, Brussels, Belgium. CS/EMU/67.
3. FMC Corporation (1997). Submission of a request for review of cross linked sodium carboxymethyl cellulose for use in solid dietary supplements. Summary SCF Dossier EC 163.01. CS/ADD/EMU/162. FMC Corporation NV, Brussels, Belgium.
4. FMC Corporation (1997). Ac-Di-Sol SD-711 and modified cellulose gum ninety-day feeding study in rats. Study number 195-2054. April 4, 1997. FMC Corporation, Princeton, New Jersey, USA.