**Advice on the selection of excipients for zinc sulfate tablets and solutions**

The potential impact of interactions between zinc ions and pharmaceutical excipients on absorption is very difficult to predict. In general, during formulation development a good excipient reference should be consulted on the compatibility of all proposed excipients, for example the Handbook of Pharmaceutical Excipients indicates several excipients, including croscarmellose sodium, that are incompatible with zinc and zinc salts.

There is particular concern with respect to the potential impact of sweeteners and flavours on the *in vivo* absorption of zinc. For this reason, as indicated in the WHO Prequalification document ‘Q&A for submission of applications for prequalification of Zinc Sulfate Tablets and Zinc Sulfate Oral liquid (solution)’, applicants to prequalification must provide evidence that the sweeteners/flavours present in their zinc sulfate products do not negatively impact the absorption of zinc.

As an aid to the development of zinc sulfate formulations, the prequalification team has determined that the following pharmaceutical sweeteners and flavours can be employed as excipients in zinc sulfate formulations, without providing additional evidence that the ingredient does not negatively impact the absorption of zinc:

- Aspartame
- Ethyl vanillin (in quantities <1mg per 20 mg zinc sulphate tablet)
- Mannitol
- Mono ammonium glycyrrhizinate*
- Saccharin sodium (in quantities <1mg per 20 mg zinc sulphate tablet)
- Sorbitol
- Trusil flavours*

It is important that these excipients be employed in the smallest quantities possible to achieve the desired sweetening/flavouring effect. In particular, the identified excipients (*) should be employed in quantities of no more than approximately 2% of the formulation by mass. If it is judged that the above-noted excipients are employed in quantities above the limit for which we have confidence that their impact will be negligible, additional information on the impact of that quantity of excipient on zinc absorption may be requested.

It is important to note that this advice does not indicate that other sweetening/flavouring excipients are not acceptable; it indicates that the use of other sweetening/flavouring excipients must be justified with supporting information on their impact on zinc absorption.