Advice on the Selection of Excipients for Zinc Tablets and Solutions

The potential impact of interactions between zinc ions and pharmaceutical excipients on absorption is very difficult to predict. 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 guidance document *Q&A: Submission of Applications for Prequalification of Zinc Tablets and Zinc 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. Although this document mainly refers to Zinc sulfate products, the principles discussed are also applicable for the other invited Zinc salts (i.e., gluconate, acetate and citrate).

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 sulfate tablet)
- Mannitol
- Mono ammonium glycyrrhizinate*
- Saccharin sodium (in quantities <1mg per 20 mg zinc sulfate 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.