All interested parties,

As you are probably aware, the ICH Q3D Expert Working Group ("EWG") is developing "Impurities: Guideline for Metal Impurities" ("the Guideline") that addresses toxicity data for potential metal impurities, establishment of a permitted daily exposure ("PDE") for metals of toxicological concern, and development of a control strategy for limiting metal impurities in drug products consistent with the PDE. The EWG has sought preliminary feedback from interested stakeholders prior to releasing the Step 2 Guideline later in 2012.

To facilitate discussion of the matters raised in and by the Guideline, IPEC-Americas would like to request the following information. If you would prefer to have this information blinded before it is used, please specify that when you submit the data.

1. **Extractables information:** Several members of the coalition have expressed concern regarding the application of total metals vs. the amount of metal that is bioavailable or extractable. It is critically important that companies that have information about this issue submit the information to the ICH EWG. We request that you submit any studies you may have about extractable levels of metals in excipients (either produced by your company or ones which you are aware of), any information which you may have about extractable methodologies and any other relevant information you may have regarding this issue.

2. **Components Data:** While the PDE limits apply to the finished product – it is also necessary to understand the levels in the API and excipient components (as they can contribute to the overall metals in the finished dosage form). Any data that you have regarding the actual levels of metals in various APIs and excipients and the test methods used to make these determinations should be submitted to the ICH EWG.

3. **Finished Drug Product Data:** Since the PDE limits apply to the finished product it is important for industry to look at their products to determine if there are issues with the limits. For example, a product with a high level of a mined excipient that can be dosed up to 10 tablets a day may have difficulty meeting the PDE limits. This type of data is needed by the EWG to properly assess the state of understanding in the industry and the types of issues with finished dosage forms that may exist when trying to comply with the PDE limits. Please supply any data you have to EWG regarding the actual levels of metals that may exist in finished dosage forms and how these may compare to the proposed PDE limits when assessing the daily dose of the product. Information related to methodologies used for determinations would also be helpful.
International Pharmaceutical Excipients Council
Of The Americas

It is very important that this information reach the EWG in time for evaluation BEFORE their meeting in November. Therefore, please try to submit this type of data to the EWG representatives in the Coalition by October 10, 2012.

Please submit your data directly to Janeen.Skutnik@pfizer.com and Douglas.j.ball@pfizer.com.

Regards,

David R. Schoneker
Chair – Coalition for Rational Implementation of USP’s Elemental Impurities Requirements