properties of the material as it relates to the end use of the API final intermediate or the final API. As far as the API manufacturer is concerned, any change will become incorporated into the Annual DMF report. With respect to the user of the API, the issue is how to report certain types of changes (Annual Report, Supplement Changes Being Effected, or a Prior Approval Supplement). As previously noted, the DMF holder has a legal obligation to notify an ANDA sponsor of changes that have been implemented in the manufacture, processing, or controls of the API. The critical point in the BACPAC guidance is that the API manufacturer is expected to obtain comparison data of the material that underwent the change with the prior process material. Typically, a comparison of the prematerial and postmaterial at the level of multiple batches is requested [9]. Both the API-DMF holder and the ANDA holders need to have clear consensual views of what changes have been made and how to deal with the changes in a very consistent manner. The BACPAC concept came at the heels of the scale-up, postapproval changes concept for the finished dosage form. The simple fact is that some changes can be made and, based on the comparison data, may fall into the category of Annual Report in today's climate. This is a savings of time, energy, and resources for all parties concerned: DMF holder, approved ANDA holder, and the FDA. What is a surprise is that at the beginning of June 2006, the FDA announced that the BACPAC I guidance was being withdrawn. The FDA rationale for this action was that the issued BACPAC guidances "were not consistent with the cGMP for the 21st Century." One can infer that efforts are underway to replace the withdrawn guidances to better harmonize the regulatory efforts for both APIs and finished drug products [9].

TECHNICAL PARTNERSHIP BETWEEN THE API MANUFACTURER AND THE DRUG PRODUCT MANUFACTURER

A strong interactive working relationship between the API source and the API consumer is important to assure that there is harmony and consensus in the filing of ANDA specifications for the drug substance with the filed DMF of the API supplier. This relates, in particular, to specifications and test methods. The auditing of the API source by the API consumer should be based on mutual respect and understanding of differences. Such a relationship will lead to timely resolution of technical issues. Further with the implementation of BACPAC I and BACPAC II, it is even more critical that each side understands the issues and practices of the other side. An initial site audit of an API supplier is common practice when working with a new source of an API. This audit should be followed up on some periodic basis, particularly if some issues were discovered during the initial audit. As the FDA inspectional history for an API supplier evolves, some determination can be made about the need and frequency for follow-up audits.

IDENTIFYING AND QUALIFYING API SOURCES

The DMF track record and FDA inspectional history are typically a starting point for establishing the qualifications for an API source. As previously noted, one can go online to the FDA website for a listing of all DMFs for a particular API. The FDA inspectional history can be obtained under Freedom of Information from various