search engine services for any given API manufacturer. One needs to know the particular site of manufacture for the API supplier for the particular API of interest, if the API manufacturer has multiple sites. The FDA inspectional history includes FDA "483s" and "EIRs." The FDA "483" is the inspection report listing "observations" issued to a firm immediately following a site inspection. The FDA Establishment Inspection Report or "EIR" is the FDA's internal report about the inspection findings. For both types of documents, the FDA dockets management branch issues "purged" documents, which exclude certain "confidential information."

A number of search engine services can provide detailed information about current manufacturers/marketers of specific APIs. The input requirements to get the search started are the CAS number and any recognized/official names for the API. By pooling the information from the DMF database, FDA inspectional history, and listings of identified suppliers (which often includes some marketing statistics for the firm and API), one can very quickly identify the pool of suppliers for just about any API. Following the identification of a primary source for an API, it is often common practice to establish alternate sources in the case of an unexpected event, which might block the primary source from serving the needs of the ANDA drug product developer.

A critical factor in moving ahead with an alternate source of the raw material (frequently referred to as "ASRM") is to have established and well-defined specifications for all critical quality-control attributes to minimize any adverse effect on the ANDA drug product formulation and manufacturing process. These specifications are provided to the potential ASRM and based on the response information provided as well as the evaluation of samples of the API can provide the basis for determining whether the ASRM material will fit the "boundaries for the filed ANDA." Here, the issue of comparability, previously discussed in the context of the primary source of the API versus the "innovator," now becomes the comparability of the primary API source versus the ASRM [10]. The timing to complete the qualification of an ASRM typically can vary from 6 to 12 months, if the testing includes manufacture and accelerated stability studies of test batches of the drug product. The completion of qualification would then be followed by filing an amendment to the filed ANDA.

A frequent issue for identifying an API source for an NCE is that, at the early stages of the NCE history, there may not be any listed source for the API. Further, there may not be any solicitation for the compound. Here, the best approach is to understand the chemistry of the NCE and identify API sources that have been involved with that chemistry before. Alternatively, look for API sources that typically stay on the forefront of NCEs. A strategy that may be worth pursuing is to start the API sourcing process immediately after an NCE enters the marketplace and when it is clear that the NCE will achieve an attractive market share.

CONCLUSION

The successful development of a generic drug product starts with the API. It is critical to understand the basic science underlying the targeted listed drug API as well as the intellectual property that "limits" the horizons for the synthesis and specifications for the generic API. Further, companion challenges that confront both the API