drug-product manufacturers with the "open part" of a DMF, because the information therein may be necessary and useful in formulating a drug product. An open part of the DMF would typically include the following:

A. Drug substance
   - Description of API
   - Manufacture of drug substance (synthetic pathway only), which includes
     - Flow chart
     - Impurity profile
     - Demonstration of chemical structure
     - Physical characteristics of the product (spectroscopic analysis)
   - Purity of the reference material
   - Packaging and labeling

B. Laboratory controls
   - Specifications and test methods used for the API
   - Scheme of the stability evaluation protocol
   - Batch size

C. Complaints file

D. Environmental impact analysis

Alternate Vendor Sourcing

It is useful to secure approval of an alternate API manufacturer. However, different API manufacturers may have applied different strategies to overcome process patents. In such cases, there is a high probability that the impurity and residual solvent profiles will vary significantly, necessitating full analytical methods revalidation.

Where polymorphism is an issue, it is essential that both suppliers provide the identical form. From a regulatory perspective, the preferred situation would be if both manufacturers' materials were synthesized utilizing the same [very difficult to achieve if patent(s) has been filed] or a similar synthetic approach, which is likely to result in similar impurity and residual solvent profiles and polymorphic form.

The need to change sources of raw material during formulation development is unfortunately not a rare occurrence. Such situations may arise when there may initially only be a single source of supply of R&D quantities of API. Formulation development thus commences with relatively costly raw material and often, in time, additional bulk API suppliers emerge to provide raw material at more favorable prices. If the formulation scientist is required to change the raw material source for scale-up or exhibit-batch manufacture, the formulation may need to be redeveloped, because the physicochemical characteristics of the new supplier's raw material may bear scant resemblance to that used initially, and as a consequence, this may slow the project down considerably.

Even if another supplier's raw material is similar, if not identical to that employed initially, a simple substitution of the latter by the former may not result in an identical product being produced even when the raw material specifications appear identical. When faced with such a situation, it is always in the formulation scientist's best interests to undertake a series of trials, preferably at pilot-batch scale, to confirm acceptability of the alternate API from both the production and analytical points of view.