raw material can be incorporated into a non-patent-infringing formulation, which will be at least as stable as the innovator drug product and also bioequivalent (BE).

Sourcing of the Active Raw Material(s)

Purchasing an API raw material can be quite demanding and is not as straightforward as one might perceive. Databases are consulted as to which manufacturers have the required material available, and once the potential vendors are identified, each is requested to furnish the following information:

1. The detailed synthetic pathway whereby the API is produced, including all solvents, catalysts, materials, etc., utilized at every step.
2. A statement indicating that the process pathway does not infringe any patent(s) that may be in force and must be verified by the generic company's patent lawyers.
3. A statement indicating the possible polymorphic nature of the active drug in question, where relevant.
4. The batch size(s) of API, which has been manufactured to date.
5. Any validation data that may be available to provide some degree of assurance that the synthetic process has been evaluated/controlled.
6. Samples of 50 to 100 g from three discrete batches of material manufactured according to the synthetic pathway provided. In each case, the batch size should be made available.
7. A complete list of synthetic impurities and potential degradation products that may be used to fingerprint the API, together with full chemical characterization of each as well as 50 to 100 mg samples of each synthetic impurity/degradation product alluded to. Appropriate methodologies such as mass spectroscopy, high-performance liquid chromatography (HPLC), x-ray diffraction (where polymorphs may be present), nuclear magnetic resonance, and electron spin resonance, among others, are generally used for the characterization. In some instances, one of the recognized international compendia such as the United States Pharmacopoeia (USP) [29] and/or Pharmacopoeial Forum [30], the British Pharmacopoeia [31], and the European Pharmacopoeia [32] may list potential impurities and/or degradation products for the API in question. Depending on the route of synthesis followed, there may be no possibility for a listed impurity to be present in the API. Should such a situation present itself, the onus is on the API manufacturer to provide a statement as to why there is no possibility for the stated impurity to be present. Note: Such a statement would have to be supported by actually demonstrating the absence of said impurity by HPLC analysis, and in order that this be done, it is essential that the impurity be synthesized (and chemically characterized) either by the API manufacturer or by a contract laboratory.
8. A complete list of solvents used in the synthetic process (which should relate to those claimed in the detailed synthetic pathway) together with those that should be monitored in the API. Where appropriate, a statement must be