GPhA
Generic Pharmaceutical Association

2300 Clarendon Blvd. • Suite 400 • Arlington, VA. 22201
703-647-2480 • Fax: 703-647-2481 • Email: info@gphaonline.org

July 7, 2003

Food and Drug Administration
Dockets Management Branch
5630 Fishers Lane, Room 1061 (HFA-305)
Rockville, MD, 20852

RE: Docket Number: 02D-0526

Draft Guidance: Drug Product Chemistry, Manufacturing and Controls Information

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Dear Sir or Madam:

The Generic Pharmaceutical Association (GPhA) appreciates the opportunity to respond to the Guidance for Industry: Drug Product Chemistry, Manufacturing and Controls Information. GPhA represents 98% of generic drug manufacturers whose drugs are dispensed for almost half of all prescriptions filled in the United States, but representing less than 10% of all drug expenditures. GPhA is the united voice of the generic drug industry and is committed to patient health and safety, and strongly supports any measures that will improve our health care system.

GPhA provides the following comments regarding the above referenced Draft Guidance. This Draft Guidance provides comprehensive recommendations to the pharmaceutical industry in regard to information to be included in marketing applications. In assessing the proposed recommendations, GPhA is also cognizant of the Commissioner's initiative to assure high quality submissions and to streamline the ANDA review process. GPhA is providing comments within the context of these initiatives.

Comments:

GPhA has concerns related to the proposed recommendations that comprehensive Pharmaceutical Development reports are to be submitted with each application. The Draft Guidance does not appear to provide for flexibility in regard to content of the reports or when such reports may not be necessary. It is believed that there is a substantial number of ANDAs for which Pharmaceutical Development reports are either not necessary, or could be provided in an abbreviated format. Reducing the content of theses reports or eliminating inclusion of Pharmaceutical Development reports when such reports are unnecessary will conserve valuable FDA resources while continuing to assure that all critical technical information is available for agency review. Providing flexibility

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in the final guidance document will work to streamline the review process without sacrificing scientific information that is essential to the review and approval process.

An ANDA for a generic version of a brand-name drug product (the reference product) must be pharmaceutically equivalent and bioequivalent to that reference product. ANDA applicants must show that the generic drug contains the same active ingredient(s) as the brand-name drug product, is identical in dosage form, strength, and route of administration, has the same conditions of use, and is bioequivalent to the reference product. Generic drugs must meet all drug product quality characteristics established by the agency as well as any compendial requirements for identity, strength, quality, and purity. Additionally, all drug products must be manufactured under the same strict good manufacturing practice regulations.

For certain dosage forms, ANDA applicants must use the same inactive ingredients in the same concentrations as the reference products. For example, 21 CFR 314.94(a)(9) identifies certain regulatory requirements for parenteral, ophthalmic and topical dosage forms that are submitted as ANDAs. For parenteral and ophthalmic drug products, the formulation of the generic product must be essentially the same as the brand product. Thus, the value of product development reports for formulations that are either identical or essentially the same as the brand product that have been carefully reviewed and found to be acceptable by FDA is questionable. In these circumstances, FDA would be re-reviewing duplicative information that provides no additional insight into the quality characteristics of the drug product.

As noted, the Draft Guidance does not appear to contemplate those situations when Pharmaceutical Development reports do not provide any useful scientific information. For example, at line 364, the Draft Guidance states that "The Pharmaceutical Development section should contain information on the development studies conducted to establish that the dosage form, formulation, manufacturing process, container closure system, microbial attributes, and usage instructions are appropriate for the purpose specified in the application." This statement indicates that a Pharmaceutical Development report will be required even though many generic products are identical in formulation and container closure system to the brand product.

Product attributes for generic versions of brand-name drug products such as dosage form, and in many cases formulation and usage instructions (conditions of use), are predetermined by those of the reference product. The ANDA applicant therefore would not likely need to conduct development studies to determine if these attributes are appropriate since they mimic the innovator product. Similarly, microbial and container closure system attributes (e.g., tight, light resistant container) may be specified in an official monograph and ANDAs must contain information showing that the selected container closure systems are suitable and appropriate for their intended use. Thus, ANDAs already contain substantial information related to the container closure system and whether a particular type of container is identified in the USP monograph. Reviewing the same Pharmaceutical Development information in one or multiple ANDAs that has already been found acceptable by the agency results in a waste of

resources that could be better used to review other technical issues within the application or to review additional pending applications.

Also, beginning at line 383, the draft guidance states that "Key physicochemical characteristics... ...should be discussed. However, for ANDAs, characteristics such as water, solubility, particle size (e.g., "micronized"), polymorphic form, etc., may be predetermined by an official monograph, or may be specified in the reference product labeling. Thus, the critical attributes have already been established in many cases. It is expected that the Pharmaceutical Development reports for these examples would have little relevant value.

The NDA applicant must conduct compatibility studies to provide information to establish and support anticipated usage. The ANDA applicant must duplicate compatibility studies of the drug product admixed with diluents identified in the reference product labeling to show that the generic drug will be compatible under the same conditions of use as the reference product. Pharmaceutical development activity for the ANDA applicant is designed to duplicate the compatibility and conditions of the reference product. From a development standpoint, the objective of the generic applicant is to demonstrate that the product performs the same as the brand product and not to introduce new or novel information related to the formulation or labeling claims.

Recommendation:

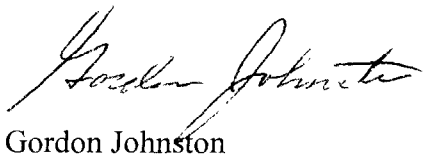
The Draft Guidance does not describe the need or relevance of Pharmaceutical Development reports for a substantial portion of the ANDAs submitted to FDA. GPhA requests that FDA reconsider the requirements set forth in the Draft Guidance as they pertain to Pharmaceutical Development reports. It is requested that the final guidance provide for a flexible approach that seeks such reports when justified for the limited subset of products for which knowledge of pharmaceutical development activities may substantially contribute to the assessment of drug product quality. For many products, a simple confirmation that the formulation is essentially the same as the reference listed drug, the container closure is the same as that used by the brand product, or the product and container complies with a compendial monograph, provides assurance that there are no new issues raised in regard to the development of the proposed drug product.

In summary, a Pharmaceutical Development section should be requested for ANDAs only if it adds reasonable value to the review and approval process. FDA should consider identifying the types of ANDAs that may warrant submission of a pharmaceutical development report and request the reports only in those instances. As stated, a significant number of ANDAs are the same or essentially the same in formulation, container closure system, physiochemical properties, etc., as the reference listed drug. For these applications, a substantive pharmaceutical development report provides no new or relevant information to support drug product quality concerns nor would these reports represent additional scientific support for the proposed drug product. Rather, the resources required to review duplicative pharmaceutical development reports that do not

add value to the scientific body of knowledge would not be justified, especially as the agency works towards a more streamlined and scientifically based review process.

GPhA appreciates your consideration of these comments.

Respectfully submitted,



Gordon Johnston
Vice President Regulatory Affairs