

NAPM



NATIONAL ASSOCIATION OF PHARMACEUTICAL MANUFACTURERS

3279 Veterans Memorial Highway, Suite D-7 • Ronkonkoma, NY 11779 • (631) 580-4252 • Fax: (631) 580-4236
E-mail: napm@npx.com • Website: www.napmnet.org

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

RE: Docket No. 99D-4809 - Guidance for Industry: Applications Covered by Section 505(b)(2)

The National Association of Pharmaceutical Manufacturers (NAPM) appreciates the opportunity to comment on the document, "Guidance for Industry: Applications Covered by Section 505(b)(2)" [Docket No. 99D-4809]. These comments represent the consensus of leading manufacturers of generic drug products. NAPM feels that the first bullet item on p. 6 of this guidance document (discussed below) describing products that can not be included in a 505(b)(2) application is a very restrictive interpretation of the original statute and implementing regulation. As discussed below, we request that the bullet point be modified by making it more consistent with 21 CFR 314.10(d)(9).

p. 6: IV. WHAT CAN'T BE SUBMITTED AS 505(b)(2) APPLICATIONS?

- An application that is a duplicate of a listed drug and eligible for approval under section 505 (j) (see 21 CFR 314.10(d)(9)):

There are many pharmaceutically equivalent drug products for which the *in vivo* bioequivalence to the reference listed drug product (RLD) can not be demonstrated objectively by measuring plasma concentrations of the active drug. For example, drug products such as inhalation aerosols and products intended for local application may have limited systemic drug absorption, such that the objective measurement of plasma drug concentrations from these products can not under our current scientific understanding be related to bioequivalence.

Presently, FDA has not provided guidances for the establishment of bioequivalence of these and similarly situated products. Forcing the generic drug product manufacturer into a 505(j) application when no guidances are available for establishing bioequivalence allows the innovator company many years of free exclusivity beyond the patent expiration date. Moreover, the high cost of performing comparative clinical studies with a variable pharmacodynamic

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endpoint as required for a 505(j) application is prohibitive for smaller drug product manufacturers.

Pharmaceutical firms who manufacture pharmaceutically equivalent drug products should be allowed to use the 505(b)(2) application for product approval when bioequivalence to the reference listed product can not be determined by scientifically objective measurements. Approval of such pharmaceutically equivalent products using the 505(b)(2) application and review process will increase market competition for these products and provide the public with less expensive, more affordable drug products that have comparable drug efficacy.

NAPM requests that first bullet item on p. 6 of this guidance document describing products that can not be included in a 505(b)(2) application be modified or deleted. The guidance is an overly restrictive interpretation of the original statute and pharmaceutical firms who manufacture pharmaceutically equivalent drug products should be allowed to use the 505(b)(2) application for product approval when bioequivalence to the reference listed product can not be determined by objective measurements.

NAPM also notes that the guidance is an unduly restrictive interpretation of the statute. Nothing in 505(b)(2) requires FDA to conclude that a drug product eligible for approval under § 505(j) cannot be the subject of a 505(b)(2) application. In fact, the guidance is more restrictive than 21 C.F.R. § 314.101(d)(9), which provides that a 505(b)(2) application "may" be rejected for filing if the product could be the subject of a 505(j) application. It gives FDA the discretion to refuse to accept for filing a 505(b)(2) NDA when an ANDA is reasonably possible. At the same time, it allows FDA to accept an application for the products discussed above, where bioequivalence to the reference listed product cannot be determined by objective measurements. NAPM urges FDA to revise the guidance to be consistent with 21 C.F.R. § 314.101(d)(9).

NAPM is the national trade organization representing manufacturers, distributors and repackagers of generic multisource prescription drugs, OTC drugs, dietary supplements and veterinary drugs. The organization prides itself in serving the needs of its members and has been heavily involved in legislative, legal, regulatory and technical issues.

We thank you for the opportunity to submit our views.

Sincerely,


Leon Shargel, Ph.D.
Vice President and Technical Director

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