



MYLAN TECHNOLOGIES INC.

December 23, 2004

VIA FEDERAL EXPRESS

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

**RE: Comments of Mylan Technologies Inc. on Docket No. 2004P-0540:
Refuse Final Approval for ANDAs for Fentanyl Transdermal Systems
Without Either Clinical Safety and Efficacy Studies or More Restrictive
Bioequivalence Criterion**

Dear Sir or Madam:

Mylan Technologies Inc. ("Mylan") submits these comments in response to the above-referenced Citizen Petition filed by London & Mead ("Petitioner") on December 3, 2004 (the "Petition").

Mylan has an interest in the Petition because Mylan has submitted an abbreviated New Drug Application ("ANDA") for a generic fentanyl transdermal system ("FTS") and Petitioner has recommended that FDA restrict the approval of generic fentanyl transdermal systems.

The Petition should be denied because Petitioner¹ has presented no evidence whatsoever to support its request that FDA impose standards for approval of ANDAs for generic fentanyl transdermal systems that are inconsistent with FDA's current practices and the governing statute. Petitioner asks that FDA adopt two entirely novel approaches to the approval of any fentanyl transdermal system: requiring transdermal systems with different rate control mechanisms to conduct clinical safety and efficacy studies as if they were entirely different dosage forms and to require even systems with the same rate control mechanism to show bioequivalence using different criteria than those established by FDA. Despite seeking such a drastic change in the standards for approval of ANDAs for fentanyl transdermal systems – relief that would prevent the long-awaited introduction of generic fentanyl transdermal systems – Petitioner fails to provide even the slightest scientific basis for the requested actions. Therefore, the Petition should be denied immediately.

First, Petitioner's request that FDA require clinical safety and efficacy studies before approving generic fentanyl transdermal systems is inconsistent with FDA practice and is not

2004P-0540

C1

¹ Petitioner, a Washington, D.C. law firm, does not explain on whose behalf it prepared this petition, what if any interest it or any of its clients has in the decision of this petition, or what scientific expertise or knowledge it has brought to making its submission.

premised on any evidence or data suggesting that generic fentanyl transdermal systems showing bioequivalence to the referenced product are unsafe or ineffective. As already addressed extensively in Mylan's response to the Petition from Alza Corporation (Docket 2004P-0506), FDA has already determined that use of a different mechanism for rate control is not a basis for requiring anything beyond the normally applicable requirements for approval of a generic product, i.e., bioequivalence. See Mylan's Response to Alza Petition at 3. The Mylan FTS has demonstrated bioequivalence to the reference product in an appropriately designed human bioequivalence study and FDA has determined that the Mylan product is bioequivalent to the RLD, is safe and effective for use as recommended in the submitted labeling, and meets all other approval requirements. Petitioner has presented no basis for questioning FDA's original approval decision of the Mylan product neither has it presented any evidence upon which the agency should revise its position. For that reason alone, Petitioner's request should be denied.

In addition to the utter lack of scientific basis for Petitioner's request, the action requested is not authorized by the governing statutory framework for the approval of generic products. Section 355(j)(2)(A) specifies the items that must be included in an ANDA and does not require clinical and safety testing. Congress has mandated that FDA "shall approve" an ANDA unless it fails to provide the information required by section 355(j)(2)(A) or if the information so provided indicates that the new product has failed to satisfy one of the requirements of that section. 21 U.S.C. § 355(j)(4). The position of Petitioner that fentanyl transdermal systems with different release systems should be treated as different dosage forms than the referenced product (and therefore require clinical safety and efficacy testing) has been rejected by FDA and the courts. See Pfizer Inc. v. Shalala, 1 F.Supp. 2d 38 (D.D.C. 1998) (rejecting view that release mechanism of generic product must be the same as the referenced drug to satisfy ANDA requirements). Thus, there is no legal authority under which FDA could condition the approval of generic products on the submission of clinical safety and efficacy testing.

Second, Petitioner's request that all ANDA products (regardless of the rate control mechanisms) should be required to meet different bioequivalence criteria than that used by FDA is unsupported by any data or scientific evidence. FDA has consistently rejected requests that it change the bioequivalence criteria applied to ANDAs for particular products, especially where there is no data presented to support the request. See FDA Response to Berlex Laboratories, Inc. and 3M Pharmaceuticals SBC (Docket 1998P-0434). Petitioner points only to the Schedule II opioid status of fentanyl as a basis for its request for revised bioequivalence. See Petition at 3. Yet, FDA did not apply such a "restrictive" bioequivalence requirement for the approval of the generic OxyContin®, which is also a potent Schedule II opioid. The schedule II status is in itself not a basis for different approval requirements. Here, Petitioner's request for a change in the bioequivalence criteria does not even include any evidence supporting its argument that fentanyl transdermal systems should be subject to such different bioequivalence criteria. There is no scientific basis for believing that the rate control mechanism used by the Mylan FTS, which FDA has already determined meets all approval requirements, is any less effective than the rate control membrane used in Duragesic®. Petitioner has given FDA no basis for concluding that revised bioequivalence criteria should apply to generic fentanyl transdermal systems and, therefore, the Petition should be immediately denied in its entirety.

Respectfully submitted,



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