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(OVERNIGHT COURIER 2/20/03)

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

Re: Docket # 02P-0478 CP1 - Response to Comments Submitted by Alza Corporation

Dear Sir or Madam:

Reference is made to the Docket cited above for the ANDA suitability petition submitted by Lachman Consultant Services, Inc. (LCS), on behalf of a client, requesting the Food and Drug Administration to make a finding that a Fentanyl Transdermal System, 12.5 mcg / hr is suitable for submission as an abbreviated new drug application (ANDA).

Reference is also made to comments submitted by Alza Corporation to the above-referenced Docket on January 7, 2003, requesting that the FDA deny the petition. The petitioner provides the following responses to Alza's comments.

The commenter contends that the petition should be denied by the Agency for three reasons. For clarity, each of the comments provided is reproduced below with the response directly following each comment.

1) Alza contends that "[C]urrent class labeling would be incomplete with the addition of a new "low-dose" fentanyl strength. The safe use of a new, lower-dose, strength would require significant changes to the label information and warnings. This alone requires the FDA to disapprove the ANDA.

The commenter is incorrect in assuming that the proposed change in strength is for a new "low-dose" fentanyl product. The petitioner seeks to label and market the proposed 12.5 mcg / hr product to provide a means of titrating a patient to an appropriate intermediate dose between two currently approved safe and effective doses of the reference-listed drug product, not as a new, low starting dose. Providing the physician the flexibility to be able to titrate a patient's dose between two existing safe and effective doses of a powerful narcotic agent like fentanyl would appear to provide a reasonable dosing option not currently available with the approved product.

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The current approved labeling of the reference-listed drug product contemplates the addition of multiple patches for achieving certain dosages. In that regard, the physician should already be aware that multiple patch application can be useful in obtaining a specific desired dose of the drug product that in some cases cannot be offered by a single patch.

The commenter claims that the approval of a suitability petition may not occur if "[a]ny of the proposed changes from the listed drug would jeopardize the safe or effective use of the product so as to necessitate significant labeling changes to address the newly introduced safety or efficacy problem"; 21 CFR 314.93(e)(1)(iv). However, the commenter has not identified any newly introduced safety or efficacy problem. There are no new warnings that will be included or required, nor are there any warnings that would be excluded. There would only be the addition of specific instructions regarding the proposed use of the 12.5 mcg / hr patch to achieve an intermediate dose between two approved dosage strengths by adding a 12.5 mcg / hr patch to the use of an existing strength patch (e.g., 25 mcg / hr, 50 mcg / hr, 75 mcg / hr or 100 mcg / hr patch). Such labeling changes are routine and clearly contemplated for drug product applications submitted pursuant to an approved suitability petition for this type of change. (21 CFR 314.94(a)(6))

2) Prescriber confusion is likely with a new fentanyl dose, as is increased off-label use.

The client does not believe that the approval of this petition will create prescriber confusion. Physicians are accustomed to monitoring patients on potent medications, and often will make necessary and appropriate dosage adjustments based on the individual patient's response. Providing a product capable of more finely titrating a patient to a specific intermediate dose of fentanyl when deemed appropriate by the prescribing physician should not be a cause for prescriber confusion.

The change proposed by this petition is for a product that can be used to titrate between the currently approved doses of the reference-listed drug product. The product will be labeled in accordance with the same uses, warnings, contraindications and indications as that of the reference-listed drug product. Because the uses, safe and effective dosage range, appropriate patient population, warnings and precautions are clearly defined in the labeling of the reference-listed drug product, and since an ANDA cannot seek uses that have not been previously approved for the reference-listed drug, we do not believe that a properly labeled product would promote off-label use.

3) Re-formulations and new dosage strengths of Schedule II controlled drugs will likely result in new uses of the product in inappropriate populations and changes in abuse potential. The risk of these new uses and increased abuse should be investigated before a new dose strength is approved.

Again, the purpose of the proposed product is not to create new uses or treat different patient populations. As a matter of fact, an ANDA suitability petition cannot be approved for such a change. The labeling proposed for the proposed product seeks approval for the same uses and patient populations as are currently approved for the reference-listed drug product. As such, there are no "newly introduced safety or efficacy problems", as is suggested in the comments, since the petitioner seeks approval for only the same uses and in exactly the same patient

population as that of the approved product. The product is intended solely for titrating patients between two currently approved doses of the innovator product.

Respectfully submitted,

Robert W. Pollock/ji

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RWP/ji

cc: L. Lachman
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