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June 4, 2003

(OVERNIGHT COURIER)

Dockets Management Branch
Food and Drug Administration (HFA-305)
Department of Health and Human Services
5630 Fishers Lane, Room 1061
Rockville, MD 20853

Re: Comments to Docket # 02P-0478/CP1

Dear Sir or Madam:

Reference is made to the Docket cited above and to comments submitted by Lachman Consulting Services Inc. dated February 20, 2003 in response to comments submitted by ALZA Corporation on January 7, 2003.

Notwithstanding the additional comments submitted by the petitioner, ALZA respectfully urges that FDA deny the petition for the reasons stated in ALZA's January 7 submission and as supplemented herein.

As previously indicated, the FFDCA states that a suitability petition should be denied, among other reasons, if FDA finds that investigations are necessary to show the safety and effectiveness of a generic drug candidate when its strength differs from that of the reference listed drug, 21 USC 355(j)(2)(c)(i); 21 CFR 314.93(e)(1)(i).

Petitioner seeks to market a 12.5 mcg/hr transdermal fentanyl product "...to provide a means of titrating a patient to an appropriate intermediate dose...", however, the petitioner offers no evidence or support whatsoever that intermediate doses of 37.5 mcg/hr, 62.5 mcg/hr or 87.5 mcg/hr are "reasonable dosing options" commonly used by physicians in their prescribing habits. Nor does petitioner offer any assurances whatsoever that the proposed 12.5 mcg/hr product would not be used as an initiation dose of opioid therapy in opioid naïve children or in cachetic individuals weighing less than 50 kg, contrary to safety information contained in the current boxed warning for the reference product. Assuming, for the purpose of discussion only, that petitioner's stated intent of seeking to market a new dose of an existing product to "...titrate a patient's dose between two existing safe and effective doses of a powerful narcotic..." is sincere, and that such intermediate doses are indeed necessary for physicians to appropriately prescribe the product, then in such event, petitioner has the

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alternative of requesting approval to market the intermediate dosage forms of 37.5 mcg/hr, 62.5 mcg/hr and 87.5 mcg/hr themselves rather than the 12.5 mcg/hr dosage form. Such a proposal would reduce the serious risk of off-label use of the 12.5 mcg/hr product in inappropriate patients as more fully described in our January 7 submission.

In addition, any introduction of a 12.5 mcg/hr product should be supported by relevant clinical studies, other than bioequivalence studies, in order to provide information on the safety and clinical utility of the starting dose of 12.5mcg/hr. We believe such a view is consistent with the position of FDA's Division of Anesthetic, Critical Care and Addiction Drug Products

Accordingly, for the reasons stated in our January 7 submission and as stated herein, the petition should be denied.

Thank you for your timely consideration of these comments. I would be happy to discuss further the issues raised in this docket submission. Please contact me at 650-564-4282.

Sincerely,

Janne Wissel
Senior Vice President
ALZA Corporation

Xc Dr Bob Rapport
Division of Anesthetic,
Critical Care and Addiction
Drug Products