



# OTSUKA AMERICA PHARMACEUTICAL, INC.

2440 Research Boulevard, Rockville, Maryland 20850  
Telephone (301) 990-0030    Telefax (301) 990-0036

September 25, 2000

0610 \*00 SEP 26 A9:14

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

**Re: Docket No. 94D-0325 and 96D-0009**

Dear Sirs:

This letter supercedes our letter dated September 17, 2000 and corrects an error in our comments.

Following are the corrected comments from Otsuka America Pharmaceutical Inc. (OAPI) on the International Conference on Harmonisation: Draft Revised Guidance Q3A(R), Impurities in New Drug Substances and Q3B(R), Impurities in New Drug Products.

Both draft guidances now allow for rounding of significant digits. The rounding may effectively increase allowable unqualified and unidentified impurity levels in the drug substances and degradation products in the drug product. For example, in Q3A(R) for a drug substances with a daily dose greater than 2grams, an impurity level of 0.14% will now be rounded down to 0.1%. However, the guidance sets the qualification and identification threshold at greater than 0.1%. Therefore, since the rounded down figure does not exceed the allowable 0.1% limit the impurity may not be identified or qualified. In this instance, rounding may result in an increase of up to 40% of an unidentified and unqualified impurity in the drug substance.

We trust that the Expert Working Groups for both Q3A and Q3B guidances have taken the toxicological and quality impact of this potential increase in unqualified and unidentified impurity and degradation product levels into consideration.

Please feel free to contact me at (301) 527-4701 should you need additional information or clarification.

Sincerely yours,

Suva B. Roy, Ph.D.  
Senior Director, Regulatory Affairs CMC

96D-0009

CR1

OTSUKA PHARMACEUTICALS  
2440 RESEARCH BLVD.

SHIP DATE: 25SEP2000

ROCKVILLE, MD 20850  
301/990-0030

ACTUAL WGT: 0.23 LBS

TO: DOCKETS MANAGEMENT BRANCH (HFA-305)  
FOOD AND DRUG ADMINISTRATION  
5830 FISHERS LANE  
ROOM 1081  
ROCKVILLE, MD 20852

**FEDEX**

PKID: 81870  
REF:

**STANDARD OVERNIGHT**

**TUE**  
DELIVER BY:  
26SEP2000

SYSTEM # 5005 25SEP2000

TRK# 7514 1436 0571 FORM 202 IAD

20852-MD-US

**19 GAIA**

