GILBERT'S

May 8, 2002

Via Facsimile & Email

Dockets Management Branch
U.S. Food and Drug Administration (HFA-305)
Room 1061
5630 Fishers Lane
Rockville, Maryland 20852
U.S.A.

Re: Docket 02P-0191: Teva Inc. Citizen Petition re Ultram (tramadol)
Docket 01P-0495: Apotex Corp. Citizen Petition re Ultram (tramadol)

The following are the comments of Apotex Corp. and Torpharm Inc. (collectively "Apotex") in response to Teva's Citizen Petition (Docket 02P-0191) respecting generic tramadol.

Apotex has filed its own petition on October 24, 2001 (Docket 01P-0495) seeking approval for labeling that does not include a dosing schedule protected by exclusivity. On April 23, 2002, FDA responded by stating:

> "FDA has been unable to reach a decision on your petition due to the need to address other Agency priorities. This interim response is provided in accordance with FDA regulations on citizen petitions (21 CFR 10.30(e)(2)). We will respond to your petition as soon as possible given the numerous demands on the Agency's resources."

In Teva's petition filed on April 30, 2002, Teva suggests that its approach to the labeling of generic tramadol is somehow different than that proposed by Apotex:

> "The Agency must recognize that Teva's approach to tramadol labeling is completely different than the "discontinued labeling" approach advocated by other applicants, which would require a determination by FDA that the discontinued 50 mg titration schedule was not withdrawn for safety reasons. Teva respectfully suggests that the discontinued labeling approach is unnecessary and inappropriate in this situation, because the use for which it is

01P-0495 C6

LAW OFFICE – THE FLATIRON BUILDING
49 Wellington Street East, Toronto, Canada M5E 1C9 T 416.703.1100 F 416.703.7422 www.gilbertslaw.ca

labeled, Teva's tramadol has the same dosage labeling as the *currently* approved innovator labeling. Moreover, Teva's approach differs from other applicants who have focused on the definition of 'safety" and comparisons between reducing adverse events and reducing drug withdrawal due to adverse events, *see eg.*, Docket No. 01P-0495, comments of Apotex, April 11, 2002."

Although Apotex' citizen petition follows the procedure set out in the draft discontinued labeling guidance, Apotex' proposed labeling does not require this draft guidance for approval of its labeling. Apotex stated in footnote 1 to its citizen petition:

"On October 26, 2000, FDA published a "Draft Guidance for Industry on Referencing Discontinued Labeling for Listed Drugs in Abbreviated New Drug Applications." 65 Fed. Reg. 64225. Although the draft guidance is consistent with the relief sought, this citizen petition is submitted pursuant to the above-listed statute and regulations, not pursuant to the draft guidance."

Teva characterizes its labeling as the "current" labeling without the use for chronic pain through the 25 mg/16 day titration dosing schedule. Similarly, Apotex' proposed labeling is in effect the current labeling without the 25 mg/16 day titration dosing schedule. In substance there is no difference between Teva's labeling and Apotex' labeling, whether it is characterized as current labeling without the chronic pain 25 mg/16 day titration dosing schedule use or whether it is characterized as the discontinued labeling.

In any event, Apotex' labeling relies upon the existing statute and regulations, namely 21 USC §355(j)(2)(A)(viii), 21 CFR§314.94(a)(8)(iv) and 21 CFR§314.127(a)(7). Teva correctly points out that a company may carve out certain labeling protected by exclusivity, ie the 25 mg/16 day titration dosing schedule. Apotex concurs with Teva's view that the generic is entitled, as of right, to carve out this labeling. Like Teva, Apotex is not seeking approval for the 25 mg/16 day dosing schedule covered by the D-63 exclusivity as well as by US patent 6,339,105, which is listed in the Orange Book.

Apotex and Teva have both requested a decision on the proper labeling of a generic tramadol product. FDA must make a decision on the content of the appropriate labeling that is permitted for any generic tramadol product. It is submitted that if FDA has any concerns about the particular form of an individual applicant's request, the applicant should be given the opportunity to address this language in order to ensure that similar applicants are treated similarly.

Finally we note that Teva has requested an answer within 10 days failing which it will "treat a failure to respond as a final Agency decision not to approve Teva's ANDA". Similarly, Apotex requests immediate final approval of its ANDA for tramadol, and a response to the citizen petition that has been outstanding since October 2001. Apotex would request that FDA answer the Apotex citizen petition no later than the answer provided to Teva and grant approval no later than that granted to Teva for its generic tramadol product

We would be pleased to provide further information upon request.

Yours very truly,

for Tim Gilbert

TG:SM:tm

GILBERT'S

FAX COVER PAGE

DATE: May 8, 2002
FILE NO.: 7002

TO:	FDA Docket Management Branch		
FAX NO.:	301-827-6870	TELEPHONE NO.:	301-827-6860
FROM:	Tim Gilbert		
FAX NO:	416-703-7422	TELEPHONE NO.:	416-703-1100

MESSAGE:

Re: Docket No. 02P-0191: Teva Inc. Citizen Petition re Ultram (tramadol)
Docket No. 01P-0495: Apotex Corp. Citizen Petition re Ultram (tramadol)

TOTAL NO. OF PAGES INCLUDING THIS PAGE: 4

ORIGINAL SENT BY: ___ MAIL ___ COURIER ___ TDX ___ NOT SENT ✓ OTHER email

CONFIDENTIAL:
THE INFORMATION CONTAINED IN THIS MESSAGE IS CONFIDENTIAL AND PRIVILEGED. IT IS INTENDED ONLY FOR THE USE OF THE INDIVIDUAL OR ENTITY TO WHICH IT IS ADDRESSED. IF YOU ARE NOT THE INTENDED RECIPIENT, YOU ARE HEREBY NOTIFIED THAT ANY DISTRIBUTION, COPYING, DISCLOSURE OR TAKING OF ANY ACTION IN RELIANCE ON THE CONTENTS OF THIS TRANSMISSION IS STRICTLY PROHIBITED AND REVIEW BY ANYONE OTHER THAN THE INTENDED RECIPIENT SHALL NOT CONSTITUTE WAIVER OF PRIVILEGE. IF YOU HAVE RECEIVED THIS FAX IN ERROR, PLEASE NOTIFY US IMMEDIATELY BY TELEPHONE.

LAW OFFICE – THE FLATIRON BUILDING
49 Wellington Street East, Toronto, Canada M5E 1C9 T 416.703.1100 F 416.703.7422 www.gilbertslaw.ca