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Dockets Management Branch
Food & Drug Administration
Department of Human Services
Room 1061
5630 Fishers Lane
Rockville, MD 20852

Re: Docket Number 2003P-0366

Dear Sir or Madam:

Procter & Gamble submits this in response to Mylan Laboratories' October 29, 2004 filing in support of the Mattingly petition, citizen petition No. 2003P-0075. The Mattingly petition asks the Agency to take the literally unprecedented step of forcing a name change of a Rx-to-OTC switch drug, so that the marketer could not use any form of the name of the Rx product.

The new basis Mylan argues for this action is that a filing for a patent extension stated that omeprazole and omeprazole magnesium are "different active ingredients" for patent extension purposes. Mylan's letter adds no new, relevant information justifying the extraordinary consumer confusion that would result if P&G were forced to rename Prilosec OTC.

The Mattingly petition should be denied for the following reasons:

- I. TECHNICALITIES OF PATENT-EXTENSION AND DRUG-EXCLUSIVITY LAW HAVE NO RELEVANCE TO CONSUMERS, TO THERAPEUTIC EFFECT, OR TO PRODUCT NAMES.

Whether an ingredient and its salt are legally the "same" or "different" depends purely on context. To illustrate: The Federal Circuit has recently held that drug active ingredients and their salts are the "same" for the purpose of defining the scope of extended patents. *Pfizer, Inc. v. Dr. Reddy's Laboratories, Ltd.*, 359 F.3d 1361, 1366 (Fed. Cir.), *reh. den.* 2004 U.S. App. Lexis 10307 (2004). Under other precedent, omeprazole and omeprazole magnesium would be "different" active ingredients for purposes of determining eligibility for patent extension based on a regulatory review. *See Glaxo v. Quigg*, 706 F.Supp. 1224 (E.D. Va. 1989) *aff'd*, 894 F. 2d 392 (Fed. Cir. 1990).¹ Active ingredients and salts are the

¹ The logic of *Glaxo* suggests that a different conclusion could be possible if approval of a salt preceded approval of an acid or base.



same for purposes of determining the length of regulatory exclusivity for newly approved drugs. 21 USC Sec. 355(j)(5)(D).

There is no question that omeprazole and omeprazole magnesium share the same “active moiety,” that is, the same molecular form “responsible for the ... pharmacological action of the drug substance.” See 21 CFR 314.108(a). Omeprazole magnesium is not a “new chemical entity” compared with omeprazole. *Id.*

Mylan’s letter, which relies selectively on one small element of this complex structure, adds nothing of substance to the Agency’s careful consideration of the naming of Prilosec OTC.

The consumer-relevant fact is that Prilosec Rx and Prilosec OTC share the same therapeutic moiety, which works the same way in each product. The Agency implicitly found this when it approved the labeling of the OTC product, which states that Prilosec OTC is “omeprazole delayed-release tablets 20 mg” with an active “equivalent to 20 mg omeprazole.”

II. THE AGENCY THOROUGHLY CONSIDERED THE MINOR PRODUCT DIFFERENCES BETWEEN PRILOSEC AND PRILOSEC OTC IN ALLOWING THE NAME “PRILOSEC OTC”

The Agency, as well as members of two Advisory Committees, relied on the extensive safety database on Rx Prilosec capsules to approve Prilosec OTC. Bioavailability studies were conducted to bridge the omeprazole Rx capsule safety data to the omeprazole magnesium (Prilosec OTC) tablet efficacy and safety data. As noted in our March 29, 2004 submission to this Docket, the FDA’s medical reviewer stated the following in the public briefing materials for the October 20, 2000 Advisory Committee meeting on the Prilosec Rx-to-OTC switch:

Results of bridging studies to compare Ome-Mg and Omeprazole indicate their toxicokinetic and toxicological profile are equivalent. Pharmacokinetic studies have demonstrated relative bioavailability between Omeprazole capsules and Ome-Mg tablet formulations.

It’s therefore noteworthy (but not surprising) that the use of the Prilosec name for Prilosec OTC was not discussed as a concern by any committee members in two joint meetings of the Nonprescription Drugs Advisory Committee and the Gastrointestinal Drugs Advisory Committee, nor by any witnesses at those public hearings.

The Agency’s consideration of the minor differences between the two formulations was also illustrated through the requirement of demonstrating safe, effective and correct consumer usage of Prilosec OTC tablets, bearing a “Prilosec” name, in an OTC setting. In its response to the Andrx Citizen Petition, the Agency noted that this was achieved through five actual use studies and five label comprehension studies.²

² CDER Memorandum, June 20, 2003, Dr. Charles Ganley’s Response to Andrx’s Citizen Petition.



III. IT WOULD BE ARBITRARY FOR THE AGENCY TO DENY THE USE OF THE NAME “PRILOSEC OTC”

It is arbitrary to treat similar situations differently. The use of the same tradename for acids or bases and their salts is common in both the Rx and OTC settings, and has been repeatedly approved by the Agency. The following are just a few examples:

Tradename	Acid or base	Salt
Proventil/Proventil HFA	Albuterol	Albuterol sulfate
Celestone	Betamethasone	Betamethasone sodium phosphate
Cefobid	Cefoperazone	Cefoperazone sodium (salt sold under ingredient name “cefoperazone”)
Thorazine	Chlorpromazine	Chlorpromazine hydrochloride
Tagamet	Cimetidine	Cimetidine hydrochloride
Vibramycin	Doxycycline	Doxycycline calcium Doxycycline hyclate
Edecrin	Ethacrynic acid	Ethacrynate sodium
Cytovene/Cytovene IV	Ganciclovir	Ganciclovir sodium
Haldol	Haloperidol	Haloperidol lactate
Bactroban	Mupirocin	Mupirocin calcium
Zofran/Zofran ODT	Ondansetron	Ondansetron HCL
Advil/Advil Migraine	Ibuprofen	Ibuprofen (free acid and potassium salt)
Children’s Benadryl	N/A	Diphenhydramine HCL Diphenhydramine citrate

The list could be readily expanded.

Within the heartburn remedy category, the Agency has allowed the use of the Rx brand name in every Rx-to-OTC switch. This is true even though almost every previous switch did not switch an Rx strength product (unlike with Prilosec OTC), and even though the Rx and OTC indications are different.

The relevant heartburn products and names are:

Rx Tradename	OTC Tradename
Pepcid	Pepcid AC, Pepcid Complete, Maximum Strength Pepcid AC
Tagamet	Tagamet HB 200
Zantac	Zantac 75
Axid	Axid AR



Thus, if the Mattingly petition were granted, Prilosec OTC would be the only branded OTC acid reducer not sold under a variant of the Rx product's tradename.

There is no evidence that the coexistence of all these products under the same root brand names (in some cases for nearly a decade) has caused any consumer harm or confusion.

IV. IT WOULD BE CAPRICIOUS FOR THE AGENCY TO REVOKE THE USE OF THE NAME "PRILOSEC OTC"

Omeprazole magnesium tablets were chosen for Prilosec OTC because the tablet form is consumer-preferred; the base ingredient in capsule form could have been more easily switched. There was no notice, throughout a regulatory review that included two advisory committee hearings, that use of the tablet form of magnesium salt would affect use of the word "Prilosec" in the product name. To deprive the sponsor of that use, after reliance on the Agency's decision, and subsequent very significant investment in the name, would be inequitable and capricious, particularly where, as here, the case for this unprecedented step rests on little more than irrelevant legalism.

More significantly, massive consumer confusion would result from the forced renaming of what is now the best selling OTC heartburn remedy. The high consumer satisfaction with the product shows that the consumer harms asserted by Mylan simply don't exist. No basis exists for forcing consumers to search out a renamed brand, or for forcing a product marketer to establish a new brand name over a year after a significant product launch.

Prilosec OTC is a version of Prilosec. Nothing in the Mattingly petition or Mylan's comments shows otherwise. The Mattingly petition should and must be denied.

Respectfully submitted,

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cc: Dr. Janet Woodcock
Jane Axelrad, Esq.
Dr. Charles Ganley