



NDA 21-042/S-007, S-008, S-010, S-012, S-013, S-014
NDA 21-052/S-004, S-005, S-006, S-007, S-008, S-009

Merck & Co., Inc.
Ned Braunstein, M.D.,
Director, Regulatory Affairs
P.O. Box 2000
RY 33-720
Rahway, NJ 07065

Dear Dr. Silverman:

Please refer to your supplemental new drug applications:

NDA 21-042/S-007 dated June 29, 2000 received June 29, 2000;
S-008 dated July 10, 2000, received July 11, 2000;
S-010 dated September 29, 2000, received October 02, 2000;
S-012 dated February 28, 2001 received March 01, 2001;
S-013 dated April 05, 2001, received April 05, 2001, and
S-014 dated October 02, 2001, received October 03, 2001;

NDA 21-052/S-004 dated June 29, 2000 received June 29, 2000;
S-005 dated July 10, 2000, received July 11, 2000;
S-006 dated September 29, 2000, received October 02, 2000;
S-007 dated February 28, 2001 received March 01, 2001;
S-008 dated April 05, 2001, received April 05, 2001, and
S-009 dated October 02, 2001, received October 03, 2001,

submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Vioxx (rofecoxib tablets) Tablets 12.5 mg, 25 mg, 50 mg and Vioxx (rofecoxib suspension) Suspension 12.5 mg/5 mL, 25 mg/5 mL, respectively.

We acknowledge receipt of your submissions for NDA 21-042/S-007 dated October 6, 13, and 27; November 13; December 5, 6, 18, 20 (2), and 21, 2000; January 12 (2), 13 (2), 15, 17, 19 (3), 20, 23, 25 (2), 29, and 30 (3); February 1, 2 (2), 5, 6, 7, 15, 16 (2) 21, 23, 27 (2), and 28; March 2, 8, 13, 15 (2), 16, 22, and 30; April 13, 16, and 30; May 16, 21, and 25; June 12, 14, 19, 22, and 29; July 9, 12, 26, 27, and 30; August 3, and 17; October 1, 3, 5, and 8; November 5, 6, 9, 16, and 26; December 5 (2), and 18, 2001; January 7, 17, and 21; February 5, 19 (2), and 25; March 5, 21 (2), 22, and 29; April 2, and 3, 2002 .

We acknowledge receipt of your submissions for NDA 21-042/S-012 dated March 23; April 30; May 04, and 16; June 22, 27 (2); July 20, and 27; August 13; September 20, and 21; October 11; November 09, December 5, and 21, 2001; and April 3, 2002.

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We acknowledge receipt of your submissions for NDA 21-052/S-004 dated October 6, and 13; March 2, and 21; April 13; May 21; October 11; November 06; December 05, 2001; January 7, 17, and 21; February 5, and 19; March 21; and April 3, 2002.

We acknowledge receipt of your submissions for NDA 21-052/S-007 dated March 23; June 27, 2001; January 4; and April 3, 2002.

Your submission of April 03, 2002 constituted a complete response to our January 11, 2002 action letter.

These supplemental new drug applications provide for the use of Vioxx (rofecoxib) Tablets 12.5 mg, 25 mg, Vioxx (rofecoxib) Suspension 12.5 mg/5 mL, 25 mg/5 mL:

NDA 21-042/S-007 and NDA 21-052/S-004 provide for proposed labeling changes in the Clinical Pharmacology, Clinical Studies, Warnings, Precautions, and Adverse Reactions sections;
NDA 21-042/S-008 and NDA 21-052/S-005 provide for changes in the Clinical Pharmacology and Precautions section to include pharmacokinetic data in patients with moderate hepatic insufficiency, drug interaction with theophylline, drug interaction with methotrexate;
NDA 21-042/S-010 and NDA 21-052/S-006 provide for inclusion of post-marketing adverse reactions and post-marketing experience of concurrent administration of clinical doses of Vioxx with lithium;
NDA 21-042/S-012 and NDA 21-052/S-007 provide for indication of rheumatoid arthritis;
NDA 21-042/S-013 and NDA 21-052/S-008 provide for post-marketing adverse reactions and post-marketing experience of hypersensitivity vasculitis and hyperkalemia; and
NDA 21-42/S-014 and NDA 21-052/S-009 provide for post-marketing adverse reactions and post-marketing experience of hepatic failure, bronchospasm, toxic epidermal necrolysis, and anaphylactic reaction.

We have completed the review of these supplemental applications, as amended, and have concluded that adequate information has been presented to demonstrate that the drug products are safe and effective for use as recommended in the agreed upon enclosed labeling text. Accordingly, these supplemental applications are approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert).

Please submit the copies of final printed labeling (FPL) electronically to each application according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, these submissions should be designated "FPL for approved supplement NDA 21-042/S-007, S-008, S-010, S-012, S-013, S-014, 21-052/S-004, S-005, S-006, S-007, S-008, S-009." Approval of these submissions by FDA is not required before the labeling is used.

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 *FR* 66632). We note that you have not fulfilled the requirements of 21 CFR 314.55 (or

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601.27); however we acknowledge your Pediatric Written Request issued on December 06, 2001 for pediatric studies to be submitted on or before December 31, 2003.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Barbara Gould, Project Manager, at (301) 827-2090.

Sincerely,

{See appended electronic signature page}

Lawrence Goldkind, M.D.
Deputy Division Director
Division of Anti-Inflammatory, Analgesic and
Ophthalmic Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

Enclosure

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Lawrence Goldkind
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