CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

21-042 / S-016  
21-052 / S-010

Trade Name: Vioxx  
Generic Name: Rofecoxib  
Sponsor: Merck & Co  
Approval Date: June 25, 2002
## Reviews / Information Included in this NDA Review.

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
21-042 / S-016
21-052 / S-010

APPROVAL LETTER
NDA 21-042/S-016
NDA 21-052/S-010

Merck & Co., Inc.
Attention: Ned S. Braunstein, M.D.
Director, Regulatory Affairs
PO Box 2000, RY33-720
Rahway, NJ 07065-0900

Dear Dr. Braunstein:

Please refer to your supplemental new drug applications dated January 15, 2002, received January 16, 2002, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Vioxx (rofecoxib) tablet, 12.5 mg/25 mg/50mg (NDA 21-042) and oral suspension, 12.5 mg/5 ml, 25 mg/5/ml (NDA 21-052).

These supplemental new drug applications provide the addition of Merck's or the manufacture of rofecoxib active drug substance for U.S. market.

We have completed the review of these supplemental applications, and they are approved.

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 Jane A. Dean, RN, MSN, Regulatory Health Project Manager, at 301-827-2090.

Sincerely,

[See appended electronic signature page]

John Smith, Ph.D.
Chemistry Team Leader for the
Division of Anti-Inflammatory, Analgesic and Ophthalmic Drug Products, (HFD-550)
DNDC III, Office of New Drug Chemistry
Center for Drug Evaluation and Research
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/
-----------------------
John Smith
6/25/02 03:17:52 PM
APPLICATION NUMBER:
21-042 / S-016
21-052 / S-010

CHEMISTRY REVIEW(S)
Chemistry Review #1

1. Division, HFD-550 2. NDA 21-042 & 21-052

3. Name and Address of Applicant
   Merck & Co. Inc., Summitytown Pike,
   P O. Box 4, BLA-20,
   West Point PA 19486

4. Supplement Number: SCM-016 (21-042)
   SCM-010 (21-052)

   Letter Date 1-14-02  Stamp Date 1-15-02  Due Date 5-15-02, primary


7. Supplement Provides for:
   To add __________________________ for manufacture of rofecoxib active drug substance for the US market.

8. Amendment(s): None


12. Dosage Form: Tablets (21-042)
    Suspension (21-052)

13. Potency(ies), 12.5, 25 & 50 mg (21-042)
    12.5 mg and 25 mg per 5 mL (21-052)

14. Chemical Name and Structure: See USAN

15. Supporting Document: NA

16. Comments:
   There are no changes in the methods of manufacture of the drug substance. The only difference is the batch size, _______.

   The approved tests and acceptance criteria, which are currently used in ______, will continue to be used in this ______.

   ______. Test results for batches manufactured at the two sites are comparable.

   Merck is requesting a categorical exclusion from the requirements to prepare an Environmental Assessment under 21 CFR §25.31(a). The supplement meets the requirements of a categorical exclusion under 21 CFR §25.31(a) because it will not increase the use of the drug. To the best of the firm’s knowledge no extraordinary circumstances exist in regards to this action.

   The Merck’s facility at ______ has been inspected by the compliance and was found acceptable.

   A copy of the EER is attached at the end of this review.

17. Conclusions and Recommendations: Recommend Approve

18. Name: Signature: Date

   Review Chemist: Bart Ho 06/28/02

   Team Leader: John Smith
3 Page(s) Withheld

✓ Trade Secret / Confidential

Draft Labeling

Deliberative Process
Application: NDA 21042/016
Stamp: 15-JAN-2002  Regulatory Due: 15-MAY-2002
District Goal: 10-APR-2002
Brand Name: VIOXX (ROFECOXIB) 12.5/25MG TABLETS
Applicant: MERCK RES
SUMNEYTOWN PIKE BLA 20
WEST POINT, PA 194860004

Priority: 1P
Org Code: 550

Established Name: ROFECOXIB
Generic Name: TAB (TABLET)
Dosage Form: 12.5 & 25 MG
Strength: 301-827-2090, Project Manager
B. GOULD (HFD-550)
B. HO (HFD-550)
J. SMITH (HFD-550)
301-827-2050, Review Chemist
301-827-2529, Team Leader

Overall Recommendation: ACCEPTABLE on 13-JUN-2002 by S. ADAMS (HFD-324)301-594-0095

Establishment ( )

DMF No: OAI Status: NONE
Profile: CSN
Responsibilities: ( )
Last Milestone: OC RECOMMENDATION
Milestone Date: 13-JUN-2002
Decision: ACCEPTABLE
Reason: DISTRICT RECOMMENDATION
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Bartholomew Ho
6/28/02 01:18:36 PM
CHEMIST

John Smith
6/28/02 01:41:11 PM
CHEMIST
Approval letter was signed on 6/25/02.
CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
21-042 / S-016
21-052 / S-010

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS
NDA 21-042/S-016
NDA 21-052/S-010

PRIOR APPROVAL SUPPLEMENT

Merck & Co., Inc.
Attention: Robert E. Silverman, M.D., Ph.D.
Senior Director, Regulatory Affairs
Sunnystown Pike
P.O. Box 4, BLA-20
West Point, PA 19486

Dear Dr. Silverman:

We have received your supplemental drug applications submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

<table>
<thead>
<tr>
<th>NDA Number</th>
<th>Supplement Number</th>
<th>Drug Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>21-042</td>
<td>S-016</td>
<td>VioxxTM (rofecoxib) Tablets 12.5 mg, 25 mg, 50 mg</td>
</tr>
<tr>
<td>21-052</td>
<td>S-010</td>
<td>VioxxTM (rofecoxib) Tablets 12.5 mg/5 mL, 25 mg/5 mL</td>
</tr>
</tbody>
</table>

Date of Supplements: January 14, 2002

Date of Receipt: January 15, 2002

These supplements propose the addition of a dose of rofecoxib.

Unless we notify you within 60 days of our receipt date that the applications are not sufficiently complete to permit a substantive review, these applications will be filed under section 505(b) of the Act on March 15, 2002 in accordance with 21 CFR 314.101(a). If the applications are filed, the primary user fee goal date will be May 15, 2002 and the secondary user fee goal date will be July 15, 2002.

Please cite the application numbers listed above at the top of the first page of any communications concerning these applications. All communications concerning these supplemental applications should be addressed as follows:
U.S. Postal Service:  
Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Anti-Inflammatory, Analgesic and Ophthalmic Drug Products, HFD-550  
Attention: Division Document Room  
HFD-550  
5600 Fishers Lane  
Rockville, Maryland 20857

Courier/Overnight Mail:  
Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Anti-Inflammatory, Analgesic and Ophthalmic Drug Products, HFD-550  
Attention: Division Document Room  
HFD-550  
9201 Corporate Blvd.  
Rockville, Maryland 20850-3202

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

Sincerely,

{See appended electronic signature page}

Carmen DeBellas, R.Ph.  
Chief, Project Management Staff  
Division of Anti-Inflammatory, Analgesic and Ophthalmic Drug Products  
Office of Drug Evaluation V  
Center for Drug Evaluation and Research
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/
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Barbara Gould
2/28/02 05:28:41 PM
for Carmen DeBellas