

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20-998

CORRESPONDENCE

SEARLE

October 16, 1998

SEARLE
4901 SEARLE PARKWAY
SKOKIE, ILLINOIS 60077
PHONE (847) 982-7000
FAX (847) 982 4701

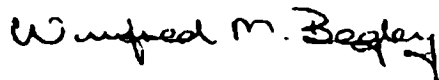
Robert DeLap, M.D., Ph.D., Acting Director
Division of Anti-Inflammatory, Analgesic,
and Ophthalmologic Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research (HFD-550)
9201 Corporate Boulevard
Rockville, Maryland 20850

RE: NDA 20-998
Celebrex™ (celecoxib)

Dear Dr. DeLap:

This is to advise that we have decided to adopt the tradename Celebrex™ in place of Celebra™ as a consequence of the finding of the Labeling and Nomenclature Committee that there is a possibility of aural and written confusion with the approved product Celexa. Our future correspondence will therefore refer to Celebrex™ which has been approved for use by the LNC.

Sincerely,



Winifred M. Begley
Director, Regulatory Affairs
(847) 982-8155
(847) 982-8090 Fax

WMB/pl

HFD-558 Lutwak



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-998

SEP 24 1998

G.D. Searle & Co.
Attention: Winifred M. Begley
Director, Regulatory Affairs
4901 Searle Parkway
Skokie, Illinois 60077

Dear Ms. Begley:

Please refer to your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: Tradename (celecoxib capsules)
Therapeutic Classification: Priority (P)
Date of Application: June 29, 1998
Date of Receipt: June 30, 1998
Our Reference Number: 20-998

Please also refer to our acknowledgment letter dated August 20, 1998. The reference to Subpart H was not applicable to this application.

This application was filed under section 505(b) of the Act on August 29, 1998, in accordance with 21 CFR 314.101(a). The user fee goal date is December 31, 1998.

This letter supersedes the previous acknowledgment letter dated August 20, 1998. If you have any questions, contact Victoria Lutwak at (301) 827-2090.

Sincerely,

Chin Koerner ^{OCK}
9/24/98

Chin Koerner, M.S.
Project Manager
Division of Anti-Inflammatory, Analgesic and
Ophthalmic Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

NDA 20-998

Page 2

cc:

Archival NDA 20-998

HFD-550/Div. Files

HFD-550/Lutwakv

DISTRICT OFFICE

filename:ack8.925

ACKNOWLEDGMENT (AC)

SEARLE

June 29, 1998

SEARLE
4901 SEARLE PARKWAY
SKOKIE, ILLINOIS 60077
PHONE (847) 982-7000
FAX (847) 982-4701

Robert DeLap M.D., Ph.D., Deputy Director,
Division of Anti-inflammatory, Analgesic,
and Ophthalmologic Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research (HFD-550)
9201 Corporate Boulevard
Rockville, MD 20850

Re: NDA 20-998
Celebra™ (celecoxib)

Dear Dr. DeLap,

Pursuant to 21 CFR 314.50, we are submitting a New Drug Application for Celebra™ (celecoxib) capsules and we are requesting a Priority Review.

The proposed indications include:

Acute or chronic use in the treatment of the signs and symptoms of osteoarthritis and rheumatoid arthritis; and

Management of pain

Reference is made to Manual of Policies and Procedures (MAPP) 6020.3, entitled Priority Review Policy. A priority review classification is based upon whether "the drug if approved would be a significant improvement compared to marketed products in the treatment, diagnosis and prevention of a disease. Improvement can be demonstrated by, for example: (1) evidence of increased effectiveness in treatment, prevention, or diagnosis of disease; (2) elimination or substantial reduction of a treatment-limiting drug reaction; (3) documented enhancement of patient compliance; or (4) evidence of safety and effectiveness in a new sub-population." Our data presented in this NDA justify the Priority classification referenced in item (2) above, and we hereby request a priority review classification.

Celecoxib selectively inhibits cyclooxygenase-2 (COX-2), the inducible form of the enzyme cyclooxygenase (COX). The ability to selectively inhibit COX-2 serves the basis for the therapeutic efficacy of celecoxib, and importantly, provides clinically important mechanism-based safety characteristics that significantly distinguish it from currently available non-selective COX inhibitors. The combination of substantial efficacy comparable to the class of non-steroidal anti-inflammatory drugs (NSAIDs), with a superior safety profile endows celecoxib with a superior benefit/risk profile compared to available anti-inflammatory therapies for the pain and the signs and symptoms of arthritis.

Division of Anti-Inflammatory, Analgesic
and Ophthalmologic Drug Products
NDA 20-998, Celebra™ (celecoxib)
June 29, 1998
Page 3

Should you have any questions regarding the content of the NDA, please contact the undersigned at (847) 982-8155 or (847) 982-8090 (FAX).

Sincerely,



Winifred M. Begley
Director
Regulatory Affairs

Enclosures
WMB/tb

References and location within the NDA:

1. N49-98-07-807; Vol 1.3:p203
2. N49-98-06-021; Vol. 1.183:p155-169
3. N49-98-06-022; Vol. 1.284:p162-183
4. N49-98-06-062; Vol. 1.251:p60-78
5. N49-98-06-071; Vol. 1.240:p62-83
6. ISS; Vol. 1.425: p150
7. ISS Text Table 88; Vol. 1.425: p146
8. N49-98-06-021; Vol. 1.183:p52
9. N49-98-06-022; Vol. 1.284:p51
10. N49-98-06-062; Vol. 1.251:p39
11. N49-98-06-071; Vol. 1.240: p42
12. ISS Table 31.1.3; Vol. 1.428:p348
13. N49-98-06-021; Vol. 1.183: p24
14. N49-98-06-022; Vol. 1.284: p25
15. N49-98-06-062; Vol. 1.251: p22
16. N49-98-06-071; Vol. 1.240: p22
17. ISS Figure 5; Vol.; 1.425: p158
18. ISS Text Table 220; Vol. 1.425:p378
19. ISS Table 11.1; Vol 1.427:p1
20. N49-97-06-012; Vol. 1.334: p36
21. N49-97-16-013; Vol. 1.235: p29
22. N49-98-06-020; Vol. 1.150: p47
23. N49-98-06-021; Vol. 1.183: p52
24. N49-98-06-022; Vol. 1.284:p51
25. N49-98-06-023; Vol. 1.258: p42
26. I49-98-06-041; Vol. 1.311: p43
27. I49-98-06-042; Vol. 1.225: p37
28. N49-97-06-047; Vol. 1.218: p40
29. N49-98-06-054; Vol. 1.167: p45
30. N49-98-06-060; Vol. 1.203: p39
31. N39-98-06-062; Vol. 1.251: p39
32. N49-98-06-071; Vol. 1.240: p42
33. N49-98-06-087; Vol. 1.211: p36
34. ISS Text Table 220; Vol. 1.425: p378, 160-173

SEARLE

June 29, 1998

SEARLE
4900 SEARLE PARKWAY
SKOKIE, ILLINOIS 60077
PHONE (847) 982-7000
FAX (847) 982-4701

Food and Drug Administration
Office of Regulatory Affairs
San Juan District
466 Fernandez Juncos Avenue
San Juan, PR 00901-3223

RE: NDA 20-998
Celebra™ (celecoxib)

Gentlemen:

In accordance with 21 CFR 314.50(k)(3), included in this submission is the Field Copy of the New Drug Application for Celebra™ (NDA 20-998). Per the CFR, a copy of the NDA application form and application summary are also provided.

The full New Drug Application was submitted to the Division of Anti-inflammatory, Analgesic, and Ophthalmologic Drug Products on June 29, 1998. A certification that this Field Copy is a true copy of technical sections contained in the original NDA is also attached.

If you require further information, please contact the undersigned directly.

Sincerely,

Winifred M. Begley
Winifred M. Begley
Director
Regulatory Affairs
(847) 982-8155
(847) 982-8090 FAX

bj/enclosures
Vols. 1.1 through 1.7

SEARLE

NDA MASTER FILE

July 6, 1998

SEARLE
4901 SEARLE PARKWAY
SKOKIE, ILLINOIS 60077
PHONE (847) 982-7000
FAX (847) 982-1701

Ms. Chin Koerner, Consumer Safety Officer
Division of Anti-inflammatory, Analgesic,
and Ophthalmologic Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research (HFD-550)
9201 Corporate Boulevard
Rockville, MD 20850



Re: NDA 20-998
Celebra™ (celecoxib)

Dear Ms. Koerner:

Please could you confirm that the tradename Celebra™ is acceptable. We had initial feedback that it was acceptable prior to the submission of the NDA but you advised that until the NDA is submitted the decision was not final. Since the NDA has now been submitted we would appreciate a final decision on this matter.

If you have additional questions, please do not hesitate to contact me.

Sincerely,

Winifred M. Begley

Winifred M. Begley
Director,
Regulatory Affairs
(847) 982-8155
(847) 982-8090 (fax)

WMB/tb

4/6
the
chrono

SEARLE

July 7, 1998

SEARLE
4001 SEARLE PARKWAY
SKOKIE, ILLINOIS 60077
PHONE (847) 982-7000
FAX (847) 982-2701

Robert DeLap M.D., Ph.D., Deputy Director
Division of Anti-inflammatory, Analgesic,
and Ophthalmologic Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research (HFD-550)
9201 Corporate Boulevard
Rockville, MD 20850

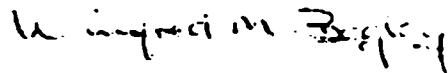
Re: NDA 20-998
Celebra™ (celecoxib)

Dear Dr. DeLap,

Enclosed is a resubmission of tapes sent June 29, 1998 to replace a tape which was missing full text indexing of the NDA (tape 1 of 1 - labeled "COMPLETE NDA - ELECTRONIC REVIEW). None of the contents of the submission have been changed.

Should you have any questions or concerns regarding this submission, please contact the undersigned.

Sincerely,



Winifred M. Begley
Director
Regulatory Affairs
(847) 982-8155
(847) 982-8090 (fax)

Enclosures
WMB/tb

SEARLE

NDA MASTER FILE

July 14, 1998

SEARLE
4901 SEARLE PARKWAY
SKOKIE, ILLINOIS 60077
PHONE (847) 982-7000
FAX (847) 982-4701

Ms. Chin Koerner, Consumer Safety Officer
Division of Anti-inflammatory, Analgesic,
and Ophthalmologic Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research (HFD-550)
9201 Corporate Boulevard
Rockville, MD 20850



Re: NDA 20-998
Celebra™ (celecoxib)

Dear Ms. Koerner:

In response to your question regarding resources to assist in supporting the electronic NDA 20-998 for Celebra™ please contact directly:

Joel Finkle

or back-up

Jan Gyzen

I will be out of the office July 20-27, in my absence questions regarding the organization of the NDA can be addressed by Pam Larsen or Barb Johnson Questions regarding data should be directed to Dr. Rich Spivey or as back-up Peter East

If you have any questions, please do not hesitate to contact me.

Sincerely,

A handwritten signature in black ink that reads "Winifred M. Begley".

Winifred M. Begley
Director,
Regulatory Affairs
(847) 982-8155
(847) 982-8090 (fax)

WMB/tb

SEARLE

July 16, 1998

SEARLE
4901 SEARLE PARKWAY
SKOKIE, ILLINOIS 60077
PHONE (847) 982-7000
FAX (847) 982-4701

Chin Koerner, CSO
Division of Anti-inflammatory, Analgesic,
and Ophthalmologic Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation & Research (HFD-550)
9201 Corporate Boulevard
Rockville, Maryland 20850

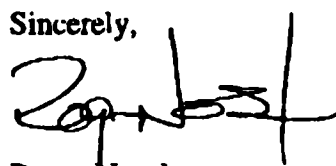
RE: NDA 20-998
Celebra™
(celecoxib)

Dear Ms. Koerner:

In response to your telephone request of 15-July-1998, enclosed is an updated NDA document entitled: "Establishment Description" for inclusion in the Celebra NDA 20-998. This document has been amended to include Central File Numbers for each establishment. This document replaces the version included in the original NDA application of 29-Jun-1998 (Volume 1.1, page 11).

If you have any questions concerning this information, please contact the undersigned.

Sincerely,



Roger Nosal
Director,
CMC Regulatory Affairs
(847) 982-7250
(847) 982-8961

Enc.
RN/pl

SEARLE

July 21, 1998

SEARLE
4901 SEARLE PARKWAY
SKOKIE, ILLINOIS 60077
PHONE (847) 982-7000
FAX (847) 982-4701

Robert DeLap, M.D., Ph.D., Deputy Director
Division of Anti-inflammatory, Analgesic,
and Ophthalmologic Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research (HFD-550)
9201 Corporate Boulevard
Rockville, MD 20850

Re: NDA 20-998
Celebra™ (celecoxib)

Dear Dr. DeLap,

As requested by Chin Koerner (CSO, Division of Anti-inflammatory) on 15 July 1998, we are providing the NONMEM data files and control streams for the analyses for the population PK, document N49-98-07-824 and the population PK/PD, document N49-98-07-826.

Sincerely,

Winifred M. Begley

Winifred M. Begley
Director,
Regulatory Affairs
(847) 982-8155
(847) 982-8090 (fax)

WMB/bj
attachment

cc: desk copy to Ms. C. Koerner, CSO, Division of Anti-inflammatory, Analgesic and
Ophthalmologic Drug Products

SEARLE

NC
NEW CORRESP
ORIGINAL

July 22, 1998

SEARLE
4901 SEARLE PARKWAY
SKOKIE, ILLINOIS 60077
PHONE (847) 982-7000
FAX (847) 982-4701

Chin Koerner, Consumer Safety Officer
Division of Anti-inflammatory, Analgesic
and Ophthalmologic Drug Products (HFD-550)
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Blvd.
Rockville, MD 20850



Re: NDA 20-998
Celebra™ (celecoxib)

Dear Ms. Koerner :

As discussed in our joint teleconference today, Dr. Witter identified a problem with the patient count in Table 46 of celecoxib study No. I49-96-02-041 (Report No. I49-98-06-041). As indicated during our discussion, this mis-count was the result of a programming error which also affected two other studies - N49-96-02-021 and N49-96-02-022.

As a temporary measure, enclosed are copies of the corrected tables for the three affected studies:

Report I49-98-06-041	Table 46
Report N49-98-06-021	Table 47
Report N49-98-02-022	Table 45

We will submit to the NDA revised, corrected pages for the reports as soon as they are completed.

Sincerely,

Peter F. East
Associate Director,
Regulatory Affairs
Tel: (847) 982-8606
Fax: (847) 982-8152

Master

SEARLE

July 30, 1998

SEARLE
4901 SEARLE PARKWAY
SKOKIE, ILLINOIS 60077
PHONE (847) 987 7000
FAX (847) 987-4701

Robert DeLap, M.D., Ph.D., Deputy Director
Division of Anti-inflammatory, Analgesic, and
Ophthalmologic Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research (HFD-550)
9201 Corporate Boulevard
Rockville, MD 20850

Re: NDA 20-998
Celebra™ (celecoxib)

Dear Dr. DeLap:

Per request, enclosed are Endoscopy Data Location sheets to aid Dr. L. Goldkind in his review of the Celecoxib GI Studies (N49-98-06-021, N49-98-06-071, N49-98-06-062, N49-98-06-022 and I49-98-06-041).

Copies of these were faxed to Dr. Goldkind as well as Vicky Lutwak/Chin Koerner on the 30-Jul-1998.

Please contact the undersigned with any questions concerning this submission.

Sincerely,

Winifred M. Begley

Winifred M. Begley
Director
Regulatory Affairs

Enclosures

WMB:pl

SEARLE

Master

July 30, 1998

SEARLE
4901 SEARLE PARKWAY
SKOKIE, ILLINOIS 60077
PHONE (847) 982-7000
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Robert DeLap, M.D., Ph.D., Deputy Director
Division of Anti-inflammatory, Analgesic, and
Ophthalmologic Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research (HFD-550)
9201 Corporate Boulevard
Rockville, MD 20850

Re: NDA 20-998
Celebra™ (celecoxib)

Dear Dr. DeLap:

Enclosed are revised Section Indices, as follows: Section 6 - Human Pharmacokinetics and Section 8 - Clinical Data for the Celebra NDA 20-998. These Indices have been revised to include volume/page locations of study report appendices. This request was made by Chin Koerner of the Division on 24-July-1998.

Please replace the enclosed Indices in the NDA, as follows:

Section 6 - Volume 1.81 ; pages 1-58
Section 8 - Volume 1.129 ; pages 1-14

Copies of these Indices were faxed to Vicky Lutwak/Chin Koerner on the 28/29-Jul-1998. Please disregard the faxed copies as corrections have since been made to these Indices.

Please contact the undersigned with any questions concerning this submission.

Sincerely,

Winifred M. Begley

Winifred M. Begley
Director
Regulatory Affairs

Enclosures

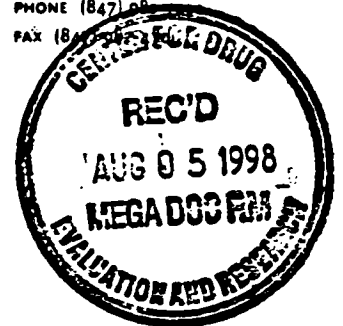
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SEARLE

August 4, 1998

Ms. Chin Koerner, Consumer Safety Officer
Division of Anti-inflammatory, Analgesic,
and Ophthalmologic Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research (HFD-550)
9201 Corporate Boulevard
Rockville, MD 20850

NC
NEW CORRESP
DUPLICATE
SEARLE
4901 SEARLE PARKWAY
SKOKIE, ILLINOIS 60077
PHONE (847) 982-8155
FAX (847) 982-8090



Re: NDA 20-998
Celebra™ (celecoxib)

Dear Ms. Koerner:

Enclosed you will find revised pages for NDA 20-998. These pages contain copies of corrected tables for three studies, as discussed in a joint teleconference on July 22, 1998 (see submission to NDA 20-998 of that same date). The correction was made due to an error in the programming of the tables and the corrected data do not alter the original interpretation of the results.

<u>Report Number:</u>	<u>NDA 20-998 Volume Number:</u>	<u>Revised Page Numbers:</u>
I49-98-06-041	1.311	page 253-254
N49-98-06-021	1.183	page 293-294
N49-98-06-022	1.284	page 294-295

If you have additional questions, please do not hesitate to contact me.

Sincerely,

Winifred M. Begley

Winifred M. Begley
Director,
Regulatory Affairs
(847) 982-8155
(847) 982-8090 (fax)

WMB/bj

SEARLE

NC
ORIGINAL

August 7, 1998

SEARLE
4901 SEARLE PARKWAY
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Chin Koerner, CSO
Division of Anti-Inflammatory, Analgesic
and Ophthalmologic Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research (HFD-550)
9201 Corporate Blvd.
Rockville, MD 20850

RE: NDA 20-998
Celebra™ (celecoxib)
Correspondence

Dear Ms. Koerner,

With reference to the request from Dr. Talarico for data listings of individual patients in the platelet aggregation studies I have enclosed a cross-reference to the volume and page numbers in the NDA where the patient listings can be found. In addition I have provided individual patient plots for each of the studies.

Please contact me if you have any questions regarding this information.

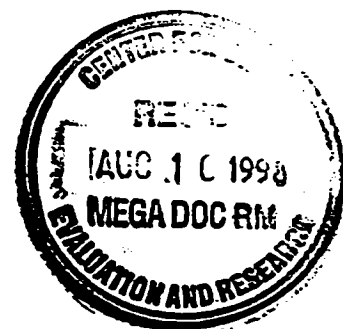
Sincerely,

Winifred M. Begley

Winifred M. Begley, Director
Worldwide Regulatory Affairs

WMB:vr

Fax copy to: Dr. D. Throckmorton



SEARLE

NDA MASTER FILE

SEARLE
4901 SEARLE PARKWAY
SKOKIE, ILLINOIS 60077
PHONE (847) 982-7000
FAX (847) 982-4701

GENERAL CORRESPONDENCE

August 7, 1998

Dr. Douglas C. Throckmorton, M.D.
Division of Cardio-Renal Drug Products
1451 Rockville Pike (HFD-110)
Rockville, Maryland 20852

RE: NDA 20-998
Celebra™



Dear Dr. Throckmorton,

To confirm our conversation of August 5, 1998, we have checked the clinical studies in our NDA 20-998 and can confirm that there are no studies which tested for bicarbonate either by determination or in serum.

Sincerely,

Winifred M. Begley
Winifred M. Begley
Director, Regulatory Affairs

cc: Ms. C. Koerner

WMB/iw

SEARLE

August 17, 1998

SEARLE
 4901 SEARLE PARKWAY
 SKOKIE, ILLINOIS 60077
 PHONE (847) 982-7000
 FAX (847) 982-4701

Robert DeLap, M.D., Ph.D., Deputy Director
 Division of Anti-inflammatory, Analgesic,
 and Ophthalmologic Drug Products
 Office of Drug Evaluation V
 Center for Drug Evaluation and Research (HFD-550)
 9201 Corporate Boulevard
 Rockville, MD 20850

Re: **NDA 20-998**
Celebra™ (celecoxib)
Minor Clinical Amendment

Dear Dr. DeLap,

Per a request from Dr. L. Goldkind we are providing individual patient endoscopy CRFs and patient's endoscopy reports. Per my discussion with Ms. Koerner, we were requested to submit this information as a Minor Clinical Amendment which would not affect the review clock. The initial request from Dr. Goldkind was just for the individual patient endoscopy reports for which we had estimated about 40 volumes. However in a subsequent conversation with Dr. Goldkind on August 7, 1998 he also requested the endoscopy CRFs, this additional request has increased the volume number to 97 (see below):

<u>Volume Number:</u>	<u>Content:</u>
2.1	Cover letter, master index
2.2-2.22	Endoscopy CRFs and reports study N49-98-06-021
2.23-2.56	Endoscopy CRFs and reports study N49-98-06-071
2.57-2.72	Endoscopy CRFs and reports study N49-98-06-062
2.73-2.91	Endoscopy CRFs and reports study N49-98-06-022
2.92-2.96	Endoscopy CRFs and reports study I49-98-06-041
2.97	Endoscopy CRFs study I49-97-16-014

The master index contains a listing of all the above by investigator within a study, with a cross-reference to the volume and page number where each patient's information can be found. The index also has an asterisk by each patient that withdrew for any reason.

NDA 20-998, Celebra™ (celecoxib)
August 17, 1998
Page 2 of 2

The above information is being provided as one archival copy and one desk copy to Dr. Goldkind. Dr. Goldkind was advised of the size of the submission August 13, 1998.

Sincerely,

Winifred M. Begley
Director,
Regulatory Affairs
(847) 982-8155
(847) 982-8090 (fax)

WMB/bj
attachment

cc: Dr. Goldkind, Division of GI/Coagulation Drug Products

SEARLE

August 24, 1998

ORIGINAL

SEARLE
4901 SEARLE PARKWAY
SKOKIE, ILLINOIS 60077
PHONE (847) 982-7000
FAX (847) 982-4701

Robert DeLap, M.D., Ph.D., Deputy Director
Division of Anti-inflammatory, Analgesic,
and Ophthalmologic Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research (HFD-550)
9201 Corporate Boulevard
Rockville, MD 20850

ORIG AMENDMENT

BE

RE: NDA 20-998
Celebra™ (celecoxib)

Dear Dr. DeLap:

Enclosed are clarification responses to 3 questions posed by the PK reviewer. We have also provided supporting information for the responses to questions 1 and 2. Please contact me if you require any further clarification.

Sincerely,

Winifred M. Begley

Winifred M. Begley
Director,
Regulatory Affairs
(847) 982-8155
(847) 982-8090 Fax

Enc.
WB/pl



SEARLE

NEW CORRESP
NC

August 24, 1998

SEARLE
4901 SEARLE PARKWAY
SKOKIE, ILLINOIS 60077
PHONE (847) 982-7000
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Robert DeLap, M.D., Ph.D., Deputy Director
Division of Anti-inflammatory, Analgesic,
and Ophthalmologic Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research (HFD-550)
9201 Corporate Boulevard
Rockville, MD 20850

ORIGINAL

RE: NDA 20-998
Celebra™ (celecoxib)

Dear Dr. DeLap:

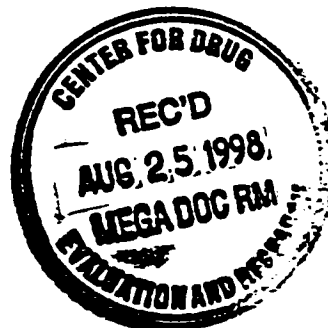
Enclosed are 2 sets of 3 CDROMs; one for the archival copy and one desk copy for Chin Koerner. A third set of the 3 CDROMs has been sent directly to Dr. L. Goldkind as a desk copy. These CDROMs are the electronic format of a minor clinical amendment (2.1) which was submitted August 17, 1998 containing individual patient endoscopy CRFs and endoscopy reports. Accompanying this letter is a Table of Contents for the electronic submission with a Description and File Name and also a document entitled Electronic Submission Installation Instructions.

If you have any questions regarding installation or navigation through the electronic files please contact Joel Finkle: 847-982-8010 (tel); 847-982-8973 (fax)

Sincerely,

Winifred M. Begley

Winifred M. Begley
Director,
Regulatory Affairs
(847) 982-8155
(847) 982-8090 Fax



Enc.
WB/pl

cc: Dr. L. Goldkind, Division of GI/Coagulation Drug Products

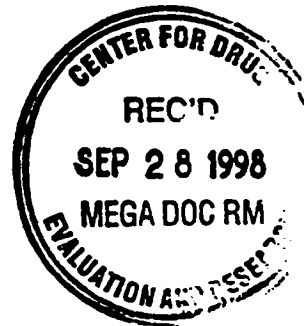
SEARLE

NDA MASTER FILE

August 27, 1998

SEARLE
4001 SEARLE PARKWAY
SKOKIE, ILLINOIS 60077
PHONE (847) 682-7000
FAX (847) 682-1700

Chin Koerner, Project Manager
Division of Anti-Inflammatory, Analgesic,
and Ophthalmologic Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research (HFD-550)
9201 Corporate Boulevard
Rockville, MD 20850



RE: NDA 20-998
Celebra™ (celecoxib)

Dear Ms. Koerner,

To confirm our telephone conversation today, calls to FDA concerning Compassionate Use of celecoxib should be referred to the Searle Healthcare Information Services toll-free number 1-800-323-4204. As discussed with you Searle do not have a Compassionate Use program with celecoxib, but patients can receive information about clinical trials that are ongoing with the drug when they call the above number.

Sincerely,

Winifred M. Begley
Winifred M. Begley
Director,
Regulatory Affairs
(847) 982-8155
(847) 982-8090 Fax

Enc.
WB/pl

September 3, 1998

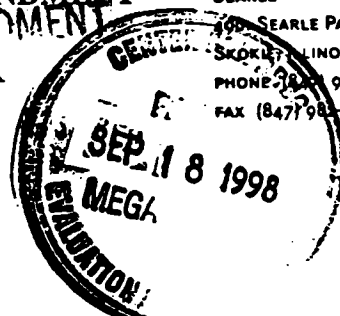
SEARLE
ORIGINAL

MINOR PHARMACOKINETIC AMENDMENT

NDA ORIG AMENDMENT

Robert DeLap, M.D., Ph.D., Deputy Director
Division of Anti-Inflammatory, Analgesic,
and Ophthalmologic Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research (HFD-550)
9201 Corporate Boulevard
Rockville, Maryland 20850

SEARLE
400 SEARLE PARKWAY
SKOKIE, ILLINOIS 60077
PHONE (847) 982-7000
FAX (847) 982-4701



RE: NDA 20-998
Celebra™ (celecoxib)

Dear Dr. DeLap:

With reference to the telephone conversation between Mr. Joel Finkle of Searle and Ms. Chin Koerner on 2-Sept-1998, we are providing the following:

Corrected Appendix 3 (dated 2-Sept-1998) for the report entitled, "Celecoxib Population Pharmacokinetic Modeling In Arthritis Patients", document number N49-98-07-824. The full report is located in Volume 1.103 of 1.452 of the initial NDA application of 29-Jun-1998.

Appendix 3.6 of this report inadvertently contained duplicate text from Appendix 3.4. The attached corrected Appendix has been paginated in the upper right-hand corner to reflect its location within the initial application.

In addition, 3 copies of a CD have been included in this submission: 1 for the Archive, 1 for Ms. Chin Koerner, 1 for Dr Li/PK Reviewer along with a diskette containing this appendix. Each CD is identical, and contains the following four files:

- NDATOC.PDF - Table of contents for the amendment
- README.PDF - Instructions for installation and use
- CPBIO-N4987824.PDF - Corrected Report in Acrobat Format
- CPBIO-N4987824.DOC - Corrected Report in MS Word Format

If you need further clarification please contact the undersigned.

Sincerely,

Winifred M. Begley *for*
Director, Regulatory Affairs
(847) 982-8155
(847) 982-8090 Fax

CC: Desk Copy: Dr. Li
Enc.

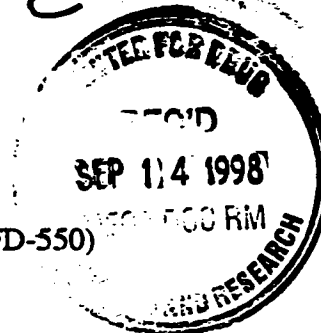
SEARLE

September 11, 1998

NEW CORRESPONDENCE

SEARLE
4901 SEARLE PARKWAY
SKOKIE, ILLINOIS 60077
PHONE (847) 982-7000
FAX (847) 982-4701

Robert DeLap, M.D., Ph.D., Deputy Director
Division of Anti-Inflammatory, Analgesic,
and Ophthalmologic Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research (HFD-550)
9201 Corporate Boulevard
Rockville, Maryland 20850



RE: NDA 20-998
Celebra™ (celecoxib)

Dear Dr. DeLap:

The correlation coefficients between WOMAC composite score and each of the three domain scores were calculated and are attached per FDA request.

The results showed highly correlated relationship of each domain score with the composite score across treatment groups and studies. In general, the correlation coefficient for stiffness score and composite averaged a little less than 0.8. For pain, it is around 0.9 and for physical function it approaches 1.

Please contact the undersigned if you require any further information.

Sincerely,

Winifred M. Begley

Winifred M. Begley
Director, Regulatory Affairs
(847) 982-8155
(847) 982-8090 Fax

Enc.
WB/pl

Desk Copy: Dr. Witter

SEARLE

September 17, 1998

Robert DeLap, M.D., Ph.D., Deputy Director
Division of Anti-Inflammatory, Analgesic,
and Ophthalmologic Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research (HFD-550)
9201 Corporate Boulevard
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SEARLE
4901 SEARLE PARKWAY
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RE: NDA 20-998
Celebra™ (celecoxib)

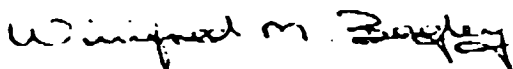
Dear Dr. DeLap:

Please find attached a table of medical history for patients in the long term open label trial -024 requested by Chin Koerner for Dr. Throckmorton September 9, 1998. (Attachment 1)

In our discussion with Dr. Throckmorton on September 14, 1998 he asked whether calcium had been included in the -024 study and our answer is that calcium has not, nor is currently, being done in this study.

In a telecon with Dr. Throckmorton on September 15, 1998 he asked for clarification as to why in Table 31.3.2 the renal ADRs did not tie up with Table 6.2 of the ISS with respect to peripheral edema, our response to this question is attached. (Attachment 2)

Sincerely,



Winifred M. Begley
Director, Regulatory Affairs
(847) 982-8155
(847) 982-8090 Fax

Enc.
WB/pl

CC: Desk Copy - D. Throckmorton

SEARLE

(resent DISKETTE)

September 17, 1998

ORIGINAL



Ms. Chin Koerner, Project Manager
 Division of Anti-Inflammatory, Analgesic,
 and Ophthalmologic Drug Products
 Office of Drug Evaluation V
 Center for Drug Evaluation and Research (HFD-550)
 9201 Corporate Boulevard
 Rockville, Maryland 20850

NEW CORRESP
 NC

RE: NDA 20-998
 Celebra™ (celecoxib)

Dear Ms. Koerner,

Enclosed is a diskette to decode the following files in study -020:

MASTRSAS.WHODIC
 MASTRSAS.SYSORG

The diskette and this letter have been sent to you only, if you need a copy for the NDA archival file please let me know.

Sincerely,

Winifred M. Begley

Winifred M. Begley
 Director, Regulatory Affairs
 (847) 982-8155
 (847) 982-8090 Fax

Enc.
 WB/pl

ORIGINAL

SEARLE

(C) BM

NEW CORRESP

September 17, 1998

SEARLE
4901 SEARLE PARKWAY
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PHONE (847) 982-7000
FAX (847) 982-4701

NC

Robert DeLap, M.D., Ph.D., Deputy Director
Division of Anti-Inflammatory, Analgesic,
and Ophthalmologic Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research (HFD-550)
9201 Corporate Boulevard
Rockville, Maryland 20850

RE: NDA 20-998
Celebra™ (celecoxib)

Dear Dr. DeLap:

Attached are the VAS scales graphed for studies -013, 042 and 047 as requested by
Chin Koerner September 14, 1998 for Dr. Witter.

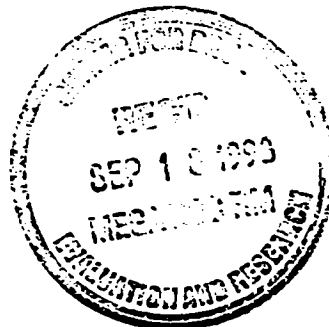
Sincerely,

Winifred M. Begley

Winifred M. Begley
Director, Regulatory Affairs
(847) 982-8155
(847) 982-8090 Fax

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WB/pl

CC: Desk Copy - Dr. Witter



SEARLE
ORIGINAL

BZ

September 18, 1998

NDA ORIG AMENDMENT

Robert DeLap, M.D., Ph.D., Deputy Director
Division of Anti-Inflammatory, Analgesic,
and Ophthalmologic Drug Products
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9201 Corporate Boulevard
Rockville, Maryland 20850

N/BZ

SEARLE
4901 SEARLE PARKWAY
SKOKIE, ILLINOIS 60077
PHONE (847) 982-7000
FAX (847)



RE: NDA 20-998
Celebra™ (celecoxib)

Dear Dr. DeLap:

In response to a request from Dr. L. Lu we have prepared on diskette and paper copy the tables of integrated results for studies -022 and -023 according to the template provided on September 14, 1998.

Please contact the undersigned if you have further questions.

Sincerely,

Winifred M. Begley
Winifred M. Begley for:
Director, Regulatory Affairs
(847) 982-8155
(847) 982-8090 Fax

Enc.
WB/pl