

# SEARLE

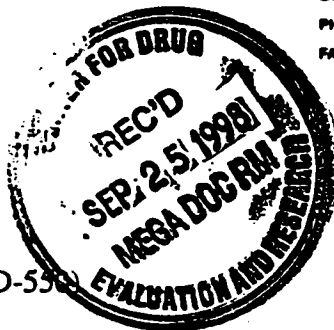
# ORIGINAL

NEW CORRESP

September 24, 1998

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

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



RE: NDA 20-998  
Celebra™ (celecoxib)

Dear Dr. DeLap:

Enclosed are the WOMAC pain subscale and pain domain correlations for studies -020, -021, and -054 requested by Dr. Witter. Per a conversation with Ms. Koerner we were advised that these were not needed for studies -060 and -087.

Sincerely,

*Winifred M. Begley*

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

Enc.

WMB/pl

CC: Desk Copy - Dr. Witter/Division of Cardio-Renal

**SEARLE**

ORIG AMENDMENT

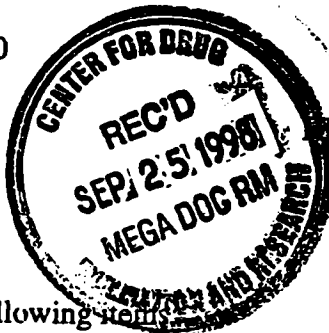
BM

ORIGINAL

September 24, 1998

Robert DeLap, M.D., Ph.D., Acting Director  
Division of Anti-Inflammatory, Analgesic,  
and Ophthalmologic Drug Products  
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FAX (847) 982-4701



NDA 20-998  
Celebra™ (celecoxib)

Dear Dr. DeLap:

Please find enclosed the following items:

- Final minutes of FDA telecon of 10-Sept-1998.
- Response to Action items listed in the above minutes:
  1. See Part II (Additional Ulcer Data Analyses Target sample Size Cohort)
  2. FDA action item if necessary
  3. See Part I (Enrollment Histogram)
  4. See Part III (Subgroup analyses of Ulcer Data based on Alcoholism and Tobacco Use Status)
  5. Not yet available

A desk copy of the above items is being sent directly to Dr. Goldkind in the GI Division.

Sincerely,

*Winifred M. Begley*

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

Enc.

WMB/pl

CC: Desk Copy - Dr. L. Goldkind/Division of GI & Coagulation

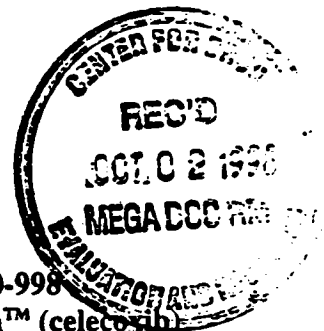
# SEARLE ORIGINAL

October 1, 1998

NEW CORRESP.

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

Dear Dr. DeLap:

Please find enclosed a response to question A. from the PK reviewer which was sent to us by fax September 28, 1998. The rest of the responses to questions listed under B. will be sent under separate cover at a later date.

Sincerely,

A handwritten signature in cursive that reads "Winifred M. Begley".

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

WMB/pl

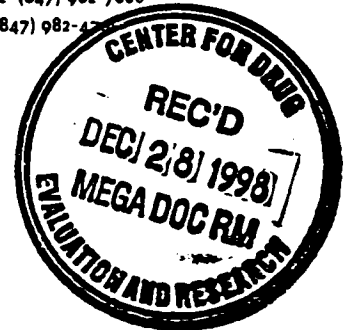
**SEARLE**

BB DUPLICATE  
NDA ORIG AMENDMENT

December 24, 1998

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4901 SEARLE PARKWAY  
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PHONE (847) 982-7000  
FAX (847) 982-4200

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:

Enclosed please find our response to a request from Dr. S. Lee in a fax received 21-Dec-1998. The attached tables were faxed to Ms. V. Lutwak 23-Dec-1998.

Sincerely,

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

WMB/pl

Enc.

# SEARLE

SEARLE  
4901 SEARLE PARKWAY  
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PHONE (847) 982-7000  
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December 29, 1998

Dr. 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, MD 20850

Re: NDA 20-998  
Celebrex™ (celecoxib)

Dear Dr. DeLap,

With reference to the FDA request of December 29, 1998, regarding a phase 4 commitment, Searle commits to study the effects of Celebrex on acid-base status, including assessment of changes in serum bicarbonate, using a protocol agreed to by this Division.

The assessment for changes in serum bicarbonate are planned for studies N49-98-22-035 and N49-98-12-102 which have already been submitted to the IND (SN 364 and SN 372).

Sincerely,



Winifred M. Begley  
Director, Regulatory Affairs

WMB/iw



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville MD 20857

AUG 20 1998

NDA 20-998

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

Dear Ms Begley:

We have received 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: Celebra (celecoxib capsules)

Therapeutic Classification: Priority (P)

Date of Application: June 29, 1998

Date of Receipt: June 30, 1998

Our Reference Number: 20-998

Unless we notify you within 60 days of our receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on August 29, 1998 in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be December 31, 1998.

We have determined that this application will be reviewed under 21 CFR 314 Subpart H (accelerated approval). We remind you that as required under 21 CFR 314.550, unless otherwise informed by the Agency, you must submit for Agency review before approval of this application copies of all promotional materials, including promotional labeling as well as advertisements, intended for dissemination or publication within 120 days after marketing approval.

NDA 20-998

Page 2

Under 21 CFR 314.102(c) of the new drug regulations, you may request an informal conference with this Division (to be held approximately 90 days from the above receipt date) for a brief report on the status of the review but not on the application's ultimate approvability. Alternatively, you may choose to receive such a report by telephone.

Please cite the NDA number listed above at the top of the first page of any communications concerning this application.

If you have any questions, contact me at (301) 827-2090.

Sincerely,



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



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



# SEARLE

## ORIGINAL

October 1, 1998

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

SEARLE  
4901 SEARLE PARKWAY  
SKOKIE, ILLINOIS 60077



RE: NDA 20-998  
Celebra™ (celecoxib)

Dear Dr. DeLap:

Enclosed is a response to Dr. Throckmorton's requests as follows:

FDA telephone contact 16 September 1998 for survival curves/ Kaplan-Meier estimates for patients with Cardiovascular mortality.

FDA fax of September 22 and 23, 1998

FDA telephone contact 23 September 1998 regarding incidence of MI and angina as AEs, SAEs or deaths and whether they overlap.

Sincerely,

A handwritten signature in cursive that reads "Winifred M. Begley".

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

WMB/pl

Desk Copy: Dr. Throckmorton/Division of Cardiorenal

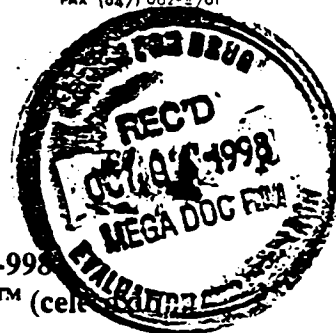
# SEARLE

# ORIGINAL

October 5, 1998

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  
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4901 SEARLE PARKWAY  
SKOKIE, ILLINOIS 60077  
PHONE (847) 982-7000  
FAX (847) 082-2701



RE: NDA 20-998  
Celebra™ (celecoxib)

Dear Dr. DeLap:

Enclosed are copies of 2 sets of data that were requested by Dr. Throckmorton and which were faxed to him on October 2, 1998:

1. Corrected table from Dr. Throckmorton's assessment report and supporting data from Table 2.9 of the ISS.
2. Kaplan-Meier plots of time to all deaths and cardiovascular deaths from controlled studies and the open-label long term safety study. A Win-Zip disc (this does not need a Zip drive to open, a regular disc drive will open) copy of these data in MS-Word 7 are being sent to Dr. Throckmorton only for him to use in his assessment report, a photocopy of the Win-Zip disc is enclosed for your records.

Sincerely,

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

WMB/pl

Desk Copy: Dr. D. Throckmorton/Division of Cardio-Renal

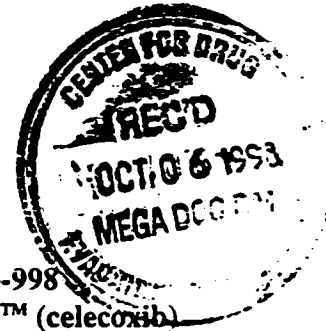
NDA ORIG AMENDMENT  
**SEARLE**

ORIGINAL

October 5, 1998

Robert DeLap, M.D., Ph.D., Acting Director  
Division of Anti-Inflammatory, Analgesic,  
and Ophthalmologic Drug Products  
Office of Drug Evaluation V  
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RE: NDA 20-998  
Celebra™ (celecoxib)

Dear Dr. DeLap:

On September 17, 1998 Dr. Goldkind requested listings of patients with ulcers and their assigned treatment to aid him in his review of the ulcer data. Please find enclosed in response to this request the following:

Appendix 1 - Listing of patients with ulcer: North American Endoscopy Studies

Appendix 2 - Listing of patients with ulcer: North American Active-Controlled Arthritis Studies

Appendix 3 - Listing of patients with ulcer: International RA/Endoscopy study.

A copy of the above was faxed and sent as a desk copy to Dr. Goldkind.

Sincerely,

*Winifred M. Begley*

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

WMB/pl

Desk Copy: Dr. L. Goldkind/Division of GI & Coagulation

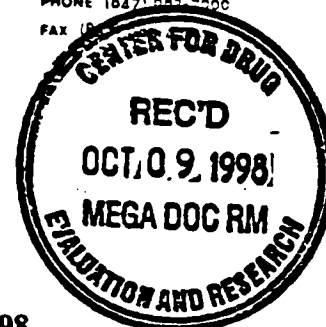
# SEARLE

October 8, 1998

DUPLICATE

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

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4901 SEARLE PARKWAY  
SKOKIE, ILLINOIS 60077  
PHONE (847) 282-7200  
FAX (847) 282-7200



RE: NDA 20-998  
Celebra™ (celecoxib)

Dear Dr. DeLap:

In response to a request from Dr. Throckmorton sent by fax 9.16.98 enclosed please find the SAS analysis of renal labs and AEs.

In all of the analyses requested by Dr. Throckmorton the following programming conventions were followed:

Patients with baseline serum chloride levels  $>110$  mmol/L were included in the analyses if their serum chloride levels increased 2mmol/L or more at any point during the treatment period.

For all other laboratory determinations (calcium, phosphate, urine protein, urine pH, urine glucose), patients with baseline values greater (less) than the limit that was defined for a given lab were included in the analysis when their lab values increased (decreased) by any amount during the treatment period. Patients whose lab values were unchanged or whose lab values decreased (increased) toward normal values were not counted as extremes.

In addition to the above tables we have provided corrected ISS tables:

Table 31.3.5 Incidence of Renal Adverse Events (Cluster 2): North American 12-week Arthritis Trials Edema generalized/Edema peripheral and BUN/Creatinine/Chloride.

Table 31.3.6 Analysis of Renal Adverse Events (Cluster 2): North American 12-week Arthritis Trials Edema generalized/Edema peripheral and BUN/Creatinine/Chloride.



Division of Anti-Inflammatory, Analgesic  
& Ophthalmologic Drug Products  
NDA 20-998/Celebra™ (celecoxib)  
October 8, 1998  
Page -2-

Tables 31.3.5 and 31.3.6 submitted in Volume 1.428, volume pages 363 and 364 (summary pages 1578 and 1579 of 1640) of the ISS were incorrect as chloride levels were not measured in all of the studies that were pooled (a common denominator was used incorrectly) in the analysis that was provided. The new tables (also identified as Tables 31.3.5 and 31.3.6 see above) have been programmed for only those (5) studies that included both placebo and active controls and chloride levels were measured.

Please contact me if you have any questions concerning the above information.

Sincerely,

*Winifred M. Begley*

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

WMB/pl

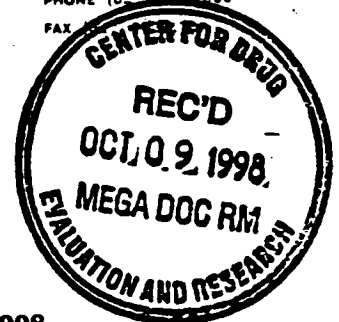
Desk copy: V. Lutwak  
Desk copy: Dr. Throckmorton/Division of Cardio-Renal

**SEARLE**  
DUPLICATE

October 8, 1998

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



RE: NDA 20-998  
Celebra™ (celecoxib)

Dear Dr. DeLap:

Please find enclosed the responses to the questions from the PK reviewer under item B sent by fax September 28, 1998 (attached). The response to question A was previously submitted on Oct 1, 1998. In this response I have provided both the individual report page numbers and corresponding NDA volume numbers and page numbers.

If you have any questions please contact the undersigned.

Sincerely,

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

WMB/pl

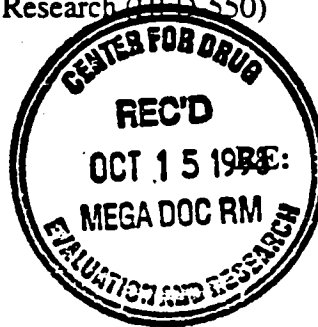
NEW CORRESP

**SEARLE** ORIGINAL *NC*

October 14, 1998

Robert DeLap, M.D., Ph.D., Acting Director  
Division of Anti-Inflammatory, Analgesic,  
and Ophthalmologic Drug Products  
Office of Drug Evaluation V  
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FAX (847) 982-4701



NDA 20-998  
Celebra™ (celecoxib)

Dear Dr. DeLap:

In response to a request from Dr. Throckmorton enclosed is Appendix B.1.3 Listings of hyperchloremia and bony AEs (Cluster 1) Long-term open label trial. A copy of these tables is being sent by fax and desk copy to Dr. Throckmorton.

Please note on the first page patient 0010079 has two identical chloride values, this is because they were rolled-over from a controlled trial into the open-label trial, hence one value is from the final visit of the controlled and the second value is for the first visit open-label trial.

Sincerely,

*Winifred M. Begley*

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

WMB/pl

Desk Copy: Dr. Throckmorton/Division of Cardio-Renal

NDA ORIG AMENDMENT  
**SEARLE**

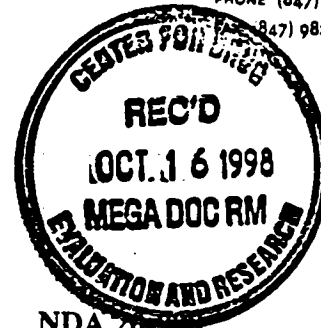
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ORIGINAL

October 15, 1998

Robert DeLap, M.D., Ph.D., Acting Director  
Division of Anti-Inflammatory, Analgesic,  
and Ophthalmologic Drug Products  
Office of Drug Evaluation V  
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(847) 982-4701



RE: NDA 20-998  
Celebra™ (celecoxib)

Dear Dr. DeLap:

Enclosed please find the remaining tables requested by Dr. Throckmorton:

Appendix F.1.2 Listing of proteinuria and abnormal creatinine (Cluster 1) North American 12-week Arthritis trials

Appendix F.2.1 Listing of proteinuria and abnormal creatinine (Cluster 2) North American 12-week Arthritis trials

Appendix F.2.3 Listing of proteinuria and abnormal creatinine (Cluster 2) Long term open label trial

Sincerely,

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

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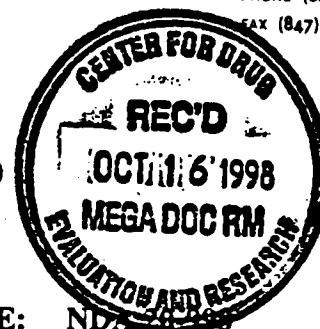
Desk Copy: Dr. D. Throckmorton/Division of Cardio-Renal



October 14, 1998

SEARLE  
4901 SEARLE PARKWAY  
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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 125-388  
Celebra™ (celecoxib)

Dear Dr. DeLap:

Further to a telecon request from Dr. Throckmorton October 14, 1998 please find enclosed the following listings:

Appendix A.3.2 Listing of hyperchloremia and abnormal renal function (Cluster 3)  
North American 12-week Arthritis trials

Appendix C.3 Listing of hypophosphatemia and bony AEs: Long-term open label trial

Appendix E.1.2 Analysis of metabolism (Cluster 1) North American 12-week Arthritis trials

The remaining 3 sets of listings (F.2.3, F.1.2 and F.2.1) will be sent in a separate package once complete.

Sincerely,

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

WMB/pl

Desk Copy: Dr. D. Throckmorton/Division of Cardio-Renal

# SEARLE

# ORIGINAL

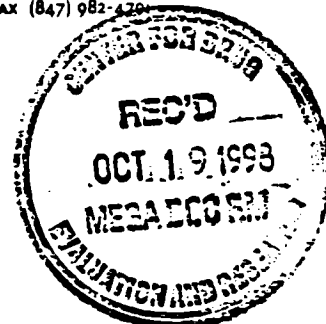
October 16, 1998

NDA 0718 AMENDMENT

SEARLE  
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*BZ*

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  
Celebra™ (celecoxib)

Dear Dr. DeLap:

Below are responses to 2 questions provided to us on October 13, 1998:

**Q.1. Request from L. Goldkind**

The data that was never supplied by Searle was a table from study 071. Table 16 7 of 12 parts. This was data on H. pylori assayed by histology and CLO test.

**A.1. subgroup analysis of endoscopy.**

For 062,  
by the biopsy (histology) test,  
by the CLO test.

The subgroup analysis determined by biopsy and CLO test has been included in the final report for 062.

For 071  
by the biopsy (histology) test,  
by the CLO test,  
by the biopsy and CLO test.

Some p-values were not displayed due to low frequency cells.

**Q.2 Request from M. Averbuch and L. Patrician**

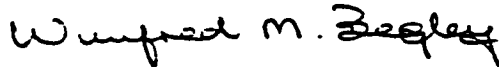
For the dental pain studies 025, 027, 070, please provide the p-values for the pair-wise comparisons between the different celecoxib doses and placebo/active control for the PID, PR and PRID (BOCF technique) analyses. Also please clarify if a multiplicity adjustment has been done on these analyses.

Division of Anti-Inflammatory, Analgesic,  
and Ophthalmologic Drug Products  
NDA 20-998/Celebra™ (celecoxib)  
October 16, 1998  
Page -2-

A.2. Pairwise p-values between each dose of celecoxib and placebo/active control for the PID, PR and PRID (BOCF) for dental pain studies 025, 027 and 070.

For the original reports, the analyses were performed according to FDA's "presentation of efficacy results of single-dose analgesics for studies using acute pain models". Fisher's protected LSD procedure was applied for multiple comparison.

Sincerely,



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

WMB/pl  
QRSid# 99,Q#2 and 3

Desk Copy: Dr. L. Goldkind/Division of GI & Coagulation  
Dr. M. Averbuch  
Dr. L. Patrician

ORIGINAL

**SEARLE**

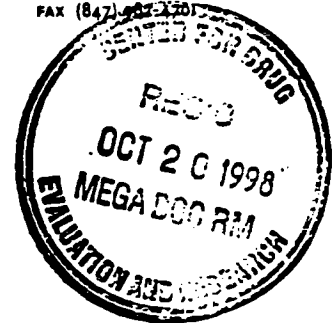
NDA CRIG AMENDMENT

BM

October 16, 1998

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FAX (847) 982-7001

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  
Celebra™ (celecoxib)

Dear Dr. DeLap:

In response to a clarification requested by Dr. Throckmorton October 15, 1998 our response is as follows:

There are 615 patients who received 400 mg in the controlled trials.

When we started working on the renal requests we reduced down to the 5 main North American studies 020, 021, 022, 023, 054 (all with 12 weeks, pbo and active comparator, and all have chloride measurements).

Of the 5 studies there are 434 400mg patients in studies 022 & 023 only; as follows:

615 in 4 studies with 400 mg groups  
99 deleted from 047 (Phase II, no active control)  
82 deleted from 012 (Phase II, no active control)

434 in 022 and 023

Division of Anti-Inflammatory, Analgesic,  
and Ophthalmologic Drug Products

NDA 20-998/Celebra™ (celecoxib)

October 16, 1998

Page -2-

If you require any further information please contact me.

Sincerely,

*Winifred M. Begley*

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

WMB/pl  
QRS id#95

Desk Copy: Dr. Throckmorton/Division of Cardio-Renal

**SEARLE**

B2

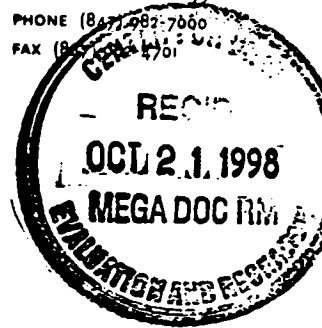
October 20, 1998

**ORIGINAL**  
**ORIG AMENDMENT**

SEARLE  
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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

B2



RE: NDA 20-998  
Celebrex™ (celecoxib)

Dear Dr. DeLap:

In response to a request from Dr. Josie Yang for an additional statistical analysis of tumors data in the rat and mouse carcinogenicity studies please find enclosed our response.

Sincerely,

*Winifred M. Begley*

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

WMB/pl

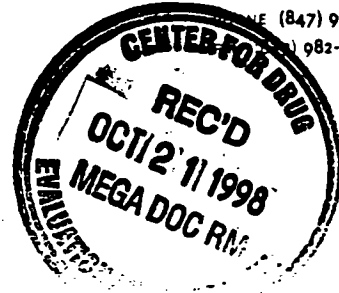
BM  
**SEARLE**

October 20, 1998

ORIGINAL  
ORIG AMENDMENT

BM

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Division of Anti-Inflammatory, Analgesic,  
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Office of Drug Evaluation V  
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9201 Corporate Boulevard  
Rockville, Maryland 20850

RE: NDA 20-998  
Celebra™ (celecoxib)

Dear Dr. DeLap:

In response to a follow-up fax request dated Oct 18, 1998 from Dr. Goldkind concerning antacid use we would like to clarify the response which was provided on September 3, 1998. The response then was made in the context of Studies 021,022,062 and 071. In these studies, the criteria for the endoscopy evaluable cohort was changed to allow for some use of antacids during the study. This change was not made to the 041 protocol, i.e., the original evaluability criteria for the endoscopy evaluable cohort excluded antacid use was not subsequently amended.

We trust this fully answers the question.

Sincerely,

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

WMB/pl

**SEARLE**

DUPLICATE

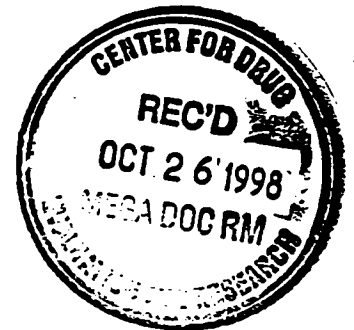
October 23, 1998

**NEW CORRESP**

NC

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9201 Corporate Boulevard  
Rockville, Maryland 20850



**RE: NDA 20-998**  
**Celebrex™ (celecoxib)**

Dear Dr. DeLap:

In response to a request from Dr. Throckmorton of Oct 22, 1998 please find enclosed a listing of concomitant medications for celecoxib and bicarbonate.

Sincerely,

*Winifred M. Begley*

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

WMB/pl

Desk Copy: Dr. Throckmorton/Division of Cardio-Renal



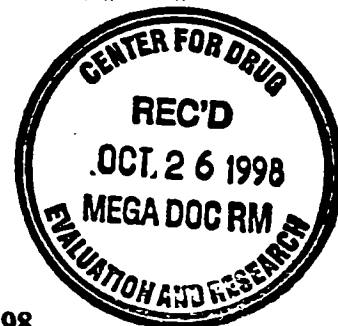
**SEARLE**

October 23, 1998

**DUPLICATE**  
**ORIG AMENDMENT**

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



RE: NDA 20-998  
Celebrex™ (celecoxib)

Dear Dr. DeLap:

In response to the fax dated Oct 23, 1998:

Page 199 of vol. 5 indicates that the 100 as well as the 200mg capsules are also supplied in counts of 14 capsules in 60cc HDPE bottles. The "How Supplied" section does not reflect this. This point needs to be clarified with the Co.

The 14 count capsule bottle is a sample only and will not be marketed.

Sincerely,

*Winifred M. Begley*

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

WMB/pl  
QRS #126

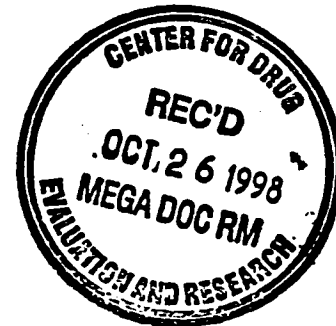
**SEARLE**

October 23, 1998

**DUPLICATE  
ORIG AMENDMENT**

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9201 Corporate Boulevard  
Rockville, Maryland 20850



**RE: NDA 20-998  
Celebrex™ (celecoxib)**

Dear Dr. DeLap:

Please find attached our response to a question from Dr. J Yang on perivascular/  
periventricular lymphocytic infiltrates in the brain of dogs for other COX-2 agents  
valdecoxib and parecoxib.

Sincerely,

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

WMB/pl  
QRS #111

CC: Dr. J. Yang

# SEARLE

October 26, 1998

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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:

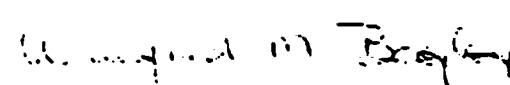
Enclosed are additional listings requested by Dr. Throckmorton on Oct 22, 1998 for the following:

Appendix A.3.3 Listing of hyperchloremia and abnormal renal function (Cluster 3)  
Long term open label trial

Appendix E.1.3 Listing of metabolism (Cluster 1) long term open label trial

This completes the request for Oct 22, 1998.

Sincerely,

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

WMB/pl  
QRS#118

Desk Copy: Dr. Throckmorton/Division of Cardio-Renal

# SEARLE

ORIGINAL  
BM

NDA ORIG AMENDMENT

October 26, 1998

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Rockville, Maryland 20850



RE: NDA 20-998  
Celebrex™ (celecoxib)

Dear Dr. DeLap:

Enclosed is a table of locations for Volume 1.442 of the NDA which contains the supplement to the ISS including the contingency tables (N49-98-17-819). The pages referenced are to the volume page number in the top right hand corner of the page on the hard copy. Dr. Witter in a telecon today asked that we provide him with the location of the listings and patient profiles for Tables 1.1, 1.2, 2.1, 2.2, 3.1, 4.1, 4.2.

Please contact me if further assistance is needed on this.

Sincerely,

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

WMB/pl  
QRS#128

Desk Copy: Dr. Witter

# SEARLE

# ORIGINAL

## NDA ORIG AMENDMENT

October 27, 1998

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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:

In response to a question from Dr. Goldkind on Oct 20, 1998 we are now able to confirm that the evaluable cohort of the -041 study did include individuals who used low dose antacids.

Sincerely,

A handwritten signature in cursive script that reads "Winifred M. Begley".

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

WMB/pl  
QRS#110

Desk Copy: Dr. Goldkind/Division of GI & Coagulation

**SEARLE** NDA ORIG AMENDMENT ORIGINAL  
SU

October 28, 1998

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Division of Anti-Inflammatory, Analgesic,  
and Ophthalmologic Drug Products  
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Center for Drug Evaluation and Research (HFD-550)  
9201 Corporate Boulevard  
Rockville, Maryland 20850



RE: NDA 20-998  
Celebrex™ (celecoxib)

Dear Dr. DeLap:

In accordance with CFR 314.50 (vi)(b)(1) we are providing the 120 day Safety Update for celecoxib.

Sincerely,

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

WMB/pl

Enc: 1 archival; 1 review; 2 desk copies