CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-402/SCM-001/S-002/S-003/S-004/S-005

ADMINISTRATIVE DOCUMENTS

MINUTES OF A MEETING
June 30, 1999
9201 Corporate Blvd.
Rockville, MD
Conference Rm. S200B

Fileability Meeting for NDA 20-402/SE1-005, Advil Migraine

CDER Participants:

Division of OTC Drug Products, HFD-560
Charles Ganley, Director
Linda Katz, Deputy Director
Rosemary Cook, Supervisory Project Manager
Kerry Rothschild, Project Manager
Rosemarie Neuner, Medical Officer
Debbie Lumpkins, Team Leader
Stephanie Mason, IDS

Division of Neuropharmaceutical Drug Products, HFD-120
Russel Katz, Acting Director
Lana Chen, Project Manager
Armando Oliva, Medical Officer
Kallapa Koti, Statistician

Meeting Objective: To determine the fileability of the efficacy supplement to NDA 20-402 and establish timelines for its review.

Whitehall-Robins submitted supplemental NDA 20-402/SE1-005 as an efficacy supplement for Advil Liqui-gels. The supplement provides for the new indication as follows:

For treatment of mild to moderate migraine headache.

The supplement was received on May 17, 1999 the user fee goal date is March 17, 2000, and, if fileable, the filing date will be July 16, 1999.

Fileability issues are as follows:

1. Project mgmt. - Kerry Rothschild. The submission was missing (1) a statement that all non-clinical laboratory studies were conducted in compliance with the requirements of 21 CFR Part 58, or an explanation why the requirements were not met; (2) a statement that all clinical trials were conducted in accordance with the IRB/Declaration of Helsinki provisions of the CFR; and (3) a statement that the integrated summary of safety includes all safety data from all sources.

Project management, nevertheless, considers the application fileable. Sponsor will be asked to submit the above.

2. Biostatistics - Kallapa Koti. Application Fileable. Statistical review to be completed by November 1, 1999.

3. Clinical HFD-560 - R.Neuner. Application Fileable. Application does not contain all current safety data regarding the product. Will request adverse event case reports. Review to be completed by November 1, 1999.

4. Clinical HFD-120 - A. Oliva. Application Fileable. Review to be completed by November 1, 1999.

5. IDS HFD-560 - S. Mason. Application Fileable. Review to be completed by November 22, 1999.

6. Filing Decision - C. Ganley/R. Katz Application fileable.

Agreements:

Application to be filed. K. Rothschild to contact sponsor regarding information to be requested. Monthly team meetings and labeling day to be scheduled as well.

Minutes Preparer: /S/

Kerry Rothschild,
Project Manager

PROJECT MANAGEMENT FILABILITY CHECKLIST:

NDA 20-402/SE1-005

On initial overview of the NDA application:

1. Do any of the following apply to this application (i.e., if YES, the application MUST BE REFUSED TO FILE under 314.100 (e) and there is no filing over protest):

	Yes	No
(a) Is the drug product already covered by an approved application?		X
(b) Does the submission purport to be an abbreviated application under 314.55: however the drug product is not one for which FDA has made a finding that an abbreviated application is acceptable under 314.55 (b)?		X
(c) Is the drug product subject to licensing by FDA under the Public Service Act and Subchapter F of Chapter I of Title 21 of the CFR?		X

2. Do any of the following apply to this application (i.e., if NO, the application MAY BE REFUSED TO FILE under 314.100 (d) and there is the potential for filing over protest):

	Yes	No
(a) Does the application contain a completed application form as required under 314.50 or 314.55?	X	
(b) On its face, does the application contain the sections of an application required by regulation and Center guidelines?	X	
(c) Has the applicant submitted a complete environmental assessment which addresses each of the items specified in the applicable format under 25.31 or has the applicant submitted evidence to establish that the product is subject to categorical exclusion under 25.24 of the CFR?	X	
(d) On its face, is the NDA formatted in compliance with Center guidelines including integrated efficacy and safety summaries?	X	
(e) Is the NDA indexed and paginated?	X	
(f) On its face, is the NDA legible?	X	
(g) Has the applicant submitted all required copies of the submission and various sections of the submission?	X	
(h) Has the sponsor submitted all special studies/data requested by the Division during pre-submission discussions with the sponsor?	X	

	Yes	No
(i) Does the application contain a statement that all nonclinical laboratory studies was conducted in compliance with the requirements set forth in Part 58 or a statement why a study was not conducted in compliance with those requirements?		X
(j) If required, has the applicant submitted carcinogenicity studies?	NA	
(k) On its face, does the application contain at least two adequate and well-controlled clinical trials?	AM-98-01; AM-98-02	
(l) Does the application contain a statement that all clinical trials were conducted in accord with the IRB/Declaration of Helsinki provisions of the CFR?		X
(m) Have all articles/study reports been submitted either in English or translated into English?	X	
(n) Has the applicant submitted draft labeling in compliance with 210.56 and 210.57 of the CFR?	X	
(o) Has the applicant submitted the required FRAUD POLICY notice?	X	
(p) Has the applicant submitted copies of all package inserts (or their equivalent) from all countries in which this product has been previously approved for marketing? Have all non-English package inserts been translated?	NA	
(q) Has the applicant stated that the integrated summary of safety includes all safety data for this product of which they are aware from all sources, domestic and foreign? What is the cut-off date for the preparation of the ISS?		X
(r) If this is a CANDA submission, has the applicant submitted a statement to the archival NDA that the text, tables, and data in the CANDA and the archival hardcopy NDA are identical? If they are not identical, is there a letter to the archival NDA that specifies distinctly ALL of the differences in the two submissions?	NA	

3. From a project management perspective, is this NDA fileable? If "no", please state why it is not.
Conclusion: Application fileable

Information to be requested from applicant:

(i) GLP statement
(l) IRB/Declaration of Helsinki statement
(q) Statement that integrated summary of safety includes all safety data.

/S/

Project Manager

HFD-510

/S/

Supervisory Project Manager

HFD-120
Adult Migraine
20-402/SE1-005

45 DAY MEETING CHECKLIST

FILEABILITY:

On initial overview of the NDA application:	YES	NO

CLINICAL:

(1)	On its face, is the clinical section of the NDA organized in a manner to allow substantive review to begin?	✓
(2)	Is the clinical section of the NDA indexed and paginated in a manner to allow substantive review to begin?	✓
(3)	On its face, is the clinical section of the NDA legible so that substantive review can begin?	✓
(4)	If needed, has the sponsor made an appropriate attempt to determine the most appropriate dosage and schedule for this product (i.e., appropriately designed dose-ranging studies)?	✓
(5)	On its face, do there appear to be the requisite number of adequate and well-controlled studies in the application?	✓
(6)	Are the pivotal efficacy studies of appropriate design to meet basic requirements for approvability of this product based on proposed draft labeling?	✓
(6)	Are all data sets for pivotal efficacy studies complete for all indications (infections) requested?	✓
(7)	Do all pivotal efficacy studies appear to be adequate and well-controlled within current divisional policies (or to the extent agreed to previously with the applicant by the Division) for approvability of this product based on proposed draft labeling?	✓
(8)	Has the applicant submitted line listings in a format to allow reasonable review of the patient data? Has the applicant submitted line listings in the format agreed to previously by the Division?	✓ but (requested)

(9) Has the application submitted a rationale for assuming the applicability of foreign data (disease specific microbiologic specific) in the submission to the US population? N/A

(10) Has the applicant submitted all additional required case record forms (beyond deaths and drop-outs) previously requested by the Division? N/A

(11) Has the applicant presented the safety data in a manner consistent with Center guidelines and/or in a manner previously agreed to by the Division? ✓

(12) Has the applicant presented a safety assessment based on <u>all</u> current world-wide knowledge regarding this product? N/A

(13) Has the applicant submitted draft labeling consistent with 201.56 and 201.57, current divisional policies, and the design of the development package? ✓

(14) Has the applicant submitted all special studies/data requested by the Division during pre-submission discussions with the sponsor? N/A

(15) From a clinical perspective, is this NDA fileable? If "no", please state below why it is not. ✓

If certain claims are not filable, please state which claims they are and why they are not filable.

/S/ HFD-120

Reviewing Medical Officer

Supervisory Medical Officer

6/30/90

OTC - Global Safety

45 DAY MEETING CHECKLIST

ILEABILITY: Advil Liquigel 200mg

n initial overview of the NDA application: YES NO

NDA 20-402

CLINICAL:

(1) On its face, is the clinical section of the NDA organized in a manner to allow substantive review to begin?

(2) Is the clinical section of the NDA indexed and paginated in a manner to allow substantive review to begin?

(3) On its face, is the clinical section of the NDA legible so that substantive review can begin?

(4) If needed, has the sponsor made an appropriate attempt to determine the most appropriate dosage and schedule for this product (i.e., appropriately designed dose-ranging studies)?

(5) On its face, do there appear to be the requisite number of adequate and well-controlled studies in the application?

(6) Are the pivotal efficacy studies of appropriate design to meet basic requirements for approvability of this product based on proposed draft labeling?

(6) Are all data sets for pivotal efficacy studies complete for all indications (infections) requested?

(7) Do all pivotal efficacy studies appear to be adequate and well-controlled within current divisional policies (or to the extent agreed to previously with the applicant by the Division) for approvability of this product based on proposed draft labeling?

(8) Has the applicant submitted line listings in a format to allow reasonable review of the patient data? Has the applicant submitted line listings in the format agreed to previously by the Division? Yes

→ for post-marketing [illegible] reports + for clinical study [illegible] case.

(9) Has the application submitted a rationale for assuming the applicability of foreign data (disease specific microbiologic specific) in the submission to the US population? yes

(10) Has the applicant submitted all additional required case record forms (beyond deaths and drop-outs) previously requested by the Division? Ø

(11) Has the applicant presented the safety data in a manner consistent with Center guidelines and/or in a manner previously agreed to by the Division? yes

(12) Has the applicant presented a safety assessment based on <u>all</u> current world-wide knowledge regarding this product? Linear Tests Only

(13) Has the applicant submitted draft labeling consistent with 201.56 and 201.57, current divisional policies, and the design of the development package?

(14) Has the applicant submitted all special studies/data requested by the Division during pre-submission discussions with the sponsor?

(15) From a clinical perspective, is this NDA fileable? If "no", please state below why it is not.

If certain claims are not filable, please state which claims they are and why they are not filable.

/S/
Reviewing Medical Officer

/S/
Supervisory Medical Officer