CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-565

PHARMACOLOGY REVIEW(S)

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

PHARMACOLOGY/TOXICOLOGY REVIEW AND EVALUATION

NDA NUMBER:	22-565 (see submission #22-112)
SERIAL NUMBER:	000
DATE RECEIVED BY CENTER:	July 28, 2009
PRODUCT:	Advil Cold & Sinus PE caplets (Ibuprofen 200 mg/ Phenylephrine PE, 10mg)
INTENDED CLINICAL POPULATION:	Temporary relief of symptoms associated with the common cold or flu
SPONSOR:	Wyeth Consumer HealthCare (WCH)
DOCUMENTS REVIEWED:	No new nonclinical studies
REVIEW DIVISION:	Division of Nonprescription Clinical Evaluation (DNCE; HFD-560)
PHARM/TOX REVIEWER:	Wafa Harrouk, Ph.D.
DIVISION DIRECTOR:	Andrea Leonard-Segal, M.D.
PROJECT MANAGER:	Janice Adams-King, RN, BSN, MS

EXECUTIVE SUMMARY

I. Recommendations

A. Recommendation on approvability: Approvable from the standpoint of pharmacology/toxicology as previously assessed under NDA 22-112.

B. Recommendation for nonclinical studies: None

C. Recommendations on labeling: None

II. Summary of nonclinical findings: No new nonclinical studies were conducted. This is a 505(b)(2) application where the sponsor is relying on the Agency's findings of safety and effectiveness for the nonclinical data submitted under NDA # 22-112. No changes were made to the inactive ingredients list used previously in NDA 22-112.

III. Regulatory history

The Sponsor submitted this NDA, # 22-565, in response to a "Not Approvable Letter" (NAL) which was issued by the FDA on May 7, 2008 for NDA # 22-112 for an ibuprofen 200 mg/ PE 10 mg formulation. The NAL was based on a flawed assay methodology used in a pharmacokinetic (PK) trial which results were used to demonstrate bioequivalence for a single ingredient PE formulation. The Agency recommended that the Sponsor submit new PK data using an adequately validated assay for quantifying free PE in plasma.

In this NDA, # 22-565, WCH conducted two PK studies, AQ-08-12 and AQ-08-13, using the final formulation where a new assay was used to measure the free PE. These two studies investigated drug interactions, formulation effects and food effects in treated subjects. In addition, samples were assayed for total PE using a new and revised total PE assay compared to the assay used under NDA # 22-112.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22565	ORIG-1	WYETH CONSUMER HEALTHCARE	ADVIL COLD & SINUS PE(IBUPROFEN 200MG/PH

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/s/

WAFA HARROUK
01/05/2010

PHARMACOLOGY/TOXICOLOGY FILING CHECKLIST FOR A NEW NDA/BLA

NDA Number: 22-565 (previously under 22-112)

Applicant: Wyeth Consumer Healthcare

Stamp Date: Resubmission July 28, 2009

Drug Name: Advil Allergy Sinus Relief PE

NDA Type: 505(b)(2)

Background: this NDA was originally reviewed under NDA 22-112 and was not approved mainly due to clinical pharmacology issues. No pharm/tox issues were included in the complete response letter. This NDA is referencing the nonclinical portion of NDA 22-112 and will not have any additional pharm/tox issues added.

On **initial** overview of the NDA application for RTF:

	Content Parameter	Yes	No	Comment
1	On its face, is the pharmacology/toxicology section of the NDA organized (in accord with 21 CFR 314 and current guidelines for format and content) in a manner to allow substantive review to begin?			N/A
2	Is the pharmacology/toxicology section of the NDA indexed and paginated in a manner allowing substantive review to begin?			N/A
3	On its face, is the pharmacology/ toxicology section of the NDA legible so that substantive review can begin?			N/A
4	Are all required (*) and requested IND studies (in accord with 505 b1 and b2 including referenced literature) completed and submitted in this NDA (carcinogenicity, mutagenicity*, teratogenicity*, effects on fertility, juvenile studies, acute and repeat dose adult animal studies*, animal ADME studies, safety pharmacology, etc)?			N/A
5	If the formulation to be marketed is different from the formulation used in the toxicology studies, have studies by the appropriate route been conducted with appropriate formulations? (For other than the oral route, some studies may be by routes different from the clinical route intentionally and by desire of the FDA).			N/A
6	On its face, does the route of administration used in the animal studies appear to be the same as the intended human exposure route? If not, has the sponsor submitted a rationale to justify the alternative route?			N/A

PHARMACOLOGY/TOXICOLOGY FILING CHECKLIST FOR A NEW NDA/BLA

	Content Parameter	Yes	No	Comment
7	Has the sponsor submitted a statement(s) that all of the pivotal pharm/tox studies have been performed in accordance with the GLP regulations (21 CFR 58) or an explanation for any significant deviations?			N/A
8	Has the sponsor submitted all special studies/data requested by the Division during pre-submission discussions with the sponsor?			N/A
9	Are the proposed labeling sections relative to pharmacology/toxicology appropriate (including human dose multiples expressed in either mg/m2 or comparative serum/plasma levels) and in accordance with 201.57?			N/A
10	If there are any impurity – etc. issues, have these been addressed? (New toxicity studies may not be needed.)	x		A 14-day general toxicity study, an Ames Salmonella study & a study for chromosome aberration in human lymphocyte were submitted under 22-112
11	Has the sponsor addressed any abuse potential issues in the submission?			N/A
12	If this NDA is to support a Rx to OTC switch, have all relevant studies been submitted?			N/A
13	From a pharmacology/toxicology perspective, is the NDA fileable? If ``no`` please state below why it is not.	x		

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/s/

WAFA HARROUK
10/16/2009