CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

022063Orig1s000

NON-CLINICAL REVIEW(S)

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

PHARMACOLOGY/TOXICOLOGY NDA REVIEW AND EVALUATION

Application number:	NDA 22063
Supporting document/s:	Supporting Document Number 44, Applicant Serial number 22
Applicant's letter date:	December 20, 2016 (Resubmission/Class 2)
CDER stamp date:	December 20, 2016
Product:	SPD 465; Mydayis™ (Mixed salts of a single-entity Amphetamine)
Indication:	Attention Deficit Hyperactivity Disorder (ADHD)
Applicant:	Shire Development LLC
Review Division:	Division of Psychiatry Products
Reviewer:	Deepa B. Rao DVM, PhD
Supervisor/Team Leader:	Ikram Elayan, PhD
Division Director:	Mitchell V. Mathis MD
Project Manager:	Latrice Wilson, Pharm D

Disclaimer

Except as specifically identified, all data and information discussed below and necessary for approval of NDA 22063 are owned by Shire Development LLC or are data for which Shire Development LLC has obtained a written right of reference.
Any information or data necessary for approval of NDA 22063 that Shire Development LLC does not own or have a written right to reference constitutes one of the following: (1) published literature, or (2) a prior FDA finding of safety or effectiveness for a listed drug, as reflected in the drug's approved labeling. Any data or information described or referenced below from reviews or publicly available summaries of a previously approved application is for descriptive purposes only and is not relied upon for approval of NDA 22063.

TABLE OF CONTENTS

Abbreviations

ADHD	Attention Deficit Hyperactivity Disorder
MAS	Mixed Amphetamine Salts
MRHD	Maximum Recommended Human Dose

1 Executive Summary

1.1 Introduction

Shire Development LLC is seeking approval of SHP465 (under the trade name Mydayis™), for their once-daily new formulation, single-entity mixed amphetamine salt (MAS) drug product for oral administration in patients (b) (4) years old diagnosed with Attention Deficit Hyperactivity Disorder (ADHD). This new triple-bead formulation is based on the approved product Adderall® XR (NDA 21303), but allows relatively sustained-release delivery that extends up to 16 hours post-administration to provide ADHD patients with symptom control throughout the day following a convenient single morning dose.

This NDA 22063 is currently a Class 2/Resubmission by Shire Development LLC (filed under a 505(b)(1) application on 12 December, 2016). The original application was filed on 21 July 2006. An Approvable Letter was issued by FDA 18 May, 2007 under the trade name (b) (4) This current Class2/Resubmission aims to address all the deficiencies identified in the Approvable Letter.

1.2 Brief Discussion of Nonclinical Findings

From a nonclinical perspective, the original application was considered approvable pending the incorporation of the findings from additional nonclinical studies [pre- and postnatal developmental reproductive toxicology study and the juvenile animal study] into the drug's label.

Review of the pre- and postnatal reproductive toxicology study and the juvenile animal study were completed under the original application for this NDA 22063 by Dr.Ikram Elayan (dated May 10, 2007). Changes in activity, body weight, and reproductive performance were observed in the reproductive toxicology study as a result of treatment with amphetamine during pregnancy and lactation on the dams and the pups (F1 generation). Results from juvenile rat study indicated changes in activity, learning, and memory in pup rats treated with the MAS at a critical stage of their development (starting from post natal day 7 to maturation). Relevant changes from both studies are to be described in the labeling (see Section 1.3.3). Changes in the label (Sections 8 and 13) have been incorporated to include findings from these studies and to reflect consistency with the dose multiples based on the most sensitive and appropriate population age group of patients.

Information on nonclinical findings for carcinogenicity studies, genotoxicity studies, and fertility studies are minimally modified from the label for Adderall® XR to reflect dose multiples based on the most sensitive and appropriate population group of patients.

The new formulation includes an excipient (b) (4) Nonclinical studies for qualification of this excipient were reviewed under DMF (b) (4) (see Dr.Elayan's review dated May 10, 2007 under NDA 22063), and were considered adequate based on the results indicating that the excipient is not absorbed systemically in the rat and clinical data submitted by the sponsor (see Section 2.4).

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS
Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.