CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

022063Orig1s000

PRODUCT QUALITY REVIEW(S)

Recommendation: Approval

NDA 022063
Review# 2

Drug Name/Dosage Form	**Mydayis** (mixed salts of a single-entity amphetamine product) extended-release capsules
Strength	12.5 mg, 25 mg, 37.5 mg, 50 mg
Route of Administration	Oral
Rx/OTC Dispensed	Rx
Applicant	Shire Development LLC

SUBMISSION(S) REVIEWED	DOCUMENT DATE	DISCIPLINE(S) AFFECTED
N-0044	*12/20/2016*	*All*
N-0028	*04/26/2017*	*Drug product*
N-0032	*5/16/2017*	*Process*
N-0033	*5/18/2017*	*Process*

Quality Review Team

DISCIPLINE	PRIMARY REVIEWER	SECONDARY REVIEWER
Drug Master File/Drug Substance	Haripada Sarker	Ben Stevens
Drug Product	Dan Berger	Wendy Wilson-Lee
Process	Yahong Wang	Akm Khairuzzaman
Microbiology	Yahong Wang	Akm Khairuzzaman
Facility	Zhong Li	Peter Zhihao Qiu
Biopharmaceutics	Jing Li	Ta-Chen Wu
ORA Lead	Adam Cooke	Johnetta Walters
Regulatory Business Process Manager	Grafton Adams	
Application Technical Lead	David Claffey	

Quality Review Data Sheet

1. RELATED/SUPPORTING DOCUMENTS

A. DMFs:

DMF #	Type	Holder	Item Referenced	Status	Date Review Completed	Comments
(b) (4)	Type II	(b) (4)	Dextroamphetamine saccharate	Adequate	12 MAY 2017	
	Type II		Amphetamine aspartate	Adequate	4 Nov 2016	
	Type II		Dextroamphetamine sulfate	Adequate	12 MAY 2017	
	Type II		Amphetamine sulfate	Adequate	9 Nov 2016	
	Type III		(b) (4)	*		
	Type III			*		
	Type IV			*		
	Type IV			*		
	Type IV			*		
	Type IV			*		

*adequate information in application.

B. Other Documents: *IND, RLD, or sister applications*

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
IND	66329	IND for this product
IND	58037	Adderall XR
NDA	21303	Adderall XR
NDA	11522	Adderall

2. CONSULTS

None

Executive Summary

I. Recommendations and Conclusion on Approvability

Recommend approval from a product quality perspective. The applicant resolved the drug product dissolution deficiencies and demonstrated that they are still capable of manufacturing product of adequate quality.

II. Summary of Quality Assessments

A. Product Overview

The proposed product, Mydayis extended release capsules, is similar to Adderall XR, but with a longer period of efficacy. Four strengths are proposed - 12.5 mg, 25 mg, 37.5 mg, and 50 mg. It is indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD). The applicant currently markets both Adderall and Adderall XR. These are immediate and extended release formulations of amphetamine mixed salts, with efficacy lasting ca. 4 and 8 hours, respectively. Patients sometimes take a dose of the immediate release product in the afternoon in order to extend the duration of efficacy of the extended release product through the evening hours. This NDA proposes the marketing of an extended release formulation of mixed amphetamine salts in a capsule dosage form with up to 16-hour duration of effect – this is intended to eliminate the need for the additional dosing of the of IR product. The pharmacokinetic profile of the formulation was targeted to be similar to a 20 mg dose of Adderall XR® followed by a 10 mg dose of ADDERALL® administered 8 hours later.

In the first review cycle an approval recommendation was made from a CMC perspective, however an approvable action was taken in 2007, because of deficiencies related to the drug product dissolution method. In this resubmission these deficiencies were adequately addressed. Several manufacturing and control changes were made since the previous submission. Additional data were provided which supported the changes. A drug product expiry period of 24 months was found acceptable.

Non-Proprietary Name Issue: Note that the non-proprietary name for this product will be (mixed salts of a single-entity amphetamine product) extended-release capsules. This is identical to Adderall XR's non-proprietary name. It is also noted that each has a 25 mg dosage strength. OPQ recognizes the potential for confusion and prescribing errors, however the non-proprietary name alone cannot be expected to describe the entire product, including its specific pharmacokinetics. Other labeling elements will be required to distinguish this product from Adderall XR, including proprietary name, ancillary carton statements, capsule colors and markings, NDC number, etc. This issue is outlined in more detail towards the end of this Executive Summary section.

Proposed Indication(s) including Intended Patient Population	***ADHD in patients (b) (4) years and older***
Duration of Treatment	***Chronic***
Maximum Daily Dose	***50 mg for adults, 25 mg pediatrics***
Alternative Methods of Administration	***Sprinkle capsule contents on apple sauce.***

B. Quality Assessment Overview

DRUG SUBSTANCE: The drug product contains equal amounts (by weight) of four amphetamine salts: dextroamphetamine sulfate and amphetamine sulfate, dextroamphetamine saccharate and amphetamine aspartate monohydrate. This results in a (b) (4) mixture of dextro- to levo- amphetamine base equivalent. All drug substance information is referenced to NDA 21303 and the related DMFs (DMF (b) (4) (dextroamphetamine saccharate), DMF (b) (4) (amphetamine aspartate), DMF (b) (4) (dextroamphetamine sulfate), DMF (b) (4) (amphetamine sulfate). Each was found adequate to support this application. This same salt mixture is used in several other amphetamine products.

DRUG PRODUCT:
The drug product will be marketed in capsule strengths of 12.5 mg, 25 mg, 37.5 mg, and 50 mg. All strengths are expressed in terms of the amount of mixed amphetamine salts. Each capsule contains immediate release beads and delayed release beads. The beads are composed of a sugar sphere core coated in a drug layer and further coated with (b) (4) layer(s) – then filled into hard gelatin capsules. The three larger strengths are dose proportional – just differing in capsule fill. The 25 mg, 37.5 mg and 50 mg strength capsule contains three types of drug-releasing beads - an immediate release and two types of delayed release beads - which release amphetamine at either pH 5.5 or pH 7.0. The former releases drug after release from the stomach while the latter will not release the drug until it reaches further down the GI tract where the pH is more neutral. The 12.5 mg strength capsules also contain immediate release beads and two types of delayed release beads. However the immediate release and first (pH 5.5) delayed release bead differs from that of the other strengths (b) (4)

Full CMC details are found in the 2007 Review #1 where an approval action was recommended from a CMC perspective – although changes to the dissolution test and acceptance criteria were requested. In this resubmission the applicant provided support

for the generally minor manufacturing and control changes. Three batches of each drug product strength were manufactured in 2014 to support the resubmission. They all met specification. Stability data through 12 months were provided for three commercial-scale batches of each strength. No significant changes were seen in these or during accelerated storage. 48 month long term stability data were provided for the pilot-scale batches from the original 2007 submission – again no significant changes were apparent. The totality of these data support the proposed 24 month drug product expiry period.

Dr. Yahong Wang, the OPF process reviewer, participated in the PAI at the (b) (4) drug product manufacturing site. Additional supporting data were requested which supported the proposed commercial manufacturing process. The manufacturing process utilizes (b) (4) to produce the beads for the 12.5 mg strength capsules (b) (4) and for the higher three strengths (b) (4). The manufacturing process for commercial scale retains the same unit operations and utilizes equipment of the same design and operating principles as those for the exhibit batches. A risk assessment was carried out on the drug product manufacturing process, with the process for each bead type undergoing a Design of Experiments (DoE) a (b) (4) batch size to examine the effects of key processing parameters. This demonstrated that the process was adequately controlled and robust.

The dissolution specifications for the release and stability were updated at Agency request (approvable letter (May 18, 2007) and the Agency's response to the Sponsor's Type C Meeting request (April 25, 2014). A (b) (4) minute dissolution time point was added, and dissolution acceptance criteria were tightened to a (b) (4) range. The method was found to have some (b) (4) and was found adequate as a quality control. In vitro dose dumping was found at ethanol levels above 20%. The extended release claim was found to be acceptable.

The preapproval inspection of the (b) (4) drug product manufacturing site found that the drug substance analytical methods were not transferred from the (b) (4) drug substance manufacturing sites. Method transfer and validation data were requested by the investigator and OPF. This was received on (b) (4). Although the data did not completely meet Agency GMP expectations it was determined to be a low risk issue and the site was found to be acceptable to support this application. (b) (4) is expected to continue working this issue and ORA will ensure that this is followed-up in the next inspection of this site.

Non-Proprietary Name Issue: Note that the non-proprietary name for this product will be (mixed salts of a single-entity amphetamine product) extended-release capsules. This is identical to Adderall XR's non-proprietary name. It is also noted that each has a 25 mg dosage strength. The applicant proposed using (b) (4) to aid in distinguishing these products. This was found unacceptable in-line with the Nomenclature Guidelines referenced by USP <1121>, which specifically states that

" (b) (4) should not be used. DMEPA were made aware of this issue – as were the OPQ and OGD labeling groups. The Agency has requested that the applicant propose ways to educate consumers and HCPs on the difference between these products. Such educational materials were submitted for review in a 12 MAY 2017 amendment. These materials used the term ' (b) (4) to distinguish the products – DMEPA and OPDP were made aware that this term was unacceptable. The bottom-line is that OPQ recommends the nonproprietary name be (mixed salts of a single-entity amphetamine product) extended-release capsules. We recognize the potential for prescribing errors and confusion that this name may cause – especially as Mydayis and Adderall XR share a 25 mg dosage strength. However, the Agency has requested that the applicant to propose ways to distinguish these products since at least the 2007 action letter. The non-proprietary name alone cannot be expected to describe the entire product, including its specific pharmacokinetics. Other labeling elements will be required to distinguish this product from Adderall XR, including proprietary name, ancillary carton statements, capsule colors and markings, NDC number, etc. Recognizing that the proprietary name will likely be a prominent distinguishing feature for this product, OGD were alerted to this issue, as generic products generally do not have a nonproprietary name. They discussed this within their labeling teams and indicated that they acknowledge this issue, but did not have any recommendations on alternatives (email Sarah Kurtz 15 MAY 2017).

C. Special Product Quality Labeling Recommendations

- Ensure that the product is used immediately after sprinkling on food as prolonged exposure may impact the beads' enteric coating.
- Ensure that the product's dosage form designation in the nonproprietary name is 'extended release capsules'.
- Alcohol dose dumping language has been added by the biopharm review team.
- Labeling elements will be required to distinguish this product from Adderall XR, including proprietary name, ancillary carton statements, etc.

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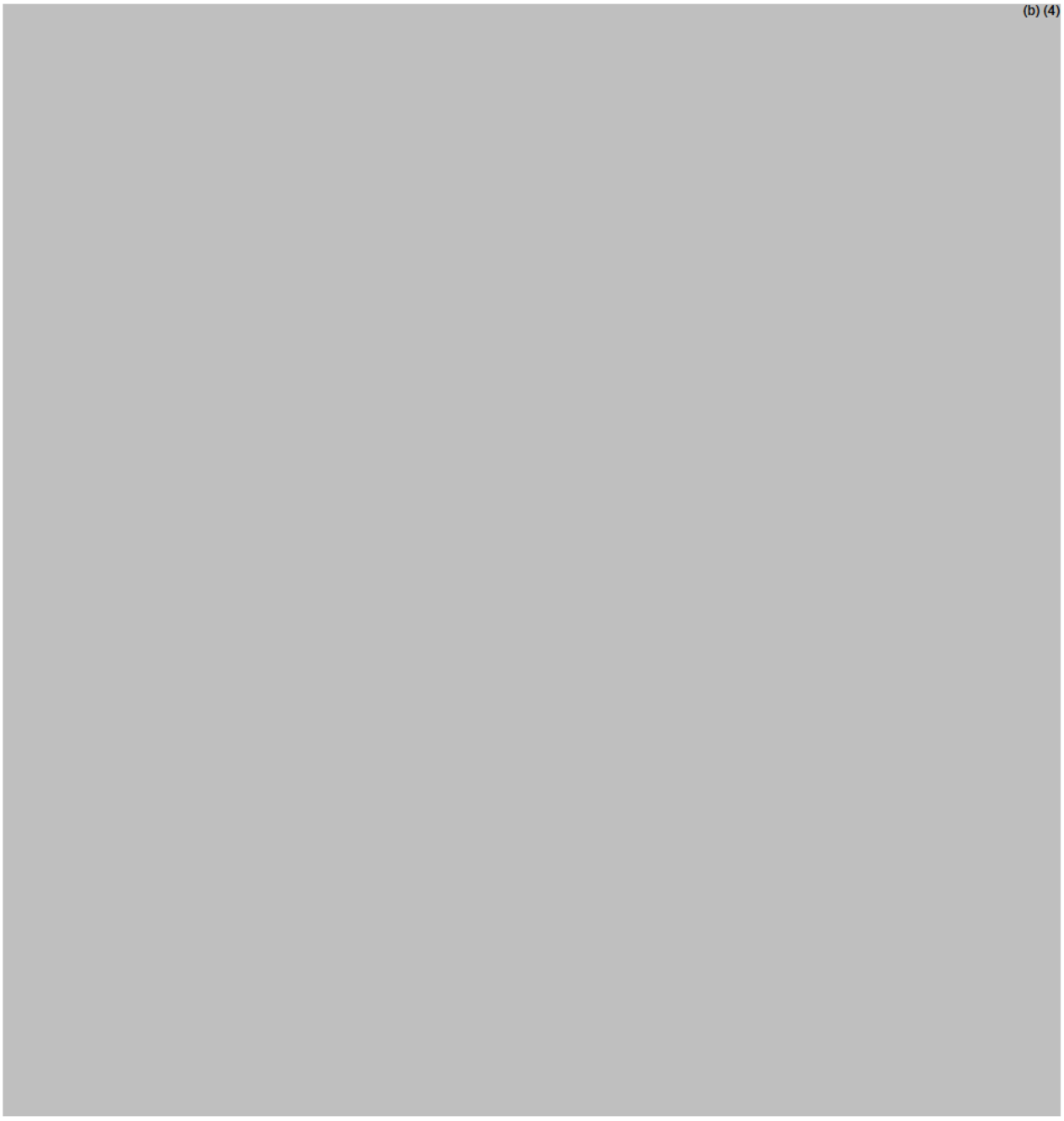
LABELING

NDA 22063

R Regional Information

1.14 Labeling

(b) (4)



(b) (4)

Reviewer's Assessment:

Item	Comments on the Information Provided in NDA	Conclusions
Proprietary name, established name (font size and prominence (21 CFR 201.10(g)(2))		Adequate
Strength (21CFR 201.10(d)(1); 21.CFR 201.100(b)(4))		Adequate
Route of administration 21.CFR 201.100(b)(3))	Dosage form should be modified to state: extended-release capsules	Needs revision
Net contents* (21 CFR 201.51(a))		Adequate
Name of all inactive ingredients (Quantitative ingredient information is required for injectables) 21CFR 201.100(b)(5)**		N/A for oral dose
Lot number per 21 CFR 201.18		Adequate
Expiration date per 21 CFR 201.17		Adequate
"Rx only" statement per 21 CFR 201.100(b)(1)		Adequate
Storage (not required)	Storage should be modified to: Store at room temperature, 20ºC to 25ºC (68ºF to 77ºF). Excursions permitted between 15 ºC to 30º C (59ºF to 86º F)	Needs revision

NDC number (per 21 CFR 201.2) (requested, but not required for all labels or labeling), also see 21 CFR 207.35(b)(3)		Adequate
Bar Code per 21 CFR 201.25(c)(2)***		Adequate
Name of manufacturer/distributor (21 CFR 201.1)		Adequate
Others		

*21 CFR 201.51(h) A drug shall be exempt from compliance with the net quantity declaration required by this section if it is an ointment labeled ''sample'', ''physician's sample'', or a substantially similar statement and the contents of the package do not exceed 8 grams.
**For solid oral dosage forms, CDER policy provides for exclusion of "oral" from the container label.
**Not required for Physician's samples. The bar code requirement does not apply to prescription drugs sold by a manufacturer, repacker, relabeler, or private label distributor directly to patients, but versions of the same drug product that are sold to or used in hospitals are subject to the bar code requirements.

Information Request, 18 May, 2017: *Revise the description "* [redacted] (b) (4) *Capsule" to "Extended-Release Capsule" to meet USP guidelines.*

Sponsor's Response Summary (19 May, 2017):

Shire has requested reconsideration of the change to the description of the extended-release capsules. The Applicant's request is based on the Applicant's efforts to differentiate the drug product from Adderal XR (extended-release) in proposed educational materials, and the Applicant further contends that the description more accurately reflects the drug product formulation.

FDA Response (24 May, 2017):

We acknowledge your 19 MAY 2017 email response to the 18 MAY 2017 request to change the dosage form designation from [redacted] (b) (4) to 'extended release' and recognize the need to distinguish this product from products for shorter duration. However it is not possible to do so based on the nonproprietary name. The Nomenclature Guidelines referenced by USP <1121> states that "Expressions such as "prolonged-release", "repeat-action", "controlled-release", "sustained-release", and their corresponding acronyms should not be used to describe such dosage forms." Therefore we request that you revise all labeling to reflect 'extended release' dosage form designation.

QUALITY ASSESSMENT

Information Request, 18 May, 2017: *Revise the storage condition to be consistent with USP controlled room temperature: "Store at room temperature, 20˚C to 25˚C (68˚F to 77˚F). Excursions permitted between 15˚C to 30˚C (59˚F to 86˚F)."*

Sponsor's Response Summary (19 May, 2017):

Shire has accepted the request to revise the storage condition text, and the changes will be incorporated in labels which will be submitted to NDA 022063.

Reviewer's Assessment: Inadequate

The Applicant has been advised that the container labels must be revised to describe the dosage form as extended release capsules, and that the storage condition description must be modified to be consistent with USP guidelines. In response to the request to modify the description of the dosage form, the Applicant requested reconsideration in order to differentiate from extended release Adderall. However, as USP <1121> stipulates that "extended-release" must be used for this dosage form, the Agency has reiterated the necessity to make this change to conform to USP nomenclature guidelines. The Applicant is expected comply with this revision to be USP compliant. As the Applicant has agreed to revise the storage condition text and to submit the changes, the container labels are otherwise acceptable.

Carton Labeling

Not provided

Reviewer's Assessment:
NA

List of Deficiencies:

1. *Revise the description "* (b) (4) *Capsule" to "Extended-Release Capsule" to meet USP guidelines.*
2. *Revise the storage condition to be consistent with USP controlled room temperature: "Store at room temperature, 20˚C to 25˚C (68˚F to 77˚F). Excursions permitted between 15˚C to 30˚C (59˚F to 86˚F)."*

Primary Labeling Reviewer Name and Date:

Dan Berger 5/25/2017

Secondary Reviewer Name and Date (and Secondary Summary, as needed):

Wendy Wilson-Lee 5/25/2017

Dan Berger

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Wendy Wilson- Lee

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BIOPHARMACEUTICS

Product Background:

NDA: 022-063

Drug Product Name / Strength: Mydayis (mixed salts of a single-entity amphetamine product) [redacted] Capsules (or SHP465) / 12.5, 25, 37.5, and 50 mg

Route of Administration: Oral

Applicant Name: Shire

Review Summary:

Mydayis (mixed salts of a single-entity amphetamine product) [redacted] Capsules (also known as SHP465) is a once-daily, triple-bead, [redacted] single-entity mixed amphetamine salt (MAS) product for oral administration, and is comprised of sulfate salts of dextro and levo-amphetamine, with dextroamphetamine saccharate and amphetamine aspartate monohydrate. The current formulation of SHP465 capsules is based conceptually on a frequently used combination in clinical practice, i.e., ADDERALL XR® in the morning, followed by a dose of MAS later in the day.

The proposed dissolution method was developed based on the approved method for ADDERALL XR® (extended-release) Capsules which has a similar formulation design as the proposed drug product. The proposed dissolution method is discriminating with respect to alterations in the encapsulation process. Overall, the proposed dissolution method is adequate for quality control of SHP465 capsules. The proposed dissolution acceptance criteria,based on the Agency's previous recommendations, are acceptable.

From a Biopharmaceutics perspective, NDA 022-063 for Mydayis (mixed salts of a single-entity amphetamine product) [redacted] Capsules (or SHP465) / 12.5, 25, 37.5, and 50 mg is recommended for **APPROVAL**.

The FDA recommended dissolution method and acceptance criteria for Mydayis (mixed salts of a single-entity amphetamine product) [redacted] Capsules (or SHP465) are as follows:

Apparatus	USP Apparatus II (paddles)
Paddle Speed	50 RPM
Media	Media 1: pH 1.1±0.1, Dilute HCl Media 2: pH 6.0±0.1, Phosphate Buffer Media 3: pH 7.5±0.1, Phosphate Buffer
Temperature	37.0±0.5 °C

Dissolution Volume	750mL Dilute HCl for the first 2 hours 950mL pH 6.0 Phosphate Buffer for the 3rd hour 1000mL pH 7.5 Phosphate Buffer for the remainder
Acceptance criteria	

Time (hr)	% Dissolved
0.5	(b) (4)
2	
3	
10	

List of Submissions being reviewed:

eCTD sequence #	Received Date	Document
0022	12/20/2016	Class 2 Resubmission

Highlight Key Outstanding Issues from Last Cycle:

- Lack of in vitro alcohol dose dumping study, noted in the Approvable Letter dated 18 May 2007 (http://darrts.fda.gov:9602/darrts/ViewDocument?documentId=090140af80142349)
- Pending acceptance of the final dissolution method and acceptance criteria for all strengths, noted in the Approvable Letter dated 18 May 2007 (http://darrts.fda.gov:9602/darrts/ViewDocument?documentId=090140af80142349)
- Lack of dissolution method development report, noted in the FDA written comments dated 25 Apr 2014 (\\CDSESUB1\evsprod\NDA022063\0022\m1\us\correspondence-regarding-meetings-25apr2014.pdf)
- Pending addition of the (b) (4)-min sampling time to monitor the dissolution of the immediate release component, noted in the FDA written comments dated 25 Apr 2014 (\\CDSESUB1\evsprod\NDA022063\0022\m1\us\correspondence-regarding-meetings-25apr2014.pdf)

Concise Description Outstanding Issues Remaining: None

BCS Designation

No BCS designation request was submitted. The drug product was not evaluated by the FDA BCS committee.

Reviewer's Assessment:

Solubility: All APIs are freely soluble in water independent of pH (see Table 1).

Table 1. Aqueous Solubility of the APIs

API	Aqueous solubility
Amphetamine Aspartate Monohydrate	Freely soluble in water pH: 1.3, 4.5, 6.0, 7.5 Solubility(mg/mL): 1.049, 1.013, 1.018, 1.012
Amphetamine Sulfate, USP	Freely soluble in water pH: 1.3, 4.5, 6.0, 7.5 Solubility(mg/mL): 1.048, 1.045, 1.024, 1.047
Dextroamphetamine Saccharate	Freely soluble in water pH: 1.3, 4.5, 6.0, 7.5 Solubility (mg/mL): 1.040, 1.009, 1.012, 1.046
Dextroamphetamine Sulfate, USP	Freely soluble in water pH: 1.4, 4.5, 6.0, 7.5 Solubility(mg/mL): 1.039, 1.043, 1.044, 1.012

Permeability: Not provided.

Dissolution: Refer to section "Dissolution Method and Acceptance Criteria" below.

Dissolution Method and Acceptance Criteria

The dissolution method shown in Table 2 was recommended by FDA in the Approvable letter dated 18 May 2007. The dissolution acceptance criteria were proposed based on the FDA recommendation dated 18 May 2007 (for 2, 3, and 10 hour time points) and 25 Apr 2014 (addition of 0.5 hour time point).

Table 2. The Dissolution Method and Acceptance Criteria

Apparatus	USP Apparatus II (paddles)
Paddle Speed	50 RPM
Media	Media 1: pH 1.1±0.1, Dilute HCl Media 2: pH 6.0±0.1, Phosphate Buffer Media 3: pH 7.5±0.1, Phosphate Buffer
Temperature	37.0±0.5 °C

Dissolution Volume	750mL Dilute HCl for the first 2 hours 950mL pH 6.0 Phosphate Buffer for the 3rd hour 1000mL pH 7.5 Phosphate Buffer for the remainder
Proposed Acceptance criteria	

Time (hr)	% Dissolved
0.5	(b) (4)
2	
3	
10	

Dissolution Method Development: (\\CDSESUB1\evsprod\NDA022063\0022\m3\32-body-data\32p-drug-prod\spd465-capsule-all-strengths\32p2-pharm-dev\pharmaceutical-development-drug-product.pdf)

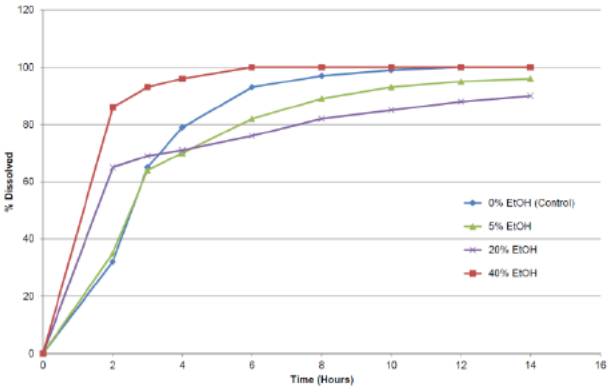
(b) (4)

dissolution acceptance criteria, and (2) the acceptance criteria are basically what FDA previously recommended based on the complete dissolution profiles. The proposed dissolution acceptance criteria are acceptable.

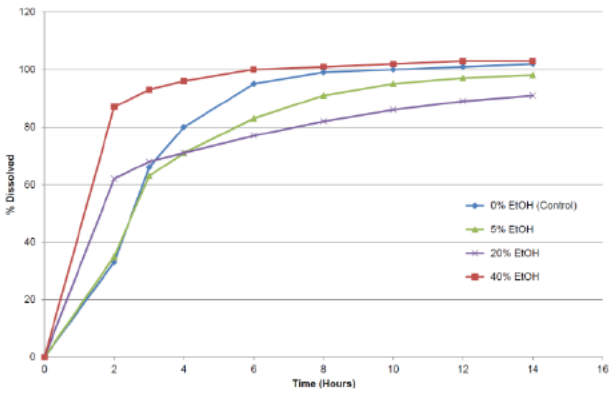
MODIFIED RELEASE ORAL DRUG PRODUCTS – In-Vitro Alcohol Dose Dumping

Two in-vitro alcohol dose dumping studies were conducted in dissolution media with 0, 10, 20, and 40% (v/v) ethanol (\\CDSESUB1\evsprod\NDA022063\0022\m3\32-body-data\32p-drug-prod\spd465-capsule-all-strengths\32p2-pharm-dev\pharmaceutical-development-drug-product.pdf).

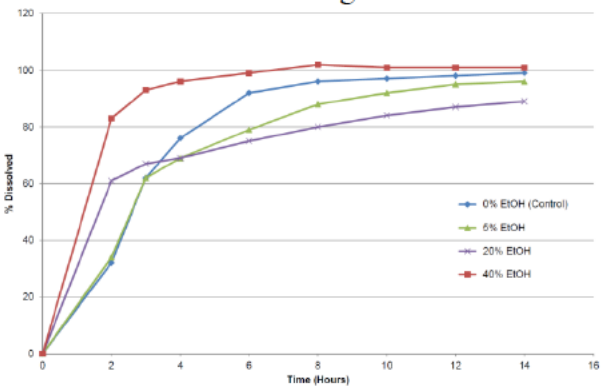
Study (1): Full dissolution profiles (up to 14 hours) were obtained at n=12 units for all strengths of SHP465 capsules (12.5, 25, 37.5, and 50 mg) using the dissolution conditions described in the original NDA submission (dated 21 Jul 2006). The mean dissolution overlay graphs for each dosage strength, comparing the drug release from SHP465 capsules as a function of ethanol content, are shown in Figure 2. Increased drug releases were observed at initial timepoints across dosage strengths in the presence of 20% and 40% ethanol.



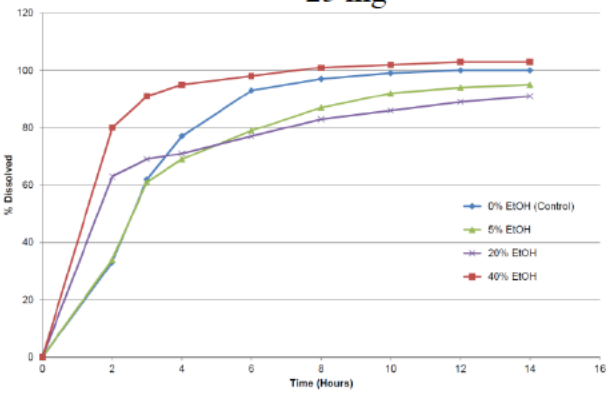
12.5 mg



25 mg



37.5 mg



50 mg

Figure 2. Overlay Graph of Mean Dissolution Results (Full Profiles) Using Ethanol Media for SHP465 Capsules

Study (2): Full dissolution profiles were obtained at n=12 units for the highest 50-mg strength of SHP465 capsule with sampling times at every 15 minutes for up to 3 hours. The graphic illustration of the mean dissolution profiles obtained in the various amounts of ethanol is presented in Figure 3.

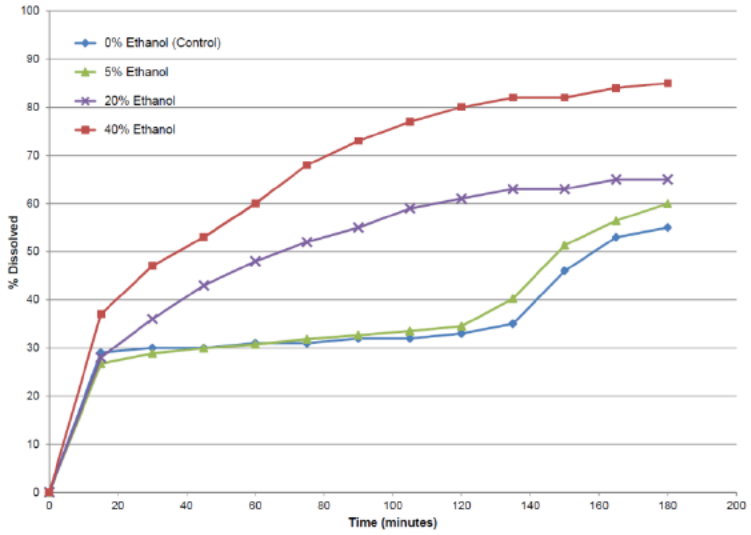


Figure 3. Mean dissolution profiles for SHP465 50 mg capsules using ethanol media (early time points)

The results showed that,with the increasing amounts of ethanol (at 20% and most noticeably at 40%), the dissolution rate for SHP465 capsules is significantly increased beyond the 20-minute test point. The results may be attributed to the alcohol solubility of the functional coatings used for the pulsatile delayed and delayed (b) (4) beads in the SHP465 capsule formulation.

Reviewer's Assessment:

The presence of increasing amount of ethanol at 20% and higher appear to proportionally increase the dissolution rate of the proposed drug product in early time points (less than 3 hours). It is noted that the following language regarding alcohol intake was included in the proposed labeling of the drug product:

****

Page 16, section 12.3:
Alcohol Effect

(b) (4)

Page 23, Medication Guide:
Tell your doctor if you or your child has ever abused or been dependent on alcohol, prescription medicines or street drugs.

****

It appears that there is no clear labeling instruction regarding the potential risk or clinica consequence as a result of concomitant use of MYDAYIS and alcohol consumption. The results of in-vitro alcohol-induced dosing dumping will be communicated to the Clinical and the Clinical Pharmacology review teams for the proper labeling recommendation.

EXTENDED RELEASE DOSAGE FORMS – Extended Release Claim

According to the OCP review for the original submission of NDA 022-063,[2] a single dose of 37.5 mg of the proposed drug product is bioequivalent to an ADDERALL® XR 25 mg + mixed amphetamine salts IR 12.5 mg administered 8 hours later. The pharmacokinetic comparison, as illustrated in Figure 4, suggested that SPD465 capsule exhibits characteristics of extended-release that appear to further extended the release (noticable the prolonged time to peak concentration or Tmax) in comparison with ADDERALL XR®. The results support the extended-release claim of the proposed drug product.

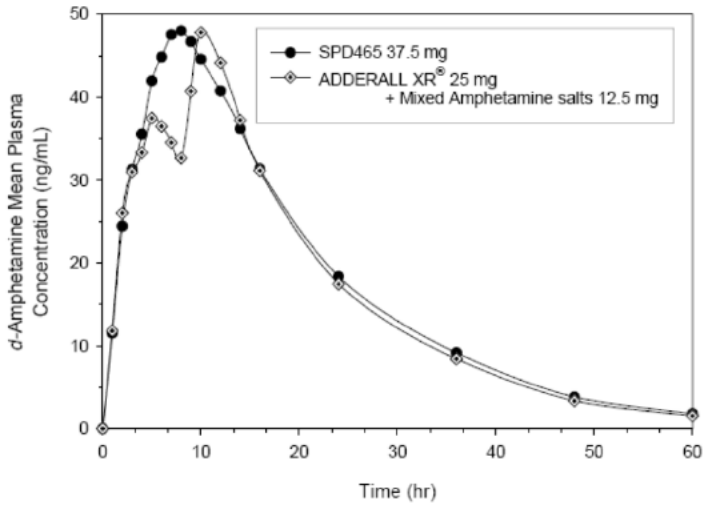


Figure 4. Mean PK profile comparison between a single dose of SPD465 37.5 mg, and an ADDERALL XR® 25 mg + mixed amphetamine salts IR 12.5 mg administered 8 hours later

List of Deficiencies:

None.

Primary Biopharmaceutics Reviewer Name and Date: Jing Li Ph.D., 3/21/2017

Secondary Reviewer Name and Date (and Secondary Summary, as needed):
Ta-Chen Wu, Ph.D., 3/28/2017.

Jing Li

Digitally signed by Jing Li
Date: 3/29/2017 10:01:34AM
GUID: 508da7420002bb05ac913303b23c39bb

Ta-Chen Wu

Digitally signed by Ta-Chen Wu
Date: 3/29/2017 10:07:28AM
GUID: 508da6df000269e151ff37cd8f4e13a1

David Claffey

Digitally signed by David Claffey
Date: 6/05/2017 10:39:54AM
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