

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**Application Number** 21-150

**STATISTICAL REVIEW(S)**

**STATISTICAL REVIEW AND EVALUATION  
STABILITY STUDY**

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**NDA Number:** 21-150  
**Applicant:** Pfizer Inc.  
**Name of Drug:** Zyrtec-D 12 Hour™ (Cetirizine HCl/Pseudoephedrine HCl 5/120 mg Bilayer Tablet)  
**Document Reviewed:** Stability data reports – Dated 2/8/01  
**Statistical Reviewer:** Feng Zhou, HFD-715  
**Chemistry Reviewer:** Prasad Peri, Ph.D., HFD-570

## I. Introduction

The sponsor submitted the stability data to support its proposed 24-month shelf lives for 100ct HDP, and 14ct HDP package types for Zyrtec-D 12 Hour™. The three package types of the product were stored at 25°C/60%RH condition. The stability data include three batches for each package type.

## II. Sponsor's Stability Analysis

The sponsor submitted the stability data reports for each testing-parameters of three package types (100ct HDP, and 14ct HDP) on February 28, 2001 and the electronic stability data (in SAS transport files) on March 5, 2001. The SAS transport files contain stability data through 24 months for the Cetirizine HCl/Pseudoephedrine HCl 5/120 mg Bilayer Tablets, NDA 21-150. The data were further divided by package type (100ct HDP, and 14ct HDP) and storage condition (25C/60%RH and 30C/60%RH). For the p-chlorobenzophenone, individual unspecified degradants, total unspecified degradants, and total degradants, the sponsor submitted only partial data in the SAS transport files. After discussing with Dr. Peri, this reviewer includes only the stability analysis for Assay of Cetirizine HCl, Assay of Pseudoephedrine HCl, Dissolution at 30 minutes, Dissolution at 1 hour, and Water Content.

There are ~~stability~~ data of three batches through 24 months for the above five parameters of 100ct HDP, and 14ct HDP package types at 25°C/60%RH. The test times for the parameters of these nine batches data were listed in Table A.

The sponsor estimated the expiration dating periods based on data of 25C/60%RH storage condition. Table B lists the specifications for the parameters the sponsor used to establish the stability for Zyrtec-D 12 Hour™. The sponsor submitted the details of its

estimation analysis and proposes an expiration dating period of 24 months for the Aclar, 100ct HDP, and 14ct HDP packaging configurations when the drug products are stored at 25°C/60%RH condition.

Table A  
Summary of all Stability Data Points Submitted by the Sponsor for  
Zyrtec-D 12 Hour™ Stored at 25C/60%RH

Test	Package	Batch	Time Points (Month)						
			0	3	6	9	12	18	24
Assay of Cetirizine HCl	100ct HDP 14ct HDP	8124, 8125, 8126	S	S	S	S	S	S	S
		8115, 8116, 8117	S	S	S	S	S	S	S
		8118, 8119, 8120	S	S	S	S	S	S	S
Assay of Pseudoephedrine HCl	100ct HDP 14ct HDP	8124, 8125, 8126	S	S	S	S	S	S	S
		8115, 8116, 8117	S	S	S	S	S	S	S
		8118, 8119, 8120	S	S	S	S	S	S	S
Dissolution/cet 30 min	100ct HDP 14ct HDP	8124, 8125, 8126			S	S	S	S	S
		8115, 8116, 8117			S	S	S	S	S
		8118, 8119, 8120			S	S	S	S	S
Dissolution/pse 1 hour	100ct HDP 14ct HDP	8124, 8125, 8126	S	S	S	S	S	S	S
		8115, 8116, 8117	S	S	S	S	S	S	S
		8118, 8119, 8120	S	S	S	S	S	S	S
Water Content	100ct HDP 14ct HDP	8124, 8125, 8126	S	S	S	S	S	S	S
		8115, 8116, 8117	S	S	S	S	S	S	S
		8118, 8119, 8120	S	S	S	S	S	S	S
p-chlorobenzhydrol	100ct HDP 14ct HDP	8124, 8125, 8126	I	I	I	I	I	I	I
		8115, 8116, 8117	I	I	I	I	I	I	I
		8118, 8119, 8120	I	I	I	I	I	I	I
p-chlorobenzophenone	100ct HDP 14ct HDP	8124, 8125, 8126	I	I	I	I	I	I	I
		8115, 8116, 8117	I	I	I	I	I	I	I
		8118, 8119, 8120	I	I	I	I	I	I	I
Individual Unspecified Degradants	100ct HDP 14ct HDP	8124, 8125, 8126	I	I	I	I	I	I	I
		8115, 8116, 8117	I	I	I	I	I	I	I
		8118, 8119, 8120	I	I	I	I	I	I	I

S = Submitted in electronic copy (March 05, 2001)

I = Incomplete in electronic copy (March 05, 2001)

Table B  
List of Specifications the Sponsor Used to Establish the Stability  
For Zyrtec-D 12 Hour™

Test Parameter	Acceptance Criteria
Assay of Cetirizine HCl	90 – 110 % of Label Claim
Assay of Pseudoephedrine HCl	90 – 110 % of Label Claim
Dissolution/cet 30 min	Q = —
Dissolution/pse 1 hour	— Label Claim Dissolved
Water Content	6% Maximum

### III. Reviewer's Stability Analysis

This reviewer analyzed the data in accordance with FDA's "Guidelines for Submitting Documentation for the Stability of Human Drugs Biologics." Data up to 24 months from three batches (8124, 8125, and 8126) of — package type, three batches (8115, 8116, and 8117) of 100ct HDP package type and three batches (8118, 8119, and 8120) of 14ct HDP package type stored at 25°C/60%RH were analyzed. The data submitted in electronic copy described in Table A with "S" indication were used in the reviewer's analyses.

The results of this reviewer's analysis presented in Table C.

In Table C, excluded the Dissolution at 30 minutes data for the three package types, the shortest estimated expiration-dating period, 36 months, is based on the Assay of Pseudoephedrine HCl data of three batches of 14ct HDP package type. Figure A shows the data of Pseudoephedrine HCl with the fitted line and the estimated expiration-dating period of the 14ct HDP package type. The data of the Dissolution at 30 minutes data of three batches of 100ct HDP package types estimated the 0 month expiration-dating period, because more than 30% of data are out of its specification. Table D shows the percentages of stability data that are out of its specification for each batch. Figures B, C, and D show the data of dissolution at 30 minutes with the fitted line and the estimated expiration-dating periods of the three package types.

### V. ~~Conclusion~~ Conclusion

The results of this reviewer's analysis using data of three batches for each package type show that the sponsor's stability data excluded the stability data of Dissolution at 30 minutes support a 24-month expiration date. The stability data of Dissolution at 30 minutes didn't support a 24-month expiration date.

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