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## RESULTS SUMMARY

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Appendix Table W summarizes the differences between the manufacturing processes of the original licensed Wyeth products and the Teva vaccines. As can be seen, the changes are minor and do not negatively influence the safety of the products.

**Appendix Table W: Comparison of the Barr and Wyeth Manufacturing Processes for Adenovirus Type 4 and Type 7 Adenovirus Drug Substances**

	Wyeth	Barr	Key Differences	Significance
<b>Cells</b>	Human Diploid Cells (WI-38)	Human Diploid Cells (WI-38)	None	None
<b>Virus</b>	ADV4 CL68578 p12 ADV7 55142 p13	ADV4 CL68578 p15 ADV7 55142 p16	None None	None None
<b>Cell Growth Medium</b>	EMEM Medium + 10% FBS and antibiotics	DMEM Medium + 10% FBS	Antibiotics removed	Increase Safety
<b>Infection Medium</b>	----- (b)(4) -----	----- (b)(4) -----	(b)(4)	(b)(4)
<b>MOI</b>	----- (b)(4) ----- -----	----- (b)(4) -----	(b)(4)	(b)(4)
<b>Incubation</b>	--- (b)(4) ---	--- (b)(4) ---	(b)(4)	(b)(4)
<b>Harvesting</b>	----- (b)(4) -----	----- (b)(4) -----	(b)(4)	(b)(4)
<b>Stabilizer</b>	----- (b)(4) -----	----- (b)(4) -----	(b)(4)	(b)(4)
<b>Lyophilizer Container</b>	----- (b)(4) -----	----- (b)(4) -----	----- (b)(4) -----	--- (b)(4) --- -----

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**Table FF: Dry Coating Raw Materials for Adenovirus Type 7**

Raw Material	Barr Product Code	Theoretical Weight (kg)
Anhydrous Lactose	---(b)(4)---	--(b)(4)--
Microcrystalline Cellulose	---(b)(4)---	--(b)(4)--
FD&C Yellow No. 6 Aluminum Lake ----- (b)(4) -----	---(b)(4)---	---(b)(4)---
Magnesium Stearate	---(b)(4)---	---(b)(4)---

**Table GG: Inner Core Raw Materials for Ad4 and Ad7**

	Barr Product Code	Theoretical Weight (kg)
Formulated Adenovirus Type 4 or 7, Lyophilized Intermediate1 (Drug Substance)	----- (b)(4) ----- -----	--(b)(4)--
Anhydrous Lactose	---(b)(4)--	--(b)(4)--
Microcrystalline Cellulose	---(b)(4)---	--(b)(4)--
Polacrillin Potassium	---(b)(4)---	---(b)(4)---
Magnesium Stearate	---(b)(4)---	---(b)(4)---

### 3.3. Coating Process for Drug Products

#### 3.3.1 Solution Preparation

**Table HH: Enteric Coating Dispersion Raw Materials for Ad4 and Ad7**

##### Enteric Coating Dispersion

Raw Material	Barr Product Code	Theoretical Weight (kg)
Cellulose Acetate Phthalate	---(b)(4)---	--(b)(4)--
Castor Oil	---(b)(4)---	--(b)(4)--
Acetone	---(b)(4)---	--(b)(4)--
Alcohol ----- (b)(4) -----	---(b)(4)---	--(b)(4)--

**Table II: Enteric Coating Dispersion Raw Materials for Ad7 batch ----- (b)(4) -----**

Raw Material	Barr Product Code	Theoretical Weight (kg)
Cellulose Acetate Phthalate	--(b)(4)--	--(b)(4)--
Castor Oil	--(b)(4)--	--(b)(4)--
Acetone	--(b)(4)--	-(b)(4)-
Alcohol----(b)(4)-----	--(b)(4)--	-(b)(4)-

### 3.3.2 Coating

### 3.5. Packaging

[(b)(4)]

**Table KK: Composition of Adenovirus Tablets, Type 4**

Ingredient	Function	Mg/Tab	%w/w
<b>Inner Core: Type 4</b>			
Formulated Adenovirus Type 4, Lyophilized Int.	Active	-(b)(4)-	-(b)(4)-
Anhydrous Lactose, NF ---(b)(4)---	Diluent	-(b)(4)-	-(b)(4)-
Microcrystalline cellulose, NF ---(b)(4)---	Diluent	-(b)(4)-	-(b)(4)-
Polacrillin Potassium, NF -----(b)(4)-----	Disintegrant	-(b)(4)-	-(b)(4)-
Magnesium Stearate, NF	Lubricant	-(b)(4)-	-(b)(4)-
<b>TOTAL</b>		-(b)(4)-	-(b)(4)-
<b>Outer Tablet; Type 4</b>			
Anhydrous Lactose, NF ---(b)(4)---	Diluent	-(b)(4)-	-(b)(4)-
Microcrystalline cellulose, NF---(b)(4)-----	Diluent	-(b)(4)-	-(b)(4)-
Magnesium Stearate, NF	Lubricant	-(b)(4)-	-(b)(4)-
<b>TOTAL</b>		-(b)(4)-	-(b)(4)-
<b>TOTAL: COMPRESSION-COATED CORE</b>		-(b)(4)-	
<b>Enteric Coating</b>			
Core	Tablet	-(b)(4)-	-(b)(4)-
Cellacelate, ---(b)(4)---	Enteric polymer	-(b)(4)-	-(b)(4)-
Castor Oil, ---(b)(4)---	Plasticizer	-(b)(4)-	-(b)(4)-
Acetone, NF – ---(b)(4)---	Solvent	*	
Alcohol -----(b)(4)-----	Solvent	*	

<b>Target Weight Gain</b>		-(b)(4)-	-(b)(4)-
<b>TOTAL OF ENTERIC-COATED TABLET</b>		-(b)(4)-	-(b)(4)-

**Table LL: Composition of Adenovirus Tablets, Type 7**

<b>Ingredient</b>	<b>Function</b>	<b>Mg/Tab</b>	<b>%w/w</b>
<b><i>Inner Core: Type 7</i></b>			
Formulated Adenovirus Type 7, Lyophilized Int.	Active	-(b)(4)-	-(b)(4)-
Anhydrous Lactose, NF –(b)(4)--	Diluent	-(b)(4)-	-(b)(4)-
Microcrystalline cellulose, NF ---(b)(4)---	Diluent	-(b)(4)-	-(b)(4)-
Polacrillin Potassium, NF ----(b)(4)-----	Disintegrant	-(b)(4)-	-(b)(4)-
Magnesium Stearate, NF	Lubricant	-(b)(4)-	-(b)(4)-
<b>TOTAL</b>		-(b)(4)-	-(b)(4)-
<b><i>Outer Tablet: Type 7</i></b>			
Anhydrous Lactose, NF –(b)(4)--	Diluent	-(b)(4)-	-(b)(4)-
Microcrystalline cellulose, NF ---(b)(4)---	Diluent	-(b)(4)-	-(b)(4)-
FD&C Yellow #6 Aluminum Lake -----(b)(4)----- -----	Colorant	-(b)(4)-	-(b)(4)-
Magnesium Stearate, NF	Lubricant	-(b)(4)-	-(b)(4)-
<b>TOTAL</b>		-(b)(4)-	-(b)(4)-
<b>TOTAL: COMPRESSION-COATED CORE</b>		-(b)(4)-	
<b><i>Enteric Coating</i></b>			
Core	Tablet	-(b)(4)-	-(b)(4)-
Cellacefate, ---(b)(4)----	Enteric polymer	-(b)(4)-	-(b)(4)-
Castor Oil, -----(b)(4)--	Plasticizer	-(b)(4)-	-(b)(4)-
Acetone, NF – ---(b)(4)---	Solvent	*	
Alcohol -----(b)(4)-----	Solvent	*	
<b>Target Weight Gain</b>		-(b)(4)-	-(b)(4)-
<b>TOTAL OF ENTERIC-COATED TABLET</b>		-(b)(4)-	-(b)(4)-

[(b)(4)]

All batches of Adenovirus Tablets, Type 4 and Type 7 have been evaluated by the established test methods and specifications. Table 40 and Table 41 summarize the methods, specifications and results for two batches only.

Tests	Methods	Limits	Results
Description	MTH-732	----- ------(b)(4)----- ----- -----	Conforms
Infectivity (Assay)		------(b)(4)-----	5.5 logTCID50
Infectivity ------(b)(4)-----		------(b)(4)-----	Mean: 5.4 logTCID50 Max: 5.7 logTCID50 Mini: 4.8 logTCID50
Identification (b)(4)		------(b)(4)-----	Positive
Identification (b)(4)		------(b)(4)-----	Positive
Disintegration ----(b)(4)---	---(b)(4)--	------(b)(4)----- -----	Conforms
Residual Solvents --(b)(4)-- --(b)(4)--- Water	MTH-732	-----(b)(4)----- -----(b)(4)----- -----(b)(4)-----	0.3% 1.3% 3.3%
General Safety		(b)(4)	Pass
------(b)(4)----- ------(b)(4)----- ------(b)(4)----- -----(b)(4)---- ------(b)(4)-----		-----(b)(4)----- -----(b)(4)----- -(b)(4)- -(b)(4)-	--(b)(4)--- --(b)(4)--- -(b)(4)- -(b)(4)-

Tests	Methods	Limits	Results
Description	MTH-732	----- ----- (b)(4) ----- -----	Conforms
Infectivity (Assay)		----- (b)(4) -----	5.8 logTCID <sub>50</sub>
Infectivity ---- (b)(4) -----		----- (b)(4) -----	Mean: 5.6 logTCID <sub>50</sub> Max: 6.0 logTCID <sub>50</sub> Mini: 5.4 logTCID <sub>50</sub>
Identification (b)(4)		----- (b)(4) -----	Positive
Identification (b)(4)		----- (b)(4) -----	Positive
Disintegration --- (b)(4) ---	-- (b)(4) --	----- (b)(4) ----- -----	Conforms
Residual Solvents	MTH-732		
-- (b)(4) --		---- (b)(4) -----	0.3%
-- (b)(4) --		---- (b)(4) -----	1.3%
Water		---- (b)(4) -----	2.5%

General Safety		(b)(4)	Pass
----(b)(4)----- ----(b)(4)----- ----- (b)(4)----- --(b)(4)-- ----- (b)(4)-----		----(b)(4)----- ----(b)(4)----- -(b)(4)- -(b)(4)-	-(b)(4)- --(b)(4)-- -(b)(4)- -(b)(4)-

[(b)(4)]

## 1. STABILITY SUMMARY AND CONCLUSION

**Table QQ: Summary of Adenovirus Vaccine Live Oral Type 4 and Type 7 Batches Used in Stability Studies**

<b>Batch Numbers</b>	----(b)(4)-----	----(b)(4)-----	----(b)(4)-----	----(b)(4)-----	----(b)(4)-----	----(b)(4)-----
<b>Batch Size (units)</b>	---(b)(4)----- -----	---(b)(4)----- -----	---(b)(4)----- -----	---(b)(4)----- -----	---(b)(4)----- -----	---(b)(4)----- -----
<b>Site of Manufacture</b>	Adenovirus Facility, Forest VA	Adenovirus Facility, Forest VA	Adenovirus Facility, Forest VA	Adenovirus Facility, Forest VA	Adenovirus Facility, Forest VA	Adenovirus Facility, Forest VA
<b>Date of Manufacture</b>	19-Jun-2006	19-Oct-2006	01-Nov-2006	23-May-2006	23-Aug-2006	24-Aug-2006
<b>Virus Type</b>	Type-4	Type-4	Type-4	Type-7	Type-7	Type-7
<b>Container Closure Description</b>	Bottle: 60cc -(b)(4)- White, Wide Mouth, Round, 38/400 Cap: -----(b)(4)----- ----- -----	Bottle: 60cc -(b)(4)- White, Wide Mouth, Round, 38/400 Cap: -----(b)(4)----- ----- -----	Bottle: 60cc -(b)(4)- White, Wide Mouth, Round, 38/400 Cap: -----(b)(4)----- ----- -----	Bottle: 60cc -(b)(4)- White, Wide Mouth, Round, 38/400 p: --- ---(b)(4)----- ----- -----	Bottle: 60cc -(b)(4)- White, Wide Mouth, Round, 38/400 Cap: -----(b)(4)----- ----- -----	Bottle: 60cc -(b)(4)- White, Wide Mouth, Round, 38/400 Cap: -----(b)(4)----- ----- -----



<b>Stability Study Number</b>	ARD_PRT-1559	ARD_PRT-2091	ARD_PRT-2092	ARD_PRT-1558	ARD_PRT-1988	ARD_PRT-1989
<b>Stability Study Start Date</b>	27-Jun-2006	14-Dec-2006	14-Dec-2006	14-Jun-2006	13-Sep-2006	13-Sep-2006

**Table RR: Summary of Adenovirus Vaccine Live Oral Type 4 and Type 7 Clinical Trial Material Used in Stability Studies**

<b>Batch Numbers</b>	----(b)(4)----- ----(b)(4)-----	----(b)(4)----- ----(b)(4)-----	----(b)(4)----- ----(b)(4)-----	----(b)(4)----- ----(b)(4)-----
<b>Packaging Configuration</b>	Bottle (1 Type 4 and 1 Type 7)	Bottle (1 Type 4 and 1 Type 7)	Bottle (1 Type 4 and 1 Type 7)	Bottle (1 Type 4 and 1 Type 7)
<b>Date of Packaging</b>	14-Jul-2006	30-Nov-2006	15-Mar-2007	15-Jun-2007
<b>Container Closure System</b>	Bottle: 30cc (b)(4), White, Wide Mouth, Round, 28/400 Cap: -----(b)(4)----- -----	Bottle: 30cc (b)(4), White, Wide Mouth, Round, 28/400 Cap: - -----(b)(4)----- -----	Bottle: 30cc (b)(4), White, Wide Mouth, Round, 28/400 Cap: - -----(b)(4)----- -----	Bottle: 30cc (b)(4), White, Wide Mouth, Round, 28/400 Cap: -----(b)(4)----- -----
<b>Stability Study Number</b>	ARD_PRT-1911	ARD_PRT-2120	ARD_PRT-2317	ARD_PRT-2318
<b>Stability Study Start Date</b>	17-Jul-2006	23-Jan-2007	27-Jun-2007	27-Jun-2007

## 1.1. Stability Protocol

**Table SS Summary of Stability Testing of Adenovirus Vaccine Live Oral Type 4 and Type 7**

<b>Storage Condition</b>	<b>Packaging Configuration</b>	<b>Testing Intervals</b>
2-8°C	Bottle (100's)	0, 3, 6, 9, 12, 18 and 24 months
----- (b)(4) ----- -----	Bottle (100's)	0, 7 days, 14 days, 1 month, 2 months, & 3 months

**Table TT: Summary of Stability Testing of Clinical Trial Materials, Adenovirus Vaccine Live Oral Type 4 and Type 7**

<b>Storage Condition</b>	<b>Packaging Configuration</b>	<b>Testing Intervals</b>
2-8°C	Bottle (1 Type 4 and 1 Type 7)	0, 1, 3, 6, 9, 12, 14.7 and 15.9 Months
----- (b)(4) ----- -----	Bottle (1 Type 4 and 1 Type 7)	0, 1, 2 and 3 months

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## Appendix Fig. VV

Table 2. Stability data for Adenovirus Tablets, Type 7, Batch (b)(4) 100 count packaging, stored at 2-8°C.

Product Description: Light peach, round, coated, unscored, biconvex tablet. Imprinted in black ink b 7 on one side and plain on the other side.  
 Container: 60cc (b)(4) White, Wide Mouth, Round, 38/400 (Thick Walled)  
 Cap Size/Style: (b)(4) 38/400. Liner printed: Sealed for Your Protection.  
 Desiccant: 1 gram, 2 in 1 canister. Printed: DO NOT EAT. (Cylindrical, plastic container, filled with clear, colorless crystals and black particles.)  
 Stability Start Date: 06/14/06

Interval		Initial	3 Months	6 Months	9 Months	12 Months	18 Months
LIMS ID		200039791	200040578	200049057	200061233	200075506	200103617
Pull Date		N/A <sup>1</sup>	9/14/2006	12/14/06	03/14/07	06/14/07	12/14/07
MTH-732 Version (s)		3.0	4.0	4.0	4.0	4.0	4.0
Test	Specification	Results					
Description		N/A	Pass	Pass	Pass	Pass	Pass
		Pass	Pass	Pass	Pass	Pass	Pass
		AC014/034 06/19/06	AC030/005 09/14/06	AC030/020 12/18/06	AC030/030 03/14/07	AC030/041 06/15/07	AC030/061 12/18/07
Disintegration		Pass	Pass	Pass	Pass	Pass	Pass
		Pass	Pass	Pass	Pass	Pass	Pass
		AC016/096 06/21/06	AC016/130 09/20/06	AC016/175 01/05/07	AC016/191 03/27/07	AC016/211 07/03/07	AC016/239 12/20/07
Water		2.5%	2.8%	2.4%	2.4%	3.1%	2.4%
		AC013/095 06/13/06	AC013/183 09/26/06	AC013/265 01/11/07	AC032/014 04/13/07	AC032/031 06/29/07	AC034/047 01/10/2008
		5.8	5.4	5.6	5.2	5.6	5.3
Infectivity (Assay)		(b)(4)	(b)(4)	(b)(4)	(b)(4)	(b)(4)	(b)(4)
		06YD28 06/27/06	06YE20 09/27/06	06YE20 12/21/06	06YE20 03/22/07	06YE20 06/21/07	06YE20 12/21/07
		(b)(4)	(b)(4)	(b)(4)	(b)(4)	(b)(4)	(b)(4)
Microbial Limits		(b)(4)	TNR <sup>2</sup>	TNR	TNR	(b)(4)	TNR
		(b)(4)	(b)(4)	(b)(4)	(b)(4)	(b)(4)	(b)(4)
		(b)(4)	(b)(4)	(b)(4)	(b)(4)	(b)(4)	(b)(4)

<sup>1</sup> Not Applicable

<sup>2</sup> Test Not Required

## Appendix Fig. WW

### Structure of the Enteric-Tablet

