



# Adenovirus Vaccine Program

**Presentation to  
Armed Forces Epidemiological Board**

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# Outline

- Program Overview
- Manufacturing
- Regulatory
- Clinical
- Quality
- Procurement
- Funding
- Moving Forward
- Program Risks



# Requirement



- Defense Health Program requirement for adenovirus vaccine type 4 and 7, Feb. 3, 2005
- Infection Disease Countermeasures-Initial Capabilities Document (IDCM-ICD)
  - Includes requirement for adenovirus vaccine type 4 and 7
  - Pending Joint Requirements Oversight Council (JROC) approval
- Adenovirus Vaccine, Types 4 and 7- Capabilities Production Document
  - Initial draft is staffed with Directorate of Combat and Doctrine Development, AMEDDC&S

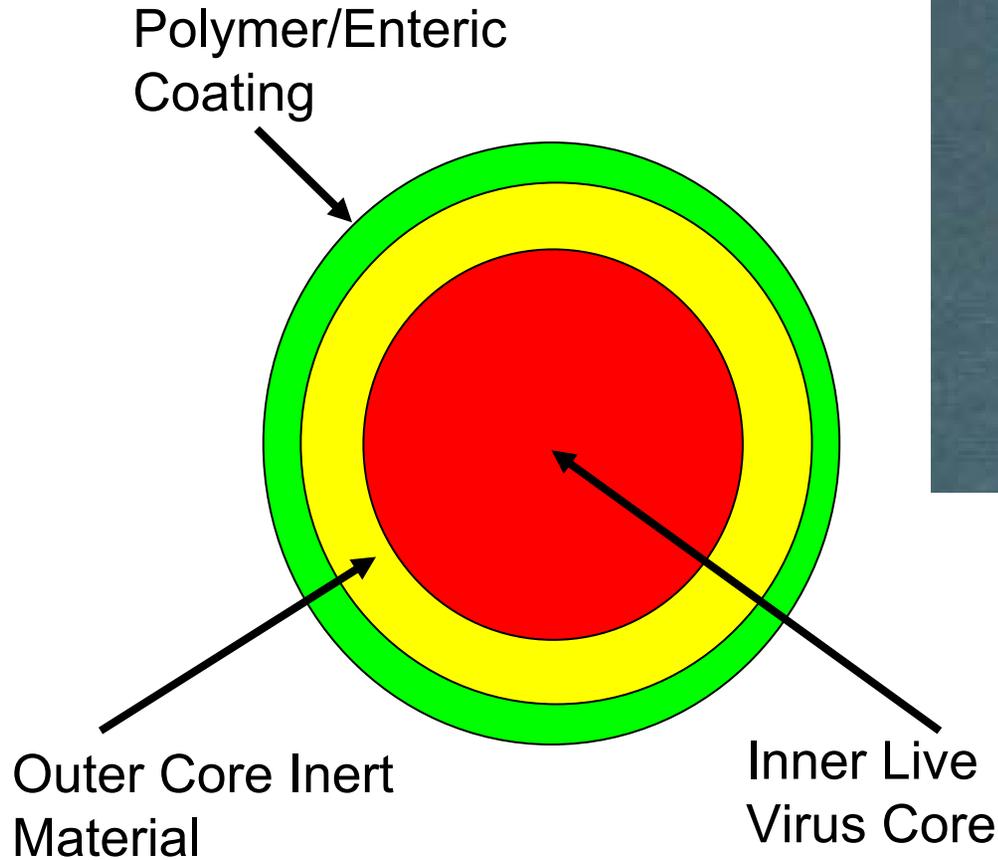


# Objective

**Provide a safe, efficacious, FDA approved Adenovirus Vaccines (Type 4 and 7) to protect US military basic trainees from adenovirus respiratory disease.**

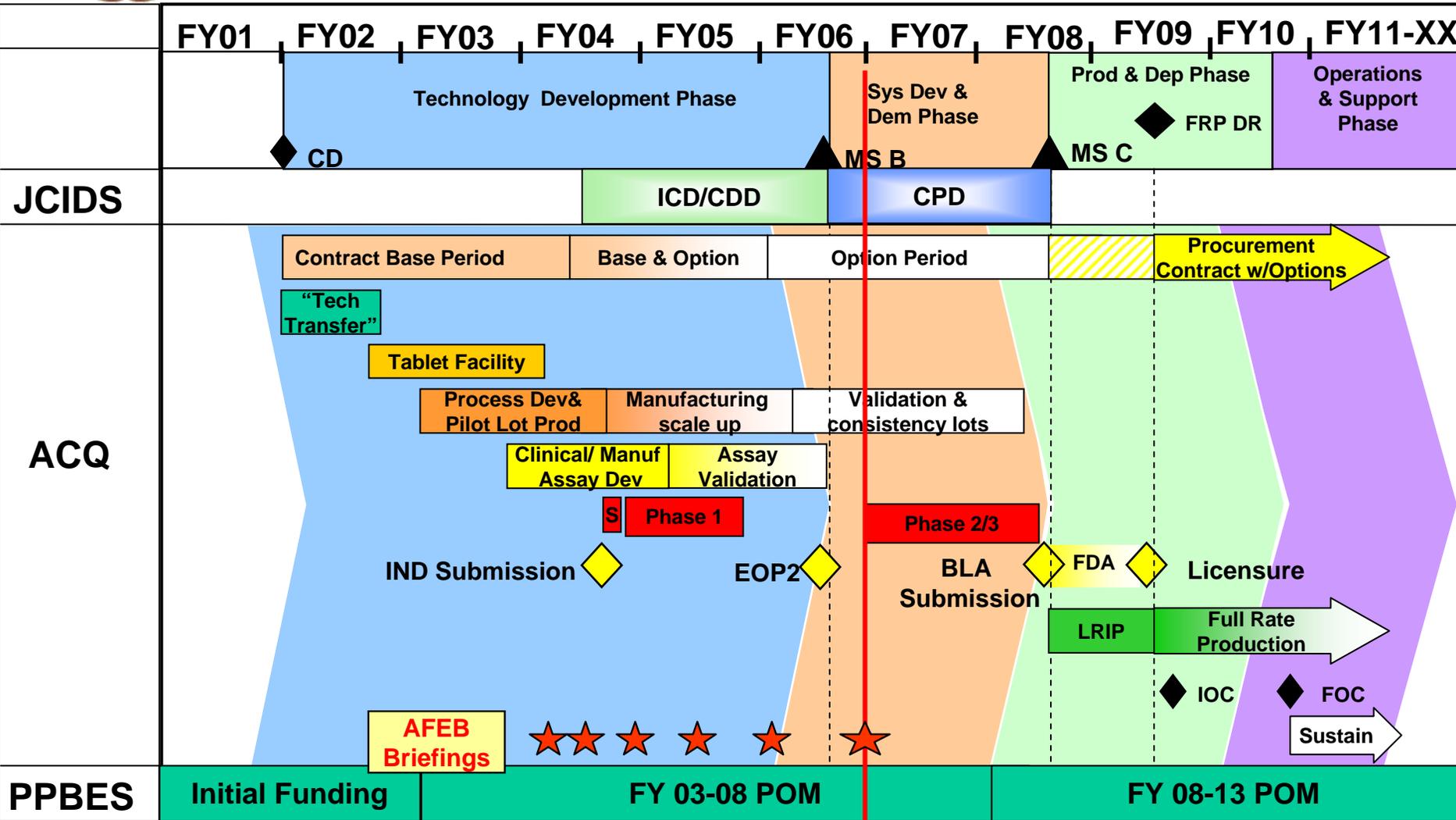


# Adenovirus Vaccine





# Acquisition Plan



26 SEP 06



# Development Plan-Dec 05



ID	Task Name	Start	Finish	2001	2002		2003		2004		2005		2006		2007		2008		2009
				H1	H2	H1	H2	H1	H2	H1	H2	H1	H2	H1	H2	H1	H2	H1	H2
1	Adenovirus Vaccine, Types 4 & 7	Mon 8/6/01	Mon 8/6/01		8/6														
2	Basic Contract	Fri 9/21/01	Wed 11/9/05																
3	DoD Contract Award	Fri 9/21/01	Fri 9/21/01		9/21														
4	Wyeth Technology and Material Transfer Agreement	Mon 10/1/01	Fri 5/17/02	10/1		5/17													
5	Wyeth Material received	Mon 5/20/02	Mon 9/16/02		5/20		9/16												
6	Facility Construction, Equipment Installation and Qualification	Fri 5/17/02	Fri 1/30/04																
12	Pilot and GMP Virus Production	Mon 1/6/03	Mon 8/23/04																
29	IND Regulatory Activities	Thu 1/9/03	Tue 8/24/04																
36	Seroprevalance Study	Wed 6/2/04	Fri 7/30/04																
40	Phase I Clinical Trial	Mon 9/1/03	Wed 11/9/05																
93	<b>Option 1</b>	Thu 1/1/04	Fri 9/5/08																
94	Vaccine Production for Phase II/III Clinical Trial	Fri 9/24/04	Wed 1/25/06																
129	Long term stability testing for the phase III product	Mon 10/24/05	Wed 10/17/07																
134	Virus Bulk Production	Thu 5/19/05	Fri 7/7/06																
147	VA Lyophilizer Qualification Schedule	Tue 10/4/05	Fri 6/16/06																
180	RA activities before next trial start	Thu 7/7/05	Mon 2/13/06																
194	Phase II/III Clinical Trial	Thu 1/1/04	Tue 5/8/07																
257	Write Reports	Mon 8/28/06	Fri 9/22/06																
260	Consistency Lot Manufacturing	Mon 10/24/05	Fri 9/5/08																
288	Quality Systems	Thu 6/16/05	Thu 12/15/05																
296	Prepare and Submit BLA	Mon 4/23/07	Mon 6/16/08																

Δ 8 m



# Schedule\*



EVENT	OBJECTIVE	THRESHOLD
Start Phase 3 Clinical Trial	SEP 06 ( $\Delta$ 5 m)**	JAN 07
Complete Execution of Phase 3 (LPO, 6 mon f/u)	FEB 08	JUN 08
Complete Study Report	APR 08 ( $\Delta$ 5 m)**	AUG 08
Submission of BLA	JUN 08 ( $\Delta$ 6 m)**	OCT 08
MS C	JUN 08	OCT 08
LRIP/Procurement Base Period Contract Award	JUL 08	NOV 08
BLA Approval	APR 09 ( $\Delta$ 10 m)**	AUG 09
FRP/Procurement Options Exercised	APR 09	AUG 09
Licensed Vaccine Available	MAY 09 ( $\Delta$ 11 m)**	SEP 09

\* **New schedule baseline approved at Milestone B review on July 5, 2006**

\*\* **Change in schedule since AFEB presentation on December 6, 2005**



# Manufacturing



Task	Status
Virus Bulk Formulation	DEVELOPED
Dedicated Manufacturing Facility	COMPLETED
cGMP Compliant Manufacturing Process	DEVELOPED
Successful Transfer of Lyophilization Process	COMPLETED
cGMP Compliant Testing	DEVELOPED AND VALIDATED



# Product Manufacturing

<b>First Clinical Batch:</b>	<b>ADV-4 Tablets</b>	<b>ADV-7 Tablets</b>
<b>Active and Placebo released</b>	✓	✓
<b>Repackaged for clinical use</b>	✓	✓
<b>Stability @ 2-8 °C</b> (labeled storage conditions; 1-month data on 9/15/06)	✓	✓

Additional lots necessary to demonstrate manufacturing lot consistency will be available for use in the Phase 3 trial by January 2007



# Regulatory Milestones

- **Pre-IND Meeting:** May 10, 2004
- **IND submitted :** July 13, 2004
- **Phase 1 Clinical Study**
  - Started: August 14, 2004
  - Completed: April 24, 2005
- **Clinical Study Report Submitted:** August 2, 2005
- **End-of-Phase 2 Meeting:** June 27, 2006
- All regulatory agreements/requirements for Phase 3 study initiation will be completed before September 30, 2006.



# Phase 3 Clinical Trial



**IND Sponsor:** Duramed Research Inc.

**Design:** Randomized, multi-center, double-blind, placebo-controlled

## Objectives:

- ADV-4 vaccine efficacy reducing attack rate of WT ADV-4 febrile ARD
- Antibody (AB) response to ADV-4 and ADV-7 vaccines
- Safety/tolerability of ADV-4 and ADV-7 vaccines

## Primary Endpoints:

- Reduction in attack rate of *febrile* ARD with throat culture positive for wild-type ADV-4 infection
- Seroconversion rate (neutralizing ABs) with  $\geq 4$ -fold titer increase in subjects with baseline titer of  $< 1:4$  for ADV-7

**Population:** 4000 military recruits (20-30% nonpregnant females)

**Nested safety study of 780 subjects**

**Interim sample size analysis at 2000 subjects**

**Two sites:** Great Lakes, IL (CDR Kevin Russell)  
Fort Jackson, SC (COL Robert Kuschner)

## Treatment groups (3:1):

- ADV-4 and ADV-7 vaccines simultaneously
- Placebos



# Site Readiness



- Fort Jackson and Great Lakes, NRTC
  - Full time CORE staff hired
  - Site renovations and equipment set up complete
  - Ancillary (part-time) staff have been trained
  - Study start 30 SEP 06 (Pending final IRB approval)



# Quality Assurance

Provide quality oversight to assure:

- Vaccine manufacturing has appropriate processes and controls in place to produce safe and effective adenovirus vaccines consistently
- Protection of rights and well-being of subjects
- Trial data are accurate, complete and verifiable
- Compliance w/protocol, GCPs, applicable regulatory requirements



# Procurement

- Revised vaccine cost estimate received in June 2006
  - Vaccine cost estimate provided greater cost detail than previous cost estimates
  - Current cost estimates are based upon limited experience manufacturing Adenovirus vaccines
- A procurement contract to support Low Rate Initial Production (LRIP) may be completed following successful completion of the Phase 3 clinical study and Milestone C program review
- LRIP is scheduled to begin during the 4QFY08 to support Initial Operational Capability in 3QFY09
  - The Initial Operational Capability is met when the ADVV has been licensed by the FDA and is available for use



# Funding

- Current program is fully funded



# Moving Forward

- Manufacturing
  - Release additional vaccine lots for Phase 3
  - Continue vaccine stability testing
- Clinical:
  - Initiate Phase 3 study
  - Data Monitoring Committee (DMC)
    - Safety Review @ 780 volunteers
    - Interim Analysis @ 2000 volunteers



# Program Risks

- Protocol review and approval (scientific and human use)
  - 8 review boards
- Regulatory (FDA) guidance
- Integration of trials with basic training schedules
  - Enrollment rate
- Vaccine performance
- Production failures
- Contract modification
- Vaccine cost

Any or all of the above could impact baseline performance, schedule, and cost