FACT SHEET

SUBJECT: Adenovirus Vaccine October 5, 2004

KEY POINTS:

A. Since late 2001, Dr Winkenwerder, ASD(HA), has made acquisition of a safe and effective adenovirus vaccine a top priority for the Military Health System.
B. The Department will spend more than $50M to obtain the vital adenovirus vaccine.
C. An accelerated schedule for acquisition and production will result in vaccine availability in 2006.

DISCUSSION:

The Military Health System (MHS) has an appointed Project Manager charged with developing sustained interaction with Food and Drug Administration (FDA) so that specific time-frames for vaccine acquisition can be established and to assure that barriers and obstacles are overcome. The Project Manager and his team work at the US Army Medical Research and Material Command (USAMRMC) and coordinate with the Defense Supply Center Philadelphia (DSCP) for the actual procurement of the vaccine.

Barr Laboratories, Forest, Virginia (Corporate headquarters in Pomona, NY) received the contract award in 2001 to develop and produce adenovirus vaccine. Construction of the vaccine manufacturing facility is complete, and necessary equipment has been installed. Barr Laboratories submitted an Investigational New Drug (IND) application to the FDA in July 2004. Phase I clinical trials are underway at Fort Sam Houston, Texas, with approximately 70 subjects. We will complete Phase I trials during fall 2004. Phase II and III combined trials will begin early in 2005 at several sites. DoD believes it will be possible to begin using the vaccine following these trials under an IND protocol so that we have vaccine available for trainees in 2006. We estimate that following the initial investments in vaccine production (over $50M), the cost of vaccine will approximate $4M annually.

Only the military services use adenovirus vaccine, and they use it at basic training installations for incoming recruit trainees. To our knowledge, Barr Laboratories is the only company, worldwide, in the process of producing this vaccine.

The Department began monitoring respiratory illnesses, including adenovirus, in recruit trainees in the late 1990's and will continue to do so until at least 2007. We conduct this population-based surveillance program at eight training installations of the military services and the U.S. Coast Guard. The sites include:

Army—Forts Benning GA, Jackson SC, Leonard Wood MO
Navy--Great Lakes Training Center IL
Marine Corps—Marine Corps Recruiting Depots Parris Island NC, San Diego CA

Air Force—Lackland AFB TX
Coast Guard—Cape May NJ

Today, nearly 90 percent of recruits are susceptible to adenovirus type 4 or 7. Since 1999 when the supply of vaccine tablets was depleted, the calculated normal rate of respiratory diseases at the training sites increased, occasionally spiking to a substantially elevated level. Measures taken to stem respiratory diseases include detailed and continued instruction on personal hygiene (such as rigorous hand-washing and covering the mouth when coughing or sneezing), spacing and head-to-toe sleeping arrangements, use of bicillin at some installations, and conceptual (no funding at this time) work on anti-viral medications. While the numbers of basic trainees at the major sites vary during the course of the year, we had about 56,000 trainees during the month of August 2003 that we estimated about 2,500 cases of adenovirus. The figure 2,500 is a calculated number based on a count of respiratory cases at training sites; the number of viral throat cultures taken, and the count of those cultures that test positive for adenovirus. Another way to view the cases of adenovirus is that we have one case for every 200 trainees each week of basic training.

We regularly conduct population-based surveillance at the major training sites, where the preponderance of cases have been seen, in order to capture early any indications of disease increases. Once detected, our preventive medicine experts work closely with the commands to ensure strict and continuous hygiene practices. On occasion, one or more of the training sites experience moderate or substantial elevation of their "normal" rate of respiratory disease. As an example, for the week ending September 5, 2004, Marine Corps Recruit Depot Parris Island experienced a substantial elevation above normal, while Marine Corps Recruit Depot San Diego, for the week ending September 26, 2004, experienced a moderately elevated rate of respiratory disease. Preliminary laboratory results suggest that these spikes were caused by adenovirus.

A small percentage of those who contract adenovirus become more significantly ill, and a smaller percentage still have died. Although death is very rare, we had three confirmed deaths from adenovirus during 2003 and no confirmed deaths in 2004.

Our population-based surveillance data are collected at the eight training sites, so we have detailed information only for those sites. However, we would expect that the experience at other training sites in the military would be similar to that of the eight sites being monitored.

BACKGROUND:

In November 1984, Wyeth Laboratories, then the only producer of adenovirus vaccine, advised the department that they needed a new facility to continue production of the vaccine. They would continue to manufacture vaccine as long as their equipment functioned. The department opened discussions with other manufacturers, but none were

interested. In 1994, Wyeth informed the department that they would fill orders from inventory, that they would no longer manufacture the vaccine unless their facilities were upgraded. The military services conducted studies regarding their continued need for the vaccine during the latter half of 1995; Army and Navy validated their need, Air Force indicated a desire to have access to the vaccine in the event of an outbreak. The Air Force discontinued use of the vaccine in 1987 and in routine surveillance thereafter found adenovirus was only sporadic. In December 1995, Wyeth informed the department that they would require two years for construction and one year for approval of the production line and product by FDA for continued manufacture of the vaccine; the estimated costs ranged from $3M to $5M. In July 1996, Wyeth indicated it preferred to transfer the technology rather than continuing to make the vaccine. Discussions within the department ultimately led to a decision to not fund the Wyeth request, or to take other procurement actions. The existing supply of vaccine was depleted or expired in 1999. The Institute of Medicine in its 2000 report concluded that DoD should expeditiously reestablish a viable adenovirus vaccine supply. That process began with an announcement in Commerce Business Daily in 2000 and contract award in late 2001 to Barr Laboratories.

Dr. Winkenwerder, ASD(HA), who assumed his position in the fall of 2001, made the acquisition of a new, safe and effective adenovirus vaccine a top priority for the Military Health System. Regular periodic meetings with the Project Management team have been held since early 2002 to ensure that all activities associated with the vaccine acquisition effort remain on schedule, and, wherever possible, accelerated to the earliest possible date for completion.

In 1998 a cost-effectiveness study examining the use of adenovirus vaccine was published in the American Journal of Preventive Medicine (14(3) 168-175). This study estimated that in the absence of the vaccine a projected 12,370 cases of respiratory disease would occur, costing $26.4M annually. A seasonally targeted vaccination program would prevent 7,800 cases of respiratory disease and save $16.1M. Year-round immunization would not prevent any additional cases, but would save $15.5M.

ADDITIONAL INFORMATION:

The conduct of the clinical trials to attain licensure for the adenovirus vaccine will require testing beyond what originally had been envisioned. Studies for reproduction toxicity will be included, plus the results of Phase I trials will instruct the final study decisions. We must adhere to the requirements of the FDA to ensure the production of a safe and efficacious vaccine. To do this we need to ensure sufficient resources for the clinical trials as well as for production. Additional dollars, theoretically, could accelerate the pace of clinical trials, but at an undetermined level. Additional funding would allow testing at more sites which affords greater participation in the trials at a faster pace.