Our vision is a U.S. Military Force that has a full medical countermeasure capability to fight and win in any CBRN battlespace worldwide.

rF1V Plague Vaccine

WHO Workshop “Efficacy trials of Plague Vaccines: endpoints, trial design, site selection”

Presented to:
World Health Organization

Dr. Lucy Ward, DVM, Ph.D.
Senior Scientist
Joint Vaccine Acquisition Program
Medical Countermeasure Systems
lucy.a.ward.civ@mail.mil

April 23, 2018

DISTRIBUTION A. Approved for public release: distribution unlimited
rF1V Plague Vaccine Target Product Profile

- rF1V is a subunit vaccine composed of recombinant *Y. pestis* F1 capsular & V proteins formulated in aluminum adjuvant
  - F1 subunit sufficient for prevention of bubonic disease; V subunit sufficient for protection against pneumonic disease

- **Indication:** For the protection of adults 18 to 55 years of age against pneumonic plague caused by aerosol exposure to *Y. pestis*

- Three dose regimen (0.5 mL per dose) administered intramuscularly on days 0, 28 & 182 (6 month schedule); annual boosters thereafter

- Storage at 2-8 C in single dose vials; vial shelf-life at 5+ years (ongoing)

- Vaccine efficacy and conferred clinical benefit data being generated per FDA guidance related to US Code of Federal Regulations Title 21 CFR 314.600 - 314.650 (drugs) or 21 CFR 601.90 - 601.95 (biological products), commonly referred to as the “FDA Animal Rule” (New Drug and Biological Products; Evidence Needed to Demonstrate Efficacy of New Drugs When Human Efficacy Studies are Not Ethical or Feasible)

Bridging Animal Efficacy to Vaccine Immunogenicity under Animal Rule

- **Top Right:** Survival curve from AR efficacy studies completed to date
  - Y axis = % NHP surviving high dose aerosol *Y. pestis* exposures as predicted by their serum rF1V ELISA titer at time of challenge
  - X axis = Log10 serum rF1V ELISA titer

- **Bottom Right:** Frequency (Y axis) of Phase 2 subjects with differing ranges (blue bars) of serum rF1V ELISA titers (X axis) at 1-3 weeks post immunization with 3rd rF1V vaccine dose

- **Red dotted-dashed lines** depict the “bridge” for rF1V ELISA titers in sera from vaccinated subjects to the same titer in sera from vaccinated NHPs to determine predicted efficacy under Animal Rule for a given vaccine-induced rF1V ELISA titer

---


---

**NOTE:** For Animal Rule licensure, >90-95% of all Phase 3 subjects receiving vaccine must develop rF1V ELISA titers above this pre-determined value negotiated with the FDA.
Kinetics of Protective Immunity per Animal Rule post-rF1V Vaccination

- **Day 35**: A portion of adult subjects (e.g. 22-25%) already develop rF1V ELISA titers above the minimal (threshold) Animal Rule (AR)-predicted protective immunity levels after dose 2 (yellow line)

- **Day 190**: Virtually all (e.g. >99%) adult subjects develop AR-predicted protective immunity following the third dose with the majority of titers at levels bridging to NHP efficacies above 80% (purple line)

- **Day 270**: The AR-predicted protective immunity as measured by the rF1V ELISA starts to wane in a portion of subjects (e.g. 20-25%) after 3 months post-vaccination to levels below that negotiated with the FDA for licensure (blue line)

- **Day 365 (or 1 year post first dose)**: The rF1V ELISA titers in subjects continue to wane and level off around 1 year post-initial vaccination with about half of the subjects above & half below the protective antibody level for licensure and identifies need for/timing of the booster immunization (gold-brown line)

Kinetic Modelling courtesy of Dr. Kevin Wingerd, MCS-JVAP
Relating $R_0$ to Vaccine Efficacy

- The relationship between $R_0$ and impact on vaccine efficacy is described below, where $P_c$ (e.g. vaccine efficacy) is the critical percentage of immune individuals required to achieve population herd immunity

$$P_c = 1 - \frac{1}{R_0}$$

- The $R_0$ for transmission of pneumonic plague has been estimated to be $0.96 - 2.3^*$

$$\text{If } R_0 = 2.3 \quad \rightarrow \quad 1 - \frac{1}{2.3} = 0.57$$

- Consequently, vaccines which elicit protective immunity against pneumonic plague disease in $\geq 57\%$ of a population have the greatest potential to ascertain rapid burn out and/or control-prevention of pneumonic plague outbreaks in endemic areas

Summary

• In ‘plague-naïve’ populations:
  – rF1V vaccine, in 3 doses IM over 6 months, is predicted to confer immunity against pneumonic plague in >98% of vaccinated subjects
  – Approximately ¼ of plague-naïve subjects have developed AR-protective immunity to pneumonic plague after 2 doses and within 5 weeks post first dose
  – By 6 months post-full vaccination regimen, about ½ of subjects showed rF1V ELISA titers waning below our pre-determined threshold for licensure suggesting need for annual boosters to maintain AR-predicted protective immunity in a naïve population

• Performance data for rF1V vaccine support its use for the control and prevention of pneumonic plague among persons in endemic disease areas
## Contact Us

<table>
<thead>
<tr>
<th>Name</th>
<th>Position</th>
<th>Organization</th>
<th>Email Address</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lucy A Ward, DVM, PhD</strong></td>
<td>Senior Scientist</td>
<td>Medical Countermeasures Systems – Joint Vaccine Acquisition Program</td>
<td><a href="mailto:lucy.a.ward.civ@mail.mil">lucy.a.ward.civ@mail.mil</a></td>
</tr>
<tr>
<td><strong>Andrew Glenn</strong></td>
<td>Acting Deputy Joint Product Manager</td>
<td>Medical Countermeasures Systems – Joint Vaccine Acquisition Program</td>
<td><a href="mailto:Andrew.glenn4.civ@mail.mil">Andrew.glenn4.civ@mail.mil</a></td>
</tr>
<tr>
<td><strong>Wai Kwan Chung</strong></td>
<td>Acting Assistant Product Manager, Plague Vaccine Program</td>
<td>Medical Countermeasures Systems – Joint Vaccine Acquisition Program</td>
<td><a href="mailto:waikwan.chung2.ctr@mail.mil">waikwan.chung2.ctr@mail.mil</a></td>
</tr>
<tr>
<td><strong>LTC Jeanne Norwood</strong></td>
<td>Joint Product Manager</td>
<td>Medical Countermeasures Systems – Joint Vaccine Acquisition Program</td>
<td><a href="mailto:jeanne.a.norwood.mil@mail.mil">jeanne.a.norwood.mil@mail.mil</a></td>
</tr>
<tr>
<td><strong>Lucy A Ward, DVM, PhD</strong></td>
<td>Senior Scientist</td>
<td>Medical Countermeasures Systems – Joint Vaccine Acquisition Program</td>
<td><a href="mailto:lucy.a.ward.civ@mail.mil">lucy.a.ward.civ@mail.mil</a></td>
</tr>
<tr>
<td><strong>Andrew Glenn</strong></td>
<td>Acting Deputy Joint Product Manager</td>
<td>Medical Countermeasures Systems – Joint Vaccine Acquisition Program</td>
<td><a href="mailto:Andrew.glenn4.civ@mail.mil">Andrew.glenn4.civ@mail.mil</a></td>
</tr>
<tr>
<td><strong>Wai Kwan Chung</strong></td>
<td>Acting Assistant Product Manager, Plague Vaccine Program</td>
<td>Medical Countermeasures Systems – Joint Vaccine Acquisition Program</td>
<td><a href="mailto:waikwan.chung2.ctr@mail.mil">waikwan.chung2.ctr@mail.mil</a></td>
</tr>
<tr>
<td><strong>LTC Jeanne Norwood</strong></td>
<td>Joint Product Manager</td>
<td>Medical Countermeasures Systems – Joint Vaccine Acquisition Program</td>
<td><a href="mailto:jeanne.a.norwood.mil@mail.mil">jeanne.a.norwood.mil@mail.mil</a></td>
</tr>
</tbody>
</table>

---

## Medical Countermeasure Systems (MCS) Project Management Offices

<table>
<thead>
<tr>
<th>Office</th>
<th>Address</th>
<th>Phone Number</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MCS-Fort Detrick (HQ)</strong></td>
<td>1564 Freedman Drive, Fort Detrick, MD 21702-5041</td>
<td>301-619-7400</td>
</tr>
<tr>
<td><strong>MCS-Frederick Annex</strong></td>
<td>110 Thomas Johnson Drive, Ste 240, Frederick, MD 21702-5041</td>
<td>301-619-2156</td>
</tr>
</tbody>
</table>