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Determining whether adsorption state is a critical attribute in aluminum adjuvanted vaccines

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Determining whether adsorption state is a critical attribute in aluminum adjuvanted vaccines

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President

"VaxForm consulting envisions a world where formulation takes a leading role in providing solutions to development of vaccines against life threatening diseases."

Understanding the antigen

- **Biophysical characterization**
  - Derivative spectroscopy, intrinsic/extrinsic fluorescence, dynamic light scattering, static light scattering etc…
- **pH/stability profile**
  - Understand how pH impacts degradation
- **Excipient screening**
  - Sugars/sugar alcohols, surfactants, antioxidants, amino acids, cyclodextrins
- **Accelerated Stability**

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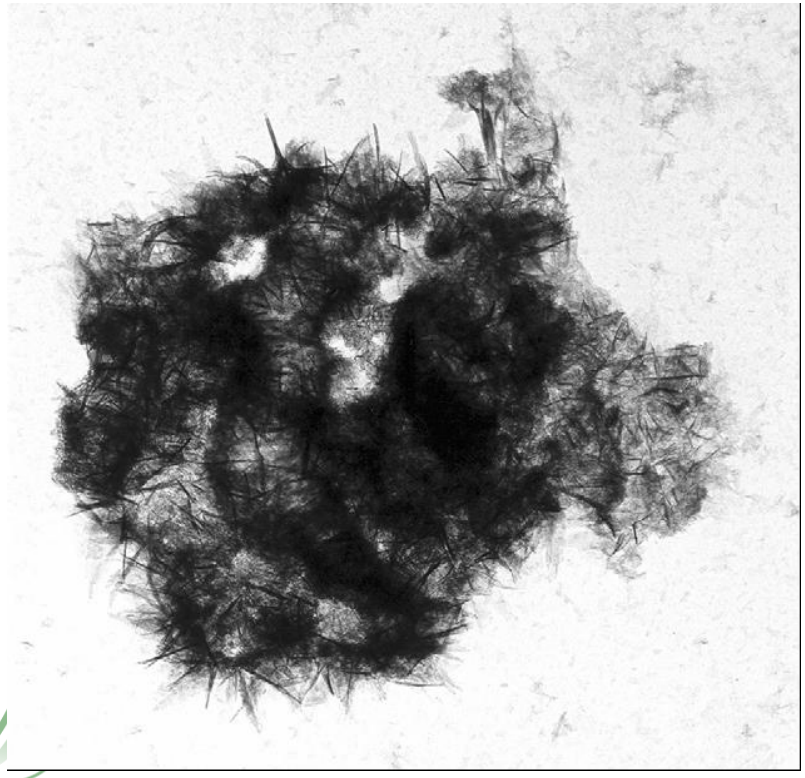
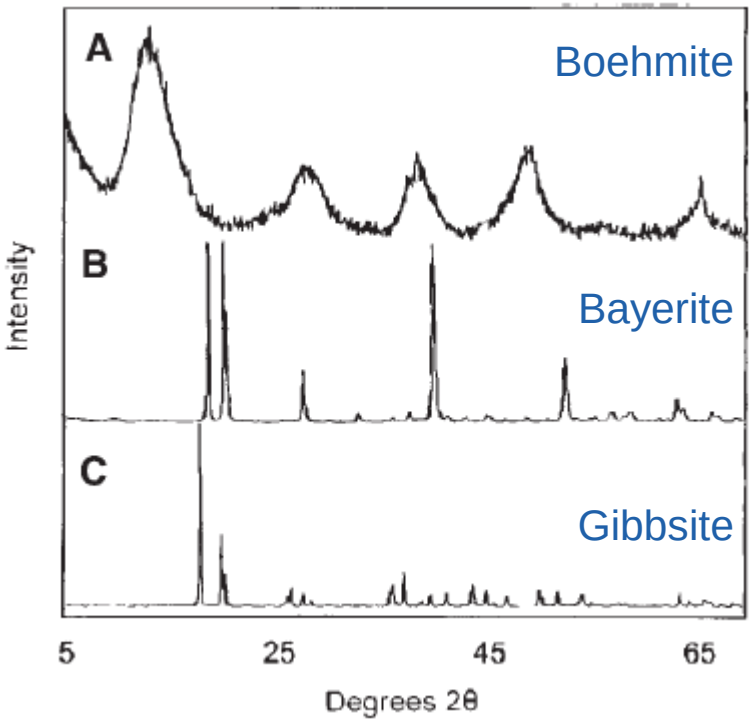
Aluminum Hydroxide Adjuvant

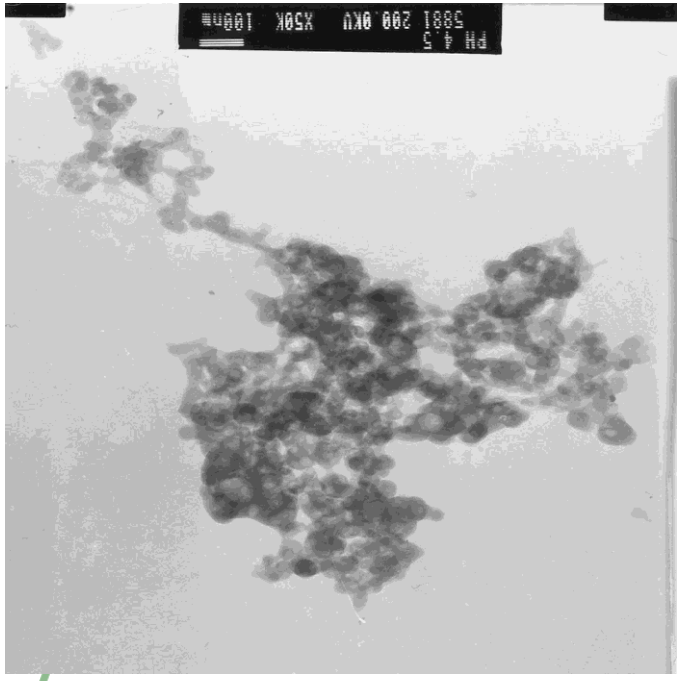
- Not $Al(OH)_3$ but AlOOH (boehmite)
- Fibrous primary particles: 4.5x2.2x10 nm^2

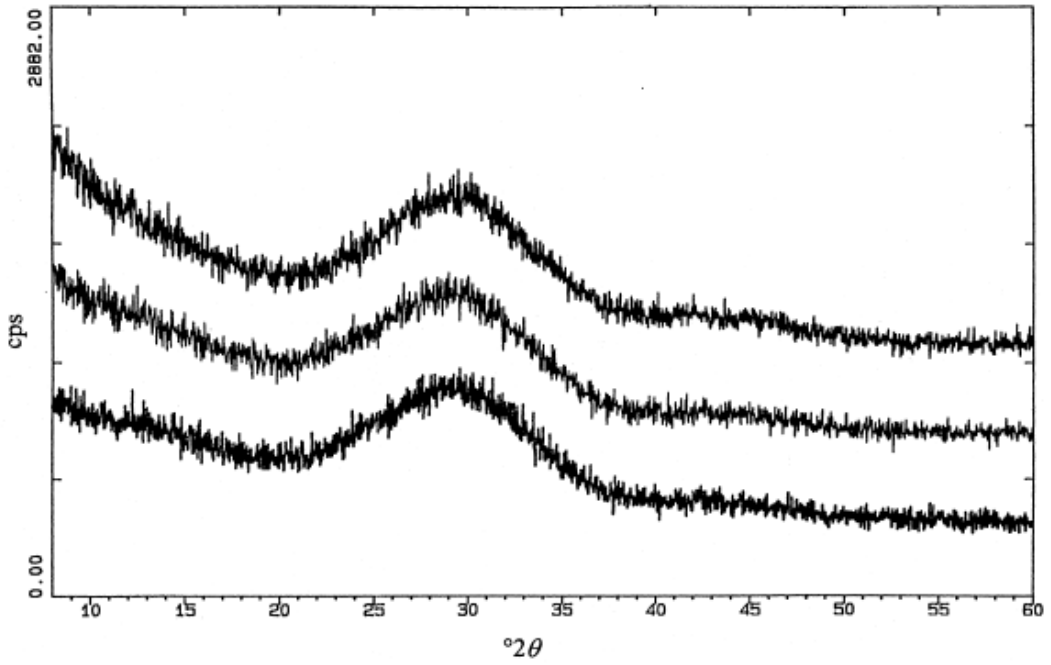




Aluminum Phosphate Adjuvant

- Not $AlPO_4$ but $Al(OH)_x(PO_4)_y$
- Non-stoichiometric
- Amorphous plate like primary particles





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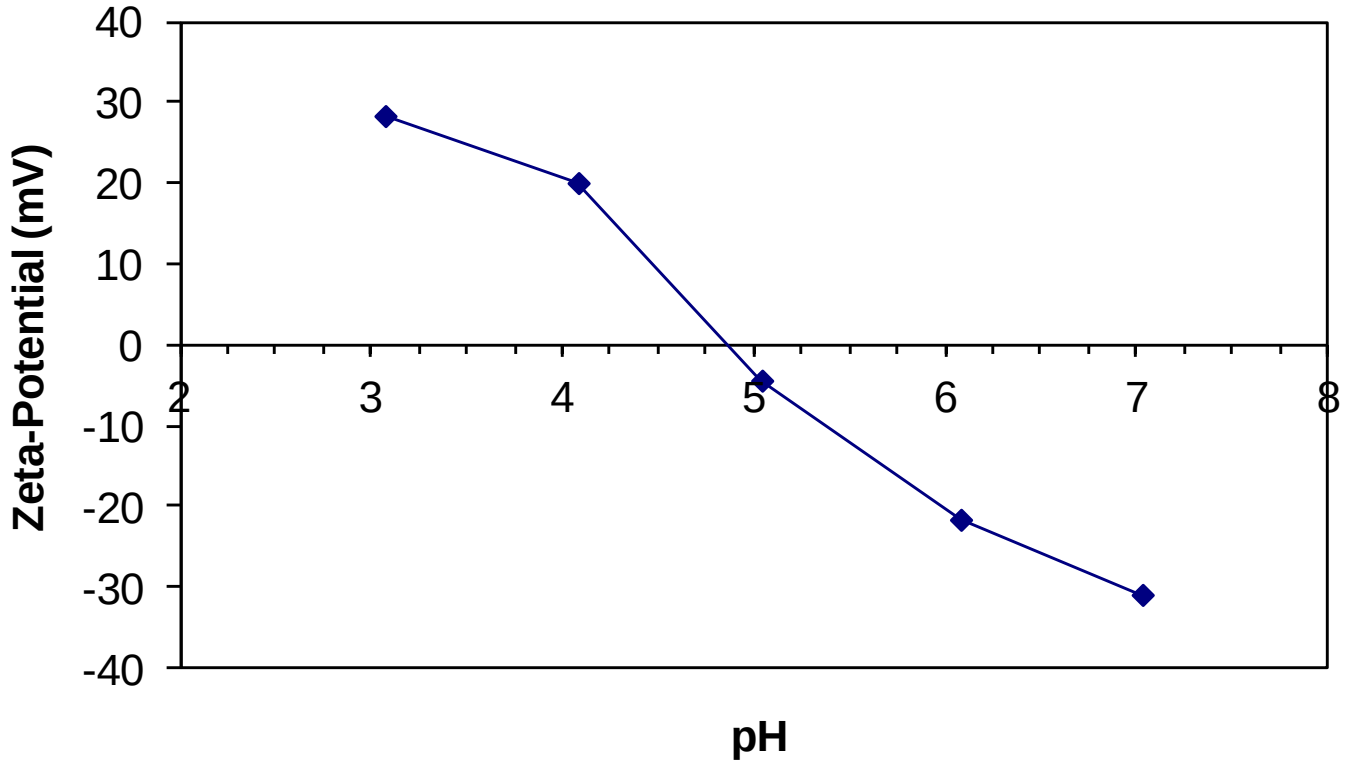
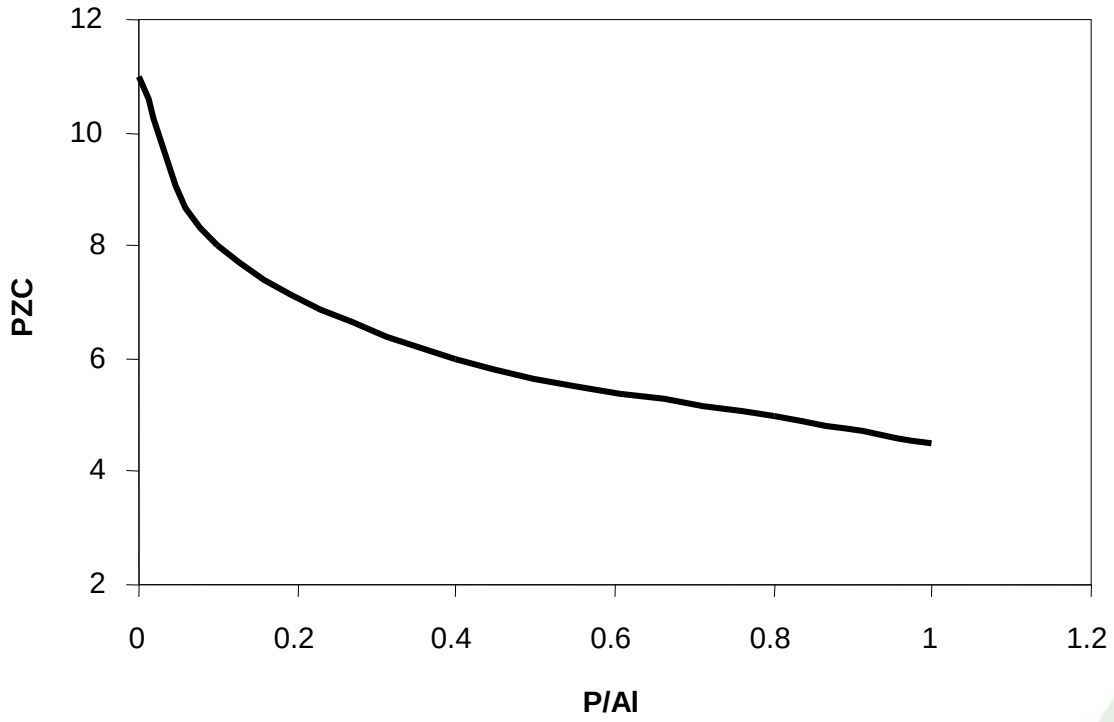
PZC – Point of Zero Charge

- **The pH at which there is no charge at the surface of the adjuvant.**



Aluminum Phosphate Adjuvant

- **PZC inversely proportional to degree of phosphate substitution.**



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Mechanisms of Adsorption

- **Balance of forces determines adsorption**
- **Electrostatic attractive forces**
  - Occurs when the adjuvant and antigen have opposite charges
  - Most frequently encountered mode of adsorption
- **Ligand Exchange**
  - PO_4 in antigen exchanges for a OH at the adjuvant surface
  - Strongest mode of adsorption
- **Hydrophobic interactions**
- **Other forces**
  - Hydrogen bonding
  - Van der Waals

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Group A Strep vaccine background

- *Streptococcus pyogenes* is a Gram-positive bacterium that causes a wide variety of diseases such as strep throat, scarlet fever, necrotizing fasciitis, streptococcal toxic shock syndrome, and impetigo. These diseases are generally referred to as Group A Streptococcal (GAS) diseases.
- VaxForm is developing a vaccine targeting GAS infection consisting of a recombinant fusion protein comprising genetically mutated SpeA and SpeB virulence factors.

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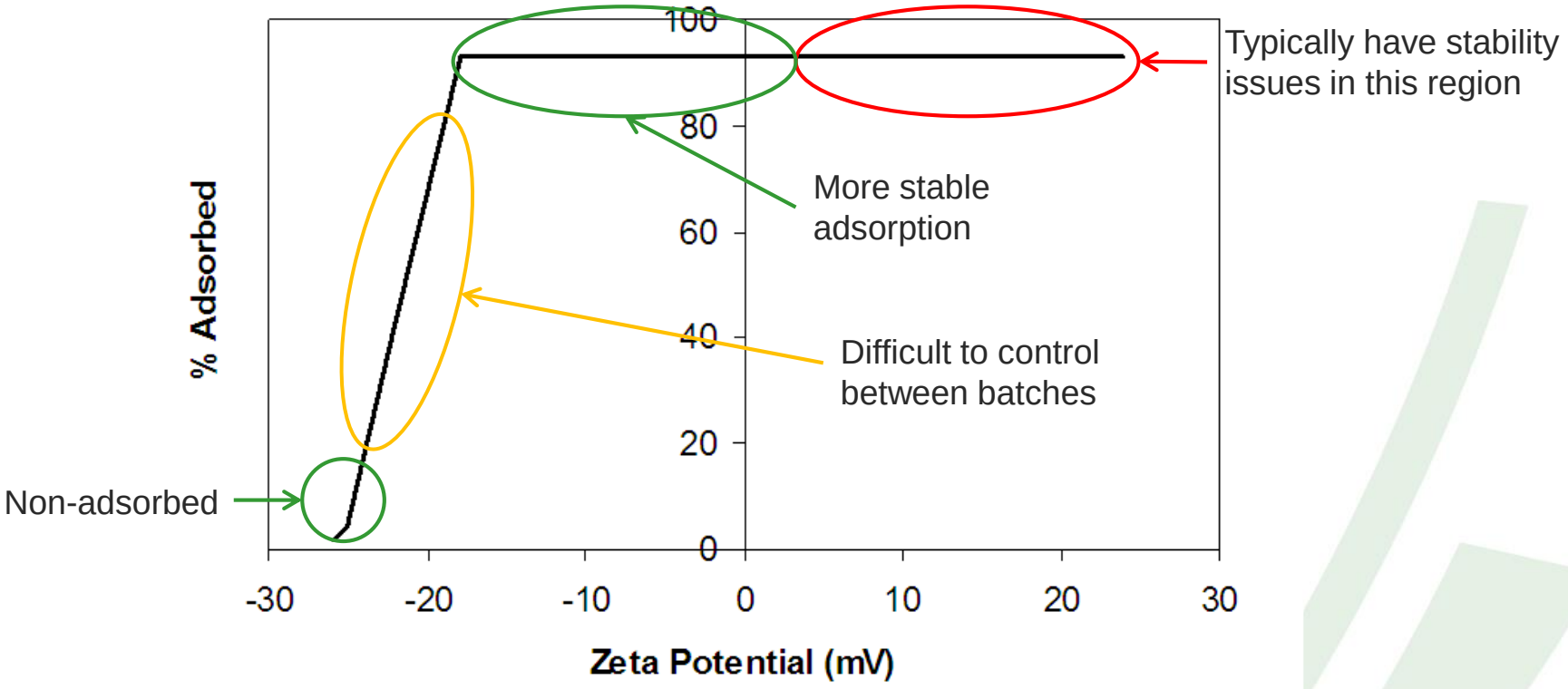
Adjuvant Surface Evaluation

- **Antigen characterization determined the antigen was stable at pH 8 and had a negative charge.**



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Formulation Comparison *In Vivo*

- BALB/c mice administered vaccine on days 0 and 14.
- 5, 2, or 0.4 μg dose of antigen
- IM administration
- Sera collected on day 28.
- Neutralizing antibody evaluated.

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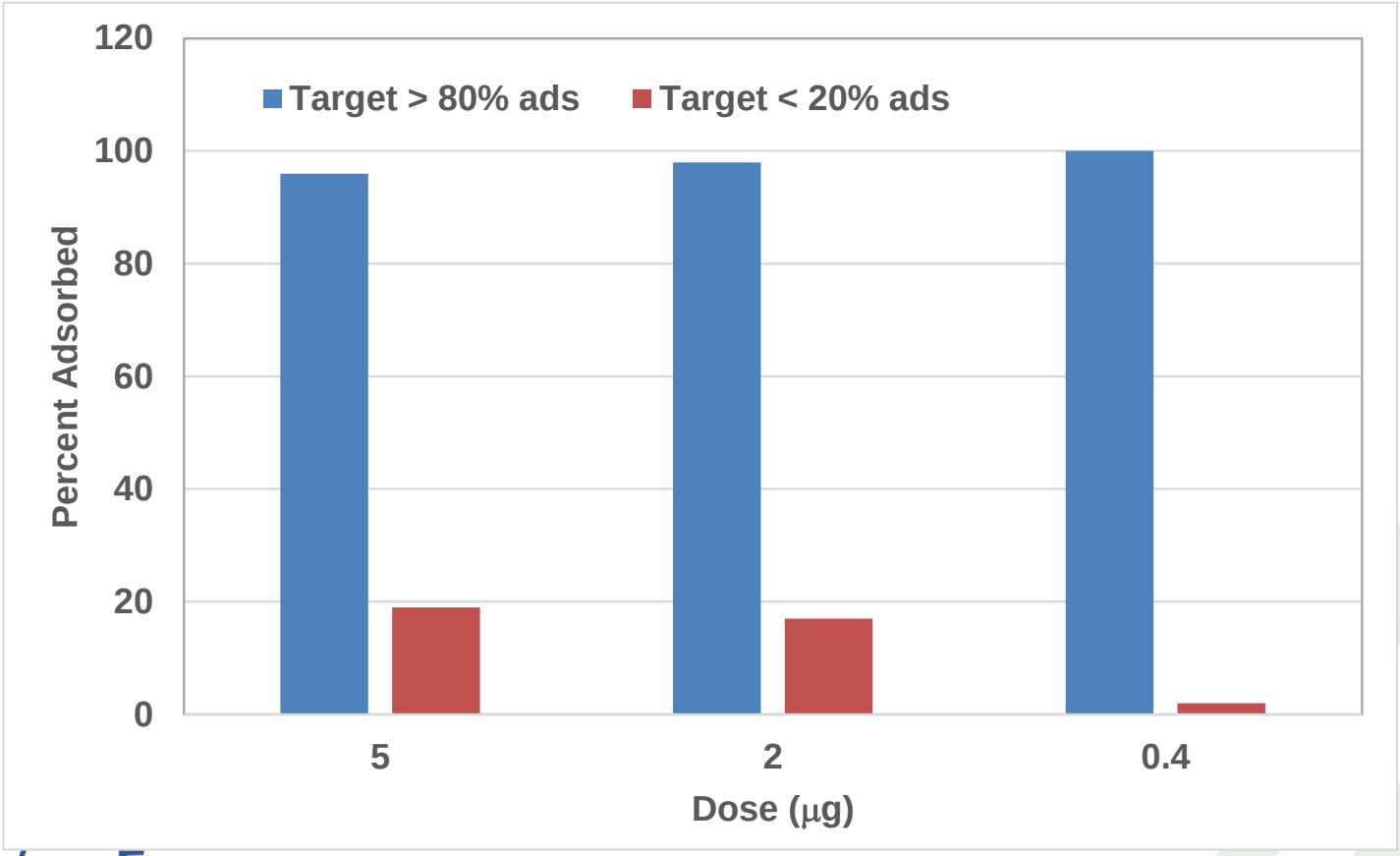
Formulation Adsorption

- **Adsorption remained within target through the duration of the study.**



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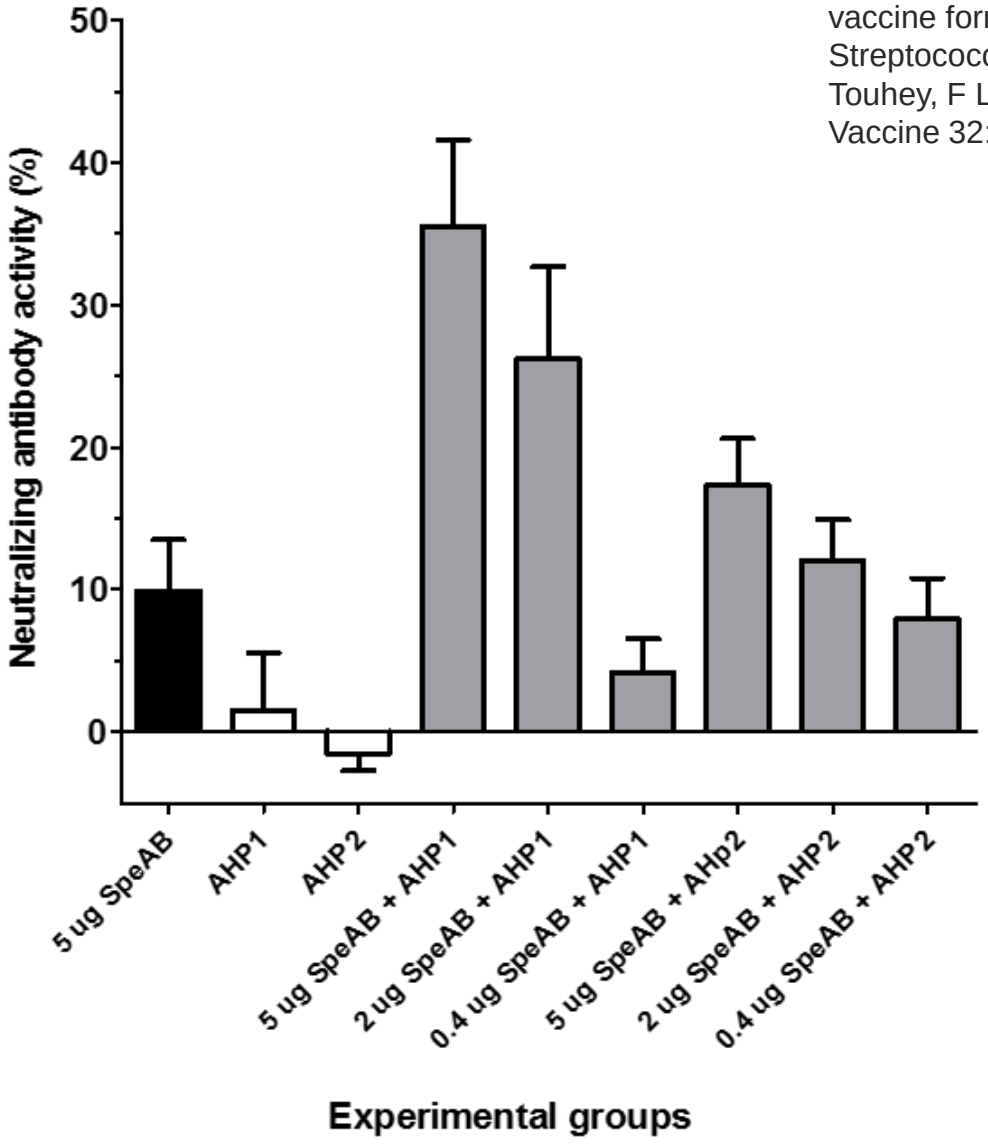
Neutralizing Antibody

Development of a recombinant fusion protein vaccine formulation to protect against Streptococcus pyogenes. G Morefield, G Touhey, F Lu, A Dunham, and H HogenEsch. Vaccine 32:3810-3815, 2014.



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Considerations once a formulation has been determined

- **Adsorption stability**
- **Impact of microenvironment pH**
  - Surface pH can vary by up to 2 pH units from that of the bulk
- **Stability assay development**
  - Can antigen stability be monitored *in vitro* on the adjuvant surface?
- **Impact of adjuvant lot to lot variability**

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Questions?

- **VaxForm**
  - Elodie Burlet, Graham Touhey, Kim Williams, Dan Paez
- **Purdue University**
  - Harm HogenEsch, Anisa Dunham, Fangjia Lu
- **DoD grant W81XWH-12-C-0183**

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