REAL-TIME, DIRECT ANALYSIS OF VACCINE STABILITY WITH NMR IMAGING

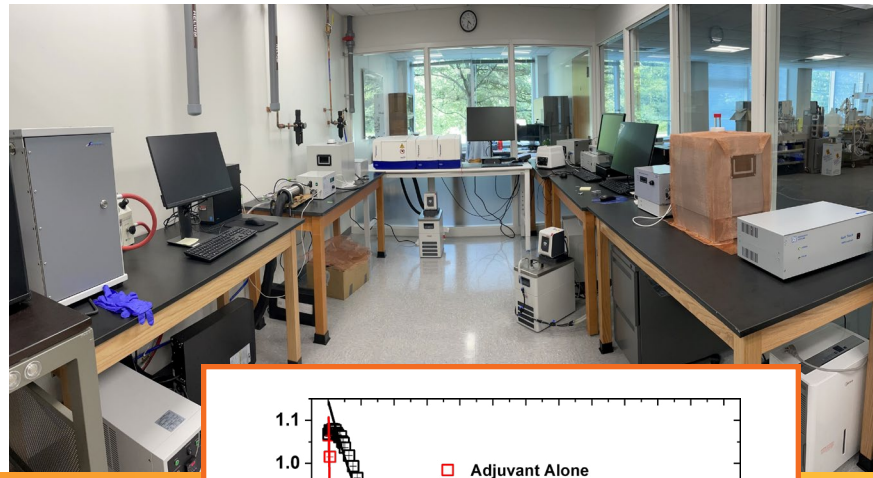
NONINVASIVE PROCESS ANALYTICAL TECHNOLOGY (PAT) FOR ALUMINUM-ADJUVANTED VACCINES

NIIMBL® The National Institute for Innovation in Manufacturing Biopharmaceuticals

University of Maryland Baltimore, Baltimore, MD

Type:
Academic Research Institution

Participating Organizations:
Merck & Co., Inc., Pfizer Inc.



Benchtop NMR Facility for PAT Development and Counterfeit Detection

» ***Bruce Yu,*** *University of Maryland Baltimore*

INDUSTRY NEED

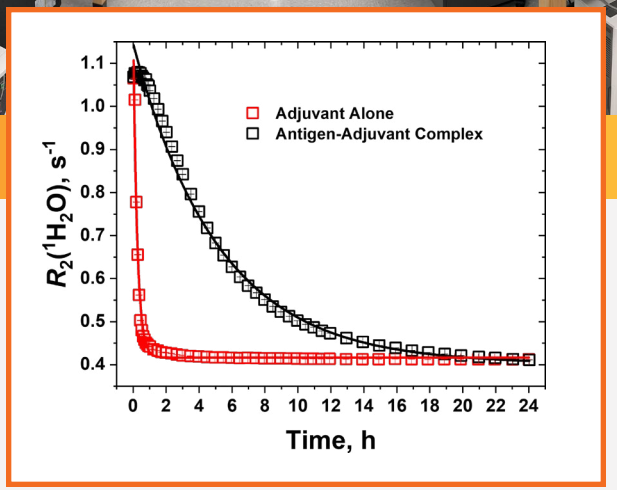
Vaccines often contain adjuvants that help boost the effectiveness of the antigen in stimulating an immune response. Analyzing the stability of adjuvanted vaccines is critical but challenging for several reasons. Adjuvanted vaccines are non-transparent suspensions, and some adjuvants, such as aluminum, can clump together and settle at the bottom of the vial, which interferes with analysis. The vaccine suspension often must be diluted before testing, which introduces the risk of contamination as vials are opened. Some vaccines must be further treated before they can be analyzed, so the vaccine is no longer in its "native" state. These issues are even more complex for vaccines that contain more than one antigen. New noninvasive approaches were needed that could analyze adjuvanted vaccines without tampering or changing the vaccine, and that could be done in real time.

SOLUTION

Led by Bruce Yu, PhD, a team of researchers at University of Maryland Baltimore (UMB) partnered with Merck and Pfizer to evaluate whether nuclear magnetic resonance (NMR) imaging could be used for non-invasive analysis of vaccines containing aluminum adjuvants. NMR can be performed directly on vaccine suspension in vials, without the need for dilution or manipulation. The antigen-adjuvant complex is an active pharmaceutical ingredient (API) of aluminum-adjuvanted vaccines. When antigen is adsorbed to the surface of the aluminum adjuvant, the sedimentation process occurs very quickly. NMR imaging is also fast, with data collected in less than a minute, so it can provide a real-time snapshot of information about the vaccines and antigen-adjuvant interactions.

OUTCOME

NMR was able to noninvasively detect the adsorption of antigens to adjuvant—an important critical quality attribute (CQA) of aluminum-adjuvanted vaccines. The team compared the ability of their wNMR technique to conventional process analytical techniques to measure the effects of gravitation, flow, and freezing/thawing on antigen-aluminum adjuvant interactions in vaccine samples. wNMR analysis performed at UMB produced similar information as conventional techniques performed at Merck and Pfizer. By removing the need for sample preparation, wNMR saved 1 hour of time for every 3 samples analyzed. Minimizing the hands-on steps also reduced the risk of analyst error or sample alteration. While further analysis is needed, the wNMR approach could significantly cut the cost of reagents, equipment, and resources needed for analysis of adjuvanted vaccines. Through this collaboration, Merck and Pfizer were able to draw on the deep knowledge of wNMR at UMB and find new ways to improve process analytics. In turn, Dr. Yu's team at UMB had their innovative NMR technology independently verified by industry and confirmed that their research was filling an industry need.



Antigen-adjuvant complex is an active pharmaceutical ingredient (API) of aluminum-adjuvanted vaccines. When antigen is adsorbed to the surface of aluminum adjuvant, the sedimentation process occurs much faster. wNMR demonstrated capability to non-invasively detect the adsorption of antigens to adjuvant—an important critical quality attribute (CQA) of aluminum-adjuvanted vaccines.

> *"By working with industry, we're able to answer their scientific questions and independently validate the benefits of our technology – it's a win-win situation."*

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