USP Biologics Roundtable on mRNA Standardization
November 14, 2018
USP–U.S. Headquarters, Rockville, MD

Executive summary: USP Staff representatives from industry at a roundtable to explore opportunities for the development of analytical methods and associated standards to support testing of mRNA-based therapies. The goal of the meeting was to facilitate a robust discussion on possible ways that documentary and performance standards could help standardize methods for assessing the quality of raw materials as well as mRNA drug substance. The roundtable participants shared challenges and discussed the need for best practices and methods in addition to physical reference standards that could be available through USP. Production of physical standards for T7 polymerase, a critical enzyme used in production, was the highest ranked opportunity with an mRNA standard ranking second.

Main bullet points from the discussion:

- The default for testing reagents for suitability is "in use" testing where if the desired result is obtained, the components are qualified
- Enzymes are the most problematic reagents. A standard kit for T7 with a specific DNA template and nucleoside triphosphates (NTPs) could be useful to standardize activity
- The DNA template size needs to be discussed as the rate of activity could change throughout transcription of a long transcript. Having a template with a functional marker gene like luciferase or Green Fluorescence Protein (GFP) would be useful for functional testing.
- A standard for RNase inhibitor would also be useful
- A standard for mRNA could be used for quantitation as well as purity

Path forward:

The participants discussed potential solutions to the analytical challenges associated with the characterization of mRNA based therapies, and prioritized ideas for standards in terms of impact/need and feasibility. The two ideas for standards that ranked the highest were the T7 RNA polymerase standard and one or more mRNA standards. USP will engage with reagent suppliers to gather information and discuss collaborative approaches to standardization. Concurrently, USP will gather individual feedback from the participants regarding the composition of proposed standards and design of round robin studies.

We ask that interested individuals please contact Jim Richardson at jim.richardson@usp.org if you have questions or clarifications for the above summary or additional thoughts on the topics that were discussed.