

Supporting the Vaccine Product Lifecycle through Standards

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United States Pharmacopeia Biologics Supporting Vaccines



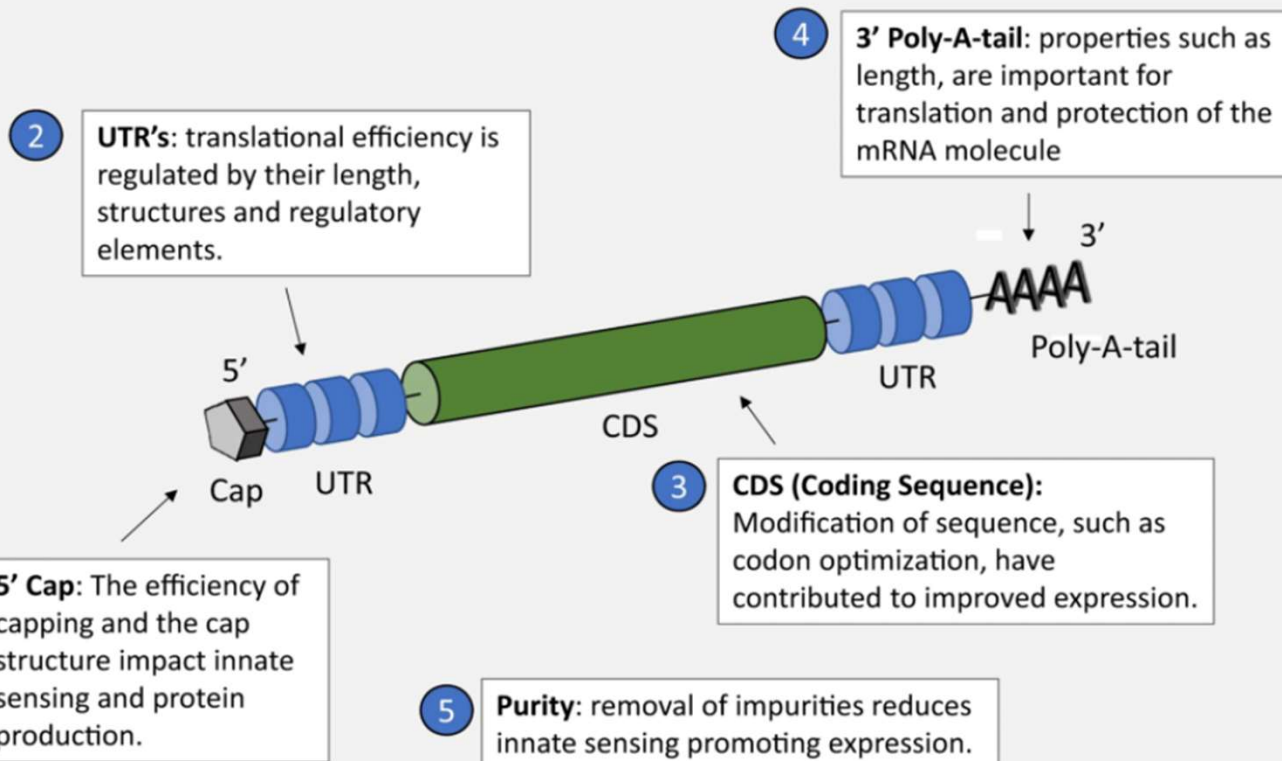
USP Independent
Scientific Standard Setting
for over 200 years

Support development,
manufacturing, regulation
and distribution of
vaccines globally

- 1** **Developing** standards, publications, and other guidance supporting potential vaccines and treatments
- 2** **Expanding** collaborations to provide these tools and facilitate global access to quality vaccines
- 3** **Supporting** analytical and regulatory systems and workforce capabilities of our partners

- ▶ Collaborate with stakeholders to build awareness and consensus on quality
- ▶ Utilize innovative approaches to gather feedback, methods and materials
- ▶ Leverage science and global reach to maximize impact
- ▶ Partner to enhance use of international best practices for informed decision making

Quality Attributes for mRNA Drug Substance



Non-replicating mRNA (NRM)



Self-amplifying mRNA (SAM)



USP Identified Analytical Quality Attributes for mRNA Drug Substance and mRNA Vaccine – Draft guidelines



Includes multiple method options for the same attribute

Learn more about USP's COVID vaccine efforts:
USP.org/COVID-19/Vaccines

Analytical Procedures for mRNA Vaccine Quality

To build public trust and confidence in innovative products like mRNA vaccines and therapies, they must be of good quality, safe and effective. To address the need for a common set of methods for determining mRNA quality—including verifying the identity of the drug substance, controlling impurities and measuring content for dosing—USP is developing a set of analytical methods to support developers, manufacturers, regulatory agencies and national control laboratories worldwide.

USP welcomes public comments on [Analytical Procedures for mRNA Vaccines Quality](#).

- 1 Submit the form below to receive the draft guidelines
- 2 Read and review the draft guidelines
- 3 Submit your comments to USPVaccines@usp.org

Available Online at: www.usp.org/mrna-quality

Table 2. Characterization and release testing for mRNA Drug Substance

Quality	Attribute	Method
Identity	mRNA sequence identity confirmation	*High throughput sequencing (HTS)
		Sanger sequencing
		Reverse Transcriptase – PCR (RT-PCR) ^v
Content	RNA concentration	Quantitative PCR (qPCR)
		digital RT-PCR (RT-dPCR)
		Ultraviolet Spectroscopy (UV)
Integrity	mRNA integrity	Fragment Analyzer ^o
		Capillary gel electrophoresis (CGE) ^{ov}
		Agarose gel electrophoresis
Purity	5' capping efficiency	Liquid chromatography mass spectroscopy (LC-MS) ^o
		*Reverse-phase liquid chromatography mass spectroscopy (RP-LC-MS/MS) ^o
		*Ion pair reverse-phase high-performance liquid chromatography (IP-RP-HPLC)
	3' poly(A) tail length	*Ion pair reverse-phase high-performance liquid chromatography (IP-RP-HPLC)
		Liquid chromatography - mass spectroscopy (LC-MS) ^{ov}
		Ion pair reverse-phase high-performance liquid chromatography (IP-RP-HPLC) ^{ov}
	mRNA purity	Ion pair reverse-phase high-performance liquid chromatography (IP-RP-HPLC) ^{ov}
	Product related impurities - dsRNA	*Immunoblot ^{ov}
		*Enzyme-linked immunosorbent assay (ELISA)
	Product related impurities - percentage of fragment mRNA	*Size exclusion-high-performance liquid chromatography (SEC-HPLC) ^o
		*Reverse-phase HPLC (RP-HPLC) ^o
	Process related impurities - residual DNA template	quantitative PCR (qPCR)
Safety	Endotoxin	Anion-exchange chromatography (AEX-HPLC) ^{ov}
		*Reverse-phase liquid chromatography mass spectroscopy (RP-LC-MS/MS) ^o
	Residual proteins	Enzyme-linked immunosorbent assay (ELISA)
Other	Endotoxin	USP <85>
	Bioburden	USP <61>, <62>, <1115>
	Appearance	USP <790>
	pH	USP <791>

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