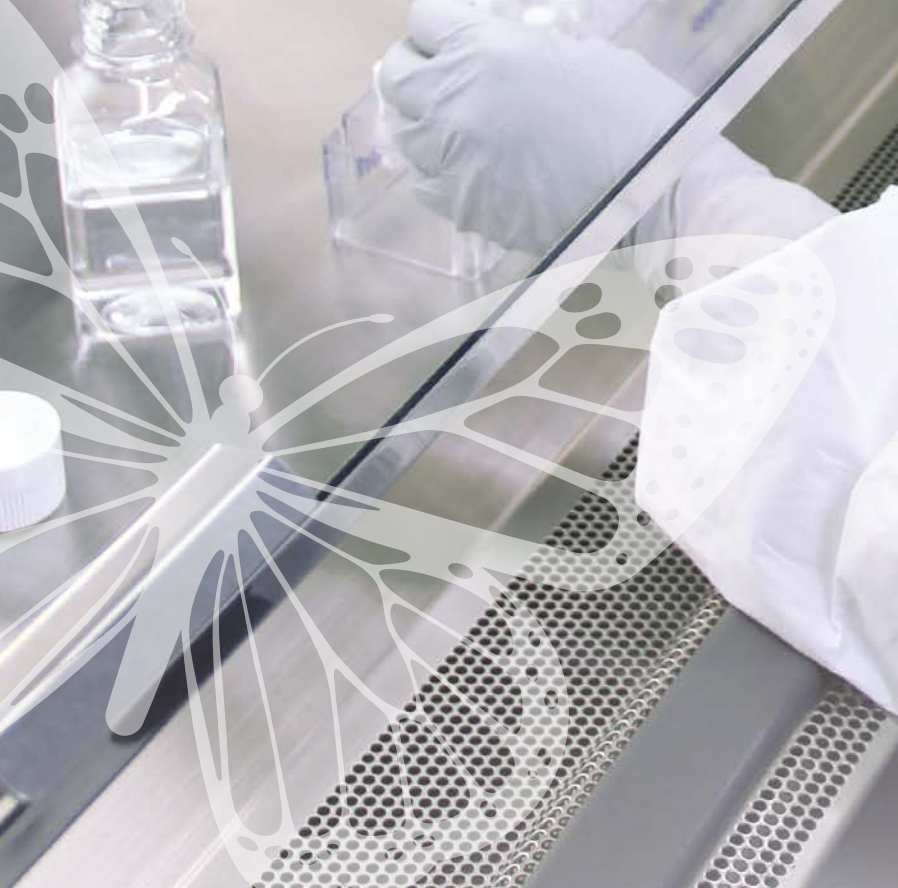


GMP-GRADE REAGENTS FOR RNA SYNTHESIS

TOOLS TO TAKE YOU FROM TEMPLATE TO TRANSCRIPT

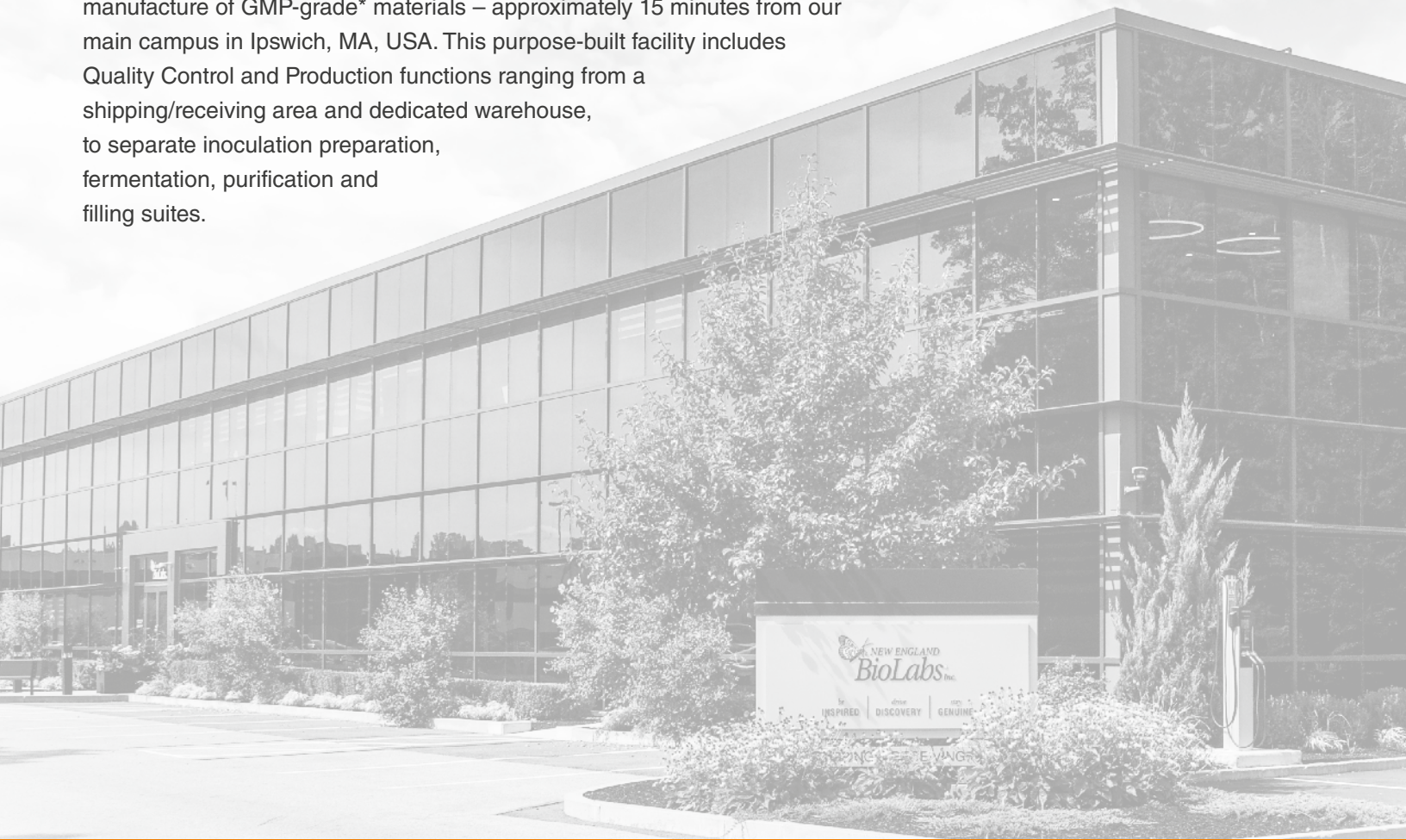


 NEW ENGLAND
BioLabs[®]

be INSPIRED
drive DISCOVERY
stay GENUINE

For over 45 years, NEB® has been a world leader in the discovery and production of reagents for the life science industry. Our **enzymology expertise** effectively positions us to supply reagents for the synthesis of high-quality RNA – from template generation and transcription, to capping, tailing and cleanup after synthesis. These products are designed and manufactured based on **decades of molecular biology experience**, so that you can **be confident they will work for your application**.

To better serve the needs of customers in regulated markets, NEB has opened a state-of-the-art, 43,000 sq. ft. production facility in Rowley, MA for the manufacture of GMP-grade* materials – approximately 15 minutes from our main campus in Ipswich, MA, USA. This purpose-built facility includes Quality Control and Production functions ranging from a shipping/receiving area and dedicated warehouse, to separate inoculation preparation, fermentation, purification and filling suites.



ENABLING GRAM-SCALE RNA SYNTHESIS

NEB manufactures and inventories the following enzyme specificities at GMP-grade, meeting customer needs with short lead times:

- Vaccinia Capping Enzyme
- RNase Inhibitor, Murine
- T7 RNA Polymerase
- Pyrophosphatase, Inorganic (*E. coli*)
- mRNA Cap 2'-O-Methyltransferase
- DNase I (RNase-free)
- BspQI
- Faustovirus Capping Enzyme (coming soon)

* "GMP-grade" is a branding term NEB uses to describe reagents manufactured and/or finished at our Rowley, MA facility, where we utilize procedures and process controls to manufacture reagents under more rigorous conditions to achieve more stringent product specifications, and in compliance with ISO 9001 and ISO 13485 quality management system standards. NEB does not manufacture or sell products known as Active Pharmaceutical Ingredients (APIs), nor do we manufacture products in compliance with all of the Current Good Manufacturing Practice regulations.



BENEFITS OF GMP-GRADE MANUFACTURING AT NEB

NEB's expertise in enzyme manufacturing positions us to best anticipate your needs and minimize the risk of transferring manufacture of your materials to our GMP-grade production facility. Examples of customer requirements that are achieved by our GMP-grade reagents include:

- Bioburden and/or endotoxin specifications on reagents
- Certified animal-free origin and manufacturing process
- Qualified equipment, utilities, QC test methods and instrumentation to deliver the highest levels of lot-to-lot consistency

Infrastructure & Approach

- Purpose-built for GMP-grade manufacturing
- Increased manufacturing output
- ISO 8 clean rooms, ISO 5 filling hoods
- Environmental monitoring of the facility
- Animal-free facility

Manufacturing Processes

- Lateral transfer from Ipswich to Rowley
- Characterized master cell banks
- Ampicillin-free processes
- Dedicated chromatography resins
- 0.22 micron-filtered final product

Product Attributes/Testing

- TSE/BSE statements – animal-free raw materials, processes and formulation
- Bioburden and endotoxin included for all products, with numerical values provided
- Appearance, protein concentration, gDNA contamination and other current QCs qualified
- Stability testing program
- Contamination and other current QCs qualified

QA & Regulatory

- ISO 9001 and ISO 13485 certification
- Batch history files/batch records
- Defined CQAs and CPPs
- Enhanced change management and lot disposition processes
- Customer support for regulatory submissions












Learn more at

www.neb.com/GMP

mRNA SYNTHESIS WORKFLOW

EXAMPLE & AVAILABLE NEB PRODUCTS

TEMPLATE GENERATION	IN VITRO TRANSCRIPTION	RNA CAPPING	POLY(A) TAILING	RNA PURIFICATION	
Q5 [®] High-Fidelity DNA Polymerase	HiScribe [®] T7 mRNA Kit with CleanCap [®] Reagent AG		<i>E. coli</i> Poly(A) Polymerase	Monarch [®] RNA Cleanup Kit (10 µg)	
	HiScribe T7 ARCA mRNA Synthesis Kit (with tailing)				
dNTP solution mixes	HiScribe T7 ARCA mRNA Synthesis Kit			Monarch RNA Cleanup Kit (50 µg)	
 BspQI*	 HiScribe T7 High Yield RNA Synthesis Components	 Faustovirus Capping Enzyme <small>COMING SOON</small>		Monarch RNA Cleanup Kit (500 µg)	
DNA Assembly • NEBuilder HiFi DNA Assembly • Golden Gate Assembly	HiScribe T7 Quick High Yield RNA Synthesis Kit	 Vaccinia Capping System		Lithium Chloride	
	HiScribe SP6 High Yield RNA Synthesis Kit	 mRNA Cap 2'-O-Methyltransferase			
	T3 & SP6 RNA Polymerases	ARCA and other mRNA cap analogs			
	 T7 RNA Polymerase				
	Hi-T7 RNA Polymerase				
	Companion Products				Companion Products
	 RNase inhibitor (Murine)				Monarch RNA Cleanup Binding Buffer
	RNase Inhibitor (Human Placental)				Monarch RNA Cleanup Wash Buffer
	 Pyrophosphatase, Inorganic (<i>E. coli</i>)				Nuclease-free Water
	Pyrophosphatase, Inorganic (Yeast)				
	 DNase I (RNase-free)				
	DNase I-XT				
	NTPs				

 = available in GMP-grade



* NEB can offer large-scale preparations of restriction enzymes using Recombinant Albumin (BSA-free)

From research to therapeutic production, NEB's *in vitro* transcription portfolio will meet your needs.

NEB's portfolio of research-grade and GMP-grade reagents support microgram scale research production to gram scale therapeutic mRNA production. Our optimized HiScribe kits enable convenient *in vitro* transcription (IVT) workflows. When it is time to scale up and optimize reaction components, our standalone reagents are readily available in formats matching our GMP-grade offering, enabling a seamless transition to large-scale therapeutic manufacturing.

To inquire about custom formats or GMP-grade reagent production, contact our Customized Solutions Team at custom@neb.com.

NOT SURE WHETHER YOU NEED **RESEARCH- GRADE (RUO)** OR **GMP-GRADE** MATERIALS?

		RUO	GMP
mRNA PRODUCTION 	Ability to produce gram to kilogram quantities of mRNA		✓
	Support production of commercially approved mRNA product(s)		✓
	Comparability reports supporting migration from RUO to GMP-grade reagents for clinical production		✓
PRODUCT CUSTOMIZATION 	Examples include but are not limited to: High-concentration enzymes, formulation, packaging and fill size	✓ Contact our Customized Solutions Team to discuss	✓ Contact our Customized Solutions Team to discuss
INFRASTRUCTURE 	Animal-free facility		✓
	Validation programs in place based on risk assessments	✓	✓
	Expanded validation requirements for facility/utilities/process equipment for GMP-grade		✓
	ISO 8 Clean Rooms ISO 5 Filling Hoods		✓
	Multiple production sites for business continuity	✓	✓
MANUFACTURING PROCESSES 	Ampicillin-free processes	Contact our Customized Solutions Team to discuss	✓
	Animal-free processes and final formulation	Contact our Customized Solutions Team to discuss	✓
	Characterized master cell banks		✓
PRODUCT ATTRIBUTES/ TESTING 	Comprehensive panel of product contamination assays performed	✓	✓
	Qualified assays with quantitative results		✓
	Compendial assays applied to all products, including bioburden and endotoxin levels		✓
	TSE/BSE statements – animal-free raw materials, processes and formulation	Contact our Customized Solutions Team to discuss	✓
QA & REGULATORY 	ISO 9001 and ISO 13485 certified	✓	✓
	Batch history files/batch history records	✓	✓
	Consolidated batch history file/batch records and defined critical quality attributes and critical process parameters and QA reviews		✓
	Change management and lot disposition by Quality Unit	✓	✓
	Regulatory support package including but not limited to the following risk statements – melamine, antibiotic, mutagenic and elemental impurities, nitrosamine and residual solvent		✓
	Validated shipping configurations	✓	✓
RECOMMENDED USE 		Research use or preclinical applications	Clinical or commercial GMP applications

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