

# R&D AND MANUFACTURING SUPPORT FOR THE BIOTECH AND BIOPHARMA INDUSTRY

EXTENSIVE EXPERIENCE. SUPERIOR QUALITY. INNOVATIVE SOLUTIONS.







## LET NEB'S SCIENTIFIC EXPERTISE HELP **DRIVE YOUR INNOVATIONS FORWARD**

In recent years, and accelerated by the COVID-19 pandemic, there has been a dramatic rise in the number of biologics and companion diagnostics being developed and commercialized. These important areas of biotechnology are more reliant than ever on cutting edge molecular biology tools and techniques. For instance, diagnostics, based on DNA amplification, can foster a better match of effective therapies with patients; personalized medicines, utilizing next-generation sequencing, can help tailor treatments for specific patients; vaccines based on DNA or mRNA are now being rapidly developed; and a wide range of biologics is now being developed as a result of advancements in recombinant technologies.

# IT'S TIME TO THINK DIFFERENTLY

At NEB, we have **decades of experience** in practicing molecular biology, which has led to the introduction of a broad product portfolio that has the potential to touch almost every stage of today's biotechnology discovery and development processes. With this expertise in hand, we are ready and able to **collaborate with biotech companies**, large and small, to support your discoveries and help them move through clinical testing, manufacturing, and quality control, and into regulated markets around the world.

\* "GMP-grade" is a branding term NEB uses to describe reagents manufactured 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.

## COLLABORATION

We're here to champion your efforts. We have **extensive scientific expertise** and can devote the necessary attention to developing solutions for your specific needs – along with the manufacturing capacity to **scale up quickly**. Whether you're looking for a custom version of an existing product, to find a new way around a development roadblock, or to license one of our technologies, our team is **ready to work with you**.

## PRODUCT PORTFOLIO

We can provide an entire **suite of enzymes** that have the potential to **accelerate your discovery efforts**. Our expertise in enzymology has enabled us to develop unique enzymes that enable **faster, more robust workflows**. Further, enzymes can be provided both in small aliquots and in bulk, in different formats (liquid, lyophilized and glycerol-free), as well as packaged into plates and complete kits. If we don't already have a solution that meets your needs, our Customized Solutions Team can help you formulate one that does.

## QUALITY

Our attention to quality is **second to none**. We are fully compliant and certified to ISO 9001:2015 and ISO 13485:2016 standards, and have recently completed building a **GMP-grade\* manufacturing facility** for reagents used in more regulated markets, including vaccine production. In addition, we are transitioning several of our buffers and enzymes to utilize recombinant Albumin (rAlbumin), for those that are moving away from animal-containing products.

## TECHNICAL SUPPORT

You can be sure that the people you contact for technical support are as knowledgeable as the scientists who work in our labs – because they're one and the same. When you pick up the phone or send an email, you **get right to the source of useful information** and effective solutions.

## GLOBAL SUPPLY CHAIN

In addition to our headquarters in the USA, NEB has warehousing capabilities in Australia, Canada, China, UK, Germany, Japan and Singapore, which can be used to not only **access our products rapidly**, but also get them to your collaborators and customers.

# THINK OF NEB AS YOUR EXPERIENCED PARTNER THROUGHOUT THE BIOTECHNOLOGY DISCOVERY PROCESS

## SYNTHETIC BIOLOGY AND DNA ASSEMBLY

A more recent expansion of the biotechnology field, synthetic biology utilizes genes and proteins as parts or devices, with the goal of re-designing and/or assembling these parts in novel ways to create a new and useful functionality.

Recent advances in biofuels generation, the production of biochemicals, and understanding the minimal genome, all benefit from synthetic biological approaches. Historically, conventional genome engineering in the agricultural industry has involved the insertion of new genes in plants. Synthetic biology approaches enable the insertion of entire genetic pathways to produce desirable traits, such as disease resistance or improved nutritional value.

The pharmaceutical industry has also benefitted from advances in synthetic biology. Examples include the design of minimal synthetic cells, containing a genetic circuit linking genetic regulators with an output signal, such as luminescence or fluorescence for phenotypic cell-based screening, the generation of small molecule libraries from the reorganization of synthetic biology parts, and cell-free metabolic engineering.

Often these projects rely on the ordered assembly of multiple DNA sequences to create large, artificial DNA structures. To this end, methods have evolved to simplify this process. Tools such as **NEBuilder® HiFi DNA Assembly (NEB #E2621, E5520, E2623)** and **NEBridge Golden Gate Assembly (NEB #E1601, E1602)** can be used to rapidly create many functional DNA structures, from a simple joining of two metabolic genes, all the way up to the creation of an artificial genome.

 NEB provides a wide range of products to support synthetic biology, DNA assembly, and other cloning techniques. Find out how these products can speed up your workflows for both simple and complex reaction design at **CloneWithNEB.com**.

## FEATURED PRODUCT: NEBuilder® HiFi DNA Assembly

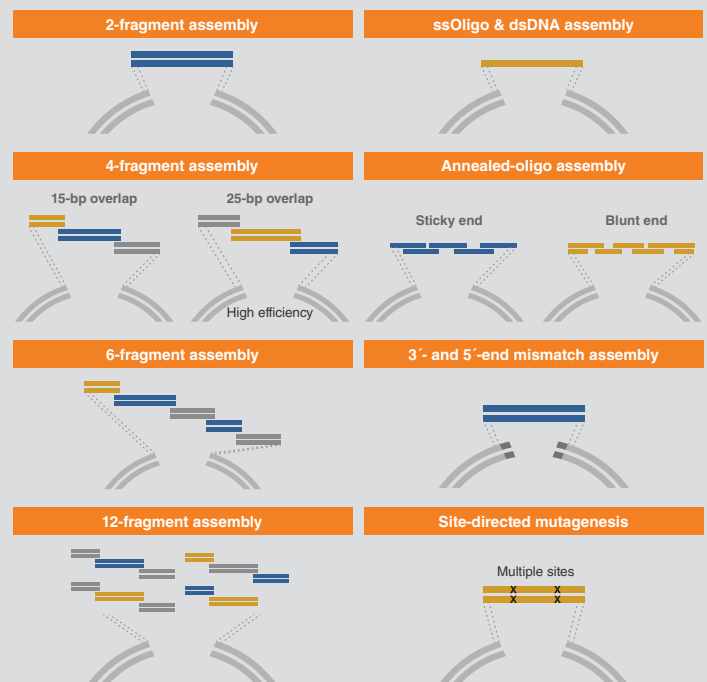
NEB #E2621S/L/X

- Enjoy simple and fast seamless cloning in as little as 15 minutes
- Use one system for both "standard-size" cloning and larger gene assembly products, up to 11 fragments
- DNA can be used immediately for transformation or as template for PCR or RCA
- Adapts easily for multiple DNA manipulations, including site-directed mutagenesis
- Design primers using our free online tool at [NEBuilder.neb.com](http://NEBuilder.neb.com)
- No licensing fee requirements from NEB for NEBuilder products



Visit [NEBuilderHiFi.com](http://NEBuilderHiFi.com) for more details.

### Not your average DNA assembly reagent



NEBuilder HiFi DNA Assembly can be used for a variety of DNA assembly methods.



## GENOME EDITING (CRISPR/CAS9)

Perhaps no other tool in genomic engineering has received more attention of late than CRISPR-based methods. Programmable nucleases enable the generation of permanent mutations by generating site-specific double stranded breaks. Knock-outs and knock-ins can be rapidly introduced in cell lines and model organisms.

The validation of small molecule targets by knocking out gene function or rescuing drug sensitivity by modifying drug resistant alleles is now a standard method for target validation. By combining next generation sequencing for the discovery of compound-resistant mutations and CRISPR-based methods for target validation, drug-target pairs can be identified and validated in model systems, such as mammalian cells, as well as model organisms.

**NEB provides reagents to support a broad variety of CRISPR/Cas9 genome editing approaches.** From the introduction of Cas9 and single guide RNA (sgRNA) into plasmids, to direct introduction of Cas9 ribonucleoprotein (RNP), and the detection of edits using next generation sequencing or enzymatic mutation detection, NEB provides reagents that simplify and shorten genome editing workflows.



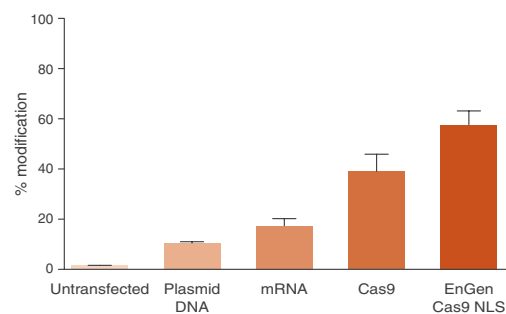
For more details on how NEB can help improve your genome editing efficiencies, visit [www.neb.com/GenomeEditing](http://www.neb.com/GenomeEditing).

## FEATURED PRODUCT: EnGen® Cas9 NLS

NEB #M0646T/M

- Ideal for direct introduction of Cas9/sgRNA complexes
- Dual NLS for improved transport to the nucleus
- Compatible with the EnGen sgRNA Synthesis Kit, *S. pyogenes* (NEB #E3322S) and the EnGen Mutation Detection Kit (NEB #E3321S)

Increased genome editing efficiency using Cas9 RNP delivery



Cas9 and sgRNA targeting a human gene were delivered to HEK293 cells by transfection. Transfected plasmid DNA contained expression cassettes for 2x NLS (N- and C-terminal) Cas9 and sgRNA. Plasmid DNA was delivered using TransIT-X2 (Mirus). Transfected mRNA was modified with pseudouridine and 5-methylcytosine and encoded 2x NLS (N- and C-terminal) Cas9. sgRNA was co-transfected with the mRNA using TransIT-mRNA. Cas9 RNPs were delivered in reverse transfections using Lipofectamine RNAiMAX (Life Technologies) using 10 nanomolar final concentration of ribonucleoprotein (RNP). Cas9 has no NLS in the protein sequence. EnGen Cas9 has N- and C-terminal NLSs. The efficiency of editing was determined using T7 Endonuclease I assay and is expressed as % modification.



Visit [www.neb.com/M0646](http://www.neb.com/M0646) for more details.





## NEXT GENERATION SEQUENCING

Next generation sequencing (NGS) has proven a valuable technology across a broad range of areas for the development and application of novel therapies. Library preparation is a critical part of the NGS workflow; successful sequencing requires the generation of high quality libraries of sufficient yield. As sequencing technologies improve and applications expand, the need for compatibility with ever-decreasing input amounts and sub-optimal sample quality grows. Scientists must balance reliability and performance with faster turnaround, higher throughput and automation compatibility.

With almost 50 years of expertise in enzyme research and manufacturing, **NEB is a world leader in the development of innovative technologies, including for sample prep for next generation sequencing.** With over 90 application-specific products available, the NEBNext® product portfolio supports a broad range of sequencing based technologies, including whole genome sequencing, transcriptome, methylome, and single-cell RNA-seq, and target enrichment.



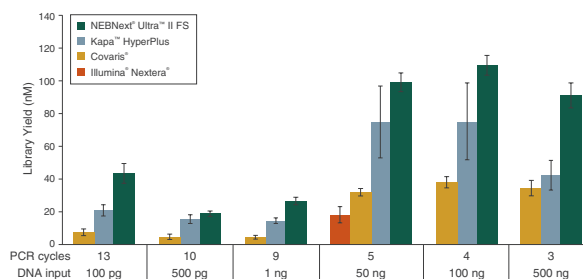
Find out how NEBNext kits can help streamline your workflows and generate high quality libraries, even with limited amounts of DNA or RNA, at [NEBNext.com](http://NEBNext.com).

## FEATURED PRODUCT: NEBNext® Ultra™ II FS DNA Library Prep Kit for Illumina®

NEB #E7805S/L

- Perform fragmentation, end repair and dA-tailing in a single enzyme mix
- Experience reliable fragmentation with a single protocol, regardless of DNA input amount or GC content
- Prepare high yields of high quality libraries from a wide range of input amounts: 100 pg – 0.5 μg
- PCR-free workflows available

NEBNext Ultra II FS DNA produces the highest yields, from a range of input amounts



*Libraries were prepared from Human NA19240 genomic DNA. For NEBNext Ultra II FS, a 20-min. fragmentation time was used. For Kapa HyperPlus libraries, input DNA was cleaned up with 3X beads prior to library construction, as recommended, and a 20-min. fragmentation time was used. Illumina recommends 50 ng input for Nextera, and not an input range; therefore, only 50 ng was used in this experiment. "Covaris" libraries were prepared by shearing in 1X TE Buffer to an insert size of ~200 bp using a Covaris instrument, followed by library construction using the NEBNext Ultra II DNA Library Prep Kit (NEB #E7645). Error bars indicate standard deviation for an average of 3–6 replicates performed by 2 independent users.*



Visit [www.neb.com/E7805](http://www.neb.com/E7805) for more details.


# ADVANCING YOUR TECHNOLOGIES FASTER WITH NEBNext

## ULTRA II LIBRARY PREP REAGENTS

The NEBNext Ultra II workflow lies at the heart of NEB's portfolio for next generation sequencing library preparation. NEBNext Ultra II kits and modules for Illumina are the perfect combination of reagents, optimized formulations and simplified workflows, enabling you to create DNA or RNA libraries of highest quality and yield, even when starting from extremely low input amounts.

The Ultra II workflow is central to many of our NEBNext solutions, including:

- Ultra II DNA & FS DNA Library Prep (standard and PCR-free version available)
- Enzymatic Methyl-seq (EM-seq™)
- Ultra II RNA & Directional RNA Library Prep
- Single Cell/Low Input RNA Library Prep
- Module products for each step in a workflow

 Find the right NEBNext product for you by using the NEBNext Selector at [NEBNextSelector.neb.com](http://NEBNextSelector.neb.com).

### The NEBNext Ultra II Workflow:



### Advantages of the Ultra II Workflow:

- Learn one central workflow and apply it to a suite of different applications
- Save time with streamlined, modular workflows, reduced hands-on time, and automation compatibility
- Benefit from low input amount requirements, fewer PCR cycles and uniform GC-coverage in all applications

## FEATURED PRODUCT:

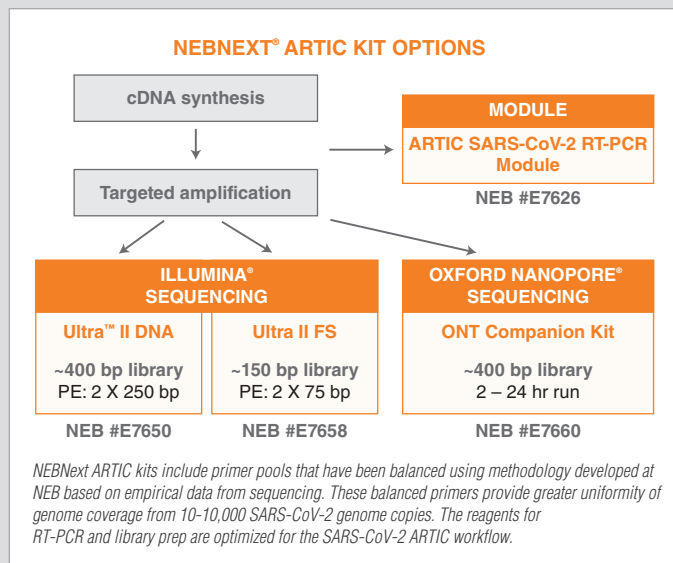
# NEBNext ARTIC SARS-CoV-2 Solutions for Illumina and Oxford Nanopore Technologies®

The ARTIC method is a multiplexed amplicon-based whole-viral-genome sequencing approach; NEB offers two kits compatible with Illumina sequencing that generate library inserts of ~150 bp or ~400 bp, for 2 x 75 or 2 x 250 sequencing, respectively. The NEBNext ARTIC SARS-CoV-2 RT-PCR Module contains only the reagents required for cDNA synthesis and targeted cDNA amplification from SARS-CoV-2 genomic RNA. Express workflow options are provided, with reduced cleanup steps.

Updated primers are now included for improved coverage with variants, including Omicron.



Visit [neb.com/ARTIC](http://neb.com/ARTIC) for more details.



# UNIQUE SOLUTIONS TO STREAMLINE YOUR WORKFLOWS AND MAXIMIZE YIELDS

## IN VITRO TRANSCRIPTION

mRNA-based medicine holds great promise for applications in infectious disease vaccination, cancer vaccination, as well as other disease treatments. Delivery of mRNA is thought to present less risk than DNA-based therapies, and has additional benefits in speed of production and personalization, versus protein delivery. Functional mRNA requires the presence of a m7G cap and poly(A) tail for recognition by the host cellular translation system. In addition, other structures may be desirable, such as the presence of modified bases or Cap-1 structures.

**NEB provides a variety of tools for the *in vitro* transcription (IVT) of RNA and mRNA.** Reagents can be purchased separately or as optimized kits. These reagents support applications ranging from benchtop research to large scale RNA production and purification for clinical applications.

**NEB also provides kits for fast and simple cleanup of synthesized RNA.** Monarch® RNA Cleanup Kits (NEB #T2030, T2040, T2050) are available for purification of 10, 50 and 500 µg of RNA, and efficiently removes reaction components, including unincorporated nucleotides, resulting in highly pure RNA for downstream applications.

**NEB also offers a wide variety of restriction enzymes that are used for linearization of plasmid,** including BspQI (NEB #R0712), SapI (NEB #R0569) and XbaI (NEB #R0145) prior to *in vitro* transcription.

\* "GMP-grade" is a branding term NEB uses to describe reagents manufactured at NEB's Rowley facility. The Rowley facility was designed to manufacture reagents under more rigorous infrastructure and process controls to achieve more stringent product specifications and customer requirements. Reagents manufactured at NEB's Rowley facility are manufactured in compliance with ISO 9001 and ISO 13485 quality management system standards. However, at this time, NEB does not manufacture or sell products known as Active Pharmaceutical Ingredients (APIs), nor does NEB manufacture its products in compliance with all of the Current Good Manufacturing Practice regulations.



NEB offers a selection of HiScribe RNA synthesis kits for the generation of high yields of high quality RNA that can be used in a wide variety of applications. Find out how NEB can streamline your RNA workflows at [NEBrna.com](http://NEBrna.com).



Looking for GMP-grade\* reagents for manufacturing therapeutic RNA? Visit [www.neb.com/GMP](http://www.neb.com/GMP) to find out how NEB can help.

## FEATURED PRODUCT:

# HiScribe™ T7 High Yield RNA Synthesis Kit

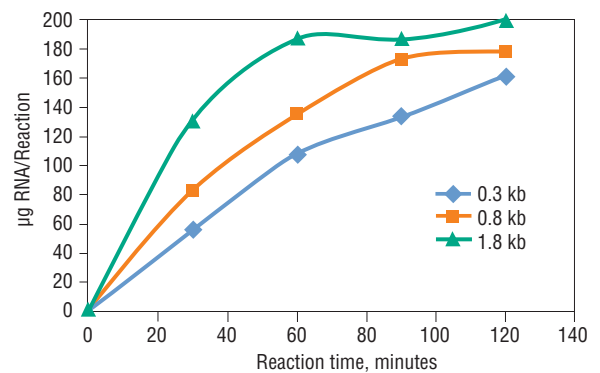
NEB #E2040S

- Up to 180 µg of RNA per reaction from 1 µg of control template
- Enables full substitution of NTPs for labeling and incorporation of modified bases
- Linearized control template included for verification of RNA synthesis



Need to clean up your RNA after synthesis? Try our Monarch® RNA Cleanup Kit (50 µg, NEB #T2040) or (500 µg, NEB #T2050) for fast recovery of highly pure RNA. Visit [www.NEBMonarch.com](http://www.NEBMonarch.com) for more details.

## Robust RNA Synthesis from a variety of template sizes using the HiScribe T7 High Yield RNA Synthesis Kit



Time course of standard RNA synthesis from three DNA templates of different sizes using HiScribe T7 High Yield RNA Synthesis Kit. Reactions were assembled according to the protocol and incubated at 37°C for the indicated time. Transcripts were purified over spin columns and quantified on a NanoDrop™ Spectrophotometer to calculate reaction yield.



Visit [www.neb.com/E2040](http://www.neb.com/E2040) for more details.





## PROTEIN EXPRESSION & PURIFICATION

Recombinant production of proteins is one of the most powerful techniques used in biotechnology. The ability to produce an abundance of a desired protein can enable a wide range of possibilities, including its use in industrial processes or to diagnose or treat disease.

At first glance, recombinant protein expression looks quite simple. However, it can be very challenging, because so many factors influence the process. For example, each protein folds in its own unique manner; some proteins require post-translational modifications, and some proteins have activities that are detrimental to their host. Thus, no single solution exists for the successful production of all recombinant proteins.

Focused on prokaryotic systems, **NEB was one of the first companies to recognize the promise of recombinant technologies, and has since developed a wide array of protein expression solutions**, including many for proteins that are difficult to express. Each NEB technology offers different advantages, which enable you to choose the strategy that best suits your protein expression and purification needs.



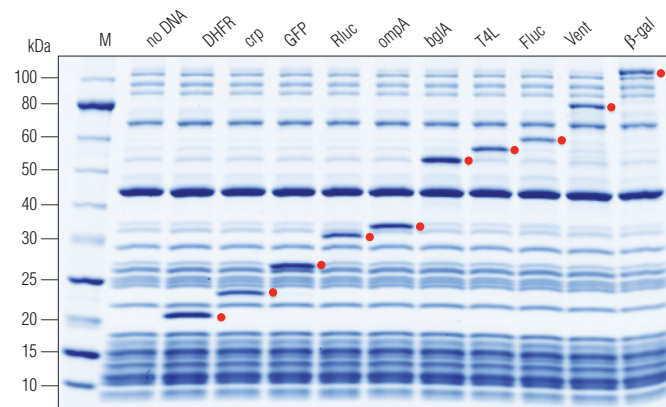
Visit [www.neb.com/ProteinExpression](http://www.neb.com/ProteinExpression) to view NEB's portfolio of products.

## FEATURED PRODUCT: PURExpress® *In Vitro* Protein Synthesis Kit

NEB #E6800S/L

- Express a wide range of proteins free of modifications and degradation
- Save valuable time with results available in just a few hours
- Use with plasmid DNA, linear DNA or mRNA
- One-step reaction requiring the mixing of only two tubes

### Protein expression using the PURExpress *In Vitro* Protein Synthesis Kit



Reactions were carried out according to manual recommendations. Red dot indicates protein of interest. Marker M is the Protein Ladder (NEB #P7703).



Also available: NEBExpress® Cell-free *E. coli* Protein Synthesis Kit. For more details on these products, visit [www.neb.com/ProteinExpression](http://www.neb.com/ProteinExpression).



## GLYCOPROTEOMICS

Over the past 20 years, the list of enzymes available for glycan analysis has steadily grown, and many of these enzymes have transitioned from academic research into workflows that both characterize glycans on biotherapeutics and support glycan-based clinical tests. As a result of this, and the growing importance and understanding of protein glycosylation in disease, new demands are being placed on the quality of reagents used for glycan analysis.

**NEB is committed to continually improving the quality of its glycosidases with the aim of supporting their routine use in biopharma and clinical diagnostic applications.** Many of these reagents are recombinant, and all undergo multiple quality control assays, enabling us to provide products with lower unit cost, higher purity, and reduced lot-to-lot variation.



Visit [www.neb.com/glycosidase](http://www.neb.com/glycosidase) to learn more, view the full list of products available, and access the articles, “Redesigning glycosidase manufacturing quality for pharmaceutical and clinical applications,” and “O-glycan analysis of therapeutic proteins enabled by O-glycoprotease.”

## FEATURED PRODUCT:

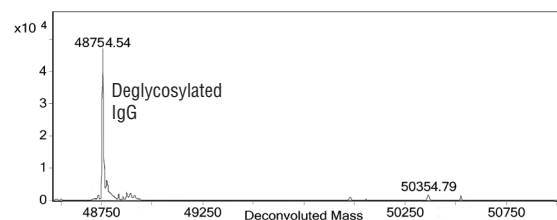
# Rapid™ PNGase F

NEB #P0710S

- Speed up deglycosylation with one-step reaction setup
- Release all N-glycans without bias
- Achieve sensitive and reproducible results with short reaction times
- Move directly to downstream analysis

Rapid PNGase F results in complete deglycosylation with a short incubation

### Rapid PNGase F (5 min. at 50°C)



*A monoclonal murine antibody was incubated for 5 min. with Rapid PNGase F, demonstrating that a short incubation is sufficient to deglycosylate every N-glycan site without bias.*



Visit [www.neb.com/PNGaseF](http://www.neb.com/PNGaseF) for more details.

# MONARCH DNA & RNA PURIFICATION KITS

FAST AND RELIABLE PURIFICATION OF HIGH QUALITY DNA & RNA USING BEST-IN-CLASS SILICA COLUMN TECHNOLOGY

Workflows for detecting, analyzing, amplifying or manipulating DNA and RNA often require extraction and purification from a biological sample and/or enzymatic reactions. Monarch nucleic acid purification kits provide fast and reliable purification of high-quality DNA and RNA from a variety of sources using best-in-class silica column technology, and a novel glass bead-based approach for HMW DNA extraction. DNA and RNA purified with Monarch kits is highly-pure and suitable for use in a wide variety of downstream applications including sequencing, cloning, PCR and other enzymatic manipulations. Monarch kits are designed with sustainability in mind; they use less plastic and are packaged in responsibly-sourced, recyclable material. For convenience, Monarch buffers and columns are also available separately.

## Monarch Kits are available for:

- Genomic DNA Extraction & Purification
- High Molecular Weight (HMW) Genomic DNA Extraction
- Total RNA Extraction & Purification
- RNA Cleanup
- DNA Cleanup & Gel Extraction
- Plasmid Purification



Learn more about Monarch Kits, and request a free sample, at **NEBMonarch.com**.

## APPLY NEB'S SCIENTIFIC AND MANUFACTURING EXPERIENCE TO HELP **DRIVE YOUR INNOVATION**

IT'S TIME TO THINK DIFFERENTLY AND CONSIDER PARTNERING WITH NEB!

- Visit [www.neb.com/DriveYourInnovation](http://www.neb.com/DriveYourInnovation) to learn more and request a discussion or visit from your NEB representative
- Developing a new life science product or technology? Contact our Customized Solutions Team at [custom.uk@neb.com](mailto:custom.uk@neb.com) to start building your solution
- Learn more about custom or bulk opportunities at [www.neb.com/CustomizedSolutions](http://www.neb.com/CustomizedSolutions)
- Starting a new laboratory or company? Contact your local NEB representative to see how we can help you! For international customers, visit [www.neb.com/internationalorders](http://www.neb.com/internationalorders) to locate your local NEB point of contact.







be INSPIRED  
drive DISCOVERY  
stay GENUINE

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