

Stock Name(SSE): Novoprotein
Stock Code: 688137.SH

novoprotein
近岸蛋白

Facilitate the Development and Industrialization of
Innovative Vaccines and Drugs

Innovative Vaccines and Drugs Development Solutions



Novoprotein Scientific Inc.

INDEX

GMP Grade animal-free, ampicillin-free

mRNA Vaccines and Drugs Enzymatic Solutions 5

The Prospect of mRNA Vaccines and Drugs Research 6

Preparation of Linear Template DNA 7

In vitro Transcription (IVT) 10

mRNA Capping 17

mRNA Tailing 19

mRNA Enzymes DIBA Kit——mRNA Enzymes Identification Reagents 21

dsRNA Residue Detection Kit 22

Enzyme Residue Detection Kit 24

Catalog mRNA 25

GMP Grade animal-free, ampicillin-free

DNA/RNA Removal 26

BenzoNuclease® 26

BenzoNuclease® ELISA Kit 34

Infectious Pathogen Vaccine Research Products 35

SARS-CoV-2 Omicron Variants Protein 35

Pseudoviruses and ACE2 Overexpressed Cell Lines 36

Respiratory Syncytial Virus (RSV) 36

Monkeypox Virus (MPXV) 36

Varicella-Zoster Virus (VZV) 37

African Swine Fever Virus (ASFV) 37

Porcine Reproductive and Respiratory Syndrome Virus (PRRSV) 37

Pseudorabies Virus (PRV) 37

Support 38



Dedicated & Professional

Novoprotein Scientific Inc. (Novoprotein) is a high-tech enterprise with more than 10 years of extensive experience in the recombinant protein industry, focusing on protein technology, and advanced in R&D, production, sales, and application solutions to raw materials and techniques for biopharmaceuticals, in vitro diagnosis, mRNA vaccines, and basic life science research. Our principal products include target proteins and cytokines, recombinant antibodies, molecular enzymes and reagents, as well as providing related technical services. Novoprotein possesses R&D and manufacturing bases in Shanghai, Suzhou, and Heze.



novoprotein
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Animal-Free Statement

STATEMENT

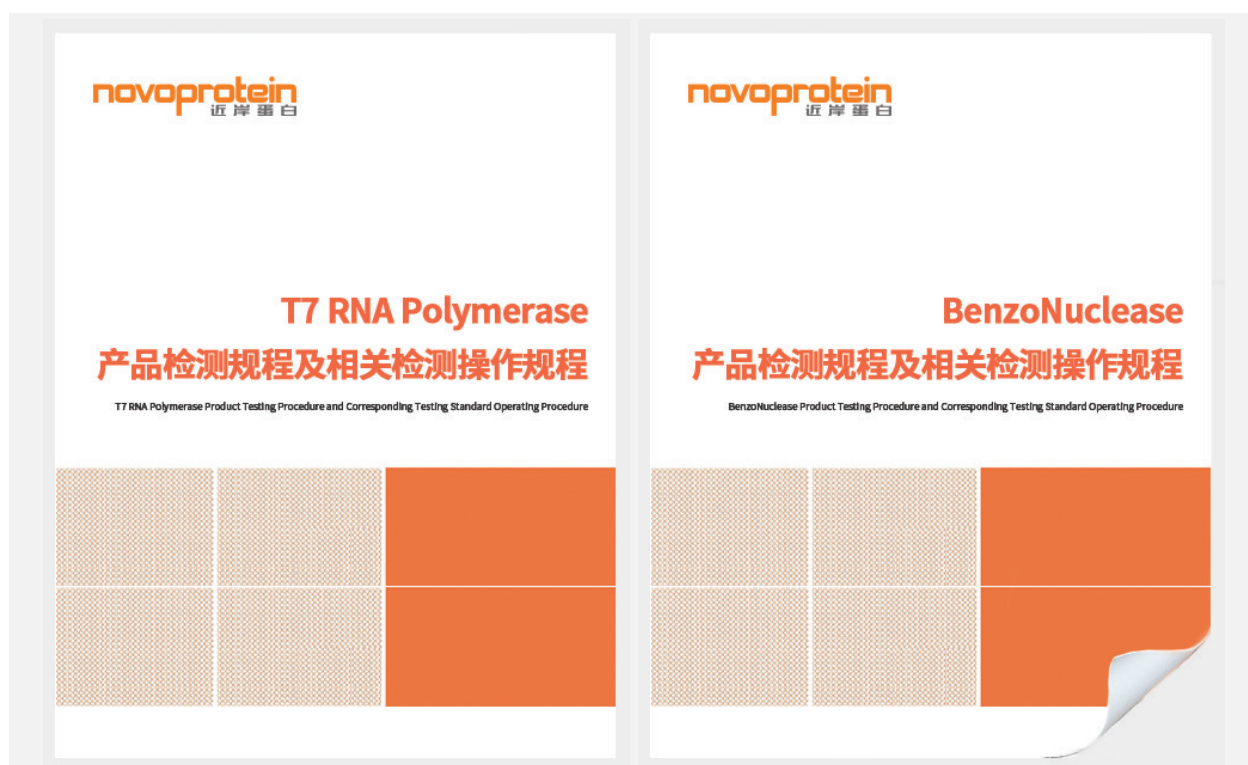
We hereby certify that our GMP series products are expressed in medium with clear chemical composition, no animal-derived and human-derived ingredients, and purified by multi-step chromatography. In the process of expression, purification and preparation of the product, no reagents containing animal-derived and human-derived ingredients. The final product is free of ampicillin, GMO, residual solvents, metal catalysts, melamine, and elemental impurities. The packing materials used in the product do not involve rubber plugs.

We do not use animal materials from or in contact with affected or quarantined animals spreading spongiform encephalopathy/bovine spongiform disease. No animals or animal products are used in our production facilities, and there is no contact with any animal pathogens.

Novoprotein Scientific (Heze) Inc.



SOP Data List



Cat. No.	Product Name
GMP-RE026	BsaI, GMP Grade
GMP-RE057	BspQI, GMP Grade
GMP-RE015	XbaI, GMP Grade
GMP-E121	T7 RNA Polymerase, GMP Grade
GMP-E131	T7 RNA Transcription Enzyme Mix, GMP Grade
GMP-M036	Pyrophosphatase, Inorganic (yeast), GMP Grade
GMP-E125	RNase Inhibitor, GMP Grade
GMP-E127	DNase I, GMP Grade
GMP-M062	Vaccinia Capping Enzyme, GMP Grade
GMP-M072	mRNA Cap 2'-O-Methyltransferase, GMP Grade
GMP-S023-S026	NTPs, GMP Grade
GMP-1707	BenzoNuclease®, GMP Grade

1

GMP Grade animal-free, ampicillin-free

mRNA Vaccines and Drugs Enzymatic Solutions



GMP Grade
Raw Material Production



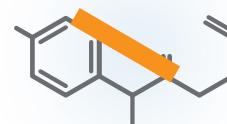
5 Billion Doses
Production Capacity



One-stop Solution for
Raw Materials/Services



Animal-free



Ampicillin-free

**Core Supplier of Raw Materials for
mRNA Vaccines and Drugs in China**



Large Packaging
Customization



Drug Master Files
(DMFs)



Halal Certification



Nearly 10,000 m²
Clean Workshop



Compliant with
Pharmacopoeia



Comprehensive QC Testing

The Prospect of mRNA Vaccines and Drugs Research

With the continuous progress of life science, mRNA is used as a drug in the fields of disease treatment and vaccine. The mRNA synthesized *in vitro* in 1990 was expressed in cells for the first time, and the mRNA vaccine in 2020 played an important role in the fight against the COVID-19. mRNA-based therapeutic modalities have caused a revolution in medicine.

mRNA vaccines have the advantages of fast development speed, flexibility, simple production process, platform-based, easy to expand production capacity, can be used for precise and personalized treatment, and can present multiple antigens at one time. mRNA vaccines belong to the third generation of vaccine technology, compared with traditional vaccines, which require the complicated procedures of artificial inactivation, attenuation and genetic engineering of pathogenic microorganisms and their metabolites, the third generation vaccines are more specific and effective, higher performance and shorter R&D cycle. The structure of mRNA vaccine is simple and can be synthesized in batches, and can be screened in high-throughput during the research and development stage, which significantly saves research and development time. Moreover, compared with DNA vaccines, mRNA vaccines do not have the genetic risk of introducing foreign genes, and have faster onset and stronger effects.

Effective mRNA vaccines have the characteristics of high yield, strong stability, low autoimmunity, high translation expression, strong antigen specificity of expression, good stimulation effect, and good delivery effect. High mRNA yields require efficiency *in vitro* mRNA synthesis methods, with T7 RNA polymerase *in vitro* transcription of choice for large-scale production. To enhance mRNA stability, reduce immunogenicity and improve translation efficiency, the most effective solution is to cap the mRNA with a capping enzyme to stabilize it inside and outside the cell, reduce autoimmunity, and allows the mRNA to be recognized by the ribosome and initiates transcription

mRNA *in vitro* Transcription and Modification Process

Preparation of Linear Template DNA

BsaI, GMP Grade

BspQI, GMP Grade

XbaI, GMP Grade

mRNA Capping

Vaccinia Capping Enzyme, GMP Grade

mRNA Cap 2'-O-Methyltransferase, GMP Grade

SAM(32mM), GMP Grade

GTP(10mM), GMP Grade

In vitro transcription (IVT)

T7 RNA Transcription Enzyme Mix, GMP Grade

T7 RNA Polymerase, GMP Grade

RNase Inhibitor, GMP Grade

Pyrophosphatase, Inorganic (yeast), GMP Grade

NTPs, GMP Grade

DNase I, GMP Grade

mRNA Tailing

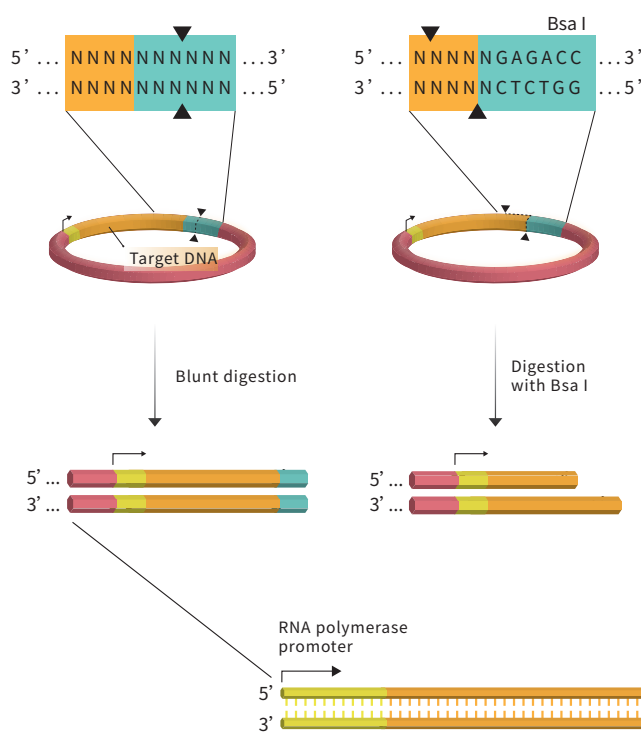
E. coli Poly(A) Polymerase, GMP Grade

10× Poly(A) Polymerase Buffer, GMP Grade

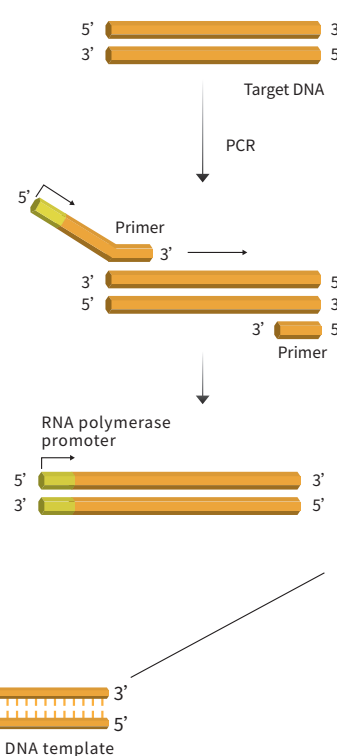
Preparation of Linear Template DNA

Linearized plasmids with double-stranded promoters, PCR products or synthetic DNA fragments can be used as templates for *in vitro* transcription. The quality of the template not only affects the efficiency of *in vitro* transcription, but also determines the integrity of the synthesized RNA. The yield of the synthesis depends largely on the purity of the template. The template can be dissolved in TE buffer or RNase-free water after purification.

A. Blunt-end or sticky-end template preparation strategy



B. PCR template preparation strategy



A. Plasmids with T7 promoter can be used as transcription templates. The linearization and purity of plasmids will affect the yield of transcription and the integrity of RNA. Since circular plasmids do not have effective termination, RNA products of different lengths will be transcribed. In order to obtain RNA of a specific length, the plasmid must be completely linearized. For linearized plasmids, please ensure that the double-strand is blunt-ended or the 5'-end of the coding strand is overhanging structure. Using a type IIS restriction endonuclease (eg. BsaI), the synthesized RNA does not contain restriction site sequences.

B. PCR products with T7 promoter can be used as templates for *in vitro* transcription. The T7 promoter was added to the 5'-end of the upstream primer of the sense strand when PCR amplifying the template. The PCR product was purified and used as a template. High-fidelity polymerase amplification is required to ensure the correctness of the template sequence.

Recommended Products

GMP Grade animal-free, ampicillin-free

BsaI

The *in vitro* transcription template can be obtained by plasmid digestion. When preparing, it is necessary to ensure that the digestion product is a blunt end or a 5'-end overhang structure of the coding chain to ensure correct transcription. The BsaI restriction endonuclease is derived from *Bacillus stearothermophilus* and is a commonly used restriction endonuclease.

This product uses recombinant protein production technology to obtain restriction endonuclease BsaI, which complies with GMP production and quality management specifications, and all raw and auxiliary materials can be traced.

Quality control standards

- Purity: $\geq 95\%$
- Heavy Metal Residues: ≤ 10 ppm
- Bacterial Endotoxin: < 1 EU/ml
- Bioburden ≤ 1 CFU/10ml
- No RNase residue

Product features

This product is highly specific and can be specifically cut for the identified DNA sequence. The identified sequence is as follows:

5'...GGTCTC(N)₁ ↓ ...3'
3'...CCAGAG(N)₅ ↑ ...5'

Product information

Cat. No.	Product Name
GMP-RE026	BsaI, GMP Grade

Recommended Products

GMP Grade animal-free, ampicillin-free

BspQI

The *in vitro* transcription template can be obtained by plasmid digestion. When preparing, it is necessary to ensure that the digestion product is a blunt end or a 5' -end overhang structure of the coding chain to ensure correct transcription. The BspQI restriction endonuclease is derived from *Bacillusphaericus* and is a commonly used IIS restriction endonuclease.

This product uses recombinant protein production technology to obtain restriction endonuclease BspQI, which complies with GMP production and quality management specifications, and all raw and auxiliary materials can be traced.

Quality control standards

- No endonuclease/exonuclease residues
- Bacterial Endotoxin: <10 EU/mg
- No RNase residue

Product features

This product is highly specific and can be specifically cut for the identified DNA sequence. The identified sequence is as follows:

5' ...GCTCTTC(N)1 ↓ ...3'
3' ...CGAGAAG(N)4 ↑ ...5'

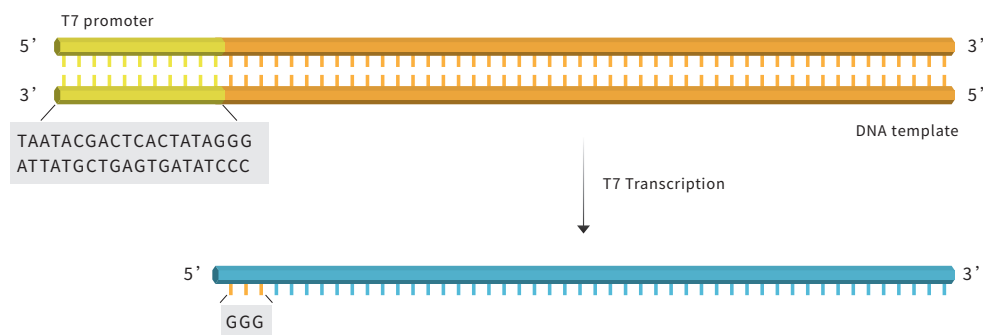
Product information

Cat. No.	Product Name
GMP-RE057	BspQI, GMP Grade

In vitro Transcription (IVT)

As a biological macromolecule, mRNA can be synthesized on a large scale by *in vitro* transcription (IVT). T7 promoter is one of the promoters with the highest transcription efficiency. *In vitro* transcription (IVT) yields more synthetic products.

Novoprotein provides GMP grade T7 RNA Polymerase and a complete kit with careful formulation and optimization. The kit contains T7 RNA Polymerase, RNase Inhibitor, Pyrophosphatase, Inorganic and DNase I. The first three components are optimized and formulated into an enzyme mix, it has the advantages of high yield, convenient operation, and reduced pollution caused by sample addition, and can be used to stably synthesize high-quality RNA.



In the template, the T7 promoter is linked to the target sequence, transcription starts from the first G after the promoter, and the sequence of the transcription product is the same as a chain in the template.

Recommended Products

GMP Grade animal-free, ampicillin-free

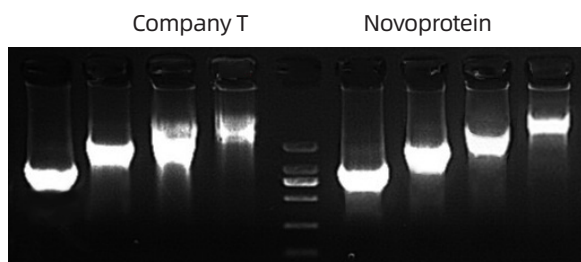
T7 RNA Polymerase

Quality control standards

- Purity: $\geq 95\%$
- Heavy Metal Residues: ≤ 10 ppm
- Bacterial Endotoxin: < 5 EU/ml
- Host-cell Protein Residues: ≤ 50 ppm
- Exogenous DNA residue: ≤ 100 pg/mg
- No RNase and endonuclease/exonuclease residues

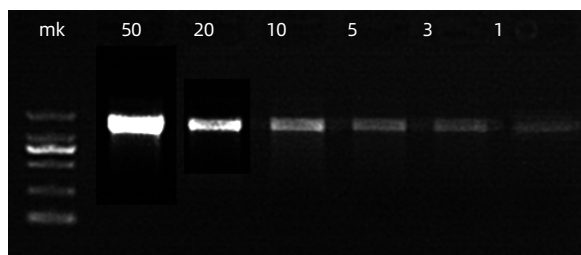
Product features

Large fragment transcription: the length of the transcription template is up to 10K



The yield of Novoprotein was higher than that of the competitive company T, and the length of the transcription template could reach more than 10K.

High sensitivity: it still has transcription function for trace template



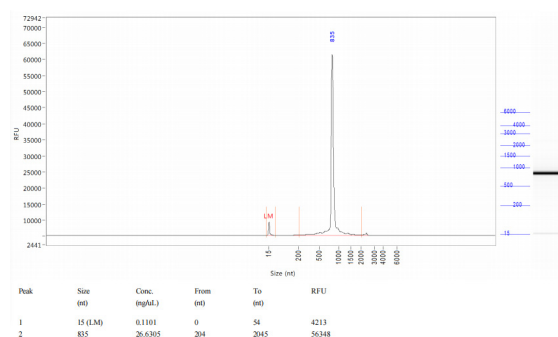
The transcription performance of Novoprotein reagent for the template as low as 1ng was better than that of the competitive company.

**High yield:
The 20μl system can harvest nearly 200μg RNA**

Magnetic bead purification (20μl)	Company T	Novoprotein
2K	121μg	129μg
4K	120μg	140μg
8k	101μg	117μg
10k	89μg	95μg

The yield of 20μl of transcription system products after magnetic bead purification is 100-150μg.

Good integrity and high purity



Capillary electrophoresis showed good integrity and high purity of the transcript.

Product information

Cat. No.	Product Name
GMP-E121	T7 RNA Polymerase, GMP Grade
GMP-E131	T7 RNA Transcription Enzyme Mix, GMP Grade
GMP-EB231	10×Transcription Buffer, GMP Grade

Recommended Products

GMP Grade animal-free, ampicillin-free

RNase Inhibitor

The murine RNase Inhibitor can specifically inhibit the activity of RNase A, B and C, and can form a 1:1 complex with RNase, thereby inhibiting its activity. In the large-scale production of mRNA, RNase Inhibitors play a very important protective role.

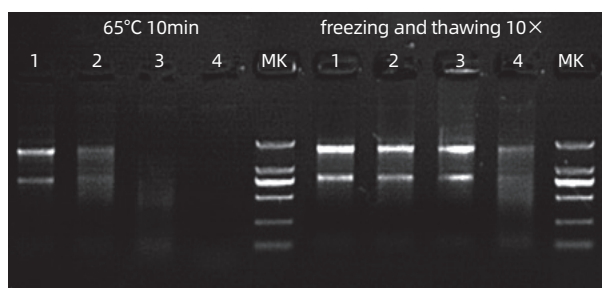
This product is a recombinant murine RNase Inhibitor with a molecular weight of about 50kD. It is expressed in *Escherichia coli* on a large scale and conforms to GMP production and quality management standards. All raw and auxiliary materials can be traced.

Quality control standards

- Purity: $\geq 95\%$
- Heavy Metal Residues: ≤ 10 ppm
- Bacterial Endotoxin: < 5 EU/ml
- Host-cell Protein Residues: ≤ 50 ppm
- Exogenous DNA residue: ≤ 100 pg/mg
- No RNase and endonuclease/exonuclease residues

Product features

Freeze-thaw stability: after repeated freezing and thawing for 10 times, the enzyme activity was not affected

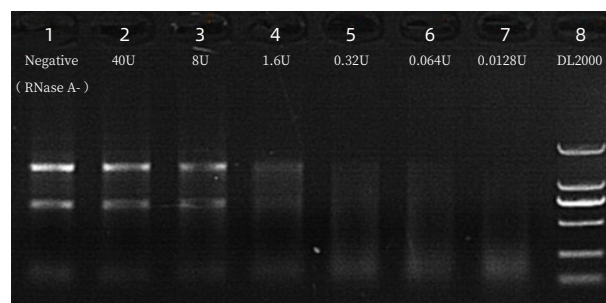


At 65 °C for 10min, more than half of the enzyme activity can be retained at 40U, and the enzyme activity is basically unaffected by freeze-thaw for 10 times.

Lane 1: 40U enzyme activity was not treated
Lane 3: 8U

Lane 2: 40U
Lane 4: 1.6U

High enzyme activity: after high dilution, it still has high enzyme activity



1μl of RNase Inhibitor was added to each system after 1/5 gradient dilution of RNase Inhibitor from 40U/μl. Finally, 1μl of 5pg RNase A was added to each system.

Product information

Cat. No.

Product Name

GMP-E125

RNase Inhibitor, GMP Grade

Recommended Products

GMP Grade animal-free, ampicillin-free

Pyrophosphatase, Inorganic (yeast)

In the process of *in vitro* transcription of mRNA in large systems, inorganic pyrophosphates will inevitably be produced. These substances have a great inhibitory effect on transcription. Inorganic pyrophosphatase (PPase) can hydrolyze the inorganic pyrophosphates generated in *In vitro* Transcription (IVT), promotes the reaction equilibrium to shift to the product forming end and increases the amount of products.

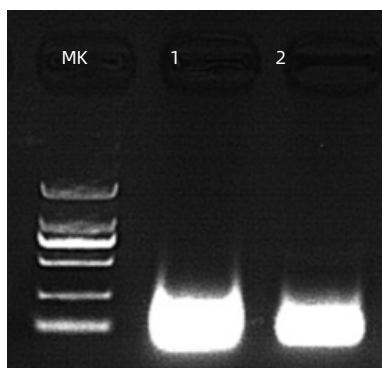
This product is a large-scale recombinant inorganic pyrophosphatase expressed in *Escherichia coli*, with a molecular weight of about 63kD. It conforms to GMP production and quality management standards, and all raw and auxiliary materials can be traced.

Quality control standards

- Purity: $\geq 95\%$
- Heavy Metal Residues: ≤ 10 ppm
- Bacterial Endotoxin: < 5 EU/ml
- Host-cell Protein Residues: ≤ 50 ppm
- Exogenous DNA residue: ≤ 100 pg/mg
- No RNase and endonuclease/exonuclease residues

Product features

Strong versatility: suitable for DNA, RNA and protein synthesis systems



1 Pyrophosphatase, Inorganic was added

2 RNase-free water was added

Inorganic pyrophosphatase significantly increases RNA transcript yield.

Product information

Cat. No.

Product Name

GMP-M036

Pyrophosphatase, Inorganic (yeast), GMP Grade

Recommended Products

GMP Grade animal-free, ampicillin-free

NTPs

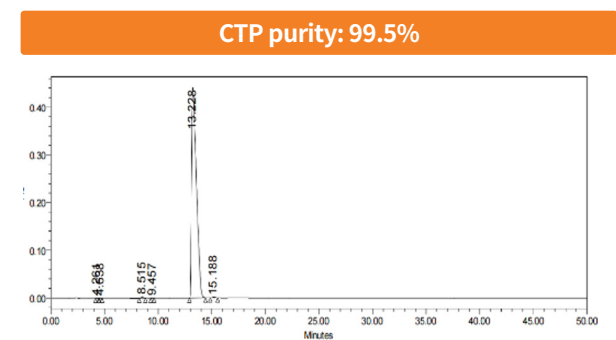
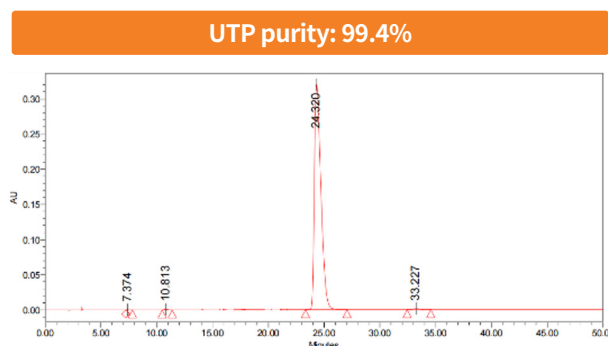
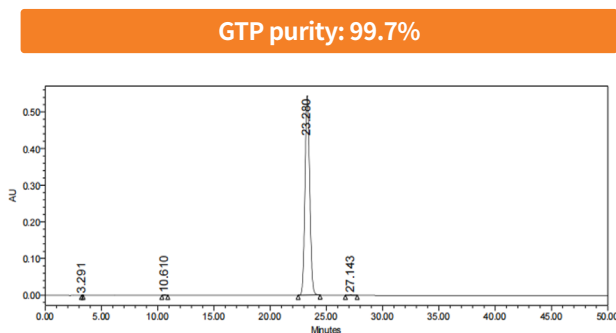
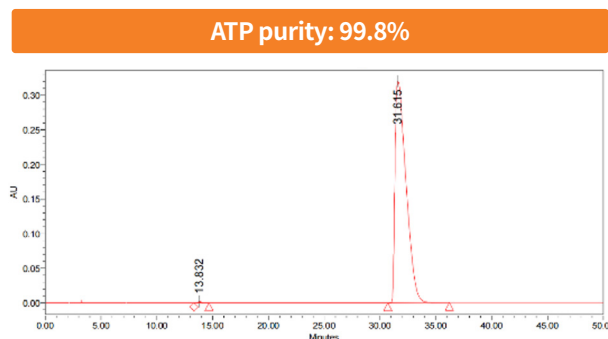
Nucleoside triphosphates (NTPs) can be used in a variety of related applications in molecular biology with product purity $\geq 96\%$ (HPLC) and no endonuclease, exonuclease and ribonuclease contamination.

This product is produced with raw and auxiliary materials of pharmaceutical specifications, and all kinds of pollution in the production process are strictly controlled. Product production and quality management procedures in line with GMP standards ensure the traceability of the production process and all raw and auxiliary materials.

Quality control standards

- Concentration: $100\text{mM} \pm 5\text{mM}$
- Purity: $\geq 96\%$
- No RNase and endonuclease/exonuclease residues

Product features



Product information

Cat. No.	Product Name	Cat. No.	Product Number
GMP-S023A	ATP, GMP Grade (100mM)	GMP-S023N	ATP, GMP Grade (10mM)
GMP-S024A	GTP, GMP Grade (100mM)	GMP-S024N	GTP, GMP Grade (10mM)
GMP-S025A	CTP, GMP Grade (100mM)	GMP-S026A	UTP, GMP Grade (100mM)

Recommended Products

GMP Grade animal-free, ampicillin-free

DNase I

In the process of large-scale mRNA production, the transcription template needs to be removed after transcription. DNase I can randomly decompose single-stranded or double-stranded DNA to the same degree to generate oligonucleotides with 5'-P terminal. Under the condition of Mg^{2+} , DNase I can cut the double-stranded DNA at will.

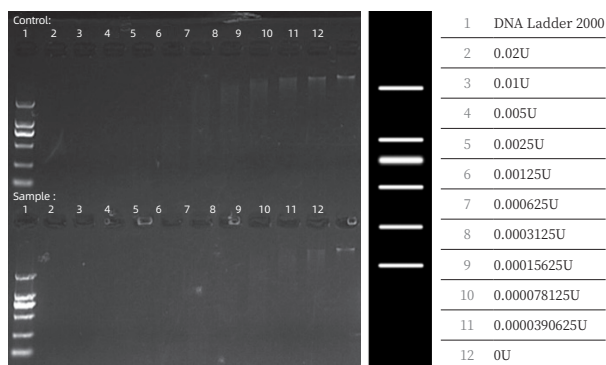
This product is a recombinant DNase I expressed by *Pichia pastoris* on a large scale, with a molecular weight of about 39kD, in line with GMP production and quality management standards, and all raw and auxiliary materials can be traced.

Quality control standards

- Purity: $\geq 95\%$
- Heavy Metal Residues: ≤ 10 ppm
- Bacterial Endotoxin: $<5EU/ml$
- Host-cell Protein Residues: ≤ 50 ppm
- Exogenous DNA residue: ≤ 100 pg/mg
- No RNase residue

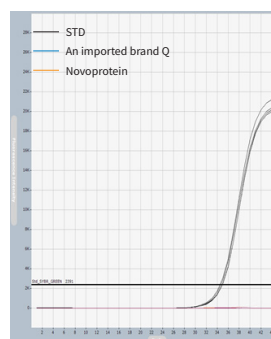
Product features

High enzyme activity: the human genome can be digested by trace amounts



Data conclusion: The sample is consistent with the control

Excellent performance: efficient removal of DNA residue in samples



Well	Sample	Ct
1	STD	34.51
2	STD	34.65
3	STD	34.92
4	STD	34.94
5	An imported brand Q	UD
6	An imported brand Q	UD
7	An imported brand Q	UD
8	An imported brand Q	UD
9	Novoprotein	UD
10	Novoprotein	UD
11	Novoprotein	UD
12	Novoprotein	UD

Sample: Mouse kidney (~20 mg) compared with an imported brand Q, both can remove DNA residue in RNA samples very well.

Product information

Cat. No.

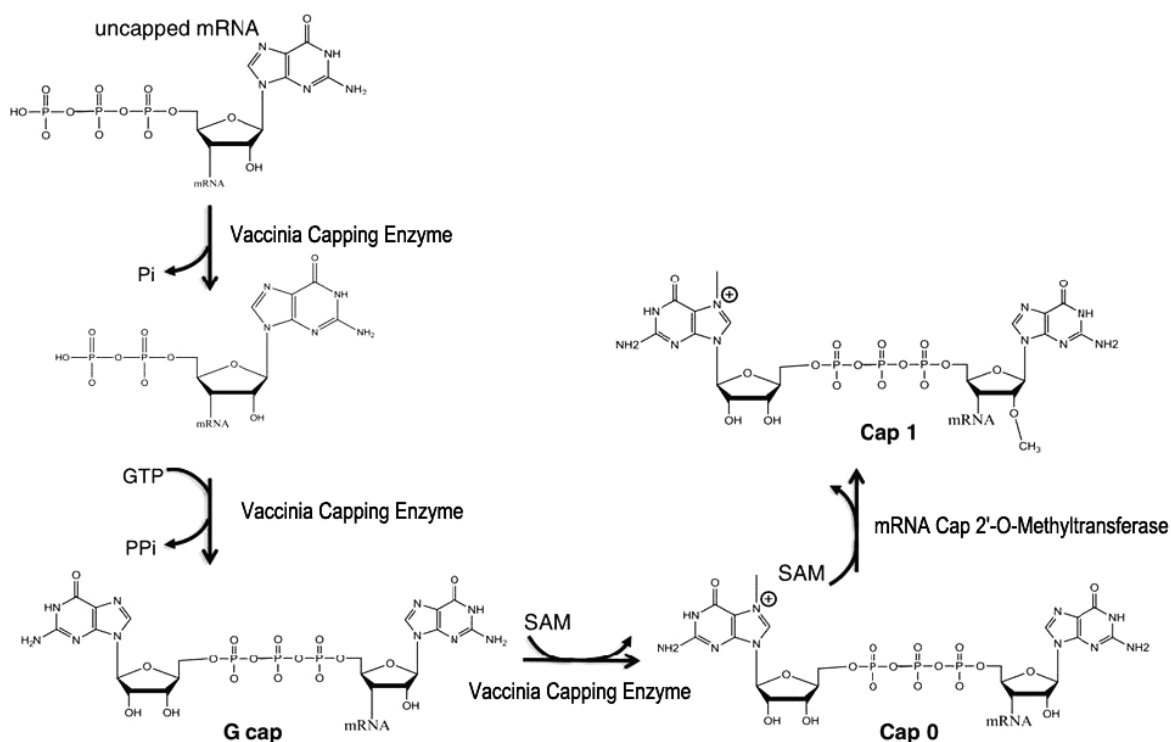
Product Name

GMP-E127

DNase I, GMP Grade

mRNA Capping

The RNA obtained by *in vitro* transcription has not been modified in cells, does not have the Cap structure and the PolyA tail, is easily degraded, easily activates the immune response, cannot bind to the ribosomal initiation protein, and cannot initiate protein translation. Therefore, in industrial mRNA production, Vaccinia Capping Enzyme needs to be used to cap the IVT RNA, so that the 5'-end of the RNA can obtain the Cap0 structure, and further use 2'-O-methyltransferase to convert Cap0 to Cap1. The Cap1 structure is known to be the least recognized structure by the body's RNA recognizer RIG-I, and is less naturally immunogenic. The cap structure introduced by enzymatic capping is completely consistent with the natural cap structure in eukaryotes, which fundamentally reduces the immunogenicity of exogenous mRNA, protects it from degradation, improves translation efficiency, and increases intracellular protein production. Capping efficiencies of up to 100% can be achieved by enzymatic capping, while capping by chemically synthesized cap analog structures is relatively inefficient, and the cap analog structures differ from natural cap structures.



Enzymatic pathways of mRNA capping. The production of Cap0 structural RNA requires the vaccinia capping enzyme: this enzyme combines the functions of a triphosphatase, a guanosine transferase, and a guanine methyltransferase. S-adenosylmethionine (SAM) is the methyl donor. Once the Cap0 structure is generated, it can be further modified by 2'-O-ribose methyltransferase to generate the Cap1 structure. This figure is quoted from Michael Beverly, Amy Dell, Parul Parmar, Leslie Houghton et al (2016). Label-free analysis of mRNA capping efficiency using RNase H probes and LC-MS. Anal Bioanal Chem.

Recommended Products

GMP Grade animal-free, ampicillin-free

Vaccinia Capping Enzyme

Quality control standards

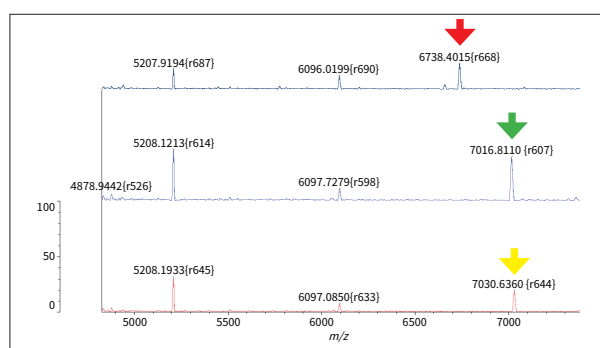
- Purity: $\geq 95\%$
- Heavy Metal Residues: ≤ 10 ppm
- Bacterial Endotoxin: < 5 EU/ml
- Host-cell Protein Residues: ≤ 50 ppm
- Exogenous DNA residue: ≤ 100 pg/mg
- No RNase and endonuclease/exonuclease residues

mRNA Cap 2'-O-Methyltransferase

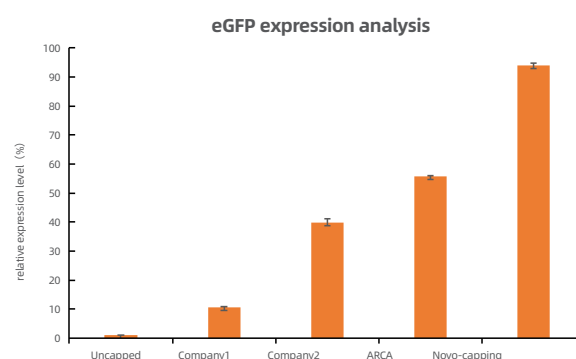
Quality control standards

- Purity: $\geq 95\%$
- Heavy Metal Residues: ≤ 10 ppm
- Bacterial Endotoxin: < 5 EU/ml
- Host-cell Protein Residues: ≤ 50 ppm
- Exogenous DNA residue: ≤ 100 pg/mg
- No RNase and endonuclease/exonuclease residues

High capping efficiency: up to 100%, significantly better than cap analogs



Mass spectrometry detection shows that the capping efficiency of Cap0 and Cap1 reaches 100%.
From top to bottom: uncapped, Cap0, Cap1.



Detection of intracellular expression levels after mRNA capping. The results showed that Novoprotein reagents performed best.

Product information

Cat. No.	Product Name
GMP-M062	Vaccinia Capping Enzyme, GMP Grade
GMP-M072	mRNA Cap 2'-O-Methyltransferase, GMP Grade
GMP-EB62	10× Capping Reaction Buffer, GMP Grade
GMP-S062	SAM, GMP Grade
GMP-S024N	GTP, GMP Grade (10mM)

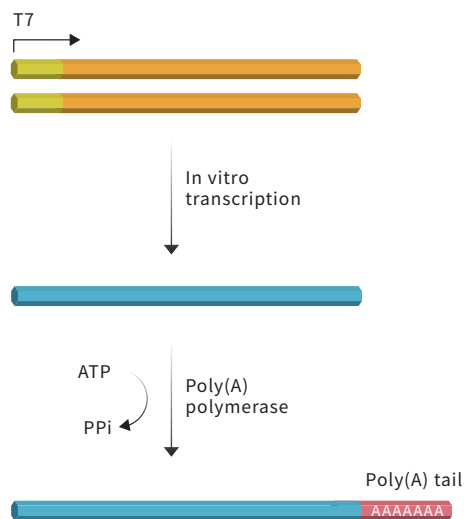
mRNA Tailing

In the complete structure of mRNA, the Poly(A) tail is an important part, which has the effect of improving the stability and translation efficiency of mRNA. There are two main ways of adding tails to synthesize mRNA *in vitro*:

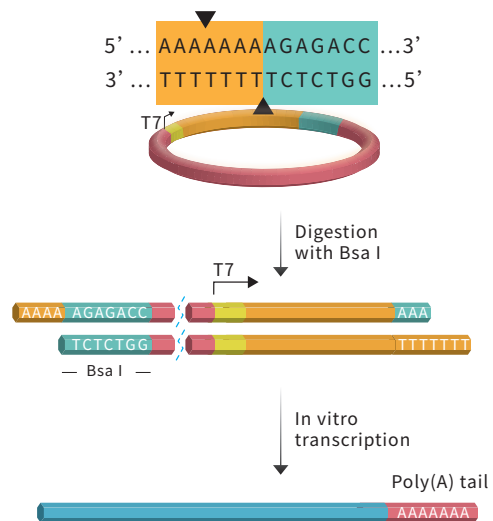
Enzymatic tailing;

A sequence encoding PolyA was introduced on the template.

A. Post-transcriptional enzymatic tailing



B. The plasmid template is introduced into Poly(A), and the transcription is tailed



The tailing is completed by the above methods: (A) post-transcriptional enzymatic tailing; (B) the template is linearized with BsaI and then transcribed.

Recommended Products

GMP Grade animal-free, ampicillin-free

E. coli Poly(A) Polymerase

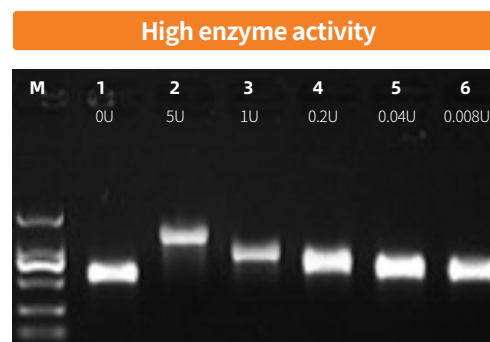
Quality control standards

- Purity: $\geq 95\%$
- Heavy Metal Residues: ≤ 10 ppm
- Bacterial Endotoxin: < 10 EU/mg
- Host-cell Protein Residues: ≤ 50 ppm
- No RNase and endonuclease/exonuclease residues

Product features



Taking RNA as the template, adding 5U enzyme amount and completing the addition of 200 A bases in 10min.



A small amount of Poly(A) Polymerase was added to the reaction system to efficiently add the Poly (A) tail.

Product information

Cat. No.	Product Name
GMP-M012	<i>E. coli</i> Poly(A) Polymerase, GMP Grade
GMP-EB12	10×Poly(A) Polymerase Buffer
GMP-S023N	ATP, GMP Grade (10mM)

mRNA Enzymes DIBA Kit

According to the Technical Guidelines for Pharmaceutical Research of mRNA Vaccines for SARS-CoV-2 Prevention (Trial) in 2020, the raw materials for mRNA vaccine production should comply with the relevant provisions of the current version of the Pharmacopoeia of the People's Republic of China and/or be consistent with international requirements. For production raw materials (such as T7 RNA Polymerase, pyrophosphatase, RNase inhibitors, etc.) prepared by recombinant technology or biological/chemical synthesis technology, corresponding production process and quality research data should be provided. Therefore, identification testing of raw materials is required to confirm whether the raw materials stored in the labelled containers are the raw materials as indicated. Various enzymes (such as T7 RNA Polymerase, inorganic pyrophosphatase, RNase inhibitors, vaccinia capping enzymes, mRNA Cap 2'-O-methyltransferases) are used in the *in vitro* transcription and modification of mRNA, as a protein substance, the enzymes can be identified by the Dot Immunobinding Assay (DIBA, 2020 edition of the Chinese Pharmacopoeia, Part IV, General Principles 3402).

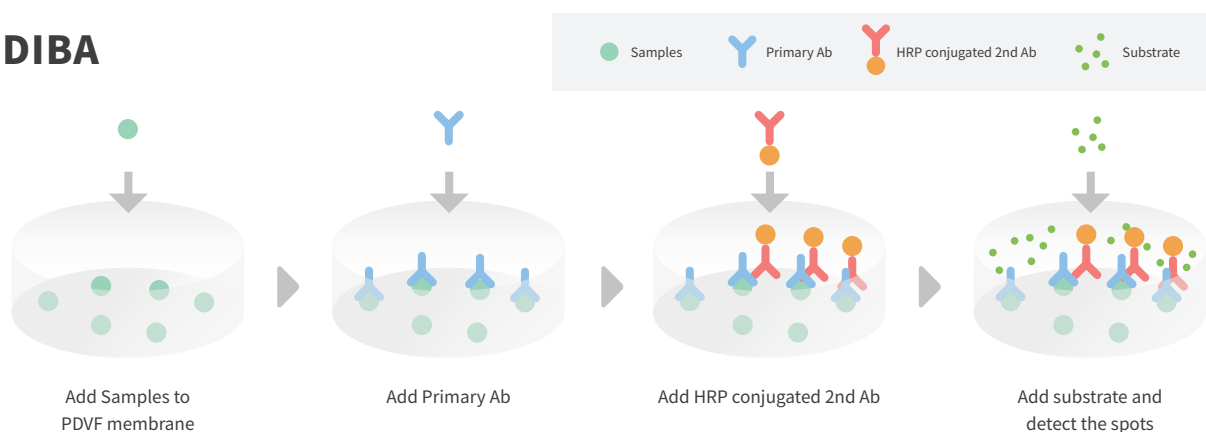
The mRNases DIBA Kit uses polyvinylidene fluoride (PVDF) as the solid phase, and carries out antigen-antibody reaction by immunospot method to carry out the identification test of various raw materials.

Product features

- Strong exclusivity
- Good durability

Reaction principle

DIBA



Product information

Cat. No.

PA007

Product Name

mRNases DIBA Kit

dsRNA Residue Detection

According to the 2020 Technical Guidelines for Pharmaceutical Research of mRNA Vaccine for Coronavirus Prevention (Trial) and the Analytical Procedures for mRNA Vaccine Quality-Draft Guidelines-2nd Edition of US Pharmacopoeia, mRNA vaccines need to be detected for process control, such as capping efficiency, length of Poly(A) tailing product, mRNA sequence integrity, sequence accuracy, purity, mRNA concentration, concentration of by-products (incomplete mRNA, double-stranded RNA, truncated RNA, long-stranded RNA, etc.), residual protein, residual DNA, sterility, Bacterial Endotoxin, etc. As one of the by-products of transcription, dsRNA significantly affects the quality of mRNA vaccine which needs strict control and detection.

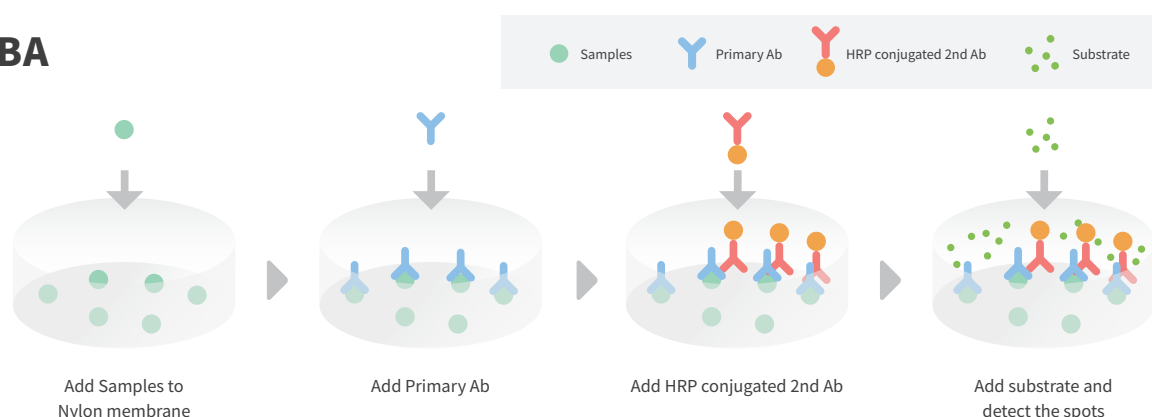
dsRNA DIBA Kit uses immunoblot method to attach antigen on Nylon film and use it as solid phase for antigen-antibody reaction. When the primary antibody is added, it can interact with the antigen on the membrane, and then the HRP conjugated 2nd antibody is added. The HRP is indirectly linked to Nylon film through the combination of the secondary antibody and the corresponding primary antibody. Finally, the corresponding substrate of the HRP is added, then judge the result according to a chromogenic reaction.

Product features

- High sensitivity: Under the condition of concentration of $1\mu\text{g}/\mu\text{l}$, it can recognize dsRNA
- High specificity: The antibody does not react with ssRNA, dsDNA, ssDNA
- High durability: The identification is not affected by the small changes in the temperature, time and other conditions

Product principle

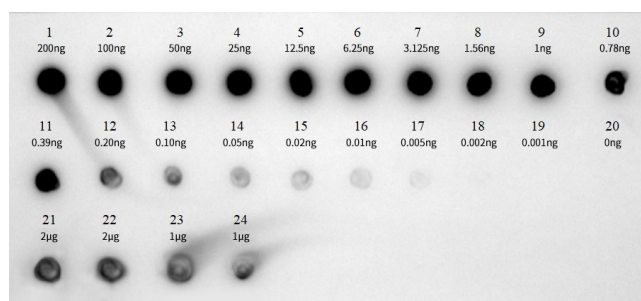
DIBA



dsRNA Residue Detection Kit

Result analysis

After a series of reactions, spots appeared in the detection sample and the positive control. According to the brightness of spots and the loading volume, the dsRNA content in the detection sample could be preliminarily determined.



Caption)

1-20: the results of Positive Control 1 (Non-modified) of the kit according to 1/2 gradient.

21-24: the results of 2μg and 1μg respectively for different ssRNA detection samples.

Product information

Cat. No.

Product Name

RD009

dsRNA DIBA Kit

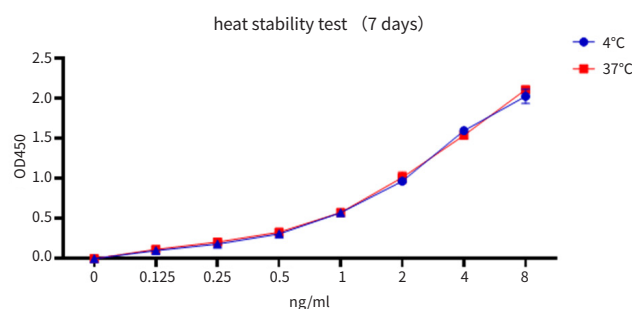
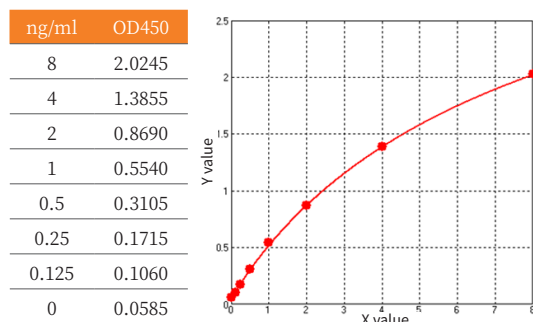
Enzyme Residue Detection Kit

According to the 2020 Technical Guidelines for Pharmaceutical Research of mRNA Vaccine for Coronavirus Prevention (Trial) and the Analytical Procedures for mRNA Vaccine Quality-Draft Guidelines-2nd Edition of US Pharmacopoeia, mRNA vaccines need to be detected for process control, such as capping efficiency, length of Poly(A) tailing product, mRNA sequence integrity, sequence accuracy, purity, mRNA concentration, concentration of by-products (incomplete mRNA, double-stranded RNA, truncated RNA, long-stranded RNA, etc.), residual protein, residual DNA, sterility, Bacterial Endotoxin, etc.

Pyrophosphatase, Inorganic ELISA Kit was precoated with PPase capture antibody. After adding samples, the samples were captured to form antibody-antigen complex, and then HRP conjugated PPase detection antibody was added which form an antibody-antigen-antibody "sandwich" complex. Finally, TMB was added for color development. After the reaction was terminated, the absorption value (OD value) was read at the wavelength of 450nm/630nm. The content of PPase in the sample was positively correlated with OD value.

Product features

- High sensitivity: 0.125ng/ml, detection range: 0.125-8ng/ml
- Strong stability: stored at 37°C for 7 days, the detection effect has no significant difference



Product information

Cat. No.	Product Name
PA101	Pyrophosphatase, Inorganic ELISA Kit

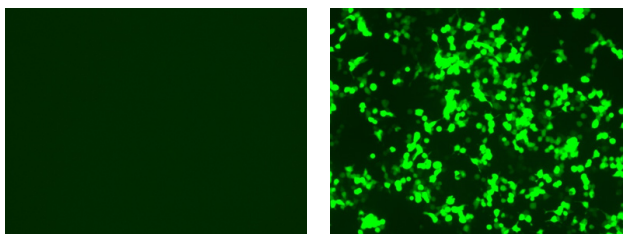
Catalog mRNA

GFP mRNA encodes a green fluorescent protein that can be expressed in mammalian cells. The eGFP mRNA of novoprotein has 5' Cap1 and 3' poly (A) tail, and is an ideal target for studying transfection and expression using various assays. Luciferase is a general term of enzymes that can produce bioluminescence in nature, and the most representative one is the luciferase from *Photinus pyralis*. luciferase from *Photinus pyralis* can show luciferase activity without post-translational modification. The mRNA sequence of Luciferase of novoprotein was derived from *Photinus pyralis*, and point mutation was performed on the wild-type sequence, which significantly improved the thermal stability and pH range of the protein.

Product features

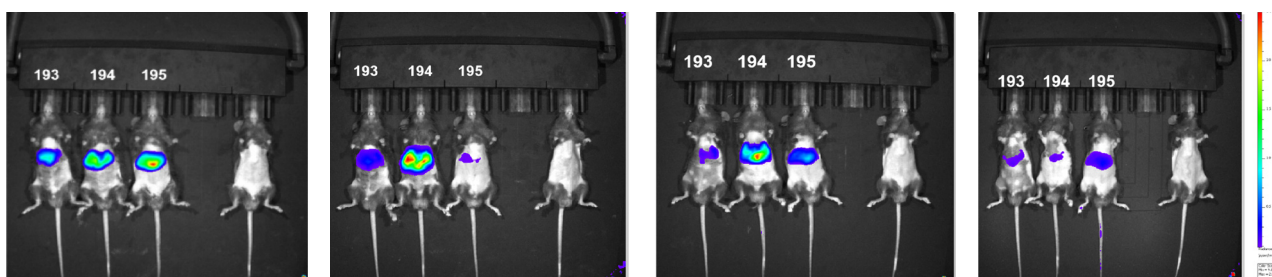
- Large supply of mRNA
- Customized mRNA

eGFP mRNA



eGFP mRNA was translated and expressed successfully after transfecting into cells.

Luciferase mRNA



Luciferase mRNA was encapsulated and injected into mice and translated successfully.

Product information

Cat. No.	Product Name
MR008/MR010	eGFP mRNA/eGFP mRNA (N1-Me-Pseudo UTP)
MR201	eGFP circRNA
MR009/MR011	Luciferase mRNA/Firefly Luciferase mRNA (N1-Me-Pseudo UTP)
MR105	mCherry mRNA (N1-Me-Pseudo UTP)
MR016	hEPO mRNA (N1-Me-Pseudo UTP)
MR015	OVA mRNA (N1-Me-Pseudo UTP)



GMP Grade animal-free, ampicillin-free

BenzoNuclease®

BenzoNuclease® is a genetically engineered recombinant endonuclease derived from *Serratia marcescens*, BenzoNuclease® has been shown to exert a broad spectrum of substrate specificity to degrade both DNA and RNA into 5'-monophosphate-terminated oligonucleotides, which are three to five bases in length—whether single-stranded, double-stranded, linear, circular or supercoiled. It is also known as "omnipotent nuclease" because of its high efficiency in degrading any form of DNA and RNA. BenzoNuclease® is an effective tool enzyme for the removal of all forms of DNA and RNA from biologicals, both in laboratory studies and in industrial-scale production. Through efficient nucleic acid removal, the effect and yield of follow-up experiments and production can be significantly improved, and the performance is better than other nucleic acid removal methods.

Novoprotein provides BenzoNuclease® produced under GMP conditions
Reliable quality, performance and supply capacity, to help your research and production

Applications

- Used to remove exogenous nucleic acid from vaccine products, reduce the risk of residual toxicity of nucleic acid and improve product safety
- Used to reduce the viscosity of feed liquid caused by nucleic acid, shorten the processing time and increase the protein yield
- Used to remove nucleic acid winding on the surface of particles (viruses, inclusion bodies, etc.), which is conducive to the release and purification of particles
- Used to prepare samples for ELISA, column chromatography, 2D electrophoresis and western blot analysis. The resolution and recovery can be improved after BenzoNuclease® treatment
- Used to prevent cell clumping
-



Viral Vector Vaccine



Recombinant Protein and Antibody Drugs



Gene Therapy



Cell Therapy

GMP Grade animal-free, ampicillin-free

BenzoNuclease®

Strict quality control and production standards create reliable BenzoNuclease®:

- No animal-derived and human-derived ingredients, no ampicillin antibiotic
- Protein purity ≥ 99%
- Without protease activity
- Bacterial Endotoxin level < 0.01 EU/KU

Element Standard	Criteria
Appearance	clear, transparent solution
Visible Particles	meet the specification
pH	7.5-8.5
Activity	250-400U/μl
Specific Activity	≥ 1.1 × 10 ⁶ U/mg
Purity	≥ 99%
Protease Activity	no protease activity detectable
Bacterial Endotoxins Residues	< 0.01 EU/kU
Host-cell Protein Residues	≤ 0.005%
Sterility	meet the specification
Heavy Metal Residues	≤ 10 ppm

DMF filing, meeting the drug application specification



Your submission was successfully processed into the CDER Electronic Document Room, and is available to the assigned review division.

Application Type/Number: MF035864

GMP Grade animal-free, ampicillin-free

BenzoNuclease®

BenzoNuclease® is an endonuclease that degrades DNA and RNA in any form, including single-stranded, double-stranded, linear, circular, and hyperhelical forms. As same as all endonuclease, BenzoNuclease® hydrolyzes phosphodiester bonds between nucleotides. After complete digestion by BenzoNuclease®, all free nucleic acids in the solution are degraded into 5' -monophosphate oligonucleotides, which are 3-5 bases in length. No base preference for BenzoNuclease® was observed.

BenzoNuclease® is composed of two subunits with a molecular weight of approximately 32kDa, has an isoelectric point of 6.99, and incorporates a His tag.

Cat. No.	GMP-1707
Product Number	BenzoNuclease®, GMP Grade
Package size	100kU/200kU/5000kU
Molecular Weight	32kDa
pI	6.99
Tag	6×His
Purity	≥ 99% (SDS-PAGE, SEC-HPLC)
Specific Activity	≥ 1.1×10 ⁶ U/mg
Optimal pH	8
Optimal Temperature	37°C
Cofactor	1-10 mM Mg ²⁺
Formulation	20 mM Tris-HCl pH8.0, 2 mM MgCl ₂ , 20 mM NaCl, 50% (v/v) glycerol
Storage	Store at -20°C . Avoid repeated freeze-thaw cycles. Properly stored BenzoNuclease® is stable for at least 24 months.
Unit Definition	In a 2.625 mL reaction system at 37°C and pH 8.0, one unit of BenzoNuclease® is defined as the amount of enzyme that causes a change in absorbance at 260 nm of 1.0 absorption units within 30 minutes.

Storage conditions and shelf life

Storage buffer: 20mM Tris-HCl pH8.0, 2mM MgCl₂, 20mM NaCl, 50%(v/v) glycerol.

Storage temperature: -20°C, avoid repeated freeze-thaw cycles.

Shelf life: two years.

Transport information

Transport with ice packs.

GMP Grade animal-free, ampicillin-free

BenzoNuclease® DNA/RNA Removal

Reaction conditions

BenzoNuclease® remains active under a wide range of conditions. The specific reaction conditions are shown in the following table:

Condition	Optimal*	Effective**
Mg ²⁺	1-2mM	1-10mM
PH	8.0-9.2	6.0-10.0
Temperature	37°C	0-42°C
DTT	0-100mM	>0mM
BME	0-100mM	>0mM
Na ⁺ , K ⁺ , etc.	0-20mM	0-150mM
PO ₄ ³⁻	0-10mM	0-100mM

*: "Optimal" is defined as the condition under which BenzoNuclease® retains > 90% of its activity.

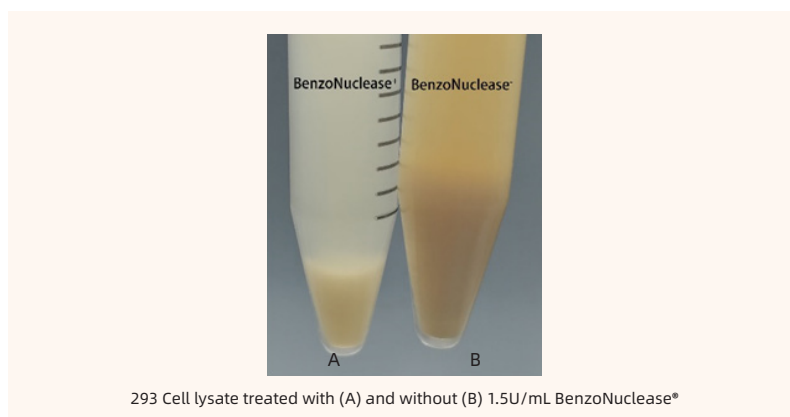
**: "Effective" is defined as the condition under which BenzoNuclease® retains > 15% of its activity.

Recommended usage table

Usage scenarios	Preparation of electrophoretic protein samples	Protein production	Production of vaccines and viruses	Cell medicine
Number of cells	1 × 10 ⁶ cells (10 mg tissue)	1 g wet weight (resuspension 10 ml)	1 L fermentation supernatant	1 L cultures
Minimum dosage	125U	250U	100U	100U
Recommended dosage	500U	2500U	25000U	5000U
Working condition	Normally the reaction time is 37°C for 15~60 min, 25°C for 30~120 min			

Viscosity reduction in 293 cell extracts

Due to the presence of nucleic acids, cell lysates often exhibit high viscosity. The high viscosity of the cell lysate is one of the main reasons for the decrease in virus/protein production, and BenzoNuclease® can solve this problem. After centrifugation, the samples without BenzoNuclease® (B) retain a high viscosity, with no clear demarcation between supernatant and pellet the samples containing BenzoNuclease® (A) show a large reduction in viscosity. The recovery of protein was significantly increased when the sample had been treated with BenzoNuclease®.

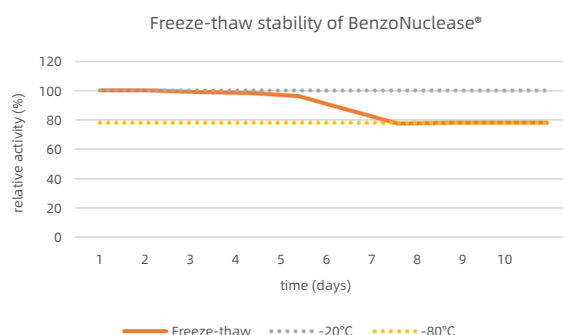


GMP Grade animal-free, ampicillin-free

BenzoNuclease® DNA/RNA Removal

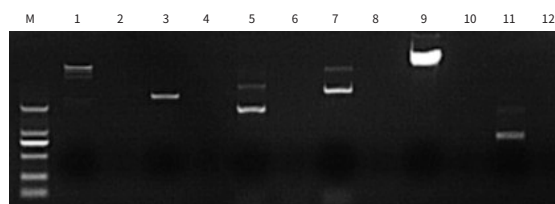
Freeze-thaw stability of BenzoNuclease®

The enzyme activity was detected after repeated freezing and thawing of BenzoNuclease®. After the sixth repeated freezing and thawing, the enzyme activity decreased significantly. Therefore, in order to prevent the freezing and loss of activity of BenzoNuclease®, the optimal storage temperature is -20°C.



Digestion of different substrates

BenzoNuclease® is excellent in digesting different types of nucleic acids.



The result of digesting different forms of DNA with 1U BenzoNuclease® in a 20μl system at 37° C for 30min.

Lane M: Marker

Lane 1: Lambda/Hind III

Lane 3: Linear pUC19

Lane 5: pUC19

Lane 7: pBAD plasmid

Lane 9: Lambda DNA

Lane 11: 800bp PCR product

Lane 2: Lambda/Hind III + 1U BenzoNuclease®

Lane 4: Linear pUC19 + 1U BenzoNuclease®

Lane 6: pUC19 + 1U BenzoNuclease®

Lane 8: pBAD plasmid + 1U BenzoNuclease®

Lane 10: Lambda DNA + 1U BenzoNuclease®

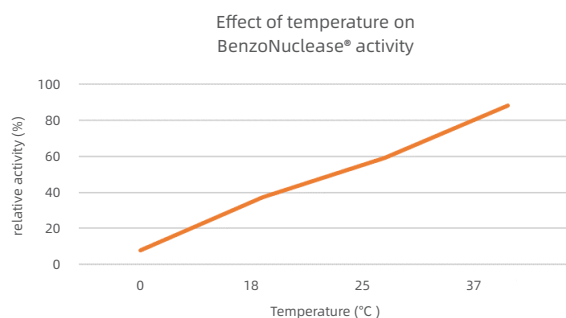
Lane 12: 800bp PCR product + 1U BenzoNuclease®

GMP Grade animal-free, ampicillin-free

BenzoNuclease® DNA/RNA Removal

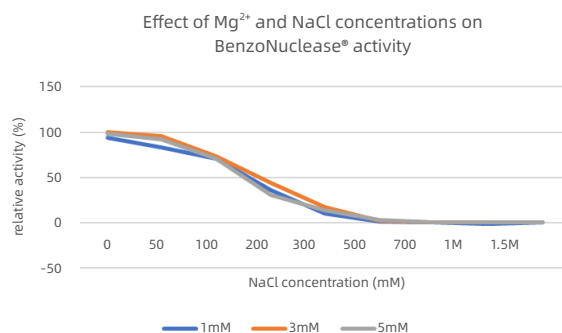
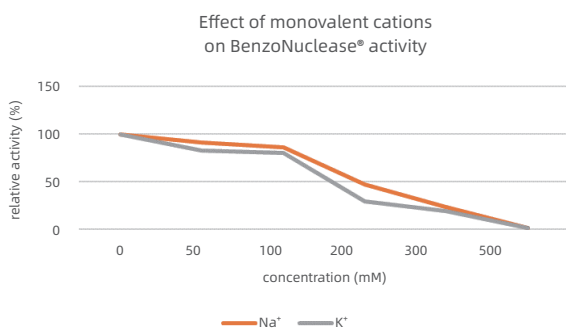
Optimum reaction temperature

The best temperature for BenzoNuclease® to degrade nucleic acid is 37°C, but it is active in the range of 0~42°C.



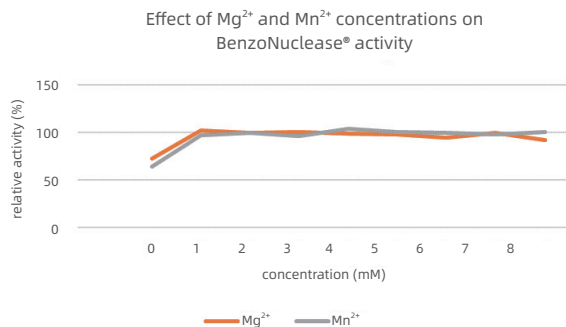
Effect of monovalent cations on BenzoNuclease® activity

Na⁺ and K⁺ have a strong inhibitory effect on BenzoNuclease® activity. When the concentration of Na⁺ and K⁺ reaches 500mM, the enzyme activity is almost completely lost.



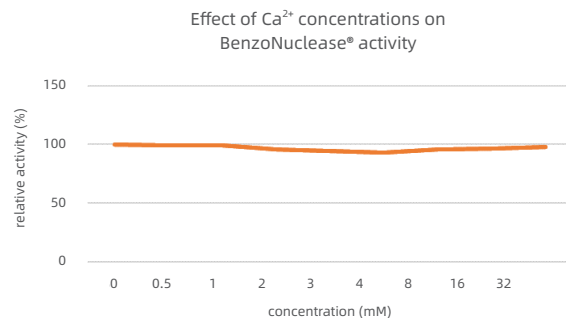
Effect of Mg²⁺ and Mn²⁺ concentrations on BenzoNuclease® activity

1-2mM Mg²⁺ or Mn²⁺ is a necessary condition for BenzoNuclease®.



Effect of Ca²⁺ concentrations on BenzoNuclease® activity

The concentration of Ca²⁺ has no effect on the enzyme activity of BenzoNuclease®.

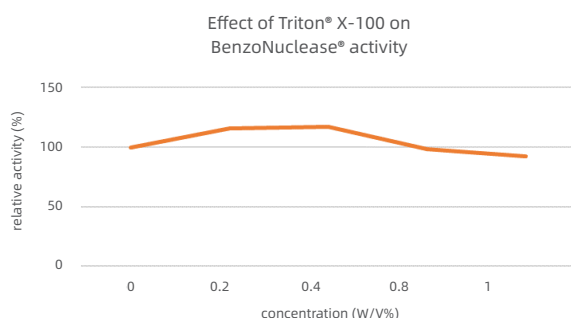


GMP Grade animal-free, ampicillin-free

BenzoNuclease® DNA/RNA Removal

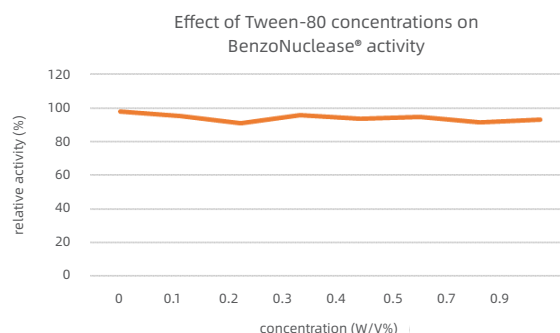
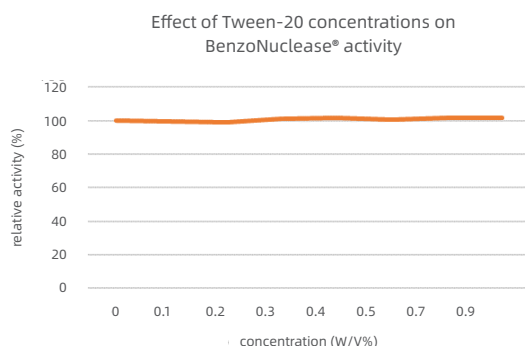
Effect of Triton® X-100 on BenzoNuclease® activity

When the concentration of Triton® X-100 is less than 1%, there is basically no effect on the activity of BenzoNuclease®.



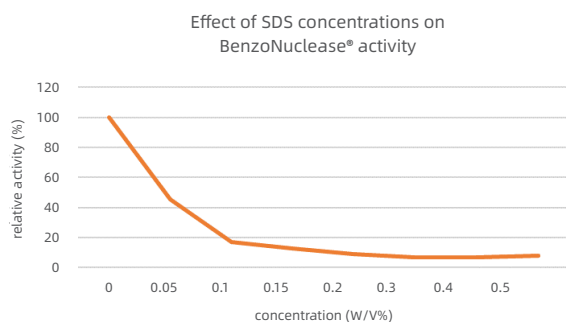
Effect of Tween-20、Tween-80 concentrations on BenzoNuclease® activity

When the concentration of Tween-20 and Tween-80 is less than 1%, there is basically no effect on the activity of BenzoNuclease®.



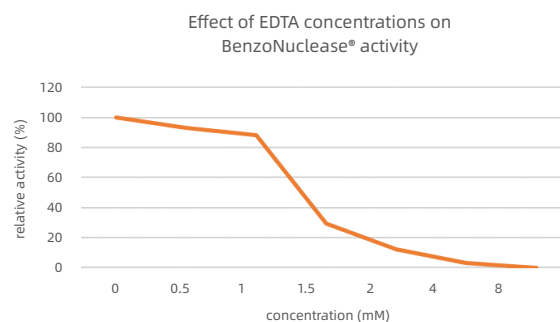
Effect of SDS concentrations on BenzoNuclease® activity

0.1% SDS has a significant effect on the activity of BenzoNuclease®.



Effect of EDTA concentrations on BenzoNuclease® activity

1mM EDTA can partially inhibit BenzoNuclease® activity.



GMP Grade animal-free, ampicillin-free

BenzoNuclease® DNA/RNA Removal

Q&A

1. At what step do we add BenzoNuclease®?

It depends on the purpose for which you use BenzoNuclease®. For example, BenzoNuclease® can be added to the sample along with a lysate reagent in the purification of proteins expressed in *E. coli*.

2. When the reaction temperature is lower than 37°C, how to ensure the digestion effect of BenzoNuclease®?

In the case of a fixed system, the digestion effect of BenzoNuclease® mainly depends on the amount of enzyme, reaction temperature and reaction time. When the reaction temperature is low, it is more recommended to extend the reaction time to ensure the digestion effect of BenzoNuclease® in order to avoid residual problems caused by excessive BenzoNuclease®.

3. How do I inhibit BenzoNuclease® activity?

There are process additives/agents that affect BenzoNuclease® activity—for example, it can be inhibited by high salts, like > 300 mM monovalent cations, > 100 mM phosphate, > 100 mM ammonium sulfate, > 100 mM guanidine HCl. Other known inhibitors are chelating agents, like EDTA, which could cause loss of free Mg²⁺-ions (EDTA concentrations > 1 mM have shown to inhibit the enzymatic reaction). This can be reversed by adding more MgCl₂.

4. BenzoNuclease® is compatible with protease inhibitor cocktails?

Yes. However, caution should be exercised, since many protease inhibitor cocktails include EDTA.

Product information

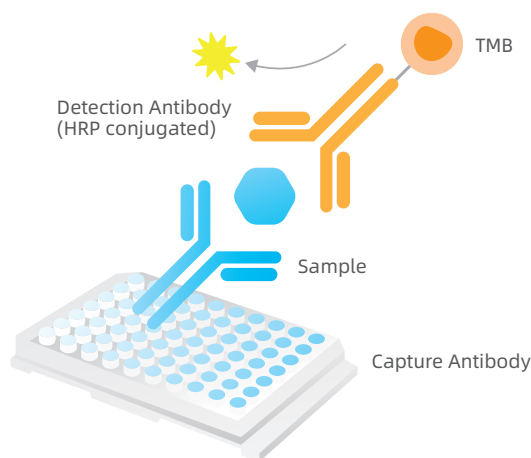
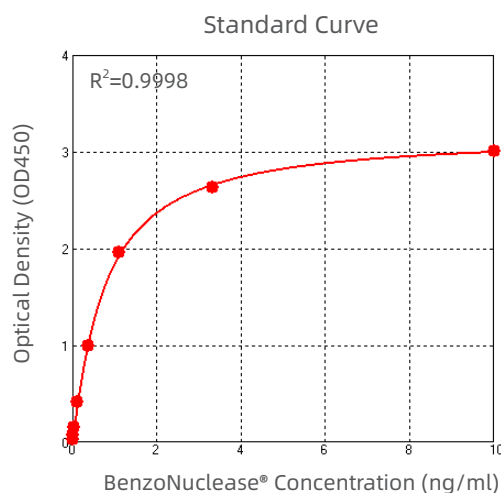
Cat. No.	Product Name	Pack Size
GMP-1707	BenzoNuclease, GMP Grade	100KU/200KU/5000KU



GMP Grade animal-free, ampicillin-free

BenzoNuclease® ELISA Kit

BenzoNuclease® ELISA Kit can detect and quantitatively analyze the residue of BenzoNuclease® in recombinant viral vectors and vaccine production with high sensitivity and specificity. The sensitivity is 0.014ng/ml, and the detection range is 0.014ng/ml-10ng/ml.



- Step 1: Test sample added to the well
- Step 2: Detection Antibody added to the well
- Step 3: Colorimetric detection with TMB substrate

Product information

Cat. No.	Product Name	Pack Size
PA018	BenzoNuclease® ELISA Kit	96T

GMP Grade animal-free, ampicillin-free

BenzoNuclease® ELISA Kit

Sensitivity

The sensitivity is 0.014ng/ml.

Blank limit

Blank limit ≤ 0.06 .

n=16 replicates	Result
AVE	0.0241
SD	0.0076
AVE+2SD ≤ 0.06	0.0393

Detection range

The detection range is 0.014ng/ml-10ng/ml.

Spike recovery

Spike recovery 80%-120%.

Theoretical concentration (ng/ml)	Back-calculated average concentration (ng/ml)	Average spike recovery
1.11	1.12	101%
0.37	0.36	97%
0.12	0.14	115%

Precision

The intra-assay precision is $\leq 10\%$, and the between-assay precision is $\leq 10\%$.

Theoretical concentration (ng/ml)	Intra-assay precision		Between-assay precision	
	Back-calculated average concentration (ng/ml)	CV	Back-calculated average concentration (ng/ml)	CV
1.11	1.21	3.6%	1.18	5.5%
	1.15		1.09	
	1.13		1.24	
0.37	0.41	8.0%	0.36	7.7%
	0.39		0.41	
	0.35		0.36	
0.12	0.13	8.3%	0.12	7.7%
	0.12		0.13	
	0.11		0.14	

4

Infectious Pathogen Vaccine Research Products

SARS-CoV-2 Omicron Variants Protein

Cat. No.	Variants	Product Name
DRA242	Omicron, CH.1.1	Recombinant SARS-CoV-2 S-trimer Protein (CH.1.1, C-6His)
DRA241	Omicron, CH.1.1	Recombinant SARS-CoV-2 S Protein RBD (CH.1.1, C-6His)
DRA237	Omicron, XBB.1.5	Recombinant SARS-CoV-2 S-trimer Protein (XBB.1.5, C-6His)
DRA234	Omicron, XBB.1.5	Recombinant SARS-CoV-2 S Protein RBD (XBB.1.5, C-6His)
DRA238	Omicron, XBB	Recombinant SARS-CoV-2 S-trimer Protein (XBB, C-6His)
DRA233	Omicron, XBB	Recombinant SARS-CoV-2 S Protein RBD (XBB, C-6His)
DRA235	Omicron, BQ.1.1	Recombinant SARS-CoV-2 S-trimer Protein (BQ.1.1, C-6His)
DRA232	Omicron, BQ.1.1	Recombinant SARS-CoV-2 S Protein RBD (BQ.1.1, C-6His)
DRA228	Omicron, BF.7	Recombinant SARS-CoV-2 S Protein RBD (BF.7, C-6His)
DRA229	Omicron, BF.7	Recombinant SARS-CoV-2 S-trimer Protein (BF.7, C-6His)
DRA236	Omicron, BA.5	Recombinant SARS-CoV-2 S-trimer Protein (BA.5, C-6His)
DRA213	Omicron, BA.4	Recombinant SARS-CoV-2 S-trimer Protein (BA.4, C-6His)
DRA205	Omicron, BA.4&BA.5	Recombinant SARS-CoV-2 S Protein RBD (BA.4&BA.5, C-6His)
DRA216	Omicron, BA.3	Recombinant SARS-CoV-2 S Protein RBD (BA.3, C-6His)
DRA218	Omicron, BA.2.75	Recombinant SARS-CoV-2 S-trimer Protein (BA.2.75, C-6His)
DRA217	Omicron, BA.2.75	Recombinant SARS-CoV-2 S Protein RBD (BA.2.75, C-6His)
DRA220	Omicron, BA.2.12.1	Recombinant SARS-CoV-2 S-trimer Protein (BA.2.12.1, C-6His)
DRA214	Omicron, BA.2.12.1	Recombinant SARS-CoV-2 S Protein RBD (BA.2.12.1, C-6His)
DRA200	Omicron, BA.2	Recombinant SARS-CoV-2 S-trimer Protein (BA.2, C-6His)
DRA198	Omicron, BA.2	Recombinant SARS-CoV-2 S Protein RBD (BA.2, C-6His)
DRA199	Omicron, BA.2	Recombinant SARS-CoV-2 S Protein RBD (BA.2, C-mFc)
DRA215	Omicron, BA.1.1	Recombinant SARS-CoV-2 S Protein RBD (BA.1.1, C-6His)
DRA194	Omicron, B.1.1.529	Recombinant SARS-CoV-2 S-trimer Protein V2 (Omicron, B.1.1.529, C-6His)
DRA196	Omicron, B.1.1.529	Recombinant SARS-CoV-2 S1 Protein (Omicron, B.1.1.529, C-10His)
DRA195	Omicron, B.1.1.529	Biotinylated SARS-CoV-2 S Protein RBD (Omicron, B.1.1.529, C-6His-Avi)
DRA190	Omicron, B.1.1.529	Recombinant SARS-CoV-2 S Protein RBD (Omicron, B.1.1.529, C-6His)
DRA197	Omicron, B.1.1.529	Recombinant SARS-CoV-2 Nucleocapsid Protein (Omicron, B.1.1.529, N-6His)

Infectious Pathogen Vaccine Research Products

Pseudoviruses and ACE2 overexpressed cell lines

Cat. No.	Product Name
XCC14	293-ACE2 Overexpressed Cells
XCV13/08/06.....	SARS-CoV-2 Pseudovirus Omicron/Alpha/Beta/Gamma.....

Respiratory Syncytial Virus (RSV)

Cat. No.	Product Name
DRA231	Recombinant RSV G Protein
DRA230	Recombinant RSV F-trimer Protein
DA091	RSV F Antibody (11A9)
DA092	RSV G Antibody (2G7)
DA101	RSV F Antibody (3C12)
DA102	RSV F Antibody (4D5)

Monkeypox Virus (MPXV)

Cat. No.	Product Name
DRA219	Recombinant MPXV A30L Protein
DRA206	Recombinant MPXV A29L Protein (110AA)
DRA207	Recombinant MPXV A29L Protein (E.coli)
DRA208	Recombinant MPXV A29L Protein (Mammalian)
DRA209	Recombinant MPXV A35R Protein
DRA210	Recombinant MPXV M1R Protein
DRA211	Recombinant MPXV B6R Protein
DRA212	Recombinant MPXV E8L Protein
NC083	Anti-MPXV A35R mAb
NC082	Anti-MPXV B6R mAb

Infectious Pathogen Vaccine Research Products

Varicella-Zoster Virus (VZV)

Cat. No.	Product Name
DRA224	Recombinant VZV (strain Oka vaccine) Envelope Glycoprotein E

African Swine Fever Virus (ASFV)

Cat. No.	Product Name
DRA160	Recombinant ASFV pS273R
DRA162	Recombinant ASFV p72 complex
DRA250	Recombinant ASFV p30

Porcine Reproductive and Respiratory Syndrome Virus (PRRSV)

Cat. No.	Product Name
DRA222	Recombinant PRRSV (strain VR2332) nsp7 Protein

Pseudorabies Virus (PRV)

Cat. No.	Product Name
DRA245	Recombinant PRV gB Protein

Support

Product Quality Control Specifications

All products have technical datasheet and COA, please e-mail to request:
support@novoprotein.com.cn

Or download via our website:
<http://www.novoprotein.com>

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