

Benzonase® endonuclease Safety Plus Emprove® Expert

Product Description

Benzonase® endonuclease—the smart solution for DNA removal in biopharmaceutical production has proven its value for over 30 years. Balancing efficiency and regulatory compliance by delivering reliability and high-quality manufacturing under GMP according to ICH Q7. Additionally, to the stringent quality control and extensive documentation packages that are part of Benzonase® endonuclease Emprove® Expert, the new Safety Plus product enhances quality level even further by adding the most recent manufacturing and analytical technologies delivering elevated risk mitigation. The Benzonase® endonuclease Safety Plus EMPROVE® Expert is manufactured using a non-animal origin chemically-defined fermentation medium. Release testing confirms the absence of mycoplasma and adventitious viruses for enhanced product safety. Tailgate samples for the large pack size are provided to avoid opening the large pack during incoming goods control, adding a further layer of safety.

Product Application

Benzonase® endonuclease Safety Plus Emprove® Expert is a companion product to our existing Benzonase® endonuclease portfolio. All Benzonase® endonuclease products share the same amino acid sequence (proven by LC-MS/MS mass spectrometry), robustness and activity. Acting as endonuclease, degrading both DNA and RNA to small 3–5 base pairs (<6 kDa) fragments with no base preference, they are the ideal tool for nucleic acid removal in virus vector and vaccine manufacturing as demanded by regulators. The use of Benzonase® endonuclease additionally increases the yield in virus purification, protects the downstream chromatography and filter devices from fouling, and reduces feed stream viscosity.

With its new features, Benzonase® endonuclease Safety Plus Emprove® Expert is ideally suited for manufacturing of cell and gene therapy agents such as adeno associated and lenti viruses, oncolytic viruses, and viral vector vaccines.

Features

Features / Application	Standard Benzonase® endonuclease	Benzonase® endonuclease Safety Plus Emprove® Expert
Origin	<i>Serratia marcescens</i> , Production: <i>E. coli</i> K12 strain W3110; 30 kDa; PI 6.85; sequence homology data	
GMP manufacturing according to ICH Q7	Yes	Yes
FDA Bulk Biological Master File (BBMF) & Emprove®	Yes	Yes
Non-Animal-Origin (NAO), recombinant from <i>E. coli</i> in chemically defined production medium	No	Yes
Shipment with temperature strips	No	Yes
Tailgate samples for large pack size	No	Yes (with 5M unit size)
Lot release <i>in vitro</i> test for absence of adventitious viruses (3 cell lines) and Mycoplasma test	No	Yes
Endotoxins (LAL) microbial testing	< 0.25 EU/1,000 U < 10 CFU/100,000 U	< 0.25 EU/1,000 U < 10 CFU/100,000 U
Target customer	Viral Vaccines	Viral & Gene Therapy
Long term product availability	Both Benzonase® products will remain in our portfolio	

Key Benefits

- Superior purity $\geq 99.0\%$
- High activity ≥ 250 U/ μ L
- No protease activity detectable
- Low bioburden (< 10 CFU/100000 U) and endotoxins ($< .025$ EU/1000 U)
- **NAO certification**
- **Lot release testing for absence of adventitious viruses and mycoplasma**
- **Tailgate Sample for large pack sizes**
- Comprehensive Emprove[®] documentation to support qualification, risk assessment and process optimization needs as well as U.S. FDA Bulk Biological Master File.
- Production according to ICH Q7 guideline

Handling and Optimization Instructions

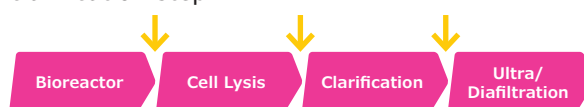
The enzyme is a protein consisting of two subunits with a molecular weight of about 30 kDa each. The protein has an isoelectric point (pI) at pH 6.85. Benzonase[®] endonuclease requires Mg²⁺ (1–2 mM) for it to be active, but retains effective under a wide range of operating conditions:

- pH 6.0–10.0
- Temperature 0–42 °C
- Concentration of monovalent ions (Na⁺, K⁺) 0–150 mM
- DDT, 2-Mercaptoethanol >100 mM
- Detergents (e.g., sodium deoxycholate or sodium dodecyl sulfate) up to 1%
- Urea up to 7 M

As Benzonase[®] endonuclease activity is influenced by the matrix it is used in, optimization of applied concentrations and incubation time is recommended ensuring the economical use of the enzyme.

1.) Screening 1.03773.1010

1. Determine DNA concentration in process
2. Calculate theoretical value of Benzonase[®] concentration needed to digest measured DNA amount based on the formula:
$$\frac{\text{DNA in } \mu\text{g/mL}}{37} = \text{XU/mL}$$
3. Set up DoE Experiments testing different Benzonase[®] concentrations (e.g., 2x; 3x; 10x and 0.5x; 0.25x; 0.1x of theoretical Benzonase[®] concentration) and varying incubation times (e.g., 1, 2, 4, 8, 12, 18 and 24 h)
4. Test optimal concentration at different steps in the process past bioreactor, cell lysis step, clarification step



5. Test scaling e.g., by moving from mL to L scale

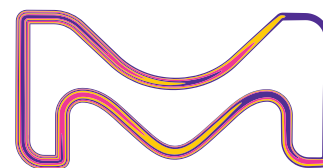
2.) Verification and manufacturing process: Large scale pack GMP grade 1.03773.0010

Ordering Information

Benzonase[®] endonuclease Safety Plus Emprove[®] Expert is available in different pack sizes to support different applications from R&D over process development up to production-scale operations.

Cat. No.	Product Name	Units Activity
1.03773.1010	Benzonase [®] endonuclease Safety Plus EMPROVE [®] Expert	100,000 U
1.03773.0001	Benzonase [®] endonuclease Safety Plus EMPROVE [®] Expert	500,000 U
1.03773.0010	Benzonase [®] endonuclease Safety Plus EMPROVE [®] Expert + Tailgate sample in same outer package	5,000,000 U +50,000 U
1.01681.0001	Benzonase [®] ELISA kit II for residual Benzonase [®] Detection	NA

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