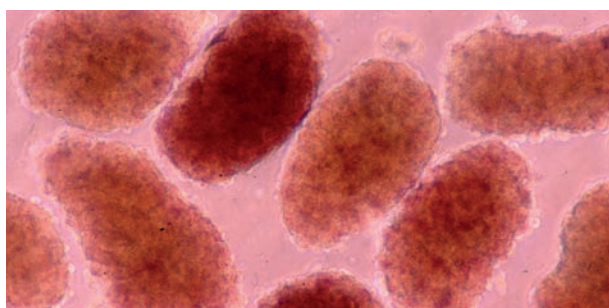


Technical Notes

Collagenase NB 1 GMP Grade Neutral Protease NB GMP Grade

GMP Collagenase for Islet Isolation

Chromatographically highly purified **Collagenase NB 1 GMP Grade** from *Clostridium histolyticum* containing class I and class II collagenase is designed for isolation of pancreatic islets. Very low levels of secondary proteases and bacterial endotoxins guarantee high yields and viability of isolated cells.



Islet isolated with Collagenase NB 1, Photo: H. & D. Brandhorst, Uppsala University Hospital

Neutral Protease NB GMP Grade from *Clostridium histolyticum* is chromatographically purified and is an essential additive for tissue dissociation with Collagenase NB 1 GMP Grade. It is provided separately allowing **individual dosage** for optimal tissue dissociation and **high stability** of the enzymes.



Collagenase NB 1 GMP Grade and Neutral Protease NB GMP Grade are manufactured at the pharmaceutical company Nordmark Arzneimittel, Germany, which is the world's largest manufacturer of collagenase. The application of pharmaceutical manufacturing standards guarantees a high quality of the products with a reliable **lot-to-lot consistency**.

Production Compliant to GMP

Pancreatic islet isolation for human transplantation requires production standards according to GMP guidelines. As collagenase is regarded as a critical raw material, Collagenase NB 1 GMP Grade and Neutral Protease NB GMP Grade are produced in compliance with the EU-Guide to current Good Manufacturing Practice (GMP) for active pharmaceutical ingredients.

GMP Compliant Production

- > Reproducible batches
- > Traceability
- > Production in a dedicated facility
- > Application of pharmaceutical manufacturing standards
- > Experienced manufacturer, GMP certified, FDA inspected, qualified supplier for Clinical Islet Transplant Consortium (CIT)

Safety

- > Absence of cross contamination
- > Carefully selected, natural production strain (*C. histolyticum*)
- > Abnormal toxicity tested for each lot (Ph. Eur.)
- > Virus validation studies
- > Production fulfills requirements of TSE (transmissible spongiform encephalopathy) guideline (Ph. Eur.)
- > TSE safety of raw materials certified by European Authorities, EDQM

Documentation

- > Batch records
- > Certificate of Analysis
- > Validation reports
- > Stability acc. to ICH guidelines
- > Qualification documents
- > US DMF (Drug Master Files) filed with FDA

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Technical Notes

Product Information

Enzyme	Collagenase NB 1 GMP Grade		Neutral Protease NB GMP Grade	
Origin	<i>Clostridium histolyticum</i>		<i>Clostridium histolyticum</i>	
Composition	Collagenase class I and class II		Neutral Protease	
Molecular weight	70 – 120 kDa (collagenases)		34 kDa	
Special features	Manufactured according to international GMP guidelines		Manufactured according to international GMP guidelines	
Characters	White to almost white, 0.2 µm filtered, chromatographically highly purified, lyophilisate		Beige to brown, 0.2 µm filtered, chromatographically purified, lyophilisate	
Protein content	Lowry assay	approx. 95%	Lowry assay	approx. 85 %
Identification	SDS-PAGE	Position of main bands must comply	SDS-PAGE	Position of main bands must comply
Test	Water	≤ 15 % (w/w)	Water	≤ 15 % (w/w)
Microbiological examination	TAMC (Total Aerobic Microbial Count)	≤ 10/Vial	TAMC (Total Aerobic Microbial Count)	≤ 10/Vial
	TYMC (Total Yeasts/ Moulds Count)	≤ 10/Vial	TYMC (Total Yeasts/ Moulds Count)	≤ 10/Vial
	Absence of Clostridia	Must comply	Absence of Clostridia	Must comply
	Abnormal toxicity (General Safety Test; Ph. Eur.)	Must comply	Abnormal toxicity (General Safety Test; Ph. Eur.)	Must comply
Activities	Collagenase (PZ activity according to Wünsch, 25 °C)	≥ 2000 U/Vial	Neutral Protease (DMC assay)	≥ 100 U/Vial
	Collagenase (PZ activity according to Wünsch, 25 °C)	≥ 3.000 U/mg lyophilisate	Neutral Protease (DMC assay)	≥ 0.50 U/mg lyophilisate
	Neutral Protease (DMC assay)	≤ 0.05 U/mg lyophilisate		
	Trypsin-like activities (BAEE assay)	Status		
	Clostripain, native state (BAEE assay)	Status		
Bacterial endotoxins	LAL assay	≤ 10.0 EU/mg lyophilisate	LAL assay	≤ 100.0 EU/mg lyophilisate
Long term storage	+2 to +8 °C		+2 to +8 °C	
Long term stability data	5 °C ± 3 °C 5 years (after manufacture)		5 °C ± 3 °C 5 years (after manufacture)	

Ordering Information

Enzyme	Cat. No.	Pack Size
Collagenase NB 1 GMP Grade from <i>C. histolyticum</i>	N0002937	≥ 2000 PZ U/Vial
Neutral Protease NB GMP Grade from <i>C. histolyticum</i>	N0002936	≥ 100 DMC U/Vial



AMSBIO | www.amsbio.com | info@amsbio.com

 **UK & Rest of the World**
184 Park Drive, Milton Park
Abingdon OX14 4SE, U.K.
T: +44 (0) 1235 828 200
F: +44 (0) 1235 820 482

 **North America**
1035 Cambridge Street,
Cambridge, MA 02141.
T: +1 (617) 945-5033 or
T: +1 (800) 987-0985
F: +1 (617) 945-8218

 **Germany**
Bockenheimer Landstr. 17/19
60325 Frankfurt/Main
T: +49 (0) 69 779099
F: +49 (0) 69 13376880

 **Switzerland**
Via Lisano 3
(CP.683)
6900 Massagno
T: +41 (0) 91 604 55 22
F: +41 (0) 91 605 17 85