PAN™ CELLTECH

Certificate of Analysis

WFI Beyond,

Water for Injection, acc. to EP monograph 0169 and beyond compendial

FDA Drug Master File: Type IV (excipient) MF044505

Product	Description	Art. No.	Size
WFI Beyond	**Water for Injection, acc. to EP monograph 0169 and beyond compendial**	**CT-981000**	**1000 mL**

Lot No.: 2560826

Date of production: August 18, 2026

Storage conditions and stability:

Storage: +15°C to +25°C (RT)
Stability: 2 years from date of production
Based on stability studies performed for the microbiological parameters sterility and endotoxins.

Specification:	**Acceptance criteria**		**Result**
	acc. to EP monograph 0169	acc. to beyond compendial	(B, E: Beginning and End of Filling process)
Appearance Turbidity (Ph. Eur. 2.2.1.)	N/A	clear	B: pass E: pass
Appearance Coloration (Ph. Eur. 2.2.2. Method II)	N/A	colorless	B: pass E: pass
Conductivity (at 20°C) (Ph. Eur. 2.2.38.) (Measured continuously in the storage loop before filtration)	≤ 1.1 µS/cm	< 0.2 µS/cm	0.128 µS/cm
Total organic carbon (TOC) (Ph. Eur. 2.2.44.) (Measured continuously in the storage loop before filtration)	≤ 0.5 mg/L	< 0.05 mg/L	0.011 mg/L
Endotoxin (Ph. Eur. 2.6.14., Method C)	< 0.25 EU/ml	< 0.005 EU/mL	B: < 0.005 EU/mL E: < 0.005 EU/mL

Specification:	**Acceptance criteria:**		**Result:**
	acc. to EP monograph 0169	acc. to beyond compendial	(B, E: Beginning and End of Filling process)
RNase activity (AA 4.1.10, fluorometric method)	N/A	No RNase activity detected	B: not detected E: not detected
DNase activity (AA 4.1.10, fluorometric method)	N/A	No DNase activity detected	B: not detected E: not detected
Sterility (Ph. Eur. 2.6.1.) Full product-specific verification not included	no growth	no growth	no growth
Elemental Impurities (Ph. Eur. 2.4.20., Procedure 2 (ICP-MS), 24 elements)	see the list below		B: complies E: complies

Class 1 - Human toxicants, evaluation always required

	limit acc. to ICH Q3D(R2)	limit acc. to beyond Compendial	LOQ = limit of quantification	Result
Arsenic (As)	≤ 1500 µg/L	≤ 750 µg/L	0.30 µg/L	B: < 0.30 µg/L E: < 0.30 µg/L
Cadmium (Cd)	≤ 200 µg/L	≤ 100 µg/L	0.04 µg/L	B: < 0.04 µg/L E: < 0.04 µg/L
Mercury (Hg)	≤ 300 µg/L	≤ 150 µg/L	0.06 µg/L	B: < 0.06 µg/L E: < 0.06 µg/L
Lead (Pb)	≤ 500 µg/L	≤ 250 µg/L	0.10 µg/L	B: < 0.10 µg/L E: < 0.10 µg/L

Class 2A - High probability of occurrence, evaluation always required

	limit acc. to ICH Q3D(R2)	limit acc. to beyond compendial	LOQ = limit of quantification	Result
Cobalt (Co)	≤ 500 µg/L	≤ 250 µg/L	0.10 µg/L	B: < 0.10 µg/L E: < 0.10 µg/L
Nickel (Ni)	≤ 2000 µg/L	≤ 1000 µg/L	0.40 µg/L	B: < 0.40 µg/L E: < 0.40 µg/L
Vanadium (V)	≤ 1000 µg/L	≤ 500 µg/L	0.20 µg/L	B: < 0.20 µg/L E: < 0.20 µg/L

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Class 2B - Low probability of occurrence, evaluation required if intentionally added

	limit acc. to ICH Q3D(R2)	limit acc. to beyond Compendial	LOQ = limit of quantification	Result
Silver (Ag)	≤ 1500 µg/L	≤ 750 µg/L	0.20 µg/L	B: < 0.20 µg/L E: < 0.20 µg/L
Gold (Au)	≤ 30000 µg/L	≤ 15000 µg/L	2.0 µg/L	B: < 2.0 µg/L E: < 2.0 µg/L
Iridium (Ir)	≤ 1000 µg/L	≤ 500 µg/L	0.20 µg/L	B: < 0.20 µg/L E: < 0.20 µg/L
Osmium (Os)	≤ 1000 µg/L	≤ 500 µg/L	0.20 µg/L	B: < 0.20 µg/L E: < 0.20 µg/L
Palladium (Pd)	≤ 1000 µg/L	≤ 500 µg/L	0.20 µg/L	B: < 0.20 µg/L E: < 0.20 µg/L
Platinum (Pt)	≤ 1000 µg/L	≤ 500 µg/L	0.20 µg/L	B: < 0.20µg/L E: < 0.20 µg/L
Rhodium (Rh)	≤ 1000 µg/L	≤ 500 µg/L	0.20 µg/L	B: < 0.20 µg/L E: < 0.20 µg/L
Ruthenium (Ru)	≤ 1000 µg/L	≤ 500 µg/L	0.20 µg/L	B: < 0.20 µg/L E: < 0.20 µg/L
Selenium (Se)	≤ 8000 µg/L	≤ 4000 µg/L	1.60 µg/L	B: < 1.60 µg/L E: < 1.60 µg/L
Thallium (Tl)	≤ 800 µg/L	≤ 400 µg/L	0.16 µg/L	B: < 0.16 µg/L E: < 0.16 µg/L

Class 3 - Low oral toxicity, evaluation required for the parenteral route

	limit acc. to ICH Q3D(R2)	limit acc. to beyond Compendial	LOQ = limit of quantification	Result
Barium (Ba)	≤ 70000 µg/L	≤ 35000 µg/L	14.00 µg/L	B: < 14.00 µg/L E: < 14.00 µg/L
Chromium (Cr)	≤ 110000 µg/L	≤ 55000 µg/L	22.00 µg/L	B: < 22.00 µg/L E: < 22.00 µg/L
Copper (Cu)	≤ 30000 µg/L	≤ 15000 µg/L	6.00 µg/L	B: < 6.00 µg/L E: < 6.00 µg/L
Lithium (Li)	≤ 25000 µg/L	≤ 12500 µg/L	5.00 µg/L	B: < 5.00 µg/L E: < 5.00 µg/L
Molybdenum (Mo)	≤ 150000 µg/L	≤ 75000 µg/L	30.00 µg/L	B: < 30.00 µg/L E: < 30.00 µg/L
Antimony (Sb)	≤ 9000 µg/L	≤ 4500 µg/L	1.80 µg/L	B: 2.6 µg/L E: < 1.80 µg/L
Tin (Sn)	≤ 60000 µg/L	≤ 30000 µg/L	12.00 µg/L	B: < 12.00 µg/L E: < 12.00 µg/L

Limits are calculated in accordance with ICH Q3D(R2), Section 7, Option 1, using the parenteral permitted daily exposures (PDE) listed in Table A.2.1:
Limit [µg/g] = parenteral PDE [µg/day] / 10 g/day.
For aqueous solutions with a density of 1.00 g/mL at 20 °C, 1 µg/g corresponds to 1 mg/L. The assumed daily intake is to be verified by the manufacturer of the finished medicinal product against its actual maximum daily intake.

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Suitability
FOR FURTHER MANUFACTURING
User is responsible to assure product suitability for the intended use.

GMP compliance:
This batch has been manufactures according to EU-GMP guidelines.

Manufactured in Germany

Date: 13. OKT. 2026

Quality Assurance

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Addendum to Certificate of Analysis

WFI Beyond,

Water for Injection, acc. to EP monograph 0169 and beyond compendial

FDA Drug Master File: Type IV (excipient) MF044505

Product	Description
WFI Beyond	**Water for Injection, acc. to EP monograph 0169 and beyond compendial**

Lot No.: 2560826

Additional elemental characterisation

Trace Metals: Copper, Iron, Manganese and Zinc

This addendum reports the results for copper, iron, manganese and zinc for this batch. Copper is part of the ICH Q3D(R2) panel and is also reported on the Certificate of Analysis. Iron, manganese and zinc are not covered by ICH Q3D(R2); they are reported as additional characterisation and evaluated against in-house reference limits. Method: Ph. Eur. 2.4.20 / USP <233> (ICP-MS).

Element	Relevance	Reference limit [µg/L]	LOQ [µg/L]	Result [µg/L]
Oxidation-relevant: proteins, unsaturated lipids and DNA				
Copper (Cu)	Catalyst of metal-catalysed oxidation (MCO)	30000 (ICH Q3D, Class 3)	6	B: < 6 E: < 6
Iron (Fe)	Catalyst of metal-catalysed oxidation (MCO)	25000 (in-house ref.)	5	B: < 5 E: < 5
RNA-relevant: RNA (e.g. mRNA, siRNA)				
Manganese (Mn)	Can cleave the RNA backbone	25000 (in-house ref.)	5	B: < 5 E: < 5
Zinc (Zn)	Can cleave the RNA backbone	25000 (in-house ref.)	5	B: < 5 E: < 5

LOQ = the LOQ is the accredited laboratory's limit of quantification for the executed method. The method is validated.

Results are reported for the beginning (B) and end (E) of the filling process.

The limit for copper is calculated in accordance with ICH Q3D(R2), Section 7, Option 1, using the parenteral permitted daily exposures (PDE) listed in Table A.2.1: Limit [µg/g] = parenteral PDE [µg/day] / 10 g/day. For aqueous solutions with a density of 1.00 g/mL at 20 °C, 1 µg/g corresponds to 1 mg/L. The assumed daily intake is to be verified by the manufacturer of the finished medicinal product against its actual maximum daily intake. Iron, manganese and zinc are evaluated against in-house reference limits.

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Background: relevance of the reported elements

Copper and iron are catalysts of metal-catalysed oxidation of proteins and of unsaturated lipids and can generate radicals that damage DNA. Manganese and zinc can cleave the phosphodiester backbone of RNA. In cell culture media, iron, copper, manganese and zinc are essential trace elements and are added deliberately.

Monoclonal antibodies

Copper and iron catalyse the oxidation of amino-acid residues such as histidine and methionine.

Cell & gene therapy

Iron and copper can generate radicals that cause DNA strand breaks; capsid proteins of viral vectors are subject to metal-catalysed oxidation.

Vaccines

Protein and conjugate antigens are subject to metal-catalysed oxidation by copper and iron. For mRNA-based vaccines, the information for mRNA and Liposomes & LNP applies.

mRNA

Manganese and zinc can cleave the RNA backbone.

Liposomes & LNP

Iron and copper can catalyse the oxidation of unsaturated lipids. For RNA payloads, manganese and zinc can additionally cleave the RNA backbone.

This information is provided to support the user's risk assessment. The suitability for the intended use is to be confirmed by the user; the evaluation of the finished medicinal product remains with its manufacturer.

Date: 29. OKT. 2026

Quality Assurance

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