Limited Liability Company
“Center for quality control BIOLIFE”
115478, Moscow, Kashirskoe Hwy, 24, bldg. 2. Tel: 8 (495)781-20-42, 8 (495) 781-20-43
Accreditation certificate № RA.RU.21.ЦК01 dated 22.07.2015

APPROVED
The Head of Testing Laboratory
Of CQC Biolife, LLC
Razlivayeava O.V.

<signature>
“6” June 2019
Round Seal: /limited liability company “Center for quality control BIOLIFE”, PSRN 1147746879280, MOSCOW/

PROTOCOL
TOXICOLOGY TESTING OF MEDICAL DEVICES (MATERIALS) FOR THE PURPOSE TO ESTABLISH THEIR SAFETY

№ 147-04П DATED 6TH OF JUNE, 2019

Total pages: 4

Name of device (material)	HBIS Endoprosthesis of synovial fluid NOLTREX, Technical Specification file (TU) 9398-001-52820385-2015 (see Annex on 1 page).
Manufacturer	RESEARCH CENTER BIOFORM, LLC located 142784, Moscow, s.Moskovskiy, Kievskoe Hwy, 22nd km, house 4, bldg. 2, floor 5, block G Manufacturing address: 142784, Moscow, s.Moskovskiy, Kievskoe Hwy, 22nd km, house 4, bldg. 2, floor 5, block G
Applicant	RESEARCH CENTER BIOFORM, LLC 142784, Moscow, s.Moskovskiy, Kievskoe Hwy, 22nd km, house 4, bldg. 2, floor 5, block G
Date of sample presented for testing	23.05.2019
Risk class	3
No of application for testing	№1

The testing is performed in accordance with (list of standards and other normative documents):
GOST R ISO 10993-2-2009
GOST ISO 10993-1-2011, 10993-5-2011, 10993-6-2011, 10993-7-2011, 10993-9-2015, 10993-10-2011, 10993-11-2011, 10993-12-2015 “Biological evaluation of medical devices”
GOST R ISO 52770-2016 “Medical devices. Safety requirements. Methods of sanitary-chemical and toxicological tests”
GOST 31214-2016 “Medical devices. Requirements for samples and documentation presented for toxicological tests, sanitary and chemical analyses, tests for sterility and pyrogenicity”

GOST 31209-2003 Containers for blood and its components. Requirements for chemical and biological safety and methods of testing., article 5.3
GOST 31576-2012 Evaluation of biological hazard of medical dental materials and articles. Classification and sampling.

TESTING RESULTS

№	Parameter	Permissible values	Results	Conclusion
1.1	Reducing impurities	less than 1,0ml. (0,02H sodium thiosulfate solution)	0.22 – 0.78	complies
1.2	Change in pH	less than 1,0	0.36-0.87	complies
1.3	Ultraviolet absorption	less than 0,3 (range 230-260nm.)	0.0411-0.1049	complies
1.4	**Concentration of hazard impurities and heavy metals in aqueous extracts**			
	Zinc	1.000 mg/l	Below determination limit of 0.005 mg/l	complies
	Iron	0.030 mg/l	Below determination limit of 0.005 mg/l	complies
	Chromium	0.100 mg/l	Below determination limit of 0.0025 mg/l	complies
	Copper	1.000 mg/l	Below determination limit of 0.0005 mg/l	complies
	Aluminum	0.500 mg/l	Below determination limit of 0.002 mg/l	complies
	Silver	0.050 mg/l	Below determination limit of 0.00005 mg/l	complies
	Formaldehyde	0.100 mg/l	Below determination limit of 0.01 mg/l	complies
	Acetaldehyde	0.200 mg/l	Below determination limit of 0.005 mg/l	complies
	Acetone	0.100 mg/l	Below determination limit of 0.005 mg/l	complies
	Methanol	0.200 mg/l	Below determination limit of 0.005 mg/l	complies
	Propyl alcohol	0.100 mg/l	Below determination limit of 0.005 mg/l	complies
	Isopropyl alcohol	0.100 mg/l	Below determination limit of 0.005 mg/l	complies
	Acrylonitrile	0.020 mg/l	Below determination limit of 0.002 mg/l	complies
2	**Toxicology test results**			
2.1	***Irritating effect on the skin and mucous membrane of animals in points***			
	Skin	0	0	complies
	Conjunctiva	0	0	complies
2.2.	**Cytotoxicity**			
	Cytotoxicity with culture of fibroblasts of mice NIH/3T3	Permissible value ≤ 30%	0-5%	complies
2.3.	***Acute toxicity in white mice at intra-abdominal introduction***			
	Deaths	none	none	complies
	Clinical symptoms of intoxication	none	none	complies
	Macroscopic changes of organs	none	none	complies
	Weight coefficient of visceras (observed changes)	none	none	complies

Conclusions as per results of testing:
Tested samples comply with the requirements for medical devices, do not cause negative effects on biological objects.

CONCLUSION

HBIS Endoprosthesis of synovial fluid NOLTREX, technical file specification TU 9398-001-52820385-2015 (see Annex 1 on 1 page), manufactured by RC BIOFORM, LLC complies with normative documentation as per toxicity parameters for medical devices.

GOST R ISO 10993-2-2009
GOST ISO 10993-1-2011, 10993-5-2011, 10993-6-2011, 10993-7-2011, 10993-9-2015, 10993-10-2011, 10993-11-2011, 10993-12-2015 “Biological evaluation of medical devices”
GOST R ISO 52770-2016 “Medical devices. Safety requirements. Methods of sanitary-chemical and toxicological tests”
GOST 31214-2016 “Medical devices. Requirements for samples and documentation presented for toxicological tests, sanitary and chemical analyses, tests for sterility and pyrogenicity”

GOST 31209-2003 Containers for blood and its components. Requirements for chemical and biological safety and methods of testing., article 5.3
GOST 31576-2012 Evaluation of biological hazard of medical dental materials and articles. Classification and sampling.

The testing was done in accordance with normative documentation for such type of tests and using verified laboratory equipment;
Spectrophotometer LEKI SS2109UV; atomic absorption spectrometer ICE 3500; gas chromatograph 6000 Vega Series 2GC; gas chromatograph Crystal 2000M; gas chromatograph Chromatech-Crystall 5000; pH-meter pH-150МИ; microscope Standard 25

RECOMMENDED for use as per toxicity parameter.

Note: the present protocol is applicable to the tested samples only, that were presented by the applicant. The partial copy or full reprint of this protocol is prohibited.

Responsible for testing:
A.A. Zabegaeva
Head of medical device testing department of CQC Biolife, LLC

K.V. Taraban
Specialist of medical device testing department of CQC Biolife, LLC

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PSRN 1147746879280, MOSCOW/

Annex 1 to the toxicology testing protocol №147-04П

HBIS Endoprosthesis of synovial fluid NOLTREX as per technical specification file TU 9398-001-52820385-2015, device variations:

1. – NOLTREX 2.5
2. – NOLTREX 3.0
3. – NOLTREX 5.0

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