NEST®

Wuxi NEST Biotechnology Co.,Ltd.

High Efficiency Erlenmeyer Flasks Validation Binder

Version: 2024 1st Edition

Table of contents

Scope and Disclaimer

Dear customer, thank you for choosing NEST products. The information provided in this document is intended to assist you in applying NEST products to your production, processes, or systems.

Please note that, unless otherwise stated, NEST is only responsible for the authenticity of the NEST issued test or validation reports in this document. Additionally, NEST guarantees the authenticity of the statements made by NEST in this document. NEST also relies on test reports, documents, and other information provided by raw material suppliers and direct component suppliers to provide you with validation results. Documents from supplier sources may be requested to be provided by NEST or directly obtained from the supplier.

NEST has also commissioned third parties to conduct some tests or validations, and the authenticity of the results is guaranteed by the commissioned third parties. As of the revision date of this version, NEST believes that all the information contained in this document is accurate and reflects our knowledge truthfully. Key information of the product, such as raw materials and processing technology, will not be changed until NEST completes the full validation. If you find any discrepancies between the key information in the more recent document issued by NEST and the content of this validation report, it means that the relevant content of this validation report has expired. Please contact us to obtain an updated validation report. We will regularly review and update this document to ensure that you receive the most accurate information possible.

The tests and reports provided in this document apply to NEST products listed in the "Product List" and the scope of validation is limited to the recommended performance and application conditions of NEST products. Extra validation is required for the use beyond the performance and application scope stated by NEST, or contact us for additional testing.

Finally, if you have any feedback on the content of this document or have more detailed requirements for the information in this document, please feel free to contact NEST via the phone or email provided below. We are happy to have our products undergo more testing and challenges, and further improve our products and services.

Below are our contact details:

NEST Biotechnology Co., Ltd.

Email: info@NEST-wuxi.com

Chapter 1 Introduction and Overview

1-1 Company Profile

Leading comprehensive service provider in the field of life sciences

NEST Biotechnology Co., Ltd. (hereinafter referred to as "NEST") was established in 2009 and created the NEST® brand. With the belief of "producing high-end consumables and creating internationally renowned brands," NEST focuses on the research and development and manufacturing of products in the field of life sciences. NEST has 6,800m2 of Class 100,000 clean-rooms, 2,700m2 of Class 10,000 clean-rooms, mature production processes, advanced machinery and equipment, a professional research and development center, and a senior management team. It is a leading comprehensive service provider for the multi-field development in the life sciences industry.

In 2013, the US subsidiary was officially established. In 2022, subsidiaries in Rotterdam, the Netherlands, Sharjah, United Arab Emirates, and Tokyo, Japan were established. The new warehouse in the western United States has been completed, providing integrated storage, transportation, and sales services, guaranteeing the supply of NEST products in worldwide markets. With the continuous increase in business volume, NEST's footprint has spread all over the world and is exported to many countries and regions including North America, Europe, Southeast Asia, the Middle East, Japan, South Korea, and India.

Introduction of advanced equipment to ensure quality stability

To ensure stable quality and achieve seamless integration of "raw material procurement - production - packaging - sterilization - delivery," NEST invested 150 million in 2012 to build a 27,000m^2 plant with dust-free clean-rooms and introduced the international advanced electron irradiation equipment Rhodotron-TT200 (irradiation sterilization process certified by ISO13485 and ISO11137 quality systems). NEST also imports medical-grade raw materials that meet USP Class VI standards and standardized production in accordance with GMP quality management specifications. It has obtained ISO 9001, ISO 13485, ISO 11137, FDA, CE certification, and medical device production licenses. In 2021, NEST added 4,500m^2 of Class 100,000 clean-rooms

and 1,500m^2 of Class 10,000 clean-rooms for the production of medical devices and pharmaceutical packaging consumables.

NEST product line - laboratory consumables, medical devices, pharmaceutical packaging consumables, laboratory instruments, biological reagents

NEST products mainly include disposable consumables (cell biology, bioprocessing, liquid handling, general testing, molecular biology consumables), medical devices, innovative pharmaceutical packaging consumables, laboratory instruments, and biological reagents (cell culture reagents, testing reagents, etc.). They are widely used in new drug development, vaccine research and production, cell therapy, medical aesthetics, biomedical research, *in vitro* diagnostics, and other fields. NEST products have wide coverage, comprehensive specifications, and complete qualifications to meet different customer needs.

Customization services

NEST Biotechnology Co., Ltd. has strong capabilities in mold design, precision machining of machine tools, and plastic molding. In addition to selling standard products, we also provide various customized services to the industry.

1-1-1 Production Base and Warehouses

Chinese Branch

Departments and Functions: Research, Production, Marketing, Sales, Warehousing.

Mainly serving countries and regions: China

Jiangsu, China R&D and Warehousing Base

Production and Storage Area: 26,888 m²

Location: Wuxi, Jiangsu, China

US Branch

Departments and Functions: Marketing, Sales, Warehousing.

Mainly serving countries and regions: North America, South America

Research and Warehousing Base in Woodbridge, New Jersey, USA

Warehousing area: 3300m^2

Location: Woodbridge, New Jersey, USA

Warehouse in Phoenix, Arizona, USA

Warehousing area: 4500m^2

Location: Phoenix, Arizona, USA

Netherlands Branch

Departments and Functions: Sales, Warehousing

Location: Rotterdam, Netherlands

Mainly serving European regions

United Arab Emirates Branch

Departments and Functions: Sales, Warehousing

Location: Sharjah, United Arab Emirates

Mainly serving the Middle East and North Africa regions

Japan Branch

Departments and Functions: Sales

Location: Tokyo, Japan

Mainly serving East Asia regions

We are also actively expanding our warehouse network and business scope to better serve our customers. We believe that NEST's global vision and warehouse layout will bring more value and advantages to our customers.

1-2 Quality Compliance, Registration and Certification

NEST evaluates, controls and manages the quality of its products according to international standards. NEST also ensures quality compliance and registration certification to ensure the safety, reliability, and effectiveness of its products, as well as to meet international legal requirements. These measures aim to reduce product quality issues and risks and improve production efficiency and management level. If you need to obtain NEST's quality compliance and registration certificates, please refer to the appendix or download them from the official website www.cell-NEST.com.

1-2-1 ISO9001, ISO 13485

ISO9001 is a certification for quality management systems applicable to organizations of various types and sizes. Its purpose is to help organizations achieve customer satisfaction and continuously improve their business processes. ISO13485 is a certification for medical device quality management systems, applicable to manufacturers, suppliers, and distributors, ensuring that their products comply with relevant regulations and legal requirements for medical devices.

NEST's ISO9001 and ISO13485 certifications are authorized by TÜV Rheinland, an authoritative EU notified body. TÜV Rheinland Group is authorized to conduct assessments for industrial and consumer products to ensure that NEST's products comply with most EU directives and regulations.

1-2-2 CE Certification: EU MDR

CE MDR is the latest European Union regulation for medical devices. Its implementation strengthens the regulation of the safety and effectiveness of medical devices, standardizes the medical device market, and ensures public drug safety and health. NEST's relevant products comply with the regulations of CE MDR, ensuring that the production of medical devices meets the relevant EU laws, regulations, and technical standards, and possesses safety and effectiveness. NEST obtained the CE certificate authorized by TÜV SÜD, an authoritative institution accredited by the European Union, in 2020.

1-2-3 FDA Registration

Since 2011, NEST has registered and sold its products with the US FDA. Our products comply with relevant US laws, regulations, and technical standards, and possess safety and effectiveness.

1-2-4 Medical Device Production License

NEST obtained a medical device production license in 2021. We have various medical device products, including reusable pen injectors, disposable pen injectors and disposable nasal drug delivery atomization devices. High-precision pen injectors are challenging medical devices that require high-precision processing equipment and technology, as well as strict quality control. Therefore, for companies to obtain a production license for high-precision pen injectors, they need to have high technical capabilities and quality assurance. We apply the same technical capabilities and quality control requirements to our laboratory consumables.

1-3 Quality Management System

NEST quality management system is implemented in accordance with the requirements of ISO9001, ISO13485, and international regulations, and has obtained relevant certifications. NEST takes various measures such as employee management and training, equipment validation, supply chain management, and production environment control to ensure the stability and reliability of product quality. If you need to review related system documents, records, etc., please contact us for on-site factory inspection, and we will provide corresponding information.

1-3-1 Personnel

NEST emphasizes the management and training of employees, ensuring that all employees strictly adhere to the requirements of the operating instructions through on-boarding training, job training, regular rotation training, and job rotation training, to ensure that the entire product production process complies with the validated process requirements.

1-3-2 Production and Testing Equipment Validation

NEST releases all machinery and equipment (including production equipment and testing equipment) for the production process through three stages: installation qualification (IQ), operational qualification (OQ), and performance qualification (PQ), to ensure that the equipment parameters meet the design requirements and can guarantee stable and reliable product performance. Testing equipment is also regularly tested and calibrated. These equipment include but are not limited to:

Production equipment:

- Injection molding machine and corresponding molds
- Automatic assembly equipment, welding equipment, surface treatment equipment, automatic packaging equipment, etc.

Testing equipment:

- Leak testers, flatness gauges, insoluble particle detectors, angle measurement devices, etc.

1-3-3 Incoming Material Control

NEST also implements strict control over supplier admission and approval of raw materials/packaging materials. The company ensures that all raw materials/packaging materials meet product technical requirements through layered control in the following steps:

- Supplier questionnaires
- Supplier on-site audits
- Raw material/packaging material report review
- Raw material/packaging material performance validation
- Raw material/packaging material batch inspection

The implementation of these measures ensures the stability of the supply chain and the quality of the products. This section will also include NEST's relevant statements regarding the control of raw materials and packaging materials.

1-3-3-1 Raw Material Compliance Statement (USP Class VI)

The raw material particles or finished products used in NEST products are provided by manufacturers that meet relevant tests for USP Class VI, ISO 10993, or GB/T 16886, including but not limited to PS, PC, PET, PETG, PP, and others. At the same time, NEST products are

rigorously tested by third-party laboratories (with CNAS or CMA qualifications) according to the following standards to ensure compliance with the relevant requirements.

Test Item	Test Standard
In vitro cytotoxicity test	GB/T 16886.5-2017 / ISO 10993-5:2009, USP<87>
Skin sensitization test	GB/T 16886.10-2017 / ISO 10993-10:2010, USP<88>
Acute systemic toxicity test	GB/T 16886.11-2011 / ISO 10993-11:2017, USP<88>
In vitro hemolysis test	GB/T 16886.4-2003 / ISO 10993-4:2002
Skin irritation test	GB/T 16886.10-2017 / ISO 10993-10:2010, USP<88>

1-3-3-2 TSE/BSE/GMO Statement

All products in this binder produced by NEST do not use any animal-derived or genetically modified ingredients or tissues throughout the entire production process, and have no TSE/BSE/GMO risks.

1-3-3-3 REACH

NEST strictly complies with the EU regulation "Registration, Evaluation, Authorization and Restriction of Chemicals" (2006/1907) (REACH) and controls the highly concerned substances (SVHC) in the raw materials.

1-3-4 Production Environment Control

1-3-4-1 Qualification of 100,000 and 10,000 Level Clean-Rooms

NEST has multiple clean-rooms that meet ISO14644 Class 7/8 standards. They undergo periodic monitoring by third parties to ensure compliance with product manufacturing and packaging requirements. Please contact us through our official website or email to obtain the clean-room qualification testing report.

1-3-4-2 Methods for Clean-Room Environmental Control

NEST conducts periodic monitoring of dust particles, airborne bacteria, settle plate counts, air exchange rates, temperature, humidity, pressure differentials, and compressed air in clean-rooms, in accordance with ISO14644 requirements and company procedures, to ensure compliance with regulatory requirements for clean-room environments.

1-3-4-3 Qualification of Sterility Testing Laboratory

NEST has a Biosafety Level 2 (BSL-2) sterility testing laboratory. It conducts testing of the production environment according to clean-room environmental testing procedures to ensure the safety and reliability of the production environment, and that the final products meet customer requirements.

1-3-4-4 Purified Water System Validation

NEST has multiple purified water systems used for cleaning clean-rooms, clean-room garments, and tools, ensuring the quality of water used in clean-rooms. The company conducts periodic water point testing to test the properties, acidity/alkalinity, ammonia, conductivity, nitrates, nitrites, oxidizable substances, non-volatile matter, heavy metals, and microbiological limits of purified water, to ensure compliance with the requirements of the Chinese Pharmacopoeia (2020 edition) and European Pharmacopoeia(2020) <Purified Water> section.

1-4 Product Verification and Quality Control

During the product validation process, NEST will test all performance items of the product according to internal product technical requirements to ensure that the product meets the design requirements. NEST products go through product design validation, process window validation, performance validation, small-batch trial production, and three-batch production tracking during the development stage to ensure that the products are produced stably and reliably, meeting the product design requirements.

After the product validation is completed and mass production is achieved, some of the early-stage validated product performance test items will be transformed into periodic monitoring and batch testing items to control the consistency of product quality. Periodic monitoring is conducted regularly based on different products and test items, while batch testing is conducted before each batch of product processing and release to ensure that any product quality issues are promptly identified, intercepted, and corrected during the production process.

1-4-1 Product Performance Validation

Product performance validation refers to a series of tests and validations to check whether the product meets the predetermined performance parameter requirements and user usage needs. The results of the validation can be used to determine whether the product can enter the next stage of development or production. These validations include, but are not limited to:

- Application performance validation of finished products
- Biocompatibility testing of finished products
- Extractable and leachable substance testing of finished products
- Shelf life validation of finished products
- Transportation validation of finished products

1-4-2 Periodic Monitoring

Periodic monitoring of products refers to regular testing and evaluation of finished products to ensure that they continue to meet quality and performance requirements during use. This type of monitoring helps identify problems with the production process or quality testing process that have a moderate level of risk and take necessary measures for repair or replacement in a timely

manner. Periodic monitoring varies depending on the product type and purpose, including, but not limited to:

- Sterility testing
- Nuclease testing
- Endotoxin testing
- Insoluble particle testing

1-4-3 Batch Testing

Process inspection and batch release testing are important methods for product quality management, which can control the quality of semi-finished products and pre-released finished products, ensuring stability and consistency of product quality. The advantage of batch testing is the ability to detect problems as soon as possible throughout the entire process, thereby reducing production costs and improving product quality. These testing items include, but are not limited to, the following for semi-finished and finished products:

- Dimensional inspection
- Appearance inspection
- Semi-finished product application performance testing
- Component compatibility testing
- Random sampling of finished product application performance
- Packaging and boxing inspection

1-5 Electron Beam Sterilization and Sterility Assurance

Electron beam sterilization is an efficient sterilization method that has been widely used in industries such as medical devices, pharmaceuticals, and food. It has many advantages compared to gamma radiation sterilization, including lower maintenance costs, faster processing time, higher processing capacity, and no generation of radioactive waste or hazardous substances. The use of electron beam sterilization is a trend driven by policies and environmental requirements.

1-5-1 ISO 11137

NEST's electron beam sterilization process complies with the ISO11137 quality system, which adds a certification system for product sterilization on the basis of ISO13485. NEST's subsidiary, Futen, obtained the ISO certification authorized by TÜV SÜD, an authoritative institution accredited by the European Union, in 2020. The electron beam sterilization process of NEST products is validated and carried out by Futen, including the validation process of bioburden assessment, sterilization dose setting and loading method validation, sterile packaging validation, and sterility inspection.

After electron beam sterilization, NEST products can achieve a sterility assurance level (SAL) of 10^{-6}, ensuring the sterility of the parts in contact with liquids. The basis for electron beam sterilization includes the sterilization label on the product outer packaging, COA, COC, and irradiation process validation report. If you need to obtain the relevant test reports, please contact us.

1-5-2 Bioburden Assessment

Bioburden refers to the number and types of microorganisms present on the surface or object before sterilization. Its assessment is carried out to ensure an appropriate sterilization dose is applied to all microorganisms present on the product, effectively killing them. NEST's bioburden assessment method for products involves initial microbial contamination testing according to the relevant standard ISO 11737-1 and GB/T 19973.1-2015. In addition, NEST also controls the level of initial contaminants by periodically monitoring the cleanliness of the clean-rooms.

1-5-3 Sterilization Dose Setting and Loading Method Validation

After setting the minimum sterilization dose based on the initial contamination level, irradiation is performed during the actual production of the product according to the recommended optimal dose of ±10% as per ISO11137-2, and GB/T 19973.1-2015. The loading method for NEST products during sterilization is based on the characteristics of the internal structure of the product. Through operational qualification (OQ) testing, an optimized distribution of sterilization dose is achieved, ensuring a sterility assurance level (SAL) of 10^{-6} for NEST products.

1-5-4 Sterile Packaging Validation and Sterility Inspection

NEST performs sterile packaging validation on products that have undergone accelerated aging according to ASTM's packaging leakage standard test methods. Regular sterility inspections are conducted to provide additional validation of the electron beam sterilization process.

NEST's Biosafety Level 2 (BSL-2) sterility testing laboratory conducts sterility inspections of products according to the product testing specifications to ensure the safety and reliability of the production environment, as well as the effectiveness and reliability of the electron beam sterilization process, in order to produce final products that meet customer requirements.

1-6 Supply Chain Stability and Lead Time

To ensure the stability of the supply and timely delivery, NEST employs the following measures to manage the supply chain and lead time:

- Long-term supply contracts: NEST signs long-term supply contracts with customers to ensure stable supply over a certain period of time.
- Safety stock: To address unforeseen circumstances during production, the company maintains a certain quantity of safety stock.
- Timely scheduling: Based on customer orders and inventory status, NEST adjusts production plans promptly to ensure timely delivery.

1-7 Traceability

NEST maintains the following methods to trace the production and transportation processes of its products:

- Batch information: Information about each product batch is recorded through batch coding, which enables traceability of key process inspection data and test results. Customers can use this information to trace the production of the product.
- Production records: In NEST's production process, process inspection data is retained at each process step, including raw materials, injection molding, and other product processing techniques. This data can be used to trace the production of the product.
- Sample retention: Samples are retained for each batch of products, allowing customers to trace the production of the product.
- Transportation process inspection: In addition to the production process, NEST also conducts inspections of the transportation process to ensure that the products are not damaged or compromised in quality during transportation.

1-8 Shelf Life

NEST determines the shelf life of products by conducting accelerated aging tests in accordance with YY/T 0681.1-2018 or ASTM F1980. The start time for calculating the shelf life is the production period of the product, as indicated by the batch-numbered accompanying COA/COC of NEST products. The duration of the shelf life for general products can be found in the COA/COC and the official product technical documents on the website.

Unless otherwise specified, the general storage conditions for NEST consumable products include a relative humidity not exceeding 80%, an ambient temperature of 10-30℃, and a light-free environment. During transportation, precautions should be taken to prevent mechanical impact or contact with sharp objects, avoid exposure to sunlight and rain, ensure intact packaging, and prevent product contamination. Air transportation is not recommended.

Chapter 2 NEST High Efficiency Erlenmeyer Flask

2-1 Introduction

NEST high efficiency Erlenmeyer flask is upgraded and optimized on the basis of the NEST Erlenmeyer flask. It has a larger culture space and oxygen flow than Erlenmeyer flask, providing a new solution for the expansion of cell culture. Its bottom size has been optimized to accommodate more flasks in the same incubator. NEST high efficiency Erlenmeyer flasks are a safer alternative to glass Erlenmeyer flask. It can be used for preparation and storage of culture media, which is suitable for a variety of culture techniques, and is safer than glass culture flask when used in the shaker. These high efficiency Erlenmeyer flasks won't crack, break or chip during the busy and challenging daily routine of a lab. They are lightweight and easy to handle, making them a valuable component of a laboratory safety plan. NEST high efficiency Erlenmeyer flasks are made from high-quality polycarbonate (PC) and are trusted for its reliable low extractable profile in a variety of laboratory applications.

NEST chooses PC material because of its high transparency, which makes it an ideal culture flask. High efficiency Erlenmeyer flasks made of PC can be autoclaved, but repeated autoclaving may result in the loss of some mechanical strength. To ensure good sterility, disposable use is recommended.

NEST high efficiency Erlenmeyer flask is available in flat-bottomed and baffled specifications, and the baffled high efficiency flask once again increases the efficiency of gas exchange. The cap is made of PP material, and the cap type can be divided into sealed cap and vent cap. The membrane in the vent cap is PTFE material, which can effectively prevent microorganisms from entering.

The scale of the NEST high efficiency Erlenmeyer flask is clear and accurate, making it easy to observe the medium capacity. It is recommended that the volume of the medium should be

30-40% of the total volume of the Erlenmeyer flask during culture.

2-2 Product Line Overview of High Efficiency Erlenmeyer Flasks

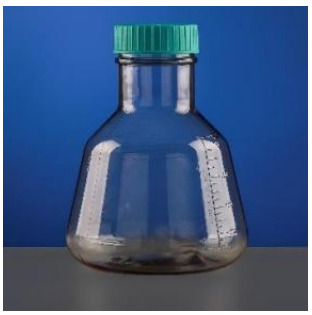
NEST high efficiency Erlenmeyer flask product line in this report includes the following different specifications:

- Specification I: Material (PC);
- Specification II: Volume (2L, 3L, 3L wide-mouth, 5L);
- Specification III: Cap type (sealed cap, vent cap);
- Specification IV: Flat bottom, baffled bottom;
- Closed system accessories: two-way liquid transfer cap, multi-functional liquid transfer cap, inverted liquid transfer cap;

Please refer to the appendix for specific product codes and specifications.

Product photo

High efficiency Erlenmeyer flask



2L (flat bottom)

2L (with baffle)

3L (flat bottom)

3L (with baffle)

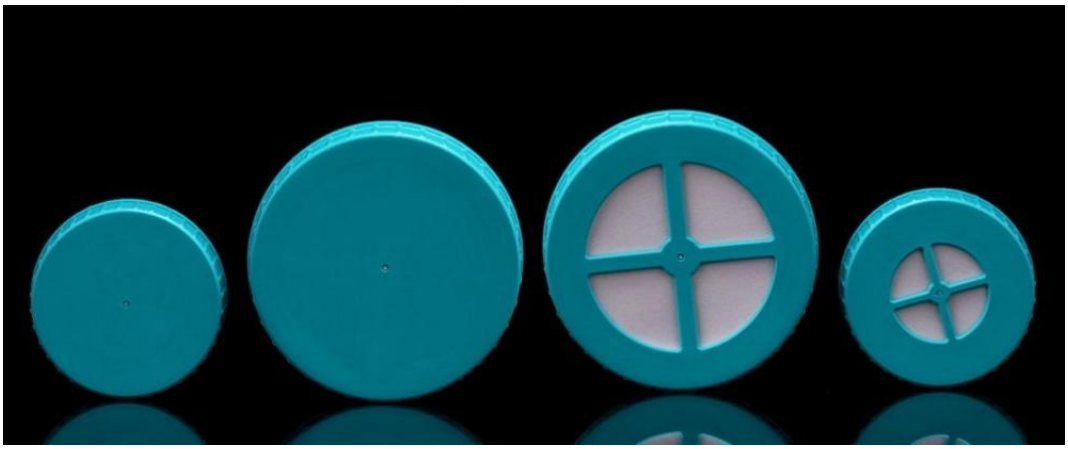
3L Wide-mouth (flat bottom)

3L Wide-mouth (with baffle)

5L (flat bottom)

5L (with baffle)

Cap



2L/3L high efficiency Erlenmeyer flask with sealed cap 786903

5L/3L wide-mouth Erlenmeyer flask with sealed cap 787903

5L/3L wide-mouth Erlenmeyer flask with vent cap 787913

2L/3L high efficiency Erlenmeyer flask with vent cap 786913

Closed system



From left to right:

Two-way liquid transfer cap (Customized)

Multi-functional liquid transfer cap

Inverted liquid transfer cap

2-3 Product Parameters

Product name	High efficiency Erlenmeyer flask
Material	Body: Polycarbonate (PC), USP Class VI compliant Cap: Polypropylene (PP), USP Class VI compliant Gas-permeable membrane: Polytetrafluoroethylene (PTFE), USP Class VI compliant
Dimensions	See appendix for details
Sterilization	Electron beam sterilization, sterility assurance level: SAL= 10^{-6}. This product has been irradiated and dose released in accordance with ANSI/AAMI/ISO 11137.
Shelf life	3 years from the date of production (assuming intact packaging)
Non-pyrogenic	Reference USP<85> and "Chinese Pharmacopoeia" endotoxin test method, endotoxin level <0.05 EU/mL.
Insoluble particles	Reference USP<788> and "Chinese Pharmacopoeia", insoluble particle test method, ≤ 25 particles/mL for particles ≥10μm, ≤ 3 particles/mL for particles ≥ 25μm.
DNase/RNase-free	Reference USP<1225><1130> and "Chinese Pharmacopoeia",

	nucleic acid enzyme test method, tested DNase/RNase-Free.
BSE/TSE/GMO	No animal-derived or genetically modified ingredients or tissues, no TSE/BSE/GMO risks.
Cell culture performance	CHO cells of logarithmic growth stage were taken and made into cell suspension with appropriate concentration. The cells were inoculated and cultured in a combined shock incubator at 37℃ and 5% carbon dioxide. The samples were counted and observed every 24 hours during 24-192h, and the proliferation multiple and cell morphology were normal, with uniform distribution and good growth.
Production environment and raw materials	Production in a class 100,000 clean environment, raw materials comply with USP Class VI standards.
Structural design features	◦ Integrated injection molded openings ensures good sealing performance and firmness. ◦ The expansion of the bottle neck and the large vent membrane make the gas exchange efficiency one step higher than that of Erlenmeyer flask, providing higher oxygen flux to the cultured cells. ◦ The bottom of the baffled flask can improve the efficiency of gas exchange again and increase the dissolved oxygen. ◦ The vent cap of the 0.22μm hydrophobic filter is used for contamination-free gas exchange. ◦ The scale is clear, accurate, easy to observe and add liquid. ◦ Match with sterile closed systems for more efficient and sterile liquid transfer. ◦ A variety of closed systems can be customized according to clients' requirements.

Process features	◦ One-step, or integrated injection-pulling-and-blowing process is applied. It does not contain any foreign ingredients or added chemicals, eliminating the risk of unknown leachables. One-piece molding improves mechanical strength. ◦ The inner surface has a uniform finish and is not easy to hang on the wall, which is suitable for large-scale culture of suspended cells. ◦ Passed the sealing pressure test to prevent leakage, suitable for peristaltic pump pressurization.
Packaging features	Traceable code on the packaging for product traceability. One-layer to three-layer packaging to ensure product cleanliness and adaptability to clean environment use.

2-4 Product Raw Materials and Packaging Information

◦ Body of high efficiency Erlenmeyer flask

PC - Finished product passed USP VI testing

◦ Main components

Vent cap 786913 787913

Sealed cap 786903 787903

PP - USP Class VI

PTFE - USP Class VI

◦ Product inner packaging

Multi-layer composite plastic: Compliant with the standards of USP<661>, QB/T 1571-1993 and YBB00132002-2015 "General Rules for Medicinal Composite Films and Bags"

Chapter 3 Product Testing

3-1 Product Testing Summary

Product Performance Verification Tests	Periodic Monitoring Tests	Batch Release Tests
Cell Culture and Evaporation Rate Test	Sterility Test	Sealing Test
Shelf Life Validation	Endotoxin Test	Appearance Inspection
Alkali Resistance and High Temperature High Pressure Test	Nuclease Test	Fitting Test of Cap and Bottle Mouth
Drop and Transport Test		Bottom Flatness and Wall Thickness Test
Biocompatibility Test		
Extractables and Leachables Test		
Initial Contaminant Test		

In addition to the test report attached to this chapter, please contact us for the originals of other test reports.

Product Performance Verification Tests

Cell Culture Testing: CHO suspension cells were cultured using high-efficiency Erlenmeyer flasks. During the culture process and after the end of the culture, samples were observed and counted under the microscope. The cells were in normal shape, in good growth state, with uniform growth and uniform distribution.

Evaporation Rate Test: The total weight was measured before cell culture, and the weight was measured to calculate the evaporation rate of the high-efficiency flask, and the test results were in line with the experimental requirements.

Shelf Life Verification: Verify that the samples meet the requirements for sealing and sterility after accelerated aging, confirming the validity of the packaged products. The experimental conditions were as follows: select a 5L high-efficiency Erlenmeyer flask that has undergone natural aging for 1 year. Accelerate aging and perform sterility and sealing tests. The results show that after aging, both sterility and sealing tests passed, and the packaged product can guarantee a 5-year shelf life.

Alkali Resistance, High Temperature and High Pressure Test: Verify that the sample is valid after being soaked in alkali solution and then subjected to high temperature and high pressure, in order to test the resistance of the sample to alkali and high temperature and high pressure. The experimental conditions were as follows: the flask made of PC material was immersed in a container containing 0.25mol/L sodium hydroxide solution (pH was about 13.4), placed for 4h, washed with pure water, and then placed in a high temperature and pressure container at 121 ℃ for 20min, repeated 10 times, to observe whether defects, deformation and melting occurred. The results show that the shaker made of PC material has good tolerance to 0.25mol/L sodium hydroxide solution and high temperature and pressure (this verification only applies to the sample used in this time).

Drop and Transportation Test: Performs long-distance transportation and drop tests on the packaged finished products using actual transportation methods. The products and packaging are not damaged during transportation, including during vibrations, handling, and drops.

Biocompatibility Test: Conducting USP Class VI verification of the product according to the relevant testing methods in ISO10993 and GB/T 16886.

Extractables Test: According to GB/T 14233.1-2008 and USP<665><1665> standards, heavy metal content (lead, tin, cadmium, chromium) and incandescent residue, dissolved matter (reducing substance, pH, UV absorbance, appearance) shall be detected, which shall not be higher than the standard detection line.

Initial Contaminant(Bioburden) Test: Conducting a bioburden assessment of the product and controlling the level of initial contaminants according to the relevant standards in ISO 11737-1 and GB/T 19973.1-2015.

Periodic Monitoring Tests

Sterility Check: After sterilization treatment of the packaged products, conduct sterility testing on the samples referencing ISO11737-2:2019, Chinese Pharmacopoeia(2020) and GB/T 19973:2-2018. The test samples show no microbial growth, and the positive and negative controls show no abnormalities.

Endotoxin Check: Test the endotoxin content of the samples referencing USP<85> and relevant methods in Chinese Pharmacopoeia(2020). The endotoxin content should be ≤ 0.05 EU/mL.

Nuclease Check: Use qPCR to amplify the extract from the cell culture bottles referencing USP<1225><1130> and relevant methods in Chinese Pharmacopoeia(2020). The samples should not detect Dnase and Rnase, under the condition that the positive and negative controls show no abnormalities.

Batch Release Tests

Tightness Performance Test: According to the inspection standard of the high efficiency Erlenmeyer flask, the cap is matched with the corresponding bottle body and the air tightness test is carried out to control the leakage phenomenon. The test condition is that after the high-efficiency Erlenmeyer flask is matched with the vent cap/sealed cap, it is inverted to test its tightness. See the test report for details about the test procedure.

Appearance Inspection: According to the high efficiency Erlenmeyer flask inspection standards, the appearance of the product is controlled by visual and point gauge measurement. The control points are black spot impurities, burrs, flash edges, bubbles, black spots/oil stains, etc. See Annex COA for specific control standards

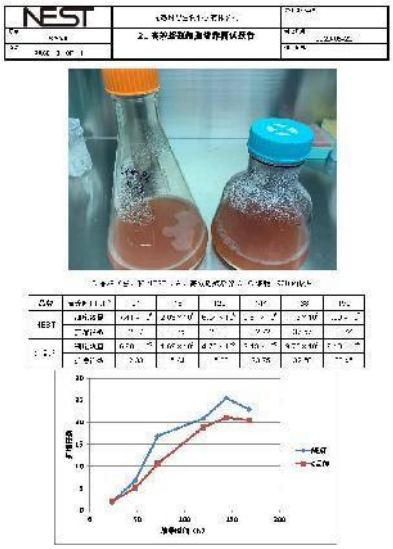
Fitting Test of Cap and Bottle Mouth: According to the inspection standard of the high

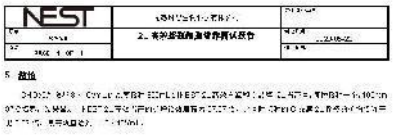
efficiency Erlenmeyer flask, test the good fit of the thread and the cap, control the phenomena of being too tight, loose or jammed, and control the product to meet the test requirements.

Bottom Flatness and Wall Thickness Test: According to the inspection standard of the high efficiency Erlenmeyer flask, the flatness and wall thickness of the bottom surface of the high efficiency Erlenmeyer flask are controlled by relevant instruments and methods. The high efficiency Erlenmeyer flask is placed on a horizontal table with a gradienter to test the flatness of the bottom surface, and the bottle is stable and does not shake, Test bottle wall thickness with wall thickness meter, record the minimum and maximum values, and the thinnest point measurement value cannot be lower than the value specified in the inspection standard of the Erlenmeyer flask.

The following reports are for demonstration purposes only. If you require the original reports, please contact a NestBio sales representative.

3-2 Cell Culture Test Report





3-3 Sealing Test Report

无锡前恩生命科技股份有限公司

5L 高效摇瓶适配性及密封性验证报告

测试项目：5L 高效摇瓶适配性及密封性验证报告

报告编号：CB-BG-202309058

测试开始时间：2023-09-15

测试结束时间：2023-09-15

制表人：张慧

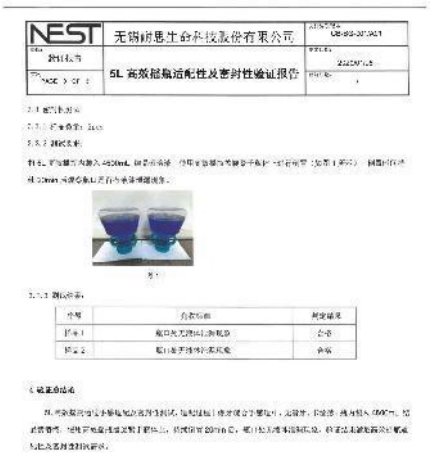
无锡前恩生命科技股份有限公司

5L 高效摇瓶适配性及密封性验证报告

1. 目的

2. 验证规格

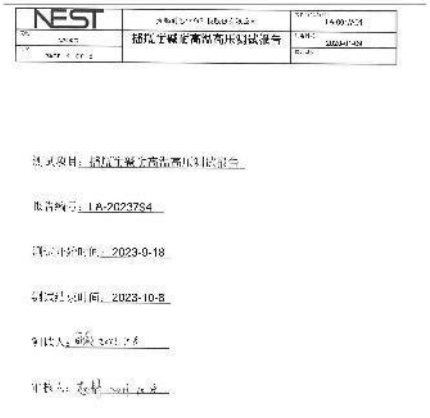
3. 测试

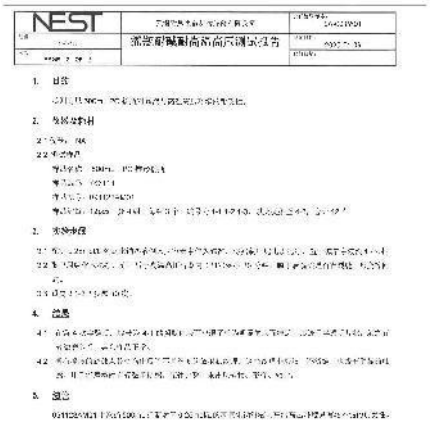


无锡前恩生命科技股份有限公司

5L 高效摇瓶适配性及密封性验证报告

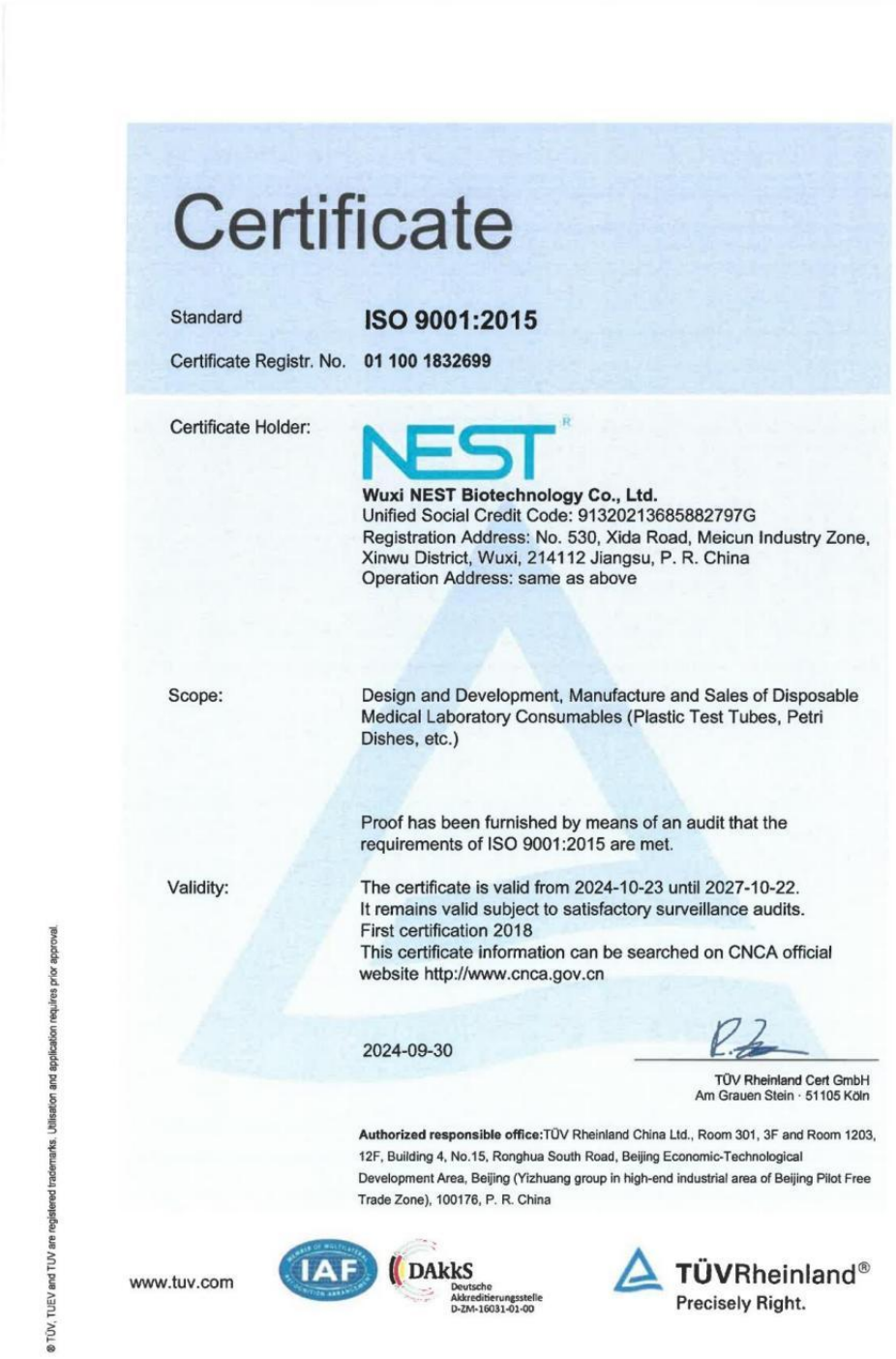
3-4 High Pressure and High Temperature Resistance Report





Annex I

Attachment-1 ISO9001



Certificate

Standard ISO 9001:2015

Certificate Registr. No. 01 100 1832699

Certificate Holder:

Wuxi NEST Biotechnology Co., Ltd.
Unified Social Credit Code: 91320213685882797G
Registration Address: No. 530, Xida Road, Meicun Industry Zone, Xinwu District, Wuxi, 214112 Jiangsu, P. R. China
Operation Address: same as above

Scope: Design and Development, Manufacture and Sales of Disposable Medical Laboratory Consumables (Plastic Test Tubes, Petri Dishes, etc.)

Proof has been furnished by means of an audit that the requirements of ISO 9001:2015 are met.

Validity: The certificate is valid from 2024-10-23 until 2027-10-22.
It remains valid subject to satisfactory surveillance audits.
First certification 2018
This certificate information can be searched on CNCA official website http://www.cnca.gov.cn

2024-09-30

TÜV Rheinland Cert GmbH
Am Grauen Stein · 51105 Köln

Authorized responsible office:TÜV Rheinland China Ltd., Room 301, 3F and Room 1203, 12F, Building 4, No.15, Ronghua South Road, Beijing Economic-Technological Development Area, Beijing (Yizhuang group in high-end industrial area of Beijing Pilot Free Trade Zone), 100176, P. R. China

www.tuv.com

DAkkS Deutsche Akkreditierungsstelle D-ZM-16031-01-00

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Attachment-2 ISO13485

TÜVRheinland®

Certificate

Quality Management System
EN ISO 13485:2016

Registration No.: SX 2181125-1

Organization: Wuxi NEST Biotechnology Co., Ltd.
No 530, Xida Road, New District,
Wuxi,
214112 Jiangsu
P.R. China

Scope: Design and Development, Manufacture and Distribution of Disposable Medical Laboratory Consumables, Disposable Nebulizers, Specimen Collection Swabs

The Certification Body of TÜV Rheinland LGA Products GmbH certifies that the organization has established and applies a quality management system for medical devices.
Proof has been furnished that the requirements specified in the abovementioned standard are fulfilled. The quality management system is subject to yearly surveillance.

Report No.: 244414889-200
Effective date: 2022-12-30
Expiry date: 2025-04-17
Issue date: 2022-12-30

TÜV Rheinland LGA Products GmbH Zertifizierstelle

DAkkS Deutsche Akkreditierungsstelle D-ZM-14169-01-02

Fuxiu Sheng
TÜV Rheinland LGA Products GmbH
Tillystraße 2 · 90431 Nürnberg · Germany

1 / 1

10/2020 d 04.08 ® TÜV, TUEV and TUV are registered trademarks. Utilisation and application requires prior approval.

Attachment-3 ISO13485、ISO11137

ZERTIFIKAT ◆ CERTIFICATE ◆ 認證證書 ◆ СЕРТИФИКАТ ◆ CERTIFICADO ◆ CERTIFICAT

DAkkS Deutsche Akkreditierungsstelle D-ZM-11321-01-00

TÜV SÜD Product Service

Certificate

No. Q8 089489 0003 Rev. 04

Holder of Certificate: **Wuxi Futeng Irradiation Technology co., LTD**
No.530, Xida Road, Meicun
Xinwu District
214112 Wuxi, Jiangsu
PEOPLE'S REPUBLIC OF CHINA

Facility(ies): **Wuxi Futeng Irradiation Technology co., LTD**
No.530, Xida Road, Meicun, Xinwu District, 214112 Wuxi, Jiangsu, PEOPLE'S REPUBLIC OF CHINA

See scope of certificate

Certification Mark:

TÜV SÜD EN ISO 13485 tuvsud.com/ps-cert

Scope of Certificate: **The provision of RHODOTRON EB Irradiation Sterilization Services for Medical Devices**

Applied Standard(s): ISO 13485:2016
(EN ISO 13485:2016/AC:2018, EN ISO 13485:2016/A11:2021)
Medical devices - Quality management systems - Requirements for regulatory purposes

The Certification Body of TÜV SÜD Product Service GmbH certifies that the company mentioned above has established and is maintaining a quality management system, which meets the requirements of the listed standard(s). All applicable requirements of the testing and certification regulation of TÜV SÜD Group have to be complied with. For details and certificate validity see: www.tuvsud.com/ps-cert?q=cert:Q8 089489 0003 Rev. 04

Report No.: SH2393501

Valid from: 2024-01-05
Valid until: 2027-01-04

Date, 2023-12-21

Christoph Dicks
Head of Certification/Notified Body

Page 1 of 1
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ZERTIFIKAT ◆ CERTIFICATE ◆ 認證證書 ◆ СЕРТИФИКАТ ◆ CERTIFICADO ◆ CERTIFICAT

Product Service

Supplement to Quality System Certificate

No. SUP 089489 0004 Rev. 03

This supplement is only valid in conjunction with the main certificate: **Q8 089489 0003 Rev. 04**

Certificate Holder:
Wuxi Futeng Irradiation Technology co., LTD
No.530, Xida Road, Meicun
Xinwu District
214112 Wuxi, Jiangsu
PEOPLE'S REPUBLIC OF CHINA

Facility(ies):
Wuxi Futeng Irradiation Technology co., LTD
No.530, Xida Road, Meicun, Xinwu District, 214112 Wuxi, Jiangsu, PEOPLE'S REPUBLIC OF CHINA

The quality system certified as stated in the main certificate additionally fulfills the applicable requirements of

EN ISO 11137-1:2015 + A2:2019 "Sterilization of health care products - Radiation - Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices (ISO 11137-1:2006/Amd 2:2018)"

Audit Report: SH2393501
Dated: 2023-10-10

The assessment was performed by auditors authorized under TÜV SÜD Product Service GmbH procedures. The audit team included an auditor authorized for sterilization.

Valid from: 2024-01-05

Christoph Dicks
Head of Certification/Notified Body

Page 1 of 1
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Attachment-4 CE: EU MDR

ZERTIFIKAT ◆ CERTIFICATE ◆ 認證證書 ◆ СЕРТИФИКАТ ◆ CERTIFICADO ◆ CERTIFICAT

Benannt durch Designated by
Zentralstelle der Länder für Gesundheitsschutz bei Arzneimitteln und Medizinprodukten
www.zlg.de
BS-MDR-099

TÜV SÜD Product Service

EU Quality Assurance Certificate (MDR)

Pursuant to Regulation (EU) 2017/745 on Medical Devices, Annex XI Part A
(Class I Devices in sterile condition, with measuring function or reusable surgical instruments)

No. G21 109429 0001 Rev. 00

Manufacturer:	**WUXI NEST BIOTECHNOLOGY CO., LTD** NO.530 XIDA Road New District 214000 Wuxi, Jiangsu PEOPLE'S REPUBLIC OF CHINA
SRN Manufacturer:	CN-MF-000002299
Authorized Representative:	SUNGO Europe B.V. Olympisch Stadion 24, 1076DE Amsterdam, THE NETHERLANDS

The Certification Body of TÜV SÜD Product Service GmbH certifies that the manufacturer has established, documented and implemented a quality management system as described in Article 10 (9) of the Regulation (EU) 2017/745 on medical devices. Details on device categories covered by the quality management system are described on the following page(s).
The Report referenced below summarises the result of the assessment and includes reference to relevant CS, harmonized standards and test reports. The conformity assessment has been carried out according to Annex XI Part A of this regulation with a positive result.
As applicable the involvement of the notified body is limited to the aspects relating to:
- establishing, securing and maintaining sterile conditions,
- conformity of the devices with the metrological requirements,
- reuse of the device, in particular cleaning, disinfection, sterilization, maintenance and functional testing and the related instructions for use.

The certified quality assurance system is subject to periodical surveillance by TÜV SÜD Product Service GmbH. All applicable requirements of the testing and certification regulation of TÜV SÜD Group have to be complied with.
For details and certificate validity see: www.tuvsud.com/ps-cert?q=cert:G21 109429 0001 Rev. 00

Report No.:	SH211724MDR01
Valid from:	2021-12-21
Valid until:	2026-12-20

Issue date: 2021-12-21

Christoph Dicks
Head of Certification/Notified Body

Page 1 of 2
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ZERTIFIKAT ◆ CERTIFICATE ◆ 認證證書 ◆ СЕРТИФИКАТ ◆ CERTIFICADO ◆ CERTIFICAT

Benannt durch Designated by
Zentralstelle der Länder für Gesundheitsschutz bei Arzneimitteln und Medizinprodukten
www.zlg.de
BS-MDR-099

Product Service

EU Quality Assurance Certificate (MDR)

Pursuant to Regulation (EU) 2017/745 on Medical Devices, Annex XI Part A
(Class I Devices in sterile condition, with measuring function or reusable surgical instruments)

No. G21 109429 0001 Rev. 00

Classification:	I
Device Group:	A020199 - SYRINGES, SINGLE-USE - OTHER A1101 - SAMPLE COLLECTION NEUTRAL SWABS
Device Properties:	MDS 1005.2 - Sterilisation by irradiation
The validity of this certificate depends on conditions and/or is limited to the following:	NA

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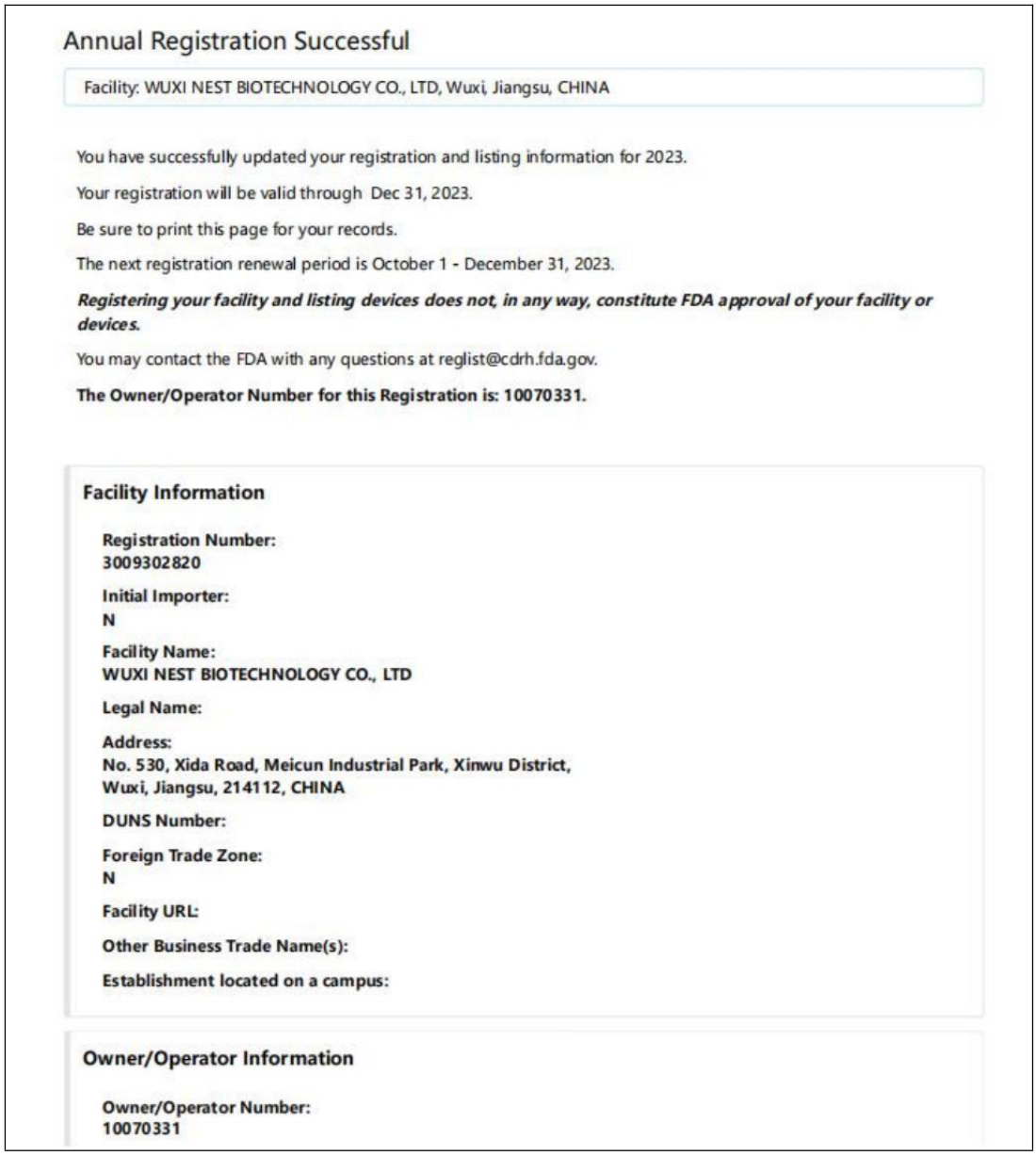
Attachment-5 FDA registration



Annual Registration Successful

Facility: WUXI NEST BIOTECHNOLOGY CO., LTD, Wuxi, Jiangsu, CHINA

You have successfully updated your registration and listing information for 2023.

Your registration will be valid through Dec 31, 2023.

Be sure to print this page for your records.

The next registration renewal period is October 1 - December 31, 2023.

Registering your facility and listing devices does not, in any way, constitute FDA approval of your facility or devices.

You may contact the FDA with any questions at reglist@cdrh.fda.gov.

The Owner/Operator Number for this Registration is: 10070331.

Facility Information

Registration Number:
3009302820

Initial Importer:
N

Facility Name:
WUXI NEST BIOTECHNOLOGY CO., LTD

Legal Name:

Address:
No. 530, Xida Road, Meicun Industrial Park, Xinwu District,
Wuxi, Jiangsu, 214112, CHINA

DUNS Number:

Foreign Trade Zone:
N

Facility URL:

Other Business Trade Name(s):

Establishment located on a campus:

Owner/Operator Information

Owner/Operator Number:
10070331

Attachment-6 Medical Device Manufacturing License

医疗器械生产许可证

许可证编号：苏药监械生产许20190045号

统一社会信用代码：91320213685882797G

企业名称：无锡耐思生命科技股份有限公司

法定代表人：杨卫东

住　　所：无锡市新吴区梅村工业园锡达路530号

企业负责人：杨卫东

生产地址：江苏省无锡市新吴区梅村工业园锡达路530号

生产范围：II类:08-05呼吸、麻醉、急救设备辅助装置，14-01注射、穿刺器械，22-11采样设备和器具

许可期限：自 2024 年 04 月 02 日

至 2029 年 04 月 01 日

发证部门：江苏省药品监督管理局

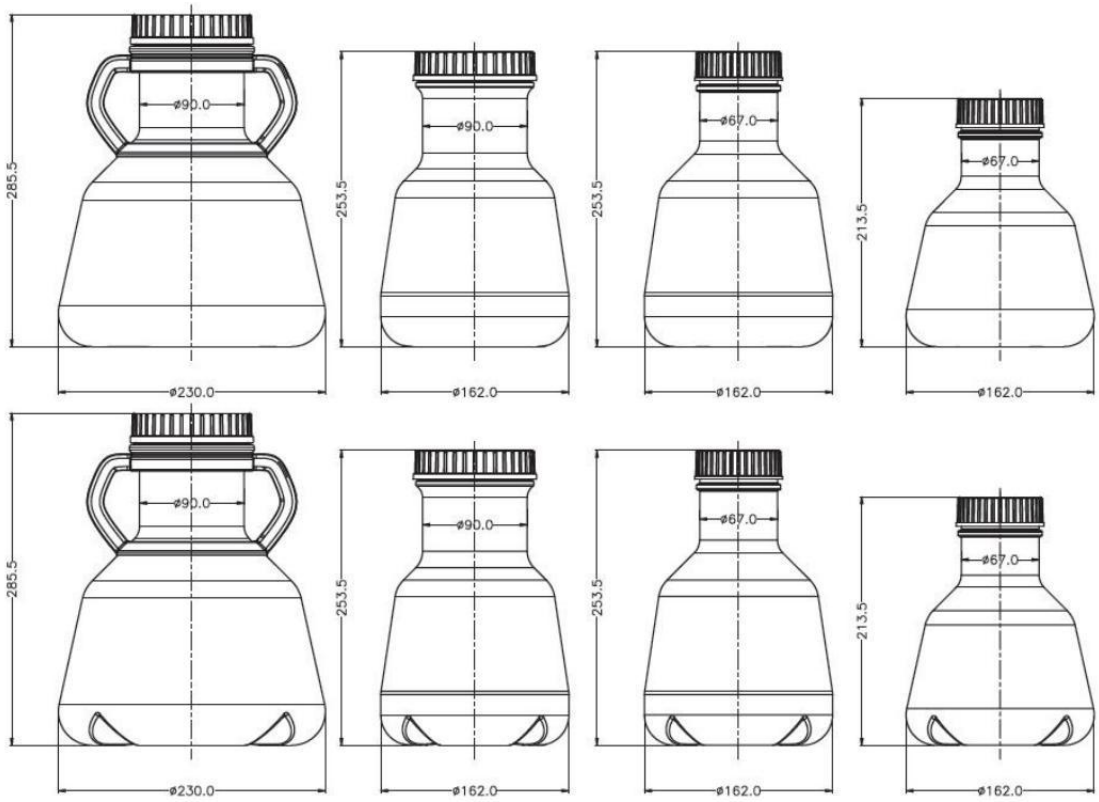
发证日期：2024 年 04 月 11 日

Attachment-7 Product code

Name	Code	Specificication
NEST high efficiency Erlenmeyer flask	785101	2L with sealed cap, flat bottom
NEST high efficiency Erlenmeyer flask	786101	3L with sealed cap, flat bottom
NEST high efficiency Erlenmeyer flask	786501	3L wide mouth with sealed cap, flat bottom
NEST high efficiency Erlenmeyer flask	787001	5L with sealed cap, flat bottom
NEST high efficiency Erlenmeyer flask	785111	2L with vent cap, flat bottom
NEST high efficiency Erlenmeyer flask	786111	3L with vent cap, flat bottom
NEST high efficiency Erlenmeyer flask	786511	3L wide mouth with vent cap, flat bottom
NEST high efficiency Erlenmeyer flask	787011	5L with vent cap, flat bottom
NEST high efficiency Erlenmeyer flask	785105	2L with sealed cap, baffled
NEST high efficiency Erlenmeyer flask	786105	3L with sealed cap, baffled
NEST high efficiency Erlenmeyer flask	786505	3L wide mouth with sealed cap, baffled
NEST high efficiency Erlenmeyer flask	787005	5L with sealed cap, baffled
NEST high efficiency Erlenmeyer flask	785115	2L with vent cap, baffled
NEST high efficiency Erlenmeyer flask	786115	3L with vent cap, baffled
NEST high efficiency Erlenmeyer flask	786515	3L wide mouth with vent cap, baffled
NEST high efficiency Erlenmeyer flask	787015	5L with vent cap, baffled
NEST high efficiency Erlenmeyer flask	786903	2L/3L flask with sealed cap
NEST high efficiency Erlenmeyer flask	786913	2L/3L flask with vent cap
NEST high efficiency Erlenmeyer flask	787903	5L/3Lhigh efficiency/wide mouth flask with sealed cap
NEST high efficiency Erlenmeyer flask	787913	5L/3Lhigh efficiency/wide mouth flask with vent cap

NEST high efficiency Erlenmeyer flask	Customized	Bi-directional Liquid Transfer Cap
NEST high efficiency Erlenmeyer flask	Customized	Multifunction Liquid Transfer Cap
NEST high efficiency Erlenmeyer flask	Customized	Inverted Liquid Transfer Cap

Attachment-8 Product drawings



Head Office Email : info@cell-nest.com
Online : www.cell-nest.com

Overseas NEST USA (New Jersey/Phoenix)
NEST scientific Co., Ltd. (Yokohama, Japan)
NEST Scientific Europe BV (Netherlands)
NEST Scientific (MENA) FZE (Sharjah, United Arab Emirates)

Attachment-9 COA certificate

Wuxi NEST Biotechnology Co., Ltd

Certificate of Analysis

Product Name	2 L, PC, Plug Seal Cap, Baffled	Product No.	785105	Lot No.	030422AP01
DOM	2022-03-04	Expiration Date		2025-02	

No.	Item	Inspection items/basis	Result
1	Appearance	Black spot impurities: Number of black spots ≤3, black spot area ≤ 0.2mm2。 Burr: Gate residue ≤0.5mm (bottle mouth, bottle bottom burr can not be scraped)。 Bubbles: Not allowed on the bottom and body of the bottle; A bottle can have one mouth, with an area ≤1mm2。 Bubbles: Thread area and sealing area are not accepted, other positions greater than 0.5mm are not accepted。 Flaring: Flaring at the cover is not acceptable, and flashing exceeding 0.2mm at other locations is not acceptable。 Black spots/oil stains: No more than 3 spots with an area less than 0.2mm2。	Pass
2	Size	Comforming to the blueprint	Pass
3	Sealing test	Inverted for 20 minutes, no water seepage	Pass
4	Packaging	Correct packaging materials and quantity; intact packaging	Pass
5	Sterilization	Red colored irrediration tag with Certificate of Irradiation	Pass
6	*Sterility testing	No microorganisms can be detected	Pass
7	*Endotoxin Detection	≤0.05EU/ml	Pass
8	*Cell culture test	The cells were evenly distributed and in good condition	Pass
9	*Rnase test	No Rnase detected	Pass
10	*Dnase test	No Dnase detected	Pass
Conclusion		Pass	

Note: Only Pass or No pass is applicable in filling in 'Result'.

Add: No. 530, Xida Road, Meicun Industrial Park, Xinwu District, Wuxi, Jiangsu, China	Tested by	Zhu yunxia	Approved by	He yun
Tel: (+86) 0510-88550090				
Fax: (+86) 0510-88550105	Date	2022-03-07	Date	2022-03-07
https://www.cell-nest.com				

Head Office Email : info@cell-nest.com
Online : www.cell-nest.com

Overseas NEST USA (New Jersey/Phoenix)
NEST scientific Co., Ltd. (Yokohama, Japan)
NEST Scientific Europe BV (Netherlands)
NEST Scientific (MENA) FZE (Sharjah, United Arab Emirates)