

密闭系统

CONTAINMENT SYSTEM

NOOZLE® 诺泽流体科技（上海）有限公司
TECHNOLOGY Noozle Fluid Technology (Shanghai) Co., Ltd.

地址：上海市松江工业区申港路3255号金地威新智造园4号楼

Add: Buiding4, No.3255, shenggang Road, songjiang District, Shanghai, 201611, P.R.China

Tel: +86-21-5408 3398 Fax: +86-21-6458 9896

Web: www.noozle.com.cn E-mail: noozle@noozle.com.cn



NOOZLE®
TECHNOLOGY

密闭的定义

WHAT IS CONTAINMENT?

○ 密闭的含义 What does Containment mean?

简而言之，是对有害物质的密封处理。主要避免两种情况的发生，避免有害物质从工作场所溢出以保护操作人员，避免产品被环境中的杂质污染。

一级密闭：防止活性物质泄露到工作环境中或生产设备中的一种防护系统。包括连续套袋系统、手套箱或蝶阀。

二级密闭：密闭系统用来减少向一级密封舱的扩散风险。比如传递窗，传递门锁和压力梯度。

Literally, it is about the encapsulation of hazardous materials. The escape of hazardous substances from the workplace (operator protection) or the contamination of a product by impurities in the environment (product protection) has to be avoided.

Primary Containment: A Containment System that avoids the escape of critical dusts or substances into the immediate working environment or the production equipment. This includes endless-liner-systems, glove boxes or butterfly valves.

Secondary Containment: A Containment system that is deployed in order to reduce any kind of spreading of expansion subsequent to the Primary Containment. This includes for example clean rooms, locks or pressure stages.

○ 封闭系统 Closed Systems

密闭应用主要在封闭系统内操作。

根据《有害物质条例》第 10 条，封闭系统是专门用于与有害物质有关的机器和设备。

作为一个基本的先决条件，环境与系统内部不能有任何的开放连接。在任何情况下都必须避免材料泄漏，同时也易于清洁和维护。因此，完整的除尘系统也属于密闭系统的基本装置。所以，在使用无尘系统时，防爆区域可以降低等级要求或完全省去。

所涉及的交互界面是特别重要的，例如取样、填充、卸料或计量。从操作人员的角度看，操作应尽可能简单，操作员的错误不应直接导致污染。

Containment applications are mainly performed within closed systems.

Closed systems are machinery and plants particularly used in connection with hazardous substances according to § 10 of the Ordinance on Hazardous Substances.

As a basic prerequisite, there must not be any open connection between the environment and the inside of the system. Leakage of material must be avoided in any case. This also applies to cleaning or maintenance. Thus, integrated dedusting systems also belong to the basic equipment of containment systems. When using dust-free systems, the Ex-zone can additionally be downgraded or may be omitted completely.

Interfaces involved e.g. when sampling, filling, discharging or metering are particularly critical. With a view to the operator, the handling should be as easy as possible, and an operator error should not automatically result in contamination.



密闭系统分级

CLASSIFICATION OF CONTAINMENT SYSTEMS

并非所有的散装固体具有相同的危险性或致敏性，因此，根据其应用和使用领域，密闭系统系统分为不同的“类别”。另外，客户或相关权威机构确定产品的特定限值。该分类的目的是为产品选择合适的生产设备或“正确的”工作流程。在实践中，对以下分类或限值进行了区分：

OEL (职业接触限值) 是指在规定的时段内测得的工作场所空气中某种物质浓度的平均负荷，以确保不会对员工的健康造成急性或慢性危害。它是根据 ADE (可接受的每日暴露量) 和其他一些值计算得出的。

OEB (职业暴露等级) 仅考虑纯物质的毒理学。产品毒性越大，OEB 越高。

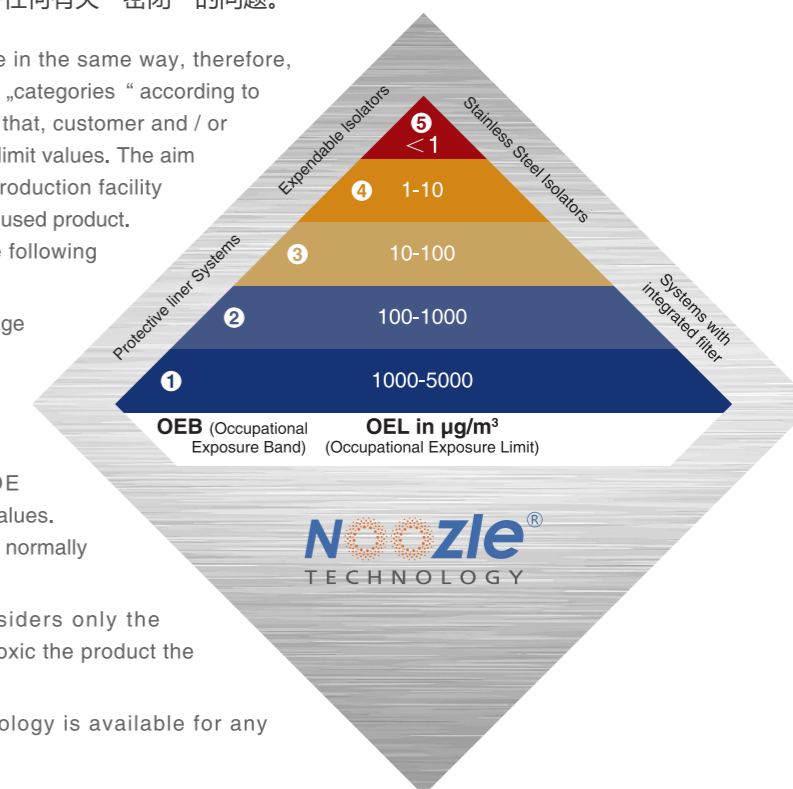
作为您的合格合作伙伴，诺泽科技可以回答任何有关“密闭”的问题。

Not all bulk solids are dangerous or sensitive in the same way, therefore, Containment systems are divided into different „categories “ according to their application and field of use. Considering that, customer and / or legislative authority determine product specific limit values. The aim of this classification is to select the suitable production facility respectively the „right “ working process for the used product. In practice, a distinction is made between the following classifications or limit values:

OEL (Occupational Exposure Limit) is the average load of concentration of a substance in the air at the workstation measured over a defined time period so that no acute or chronic harms to the health of the employee is expected. It is calculated out of the ADE (Acceptable Daily Exposure) and some other values. Are not all values known for the calculation you normally use a classification.

OEB (Occupational Exposure Band) considers only the toxicology of the pure substance. The more toxic the product the more higher will be the OEB.

As your competent partner, Noozle Technology is available for any questions about “Containment “.



操作人员防护：保护操作者免受有害物质的伤害。

产品防护：保护产品免受杂质和交叉污染。

因此，这取决于是对产品保护还是操作人员保护，亦或与两者相关的具体要求。但均可以通过封闭系统的使用实现。

Operator protection means the protection of the operator against hazardous products.

Product protection means the protection of the product against impurities and cross-contamination in particular.

So it depends on the point of view whether product protection, operator protection or both of them are relevant. What they have in common is the approach to achieve them: the use of closed systems.

工程设计 ENGINEERING

○ 密闭系统的规划 Planning of Containment Systems

用于制药环境的生产工厂规划时，需要精确地确定需要达到的密闭限定值，以便确定一级或二级密闭系统。此时应主要关注一级密闭系统，而二级密闭系统应该作为一个补充的安全措施。

OEB 值或 OEL 数值对密闭系统的选型有重要影响。为确定该数值，必须使用特殊的测量装置进行准确的风险分析，然后在有关认证的实验室进行分析评估。

客户物料的生产量和产品转换频率是决定单一多功能系统或机械自动化水平的关键因素。需要完全遵守所有当前的标准和准则。此外，操作员执行的所有过程交互界面和操作都是重要的方面，应仔细考虑，还需要对产品的流动性和特性进行评估。根据产品的不同，还必须保证防爆要求。

密闭系统的规划必须从内到外进行，并且需要对各自的过程及其注意点有充分的了解。这些技术难点就广泛存在于加药系统、各个阀门或排气系统和过滤器装置中。

为了避免交叉污染，产品污染和产品扩散风险，设备的清洁能力尤为重要。在这种情况下，建议使用带有 WIP，CIP 或 DIP 清洗功能的辅助系统，但是需要事先评估清洗过程。后添加的功能，安装起来总是带来不必要的高成本。

另一关键点是密闭系统的维护和保养。根据系统类型的不同，在成功执行清洗后，有必要打开设备单元。系统必须进行定期监测和维护。通过润湿表面，可以避免粉尘的排放和泄漏。

Long before planning a Containment production plant that is used in a pharmaceutical environment the threshold values of the Containment to be achieved need to be defined very precisely in order to determine either a primary or a secondary Containment System. At this point the main focus should be on a primary Containment, whereas the secondary should function as a supplementary security measure.

OEB-values or **OEL-levels** have a significant influence on the selected Containment System. To define this value an accurate risk analysis with special measuring devices is necessary, followed by an analytical evaluation in a certified laboratory.

The production quantities processed by the customer as well as the product changeover frequency are crucial factors for the decision on a **mono- or multifunctional system** or the automation level of the machinery. Another essential point is the full compliance with all current standards and guidelines. Furthermore, all process interfaces and actions performed by the operator are important aspects that should be considered carefully. In addition, the fluidity and characteristics of the product have to be evaluated. Depending on the product, explosion protection must be guaranteed.

Planning of the system has to be performed from the inside to the outside and requires extensive knowledge of the respective processes and their weak points. These can be found, for instance, in dosing systems, valves or within the exhaust air system and filter units.

In order to avoid cross-contamination, product contamination and product spreading, an optimum cleaning capability of the machinery is of particular importance. In this case supplementary systems with **WIP-, CIP- or DIP-cleaning methods** are recommended but of course the process needs to be evaluated in advance. A subsequent installation always involves unnecessary high costs.

One more crucial point is maintenance and servicing of the Containment System. Depending on the kind of system, an opening of the processing unit will be necessary but can only be performed after a successful cleaning. A regular monitoring and maintenance are mandatory. By wetting the surfaces, dust emission and leakage can be avoided.

要求 REQUIREMENTS

○ 系统需求 System Requirements

通常，采用密封系统是为了避免粉尘和其他活性物质污染环境。密闭系统的需求取决于产品本身特性，并且必须为每个新项目重新规定要求。

密闭等级可以根据诺泽自身的金字塔等级来划分。具体可以分为几大类，比如 OEB(职业暴露等级)和 OEL(职业接触限值)或 TOX (毒性值)。产品的毒性值是指每单位空气中允许存在的颗粒数量。在对您的产品进行分类后，诺泽科技将提供适当的解决方案(取决于您的需求)。系统的设计必须以各自满足规定要求为重点。基本的卫生设计方法应该包括无死角设计、封闭的系统或易于清洁的。

Generally, Containment systems are applied in order to avoid contamination of the environment by dust and other critical substances. The systems requirements depend on the products and have to be repeatedly defined for each new project.

Containment levels can be classified with our Noozle pyramid. It shows several classification levels: **OEB (Occupational Exposure Band)** and **OEL (Occupational Exposure Limit)** or **TOX (Toxicity)**. The classification refers to the toxicity of the products and permits to determine the amount of particles per air quantity. Having classified your product, Noozle Technology offers the appropriate solution (depending on you requirements). Systems then have to be designed with focus on the respective meet the specification level. Basic hygienic design approaches include dead space free design, closed systems or easy accessibility for cleaning .

○ 系统的确认 System Qualification

密闭系统密封性应该在客户的充分使用中得到确认和验证。为了使这一程序标准化，ISPE 在 2004 年发布了一个良好实践指南“评估制药设备中的微粒控制性能 (APCPPE)”即 SMEPAC。同时，本文件已被确立为密闭系统的检测标准。

新的 ISPE 密闭系统手册也可以作为支持文件。诺泽科技的密闭系统也根据 SMEPAC 标准来检测。我们的套袋连接组合系统，比如集装袋或其他套袋，允许达到小于 $1\mu\text{g}/\text{m}^3$ 的 OEL (职业接触限值)。

Containment systems should be qualified and validated with respect to their tightness and their adequate use in the company. In order to standardize this procedure, the ISPE issued a Good Practice Guide "Assessing the Particulate Containment Performance of Pharmaceutical Equipment " (APCPPE), better known as SMEPAC, in the year 2004. In the mean time, this document has been established as the standard for measurements of containment systems.

Also the new ISPE containment manual can be a support. Noozle Technology containment systems have also been measured according to SMEPAC. Our liner connection system for FIBCs or pouches, for example, permits to reach an OEL (Occupational Exposure Limit) of smaller than $1\mu\text{g}/\text{m}^3$.

一次性技术

SINGLE USE TECHNOLOGY

防护型软舱隔离器 Safe-Flex Isolator

○ 密闭系统的柔性解决方案

The flexible solution for contained processes

在防护型软舱隔离器的开发过程中，诺泽科技密闭隔离解决方案优先考虑易操作性、高劳动安全性和通用性。

我们的隔离器是概念化的，定制的，适用于微粉化、分料，取样和进料过程以及各种特殊应用。Safe-Flex 薄膜材料提供安全保护，具有高抗撕裂性和最佳性能，便于手动工具操作。生产完毕后，隔离器闭合，易于清洁处理。因此，清洁和验证工作减少了一倍。

Noozle Technology Containment Solutions has set priority during development of the Safe-Flex isolator on easy handling, high labor safety and universal in use.

Our isolators are conceptualized, custom made and are suitable for Micronizing, dispensing, sampling and feed processes as well as special applications. The Safe-Flex film-material offers a safe protection with high tear resistance and optimum properties for manual handling with tools. After the process, the isolator is closed and can be easily disposed. The cleaning and validation effort is thus reduced by a multiple.

安全性 Safety

- ▶ 薄膜保护用于一级密闭
- ▶ 正负压对操作员和产品的保护
- ▶ 对每一个软膜隔离器泄漏测试，保证安全
- ▶ 高密封等级 OEL：高达 $1\mu\text{g}/\text{m}^3$ (OEB5)
- ▶ 无交叉污染
- ▶ Primary Containment due to protective foil
- ▶ Operator and product protection due to negative and positive pressure
- ▶ Leakage test for every foil isolator
- ▶ High Containment-OEL: up to $1\mu\text{g}/\text{m}^3$ (OEB5)
- ▶ No cross-contamination

经济性 Cost Effective

- ▶ 投资和维护成本低
- ▶ 极低的清洁和验证成本
- ▶ 缩短更换时间
- ▶ Low investment and maintenance costs
- ▶ Hardly and costs for cleaning and validation
- ▶ Short changeover time

灵活性 Flexibility

- ▶ 适用于不同类型的箱体和应用场合
- ▶ 过程控制可适应 OEL 数值要求
- ▶ 可移动和灵活的位置
- ▶ 一次性使用技术，快速更换配件
- ▶ 可使用带套袋的不同料仓
- ▶ 一个框架内可单独设计各种独立的软舱隔离器
- ▶ Adaptable to different kinds of bins and applications
- ▶ Process control can be adapted to OEL-requirements
- ▶ Mobile and location-independent
- ▶ Quick product change due to single-use technology, short setup times
- ▶ Different bins with liners useable
- ▶ Various foil isolators within one frame individually designable



一次性技术

SINGLE USE TECHNOLOGY

连续套袋系统

Continuous Liner System

为了人员的安全和产品的保护，连续套袋的使用是非常有效和普遍的。

For the safety of the personnel and the protection of the product, the use of continuous liner is very effective and popular.

优势 The advantages

- ▶ 高产和人员保护
- ▶ 易于操作
- ▶ 根据客户规范提供薄膜材料
- ▶ 可选范围内，每个装置最多可到 80 米
- ▶ High product and personnel protection
- ▶ Easy handling
- ▶ Film material supplied to customer specifications
- ▶ Optionally, up to 80 meters per unit

应用范围 Application areas

- ▶ 洁净室和隔离器的应用
 - 基本中型包装
 - 废料站
 - 产品转移
 - 取样
- ▶ 分装装备
- ▶ 原料药的装卸（高活性原料药成分）
- ▶ 毒性和高反应性产品
- ▶ Isolator and cleanroom applications
 - Primarily medium pack
 - Waste-port
 - Product transfer
 - Sampling
- ▶ Filling facilities
- ▶ Discharging of API (Active Pharmaceutical Ingredients)
- ▶ toxic and highly reactive products

○ 小批量物料转移 Transfer of small quantities

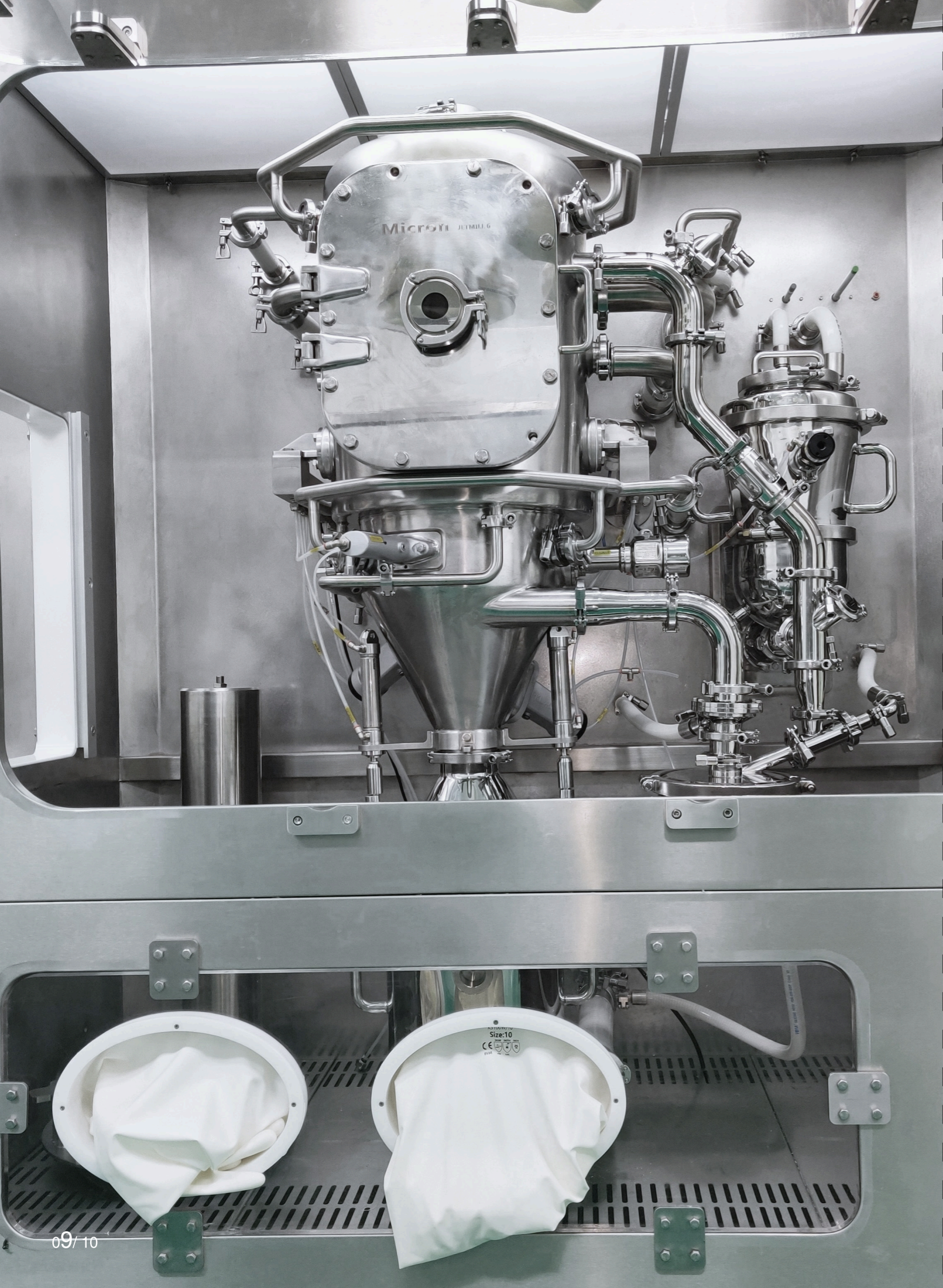
诺泽科技转运袋能满足制药和生物技术部门的高要求，也适用于小批量的物料转移。根据不同的应用，可选择最佳的连接功能和大小不同的转运袋。

标准版本的转运袋是用永久性防静电膜制成，如果需要，也可以在洁净室用客户特定的薄膜材料制造转运袋。

The Noozle Technology Transfer Bags meet the high requirements in the pharmaceutical and biotech sector and are responsible for the product transfer of small quantities. Depending on the application, the optimal connectivity and size of the Transfer Bags is selected.

Standard versions are available in a permanent antistatic film and, if desired, the bags can also be manufactured in a clean room from a customer-specific film-material.





不锈钢结构隔离器 STAINLESS STEEL ISOLATOR

无菌工艺过程生产型隔离器 Transfer of small quantities

诺泽科技的隔离器采用双层壁的结构来作为无菌工艺（微粉化、卸料和分装）的外壳。通过在操作人员和产品之间安装隔离屏障来实现人员和产品的保护。高效过滤器的提供的 A 级单向气流能有效防止颗粒涡流。产品和材料通过转运系统进出隔离器。

所有的安全和 GMP 相关功能都能始终处于地监控状态并以电子方式存档。在生产过程开始之前，隔离器用 VHP 消毒。

多种形式的空气处理方式：来自于独立的洁净室 / 进入洁净室的工艺空气供应、来自技术层或外部空调的预处理空气—诺泽科技涵盖了所有这些要求形式。

Nozzle Technology isolators double wall design serve as an enclosure for aseptic processes (Micronizing, discharging and filling). Product protection is achieved by a barrier (manipulation unit and plenum) which separates the operator and the product. HEPA filtered unidirectional air flow provides Grade A conditions preventing particle swirl. Products and materials are transferred into and out of an isolator via transfer systems.

All safety and GMP relevant functions are permanently monitored and archived electronically. Before the production process commences, the isolator is decontaminated with VHP system.

Various possibilities are available for the air treatment: independent of process air supply from the clean room/into the clean room, preconditioned air handling from the technical floor or external air conditioning -NOOZLE Technology covers all these variants.

无菌高毒性工艺过程生产型隔离器 Production isolators for aseptic toxic process

诺泽科技的单壁设计的隔离器可作为无菌 / 有毒工艺（微粉化、卸料和分装）的外壳。通过在操作人员和产品之间安装隔离屏障来实现人员和产品的保护。回风管可以实现自动清洗（CIP），清洁工作区通过自动或手动（WIP）清洗。

高效过滤器的提供的 A 级单向气流能有效防止颗粒涡流。产品和材料通过转运系统进出隔离器。

所有的安全和 GMP 相关功能都能始终处于地监控状态并以电子方式存档。在生产过程开始之前，隔离器用 VHP 消毒。

Nozzle Technology isolators in single wall design serve as an enclosure for aseptic/toxic processes (Micronizing, discharging and filling). Personnel and product protection is achieved by installing a barrier between the operator and the product. The return air ducts are cleaned automatically (CIP). The work area is cleaned automatically or manually (WIP).

HEPA filtered unidirectional air flow provides Grade A conditions preventing particle swirl. Products and materials are transferred into and or out of an isolator via transfer systems.

All safety and GMP relevant functions are permanently monitored and archived electronically. Before the production process commences, the isolator is decontaminated with VHP system.

不锈钢结构隔离器 STAINLESS STEEL ISOLATOR

高活性原料药粉体工艺过程生产型隔离器 Production isolators for HPAPI powder process

诺泽科技的单壁设计的隔离器可作为高活性原料药 / 有毒产品工艺（微粉化、排放和填充）的外壳。通过在操作员和产品之间安装隔离屏障来实现人员和环境的保护。回风管可以实现自动清洗（CIP），清洁工作区通过自动或手动（WIP）清洗。

产品和材料通过转运系统进出隔离器。

所有的安全和 GMP 要求的相关功能都能始终处于监控状态并以电子方式存档。

在微粉化工艺开始之前，对隔离器进行自动泄漏测试。

Noozle Technology isolators in single wall design serve as an enclosure HPAPIs / toxic processes (Micronizing, discharging and filling). Employees and environment protection is achieved by installing a barrier between the operator and the product. The return air ducts are cleaned automatically (CIP). The work area is cleaned automatically or manually (WIP).

Products and materials are transferred into and or out of an isolator via transfer systems.

All safety and GMP relevant functions are permanently monitored and archived electronically.

Before the micronizing process begins, automatic leak test of the isolator is performed.



VHP消毒系统 H₂O₂ decontamination system (VHP)

特殊设计专门用于隔离器的消毒系统
Designed specifically for decontamination of isolators

- ▶ 每个 VHP 系统包括汽化单元和 H₂O₂ 供应单元，以及通风管道、管路和控制系统
 - ▶ VHP 系统利用压缩空气作为蒸发 H₂O₂ 的载体空气
 - ▶ 隔离器短的除湿期
 - ▶ 系统内没有残留物
 - ▶ 每个循环前的综合泄漏测试
 - ▶ 维修费用低
- ▶ Each VHP system comprises of the vaporizing unit and the H₂O₂ supply unit with ductwork, tubing and control
 - ▶ The VHP system utilizes compressed air as the carrier air of the vaporized H₂O₂
 - ▶ Short dehumidification phase of the isolators
 - ▶ No residues inside the system
 - ▶ Integrated leak test before each cycle
 - ▶ Low maintenance



手套检漏测试仪 Glove Testing Systems

手套测试系统，用于自动测试手套的密封性。
Glove testing systems for automatically testing whether gloves are leak-tight.

- ▶ 移动的或集成的
- ▶ 易于操作
- ▶ Mobile or integrated.
- ▶ Easy to operate.

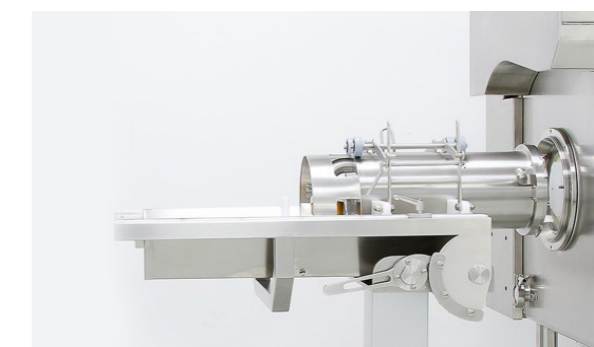
无菌/高毒性转运系统 Sterile/Toxic Transfer Systems

转运系统提供了在不破坏密封情况下将物料移入隔离器或无菌区的方法。

诺泽科技为制药生产提供了完整的解决方案。

The transfer system provides the means to move material in and out of an isolator or sterile zone without breaking containment.

Noozle Technogy provides a complete range of solutions for pharmaceutical production.



分体蝶阀(α-β 阀) Split Butterfly Valve(α-β Valve)

无菌应用，即可满足 A/B 级洁净要求，也可满足 C/D 级洁净环境应用要求。

高密闭应用，最高可满足 OEL<0.1μg/m³ 的密闭应用要求。

Aseptic application, it can meet the requirements of Grade A/B and Grade C/D also.

Containment applications, which can meet the requirements up to OEL<0.1μg/m³.



验证 Verification

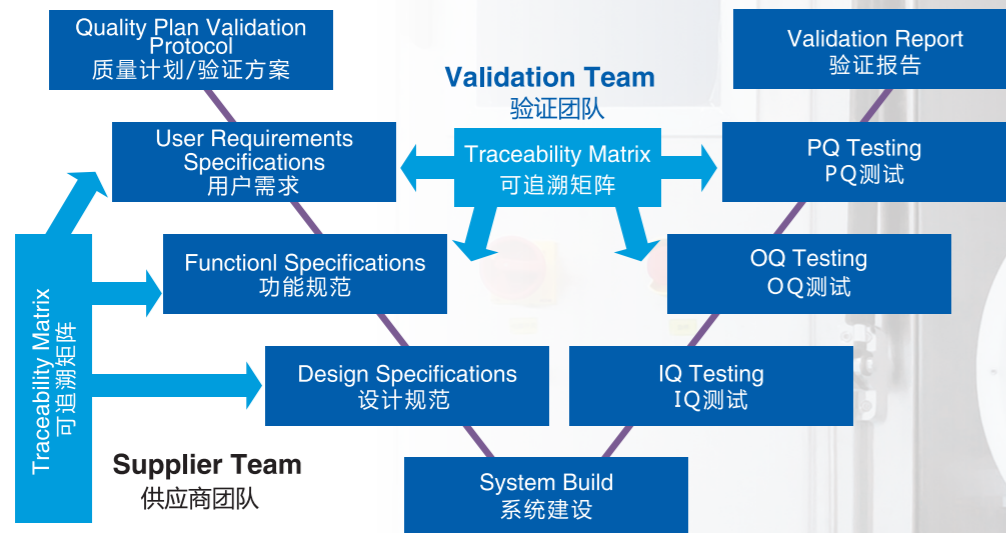
诺泽科技验证团队将会为定制的设备提供验证服务。公司为测试用仪器建立了设备管理系统，以确保测试的正确性及时效性。

The Noozle Technology qualification team provides qualification services for Noozle Technology equipment. Noozle Technology has its own equipment management system for the testing instruments, to ensure that they are always available without delay.

确认活动将基于国际标准执行：

The qualification is based on international standards and cutting-edge scientific research:

- ◎ 良好的自动化生产指南 第五版 ◎ GAMP standards
- ◎ 良好的生产制造管理规范 ◎ GMP
- ◎ 诺泽标准操作规程 ◎ Noozle Technology SOP' s
- ◎ 客户的需求 ◎ Customer requirements
- ◎ 文件可满足客户的要求 ◎ Documentation can be adapted to meet customer requirements



诺泽卓越技术中心 Noozle excellent Technical Center

测试与试验 Tests and Trials

诺泽卓越技术中心为各种类的粉体物料提供了理想的测试环境。可以为快速灵活的解决方案提供经济有效的测试。

The Noozle Excellent Technical Center offers the perfect environment for any kind of bulk handling system. We ensure cost-effective, practical trials and product testing for fast and flexible process solutions.

○ 我们可以提供以下测试和试验

In particular we offer testing and trials for

- | | |
|-----------|----------------------------|
| ▶ 微粉化 | ▶ Micronizing |
| ▶ 卸料 | ▶ Discharging |
| ▶ 分装 | ▶ Filling |
| ▶ 输送 | ▶ Conveying |
| ▶ 计量 / 称重 | ▶ Dosing / Weighing |
| ▶ 密闭应用 | ▶ Containment Applications |
| ▶ 清洗 | ▶ CIP/WIP Cleaning CIP/WIP |

访问诺泽卓越技术中心，可以找到更多的关于人体工程学和系统处理方面的信息！

Give it a try and find out more about the ergonomics and handling of our systems by visiting our Noozle excellent Technical Center!