OUR GLOBAL VISION, YOUR EMPOWERMENT

ZHOLION 众林

可见异物标准物质

VISIBLE PARTICULATES FOR INJECTABLE DRUGS

人员培训
OPERATORS TRAINING

建立缺陷样品库
SET-UP A DEFECT LIBRARY

KNAPP人机比对
KNAPP HUMAN-MACHINE COMPARISON

灯检机验证
VERIFICATION OF LIGHT INSPECTION MACHINE

可见异物定义

WHAT IS VISIBLE PARTICULATES?

中国药典2025版第四部-0904可见异物检查法中规定：可见异物系指存在于注射剂、眼用液体制剂和无菌原料药中，在规定条件下目视可以观测到的不溶性物质，其粒径或长度通常大于50μm。

Visible particulates refer to insoluble substances present in injections, ophthalmic liquid drugs and sterile raw materials that can be visually observed under specified conditions, and their particle size or length is usually greater than 50μm.

众林定制可见异物
OPTIONAL VISIBLE PARTICULATES

国际监管合规 COMPLIANCE

FDA、EMA、WHO、PIC/S、NMPA（CDE）

国际化市场验证 MARKETING PROVEN

药明、恒瑞等多家中国头部出海客户信赖。

Cooperation with top global clients, such as Apptech, Hengrui Pharma.

支持按需定制 CUSTOMIZATION

多维度标准选择，覆盖客户定制需求。

Wide ranges of options to meet your demands.

缺陷类型 DEFECT TYPE	玻璃屑、金属屑、纤维、黑点、白点、毛发、橡胶屑、白色塑料、色点、块状物、微细可见异物、液体装量差异、瓶身裂痕、铝盖缺陷、瓶身缺陷及其他定制缺陷品。 Glass, metal, fibers, black specks, white specks, hair, rubber particles, white plastic, colored specks, clumps, sub-visible particles, fill volume variation, glass crack, aluminum seal defect, and other customized defects.
粒径 Partical Size	50um-2000um
颗粒数 Qty	1-3、5-10、≥10
规格 Volume	1mL、2mL、5mL、20mL
介质 Liquid Carrier	水、药液 Water, Liquid of drugs
包装 Packaging Type	安瓿瓶、西林瓶、卡式瓶、预充针等 Ampoules, vials, cartridges, PFS, and others

建立可见异物标准物质的必要性

WHY VISIBLE PARTICULATES ARE IMPORTANT?

美国药典1790章节 USP 1790

7.5这些可见异物标准物质应组成样品缺陷库，用于挑战人工检验员的可见异物检测技术，及人员资质确认，或在自动化设备确认与验证期间用于比对。如有可能，缺陷库应按每种可见异物的类型和尺寸准备双份，以确保在标准容器破损或可见异物被卡住或丢失于容器内时，有备用可见异物可用。

7.5 These qualified defects standard units are then assembled into test sets, which may be used to specifically challenge the particle detection technique of human inspectors, used as part of a defect test set (including container-closure defects) for human qualification or for comparison during automated equipment qualification and validation. When possible, the test set should be prepared with duplicate product units per particle type and size to ensure that backup units are available in the event that a standard container is broken or the particle is trapped or lost within the container.

2022版欧盟附录1 EU GMP <Annex 1>

8.30应该生成并维护一个缺陷库，它可以捕获所有已知的缺陷类。缺陷库应用于生产和质量保证人员的培训。在对可接受的容器进行任何后续取样和检查时，不应发现严重缺陷。

8.31应使用制造商缺陷库集中的适当样品进行人员资质考核。

8.32在使用自动化检查方法的地方，工艺应被验证检测已知缺陷（可能影响产品质量或安全）的能力，并与人工检查方法相等，或优于人工检查方法。设备的性能应在启动前和在整个批次中定期使用具有代表性的缺陷进行挑战。

8.30 A defect library should be generated and maintained which captures all known classes of defects. The defect library should be used for the training of production and quality assurance personnel. Critical defects should not be identified during any subsequent sampling and inspection of acceptable containers.

8.31 The qualification should be undertaken using appropriate samples from the manufacturer's defect library sets.

8.32 Where automated methods of inspection are used, the process should be validated to detect known defects (which may impact product quality or safety) and be equal to, or better than, manual inspection methods. The performance of the equipment should be challenged using representative defects prior to start up and at regular intervals throughout the batch.

建立可见异物标准物质的必要性

WHY VISIBLE PARTICULATES ARE IMPORTANT?

2025版中国药典0904可见异物检查法 CHINESE PHARMACOPOEIA 2025

在规定条件下目视可以观测到的不溶性物质，其粒径或长度通常大于50μm。

Visible particulates are defined as insoluble matter that can be observed by the unaided eye under specified conditions, with particle size or length typically greater than 50 μm.

可见异物检查法有灯检法和光散射法。一般常用灯检法。灯检法不适用的品种，如用深色透明容器包装或液体色泽较深(一般深于各标准比色液7号)的品种可选用光散射法。

Two primary methods are available for the inspection of visible particulates: the visual inspection method and the light scattering method. The visual inspection method is generally the most commonly used approach. For products for which the visual inspection method is not suitable—such as those packaged in dark transparent containers or those with deeply colored liquids (generally darker than Standard Color Solution No. 7)—the light scattering method may be employed as an alternative.

第一法（灯检法）结果判定：供试品中不得检出金属屑、玻璃屑、长度超过2mm的纤维、最大粒径超过2mm的块状物以及静置一定时间后轻轻旋转时肉眼可见的烟雾状微粒沉积物、无法计数的微粒群或摇不散的沉淀，以及在规定时间内较难计数的蛋白质絮状物等明显可见异物。

Visual Inspection Method - Acceptance Criteria:

The test sample must not contain any of the following readily visible particulates:

- Metal particles, glass particles, fibers exceeding 2 mm in length
- Agglomerates with a maximum particle size exceeding 2 mm
- Cloudy particulate sediment visible to the unaided eye upon gentle swirling after a specified standing period
- Innumerable particles, and precipitates that cannot be dispersed by shaking
- Proteinaceous flocculent matter that is difficult to count within the specified time frame

第二法（光散射法）除另有规定外，分别用粒径为40μm和60μm的标准粒子溶液对仪器进行标定。根据标定结果得到曲线方程并计算出与粒径50μm相对应的检测像素值。

Light Scattering Method - Calibration:

The equipment shall be calibrated using standard particle solutions with particle sizes of 40 μm and 60 μm, respectively. Based on the calibration results, a curve equation shall be established, and the detection pixel value corresponding to a particle size of 50 μm shall be calculated.

建立可见异物标准物质的必要性

WHY VISIBLE PARTICULATES ARE IMPORTANT?

2023版中国GMP指南 CHINESE GMP GUIDELINES 2023

企业应采用风险评估工具，基于产品特性、生产工艺、内包材、历史缺陷数据等确定产品可能存在的缺陷类型，并主要根据缺陷对患者安全的影响对缺陷类型进行等级分类(通常分为严重、中等、轻微三种等级)，合理设定每种缺陷类型的检出率标准。

Manufacturers shall use risk assessment tools to identify potential defect types for the product, taking into account product characteristics, manufacturing processes, primary packaging materials, and historical defect data. Defect types shall be classified into severity levels-typically critical, major, and minor-based primarily on the impact on patient safety. Probability of Detection (PoD) criteria shall be rationally established for each defect type.

需要制作相应的缺陷样品用于人工目检考核或替代人工的方法比较，为保证制备的缺陷样品具备代表性，缺陷样品可来源于以下两种渠道：

- 将实际生产过程中收集到的缺陷样品通过多名具有灯检资质的人员进行目检，每瓶合计灯检30~50次，计算检出率，根据检出率将缺陷品进行分类。
- 通过实验室制备，制备材料的材质与可能污染源对应，缺陷尺寸可量化。

Defect samples shall be prepared for use in manual inspection qualification or for comparison with alternative (automated) methods. To ensure that the prepared defective samples are representative, they may be obtained from the following two sources:

- Defect samples collected from actual manufacturing processes shall be visually inspected by multiple qualified light inspection personnel, with each unit inspected 30 to 50 times in total. The detection rate (Probability of Detection) shall be calculated, and defect samples shall be classified based on the resulting detection rates.
- Defects shall be prepared in the laboratory using materials that correspond to potential contamination sources, with defect sizes that are quantifiable.

缺陷样品应设定有效期，并定期对缺陷样品进行检查，及时更替失去代表性的缺陷样品。

Defect samples shall be assigned an expiration date and shall be periodically inspected. Defect samples that are no longer representative shall be promptly replaced.

MASTERING CCIT CHALLENGES WITH EXPERIENCE

众林成立于2005年，总部位于上海，专业从事医药和医疗器械容器密封完整性测试研究和气体分析。

Founded in 2005 and headquartered in Shanghai, Zholion specializes in pharmaceutical and medical device container closure integrity testing research and gas analysis.

SOLUTIONS
Customized CCIT One-stop Solutions

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