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1. 目的PURPOSE
建立成品和中间产品取样的管理程序，规范成品和中间产品取样操作过程。
Establish a management procedure for sampling finished and in-process products, and standardize the sampling process for finished and in-process material.
2. 范围SCOPE
本文件适用于诺峰药业（成都）有限公司（ZENNOVA）所有成品、中间产品取样以及原辅料预处理的取样。
This document applies to the sampling of all finished products, intermediate products, and raw material pretreatment of ZENNOVA Pharmaceutical (Chengdu) Co., Ltd.
3. 参考REFERENCE
	1. 中国药品生产质量管理规范（2010年修订版）
	Chinese Good Manufacturing Practice for Drugs (Revised in 2010)
	2. 中国GMP指南—质量管理体系
	Chinese GMP Guidelines - Quality Management Systems
	3. FDA CFR 211
	4. SMP-PD-021《OSD车间工器具管理》
	SMP-PD-021 Tool Management of OSD Workshop
	5. SMP-QC-004《QC实验室样品管理》
	Sample Management in QC Laboratory
4. 职责 RESPONSIBILITIES
	1. 现场QA负责按照规程对成品和中间产品进行取样并送至QC检验。
	QA On-site is responsible for sampling and sending finished and intermediate products to QC for inspection in accordance with protocols.
	2. 车间人员负责协助现场QA取样。
	Workshop personnel are responsible for assisting QA on-site sampling.
	3. QC负责准备相应的取样容器、标签等，负责额外检验需要的仓库成品取样。
	QC is responsible for preparing the appropriate sampling containers, identifications and others and is responsible for additional inspection needs of the warehouse finished product sampling.
5. 定义/缩略词 DEFINITIONS/ABBREVIATIONS
	1. 中间产品：系指公司生产车间在完成部分加工步骤之后的产品，即在它成为待包装产品或成品之前必须经过进一步加工处理的产品。
	Intermediate product: refers to the product produced by the company's production workshop after completing some processing steps, that is, the product that must undergo further processing before it becomes a packaged or finished product.
	2. 取样：药品生产过程的取样是指为一特定目的，自某一总体（物料和产品）中抽取样品的操作。取样操作要保证样品的代表性。
	Sampling: Sampling during the drug production process refers to the operation of extracting samples from a specific population (materials and products) for a specific purpose. The sampling operation should ensure the representativeness of the sample.
	3. BMF法取样规则：将产品按加工顺序分成三部分，第一部分为生产中前三分之一，包括最初生产的部分产品，称为“B”，第二部分为生产中间三分之一，按相同的产品包装间隔分次取样，称为“M”，第三部分为后三分之一，包括批最终生产的部分产品，称为“F”。各部分分别取总取样量的三分之一，随机取样。
	Sampling rules of BMF method: The product is divided into three steps according to the processing order. The first part is the first third of production, including the initially produced products, called "B". The second part is the middle third of production, which is sampled in batches at the same packaging interval, called "M". The third part is the last third, including the final batch of products, called "F". Take one-third of the total sampling amount for each section and random sample.
6. 程序 PROCEDURE
	1. 人员要求
	Personnel requirements
	现场QA应经成品和中间产品取样操作培训并考核合格后，经资质确认后方可上岗独立取样。
	QA On-site should receive training on sampling operations for finished and intermediate products, pass the assessment, and obtain qualification confirmation before taking up independent sampling positions.
	2. 取样地点
	Sampling location
		1. 中间产品的取样应在对应的生产工序进行，取样过程中涉及设备的操作（如打开料斗盖等），岗位操作人员需进行协助。
		The sampling of intermediate products should be carried out in the corresponding production process, and the sampling process involves equipment operation (such as opening the hopper cover), and the post operator needs to provide assistance.
		2. 成品的取样可在内包装工序进行，如泡罩包装、瓶包工序。
		The sampling of finished products can be carried out in internal packaging processes, such as blister packaging and bottle packaging processes.
	3. 取样工具
	Sampling tools
		1. 通用要求
		General requirements
			1. 应该根据要取的样品选择合适的取样器具。取样器具应当平整、光洁、易清洗或消毒/灭菌、耐腐蚀，不得与药品发生化学反应、吸附药品或向药品中释放物质；如不锈钢、玻璃等惰性材料。
			Suitable sampling equipment should be selected based on the sample to be taken. Sampling equipment should be flat, smooth, easy to clean or disinfect/sterilize, corrosion-resistant, and should not undergo chemical reactions with drugs, adsorb drugs, or release substances into drugs like stainless steel, glass and other inert material.
			2. 用于微生物检验取样时，取样器具必须灭菌且处于灭菌有效期内。
			When used for microbiological testing sampling, the sampling equipment must be sterilized and within the sterilization period.
			3. 中间产品的取样器应专用，并标识产品名称。
			The sampler for intermediate products should be dedicated and labeled with the product name.
			4. 中间产品取样器具使用完后，应按照SMP-PD-021《OSD车间工器具管理》进行清洁，并在清洁、干燥的状态下保存，并在清洁有效期内使用。
			After using the intermediate product sampling equipment, it should be cleaned according to SMP-PD-021 Tool Management of OSD Workshop, stored in a clean and dry state, and used within the effective cleaning period.
			5. 取样器具若有损坏，必须立即停止使用。
			If the sampling equipment is damaged, it must be immediately stopped from use.
			6. 一般取样器具有粉末取样器、不锈钢勺、不锈钢铲等。
			Typical samplers include powder samplers, stainless steel spoons, stainless steel shovels, etc.
		2. 粉末取样器
		Powder Sampler
			1. 定量取样钎一般用于固体粉末类、颗粒类的取样。
			Quantitative sampling drills are generally used for sampling solid powders and particles.
			2. 使用方法：将弹簧装入驱动杆中，再将驱动杆装入套管中，安装取样头，使取样口封闭，将取样器插入需要取样的物料中，达到要求的深度后，向上拉取样器的外部管套，物料将充填在取样头周围的空隙处，再将取样器外套管向下推，使取样头退回到取样器中，样品被隔离在取样器中，将取样器从物料中抽出，将样品放出至QC已称量皮重的样品容器中（若样品容器口径较小不便于收集样品，可以将取出的样品放至称量纸上再转移至容器中）。
			Usage: Install the spring into the drive rod, then insert the drive rod into the sleeve, install the sampling head, close the sampling port, insert the sampler into the material to be sampled, reach the required depth, pull up the outer sleeve of the sampler, and the material will fill the gap around the sampling head. Then push down the outer sleeve of the sampler to retract the sampling head into the sampler, and isolate the sample in the sampler. Pull out the sampler from the material and release the sample into the container whose tare weight has been weighed (if the diameter of the sample container is small and not convenient for collecting samples, the extracted sample can be placed on weighing paper and transferred to the container).
		3. 取样勺/铲
		Sampling spoon/shovel
		用途：一些固体制剂产品生产过程中颗粒的取样，如：物料在烘箱中需要每盘取样时。
		Usage: Sampling of particles during the production process of some solid dosage forms, such as when materials need to be sampled from each tray in an oven.
		4. 样品容器
		Sample container
			1. 样品容器应能够防止受到环境、微生物、热原等污染，容器应避免与样品发生反应、吸附或引起污染，并根据样品的储存要求，能满足避光、隔绝空气与水分，防止样品出现降解、潮解、吸湿、挥发等情况。
			The sample container should be able to prevent contamination from the environment, microorganisms, pyrogens, etc. The container should avoid reacting, adsorbing, or causing contamination with the sample, and according to the storage requirements of the sample, it should meet the requirements of avoiding light, isolating air and moisture, and preventing degradation, deliquescence, moisture absorption, volatilization, of the sample.
			2. 现使用的样品容器有PE袋、蓝盖瓶、具塞玻璃瓶、称量瓶等。
			The currently used sample containers include PE bags, blue capped bottles, stoppered glass bottles, weighing bottles, etc.
			3. 特殊品种可根据工艺要求准备样品容器。
			Special varieties can have sample containers prepared according to process requirements.
	4. 取样量
	Sampling Amount
		1. 取样量应按对应的质量标准、工艺规程、批记录或方案中规定的量执行。
		The sampling amount should be executed according to the corresponding quality standards, process specifications, batch records, or the amount specified in the plan.
		2. 根据CDE和ISPE指导原则：口服固体制剂混合均匀性取样，在混合设备和/或中间体物料容器中至少选取 10 个取样点，每个取样点至少取 3 份样品。单份样品取样量通常应在 1-3 倍单位剂量范围内，样品应全量用于混合均匀度检测，应避免出现二次取样情况。（取样头的选择：可根据公式“取样体积(ml)=取样量（g）/颗粒堆密度(g/ml)”计算得出理论取样体积，再根据理论取样体积选择合适的取样头用于取样操作。各产品的堆密度可从研发部门或研究批、工艺验证等批次收集的数据中获取）。
		According to the guidelines of CDE and ISPE, for uniformity sampling of oral solid dosage forms, at least 10 sampling points should be selected in the mixing equipment and/or intermediate material container, with at least 3 samples taken from each sampling point. The sampling amount of a single sample should usually be within the range of 1-3 times the unit dose. The entire sample should be used for testing the uniformity of the mixture, and secondary sampling should be avoided. (Selection of sampling head: The theoretical sampling volume can be calculated based on the formula "Sampling volume (ml)=Sampling volume (g)/Particle bulk density (g/ml)", and then the appropriate sampling head can be selected for sampling operation according to the theoretical sampling volume.). The bulk density of each product can be obtained from data collected by the R&D department or research batches, process validation batches, etc.
	5. 请验
	Test Request
	由车间人员填写SMP-QC-003/R01《请验单》第一部分交至现场QA。成品请验时，请验单中的“数量/容器数”若未明确，可填写N/A，待数量确定后，车间人员需在《请验单》上备注“数量/容器数”并签名和日期。
	The workshop personnel shall fill out the first part of SMP-QC-003/R01 Test Request Form and submit it to the QA on-site. When requesting inspection of finished products, if the "quantity/number of containers" in the inspection form is not clear, N/A can be filled in. After the quantity is confirmed, workshop personnel need to annotate "quantity/number of containers" on the "Test Request Form" and sign and date it.
	6. 取样前检查
	Pre-sampling inspection
	必要时查阅质量标准、验证取样计划了解被取样品的性质和注意事项，准备相应的取样工具、样品容器和样品标签，若涉及取样称量操作，需提前做好衡器预热和校准工作。核对请验单上的信息是否与待取样中间产品和产品一致，确保无误后开始取样。
	When necessary, consult the quality standards, verify the sampling plan to understand the nature and precautions of the sample being taken, prepare the corresponding sampling tools, sample containers, and sample labels. If sampling and weighing operations are involved, preheating and calibration of the weighing apparatus should be done in advance. Check whether the information on the inspection form is consistent with the intermediate products and products to be sampled, and start sampling after ensuring that there are no errors.
	7. 中间产品的取样
	Sampling of intermediate products
		1. 固体制剂中间产品的取样
		Sampling of intermediate products in solid dosage
			1. 原辅料预处理后粒径样品的取样
			Sampling of particle size samples after pre-treatment of raw materials
* 原辅料预处理后物料应按照工艺规程或者方案存放在相应的包装容器中，若容器取件数总件数为n，n≤3时，每件取样；n＞3时，取样件数为。若计算出得样品数不是整数，则采用进一法修约成整数。
Raw materials and excipients after pre-treatment, they should be stored in corresponding packaging containers according to the process specifications or protocols. If the total number of containers taken is n, and n ≤ 3, samples should be taken from each container; When n>3, the number of samples taken is . If the calculated number of samples is not an integer, use the method of rounding to an integer.
* 原辅料预处理后的粒径取样，考虑原料或辅料是单一物料，用取样器在包装容器上、中、下三层取样，在取样容器中将其摇匀。
Sampling of particle size after pre-treatment of raw material and excipients, considering that the raw material and excipients are single materials, use a sampler to take samples from the top, middle, and bottom layers of the packaging container, and shake them evenly in the sampling container.
* 上、中、下取样时，三个点垂直方向应不在一条直线上，且至少有一层取样点在该层中间位置。
When sampling from the upper, middle, and the bottom, the three points should not be on a straight line in the vertical direction, and at least one layer of sampling points should be in the middle of that layer.
* 若预处理后的物料数量较少不便于从上中下取样则从三个不同的位置取样后混合。
If the quantity of preprocessed materials is small and it is not convenient to sample from the top, middle, and bottom, samples should be taken from three different positions and mixed.
* 多件包装容器的取样件应分布在预处理前中后，取样后样品可混合在一个取样容器中。
Samples of multiple packaging containers should be distributed before, during, and after pre-treatment, and the samples can be mixed in one sampling container after sampling.
	+ - 1. 制粒后粒径分布的取样
			Sampling of particle size distribution after granulation
			取样时，使用不锈钢取样瓢，接在干法制粒机出料口，接取25g~100g的颗粒（若取样量未在规定范围内，需做废弃物处理，并重新取样），取样后盖上取样瓢的盖子转移至中控间，使用烧杯或不锈钢盘等容器称量样品重量，将样品全部转移至振动筛分仪检测粒径分布，检测后的颗粒做废弃物处理。
			When sampling, use a stainless steel sampling ladle and connect it to the discharge port of the dry granulation machine. Take 25g-100g of particles (if the sampling amount is not within the specified range, it needs to be disposed as waste and resampled). Cover the sampling ladle with the lid and transfer it to the QA In-process Control Room. Use a beaker or stainless steel plate to weigh the sample, and transfer all the samples to the Sieve Shaker to detect the particle size distribution. Dispose of the detected particles as waste.
			2. 堆密度/振实密度样品的取样
			Sampling of bulk density/tap density samples
			取样时，使用不锈钢取样瓢，接在干法制粒机出料口，取样后盖上取样瓢的盖子转移至中控间，使用烧杯或不锈钢盘等容器称量样品重量，使用称量纸或漏斗等工具将样品全部转移至振实密度仪的量筒中，检测堆密度和振实密度，检测后的颗粒做废弃物处理。取样量为：物料的堆密度\*表观体积应不低于所选量筒刻度的60%的体积~物料的堆密度\*量筒100%体积，振实密度仪量筒容积分别为：25ml、50ml、100ml、250ml。
			When sampling, use a stainless steel sampling ladle and connect it to the discharge port of the dry granulation machine. Cover the sampling ladle with the lid and transfer it to the QA In-process Control Room. Use a beaker or stainless steel plate to weigh the sample, and use tools such as weighing paper or funnel to transfer all the samples to the measuring cylinder of the Tapping Apparatus. Test the bulk density and tap density, and dispose of the particles as waste after testing. The sampling amount is: the bulk density of the material multiplied by the apparent volume should not be less than 60% of the volume of the selected measuring cylinder scale~ the bulk density of the material multiplied by 100% of the volume of the measuring cylinder. The volumetric capacities of the vibrating density meter measuring cylinders are 25ml, 50ml, 100ml, and 250ml, respectively.
			3. 混合均匀度样品的取样
			Sampling of Mixed Uniformity Samples
* 方锥形物料罐中的取样点示意图如下：确认物料表面已抚平后，在混合罐的上部、转角边缘处和出料口共11个位置分别取样，每个位置取三份样品，其中两份样品备用。
The schematic diagram of the sampling points in the conical material tank is as follows: After confirming that the surface of the material has been smoothed, samples are taken at 11 positions including the upper part, corner edge, and discharge port of the mixing tank. Three samples are taken from each position, with two samples for backup.



* 取样前，需称量所有取样容器的总重量。
Before sampling, it is necessary to weigh the total weight of all sampling containers.
* 按6.4确定取样量和合适的取样头，按取样点顺序依次进行取样，每份样品均应一次取够足量且全量转移至样品容器，应避免出现分样和二次取样操作。
Determine the sampling amount and appropriate sampling head according to 6.4, and take samples in sequence according to the sampling points. Each sample should be taken in sufficient quantity at once and transferred to the sample container in full. Separation and secondary sampling operations should be avoided.
* 若有单点取样量不在要求范围内，则此份样品作废料处理并重新取样。
If the sampling volume of a single point is not within the required range, the sample will be treated as waste and resampled.
* 取样后，称量样品及容器的总重量，可计算出总取样量。
After sampling, the total weight of the sample and container can be weighed to calculate the total sampling amount.
	+ - 1. 含量、性状、水分等样品的取样
			Sampling of content, characteristics, moisture, etc
* 使用取样器在混合罐或物料罐的上、中、下三层各取一个点，并在取样袋/瓶中进行混合，至少上下翻转混合10次。
Use a sampler to take one point from each of the upper, middle, and lower layers of the mixing tank or material tank, and mix them in a sampling bag/bottle by flipping them up and down at least 10 times.
* 若物料数量较少不便于从上中下取样，则从三个不同的位置取样后混合。
If the quantity of materials is small and it is not convenient to sample from the top, middle, and bottom, samples should be taken from three different locations and mixed.
	+ - 1. 素片、包衣片、胶囊、铝塑板、塑料瓶装产品的取样
			Sampling of plain tablets, coated tablets, capsules, aluminum-plastic panels, and plastic bottled products
* 按BMF法规则或工艺规程/验证方案中的要求，在生产线上随机抽取规定量的样品（素片、包衣片、胶囊取样时应借助合适的工具，如物料铲等），装于取样容器（如PE袋等）中，并贴上样品标签。
According to the BMF method rules or process specifications/validation plans, a specified amount of samples (such as plain tablets, coated tablets, and capsules) should be randomly selected on the production line, and appropriate tools such as material shovels should be used for sampling. The samples should be placed in sampling containers (such as PE bags) and labeled.
* 取样过程中，所有物料一经取出，不得再次返回原物料中，在岗位现场进行检测的项目（如：密封性、水分）检测完成后，即便检测过的样品仍符合工艺要求，也不得返回物料中，需作为废料处理。
During the sampling process, once all materials are taken out, they must not be returned to the original material. After the testing of items (such as sealing and moisture) at the job site is completed, even if the tested samples still meet the process requirements, they cannot be returned to the material and must be treated as waste.
	+ 1. 验证时进行的中间产品取样，应注意样品的代表性。如验证搅拌时间的取样应在规定的时间点进行取样；分层取样的应注意取样的代表性。
		When sampling intermediate products during verification, attention should be paid to the representativeness of the samples. The sampling for verifying the mixing time should be taken at the specified time point; Attention should be paid to the representativeness of stratified sampling.
		2. 若因偏差额外进行中间产品取样，取样点位、取样方法、取样量按偏差处理意见执行。
		If additional intermediate product sampling is carried out due to deviation, the sampling points, sampling methods, and sampling quantities shall be handled according to the deviation handling opinions.
		3. 一个时间只取一个样品，样品容器在取样后即应贴上样品标签，以免发生差错；混合均匀度样品标签可按整份进行粘贴。
		Only one sample should be taken at a time, and the sample container should be labeled with a sample label immediately after sampling to avoid errors; The sample label for uniformity of mixing can be pasted as a whole.
		4. 要求避光保存的物料，取样时应尽量控制取样时间，取好的样品用不透光的样品容器盛装或另外增加避光处理，如套黑色PE袋。
		Materials that are required to be stored away from light should be sampled with controlled sampling time as much as possible. The collected samples should be stored in opaque sample containers or additionally protected from light, such as using black PE bags.
		5. 中间产品取样涉及取样量按重量计算的操作，通常先称取样品容器的总皮重，取样后再称取样品及容器的总毛重，用后者重量减去前者重量得出样品的净重，特殊情况下，如取样容器重量较大，可能超出天平使用范围，可取样后，转移至其他容器进行称量。
		The sampling of intermediate products involves the operation of calculating the sampling amount by weight. Usually, the total tare weight of the sample container is first weighed, and then the total gross weight of the sample and the container is weighed. The net weight of the sample is obtained by subtracting the weight of the former from the weight of the latter. In special cases, if the weight of the sampling container is large and may exceed the range of use of the balance, it can be transferred to other containers for weighing after sampling.
		6. 取样过程中，应注意观察产品有无异常，如异物、杂质、色泽不均等，若有，应立即上报。
		During the sampling process, attention should be paid to observing whether there are any abnormalities in the product, such as foreign objects, impurities, or uneven color. If there are any, they should be reported immediately.
	1. 成品的取样
	Sampling of finished products
		1. 成品通常按照BMF法规则取样，通常在完成最小销售单元的包装并贴签后进行取样。特殊情况下，可在完成内包装后进行取样。
		Finished products are usually sampled according to the BMF method rules, usually after completing the packaging and labeling of the smallest sales unit. In special circumstances, sampling can be carried out after completing the primary packaging.
		2. 如果生产过程是亚批进行的，则应从每个亚批中进行的取样，并分别进行检测。
		If the production process is carried out in sub batches, samples should be taken from each sub batch and tested separately.
		3. 稳定性试验样品通常应与成品放行样同时进行取样，特殊情况下，可填写SMP-QC-003/R05《取样申请表》进行取样。
		Stability test samples should usually be sampled simultaneously with finished product release samples. In special cases, SMP-QC-003/R05 Sampling Application Form can be filled out for sampling.
		4. 同时取样的成品的样品可按批进行样品标签的粘贴。
		Samples of finished products taken simultaneously can be labeled in batches.
	2. 记录填写
	Fill out Records
	取样后，现场QA应填写《请验单》第二部分内容，同时将中间产品和成品的取样活动记录于该批产品的批记录中。
	After sampling, the on-site QA should fill out the second part of the Test Request Form and record the sampling activities of intermediate and finished products in the batch record of the batch of products.
	3. 送样
	Send samples
		1. 完成取样后送QC检验前，样品应按其质量标准上规定的储存条件进行存放。样品转移至QC过程中应避免样品受到污染、光照和高温高湿的影响，转移时间不得超过1小时。
		Before completing the sampling and sending it to QC for inspection, the samples should be stored under the storage conditions specified in their quality standards. During the transfer of samples to QC, contamination, light exposure, and high temperature and humidity should be avoided, and the transfer time should not exceed 1 hour.
		2. 现场QA将样品送至QC样品管理室，将样品交给样品管理员，并填写样品台账，样品管理员按照SMP-QC-004《QC实验室样品管理》发放样品编号并填写相应《样品标签》中的内容。
		On site QA will send the samples to the QC sample management room, hand them over to the sample administrator, and fill out the sample logbook. The sample administrator will issue sample numbers according to SMP-QC-004 Sample Management in QC Laboratory and fill in the corresponding content in the Sample Identification.
1. 环境、健康与安全ENVIRONMENT, HEALTH&SAFETY
无
None
2. 附件ATTACHMENTS
无
N/A
3. 修订历史DOCUMENT REVISION HISTORY

| 版本号Version No. | 生效日期Effective Date | 修订内容简述Description of Revised Contents  |
| --- | --- | --- |
| 00 | 不适用N/A | 新文件New File |

1. 培训要求 TRAINING REQUIREMENT

| 部门Department | 需培训的岗位Post to be Trained | 培训要求Training Requirements |
| --- | --- | --- |
| 熟练操作Skilled Operation | 全面掌握Thorough Understanding | 了解Basic Knowledge |
| QA | 现场QAQA On-site | □ | ☑ | □ |
| QC | 主管及以上Supervisor and above | □ | □ | ☑ |