Submission requirements for pharmaceutical excipients CDMF

药用辅料的技术资料申报要求

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药用辅料

China Food and Drug Administration Nov. 28, 2016
CFDA Issued the Requirements for CDMFs of Pharmaceutical Packaging Materials and Pharmaceutical Excipients ([2016] No.155)

国家食品药品监督管理总局 CFDA
China Food and Drug Administration

总局关于发布药包材药用辅料申报资料要求（试行）的通告（2016年第155号）

2016年11月28日 发布

依据《关于药包材药用辅料与药品关联审评审批有关事项的公告》（国家食品药品监督管理总局2016年第134号），我局组织制定了《药包材申报资料要求（试行）》和《药用辅料申报资料要求（试行）》，现予公布，并就有关事项通告如下：

一、药包材、药用辅料已与药物临床试验申请关联申报的，如在药品上市申请阶段发生变化，药包材、药用辅料生产企业应及时通知药品注册申请人，并直接向国家食品药品监督管理总局药品审评中心提交相关补充资料，附药包材、药用辅料《受理通知书》，无需重复关联申报。

二、药包材、药用辅料生产企业名称、生产地址、处方工艺、质量标准等发生变更时，其生产企业应开展研究并及时通知相关药品生产企业。药品生产企业应及时掌握药包材、药用辅料变更情况，并按相关技术指导原则进行研究和评估，对影响药品质量的药包材、药用辅料变更应依据《药品注册管理办法》的相关规定申报药品补充申请，对不影响药品质量的药包材、药用辅料变更应依据《药品注册管理办法》附件4补充申请第36项向省级食品药品监管部门备案。

三、药品注册申请人在药品注册申报资料中一并提交药包材、药用辅料研究资料的，可以进行药品审评，完成审评后不对药包材、药用辅料核发核准编号。

四、本通告自发布之日起施行。

特此通告。

药用辅料

Requirements of Pharmaceutical Excipients Submission

药用辅料申报资料要求（试行）

品种名称：XXXXX

申请人：XXXXX

应用情况 □境内外上市制剂中未使用过的药用辅料。

□境外上市制剂中已使用而在境内上市制剂中未使用过的药用辅料。

□境内上市制剂中已使用，未获得批准证明文件或核准编号的药用辅料。

□已获得批准证明文件或核准编号的药用辅料改变给药途径或提高使用限量。

□国家食品药品监督管理总局规定的其他药用辅料。

拟用制剂给药途径：□注射 □吸入 □眼用 □局部及舌下 □透皮 □口服 □其他。

来源：□动物或人 □矿物 □植物 □化学合成 □其他。

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		1	Registrant Information 登记人基本信息	Basic requirements and information must be accurate. 基本要求，信息要准确无误
		1.1	Name, Address, Manufacturing address 登记人名称、地址、生产地址	More supporting documents should be provided (including approved and expired documents in the past) . 应提供更多的证明文件（包括过去已批准、过期的证明文件）
		1.2	Certification 证明性文件	
		1.3	Stored Address of Raw Data 研究资料保存地址	
3.2.S.1	Information	2	Excipients Information 辅料基本信息	
3.2.S.1.1	Name	2.1	Name 名称	
3.2.S.1.2	Structure	2.2	Structure and Composition 结构与组成	
3.2.S.1.3	Properties	2.3	Physicochemical Properties 理化性质及基本特性	
		2.4	Domestic and Foreign Approval Information and Usage 境内外批准信息及用途	
		2.4.1	Other Countries Information 其他国家的相关信息	
		2.4.2	Usage Information 用途信息	
		2.5	Domestic and Foreign Pharmacopoeia monographs 国内外药典收载情况	
3.2.S.2	Manufacturing Information	3	Manufacturing Information 生产信息	

Compare CTD in China with ICH 国内外药用辅料CTD格式比较

CTD of ICH 国外药用辅料申报实例		CTD in China 国内药用辅料申报要求		解析
3.2.S.2.1	Manufactures			
3.2.S.2.2	Manufacturing Process	3.1	Manufacturing Process Control 生产工艺和过程控制	Must be required 必须要求
3.2.S.2.3	Material Control	3.2	Material Control 物料控制	
3.2.S.2.4	Critical Process and Intermediates Control	3.3	Critical Process and Intermediates Control关键步骤和中间体的控制	
3.2.S.2.5	Process Validation and / or Evaluation	3.4	Process Validation and / or Evaluation 工艺验证和评价	Simplified if have pharmacopeia monographs
		3.5	Development of Manufacturing Process 生产工艺的开发	Development research process 开发研究过程
3.2.S.3	Specific Tests	4	Specific Tests 特性鉴定	
3.2.S.3.1	Structure and Other Properties	4.1	Structure and Physicochemical Properties 结构和理化性质研究	
3.2.S.3.2	Impurity	4.2	Impurity 杂质研究	
		4.3	Functionality-related Characteristics 功能特性	Differences in quality of excipients at home and abroad 国内外质量的差异化
3.2.S.4	Quality Control	5	Quality Control 质量控制	
3.2.S.4.1	Quality Standard	5.1	Quality Standards 质量标准	
3.2.S.4.2	Analytical Process			

Compare CTD in China with ICH 国内外药用辅料CTD格式比较

CTD of ICH 国外药用辅料申报实例		CTD in China 国内药用辅料申报要求		解析
3.2.S.4.3	Validation of Analytical Process	5.2	Validation of Analytical Process 分析方法的验证	
3.2.S.4.5	Quality Standard Establishment Basis	5.3	Quality Standard Establishment Basis 质量标准制定依据	
3.2.S.4.4	Lot Testing	6	Lot Testing 批检验报告	
3.2.S.5	Reference Substance			
3.2.S.5.1	Reference Substance			
3.2.S.6	Packaging Materials			
3.2.S.6.1	Packaging Materials			
3.2.S.7	Stability	7	Stability 稳定性研究	
3.2.S.7.1	Stability Conclusion and Summary	7.1	Stability Summary 稳定性总结	
3.2.S.7.2	Post-market Stability Promise and Project			
3.2.S.7.3	Stability Data	7.2	Stability Data 稳定性数据	
		7.3	Packaging 辅料的包装	
		8	Pharmacology and Toxicology Data 药理毒理研究	New pharmaceutical excipients, dosage and route of administration 新辅料，新用量、新给药途径

Requirements for Registration Application Dossiers of Pharmaceutical Excipients ([2016] No.155)

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	Application requirements（申报资料要求）	Interpretation（解读）
1	**Registrant Information（登记人基本信息）**	Basic Information（基本信息）
1.	Registrant Name, Address, Manufacturing address Provide the name, registered address, manufacturers, and production address of the registrant. The production address should be accurate to the production floor and production line. 登记人名称、地址、生产地址 提供登记人的名称、注册地址、生产厂、生产地址。 生产地址应精确至生产车间、生产线。	
	Certification（证明性文件）	Certification（证明文件）
	The registrant of pharmaceutical excipients must submit the following supporting documents（境内药用辅料登记人需提交以下证明文件）：	
	(1) A copy of the registrant's business license. The registrants shall submit the relevant documents such as the power of attorney and the relevant information of the producer and a copy of the business license when they entrust a third party to produce. （1）登记人营业执照复印件。对登记人委托第三方进行生产的，应同时提交委托书等相关文件及生产者相关信息及营业执照复印件。	
	(2) For domestic registrants applying for gelatin vacant capsule shell, gelatin capsule and pharmaceutical gelatin, they are required to provide: 1. the legal source certificate of gelatin should be provided, including the approval certificate for gelatin, standards, COA, business licenses for pharmaceutical gelatin manufacturers, copies of pharmaceutical production licenses, sales invoices, supply agreements, etc. 2. certificates such as types and standards, should be provided.	

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	Application requirements（申报资料要求）	Interpretation（解读）
	The registrant of overseas pharmaceutical excipients shall authorize the Chinese representative office to submit the following supporting documents: （境外药用辅料登记人应授权中国代表机构提交以下证明文件）	
	(1) The legal registrants' legal production qualification certificate, notarized documents and their Chinese translations. The registrants shall submit the relevant documents such as the power of attorney and the relevant information and certification documents (if any) of the producer when they entrust a third party to produce. （1）登记人合法生产资格证明文件、公证文件及其中文译文。对登记人委托第三方进行生产的，应同时提交委托书等相关文件及生产者相关信息及证明文件（如有）。	
	(2) The business license of the agency in China or the registration certificate of the resident representative office of a foreign company in China. (2) 中国境内代理机构的营业执照或者登记人常驻中国境内办事机构的《外国企业常驻中国代表机构登记证》。	
	(3) For the declaration of gelatin and gelatin-related products,and other bovine-derived excipients, claim of virus-free, TSE free shall be provided. (3) 申报药用空心胶囊、胶囊用明胶、药用明胶等牛源性药用辅料进口的，须提供制备胶囊的主要原材料——明胶的制备原料的来源、种类等相关资料和证明，并提供制备**原料来源于没有发生疯牛病疫情国家的政府证明文件**。境外药用辅料建议提供人源或动物源性辅料的相关证明文件。	

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	1.3 Stored address of raw data（研究资料保存地址） **The storage address of the research materials for the pharmaceutical excipients should be accurate to the house number. If the research data has multiple saved addresses, all of them must be submitted.** 提供药用辅料研究资料的保存地址，应精确至门牌号。如研究资料有多个保存地址的，均需提交。	
2	**Excipients Information(辅料基本信息)**	
	2.1 Name（名称）	
	Provide the Chinese common name of the excipient (if applicable, the Chinese Pharmacopoeia name), the English common name, the Hanyu Pinyin, the chemical name, the former name, and the Chemical Abstracts (CAS) number. If the UNII number and other names (including the names of the domestic and foreign Pharmacopoeia) are recommended, please provide them. 提供辅料的中文通用名（如适用，以中国药典名为准）、英文通用名、汉语拼音、化学名、曾用名、化学文摘（CAS）号。如有UNII号及其他名称（包括国内外药典收载的名称）建议一并提供。 **Pre-mixed excipient[Note 1] and co-processed excipient [Note 2] should clarify the single excipient used and make qualitative and quantitative descriptions. Typical formulations can be submitted for illustration. The specific formulation for practical application should be included as an annex according to the use. Provided in the registration data or at the time of drug registration.** 预混辅料[注1]和共处理辅料[注2]应明确所使用的单一辅料并进行定性和定量的描述，可提交典型配方用于说明，实际应用的具体配方应根据使用情况作为附件包括在登记资料中或在药品注册时进行提供。 Note: 1. Pre-mixed excipient means that two or more excipients are mixed by low to medium shear force, which is a simple physical mixture. The components remained as separate chemical entities after mixing, and the chemical properties of the components did not change. The premixed excipients can be either solid or liquid, with a simple physical mixing time. 注：1、**预混辅料（pre-mixed excipient）是指两种或两种以上辅料通过低至中等剪切力进行混合，这是一种简单的物理混合物。各组分混合后仍保持为独立的化学实体**，各成分的化学特性并未变化。预混辅料可以是固态的也可以是液态的，单纯的物理混合时间较短。 2. Co-processed excipient is a combination of two or more excipients whose physical properties have changed but the chemical properties have not changed significantly. This change in physical properties cannot be obtained by simple physical mixing, and in some cases, it may exist as a salt. 2、共处理辅料（co-processed excipient）是两种或两种以上辅料的结合物，该结合物的物理特性发生了改变**但化学特性无明显变化**。这种物理特性的改变无法通过单纯的物理混合而获得，在某些情况下，有可能以成盐形式存在。	**First proposed 首次提出**

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	Application requirements（申报资料要求）	Interpretation（解读）
	2.2 Structure and composition（结构与组成） **Provide the structure and composition information of the auxiliary materials, such as structural formula, molecular formula, molecular weight, polymer pharmaceut-ical excipients should be clear molecular weight range, degree of polymerization and so on. The phenomenon of three-dimensional structure and polymorphism should be specified. Premixed excipients and co-processed excipients should submit structural information for each component.** 提供辅料的结构与组成信息，如结构式、分子式、分子量，高分子药用辅料应明确分子量范围、聚合度等。有立体结构和多晶型现象应特别说明。预混辅料和共处理辅料应提交每一组分的结构信息。	
	2.3 Physicochemical property （理化性质及基本特性） **Provide known physical and chemical properties of the excipients, such as: properties (such as appearance, color, physical state), melting point or boiling point, specific rotation, solubility, solution pH, particle size, density (bulk density, tap density, etc.) Functional relevance indicator, etc. Premixed excipients should submit basic characteristics such as product traits.** 提供辅料已知的物理和化学性质，如：性状（如外观，颜色，物理状态）、熔点或沸点、比旋度、溶解性、溶液pH、粒度、密度（堆密度、振实密度等）以及功能相关性指标等。预混辅料应提交产品性状等基本特性信息。	
	2.4 Domestic and foreign approval information and usage(境内外批准信息及用途)	
	2.4.1 Domestic historical approval information（境内历史批准信息） Provide relevant information (if any) for domestic history approval. 提供境内历史批准的相关信息（如有）。	**Past domestic certif-ications or registrat-ion certifications 国内过去的证明文件/注册证**

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	2.4.2 Other countries information（其他国家的相关信息） **Provide information about the intended application of the product as a pharmaceutical excipient in foreign countries (if applicable).** 提供拟申请产品在国外作为药用辅料的相关信息（如适用）。	**Foreign approval certifications** 国外批准证明文件
	2.4.3 Usage information（用途信息） **Provide information on the route of administration of the excipients, as well as the maximum daily reference dose and reference basis. The medicines using the excipients have been approved for marketing at home and abroad, and the dosage forms and routes of administration of the related medicines are provided. If the medicines using the excipients have not been approved for marketing, the intended route of administration of the excipients should be provided and the use of the excipients should be provided. Drug information for registration of accessories. If there is a recommended route of administration or a defined dose known to the manufacturer, it should be clarified and provided with relevant reference. The above information should be provided as much as possible.** **提供本辅料的给药途径信息以及最大每日参考剂量及参考依据**。使用该辅料的药品已在国内外获准上市的，提供相关药品的剂型、给药途径等；尚未有使用该辅料的药品获准上市的，应提供该药用辅料的预期给药途径以及正在使用该辅料进行注册的药品信息。如有生产商已知的**不建议的给药途径或限定的使用剂量**，也应予以明确并提供相关参考说明。以上信息应尽可能提供。	**Provide information on the route of administration of the applied product and the maximum daily reference dose and reference basis** 提供申请产品的给药途径信息以及最大每日参考剂量及参考依据
	2.5 CHP and OTHER pharmacopoeia monographs（境内外药典收载情况） **Provide information on pharmacopoeia MONOGRAPHS.** 提供该药用辅料被国内外药典及我国国家标准收载的信息。	**Determining quality control maturity and methodology** 确定质量控制成熟度和方法学

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3	**Manufacturing Information（生产信息）**	
	3.1 Manufacturing Process Control （生产工艺和过程控制）	
	(1) Process overview: The process flow chart is provided according to the process steps, and the production process is summarized. 工艺综述：按工艺步骤提供工艺流程图，并进行生产工艺综述。	
	(2) Process details: The process parameters and the solvents used are indicated according to the process flow. For chemically synthesized pharmaceutical excipients, reaction conditions (such as temperature, pressure, time, catalyst, etc.) and their chemical reaction formulas should be provided, including starting materials, intermediates, molecular formula of the reagents used, molecular weight, chemistry and structural formula. **Representative of the commercial batch, the main process steps, the amount of each reaction material and the yield range of each step are listed, and the key production steps, key process parameters and quality control indicators of the intermediates are clarified.** **For excipients of human or animal origin, the process of production of the excipient should have clear process steps for virus inactivation and removal and must be verified.** 工艺详述：按工艺流程标明工艺参数和所用溶剂等。如为化学合成的药用辅料，还应提供反应条件（如温度、压力、时间、催化剂等）及其化学反应式，其中应包括起始原料、中间体、所用反应试剂的分子式、分子量、化学结构式。 以商业批为代表，列明主要工艺步骤、各反应物料的投料量及各步收率范围，明确关键生产步骤、关键工艺参数以及中间体的质控指标。 对于**人或动物来源的辅料**，该辅料的生产工艺中应有明确的**病毒灭活**与清除的工艺步骤，并须对其进行验证。	
	（3）Explain the batch range, commercial production, and reasons. 说明商业生产的分批原则、批量范围和依据。	

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(4) Equipment: Provides primary and special production equipment.
设备：**提供主要和特殊的生产设备**。
Production equipment information can be submitted in the form of the following form:
生产设备资料可以按照下述表格形式提交

序号	设备名称	用途		
1				
2				
…				

3.2 Material control （物料控制）

3.2.1 Key material control information（关键物料控制信息）
对关键物料的控制按下表提供信息。

关键物料控制信息

物料名称	来源注	质量标准	使用步骤

注：如动物来源、植物来源、化学合成等。

Prevent arbitrary changes
防止随意变更

3.2.2 Material control information（物料控制信息详述）
According to the process in the process flow chart, all the materials used in the product ion (such as starting materials, reagents, solvents, catalysts, etc.) are listed in the form of a table, and the steps used are illustrated as follows.
按照工艺流程图中的工序，**以表格的形式列明生产中用到的所有物料**（如起始物料、反应试剂、溶剂、催化剂等），并说明所使用的步骤，示例如下。

物料控制信息

物料名称	来源注	质量标准	使用步骤

注：如动物来源、植物来源、化学合成等。

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Provide the source of the above materials, clearly reference standards, or provide internal co ntrol standards (including projects, testing methods and limits), and provide methodological verification data if necessary.提供以上物料的来源、明确引用标准，或提供内控标准（包括项目、检测方法和限度），必要时提供方法学验证资料。

3.3 Critical Process and Intermediates Control（关键步骤和中间体的控制）
List key steps (eg, refining of the final product, purification process steps, viral inactivation/r emoval steps for excipients from human or animal sources). Where applicable, provide critic al process control parameters and provide specific research data (including research method s, findings and conclusions), could justify the reasonableness of the process parameters and control of the key steps identified. Where separate intermediates are present, their quality c ontrol criteria, including items, methods and limits, should be listed and the necessary meth odological validation information provided. 列出关键步骤（如：终产品的精制、纯化工艺步骤，人或动物来源辅料的病毒灭活/去除步骤）。适用时，提供关键过程控制及参数，提供具体的研究资料（包括研究方法、研究结果和研究结论），支持关键步骤确定的合理性以及工艺参数控制范围的合理性。存在分离的中间体时，应列出其质量控制标准，包括项目、方法和限度，并提供必要的方法学验证资料。

Prevent arbitrary changes
防止随意变更

3.4 Process validation and / orevaluation（工艺验证和评价）

For pharmacap eial excipients, simplified data

3.4.1 Process stability assessment（工艺稳定性评估）
Provide relevant assessment materials for the stability of the auxiliary materials, such as retr ospective reports on product quality of more than 5 batches.
提供辅料工艺稳定的相关评估资料，如5批以上的产品质量回顾性报告等。

3.4.2 Process Validation（工艺验证）
Provide process verification plans, verification reports, etc., and provide batch production sa mple samples if necessary 提供工艺验证方案、验证报告等资料，必要时提供批生产记录样稿。

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3.5 R&D of manufacturing process 生产工艺的开发

Provide the basis for selection of the process route (including literature basis and / or theoretical bacontrol range of the process parameters.

Describe in detail the major changes in the production process during the process development process (including changes in batch, equipment, process parameters, and process routes) and related supporting verification studies. Provide a summary of the process sis).

提供工艺路线的选择依据（包括文献依据和/或理论依据）。

Provide detailed research data (including research methods, research results and research conclusions) to illustrate the rationality of the key steps and the rationality of the research data, examples are as follows:

提供详细的研究资料（包括研究方法、研究结果和研究结论）以说明关键步骤确定的合理性以及工艺参数控制范围的合理性。

详细说明在工艺开发过程中生产工艺的主要变化（包括批量、设备、工艺参数以及工艺路线等的变化）及相关的支持性验证研究资料。提供工艺研究数据汇总表，示例如下：

工艺研究数据汇总表

批号	试制日期	试制地点	试制目的/样品用途注1	批量	收率	工艺注2	样品质量		
							含量	功能性指标	性状等

注 1：说明生产该批次的目的和样品用途，例如工艺验证/稳定性研究。

注 2：说明表中所列批次的生产工艺是否与 3.1 项下工艺一致，如不一致，应明确不同点。

Development research process
开发研究过程

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	Application requirements（申报资料要求）	Interpretation（解读）
4	**Specific tests**（特性鉴定） **4.1 Structure and physicochemical property**（结构和理化性质研究） **（1）Structural confirmation information**（结构确证信息） **Provides information that can be used to confirm the structure of pharmaceutical excipients.** 提供可用于对药用辅料的结构进行确证的相关信息。 **（2）Structural confirmation study**（结构确证研究） **The structure of the product should be analyzed in combination with the preparation route and various structural confirmation methods. For example, the problem of possible three-dimensional structure, crystal water/crystallization solvent or polymorphism should be explained in detail. For polymer pharmaceutical excipients, attention should also be paid to molecular weight and Structure confirmation information such as molecular weight distribution, degree of polymerization, and infrared spectrum. Provide the method of purification, purity, and batch number of the sample for structural confirmation; provide specific research data and maps and analyze them.** 应结合制备工艺路线以及各种结构确证手段对产品的结构进行解析，如可能含有立体结构、结晶水/结晶溶剂或者多晶型问题要详细说明，对于高分子药用辅料，还需关注分子量及分子量分布、聚合度、红外光谱等结构确证信息。提供结构确证用样品的精制方法、纯度、批号；提供具体的研究数据和图谱并进行解析。	**Combined with the preparation process route, various structural confirmation means are adopted. Focus on the three-dimensional structure, crystal water/crystallization solvent, and polymorph.** **For polymer pharmaceutical excipients: molecular weight and molecular weight distribution, degree of polymerization, infrared spectrum, and the like.** 结合制备工艺路线、采用各种结构确证手段。关注立体结构、结晶水/结晶溶剂、多晶型。 对于高分子药用辅料：分子量及分子量分布、聚合度、红外光谱等。

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	Application requirements（申报资料要求）	Interpretation（解读）
4	**In order to ensure consistency in the quality of pharmaceutical excipients derived from biological products, it is necessary to establish standards /controls or to compare excipients with their natural analogues. See ICH guidelines for biotechnology/biological products for biologic excipients.** 为了确保生物制品来源的药用辅料质量的一致性，需要建立标准品/对照品或将辅料与其天然类似物进行比较。对于生物制品类辅料具体见ICH关于生物技术/生物产品的指南。 **For premixed excipients derived from chemical synthetics or derived from animals/plants, different methods are required to describe their characteristics and to provide quantitative and qualitative descriptions, including all special information.** 对来源于化学合成体或来源于动/植物的预混辅料，需要用不同的方法描述其特性，并进行定量和定性的描述，包括所有特殊信息。	
	4.1.2 Physical and chemical properties（理化性质） **Provide research materials on auxiliary cooking properties, such as: traits (such as appearance, color, physical state), melting point or boiling point, specific rotation, solubility, hygroscopicity, solution pH, partition coefficient, dissociation constant, will be used in the production of preparations Physical form (eg polymorph, solvate or hydrate), particle size, source, etc.** 提供辅料理化性质研究资料，如：性状（如外观，颜色，物理状态）、熔点或沸点、比旋度、溶解性、吸湿性、溶液pH、分配系数、解离常数、将用于制剂生产的物理形态（如多晶型、溶剂化物或水合物）、粒度、来源等。	

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	Application requirements（申报资料要求）	Interpretation（解读）
	4.2 **Impurity** 杂质研究 4.2.1 **Impurity information**（杂质信息） **Describe the impurity conditions in combination with the excipient production process.** 结合辅料生产工艺，描述杂质情况。 **4.2.2 Impurity research**（杂质研究） **Impurities should be studied according to the molecular characteristics, sources, preparation processes, etc. of pharmaceutical excipients. For polymer excipients, the residual monomers, catalysts, and impurities from the production process should be studied. Evaluate the effects of impurities on the safety and functionality of pharmaceutical excipients and control them accordingly.** 应根据药用辅料的分子特性、来源、制备工艺等进行杂质研究，如对于高分子辅料，应重点研究残留单体、催化剂以及生产工艺带来的杂质。评估杂质对药用辅料安全性、功能性等的影响，并进行相应的控制。	
	4.3 FRCs（功能特性） **4.3.1 FRCs Information**（功能特性信息） **Combine the use of excipients in the preparation and the route of administration, and provide information on the functional indicators of the excipients (if applicable).** 结合辅料在制剂中的用途及给药途径，提供辅料有关功能性指标信息(如适用)。 **4.3.2 FRCs research**（功能特性研究） **Combined with the use of the excipients in the preparation and the route of administration, the main functional properties of the excipients are detailed and corresponding research data are provided.** 结合辅料在制剂中的用途及给药途径，详细说明该药用辅料的主要功能特性并提供相应的研究资料。	**Impurities that may be contained (including organic impurities, inorganic impurities, residual solvents and catalysts, etc.), the source of the impurities analyzed (by-products from the synthesis of raw materials, by-products produced during production, or by degradation)**

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	For example, the binder can provide applicable characteristics such as surface tension, particle size and particle size distribution, solubility, viscosity, specific surface area, and degree of accumulation. 如：粘合剂可提供表面张力、粒度及粒度分布、溶解性、粘度、比表面积、堆积度等适用的特性指标。	可能含有的杂质（包括有机杂质，无机杂质，残留溶剂和催化剂等），分析杂质的来源（合成原料带入的，生产过程中产生的副产物或者是降解产生的） **Differentiation of quality at home and abroad** 国内外质量的差异化
	5 Quality Control（质量控制）	
	5.1 Quality Standards（质量标准） Provide quality standards for pharmaceutical excipients. The quality standard shall comply with the general technical requirements and format of the current edition of the Pharmacopoeia of the People's Republic of China, and use its terminology and unit of measure. 提供药用辅料的质量标准。质量标准应当符合《中华人民共和国药典》现行版的通用技术要求和格式，并使用其术语和计量单位。	**Must meet Pharmacopoeia requirements** 必须符合药典要求
	5.2 Validation of Analytical Process（分析方法的验证） Provide methodological validation data for each of the quality standards. For the varieties currently in the Chinese Pharmacopoeia/United States Pharmacopoeia/European Pharmacopoeia/UK Pharmacopoeia/Japanese Pharmacopoeia, if the Pharmacopoeia standard method is adopted, the methodological confirmation may be carried out as appropriate. 提供质量标准中各项目的方法学验证资料。对于现行版中国药典/美国药典/欧洲药典/英国药典/日本药典已收载的品种，如采用药典标准方法，可视情况开展方法学确认。	Provide methodological validation data for each of the quality standards. For the varieties that have been included in the current version of the Chinese Pharmacopoeia, if the Pharmacopoeia standard method is adopted, the methodological confirmation may be carried out as appropriate.

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	Application requirements（申报资料要求）	Interpretation（解读）
	5.3 Quality standard Establishment basis（质量标准制定依据） Explain the considerations of each project setting, and summarize and analyze the selection of each inspection method and the basis for determining the limits. The drafting of the quality standard shall include the selection of control items in the standard, method selection, inspection, and the basis for setting the purity and limits. 说明各项目设定的考虑，总结分析各检查方法选择以及限度确定的依据。质量标准起草说明应当包括标准中控制项目的选定、方法选择、检查及纯度和限度范围等的制定依据。	Explain the considerations of each project setting, and summarize and analyze the selection of each inspection method and the basis for determining the limits 说明各项目设定的考虑，总结分析各检查方法选择以及限度确定的依据。 Technical indicators can not be lower than the pharmacopoeia 技术指标不能低于药典
6	**Lot testing**（批检验报告） Provide inspection reports for not less than three batches of production samples. If there is an item that is commissioned by an external unit, it needs to be explained. The trustee of the entrusted inspection shall have relevant qualifications. 提供不少于三批生产样品的检验报告。如果有委托外单位检验的项目需说明。委托检验的受托方需具备相关资质。	**Self-test** 可以自检 **Qualified** 有资质
7	Stability（稳定性研究）	
	Experimental data and literature on stability studies. This includes stability tests conducted in conjunction with packaging materials and containers that are in direct contact with pharmaceutical excipients. Where applicable, describe compatibility and support studies for selected packaging materials. 稳定性研究的试验资料及文献资料。包括采用直接接触药用辅料的包装材料和容器共同进行的稳定性试验。如适用，描述针对所选用包材进行的相容性和支持性研究。	

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	Application requirements（申报资料要求）	Interpretation（解读）
	7.1 Stability summary（稳定性总结） **Summarize the sample conditions, investigation conditions, investigation indicators and investigation results of the stability study conducted, analyze the trend of change, and propose storage conditions and expiration dates** 总结所进行的稳定性研究的样品情况、考察条件、考察指标和考察结果，对变化趋势进行分析，并提出贮存条件和有效期。	**Stability sample conditions, investigation conditions, investigation indicators and investigation results** **Propose packaging, storage conditions and expiration date** 稳定性样品情况、考察条件、考察指标和考察结果 提出包装、贮存条件和有效期
	7.2 Stability Data（稳定性数据） **The specific results of the stability study are provided in tabular form and the relevant maps in the stability study are attached.** 以表格形式提供稳定性研究的具体结果，并将稳定性研究中的相关图谱作为附件。	
	7.3 Packaging（辅料的包装） **Explain the packaging and selection basis of the auxiliary materials, and provide the packaging label sample.** 说明辅料的包装及选择依据，提供包装标签样稿。	
8	**Pharmacology and Toxicology Data**（药理毒理研究）	
	The pharmacological and toxicological research materials or literature materials that are generally required to be included include: 一般需提供的药理毒理研究资料或文献资料包括： **(1) Summary of pharmacological and toxicological research data.** **(2) Test data or literature on the pharmacodynamic effects of the proposed drug.** **(3) Non-clinical pharmacokinetic test data or literature.** **(4) Test data or literature on safety pharmacology.** **(5) A single dose of toxicological test data or literature.**	**New excipients, new dosage, New route of administration** 新辅料，新用量、新给药途径 **Or literature** 或者文献资料。

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Application requirements（申报资料要求）	Interpretation（解读）
(6) Repeated administration of toxicological test data or literature. **(7) Allergic (local, systemic and photosensitivity), hemolytic and local (vascular, skin, mucous membrane, muscle, etc.) irritant and other special safety test studies or literature related to local and systemic administration.** **(8) Genetic toxicity test data or literature.** **(9) Reproductive toxicity test data or literature.** **(10) Carcinogenicity test data or literature.** **(11) Other safety test data or literature.** **According to the listing status, application status and risk level of the pharmaceutical excipients, the research materials and/or literature materials to be submitted shall be determined. If a research data is not needed, it shall be explained under the corresponding research project. The pharmacological and toxicological studies of pharmaceutical excipients can be carried out separately or in combination with pharmacological and toxicological studies of rationally designed and associated preparations.** （1）药理毒理研究资料综述。 （2）对拟应用药物的药效学影响试验资料或文献资料。 （3）非临床药代动力学试验资料或文献资料。 （4）安全药理学的试验资料或文献资料。 （5）单次给药毒理性的试验资料或文献资料。 （6）重复给药毒理性的试验资料或文献资料。 （7）过敏性（局部、全身和光敏毒性）、溶血性和局部（血管、皮肤、粘膜、肌肉等）刺激性等主要与局部、全身给药相关的特殊安全性试验研究或文献资料。 （8）遗传毒性试验资料或文献资料。 （9）生殖毒性试验资料或文献资料。 （10）致癌试验资料或文献资料。 （11）其他安全性试验资料或文献资料。 根据药用辅料的上市状态、应用情况、风险程度等确定需提交的研究资料和/或文献资料，如不需要某项研究资料时，应在相应的研究项目下予以说明。药用辅料的药理毒理研究可单独进行也可通过合理设计与关联制剂的药理毒理研究合并进行。	**The pharmacological and toxicological studies of pharmaceutical excipients can be carried out separately or in combination with pharmacological and toxicological studies of rationally designed and associated preparations.** 药用辅料的药理毒理研究可单独进行也可通过合理设计与关联制剂的药理毒理研究合并进行。

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药用辅料登记资料表

资料项目	内容	1.1*	1.2*	1.3*	1.4*	2.1*	2.2*	2.3*	2.4*	3.1*	3.2*
1.	登记人基本信息	+	+	+	+	+	+	+	+	+	+
2.	辅料基本信息	+	+	+	+	+	+	+	+	+	+
3.	3.1（1）工艺综述	+	+	+	+	+	+	+			
	3.1（2）工艺详述	+	±	±	±	±	±	-			
	3.1（3）说明商业生产的分批原则、批量范围和依据	+	+	+	+	+	+	+			
	3.1（4）设备	+	+	+	+	+	+	+			
	3.2.1 关键物料控制信息	-	-	-	+	-	-	+			
	3.2.2 物料控制信息详述	+	+	+	-	+	+	-			
	3.3 关键步骤和中间体的控制	+	+	+	+	+	+	-			
	3.4.1 工艺验证性评估	-	-	-	+	+	+	+	+	+	+
	3.4.2 工艺验证	+	+	+	-	-	-	-	-	-	-
	3.5 生产工艺的开发	+	±	±	-	±	±	-	-	-	-
4.	4.1.1（1）结构确证信息	+	+	+	+	+	+	±	-	+	+
	4.1.1（2）结构确证研究	+	±	+	-	-	-	-	-	-	-
	4.1.2 理化性质	+	±	±	±	±	±	-	-	±	±
	4.2.1 杂质信息	+	+	+	+	+	+	+	+	+	+
	4.2.2 杂质研究	+	±	±	±	±	±	-	-	±	±
	4.3.1 功能特性信息	+	+	+	+	+	+	+	+	+	+
	4.3.2 功能特性研究	+	+	+	±	±	±	-	-	±	±
	5.1 质量标准	+	+	+	+	+	+	+	+	+	+

± 根据需要提供相关资料的项目

备注：*

国内外批准制剂中未有使用历史的，且

1.1 新的分子结构的辅料以及不属于第 1.2、1.3 的辅料；

1.2 由已有使用历史的辅料经简单化学结构改变（如盐基，水合物等）；

1.3 两者及两者以上已有使用历史的辅料经共处理得到的辅料；

Registration form of Pharmaceutical excipients

1.1 New molecular structure excipients and do not belong to 1.2 and 1.3

1.2 The excipients that have been used in history are changed by simple chemical structure(such as base and aquo-complex).

1.3 Excipients obtained by co-processing of two or more excipients that have been used in history.

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1.4 已有使用历史但改变给药途径的辅料。

国内外批准制剂中已有使用历史的，且

2.1 中国药典/USP/EP/BP/JP 均未收载的辅料;

2.2 USP/EP/BP/JP 已收载，但未在国内上市制剂中使用的辅料;

2.3 USP/EP/BP/JP 已收载，中国药典未收载;

2.4 中国药典已收载的辅料。

在食品或化妆品中有使用历史的辅料，且

3.1 具有食品安全国家标准的用于口服制剂的辅料；

3.2 具有化妆品国家或行业标准的用于外用制剂的辅料。

注：

（1）高风险药用辅料一般包括：动物源或人源的药用辅料；用于注射剂、眼用制剂、吸入制剂等的药用辅料。对于高风险辅料的登记资料要求，可根据辅料在特定制剂中的应用以及相应的技术要求，按需提供，或在审评过程中根据特定制剂及辅料在制剂中的应用情况根据需要补充资料。

（2）对于已有使用历史的辅料，若该辅料超出相应给药途径的历史最大使用量，应提供相关安全性数据等资料。

（3）对预混辅料，应根据其在制剂中的应用及配方组成中各辅料成分情况，选择合适的资料要求进行登记。

（4）国家食品药品监督管理总局 134 号公告及其解读中已规定不纳入关联审评审批的药用辅料，仍不纳入药用辅料登记的范围。

（5）以上登记资料分类要求作为登记人资料准备的指导，药品审评中心可根据制剂的技术审评需要提出资料补充要求。

（6）根据辅料分类不同，登记资料 3.2.1 与 3.2.2，3.4.1 与 3.4.2，4.1.1(1)与（2）中提供一组研究资料即可。

2.1 Pharmaceutical excipients are not collected in Ch.P/USP/EP/BP/JP.

2.2 Pharmaceutical excipients have been collected in USP/EP/BP/JP, but not used in domestic marketed preparations.

2.3 Pharmaceutical excipients have been collected in USP/EP/BP/JP, but not in Ch.P.

2.4 Pharmaceutical excipients have been collected in Ch.P.

The Review and Approval of pharmaceutical excipients

is a new system that strengthens the safety supervision of excipients and simplifies the testing and approval items. The implementation of the joint review system for pharmaceutical excipients plays an important role in promoting the quality supervision of pharmaceutical excipients in China.

药用辅料共同审评制度是加强药用辅料安全监管，简化审批事项的时代要求碰撞产生的新的制度。药用辅料共同审评制度的推行实施对我国药用辅料质量监管的完善具有重要的推动作用。

Drug safety is an insurmountable baseline!

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Thank You !

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