康利华咨询
A Tigermed Company

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药政法规更新摘要

目錄

法规要闻

CDE 更新 PDF 文件批量电子签章软件

1 月 3 日，国家药监局药审中心发布《关于更新 PDF 文件批量电子签章软件的通知》。更新内容主要包括：

a. 增加了对于单个 PDF 文件的电子签章功能。申请人在使用签章软件时，可打开预览单个 PDF 文件，并自定义设置签章在文件中的具体位置和页码；
b. 增加了在批量文件签章和校验签章过程中，申请人可随时手动终止执行操作的功能；
c. 优化了签章状态显示内容，在批量文件签章和校验签章过程中，申请人可实时查看每个 PDF 文件的执行状态；
d. 增加了批量签章文件数量和文件大小的建议值提示信息显示功能；
e. 优化了校验签章速度慢问题和多次签章后验章失败问题。

NMPA 印发进一步加强中药科学监管促进中药传承创新发展若干措施的通知

1 月 4 日，国家药监局印发《关于进一步加强中药科学监管促进中药传承创新发展若干措施的通知》（国药监药注〔2023〕1 号），以期全面加强中药全产业链质量管理、全过程审评审批加速、全生命周期产品服务、全球化监管合作、全方位监管科学创新，向纵深推进中国式现代化药品监管实践和具有中国特色的中药科学监管体系建设。全文从九大方面三十五项措施阐述了加强中药科学监管促进中药传承创新发展的举措，分别为：

一、加强中药材质量管理
二、强化中药饮片、中药配方颗粒监管
三、优化医疗机构中药制剂管理
四、完善中药审评审批机制
五、重视中药上市后管理
六、提升中药标准管理水平
七、加大中药安全监管力度
八、推进中药监管全球化合作
九、保障措施

五部门联合发布《药品行政执法与刑事司法衔接工作办法》

1 月 18 日，国家药品监督管理局 国家市场监督管理总局 公安部 最高人民法院 最高人民检察院联合发布了《药品行政执法与刑事司法衔接工作办法》（国药监法〔2022〕41 号），自 2023 年 2 月 1 日起施行。《食品药品行政执法与刑事司法衔接工作办法》（食药监稽〔2015〕271 号）中有关规定与新办法不一致的，以新办法为准。

NMPA 发布《药物非临床研究质量管理规范认证管理办法》

1 月 19 日，国家药监局发布《药物非临床研究质量管理规范认证管理办法》的公告（2023 年第 15 号），于 2023 年 7 月 1 日施行。

国家药监局综合司 国家卫生健康委办公厅发布关于加快推进注射用 A 型肉毒毒素追溯体系建设工作的通知

1 月 19 日，国家药监局综合司 国家卫生健康委办公厅发布《关于加快推进注射用 A 型肉毒毒素追溯体系建设工作的通知》（药监综药管〔2023〕3 号），有关事宜如下：

一、**药品上市许可持有人、进口药品境内代理人**应当按照药品信息化追溯体系建设标准要求，于 2023 年 2 月 28 日前完成对各级销售包装单元的赋码，通过自建追溯系统或使用第三方追溯系统开展追溯数据的采集和上传。在销售注射用 A 型肉毒毒素时，应通过追溯系统向下游企业提供相关追溯信息。要采取合同约定等方式要求下游企业按规定开展追溯，并及时向追溯系统上传追溯信息。

二、**药品经营企业**应当于 2023 年 3 月 31 日前在追溯系统中完成基础信息的维护，并对追溯数据进行采集与上传。在采购注射用 A 型肉毒毒素时，应通过追溯系统向上游企业索取相关追溯信息，在验收时进行核对，并将核对信息通过追溯系统反馈上游企业。在销售注射用 A 型肉毒毒素时，应通过追溯系统向下游企业或使用单位提供相关追溯信息。

三、**使用单位**应当于 2023 年 5 月 31 日前在追溯系统中完成基础信息的维护，及时采集并上传追溯数据。在采购注射用 A 型肉毒毒素时，应通过追溯系统向上游企业索取相关追溯信息，在验收时进行核对，并将核对信息通过追溯系统反馈上游企业。在使用注射用 A 型肉毒毒素时，应及时在追溯系统更新已使用的注射用 A 型肉毒毒素的状态，保障已使用的注射用 A 型肉毒毒素能通过追溯码关联到使用人。

四、**药品上市许可持有人、进口药品境内代理人建设的追溯系统**应满足国家网络安全和数据安全有关规定，并具备为监管方提供追溯数据查询的功能。追溯数据谁产生谁所有，药品上市许可持有人、进口药品境内代理人、生产企业、经营企业和使用单位应和追溯系统运营单位对追溯数据的安全和使用进行约定，未经数据所有方授权，其他各方不得泄露和使用。

五、**各级药品监督管理部门、卫生健康部门**要严格落实属地监管责任，加强对本辖区注射用 A 型肉毒毒素持有人、进口药品境内代理人、药品经营企业和使用单位的行政指导和监督检查，督促落实追溯责任，将追溯系统建设、追溯信息上传、追溯责任落实纳入日常监督检查范畴，确保追溯工作顺利开展。对未按规定建立并实施药品追溯制度的，应按照《中华人民共和国药品管理法》有关规定严肃处理。

备注：

1) *2008 年 7 月 21 日，国家食品药品监督管理局、中华人民共和国卫生部发布了《关于将 A 型肉毒毒素列入毒性药品管理的通知》（国食药监办[2008]405 号），要求各级卫生行政部门、食品药品监督管理部门应当严格按照《医疗用毒性药品管理办法》和通知要求，采取有效措施，切实强化对 A 型肉毒毒素及其制剂生产、经营和使用的监督管理，对非法生产、经营和使用 A 型肉毒毒素的单位和个人，依法严厉查处。*

2) *2016 年 7 月 8 日，食品药品监管总局办公厅发布了《总局办公厅关于加强注射用 A 型肉毒毒素管理的通知》（食药监办药化监〔2016〕88 号），要求各级食品药品监管部门要加大对行政区域内药品生产经营企业的监督力度，督促其严格按照《医疗用毒性药品管理办法》（国务院令第 23 号）和原国家食品药品监督管理局、原卫生部《关于将 A 型肉毒毒素列入毒性药品管理的通知》（国食药监办〔2008〕405 号）相关要求，自觉依法依规生产经营。*

CDE 发布《慢性淋巴细胞白血病新药临床研发技术指导原则》

1 月 19 日，国家药监局药审中心发布《慢性淋巴细胞白血病新药临床研发技术指导原则》（2023 年第 1 号），自发布之日起施行。

NMPA 发布关于适用《Q3D（R2）：元素杂质》《M10：生物分析方法验证及样品分析》国际人用药品注册技术协调会指导原则的公告

1 月 29 日，国家药监局发布了《关于适用<Q3D（R2）：元素杂质><M10：生物分析方法验证及样品分析>国际人用药品注册技术协调会指导原则的公告》（2023 年第 16 号）。公告中的有关事项如下：

一、申请人需在现行药学研究技术要求基础上，按照 Q3D（R2）指导原则的要求开展研究；自 2023 年 7 月 29 日起开始的相关研究（以试验记录时间点为准），均适用 Q3D（R2）指导原则，Q3D（R1）指导原则同时停止实施。

二、申请人需按照 M10 指导原则的要求开展研究；自 2023 年 7 月 29 日起开始的相关研究（以生物样品分析原始记录时间点为准），均适用 M10 指导原则。

三、相关技术指导原则可在国家药品监督管理局药品审评中心网站查询。国家药品监督管理局药品审评中心负责做好本公告实施过程中的相关技术指导工作。

备注（ICH Guidelines 实施阶段回顾）：

- *Step 1: Consensus Building – Technical Document*
- *Step 2a: Confirmation of consensus on the Technical Document*
- *Step 2b: Adoption of the Draft Guideline*
- *Step 3: Regulatory Consultation and Discussion*
- *Step 4: Adoption of an ICH Harmonised Guideline*
- *Step 5: Implementation*

征求意见稿-CDE

1 月 3 日，国家药监局药审中心发布《2 型糖尿病口服药物复方制剂研发指导原则（征求意见稿）》，征求意见时限为自发布之日起 1 个月。

1 月 6 日，国家药监局药审中心发布《中药改良型新药研究技术指导原则（征求意见稿）》，征求意见时限为自发布之日起 1 个月。

1 月 29 日，国家药监局药审中心发布《eCTD 实施指南 V1.1（征求意见稿）》及《eCTD 验证标准 V1.1（征求意见稿）》，征求意见时限为自发布之日起 1 个月。与《eCTD 实施指南

V1.0》(以下简称《实施指南》)及《eCTD 验证标准 V1.0》(以下简称《验证标准》)对比，主要修订内容如下：

一、删除《实施指南》2.8 章节关于纸质资料的递交要求；

二、删除《实施指南》4.1.2 章节和附件说明函中关于纸质资料的相关内容，包括“关于纸质资料与 eCTD 申报资料内容一致的承诺”和“关于按规定时限一次性提交全部纸质申报资料的承诺；

三、修改《实施指南》7.6 章节关于文件大小的要求，将单个 PDF 文件应控制在 500MB 以内修改为 200MB 以内；

四、对《验证标准》相对应部分进行了修订。

法规指南更新

《药品行政执法与刑事司法衔接工作办法》（摘自 NMPA）

国家药监局、市场监管总局、公安部、最高人民法院、最高人民检察院联合印发了《药品行政执法与刑事司法衔接工作办法》(以下简称《办法》）。《办法》自 2023 年 2 月 1 日起施行。

2022 年，为了深入贯彻落实习近平总书记重要指示和党中央、国务院决策部署，加快完善药品行政执法与刑事司法衔接工作机制，严厉打击危害药品安全违法犯罪行为，国家药监局、市场监管总局、公安部、最高人民法院、最高人民检察院等部门将出台《办法》纳入落实药品安全专项整治工作的重点任务清单。国家药监局作为牵头部门，在 2021 年研究工作的基础上，持续推动修订工作进程，会同市场监管总局、公安部、最高人民法院、最高人民检察院等部门，对原食品药品监督管理总局、公安部等 5 部门联合印发的《食品药品行政执法与刑事司法衔接工作办法》进行了修改，组织研究起草了《办法》。各部门通力合作，深入调查研究、广泛征求意见、反复研究论证，达成一致意见，顺利联合印发《办法》，圆满完成药品安全专项整治工作任务。

《办法》的制定和发布，强化多部门联合查处大案要案，加强对药品行刑衔接工作规范和指导，优化行刑衔接流程，将更好地推进“两法两条例”、《刑法修正案（十一）》和“两高”《关于办理危害药品安全刑事案件适用法律若干问题的解释》的落地实施，严厉打击药品领域违法犯罪行为，切实维护人民群众生命安全和身体健康，有力助推药品安全专项整治工作取得实效。

《办法》共六章四十六条，重点在五个方面对行刑衔接工作进行了完善。

一是明确了药品监管部门、公安机关、人民检察院、人民法院等各部门的职责边界。增加药品监管部门移送案件的具体职责，明确公安机关案件受理审查、执法联动的职责，强调检察院对药品监管部门移送涉嫌犯罪案件活动和公安机关有关立案侦查活动履行监督责任，增加人民法院对财产刑和从业限制的判罚，提高法律震慑力。

二是完善了案件移送的条件、时限和移送监督，明确了公安机关、检察机关反向移送要求，对衔接工作流程、程序和时间、材料要求等方面作出更加具体的规定，增强可操作性。

三是规范了涉案物品检验、认定、移送、保管和处置程序。规定药监部门应当设立检验检测绿色通道，积极协助公安、司法机关提供涉嫌犯罪案件涉案物品的检验结论和认定意见。与新修订的危害药品安全“两高”司法解释相衔接，完善了涉案物品认定结论。明确了涉案物品移交、保管和处置程序，规定案件移送的同时移交涉案物品。对因客观条件所限或对保管、处置有特殊要求的涉案物品，公安机关可以与药品监管部门签订涉案物品委托保管协议，委托药品监管部门代为保管和处置。相关保管、处置等费用有困难的，由药品监管部门会同公安机关等部门报请本级人民政府解决。

四是强化了协作配合与督办。各部门应推动建立地区间、部门间药品案件查办联动机制，通报案件办理工作情况，建立双向案件咨询制度。明确了公安机关提前介入、加强执法联动的责任，药监部门在工作中发现明显涉嫌犯罪的线索，应当立即通报，同级公安机关应当及时进行审查，必要时进行调查核实。对药监部门查处、移送案件过程中，发现行为人可能存在逃匿或者转移、灭失、销毁证据等情形的，应当由公安机关协助采取紧急措施，必要时和药品监管部门协同加快移送进度，依法采取紧急措施予以处置。

五是加强信息共享和通报。强调各部门应通过行政执法与刑事司法衔接信息共享平台，逐步实现涉嫌犯罪案件网上移送、网上受理、网上监督。《办法》还依据新修订的法律、法规和国务院文件，增加了行政拘留的衔接、行政处罚与刑事处罚的衔接、行纪衔接等条款，明确有关部门的分工与职责。

国家药监局、市场监管总局、公安部、最高人民法院、最高人民检察院将指导各省、自治区、直辖市药监局、市场监管局、公安厅（局）、高级人民法院、人民检察院贯彻落实相关法律、法规、国务院文件和《办法》规定，充分发挥行刑衔接工作机制的作用，加大对药品领域违法犯罪行为的打击力度，严防严管严控药品安全风险，切实保障人民群众用药用械用妆安全。

技术总结

欧盟注册要求的 QP 出具的 GMP 符合性声明出处

临床试验申请（REGULATION (EU) No 536/2014 Annex 1）

F. DOCUMENTATION RELATING TO COMPLIANCE WITH GOOD MANUFACTURING PRACTICE (GMP) FOR THE INVESTIGATIONAL MEDICINAL PRODUCT

31. As regards documentation relating to GMP compliance, the following shall apply.

32. No documentation needs to be submitted where the investigational medicinal product is authorised and is not modified, whether or not it is manufactured in the Union.

33. If the investigational medicinal product is not authorised, and does not have a marketing authorisation from a third country that is party to the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), and is not manufactured in the Union, the following documentation shall be submitted:

(a) a copy of the authorisation referred to in Article 61; and

(b) certification by the qualified person in the Union that the manufacturing complies with GMP at least equivalent to the GMP in the Union, unless there are specific arrangements provided for in mutual recognition agreements between the Union and third countries.

34. In all other cases, a copy of the authorisation referred to in Article 61 shall be submitted.

35. For processes related to investigational medicinal products set out in Article 61(5), which are not subject to an authorisation in accordance with Article 61, documentation to demonstrate compliance with the requirements referred to in Article 61(6) shall be submitted.

备注：临床试验申请时需要提交 QP 对制剂生产场地的 GMP 符合性声明。

Third Country = outside of the EU/EEA

上市许可申请

Directive 2001/83/EC、Directive 2011/62/EU

▶M11	Directive 2011/62/EU of the European Parliament and of the Council of 8 June 2011	L 174	74	1.7.2011

Article 8

▼M11

(ha) A written confirmation that the manufacturer of the medicinal product has verified compliance of the manufacturer of the active substance with principles and guidelines of good manufacturing practice by conducting audits, in accordance with point (f) of Article 46. The written confirmation shall contain a reference to the date of the audit and a declaration that the outcome of the audit confirms that the manufacturing complies with the principles and guidelines of good manufacturing practice.

Article 46

▼M11

(f) to comply with the principles and guidelines of good manufacturing practice for medicinal products and to use only active substances, which have been manufactured in accordance with good manufacturing practice for active substances and distributed in accordance with good distribution practices for active substances. To this end, the holder of the manufacturing authorisation shall verify compliance by the manufacturer and distributors of active substances with good manufacturing practice and good distribution practices by conducting audits at the manufacturing and distribution sites of the manufacturer and distributors of active substances. The holder of the manufacturing authorisation shall verify such compliance either by himself or, without prejudice to his responsibility as provided for in this Directive, through an entity acting on his behalf under a contract.

The holder of the manufacturing authorisation shall ensure that the excipients are suitable for use in medicinal products by ascertaining what the appropriate good manufacturing practice is. This shall be ascertained on the basis of a formalised risk assessment in accordance with the applicable guidelines referred to in the fifth paragraph of Article 47. Such risk assessment shall take into account requirements under other appropriate quality systems as well as the source and intended use of the excipients and previous instances of quality defects. The holder of the manufacturing authorisation shall ensure that the appropriate good manufacturing practice so ascertained, is applied. The holder of the manufacturing authorisation shall document the measures taken under this paragraph;

Module 1.2 Application form Annex

☐5.22 For each active substance, attach a declaration(s) from the Qualified Person of the manufacturing authorisation holder in Section 2.5.1 and from the Qualified Person of each of the manufacturing authorisation holders (i.e. located in EEA) listed in Section 2.5.2 where the active substance is used as a starting material that the active substance is manufactured in compliance with the principles and guidelines of good manufacturing practice for starting materials. Alternatively, such declaration may be signed by one Qualified Person on behalf of all QPs involved (provided this is clearly indicated). The declaration should refer to an audit and the date of the audit.

备注：上市许可申请时需要提交 QP 对 active substance 生产场地的 GMP 符合性声明。

EMA/196292/2014 Guidance for the template for the qualified person's declaration concerning GMP compliance of active substance manufacture "The QP declaration template"

Scope

With respect to the application of GMP for products for human use, ICH Q11[9], states, *"Each branch of a convergent drug substance manufacturing process begins with one or more starting materials. The GMP provisions described in ICH Q7 apply to each branch beginning with the first use of a starting material. Performing manufacturing steps under GMP together with an appropriate control strategy provides assurance of quality of the drug substance."*

The GMP Basic Requirements for Active Substances used as Starting Materials[2] apply to each branch beginning with the first use of the starting material(s) (as designated in the quality module / section of the regulatory submission) at all active substance manufacturing sites, including intermediate sites.

For active substances for biological medicinal products, reference should be made to volume 4 GMP Guidelines including Annex 2 "Manufacture of biological active substances and medicinal products for human use" and Annex 5 "Manufacture of immunological veterinary medicinal products."

For chemically synthesised active substances, it is acknowledged that details of the suppliers of designated starting materials may be confidential. Their suitability should be assessed indirectly by audit of the active substance manufacturer's quality system for starting materials.

化学原料药和生物制品原液均需提交 QP 的 GMP 符合性声明。分别按照 Part II 和附录 2（人用药）、附录 5（免疫类兽药）进行审计。

3. Application of the QP declaration

The QP declaration applies to all human and veterinary medicinal products.

A QP declaration is required to be submitted with all applications for new marketing authorisations, renewals and submissions of relevant quality variations, concerning changes (addition or replacement) to the manufacturer of a starting material and / or to the registered manufacturer(s) of the active substance, finished product or batch importation/certification sites[1]. This is irrespective of the means by which the data requirements for the active substance are met – by either EDQM Certificate of Suitability (CEP), Active Substance Master File (ASMF) or full details in the dossier.

If site changes are introduced during the regulatory review procedure, then a new declaration will need to be provided.

The QP declaration is not required:

- (a) for blood or blood components; these are not medicinal product and are subject to the requirements of Directive 2002/98/EC[10];
- (b) from MIAH sites that do not use the active substance as a starting material, e.g. packaging only sites, quality control testing sites.

QP 声明适用于所有的人用药品和兽用药品。

递交变更时也需要提交 QP 声明。

关于产品出口欧盟放行检验问题的汇总

一 放行检验

以下选择的是与产品输出到欧盟相关的内容，欧盟境内的要求没有摘录。

Directive 2001/83/EC 2012 整合版
TITLE IV MANUFACTURE AND IMPORTATION

Article 51，1（b）

1. Member States shall take all appropriate measures to ensure that the qualified person referred to in Article 48, without prejudice to his relationship with the holder of the manufacturing authorization, is responsible, in the context of the procedures referred to in Article 52, for securing:

(b) in the case of medicinal products coming from third countries, irrespective of whether the product has been manufactured in the Community, that each production batch has undergone in a Member State a full qualitative analysis, a quantitative analysis of at least all the active substances and all the other tests or checks necessary to ensure the quality of medicinal products in accordance with the requirements of the marketing authorisation.

Article 51，2

2. In the case of medicinal products imported from a third country, where appropriate arrangements have been made by the Community with the exporting country to ensure that the manufacturer of the medicinal product applies standards of good manufacturing practice at least equivalent to those laid down by the Community, and to ensure that the controls referred to under point (b) of the first subparagraph of paragraph 1 have been carried out in the exporting country, the qualified person may be relieved of responsibility for carrying out those controls.

EU GMP ANNEX 16 Certification by a Qualified Person and Batch Release-2015 年

注：在 ANNEX16 里出现了 Marketing Authorisation 和 Manufacturing Authorisation，其缩写在该附录里分别为 MA 和 MIA.

1. THE PROCESS OF CERTIFICATION

1.1 1.1. Each batch of finished product must be certified[2] by a QP within the EU before being released for sale or supply in the EU or for export. Certification can only be performed by a QP of the manufacturer and/or importer which are described in the MA.

1.5 1.5 For medicinal products manufactured outside the EU, physical importation and certification are the final stages of manufacturing which precede the transfer to saleable stock of the batch.

1.5.4 1.5.4 The QP certifying the finished product is responsible for ensuring that each finished medicinal product batch has been manufactured in accordance with GMP and the MA. Unless an MRA or similar agreement is in place between the EU and the exporting country, the QP is also responsible for ensuring that the finished medicinal product batch has undergone in a Member State a full qualitative analysis, a quantitative analysis of at least all the active substances and all the other tests or checks necessary to ensure the quality of medicinal products is in accordance with the requirements of the MA.

简译 每个成品批次在 EU 境内放行销售或供应或出口前，必须由 EU 境内的 QP 进行证明。证明只能由 MA 中规定的生产商和/或进口商的 QP 进行。进行成品证明的 QP 有责任确保每批成品均根据 GMP 和 MA 进行生产。除非 EU 和出口国之间有 MRA 或类似的协议，否则 QP 还有责任确保成品批次已经在成员国接受至少针对所有原

EU GMP ANNEX 16 Certification by a Qualified Person and Batch Release-2015 年

料药的全部定性分析、定量分析以及确保药品质量符合 MA 要求所必须的所有其他检验或检查。

结论：

- 根据上述引用的法规和 GMP 条款，如果产品出口欧盟，需欧盟境内的 QP 放行且在产品放行前需要在欧盟成员国内进行检验。
- 如果是临床试验药品出口至欧盟，则未从 EU/EEA 层面强制 IMPs 进行欧盟境内的检验，但 QP 是必须具备的，具体内容参见 COMMISSION DELEGATED REGULATION (EU) 2017/1569 和 EU GMP 附录 16。

二 取样

EU GMP ANNEX 16 Certification by a Qualified Person and Batch Release-2015 年

1.5.3 1.5.3 Conditions of storage and transport for the batch and the sample, if sent separately, should be taken into account by the QP before certification of a batch.

简译 如果批次与样品分开发送，QP 发放批证明之前应考虑批产品与样品的储存和运输条件。

1.5.5 1.5.5 Sampling of imported product should be fully representative of the batch. Samples may either be taken after arrival in the EU, or be taken at the manufacturing site in the third country in accordance with a technically justified approach which is documented within the company's quality system. Responsibilities in relation to the sampling should be defined in a written agreement between the sites. Any samples taken outside the EU should be shipped under equivalent transport conditions as the batch that they represent.

简译 进口药品的取样应能够代表批产品。样品可以在到达 EU 之后取样，或在第三国生产场所根据公司质量体系书面规定的经过技术论证的方法取样。与取样有关的职责应通过场所之间的书面协议进行规定。所有在 EU 境外取得样品均应在其所代表批次等同的运输条件下发运。

1.5.6 1.5.6 Where sampling is performed at a third country manufacturing site, the technical justification should include a formal Quality Risk Management process to identify and manage any risks associated with this approach. This should be fully documented and include at least the following elements:

i. Audit of the manufacturing activity including any sampling activity at the third country site and evaluation of subsequent transportation steps of both the batch and samples to ensure that the samples are representative of the imported batch.

ii. A comprehensive scientific study, including data to support any conclusions that samples taken in the third country are representative of the batch after importation. This study should at least include:

- Description of the sampling process in the third country.
- Description of the transported conditions of the sample and the imported batch. Any differences should be justified.
- Comparative analysis of samples taken in the third country and samples taken after importation.
- Consideration of the time interval between sampling and importation of the batch and generation of data to support appropriate defined limits.

iii. Provision for random periodic analysis of samples taken after importation to justify ongoing reliance on samples taken in a third country.

iv. A review of any unexpected result or confirmed out of specification result. These may have implications for reliance on sampling performed at the third country manufacturing site and should be notified to the Supervisory Authority for the site where certification is performed. Such an occurrence should be regarded as a potential quality defect and investigated in line with the guidance in Chapter 8 of EudraLex, Volume 4, Part I.

简译 如果取样是在第三国场所进行的，技术性论证应包括正式的质量风险管理程序，以识别和管理与该方法相关的全部风险。该程序应全面记录并至少包括以下要素：

i. 生产活动的审计，包括所有在第三国场所进行的取样活动，以及对批产品和样品随后运输步骤的评价，以确保样品能代表被进口的批次。

ii. 全面的科学研究，包括支持在第三国所取样品能够代表进口后批产品的所有结论的数据，该研究至少应包括：

- 第三国取样的描述。
- 样品和进口批次运输条件的描述。如有差异应进行论证。
- 在第三国所取样品与进口后所取样品的对比分析。
- 对取样和批产品进口的时间间隔进行考虑，并由数据支持被恰当定义的限度。

iii. 进口后取样的随机周期检测条款，可以证明在第三国取样持续的可靠性。

iv. 对非预期结果或确认的超标结果的审核。这些结果可能对第三国生产场所进行的取样活动的可靠性产生影响，应当向监管机构报告出具证明的场所。这种情况的发生应作为潜在的质量缺陷，根据欧盟药品法规第四卷第 I 部分第 8 章中的指南进行调查。

结论：取样可以在进口至 EU 后进行也可在第三国生产场所进行。如果在第三国生产场所进行，企业需要做上述的工作来证明取样和运输的等同性。

三、关于兽药的上市许可和批放行

法规依据是 REGULATION (EU) 2019/6，取代了 Directive 2001/82/EC.

GMP 与人用药相同，关于 QP 放行的 ANNEX 16 Certification by a Qualified Person and Batch Release 同样适用。

1. 上市许可

Article 5

Marketing authorisations

1. A veterinary medicinal product shall be placed on the market only when a competent authority or the Commission, as applicable, has granted a marketing authorisation for that product in accordance with Article 44, 47, 49, 52, 53 or 54.

2. A marketing authorisation for a veterinary medicinal product shall be valid for an unlimited period of time.

3. Decisions to grant, refuse, suspend, revoke or amend by way of a variation a marketing authorisation shall be made public.

4. A marketing authorisation for a veterinary medicinal product shall only be granted to an applicant established in the Union. The requirement to be established in the Union shall also apply to marketing authorisation holders.

上市许可仅颁发给欧盟境内的申请人。MAH 也要求为处于欧盟境内。

2. 批放行

Article 97

Qualified person responsible for manufacturing and batch release

1. The holder of a manufacturing authorisation shall have permanently at its disposal the services of at least one qualified person who fulfils the conditions laid down in this Article and is responsible, in particular, for carrying out the duties specified in this Article.

7. Where veterinary medicinal products are imported, the qualified person referred to in paragraph 1 shall ensure that each imported production batch has undergone in the Union a full qualitative and a quantitative analysis of at least all the active substances, and all the other tests necessary to ensure the quality of the veterinary medicinal products in accordance with the requirements of the marketing authorisation and that the batch manufactured is in compliance with good manufacturing practice.

QP 应确保进口兽药在欧盟境内完成检验，确保产品质量符合 MA、批生产符合 GMP。

EMA GMP&GDP Q&A 节选

Canny 康利华咨询
A Tigermed Company

GDP requirements (Updated Jan 2023)

Expand section Collapse section

1. Is it acceptable that storage conditions are not monitored for medicinal products which do not have any predefined storage conditions on the outer packaging?

No. According to the Guideline on declaration of storage conditions (CPMP/QWP/609/96 Rev. 2) , marketing authorisation holders have to provide **stability data** for storage conditions at 25°C / 60% relative humidity (RH), or 30°C / 65% RH (long term) and 40°C / 75% RH (accelerated), in order to justify not including a statement in the medicinal product labelling.

This stability data is generated according to the temperature and humidity conditions of climate zone I (temperate) and II (Mediterranean/subtropical) in Europe. For more information, see the World Health Organization Expert Committee on Specifications for Pharmaceutical Preparations forty-third report, Annex 2: Stability testing of active pharmaceutical ingredients and finished pharmaceutical products .

No labelling statement means that controls should be in place to maintain conditions relevant to climate zones I and II. Consequently, the **temperature should be monitored** during storage and transport. Appropriate limits should be set for temperature monitoring to ensure that product stability is not adversely affected.

从红框标注的意思来看，如果没有标注储存条件，则意味着应当按照气候带 I 和 II 来控制。按照国际气候带的划分（ChP 2020 第四部 通则 9001）

表 国际气候带

气候带	计算数据				推算数据
	温度①/℃	MKT②/℃	RH/%	温度/℃	RH/%
Ⅰ温带	20.0	20.0	42	21	45
Ⅱ地中海气候、亚热带	21.6	22.0	52	25	60
Ⅲ干热带	26.4	27.9	35	30	35
Ⅳ湿热带	26.7	27.4	76	30	70

因此如果不在标签上标注储存条件，会被欧盟方要求按照欧洲药典中的室温 15-25℃要求，监测、控制和验证应按此条件开展。

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