



European Directorate for the
Quality of Medicines & HealthCare

Certification of Substances Division



HB/CB

PUBLIC DOCUMENT
(Level 1)

English/Chinese

PA/PH/CEP (04) 2 3R

Strasbourg, May 2008

Certification of suitability to Monographs of the European Pharmacopoeia
欧洲药典适用性证书

**Guideline on Requirements for Revision/Renewal of Certificates
of Suitability to the European Pharmacopoeia monographs**
欧洲药典CEP证书修订/更新规定的指南

GUIDELINE ON REQUIREMENTS FOR REVISION/RENEWAL OF CERTIFICATES OF SUITABILITY TO THE EUROPEAN PHARMACOPOEIA MONOGRAPHS

欧洲药典CEP证书修订/更新规定指南

Date of implementation: 1 July 2008

执行日期：2008年7月1日

Introduction:

This guideline is revised to split the minor revision R3 and to clarify several other points.

引言

本版本将微小变更R3进行了分类并澄清了其他问题

The holder of Certificate of suitability shall inform the EDQM of any change in the information included in the certification dossier by sending an application form and all necessary documents demonstrating that the conditions laid down in the present guideline are met.

欧洲药典适用性证书持有人必须向EDQM报告所有与申报文件有关的变更，申报时应填写申请表格和所有必要的资料，证明变更符合以下指南的规定。

Classification of changes 变更分类

The changes have been classified in three categories (notification/minor/major) depending on the potential impact of the change on the quality of the final substance. These three categories are based on those (IA/IB/II) of the Commission Regulation (EC) No 1084/2003 concerning the examination of variations to the terms of marketing authorization for medicinal products for human use and veterinary medicinal products granted by a competent authority of a Member State and the Commission Regulation (EC) No 1085/2003 concerning the examination of variations to the terms of a marketing authorization for medicinal products for human use and veterinary medicinal products falling within the scope of Council Regulation (EEC) No 2309/93.

根据变更可能对最终产品产生的影响程度，变更分为三类（通知/微小/重大）。分类原则是根据EC法规1084/2003（IA/IB/II）：EC成员国审核人用和兽用制剂销售许可证变更规定、和EC法规1085/2003：欧洲议会法规（EEC）2309/93范围内审核人用和兽用制剂销售许可证变更规定。

Any change not classified as a notification or a minor change should be classified as a major change except in the following cases where a new application should be submitted:

所有未划为通知或者微小变更都是重大变更，但以下情形必须按新证书申请办理：

- addition of a new route of synthesis and/or a new manufacturing site where the specifications of the final substance are different
- transfer to a new holder that is not the same legal entity as the current one, where the transfer does not occur because of a merger or because the company is sold, and where the manufacturer does not take out the Certificate of suitability in their own name.
- 增加新合成途径或新生产场地，而且成品质量标准发生变化。
- 持有人转让，新持有人与现行法人不同，这种转让不是公司合并、出售的结果，生产厂也没有以自己名义获取原有证书。

The changes related to Ph. Eur. monograph revisions or any other regulatory requirements are treated separately and generally initiated by the EDQM.

欧洲药典修订或其它法规要求而产生的变更另论，通常由EDQM发起。

Documentation to be provided 需要申报的文件

For any change the documentation should consists in:

- a description and a justification of the change
- the application form duly filled in and enclosing a comparative list of updated sections /pages of the dossier
- the specific documents described below for each change

所有变更的申报文件必须包括以下内容：

- 变动内容并说明变动的合理性
- 填写的正式申请表格，并附上申报文件变动后的章节/页面内容
- 下述各种变动所要求的具体文件

Each time batch data are needed:

- they should be in accordance with the specifications of the current Ph. Eur. monograph and when relevant with the additional requirements included in the Certificate of suitability.
- the manufacturing site, the manufacturing date and the size of the batches should be specified.
- quantitative results should be presented numerically (i.e. not in general terms such as “complies”) and with the appropriate number of decimal places.

所有变更都需要申报批分析数据：

- 而且必须现行欧洲药典标准、以及CEP证书附加的有关要求。
- 必须说明生产场地、生产日期和生产批量。
- 应以数字形式表示定量结果（即：不得笼统表达为“合格”等），数位应合理。

The changes are presented in five sections:

Notifications (N)

Minor revisions for Certificates of suitability for chemical purity and microbiological quality (R) and minor revisions for TSE Certificates of suitability (T)

Major revisions

Renewals

Transfer of holdership

以下分五节讨论各种变更情况：

通知（N）

化学微生物质量（R）的CEP证书和TSE证书微小变动（T）

重大变动

更新

证书持有人转让

NOTIFICATIONS (N) 通知 (N)

N1) Change in the name and/or address of the certificate holder or the manufacturer of the final substance 证书持有人或生产厂原名原址变更

Conditions:

- the certificate holder/manufacturer shall remain the same legal entity (except where the company is sold or in case of a merger).

Documentation:

- a formal document from a relevant official body (e.g. Chamber of Commerce) in which the new name or the new address is mentioned
- all updated declarations (see application form)

条件:

- 证书持有人/生产法人地位不变（公司出让或被兼并除外）。

文件要求:

- 官方出具（如：商会）的有关新名称和新地址的正式文件
- 更新所有声明（见申请表）

N2) Change in the name and/or address of the manufacturing site 生产场所名称或地址改变
--

Conditions: the location of the manufacturing site shall remain the same.

Documentation:

- a formal document from a relevant official body (e.g. Chamber of Commerce) in which the new name or the new address is mentioned
- updated declarations of manufacture in accordance with the dossier and according to GMP rules and of willingness to be inspected

条件：生产场所具体位置应保持不变。

文件要求:

- 官方出具（如：商会）的有关新名称和新地址的正式文件
- 声明更新：按申报文件组织生产、GMP声明或愿意接受检查的声明

N3) Deletion of any manufacturing site
取消生产场所

Conditions: none

Documentation : none apart from a justification of the deletion

条件： 无

文件要求： 无。但必须证明取消的合理性。

N4) Deletion of a manufacturing of any intermediate/starting material
取消中间体/起始物质的生产

Conditions: none

Documentation : none apart from a justification of the deletion

条件： 无

文件要求： 无，但必须证明取消的合理性。

N5) Change in batch size of final substance or intermediate up to 10-fold compared to the original batch size.
成品或中间体批量变动，但不超过原批量10倍

Conditions:

- any changes to the manufacturing methods are only those necessitated by scale-up, e.g. use of different-sized equipment
- test results of at least two batches of the final substance complying with the approved specifications should be available for the proposed batch size
- the substance is not a biological substance or a sterile substance
- the change does not affect the reproducibility of the manufacturing process

Documentation

- the batch numbers of the tested batches having the proposed batch size
- approved and proposed batch size
- updated description of the full process specifying the new batch size

条件

- 生产方法所有变动只与批量放大有关，如：使用不同大小的设备
- 至少有符合已批准质量标准的两个成品批号检验结果（新批量）
- 产品不是生物或无菌产品
- 变动不影响生产工艺的重现性。

文件要求

- 新生产批号（新批量）
- 原批准批量和新批量
- 批量变动后，新的工艺描述

N6) Change in batch size of final substance or intermediate: downscaling 成品或中间体批量变化：变小

Conditions:

- any changes to the manufacturing methods are only those necessitated by the downscaling, e.g. use of different-sized equipment
- test results of at least two batches of the final substance complying with the approved specifications should be available for the proposed batch size
- the substance is not a biological substance or a sterile substance
- the change does not affect the reproducibility of the manufacturing process
- the change should not be the result of unexpected events arising during manufacture or because of stability concerns

Documentation

- the batch numbers of the tested batches having the proposed batch size
- approved and proposed batch size
- updated description of the full process specifying the new batch size

条件:

- 生产方法所有变动只与批量变小有关，如：使用不同大小的设备
- 至少有符合已批准质量标准的两个成品批号检验结果（新批量）
- 产品不是生物或无菌产品
- 变动不影响生产工艺的重现性
- 该变动原因不是生产过程的异常或稳定性实验出现问题引起的

文件要求

- 新生产批号（新批量）
- 原批准批量和新批量
- 批量变动后，新的工艺描述

N7) Minor changes to a test procedure for the final substance or a starting material/intermediate/reagent used in the manufacturing process of the final substance. Editorial changes to a method description annexed to a certificate of suitability.

成品检验方法微小变动、或生产过程所用起始物质/中间体/试剂的分析方法微小变动。CEP证书规定方法的表述形式变动。

Conditions:

- the method of analysis should remain the same (e.g. a change in column length or temperature, but not a different type of column or method); no new impurities are detected
- appropriate (re-)validation studies have been performed in accordance with relevant guidelines
- results of method validation show the new test procedure to be at least equivalent to the former procedure
- the final substance, starting material, intermediate or reagent is not a biological substance.

Documentation:

- updated description of the method in a format to be appended to the certificate of suitability

条件:

- 分析方法本身不变(如：柱长或柱温改变，但柱子类别或方法不变); 未检出新杂质
- 已按有关指南要求进行正确的（再）验证
- 方法验证结果证明：新检验方法至少等同于原方法
- 成品、起始物质、中间体或试剂不是生物产品

文件要求

- 更新后的方法描述，表述应符合CEP证书附件方法格式

N8) Tightening of the specification limits for the final substance, a starting material/ intermediate/reagent used in the manufacturing process of the final substance
提高成品、起始物质/中间体/试剂质量标准

Conditions:

- the change should not be the result of unexpected events arising during manufacture
- any change should be within the range of currently approved limits
- when the change regards the specifications of the final substance it must comply with the tightened specifications throughout its period of use

Documentation

- comparative table of current and proposed specifications
- when the change regards the specifications of the final substance, a commitment that it complies with the tightened specifications throughout its period of use

条件:

- 该变动不是生产过程的异常引起
- 所有变动必须符合现行已经批准的质量标准范围
- 如果是成品质量标准变动，该产品在使用期限内，完全符合更严的质量标准

文件要求

- 变动前后质量标准对照表
- 如果是成品质量标准变动，必须承诺：该产品在使用期限内，完全符合更严格的质量标准。

N9) Change in the code product/reference number and/or in the brand name of the final substance or any material used in the synthesis of the substance
成品或生产过程使用的任一物质的代码或索引号或商标名变动

Conditions:

- the change does not regard the quality of the final substance or the concerned material

Documentation:

- current and proposed code product / reference number / brand name

条件:

- 变更与成品质量或变更物料质量无关

文件要求

- 产品代码、索引号、商标名新旧对照表

N10) Amendment to stability data further to a commitment at the time of granting of the Certificate of suitability

取得CEP证书、执行原稳定性实验程序后，修改稳定性实验资料

Conditions:

- no out-of-specification results should have been observed during the stability study

Documentation:

- table of updated results

条件： 稳定性实验数据从来没有OOS结果

文件要求： 更新后的稳定性实验数据

N11) Removal/reduction of the re-test period from the Certificate of suitability
从CEP证书上取消/减少再检验日期

Conditions:

- the change should not be the result of unexpected events arising during manufacture or because of stability concerns

Documentation: none apart from the justification of the removal/reduction

条件： 该变动不是生产过程的异常或稳定性实验出现问题引起

文件要求： 无，但必须说明取消/减少再检验日期的合理性

N12) For a Certificate for TSE risk, deletion of a source country or change in source of a material used in the preparation of the final substance from a TSE risk material to a vegetable, synthetic, or non-TSE risk material

TSE风险的证书，取消该物质原产地国或变更来源，或将具TSE风险的原料更改为植物的、合成的或无TSE风险的来源

Conditions:

- no change in the manufacturing process

Documentation

- if applicable a declaration from the manufacturer of the material that it is purely of vegetable, synthetic or non-TSE risk origin

条件： 生产工艺不得改变

文件要求： 适用时，生产厂必须声明：产品是纯植物、或纯合成或无TSE风险。

**MINOR CHANGES FOR CERTIFICATES FOR CHEMICAL PURITY AND
MICROBIOLOGICAL QUALITY (R)**

化学微生物产品微小变更 (R)

R1) Minor change in the manufacturing process of the substance

生产工艺微小变化

Conditions:

- no change in qualitative and quantitative impurity profile (including related substances, residual solvents, residual catalysts) or in physico-chemical properties
- the substance is not a biological substance
- the change does not regard the sterilisation step(s) if any
- the synthetic route remains the same, i.e. intermediates remain the same. In the case of herbal medicinal products, the geographical source, production of the herbal substance and the manufacturing route remain the same.

documentation:

- direct comparison of the present process and the proposed process (full description)
- batch analysis data (in comparative tabular format) of at least two batches (minimum pilot scale) of the substance manufactured according to the present and proposed process, demonstrating that the change has no impact on the quality of the substance

条件:

- 杂质定性、定量含量均没有变化(包括相关物质、残留溶剂、残留催化剂)或者理化性质没有变化
- 产品不是生物制品
- 灭菌工序没有变动 (如果有)
- 合成途径未变, 即: 仍得到原来的中间体。植物制剂产品的原料药地理产地、生产操作和生产工艺不变

文件要求

- 变动前后工艺对照表 (完整的描述)
- 至少两个批号产品的批分析数据(变动前后对照表) (至少应为试验批), 证明变动不影响产品质量。

R2) Change in batch size of the substance or an intermediate more than 10-fold compared to the original batch size
成品或中间体批量放大不超过原申报批量10倍

Conditions:

- any changes to the manufacturing methods are only those necessitated by scale-up, e.g. use of different-sized equipment
- the substance is not a biological substance or a sterile substance
- the change does not affect the reproducibility of the manufacturing process

Documentation

- updated description of the process specifying the new batch size
- batch analysis data (in comparative tabular format) on a minimum of two production batches manufactured according to both the current and the proposed sizes. Batch data on the next two full production batches should be available upon request and reported by the certificate holder if outside specification (with proposed action).
- a commitment to provide updated stability study results demonstrating the compliance of the batches of the up-scaled size with the approved specifications when a re-test period is mentioned on the Certificate of suitability

条件:

- 生产方法所有变动只与批量放大有关，如：使用不同大小的设备
- 产品不是生物制品
- 变动不影响生产工艺重现性

文件要求

- 变动后生产工艺描述，说明新的批量
- 至少两个批号的批分析数据(批量变动前后对照表)。如果超标，之后应还有至少两个完整生产批的数据备查（还应有相应整改措施）。
- 如果在CEP证书申请了再检验日期，承诺继续提供稳定性实验数据，从而证明放大批量后，产品仍符合质量标准。

R3a) Specification of the final substance: addition of a new test parameter or changes to or replacement of a test procedure

成品质量标准：增加检验项目、或改变或替代检验方法

Conditions:

- any change should not be the result of unexpected events arising during manufacture
- any new test method does not concern a novel non-standard technique or a standard technique used in a novel way
- any new test procedure should have been appropriately (re-)validated in accordance with relevant guidelines results of method validation and should have been shown to be at least equivalent to the former procedure
- the final substance is not a biological substance
- the change does not affect tests for sterility or bacterial endotoxins
- test results of at least two batches of the final substance and complying with its approved specifications should be available

Documentation:

- comparative table of current and proposed specifications of the substance
- details of any new analytical method and validation results showing that the current method and the proposed method are at least equivalent
- batch analysis data on two production batches of the final substance for all tests in the new specifications
- a commitment to provide updated stability study results demonstrating the compliance with the changed specifications when a re-test period is mentioned on the certificate of suitability

条件:

- 所有变动不是生产过程的异常引起
- 所有检验方法不是新的非标技术、或标准技术的新用途
- 已按有关指南要求对新检验方法进行正确的（再）验证，方法验证结果证明：新检验方法至少等同于原方法
- 产品不是生物制品
- 变动不影响无菌检验或细菌内毒素检验
- 至少已有两个批号成品符合已批准的质量标准

文件要求

- 变动前后产品质量标准对照表
- 新分析方法详细描述和验证报告，证明新方法至少等同于原方法
- 至少两个批号、按新方法全检的成品分析数据
- 如果CEP证书规定了再检验日期，应承诺继续提供稳定性实验数据，证明标准改变后，产品仍符合质量标准。

R3b) Change of specification of a starting material/intermediate/reagent used in the synthesis of the final substance
产品合成所用起始物质/中间体/试剂质量标准的变动

Conditions:

- no change in the specification of the final substance
- any change should not be the result of unexpected events arising during manufacture
- any new test method does not concern a novel non-standard technique or a standard technique used in a novel way
- any new test procedure should have been appropriately (re-)validated in accordance with relevant guidelines results of method validation and should have been shown to be at least equivalent to the former procedure
- the final substance is not a biological substance
- test results of at least two batches of the final substance manufactured using the concerned starting material/intermediate/reagent and complying with its approved specifications should be available

Documentation:

- comparative table of current and proposed specifications for the concerned material
- details of any new analytical method and validation results showing that the current method and the proposed method are at least equivalent
- batch analysis data on two production batches of the final substance for all tests in the approved specifications demonstrating compliance with the approved specifications

条件:

- 成品质量标准没有变动
- 所有变动不是生产过程的异常引起
- 所有检验方法不是新的非标技术、或标准技术的新用途
- 已按有关指南要求对新检验方法进行正确的（再）验证，验证结果应证明：新检验方法至少等同于原方法
- 产品不是生物制品
- 使用该起始物料/中间体/试剂生产成品，至少已有两个批号成品检验数据符合已批准的质量标准

文件要求

- 相关物料的质量标准变动前后对照表
- 新分析方法详细描述和验证报告，证明新方法至少等同于原方法
- 两个批号、按已批准的标准全检的成品分析数据，证明产品符合已批准的质量标准

R4) Change in the manufacturer or addition of a new manufacturer of a starting material or intermediate used in the manufacturing process of the final substance
起始物质或中间体生产厂变动、或新增

Conditions:

- the specifications and the route of synthesis (including all materials used) of the concerned material are identical to those already approved
- the final substance, starting material or intermediate is not a biological substance
- when the change regards the manufacturer of a key intermediate test results of at least two batches of the concerned key intermediate and complying with its approved specifications should be available

Documentation

- a declaration from the holder of the Certificate of suitability that the specifications of the final substance are the same as those already approved
- a declaration from the holder of the Certificate of suitability that the synthetic route, the specifications and the quality control procedures of the starting material or intermediate are the same as those already approved
- batch analysis data (in a comparative tabular format) for at least two batches (minimum pilot scale) of the final substance from the current and the proposed sources of the starting material or intermediate

条件:

- 质量标准和合成途径（包括所有物料）与已批准的完全相同
- 成品、起始物质或中间体不是生物制品
- 如果是关键中间体，至少已有两个批号完全符合已批准的质量标准

文件要求

- CEP证书持有人声明：成品质量标准不变
- CEP证书持有人声明：起始物质/中间体合成途径、质量标准和检验方法不变
- 变动前后至少各两批成品分析数据（至少是实验批）对照表

R5) For a “double” Certificate of suitability (for chemical purity and microbiological quality and for TSE risk), change in source of a material used in the preparation of the final substance from a TSE risk material to a vegetable, synthetic, or non-TSE risk material

双重CEP证书（化学微生物和TSE证书），将TSE风险原料改为植物、合成或非TSE风险物料来源

Conditions:

- no change in the manufacturing process
- the specifications of the final substance remain the same
- the final substance is not a biological substance

Documentation

- updated specifications of the new source of the material
- batch analysis data (in a comparative tabular format) for at least two batches (minimum pilot scale) of the final substance from the current and proposed source of the material or intermediate
- a declaration from the manufacturer of the material that it is purely of vegetable, synthetic or non-TSE risk origin (specifying the origin)

条件:

- 生产工艺不变
- 成品质量标准不变
- 成品不是生物制品

文件要求

- 新来源原料的质量标准
- 变动前后至少各两批成品分析数据（至少是实验批）对照表
- 原料生产厂声明：该原料仅仅来源于植物、合成或无TSE风险（说明来源）

R6) Change in the manufacturing site/workshop or addition of a new manufacturing site/workshop for the final substance
成品生产场地/车间的变更或新增

Conditions:

- the quality control specifications (including in process controls, methods of analysis of all materials), method of preparation (including batch size) **and detailed route of synthesis** are identical to those already approved
- the final substance is not a biological substance or a sterile substance

Documentation

- a declaration from the holder of the Certificate of suitability that the manufacturing process, quality control procedures and specifications of the final substance are the same as those already approved
- batch analysis data (in a comparative tabular format) for at least two batches (minimum pilot scale) of the final substance from the current and the proposed sites
- updated declarations of manufacture in accordance with the dossier and according to GMP rules and of willingness to be inspected

条件:

- 质量标准（包括中间控制、所有物料分析方法）、生产方法（包括批量）和**详细的合成途径**不变
- 成品不是生物制品或无菌产品

文件要求

- CEP证书持有人声明：生产过程、质量控制方法和成品质量标准不变
- 变动前后至少各两批成品分析数据（至少是实验批）对照表
- 更新以下声明：按申报文件组织生产、符合GMP和愿意接受检查

R7) Change in the re-test period of the final substance and/or the storage conditions for the final substance when a re-test period is already mentioned on the Certificate of suitability or request to include a re-test period on the Certificate of suitability

CEP证书规定了再检验日期时，变动成品再检验日期或贮存条件；或要求在CEP证书上增加再检验日期

Conditions:

- stability studies have been done in accordance with relevant guidelines
- the change should not be the result of unexpected events arising during manufacture or because of stability concerns
- the final substance is not a biological substance.

Documentation for addition of a retest period:

- results of long-term and accelerated stability studies for at least two pilot or production scale batches
- description and specification of the commercial packaging material (section 3.2.S.6. of the CTD)

Documentation for an extension of the retest period:

- updated results of the stability studies for at least two pilot or production scale batches

条件:

- 已按有关指南完成了稳定性实验
- 变动不是生产异常引起或稳定性实验出现问题引起
- 成品不是生物制品或无菌产品

文件要求（增加再检验日期）：

- 提供至少两个实验批或生产批的长期稳定性实验数据和加速实验数据
- 商业包装材料的描述及质量标准（见CTD文件之3.2.S.6）

文件要求（延长再检验日期）：

- 提供至少两个实验批或生产批的更新稳定性实验数据

MINOR CHANGES FOR TSE CERTIFICATES (T)

TSE证书的微小变动 (T)

T1) Change in the manufacturing site or addition of a manufacturing site for the substance

生产场地变动或增加

Conditions:

- no change in the manufacturing process and in the materials and in the origin of the material used in the process
- no other TSE risk material is processed in the new manufacturing site

Documentation:

- a declaration from the holder of the Certificate of suitability that the manufacturing process is strictly identical to that already approved
- a declaration from the manufacturer that no other TSE risk material is processed in the new manufacturing site
- updated declarations of manufacture in accordance with the dossier and according to GMP rules and of willingness to be inspected
- information on the quality assurance system (including traceability) applied in the new manufacturing site

条件:

- 生产工艺不变、原材料不变、原材料来源不变
- 新厂址不生产其它具TSE风险的产品

文件要求

- CEP证书持有人声明：生产工艺完与原来申报工艺完全相同
- 生产厂声明：新厂址不生产其它具TSE风险的产品
- 更新以下声明：按申报文件组织生产、符合GMP和愿意接受检查
- 新厂址质量保证体系介绍（包括可追踪性）

T2) Minor change in the manufacturing process (including process parameters) or in the specifications of the final substance

生产工艺微小变更（包括工艺参数）或成品质量标准微小变更

Conditions:

- the change has no impact on the TSE risk
- the TSE Certificate of suitability does not cover the chemical purity and the microbiological quality

Documentation

- comparison of the approved and proposed process
- a declaration from the manufacturer that the change has no impact on the TSE risk

条件:

- 变更不影响TSE风险
- TSE证书不涉及化学微生物质量产品

文件要求

- 变动前后的工艺对比
- 生产厂声明：变动不影响TSE风险

T3) Change in the quality assurance system applied in the manufacturing site
生产场所质量保证体系变动

Conditions:

- the new quality assurance system is at least equivalent to the former one
- no change in the manufacturing process (including process parameters) or in the specifications of the final substance

Documentation

- updated information on the quality assurance system (including traceability)
- updated declaration of manufacture in accordance with the dossier and according to GMP rules and of willingness to be inspected

条件:

- 新质量体系至少与以前的体系具等同性
- 生产工艺（包括工艺参数）或成品质量标准不变

文件要求

- 新的质量保证体系介绍（包括可追踪性）
- 更新以下声明：按申报文件组织生产、符合GMP和愿意接受检查

MAJOR CHANGES

重大变更

For a certificate for chemical purity and microbiological quality

Documentation

- batch analysis data of at least three batches of the final substance (minimum pilot scale)
- fully updated information and supportive data related to the change(s) and any consequential changes including updated stability data if applicable

For a certificate for TSE risk

Documentation

- fully updated information related to the change(s) and any consequential changes

化学微生物质量的CEP证书：

文件要求

- 至少3批成品批分析数据（至少是实验批）
- 变动的详细资料和支持性数据、与该变更相关的后续变动，包括更新的稳定性实验数据（适用时）

TSE证书

文件要求

- 变动的详细资料、变动后续的变更

RENEWAL 更新

The Certificate of suitability is valid for five years from the date when the original certificate was granted. Regardless of any revisions treated in the meantime, the holder of a Certificate of suitability shall ask for the renewal of the Certificate of suitability six months prior to expiry date by providing an update of the certification dossier.

CEP证书自首次签发之日起5年有效。失效前6个月，无论是否正在办理变更手续，CEP证书持有人必须提出五年更新申请，并上报更新后的文件。

If no change has been made since the last Certificate of suitability was granted 如果自上次CEP证书签发后没有任何变动

Documentation:

- a statement that no changes that may affect the quality, safety or efficacy of the substance have been made
- certificates of analysis from at least two recent production batches
- updated declarations as appendix to the application form.

文件要求:

- 说明没有发生任何影响产品质量、安全、效力的变化
- 并提供至少两个最近批号的分析证
- 刷新申请表格后附的声明

If changes are included in the request for renewal 如果更新申请包含变动

Documentation:

- an updated dossier in CTD format
- list of changes introduced in the format of a comparative table
- relevant data supporting each change as described in this guideline
- certificates of analysis from at least two recent production batches
- updated declarations as appendix to the application form.

文件要求:

- CTD格式的更新文件
- 所做变动的对照表
- 按本指南要求，提供所有变更的支持性数据资料
- 提供至少两个最近生产批号的分析证
- 刷新申请表格后附的声明

TRANSFER OF HOLDERSHIP OF A CERTIFICATE OF SUITABILITY

CEP证书持有人转让

A transfer of the ownership of the Certificate of suitability (i.e. change in the name of the certificate holder that is not the same legal entity and where the change does not occur following a sale or a merger) is feasible in exceptional cases with the below conditions:

- the current Certificate of suitability is held by another company than the manufacturer (e.g. a broker or trader)
- the manufacturer takes out the Certificate of suitability in their own name

Documentation:

- a letter signed by both parties, i.e. the former holder and the manufacturer, agreeing that the ownership of the Certificate of suitability is passed on to the manufacturer from the date of the request
- updated declarations as annex to the application form.

This kind of request is a major change.

CEP证书可以转让（即：证书持有人变更给原法人以外的团体，这种变更不是公司出售或合并的结果），但必须符合以下条件：

- CEP证书现行持有人不是生产厂（如：中间商或贸易商）
- 生产厂以自己名义领取CEP证书

文件要求：

- 双方签字协议函，即：原持有人和生产厂同意自申请之日起，CEP证书转让给生产厂持有。
- 刷新申请表格附件的声明

这种申请属于重大变更。