

CP/CB

PUBLIC DOCUMENT

(Level 1)

公开文件

(Level 1)

中文版

PA/PH/ CEP (04) 1 4R

February 2007

**Certification of suitability of Monographs of the European Pharmacopoeia
Content of the dossier for chemical purity and microbiological quality**

**欧洲药典适用性证书
化学合成和有微生物品质要求品种的文件内容**

(Revision of Annex I Resolution AP-CSP (93) 5 as amended)

(决议AP-CSP (93) 5附件 1)

Strasbourg施特拉斯堡

Content of the dossier for chemical purity and microbiological quality

化学合成和有微生物品质要求的文件内容

The Application Form – Request for New Certificate of Suitability together with the relevant annexes should be completed (available for download from the EDQM website(<http://www.edqm.eu>).

应填写申请表格-首次申请应填写申请表与有关附件信。表格可从EDQM网站下载(<http://www.edqm.eu>)。

Dossiers should be presented according to the CTD format (see The Rules Governing Medicinal Products in the European Community – Notice to Applicants for marketing authorizations for medicinal products for human use in the member states of the European Community, Volume 2B) as presented below except when justified.

应按CTD格式申报文件（详见欧洲共同体药品管理法—Vol 2B, 对欧共体内人用药品销售许可证申请人的公告）。如无另外说明，格式见后。

References to guidelines are inserted to assist applicants. However, it remains the applicant's responsibility to ensure that all relevant legislation and guidelines, as revised or maintained, are respected in the application when applicable. The guidelines referenced in each section provide useful information on the content expected in that section. However, this list should not be regarded as comprehensive. The requirements of the general monographs Substances for Pharmaceutical Use (2034), Products of Fermentation (1468) and Products with risk of transmitting agents of animal spongiform encephalopathies (1483) should be respected in the application, when applicable.

申报文件说明还给出了指导文件的出处，方便申请人使用。但是，保证编写申报文件符合所有相关法规、指南或其修订版是申请人的责任。各章节引用的指导文件是对该章节内容的要求和规定，但只是一般性的要求。此外，适用时，申报文件还应符合欧洲药典总论“药用物质2034”、“发酵产品1468”和“有海绵状脑病风险产品1483”的要求。

The applicant should also provide the Certification Secretariat of the EDQM with samples of 1 or 2 representative commercial batches in sufficient quantity to perform a complete analysis (normally about 10 g). Where applicable, samples of impurities are required where revision of the monograph is requested and/or if an additional method(s) to limit the related substances is (are) appended to the certificate for possible checking by the laboratory of the EDQM.

申请人应向EDQM提交1或2份商业批样品，数量应能够进行全分析（约10g）。适用时，药典更新、或证书上规定必须使用其他分析方法控制相关物质时也要求提供杂质样品，以便EDQM化验室进行检测。

1 **Table of contents**

2 **内容目录**

3 **Information about the Expert (1.4)**

4 **专家信息 (1.4)**

5 The experts c.v. showing his/her experience in the concerned field should be given.

6 应提供专家简历，说明其工作经历。

7 **Quality Overall Summary (QOS) (2.3)**

8 **质量总结 (QOS) (2.3)**

9 A summary of the content of the dossier should be given in the form of a Quality Overall
10 Summary (QOS)-(see The Rules Governing Medicinal Products in the European Community
11 – Notice to Applicants for marketing authorizations for medicinal products for human use in
12 the member states of the European Community, Volume 2B). It is expected that the Quality
13 Overall Summary (QOS) should discuss the ability of the European Pharmacopoeia
14 monograph to control the quality of the drug substance, and in particular the declared
15 potential impurities, or the necessity for alternative methods. Particular attention should be
16 given to justifying cases where testing for possible impurities is omitted, for example due to
17 the fact that the impurity has not been detected in any batches or will not potentially be
18 present due to a particular method of production. The report should be signed and dated.

19 应符合质量总结形式（QOS）—（详见欧洲共同体药品管理法—Vol 2B, 对欧共同体人
20 用药品销售许可证申请人的公告）。质量总结QOS应讨论欧洲药典如何控制产品质
21 量，尤其是申报的潜在杂质、是否有必要使用其他分析方法。必须特别注意：证明可
22 能出现的杂质不做常规检测的合理性。如，由于所有批号均检测不出某项杂质、或该
23 生产工艺不可能产生该杂质的情形。QOS报告应有专家签名，并加注日期。

24

1 **General information (3.2.S.1)**

2 **一般信息 (3.2.S.1)**

3 **Commercialisation history of the substance:**

4 **该原料药商业销售历史:**

5 Summarise the licensing history for medicinal products licensed in Europe that contain the
6 substance made by the defined method of manufacture naming the countries, products and
7 commercialisation dates. It should be made clear whether the products are for veterinary use.
8 Information on the Active substance Master Files submitted to the National Licensing
9 authorities should be supplied. This information should be given in the relevant sections of the
10 administrative form.

11 使用该原料药的产品制剂在欧洲销售许可证信息汇总，包括国别、品名和上市日期。
12 应明确产品是否为兽用。在各欧洲国家申报的活性物质主文件情况也应进行说明。该
13 信息还应填写在管理表格中。

14 **Declarations:**

15 **声明:**

16 A signed declaration from the manufacturer that manufacture is conducted in accordance with
17 the presented dossier and with a specified guideline on GMP should be supplied, preferably
18 with the administrative form. The applied GMP should comply with *Vol. 4 of the Rules*
19 *Governing Medicinal Products in EU* and apply for each manufacturing step from the
20 introduction of the starting materials (see Control of materials 3.2.S.2.3). If available a copy
21 of a GMP certificate should be supplied. Other approaches to GMP of similar standards are
22 acceptable, if justified.

23 生产厂声明：按申报文件和指定的GMP要求组织生产，声明最好与管理表格一起上
24 报。工厂执行的GMP应符合*欧盟药品管理法第4卷*，并从引入起始物质生产的第一步开
25 始执行。（见物料管理3.2.S.2.3）。若有，应提供GMP证书。其它与ICHQ7A相似的
26 GMP也可能接受，但必须证明其等同性。

27 A signed declaration that the manufacturer is willing to be inspected, in accordance with the
28 relevant legislation, on the request of a relevant authority before and/or after being granted a
29 certificate of suitability should be supplied. When the proposed holder is not the manufacturer
30 this declaration should also be provided by the proposed holder together with a declaration
31 from the active substance manufacturer committing them to keep the proposed holder
32 informed of any changes to the documentation so that this may be declared to the EDQM.

33 生产厂声明：愿意按相关法律规定，应有关当局要求，在COS证书签发之前或之后接
34 受检查。证书持有人如果不是生产工厂，该持有人也必须提交此份声明，同时还必须

1 附上活性生产厂家另一声明：保证持有人及时得知文件发生的所有任何变动，以便持
2 有人及时向EDQM申报。

3 Other parties may be mentioned on the certificate where relevant. If other parties are involved
4 in certain stages of the process, details of their involvement and of other site addresses must
5 be provided and information given on the contractual arrangements regarding sole or shared
6 responsibilities. If an additional site is to provide alternative capacity batch analysis results for
7 impurity profiles must be provided to demonstrate that the alternative arrangements yield
8 product of the same quality as that produced by the first site.

9 COS证书也可列上其它相关各方。若有他人从事生产工艺中的某一步骤生产，必须详
10 细说明其从事的活动、以及生产地址，并说明合同生产协议中单方或双方的责任。若
11 另一场址生产能力不同，必须提供批分析结果，说明杂质情况，证明另一场地生产的
12 产品与原场地产品质量的等同性。

13 When the manufacturer of the final substance performs only the purification of a crude
14 substance supplied by a contract manufacturer that is a not a subsidiary of the manufacturer of
15 the final substance separate declarations on GMP and willingness to be inspected should be
16 provided for the contract manufacturer(s). This could also be the case for any other contract
17 manufacturer that is not a subsidiary including laboratories.

18 如果最终成品生产厂仅仅进行粗品的精制，而粗品由合同工厂生产，该合同工厂又不
19 是本厂的分厂，则该合同工厂必须提供GMP、愿意接受检查的声明信。此项规定适用
20 于所有非子公司的合同工厂或合同实验室。

21 A declaration on the use/non-use of material of animal or human origin during manufacture
22 should be supplied. Where materials of animal or human origin are used in the process, this
23 will be mentioned on the certificate. In this case, CEP holders and MA holders should be
24 aware that viral safety data are to be submitted in the MA dossier. If material of animal origin
25 which may be susceptible to TSE contamination is used, compliance with the European
26 Pharmacopoeia monograph *Products with risk of transmitting agents of animal spongiform*
27 *encephalopathies (1483)* should be demonstrated as described in the document *Content of the*
28 *dossier for a substance for TSE risk assessment (PA/PH/CEP (06) 2)*.

29 应声明：生产过程不使用源于动物或人体的物料。如果使用，CEP证书将加以说明。
30 CEP证书持有人和MA持有人都必须意识到MA申报文件中必须包括病毒安全数据。若
31 源于动物的物质易于感染TSE，必须证明其符合欧洲药典“有动物海绵状脑病风险的产
32 品1483”的规定，这已在 *TSE风险评估产品的CEP申报文件内容(PA/PH/CEP (06) 2)* 中
33 做出了规定。

34

1 **Nomenclature (3.2.S.1.1):**

2 **名称 (3.2.S.1.1):**

3 The European Pharmacopoeia monograph name, the INN, and other chemical name(s) should
4 be stated together with any laboratory code used in the dossier.

5 欧洲药典名称、INN名称、其他化学名称，以及申报文件中所使用的实验室代码。

6 **General properties (3.2.S.1.3):**

7 **一般性质 (3.2.S.1.3):**

8 In case more than one grade, in respect of physical characteristics, is produced, the
9 manufacturer may wish to submit one or more dossiers depending on whether or not separate
10 certificates are applied for. Examples are: compacted, special particle size, particular
11 polymorphic form (where the monograph does not restrict to one single polymorph). In any
12 case the different qualities shall comply with the general level of quality defined in the
13 monograph. If more than one grade is described in the same dossier (i.e. only one certificate is
14 asked for) the batch analysis results, in respect of impurity profiles, should include all grades.
15 It is optional to mention the different grades in the sub-title of the certificate (this should be
16 made clear on the administrative form). However, the possibility for one certificate to cover
17 different grades cannot be applicable when these different grades require different
18 specifications and/or methods for the control of impurities; in which case separate certificates
19 will be needed and the relevant grades will be mentioned in the sub-title of the certificate. For
20 grades not described in the European Pharmacopoeia the specifications describing the
21 determination of the physical grade should be given with the used analytical method as well
22 as the characterisation of the physical properties.

23 如果生产不止一个物理特性级别，生产厂可以申报一个或多个文件，这取决于是否分
24 别申报CEP证书。如，压实粉、特殊粒度、特殊晶型（药典没有限制只能是一种晶形
25 时）。所有级别必须符合药典基本要求。如果在同一文件申报不同的级别（即：只申
26 请一个证书时），必须在批分析数据中说明所有级别的杂质情况。也可在CEP证书下
27 以小标题形式加以说明（申请人必须在填写管理表格时加以说明）。不过，如果各级
28 别质量标准、或杂质分析控制方法不同时，则不能在一个证书下申请不同的级别；此
29 时，将需要不同的证书，证书小标题将说明各种级别。如果申报欧洲药典没有规定的
30 级别，必须提供确定该物理级别的标准、成熟的分析方法和物理特性的确认。

31 In other cases the manufacturer may want to present individual dossiers for each grade with a
32 view to obtaining separate certificates for each grade, which will also be mentioned in the
33 sub-title of the certificate (this should be made clear on the administrative form).

34 生产厂希望将不同级别分别申报，使每个级别取得一个证书号时，证书也会以小标题
35 形式加以说明（工厂也应在填写管理表格时说明）。

36

1 It should be noted that:

2 应注意:

3 - As explained in the general monograph *Substances for Pharmaceutical Use* (2034)
4 mixtures that are manufactured from defined active substances or excipients are only
5 acceptable if this is specifically stated in the definition of the individual monograph.
6 Suitable test methods and limits for any additives should be provided.

7 - 如“药用物质2034”所规定的，只有药典正文明确规定，才可以用指定的活性
8 物质或辅料生产混合物。应提供添加剂的检验方法和限量标准。

9 - Acceptable claims regarding sterility/freedom from pyrogens and/or bacterial
10 endotoxins should be indicated and reference given to the relevant test of the
11 monograph (sterility/LAL/pyrogens) and the method used for sterilisation should be
12 identified and which will be stated on the certificate. The document *Certificates of*
13 *suitability for sterile active substances* (PA/PH/CEP/T0(6) 13,1R) should be taken into
14 consideration. It is only possible to introduce grades for freedom from pyrogens and/or
15 bacterial endotoxins on the CEP when the monograph foresees this. Separate files will
16 be needed if both grades are produced (non-sterile and sterile, apyrogenic/bacterial
17 endotoxin-free and non-apyrogenic/endotoxin free substances).

18 - 无菌/无热原或无细菌内毒素：应进行合理的说明，并说明使用哪种药典方法
19 （无菌检验/LAL/热原检查）。应说明灭菌方法，该灭菌方法将在CEP证书上予
20 以规定。应参考“*无菌活性物质适应性证书*” (PA/PH/CEP/T0(6) 13,1R)。只有
21 药典正文预先有上述项目的规定，方可申请无热原或无细菌内毒素的CEP证
22 书。如果同时生产两个级别（非无菌或无菌，有热原/细菌内毒素和无热原/无细
23 菌内毒），必须申报两份文件。

24 In the particular case where the monograph covers different grades of the substance (i.e.
25 lactulose liquid or sodium lactate solution, various per cent concentrations or dimeticone,
26 viscosity) it is possible to mention different grades in the sub-title of the CEP if the
27 concentrations/viscosity etc are within the range of the monograph and also if the monograph
28 states that the label should mention the particular grade.

29 特殊情况下，如果药典正文包括了不同的级别（如：乳果糖液或乳酸钠溶液，不同浓
30 度或有二甲硅油，不同粘度），可以在CEP证书小标题上说明不同的级别，但那些不
31 同的浓度/粘度应该在药典规定范围内、此时药典已经规定了必须在标签上说明级别要
32 求。

33

1 **Manufacture (3.2.S.2)**

2 **生产 (3.2.S.2)**

3 **Manufacturer(s) (3.2.S.2.1):**

4 **生产厂 (3.2.S.2.1):**

5 If different sites/facilities are involved for a single defined process for manufacture and/or
6 testing this should be explained and it should be made clear which production step is
7 conducted on which site and the names and addresses of each of them should be given.

8 只有一个工艺，但涉及几个场址或设施从事生产或检验时，应在文件中予以说明，并
9 明确哪一个场地从事哪一个生产步骤，必须说明各场地的名称和地址。

10 **Description of manufacturing process and Process Controls (3.2.S.2.2):**

11 **生产工艺描述和生产控制 (3.2.S.2.2):**

12 Applicants are reminded that the requirements of the general monographs *Products of*
13 *Fermentation* (1468) and *Products with risk of transmitting agents of animal spongiform*
14 *encephalopathies* (1483) should be respected when applicable.

15 适用时，申请人应该注意符合药典通则“发酵产品1468、有海绵状脑病风险的产品
16 1483”要求。

17 The following information should be supplied:

18 应提供以下信息：

19 - An outline (flow chart, including the structural formula for the starting materials and
20 all intermediates),

21 - 工艺概述（流程图，包括起始物质和所有中间体的分子结构）

22 - The description of the manufacturing method should include all the steps of the
23 process, proceeding from the starting materials(s) to the isolated intermediates, and
24 ultimately to the active substance.

25 - 生产方法描述：应包括从起始物质到分离中间体、再到最终成品的生产工艺各
26 步描述，

27 - Detailed description of each stage of the manufacture, including information on
28 solvents and reagents, catalysts, conditions of reactions, information on intermediates,
29 which are isolated and purified, quantities of all materials used in the process to
30 produce a batch of the typical commercial size and yields for isolated intermediates
31 should be indicated for each process step. Special emphasis should be given to the
32 final steps including purification procedures.

- 1 - 生产各步详细描述：包括溶剂、试剂、催化剂使用情况，反应条件、分离出并
2 纯化的中间体，生产商业批时，各步所有物料用量、中间体得量（收率）。应
3 特别注意包括精制工序的成品步骤的描述。
- 4 - The maximum batch size for which the manufacturer has acquired experience with the
5 defined method, and which should correspond to batches referred to in the dossier,
6 should be stated. Where the substance has yet to be produced in commercial quantities
7 (only pilot scale batches manufactured) the certificate can be granted provided scale-
8 up is immediately reported to the EDQM. For a sterile product, an application for a
9 variable and/or alternative batch size should be justified.
- 10 - 该生产工艺下的最大批量：该批量应在文件中予以申报。如果产品还没有商业
11 批（仅生产了试验批），也可签发CEP证书，但必须保证一旦放大生产，必须
12 立即向EDQM申报。对于无菌产品，如果批量是可变的，或有其他批量，应说
13 明其合理性。
- 14 - In case of semi-synthetically manufactured substances the fermented starting material
15 should be well characterised, and the possibility of carrying impurities from the
16 fermentation process to the final substance should be discussed. Each supplier should
17 give a declaration on the use/non-use of material of animal origin during manufacture
18 of the starting material. Note that products obtained only by purification or salification
19 of a fermented starting material cannot be considered as semi-synthetic products and
20 should therefore be subject to the same requirements as true products of fermentation.
- 21 - 半合成产品：应充分说明发酵起始物质的特性，讨论发酵产生的杂质进入成品
22 的可能性。每个供应商必须提供生产起始物质是否使用源于动物原料的声明。
23 应该注意：仅仅对发酵起始物质精制或进行成盐反应而得到的成品，不是半合
24 成产品，必须完全符合发酵产品的要求。
- 25 - Different manufacturing sites and different manufacturing methods or alternatives
26 could be described in a single dossier provided that proof is given that for each case
27 the specifications and the impurities profiles are exactly the same. If more than one
28 manufacturer/facility is involved in manufacture, the responsibilities of each party
29 should be clearly indicated.
- 30 - 可以在一个文件中申报多个生产场地、多个生产方法或其他，但必须保证成品
31 质量标准和杂质含量完全相同。如果有不止一个生产厂商或生产场地，必须明
32 确说明各方责任。
- 33 - Whatever type of manufacturing process is used, alternatives are not allowed unless
34 they are clearly defined and detailed as part of 2nd, 3rd etc. processes. Batch analysis
35 results corresponding to the substance manufactured according to the different
36 alternatives must be provided to demonstrate that there are no significant differences
37 in impurity profiles, which may affect the specifications. If this provision is not met,

1 the application will need revision to delete one or more of the options, which results in
2 a product that does not conform to the 'standard' profile. 'Deleted' options may be
3 included in further applications for additional certificates.

4 - 无论使用什么生产工艺，只有在文件中明确指定为第二、第三...等工艺时，方
5 可使用替代工艺。必须提供各种工艺下生产批的批分析数据，证明各种方法生
6 产的产品杂质没有明确差异，否则就会影响产品质量标准。如果申报人无法满
7 足上述要求，则必须取消该产品的替代工艺，因为替代工艺致使产品不符合
8 “标准数据”。取消的工艺可以用于申报另一个证书。

9 If re-processing (i.e. re-application of a step already described in the process) is a possibility it
10 should be mentioned and should be treated as a procedural option.

11 如果有可能进行返工（如，完全重复工艺中前述的某一步），文件中应予以申报，可
12 以视为备用步骤。

13 Normally re-working (application of steps different from those of the process) is not
14 acceptable since this implies the use of different solvents, which leads to a change in the
15 specifications, and /or impurity profile of the substance. A separate certificate application
16 would therefore be necessary to cover material produced using such a procedure.

17 通常，不允许再加工（不同于原工艺的方法），因为再加工可能会使用其他溶媒，会
18 改变产品质量标准或杂质含量。此时必须单独申报CEP证书。

19 Recovery (e.g. from mother liquors or filtrates) of reactants, intermediates or the final
20 substance is considered acceptable provided that approved procedures exist for the recovery
21 and the recovered materials meet specifications suitable for their intended use. The
22 specifications should be described. However, recovery of the substance without any further
23 purification of the obtained substance according to the usual process should be considered as
24 a re-working and is not acceptable.

25 回收反应物（如，从母液回收或滤液回收）、中间体或成品是可以接受的，但是必须
26 保证回收工艺和回收物料符合质量标准，并且适用。必须申报回收物的质量标准。没
27 有按日常工艺进行精制的回收品是一种再加工过程，是不可接受的。

28 Blending of production batches of the final substance to obtain a larger size is acceptable
29 provided each batch incorporated into the blend is individually tested and found to meet
30 specifications set for the final substance prior to blending.

31 可以混和成品生产批得到大批量，但混料前，所有小批必须单独检验并符合成品质量
32 标准。

33

1 **Control of materials (3.2.S.2.3):**

2 **物料控制 (3.2.S.2.3):**

3 Appropriate specifications for raw materials and solvents should be supplied. If materials are
4 recycled then justified specifications for the recycled materials should be supplied and it
5 should be made clear in which manufacturing step they are used. When a class 1 solvent could
6 be present in a solvent used during manufacture e.g. benzene in toluene a suitable limit and
7 analytical method for its control should be introduced.

8 必须申报适当的原材料和溶媒质量标准。如果物料循环使用，应提供循环物料合理的质
9 量标准，并说明在哪个工序使用。如果溶媒的生产过程中可能存在1类溶媒，如甲苯中
10 的苯，则必须建立该溶媒中1类溶媒的限量标准和控制分析方法。

11 Applicants should propose and justify which substance(s) should be considered as the starting
12 material(s). They should be fully characterised and complete specifications should be
13 provided including an impurities profile. The possibility that impurities present in the starting
14 material may be carried through the process unchanged or as derivatives should be discussed
15 and if relevant be controlled in starting material by appropriate acceptance criteria. A
16 description of analytical controls applied to ensure the quality of the starting materials should
17 be given. Relevant viral safety and/or TSE data should be provided if any animal derived
18 material is used during the manufacturing process. Starting materials from vegetable origin
19 should be fully characterised to ascertain suitability, and a contaminant profile should be
20 established and submitted.

21 申请人应说明哪个物质是起始物质，并说明其合理性。必须充分说明起始物质特性，
22 申报完整的质量标准，包括杂质标准。必须讨论起始物质杂质进入成品、发生变化或
23 产生衍生物的可能性，必要时，应对起始物质加以控制。应详细说明起始物质分析方
24 法。如果使用源于动物原料生产起始物质，应申报有关的病毒安全数据或TSE数据。应
25 充分说明植物来源和起始物质特性，确保其适用性，应建立和申报污染物含量。

26 In the case of a route of synthesis consisting of one or only a few steps, full details of the
27 manufacture of the starting material(s) should be given and/or at least detailed specifications
28 especially regarding the impurity profile including residual solvents and catalysts.
29 Alternatively, for starting materials described in the European Pharmacopoeia certificates of
30 suitability can be provided, if available.

31 如果合成途径只有一步或很少几步反应，应详细申报起始物质生产厂家的情况，至少
32 应有详细的质量标准，尤其是杂质含量、残留溶剂、催化剂情况。如果该起始物质已
33 有CEP证书，也可只提供CEP证书。

34

1 The supplier(s) of the starting materials(s) should be declared and where more than one
2 supplier is used batch analysis results from the substance manufactured from the different
3 suppliers should be given.

4 必须申报起始物料的供应商，如果起始物质供应不止一家，必须提供各供应商的批分
5 析结果。

6 **Controls of critical steps and intermediates (3.2.S.2.4);**

7 **关键工序和关键中间体的控制 (3.2.S.2.4);**

8 Any critical steps should be identified. Tests and acceptance criteria performed at the critical
9 steps should be provided. In-process controls should be described. Information on the quality
10 and control of intermediates isolated during manufacture should be provided.

11 必须说明所有关键工序。说明关键工序所进行的检验项目和认可标准。说明过程控制
12 项目。必须提供中间体质量标准和控制方法。

13 **Process validation and/or evaluation (3.2.S.2.5);**

14 **工艺验证或评价 (3.2.S.2.5);**

15 Process validation and/or evaluation studies shall be provided as appropriate. In particular,
16 sterilisation processes including filtration and aseptic processing should be validated.
17 Therefore, when a request to mention sterile in the sub-title of the certificate is made
18 validation data should be presented in the dossier. European Pharmacopoeia General text 5.1
19 should be taken into consideration. In addition, a full description of the sterilisation process is
20 required, including for sterilisation by filtration, the maximum acceptable bio-burden prior to
21 the sterilisation, the type of microbial retentive filter used and its pore size (pore sizes of 0.22
22 µm or less are acceptable without further justification), any in-process controls (i.e. filter
23 integrity) as well as the method(s) of sterilisation of the primary packaging material. CEP
24 holders and MA holders should be aware that when the active substance is used after
25 sterilisation as a medicinal finished product e.g. sterile powder distributed in sterile packaging,
26 the sterilisation of the active substance will be considered as an intrinsic part of the
27 manufacturing process of the medicinal product. Consequently, full data must be provided in
28 the application file for a medicinal product or by the licensing authority requesting the
29 assessment report from the EDQM.

30 适当时，应提供工艺验证或评价报告。特别是无菌工艺，包括过滤和无菌工艺必须进行
31 验证。因此，如果要求在CEP证书小标题上加注无菌级别时，必须申报无菌验证资
32 料。应符合欧洲药典总论5.1要求。必须详细说明灭菌过程，包括无菌过滤、灭菌前最
33 大可接受生物负荷量、微生物截留型过滤器型号、孔径（0.22µ或以下可以直接接受而
34 不需要另外证明），所有中间控制（如，过滤器完好性检测）以及内包材灭菌方法。
35 CEP证书持有人和MA持有人必须懂得：灭菌后活性物质用于药品制剂时，如，分装于
36 无菌包装内的无菌粉针，活性物质的灭菌过程就必然是药品制剂生产过程中的一部

1 份。因此，制剂申请文件必须提供完整的资料，或由MA发证部门索取EDQM的评审报
2 告。

3 When the monograph indicates specific additional requirements for the manufacturing process
4 (i.e. in the production section of the monograph) compliance to this aspect should be
5 demonstrated when reference to a specific test(s) is given. For biological substances (such as
6 heparin sodium), and even if a specific microbial grade is not requested to be mentioned on
7 the certificate (sterile, endotoxin free, ..), the dossier should include information
8 demonstrating suitable inactivation and/or removal of any infectious agent.

9 如果药典对某一物质专门规定了生产工艺的特殊要求（如，药典正文的生产部份），
10 如果有指定的检验项目，申报人必须证明其生产符合药典规定。对于生物制品而言
11 （如肝素钠），即使CEP证书不申请特定的微生物指标质量（如无菌性、无内毒素
12 素），申报文件都必须包括相关资料，证明已除去所有易感性成份或进行了灭活。

13 **Elucidation of Structure and other Characteristics(3.2.S.3.1)**

14 **结构和其它特性解析(3.2.S.3.1)**

15 **Impurities (3.2.S.3.2)**

16 **杂质(3.2.S.3.2)**

17 **Related substances: 相关物质:**

18 The requirements of the related substances section of the general monograph *Substances for*
19 *Pharmaceutical Use (2034)* and the guideline *Control of impurities of pharmacopoeial*
20 *substances (CPMP/QWP/1529/04)* should be met. It should be demonstrated that all applied
21 methods are suitable to control impurities at the applicable levels set by the general
22 monograph. Furthermore the provisions of the general chapter *Control of impurities in*
23 *substances for pharmaceutical use (5.10)* are to be taken into consideration.

24 必须符合药典“药用物质2034”和CPMP/QWP/1529/04“药用物质杂质控制指南”的
25 要求。必须证明：所有分析方法都可以将杂质控制在药典规定的合理限量内。此外，
26 还应符合药典附录“药用物质杂质控制5.10”的规定。

27 Possible impurities originating from the route of synthesis or from degradation should be
28 listed and discussed with an indication of their origin (starting material, reagent, solvent,
29 catalyst, intermediate, degradation product). The impurities that are controlled should be
30 presented together with the analytical methods used, and a list of the related substances found
31 in the substance. The related substances found in batches of the active substance should be
32 compared with the related substances listed in the transparency statement of the monograph
33 (where one exists) together with their typical levels and the proposed limits.

34 必须列出合成途径或降解可能产生的所有杂质，讨论杂质来源（起始物质、试剂、溶
35 剂、催化剂、中间体、降解物质）。必须报告所检验的杂质以及分析方法，并列出产

1 品实际含有的相关物质清单。如果药典正文后面给出了杂质清单，应将实际含有的相
2 关物质种类、实际含量、限量标准与药典比对

3 **The suitability of the method(s) of the monograph to control the quality of the substance**
4 **must be discussed and demonstrated.** In particular, where additional impurities (i.e. those
5 not listed in the transparency statement of the monograph) are found above the relevant
6 reporting threshold and disregard limit of the monograph it must be demonstrated whether the
7 monograph controls them and where applicable retention times or Rf values and limits of
8 detection and/or quantification should be provided. If the monograph does not control the
9 additional impurities, suitably validated additional test(s), should be proposed. Evidence
10 should be given of the absence of impurities not routinely tested for in the product or its
11 intermediates.

12 必须讨论药典方法是否适合于控制产品质量，并进行证明。特别是出现了药典规
13 定之外的杂质、（如，没有列在正文后面的杂质），而这些额外杂质超过了药典规定
14 的忽略限量和报告限量时，申报人必须证明药典方法是否能够控制这些杂质，报告这
15 些杂质的保留时间或Rf值、检测限或定量限。如果药典正文不能控制这些额外杂质，
16 必须申报合理的、经过验证的方法和检验项目。如果对成品或中间体不进行日常检
17 测，必须提供证据证明：上述杂质不存在于成品或中间体中。

18 Chromatograms for production batches of the substance suitably zoomed and annotated and
19 with peak area results should be supplied.

20 必须提供生产批批分析数据的图谱，图谱应适当缩放和注释，并包括峰面积。

21 Where additional related substances are present (those not already mentioned in the
22 monograph) they should be considered according to the related substances section in the
23 general monograph *Substances for Pharmaceutical Use* (2034) (which corresponds to the
24 requirements of the ICH note for guidance Impurities in New Drug Substances
25 CPMP/ICH/2737/99). Suitable limits should be set which should be justified. In particular,
26 where present above the relevant identification threshold they are identified and when present
27 above the relevant qualification threshold they should be qualified. Alternatively, and where
28 appropriate, it may be demonstrated by other means that the impurity profile (number, nature,
29 amount) of the substance is comparable to that of products already on the market. For active
30 substances excluded from the requirements on related substances of the general monograph
31 *Substances for Pharmaceutical Use* (2034), and which contain additional impurities, qualified
32 limits should be proposed and where necessary toxicological data should be supplied.

33 如果存在额外相关物质（药典没有规定的杂质），必须符合药典“药用物质2034”
34 的规定（与ICH指南：新原料药杂质CPMP/ICH/273/99相同）。应建立合理限量标准，
35 并说明合理性。如果限量超过了鉴别限，则必须对这些杂质进行鉴别，如果超过了定
36 性限，则必须进行定性分析。也可采用其他方式来证明其合理性，如与已上市产品的
37 杂质进行对比，证明（在数量、性质和含量）可比性。如果该活性物质不属于药典
38 “药用物质2034”规定的范畴，而该产品又确实存在其他杂质，应申报定性限，必要

1 时必须申报毒性资料。

2 In the case of particularly toxic impurities, the determination of acceptable levels is a critical
3 issue to be documented. The EMEA CHMP Guideline on the Limits of Genotoxic Impurities
4 (EMEA/CHMP/QWP/251344/2006), effective as of 01 January 2007, is applicable to new
5 applications for existing active substances in conditions described in the scope of the
6 guideline. A specific discussion as part of the overall discussion on impurities should be
7 provided with regard to impurities with potential genotoxicity. If a genotoxic impurity is
8 liable to be present in the substance then conformity to the requirements of the guideline
9 should be demonstrated in the CEP application file

10 对于特别毒性杂质，确定可接受限量标准至关重要，必须申报。2007年1月1日生效的
11 “基因毒性杂质限量指导原则” (EMEA/CHMP/QWP/251344/2006)，在规定范围内，
12 适用于现有活性物质的首次申请。具潜在基因毒性的杂质，应作为杂质总论的一部分
13 进行特别讨论。如果基因毒性杂质易于出现在活性物质中，必须在CEP申请文件中，
14 证明该基因毒性物质符合上述指导原则的要求。

15 In discussing possible degradation products, reference to data from real time stability studies
16 or from stress testing or reference to the literature may be helpful. However, results from
17 formal stability studies are not a requirement when there is no request to mention a retest
18 period on the certificate.

19 讨论可能存在的降解物质时，参考文献、强迫降解实验或长期稳定性实验数据会有所
20 帮助。不过，如果不在CEP证书上申请再检验日期，则正式的稳定性实验结果不是必
21 须要求。

22 If alternative routes of synthesis are described the possible impurities are discussed separately
23 for each route.

24 如果使用了替代合成方法，必须分别讨论各合成途径可能产生的杂质。

25 **Other impurities:**

26 **其它杂质:**

27 Residues of residual toxic reagents should also be discussed and where applicable a suitable
28 limit and test method proposed if the monograph does not provide a suitable test.

29 应讨论毒性试剂残留的情况，如果药典没有规定此检验项目，适当时，应建立残留限
30 量标准，申报检验方法。

31 Residues of acids or bases that are not mentioned in the ICH guideline for residual solvents
32 (e.g. HCl, organic acids) should also be discussed if the monograph does not provide a
33 suitable test (pH, acidity or alkalinity).

34 ICH残留溶剂指南没有规定的酸碱残留（如，盐酸、有机酸）、药典又没有规定相应检

1 验项目（pH、酸值或碱值）时，应在申报文件中讨论其残留量。

2 **Residual solvents:**

3 **残留溶剂:**

4 The European Pharmacopoeia general chapter 5.4 Residual Solvents is to be applied. In
5 addition, the Annexes to: CPMP/ICH/283/95 Impurities: Guideline for Residual Solvents &
6 CVMP/VICH/502/99 Guideline on Impurities: Residual Solvents *Annex I: Specifications for*
7 *class 1 and class 2 residual solvents in active substances* (CPMP/QWP/450/03,
8 EMEA/CVMP/511/03) should be taken into consideration when setting specifications.

9 必须符合欧洲药典附录5.4“残留溶剂”的要求。建立质量标准时，应符合
10 “CPMP/ICH/283/95杂质：残留溶剂指南”的附录和“CVMP/VICH/502/99杂质指南：
11 残留溶剂附录I：活性物质中1类和2类残留溶剂”（CPMP/QWP/450/03,
12 EMEA/CVMP/511/03）的规定。

13 As indicated in the general chapter class 1 solvents should not be employed in the
14 manufacture of active substances or excipients unless there is a benefit/risk justification,
15 which should be provided. The final decision on the acceptability of the use of a class 1
16 solvent during manufacture will be taken by the Technical Advisory Board.

17 如药典附录所规定，如果未进行效益/风险评估，生产活性物质或辅料不得使用1类溶
18 剂，其评估报告应进行申报。最后由技术顾问委员会TAB决定是否同意在生产上使用1
19 类溶剂。

20 If class 2 solvents are only used in a step of the manufacturing process prior to purification,
21 the absence of such solvents in the final product should be demonstrated to justify the
22 exemption of a test. Otherwise a suitable specification should be introduced. Toxic solvents
23 (Class 1 and 2) should always be limited using a specific test, e.g. the test described in the
24 general methods of the European Pharmacopoeia.

25 如果在精制前只使用2类溶剂，应证明成品中没有2类溶剂残留，从而可以申请不进行2
26 类溶剂残留的日常检测。否则，应建立适当限量标准。应始终限制使用有毒溶剂（1、
27 2类溶剂），并采用特定的分析方法，如，欧洲药典通用方法的检验方法。

28 Any limit higher than the ICH option 1 limit should be justified according to an option 2
29 calculation, i.e. based on the daily dose (for class 2 solvents only).

30 必须按ICH方法2的计算方式，证明所有高于ICH方法1限量标准的合理性，即：根据日
31 服剂进行计算（只适用于2类溶剂）。

32 Low toxic solvents (Class 3) can be limited by a test for Loss on drying with a limit of not
33 more than 0.5%. For solvents used in previous steps and shown absent or at a low level their
34 control may be omitted. If the limit in the loss on drying test of the monograph is more than

1 0.5%, or it is not possible to introduce a loss on drying test, a specific test for residual
2 solvents should be introduced.

3 低毒性溶剂（3类）可以采用干燥失重进行控制，限量不得大于0.5%。前工序使用了溶
4 剂，而成品中没有或含量很低时，可省略日常检测。如果药典规定的干燥失重限量大
5 于0.5%、或无法进行干燥失重检测时，必须进行残留溶剂的检验。

6 For solvents not listed in the general chapter or listed in table 4 of the general chapter and
7 which need to be mentioned on the certificate toxicological justification of the proposed limits
8 should be supplied.

9 药典附录没有列出、或表4列出的溶剂，而又必须出现在CEP证书上规定限量时，必须
10 证明申报限量的合理性。

11 Solvents to be controlled will be mentioned on the certificate with the relevant test(s) and
12 limit(s) (except those mentioned in the specific monograph).

13 CEP证书将说明需要控制的溶剂，并规定检测方法和限量标准（药典个论另有规定的
14 溶剂除外）。

15 **Residual catalysts:**

16 **残留催化剂:**

17 Where catalysts are used in manufacture satisfactory information to demonstrate that there is
18 no entrainment of metal catalysts should be supplied. If there is carry over a suitable and
19 justified control limit should be proposed together with a validated method for determining
20 the residual catalyst.

21 如果使用催化剂，必须提供资料证明产品没有残留催化剂。否则，必须建立限量标准
22 和经过验证的分析方法，证明其合理性。

23

1 **Control of Drug substance (3.2.S.4)**

2 **成品控制 (3.2.S.4)**

3 **Specification (3.2.S.4.1):**

4 **质量标准 (3.2.S.4.1):**

5 The specifications should be in accordance with the current general and specific European
6 Pharmacopoeia monographs. Where the monograph has been shown not suitable to control
7 the quality of the substance, and in particular the related substances, the additional analytical
8 methods should be identified. Any additional specifications to those of the monograph shall
9 be justified.

10 质量标准应符合现行欧洲药典总论和正文要求。如果仅按药典标准无法控制产品质
11 量，尤其是相关物质时，必须说明其它的检验方法。必须证明所有药典以外附加标准
12 的合理性。

13 Where the monograph includes a production section the requirements of this section should be
14 shown respected in the application dossier.

15 药典正文对生产部份有所规定时，申报文件必须符合其要求。

16 **European Pharmacopoeia monograph under revision:**

17 **修订中的欧洲药典:**

18 If the monograph is in the process of being revised, the draft monograph will be taken into
19 consideration during evaluation since the current monograph is viewed as insufficient and
20 therefore the manufacturer may also wish to take it into consideration in the application
21 dossier. However, application of the revised monograph is not mandatory before the
22 implementation date.

23 如果药典正处于修订期，对文件的评审将考虑修订药典的规定，因为现行药典已存在
24 缺陷，因此生产厂可以在申报文件中考虑对药典修订文本的符合性。不过，修订中的
25 药典在正式生效前没有法律效应。

26 **Analytical procedures (3.2.S.4.2):**

27 **分析方法 (3.2.S.4.2):**

28 If specifications and test methods other than those described in the monograph concerned of
29 the European Pharmacopoeia are used, they must be fully described and validated (see below).
30 They would be appended to the certificate only if shown needed as a supplementary test to
31 those of the monograph (which are shown insufficient). Monographs describing a TLC
32 method to control related substances are generally not considered to comply with the
33 requirements of the general monograph Substances for Pharmaceutical Use (2034) and
34 general chapter 5.10 Control of impurities in substances for pharmaceutical use and therefore

1 a quantitative method should be proposed by applicants to control the related substances liable
2 to be present in the substance. This method would then be appended to the CEP. The TLC
3 method would be accepted in rare cases only i.e. as only rarely are the requirements of the
4 general monograph on Substances for Pharmaceutical Use and the general chapter 5.10
5 Control of impurities in substances for pharmaceutical use satisfied by a TLC method. It
6 would also be acceptable in cases where a particular related substance is controlled by a TLC
7 method but a quantitative method is also described in the monograph to control related
8 substances.

9 如果使用了欧洲药典以外的质量标准和分析方法，必须进行完整验证（见下面）。只
10 有在必须做为药典补充检验项目时（因为药典规定项目不够），才会附在CEP证书
11 上。一般认为用TLC法控制相关物质的药典个论是不符合药典总章“药用物质
12 （2034）”和附录5.10“药用物质杂质控制”的要求的，因此，为了控制可能出现的相关
13 物质，申请人应申报定量分析方法，该方法将附加在CEP证书上。只有极少数情况
14 可能接受TLC方法控制相关物质，如：TLC方法已经可以符合药典总章“药用物质”和
15 附录5.10“药用物质杂质控制”的要求。另外还有一种情况可以接受TLC方法，就是药
16 典规定了TLC方法的同时，也规定了定量方法控制某相关物质。

17 To facilitate the preparation of the certificate a separate description of any supplementary tests
18 should be presented.

19 为便于CEP证书的签发，必须申报所有附加方法。

20 **Validation of analytical procedures (3.2.S.4.3):**

21 **分析方法的验证 (3.2.S.4.3):**

22 If purity testing methods other than or supplementary to those of the European Pharmacopoeia
23 are used the analytical validation should be supplied. Where the official method of control of
24 related substances is used, and it is declared that only those related substances listed in the
25 transparency statement of the monograph are present in their substance, it should be
26 demonstrated that no other impurities are detected. Typical chromatograms should be
27 presented together with the characterisation of the reference substance(s). Where additional or
28 alternative methods are used in quality control of the final substance they should be
29 adequately validated and/or cross validated with reference to the monograph's method(s)
30 using Ph. Eur. CRS where prescribed. Where appropriate typical chromatograms should be
31 available.

32 如果使用不同于欧洲药典的纯度检验方法、或有附加的检验方法，必须申报方法验证
33 资料。如果使用官方检验方法控制相关物质，而且声明只存在欧洲药典列出的相关物
34 质时，则必须证明成品中检测不出其它杂质。应提供典型图谱，并进行特性描述。如
35 果使用其它方法或替代方法控制成品质量，必须进行方法验证，用规定的欧洲药典标
36 准品证明替代方法与药典方法的等同性。必要时，须提供典型图谱。

1 If an additional method is exactly as described in the general methods of the European
2 Pharmacopoeia (i.e. general method 2.4.24 for residual solvents) a full validation is not
3 required but the method should be described and only applicability to the concerned substance
4 should be demonstrated. For the determination of residual solvents the method of sample
5 preparation and the used system (A or B) should be specified. Methods from a specific
6 monograph of another Pharmacopoeia do not have to be fully validated (though specificity
7 and level of detection and/or quantification should be calculated). If the method of the specific
8 monograph is used to control additional impurities a minimum validation should be done
9 (specificity, limits of detection and quantification).

10 如果附加检验方法与药典附录方法完全相同（即：残留溶剂检测方法：附录2.4.24），
11 则不需要完整验证，但是必须对方法进行详细描述，只需要证明方法对成品检测的适
12 用性即可。如果是检测残留溶剂，必须规定样品制备方法、说明使用哪一个系统（系
13 统A或B）。他国药典正文规定的检验方法也不需要完整验证（但应计算专属性、检测
14 或定量限）。如果他国药典正文规定的方法用于检测附加杂质，必须进行最小程度的
15 验证（专属性、检测限和定量限）。

16 **Batch analyses (3.2.S.4.4):**

17 **批分析数据 (3.2.S.4.4):**

18 To be able to re-evaluate the monograph of the European Pharmacopoeia the results of a full
19 testing of at least two batches will be given. Results below 1.0 % for related substances
20 should be reported with two decimal places e.g. 0.25 %. When different grades, methods of
21 manufacture or alternatives or different sites are described in the dossier, the results of the
22 analysis of the batches shall be provided for each of them. The batch size, and the date of
23 manufacture and analysis will be given. The results of the analysis are given as actual figures
24 whenever possible instead of statements such as “conforms”, “complies” etc

25 为了能够对药典正文进行再次评估，必须申报至少两个批号的全分析数据。小于1.0%
26 的相关物质必须报告到两位数，如0.25%。如有多种级别、多种生产方法、或多个场
27 地，必须分别报告其批分析数据。必须报告批量、生产日期、检验日期。必须尽可能
28 以数字形式报告检验结果，避免使用“合格”“符合要求”等字眼。

29 The batch size should be in accordance with the declared maximum batch size as specified in
30 the description of the manufacturing process.

31 批量必须符合在生产工艺描述中申报的最大批量。

32 The results submitted should be discussed in relation to the limits of the European
33 Pharmacopoeia monograph and possible supplementary tests.

34 根据欧洲药典规定标准和可能增补的检验项目，对申报的批分析数据进行讨论。

35

1 **Justification of specification (3.2.S.4.5)**

2 **质量标准的合理性 (3.2.S.4.5)**

3 It should be stated if supplementary or improved tests are needed. Any additional
4 specifications or deviations should be justified. The possible need for a revision of the
5 European Pharmacopoeia monograph should be discussed.

6 必须说明是否需要补充检验或调整检验项目。必须证明附加质量标准或差异的合
7 理性。必须讨论是否需要修订欧洲药典。

8 **Omission of tests:**

9 **省略检验项目:**

10 Where the monograph mentions a test for a named impurity (metal catalyst/reagent/solvent)
11 but which is not used during manufacture, the manufacturer may omit the test in the
12 specifications which should be made clear in the dossier. If the proposal of the applicant is
13 accepted, a clear statement on this subject will be reported on the CEP. However, the
14 substance should comply with the monograph, if tested.

15 药典规定的已知杂质（金属催化剂/试剂/溶剂）、但申请人生产中不使用时，生产厂可
16 以在质量标准中省略这些项目，但必须在申报文件中明确提出。一旦这种申请得到批
17 准，CEP证书上将会予以明确说明。不过，如果进行检验，产品必须符合药典规定。

18 **Reference standards or materials (3.2.S.5)**

19 **参考标准或物质 (3.2.S.5)**

20 When in-house standards/working standards, non-official or official standards other than the
21 appropriate Ph. Eur. CRS are employed, they have to be suitably described (in terms of
22 identification, purity, assay, etc) and their establishment have to be demonstrated. If other
23 standards are used instead of their respective Ph. Eur. CRS an appropriate comparison to the
24 Ph. Eur. CRS is required.

25 如果使用内部标准/工作标准品、非法定标准而不使用欧洲药典标准品，必须进行适当
26 描述（鉴别、纯度、含量等），必须证明其合理性。如果使用其它标准品而不是
27 EPCRS，则必须证明与EPCRS的等同性。

28

1 **Container closure system (3.2.S.6)**

2 **容器包装系统 (3.2.S.6)**

3 The container closure–system should be described and the specifications (including
4 description and identification) should be supplied. Where relevant conformity to the note for
5 guidance *plastic Primary Packaging Materials* (CPMP/QWP/4359/03) should be shown. The
6 compatibility with the requirements of the storage section of the specific monograph (e.g. for
7 airtight containers) should be demonstrated.

8 必须描述容器包装系统和质量标准（包括外观和鉴别）。相关时，应证明符合“直接
9 接触药品的塑料包材(CPMP/QWP/4359/03)指南”。应证明该包装适用于药典正文规定
10 的贮存条件（如，密闭容器）。

11 **Stability (3.2.S.7)**

12 **稳定性 (3.2.S.7)**

13 As stated in the note for guidance *Stability testing of existing active substances and related*
14 *finished products* (CPMP/QWP/122/02) for substances described in an official
15 Pharmacopoeia monograph which covers the degradation products, results from formal
16 stability studies are not necessarily required. However, when a retest period is requested to be
17 mentioned on the certificate (which should be made clear on the administrative form) it
18 should be determined in accordance with Stability testing of existing active substances and
19 related finished products (CPMP/QWP/122/02 Rev 1) and the Annex: Declaration of Storage
20 Conditions for Medicinal Products Particulars and Active Substances (CPMP/QWP/609/96
21 Rev. 1)). Results from stability studies justifying the requested retest period and in accordance
22 with the note for guidance shall be supplied. In accordance with this note for guidance results
23 from accelerated stability studies should be supplied when a retest period is to be mentioned
24 on the certificate. In addition to the retest period, the commercial packaging material and
25 where necessary storage conditions will also be stated on the certificate. If no request to
26 mention a retest period on the certificate is made stability data may still be submitted in
27 particular to support the discussion on impurities and which should be summarised.

28 根据CPMP/QWP/122/02指南：“现行活性物质和其成品制剂稳定性实验”规定，法定
29 药典收载、而药典又规定了相关物质的产品可以不必申报正式的稳定性实验数据。但
30 是，如在CEP证书上申请再检验日期（这一点必须在填写管理表格时明确说明），则
31 应按照“现行活性物质和其成品制剂稳定性实验(CPMP/QWP/122/02 Rev 1)”及其附
32 件：药品和活性物质贮存条件声明(CPMP/QWP/609/96 Rev. 1)的要求来制定再检验日
33 期。必须按指南CPMP/QWP/122/02要求申报稳定性实验数据，证明申报的再检验日期
34 的合理性。依据指南CPMP/QWP/122/02，如果在CEP证书上申请再检验日期，应提供
35 加速稳定性试验结果。除再检验日期之外，商业包装、贮存条件（必要时）都会在
36 CEP证书上加以规定。如果不在CEP证书上申请再检验日期，仍然会需要申报稳定性数
37 据，尤其是用于支持有关杂质的讨论。

1 **Post-approval Stability Protocol and Stability Commitment (3.2.S.7.2);**

2 **批准后稳定性计划和承诺 (3.2.S.7.2);**

3 A re-test period may be attributed based on extrapolation proposed by the applicant under the
4 conditions described in the Nfqs *Stability testing of existing active substances and related*
5 *finished products* (CPMP/QWP122/02 revision 1) and *Evaluation of Stability Data*
6 (CPMP/ICH/420/02). In this case, and also when the retest period has been based on data
7 obtained on pilot batches, the manufacturer will be asked to supply the complementary and/or
8 additional stability data when available.

9 根据申请人按CPMP/QWP122/02修订 1指南：“现行活性物质和其成品制剂稳定性实
10 验”、CPMP/ICH/420/02“稳定性实验数据的评估”申请的再检验日期，可按外推法规
11 定产品的再检验日期。这种情况或根据试验批规定再检验日期时，生产厂应在获得新
12 的稳定性数据之后，补充报告。