Technical Guide for the Elaboration of Monographs

欧洲药典质量标准的起草技术指南

——II.7 部分

II.7 TESTS 检查

II.7.1 General 一般要求

The main purpose of the TESTS section is to limit impurities in chemical substances. General chapter *5.10. Control of impurities in substances for pharmaceutical use* gives details of the policy to be applied.

检查部分主要目的是对化学物质中的限量杂质进行检查。通则 5.10“药用物质中杂质控制”详细阐述了相关原则。

While the monograph must ensure adequate purity in the interests of public health, it is not the aim of the Ph. Eur. to impose excessive requirements that restrict unnecessarily the ability of manufacturers to produce compliant products.

虽然各论必须确保足够的纯度，以利于公众健康，但欧洲药典的目的不是强加过多的要求，不必要地限制制造商生产符合要求的产品的能力。

In the interests of transparency, information is included wherever possible on:

考虑到透明公开的原则，在可能的情况下包括以下信息：

_ the impurities controlled by a test;

由检查控制的杂质；

_ the approximate equivalent (percentage, ppm, etc.) of the prescribed limit in terms of the defined impurities or class of impurities.

在规定的杂质或杂质类别方面，规定限值的近似值（百分比，ppm 等）。

In addition to approved specifications in marketing authorisations, acceptance criteria and limits are set on the basis of analytical data at hand (i.e. batch results provided by manufacturers and data produced during monograph elaboration by the testing laboratories). In order to define limits for tests (loss on drying, residual water, etc.), the “3-sigma” rule may be used. In a normal distribution, 99.7% of values lie within three standard deviations of the mean. A minimum of 10 test results, obtained from one source, must be available to calculate the mean. However, it should be noted that the empirical rule is not applied systematically. This is especially true for the related substances test, where impurity limits should reflect more closely their real content in substances used in approved medicinal products.

除了上市许可中批准的标准外，还可根据现有分析数据（即生产商提供的批次结果和分析实验室在各论制定过程中产生的数据）设定验收标准和限值。为了定义检测限度（干燥失重、

残留水分等），可使用“3-sigma”规则。在正态分布中，99.7%的值位于平均值的三个标准差内。至少要有 10 个从一个来源获得的测试结果，才能计算出平均值。然而，应当指出的是，这个经验法则并未得到系统的应用。特别是对于有关物质的分析，杂质可接受标准应该更紧密地反映其在已批准的产品中使用的物质的实际含量。

Example 1: Determination of specification for water content(2.5.12)

例 1: 含水量限度的确定（2.5.12)

- *Batch data provided by a manufacturer:10batches*

  生产商提供的数据: 10 批
- *Min.value:3.2%,max.value:5.4%*

  最小值: 3.2%，最大值: 5.4%
- *Mean+3sigma =6.1%*

  平均值 + 3 sigma= 6.1%

Conclusion: The limit for water is set at 6.1% according to the 3-sigmarule.

结论：根据 3-sigma 规则，含水量限度被设定为 6.1%。

Example 2: Determination of specification for impurity X limit

例 2：杂质 X 限度的确定

- *Batch data for level of impurity X provided by a manufacturer:57batches*

  生产商提供的杂质 X 水平的批次: 57 批;
- *52 batches around or less 0.05%, 4 batches about 0.08%, 1 batch 0.09%*

  52 批次数据约或低于 0.05%，4 批次数据大约为 0.08%，1 个批次数据为 0.09%;
- *Mean+3sigma =0.11%*

  平均值 + 3 sigma = 0.11%;

Conclusion:The3-sigma rule is not applied. The limit for impurity X is set at 0.10%, based on batch data.

结论：不适合采用 3-sigma 规则。根据批次数据，杂质 X 的限值被设定为 0.10%。

Certain tests may apply to special grades (parenteral, dialysis solutions, etc.) or a test may have a special limit for a particular use: this is indicated within the test.

某些检查可能适用于特殊剂型（肠外、透析溶液等），或者某项检查可能对某一特定用途有特定的限度：应在该检查中注明。

II.7.2. Title of tests 检查项目名称

Wherever possible, the title includes the impurity or class of impurities limited by the test (Oxalica cid, Potassium, Copper, Chlorides, etc.).Non-specific tests carry a more general title appropriately chosen from the standard terminology of the Ph. Eur. (Appearance of solution, pH, Acidity or alkalinity, etc.) or a similar designation. Titles that merely refer to the methodology employed in the test (e.g. Absorbance) are to be avoided wherever possible.

在可能的情况下，标题包括测试所包含的杂质名称或杂质类别（例如：草酸、钾、铜、氯化物等）。非专属性试验的标题,可从欧洲药典的标准术语中适当选择（例如：溶液的外观、pH 值、酸度或碱度等）或类似的名称。应尽可能避免使用仅指试验中采用的方法作为检测项目的名称（如吸光度、比旋度）。

II.7.3. Solution S 供试品溶液

A solution of the substance to be examined, designated “Solution S”, is prepared whenever this can be used to perform more than one test (and/or identification).

只要可以用来进行一项以上的测试（和/或鉴定），就可以制备一种待检物质的溶液，命名为“溶液 S”。

If necessary, several solutions S, (designated S1, S2, etc.) may be prepared in various ways, each being used for at least two tests.

如有必要，可采用多种方法制备几种溶液 S（指定为 S1、S2 等），每种溶液至少用于两次测试。

For insoluble substances, solution S may be prepared by an extraction process.

对于不溶性物质，溶液 S 可以通过萃取来制备。

The solvent used depends on the purpose of the tests and the solubility of the substance to be examined and that of its potential impurities. It maybe:

溶剂的选用取决于测试的目的和待检物质及其潜在杂质的溶解度。可能情况如下：

- water(usually)水（常用）：
    - *carbon dioxide-free water R* in cases where the presence of carbon dioxide can appreciably influence the outcome of a test, e.g. for pH or Acidity or *alkalinity (see part II.7.5);*

      在易受到二氧化碳影响的实验中应使用无二氧化碳的水，比如测 pH 值/酸碱度（见 II.7.5)；
    - *distilled water R if solution S is used in the tests for barium, calcium and sulfates;*

      在钡、钙和硫酸盐的测试中使用的供试品溶液，要用蒸馏水制备；
    - *carbon dioxide-free water R prepared from distilled water when both previous cases apply;*

      前两条情况均存在时，要用无二氧化碳的蒸馏水制备；
- a dilute acid or an alkaline solution;

  酸或碱的稀释溶液；
- more rarely, other solvents (alcohols, tetrahydrofuran, etc.) that give solutions with a narrower field of application than aqueous solutions.

极少被使用的其他溶剂（乙醇、四氢呋喃等），这些溶剂制备的溶液比水制备的溶液适用范围更窄。

The solvent must make it possible to carry out the specified tests, either directly or after suitable dilutions explicitly specified in each test. The concentration is around 20-50 g/L, but may be(e.g. 10 g/L) or higher (100 g/L, possibly more in exceptional cases). The quantity of solution S prepared must be sufficient to carry out each of the tests for which it has been prepared and should be adapted, if necessary, if the text is revised. If solution S is to be filtered, the loss on filtering must be taken into account, and if the insoluble portion thus separated is to be used for another test, this is clearly indicated.

溶剂必须能够直接进行规定的试验，或在每次试验中经过规定的适当稀释后进行。一般溶液浓度约为 20-50 g/L，但也可能更低（如 10 g/L）或更高（100 g/L，特殊情况下可能更高）。制备的供试品溶液的数量必须足以进行每项试验，如有必要，应在修订文本时进行调整。如果供试品溶液要过滤，必须考虑到过滤时的损失，如果这样分离出来的不溶性部分要用于另一个试验，则要明确说明。

While several tests may be carried out on the same portion of solution S, this is only done for substances where there are good reasons to economise (expensive products or products whose use is subject to restrictions) and this is then clearly indicated in the monograph.

虽然可以对供试品溶液的同一部分进行多次试验，但这只适用于有充分理由节约样品的情况（昂贵的产品或使用受到限制的产品），并应在各论中明确指出。

Depending on the particular tests, the concentration of solution S is defined with varying levels of accuracy:

根据特定的测试，供试品溶液的浓度有不同的精确度要求:

- for “Appearance of solution”, “pH” and some identifications, an accuracy of 5-10% is sufficient;

  对于“溶液外观”、“pH 值”和一些鉴别项目，5-10%的精确度就足够了
- for most limit tests, an accuracy of about 2% is appropriate;

  对于大多数限度检查项目，2%左右的精确度是合适的。
- for some cases, such as the determination of specific optical rotation, specific absorbance, various chemical values and, more generally, tests where the result is obtained by calculation, a greater level of accuracy is needed.

  在某些情况下，如测定旋光度、吸光度、各种化学值，以及通过计算获得结果的检查，需要更高的精确度。

The accuracy with which the concentration of solution S is defined is that required by the most exacting test for which it is intended. The description of the preparation of solution S thus specifies:

供试品溶液浓度的精确度应基于最严格检查项目的要求。因此，对供试品溶液制备的描述包括：

- the quantity of substance to be examined with the required accuracy (see *General Notices*);

  符合精确度要求的待测物质的数量(参见凡例);

- the volume, to one decimal place (10.0 mL, 25.0 mL, etc.) when the concentration must be known to within less than 1%, without a decimal (10 mL, 25 mL, etc.) when a lower accuracy is adequate.

  当浓度必须精确到 1%以内时，量取的体积数保留一位小数(比如 10.0ml、5.0ml 等)，当准确度要求较低时， 可不保留小数(比如 10ml、25ml 等)。

II.7.4. Appearance of solution 溶液外观

This test makes it possible to ascertain the general purity of a substance through the detection of impurities insoluble in the solvent selected, or of coloured impurities.

这种检查可以通过检测不溶于所选溶剂的杂质或有色杂质，确定物质的大体纯度。

The “Appearance of solution” test is practically always prescribed for substances intended for preparations for parenteral use. A part from this, it is to be applied only if it yields useful information about specific impurities.

“溶液外观”对注射用的原料是必检项目。除上述用途外，该项检查只是用于提供一些特定的纯度信息。

It can comprise one or both of the following tests:

它可以包括以下一项或两项测试:

- *Clarity and degree of opalescence of liquids(2.2.1);*

  液体的透明度和浊度（2.2.1.）;

- *Degree of coloration of liquids(2.2.2).*

  液体的颜色（2.2.2）.

The two tests are practically always carried out on identical solutions, usually solution S, but they may be performed on different solutions.

两个试验通常采用同样的溶液。一般是供试品溶液，但也有可能采用不同的溶液。

The solvent employed is typically water but other solvents may be used depending on the solubility of the substance to be examined.

所使用的溶剂通常是水，但根据待测物质的溶解度,可以使用其他溶剂。

When an organic solvent is used to prepare solution S, it may be necessary to ensure that the solvent also complies with the test, especially where there is a very stringent requirement.

当使用有机溶剂制备供试品溶液时，需要确保溶剂也符合试验要求，特别是在要求非常严格的情况下。

The more concentrated the solution the stricter the test. For very pure substances or those used in high doses, the concentration chosen is 50-100 g/L, whereas for less pure substances or substances administered in small doses the concentration is 10-20g/L.

溶液浓度越高，测试越要严格。对于纯度很高或者大剂量使用的物质，其浓度选择为 50-100g/L。而对于纯度较低的物质或小剂量给药的物质，其浓度为 10-20g/L.

*II.7.4.1. Clarity and degree of opalescence(2.2.1)*透明度和浊度（2.2.1.）

This test is mainly performed on colourless substances or those that give only slightly coloured solutions in order to permit valid comparison with reference suspensions. Newer instruments with ratio selection are capable of measuring coloured substances.

这项测试主要是针对无色物质或溶液颜色较浅的物质，以便能够与标准浊度液进行有效的比较。较新的仪器具有比率选择功能，能够测量有色物质

The quantity of solution required depends on the diameter of the comparison tubes used; it varies from 7-20 mL for tubes with a diameter of 15-25 mm prescribed in the general chapter. Itis therefore necessary to take the larger volume into account.

所需的溶液量取决于所使用的比浊管的直径；对于通则中规定的直径为 15 mm 至 25 mm 的比浊管来说，溶液量从 7- 20mL 不等。因此选择比浊管时有必要考虑更大的溶液体积。

Most often, the solution examined must be “clear” (as defined in the Ph. Eur.). However, in certain cases (e.g. substances that are not intended to be used in solution), a more marked opalescence may sometimes be permitted.

大多数情况下，待测溶液必须是“澄清的”（如欧洲药典中的定义）。然而，在某些情况下(如非液体制剂中使用的物质)，有时允许有更高的浊度。

*II.7.4.2. Degree of coloration of liquids(2.2.2)*溶液的颜色（2.2.2）

This test applies to essentially colourless substances that contain, or may degrade to form, coloured impurities that can be controlled by limiting the colour of solution of the substance. Three methods are described in general chapter *2.2.2. Degree of coloration of liquids*:

该试验适用于含有或可能降解形成有色杂质的无色物质，可以通过限制该物质的溶液颜色进行质量控制。通则 2.2.2 中描述了溶液颜色检查的 3 种方法：

- Method I only requires 2 mL of solution but is seldom prescribed except for substances that give highly coloured solutions;

  方法 I 只需要 2mL 的溶液，但除非是那些颜色较深的样品，否则标准中很少采用该方法；

- Method II, which is more discriminating and therefore more frequently used, requires the larger volume of solution employed for the clarity test;

  方法 II 因区分力更强，因此更经常使用，需要更大体积的溶液来进行澄清度测试；
- Method III describes the instrumental determination of the coloration and provides more objective data than the subjective viewing of colours by a small number of individuals.

  方法 III 描述的是用仪器测定颜色，比主观观察颜色的方法提供更多的客观数据。

The results given by these three methods are not necessarily the same, so the one to be used is specified in the monograph.

这三种方法给出的结果不一定相同，所以要在各论中规定使用哪一种。

At present, the specifications indicated in the Ph. Eur. Are all based on visual determination and an exact correlation between visual and instrumental results is not always possible, depending on the ability of the analyst to differentiate between colour grades (visual method) and on the equipment settings. Hence, when using chapter *2.2.2*, the analyst is asked to report the results together with the method used (I, II or III).

目前，欧洲药典中规定的标准均基于目视测定，目视结果和仪器结果之间并不总是能够准确关联，这取决于分析员区分颜色等级（目视方法）和设备设置的能力。因此，当使用通则 2.2.2 时，要求分析员将结果与使用的方法（I、II 或 III）一起报告。

The solution is described as colour less when it is less coloured than reference solution B9. When the solution is slightly coloured, the appropriate reference solution is given. When the shade of colour varies depending on the samples, two or more reference solutions of the same degree of colour may be mentioned, or even only the degree of coloration without specifying the actual colour.

当溶液的颜色浅于 B9 标准比色液时，溶液的颜色规定为无色。当溶液略带颜色时，应给出合适的标准比色液。当颜色的深浅因样品不同有变化时，可以规定 2 个及以上相同等级的标准比色液，甚至只提及颜色等级而不指明实际颜色。

For material intended for parenteral use and for highly coloured solutions, especially when the use of Method I is contemplated, it is preferable to apply a limit of absorbance measured with a spectrophotometer at a suitable wavelength (usually 400-450nm). The concentration of the solution and the limit of absorbance must be stated. The conditions and limit must be based on knowledge of the absorbance curve in the range of 400-450 nm and on results obtained with appropriate samples, including stored and degraded samples, as necessary.

注射用物料和溶液颜色较深的物料，特别是当考虑使用方法 I 时，最好采用分光光度计在合适的波长（通常为 400-450nm）下测量的吸光度限度。必须说明测试溶液的浓度和吸光度的限度。测试条件和限度必须基于对 400-450nm 范围内吸光度曲线的了解，以及使用适当的样品（必要时包括储存和降解样品）获得的结果。

II.7.5. pH and Acidity or alkalinity pH、酸度/碱度检查

This test enables the limitation of acidic or alkaline impurities stemming from the method of preparation or purification or arising from degradation (e.g. from inappropriate storage) of the substance. The test may also be used to verify the stoichiometric composition of certainsalts.

该测试可以确保由于制备或纯化方法或由于物质的降解（如不适当的储存）而产生的酸性或碱性的杂质的限度。该测试也可用于验证某些盐类的化学成分。

Two types of test for protolytic impurities are used in the Ph. Eur.: a semi-quantitative titration experiment using indicators or electrometric methods to define the limits (the Acidity or alkalinity test); or a pH measurement.

在药典中采用两种方法对解离型杂质进行检测：第一种方法是采用指示剂或电化学方法半定量滴定试验确定限度值，也就是酸碱度检查；第二种方法是 pH 测定。

pH measurement is included if the material has buffering properties, otherwise a titrimetric procedure is recommended.

如果物料具有缓冲性质，应进行 pH 测定，否则推荐采用滴定方法检测。

The question of whether to prescribe an Acidity or alkalinity test or a pH measurement in a pharmacopoeial monograph can be decided on the basis of an estimation of the buffering properties of the material. To this end, a titration curve can be constructed for an aqueous solution (or, if necessary, an extract) in the intended concentration (10-50 g/L) of a sample, preferably pure, of the substance to be examined, using 0.01 M hydrochloric acid and 0.01 M sodium hydroxide, respectively, and potentiometric pH measurement.

可以根据物料缓冲能力的估计，确定在药典标准中选用酸碱度检查还是 pH 测定。最后，可以用 0.01M 盐酸和 0.01M 氢氧化钠分别对预定浓度（10-50g/L）的待检物质的水溶液（或者必要时，提取物）建立滴定曲线，并进行电位 pH 测量。

The inflexion point of the titration curve is the true pH of the solution and will, for a pure substance, be at the point of intersection with the pH-axis. The measure of the buffering capacity of the solution to be examined is the total shift in pH, (pH), read from the titration curve as the result of adding 0.25 mL of 0.01 M sodium hydroxide to 10 mL of the solution and 0.25 mL of 0.01 M hydrochloric acid to a separate 10 mL portion of the same solution. The buffering capacity is inversely proportional to the pH. For a sample that is not quite pure, carry out a parallel displacement of the titration curve so that the true pH of the solution is on the pH-axis before the pH is read from the curve.

滴定曲线的拐点是溶液的真实 pH 值，对于纯物质来说，它将位于与 pH 轴的交点处。衡量待测溶液的缓冲能力是指从滴定曲线上读出的 pH 值的总变化（ΔpH），即一方面向 10mL 的溶液中加入 0.25mL 的 0.01M 氢氧化钠，另一方面向同一溶液的另 10mL 部分加入 0.25mL 的 0.01M 盐酸。缓冲能力与ΔpH 成反比。对于不太纯的样品，对滴定曲线进行平行位移，使溶液的真实 pH 值在 pH 轴上，然后再从曲线上读出ΔpH 值。

The magnitude of ΔpH of the solution to be examined determines the choice of method for the limitation of protolytic impurities according to the following scheme. The classification is based upon the observation that the colour change for most indicators takes place over a pH range of 2 units.

待测溶液的ΔpH 值的大小决定了选择以下哪种方案进行解离性杂质的限度检查方法。该分类

是基于这样的观察：大多数指示剂的颜色变化发生在 2 个单位的 pH 范围内。

ClassA	ΔpH >4	Acidity-alkalinity test using two appropriate indicators. 使用两种适当的指示剂进行酸碱度测试。
ClassB	4 >ΔpH >2	Acidity-alkalinity test using a single appropriate indicator. 利用一种适当的指示剂进行酸碱度测试。
ClassC	2 >ΔpH >0.2	Direct pH measurement. pH 值测定法
ClassD	ΔpH <0.2	The protolytic purity cannot be reasonably controlled. Substances that are salts consisting of ions with more than one acidic and/or basic function belong to this class and for these a pH measurement can contribute to ensuring the intended composition if the limits are sufficiently narrow. 原始溶液纯度无法进行合理的控制。由 1 种以上酸性和/或碱性离子组成的盐类物质属于这一类，对于这些物质，如果限度足够窄，pH 值的测量有助于确保预期的组成比例。

It is evident that, by changing the concentration of the solution to be examined, the class of buffering properties as set out above into which the substance will fall can be altered to some extent, since the shape of the titration curve will also be modified as a result. The concentration range given above is not to be exceeded, however, unless poor water solubility means that a more dilute solution has to be used.

显然，通过改变待测溶液的浓度，可以在一定程度上改变上述物质所处的缓冲性质类别，因为滴定曲线的形状也会因此而改变。但是，除非水溶性差，必须使用浓度更低的稀溶液，否则不能超过上述规定的浓度范围。

If a test for acidity-alkalinity cannot be performed with the use of indicators due to the coloration of the solution to be examined or other complications, the limits are then controlled electrometrically. If on the other hand, the addition of a standard acid or base leads to decomposition or precipitation of the substance to be examined, it may be necessary to prescribe a pH test regardless of the buffering properties.

如果由于待测溶液的颜色或其他复杂情况，无法使用指示剂进行酸碱度测试，那么就用电化学方法控制限度。另外，如果加入标准酸或碱会导致待测物质的分解或沉淀，则可能需要规程 pH 值测试，而不考虑供试品溶液的缓冲性质。

If, for the reasons outlined above, a pH measurement has to be prescribed for solutions with little or no buffering capacity, the solution to be examined is prepared with *carbon dioxide-free water R*.

由于上述原因，如果需要对缓冲能力较弱或没有缓冲能力的溶液进行 pH 测量，则需要用不含二氧化碳的水来制备待测溶液。

Conversely, it is not necessary to use *carbon dioxide-free water R* when preparing solutions that have sufficient buffering capacity to warrant a direct pH measurement because the required accuracy, which seldom exceeds 1/10th of a pH unit, will not be affected. When anacidity requirement corresponds to not more than 0.1 mL of 0.01 M sodium hydroxide per 10 mL of solution to be examined, the solution must be prepared using *carbondioxide-freewater R*. These considerations are to be borne in mind when prescribing the composition of solution S if it is to be used in a test for protolytic impurities.

反之，没有必要使用不含二氧化碳的水来制备有足够缓冲能力的溶液，以保证直接测量 pH 值，因为所要求的精度很少超过 1/10 的 pH 单位，不会受到影响。当酸度要求相当于每 10mL 待测溶液中不超过 0.1mL 的 0.01M 氢氧化钠时，后者必须用不含二氧化碳的水来配制。在规定供试品溶液的配制时，如果它要用于解离型杂质的测试，就要考虑到上述因素。

II.7.6. Optical rotation(*2.2.7*)旋光度检查（2.2.7）

Measurements of the optical rotation of an article, though sometimes useful for identification purposes, may be used as a purity test:

尽管有时可用于鉴别，但旋光度检查主要用于药物的纯度测试：

- either to assess the general purity of an optically active substance(a liquid or a solid in solution), by calculating the “Specific optical rotation” (title of the test);

  通过计算“比旋度”（检查项目名称），可对具有光学活性的物质(液体或固体物质的溶液)的纯度进行评估；

- or to limit the presence of optically active impurities in any “optically inactive” mixture (racemate), provided that the specific optical rotation of the enantiomer at 589nm is sufficient to ensure adequate sensitivity. In this case, the optical rotation of the liquid or of the solid in solution is measured under defined conditions (temperature, concentration, path length) and the range normally given should be − 0.10° to + 0.10° (covering the substances that are not true racemates).

  或者只要对映异构体在 589nm 处的旋光度有足够的灵敏度，可以通过旋光度控制任何“无光学活性”的混合物（外消旋体）中光学活性杂质的限度。在这种情况下，在规定的条件下（温度、浓度、旋光管长度）测量液体或固体在溶液中的旋光度，通常给出的范围应该是-0.10°到+0.10°（覆盖非外消旋体的物质）。

In monographs on a single active enantiomer(eutomer), chiral chromatography (“Enantiomeric purity”) is preferred to control the other enantiomer (distomer) because specific optical rotation is generally not specific enough for an appropriate control. On the other hand, an achiral chromatographic procedure can generally be used to test for diastereoisomers.

在关于单一活性对映体（异构体）的各论中，首选手性色谱法（“对映体纯度”）来控制另一个对映体（异构体），因为比旋度通常不足以对其进行适当的控制。另一方面，非手性色谱程序一般可用于检测非对映异构体。

Although the test is not suitable for highly coloured or opalescent solutions, filtration can sometimes make the determination possible for opalescent solutions. Shortening the path length can also help to measure particular samples (e.g. for some essential oils).

该测试不适合颜色深或混浊的溶液，有时可采用过滤的方式使混浊的溶液可被检测。缩短旋

光管长度也有助于测量特定的样品（例如一些精油）。

The following aspects are taken into account in describing the test:

在描述该试验时，考虑到了以下几个方面

- the solvent, which depends on the solubility of the substance to be examined and the observed optical rotation in that solvent. In the case of non-aqueous solvents, their purity and especially their water contents may need to be carefully defined;

  溶剂。根据供试品的溶解性和样品在该溶剂中的旋光度值，确定配制供试品溶液的溶剂。如果需要使用非水溶剂，必须规定溶剂的纯度，特别是含水量。

- the quantity of substance to be used, determined with sufficient accuracy (generally 1%), and the volume to be prepared (given to one decimal place). Although the volume depends on the apparatus used, 25.0 mL is usually prescribed because it rarely exceeds that amount. The concentration of the solution must be high enough to give a reliable reading of the angle of rotation;

  供试品的用量要保证足够的准确度(浮动一般为±l%)，供试品溶液的体积也应确定（小数点后一位数字）。检测所需的溶液体积取决于所用的仪器，但是，通常很少超过 25.0ml。溶液的浓度必须足够高，以便得到可靠的旋光度读数。

- the degree of hydration or organic solvation of the substance (for the calculation of the result);

  物质的水合度或有机化程度（用于计算结果）；

- the result is the mean of at least five measurements when evaluated visually, with an instrument allowing readings to the nearest 0.01°;

  该结果是至少五次测量的平均值，仪器读数应准确至 0.01°;

- measured angles of optical rotation are given to two decimal places;

  测得的旋光度精确到小数点后两位;

- specific optical rotation values are given to two or three significant figures: values below 10 are given to two significant figures, while values of 10 and over are given to three significant figures;

  比旋度结果保留两位或三位有效数字。比旋度小于 10 时，保留两位有效数字，比旋度超过 10 时，保留三位有效数字;

- composition limit for racemates.

  外消旋体的成分限制;

The value of the specific optical rotation is calculated with reference to the dried or anhydrous substance.

旋光度应按照干燥的或无水物进行计算。

II.7.7. Absorption spectrophotometry (ultraviolet and visible)(*2.2.25*)

吸收分光光度法 (紫外和可见光)（2.2.25）

The absorption of electromagnetic radiation may be used in purity tests as a limit test for certain impurities. The typical case is that of impurities that absorb in a region where the substance to be examined is transparent, in which case the absorbance of a solution of the substance to be examined is measured. This test may be performed in the following ways:

电磁辐射吸收可用于纯度测试，作为某些杂质的限度检查。典型的情况是杂质在待测物质无吸收的区域中有吸收，在这种情况下测量待测物质溶液的吸光度。该测试可通过以下方式进行：

- by direct measurement on the solution, where the absorbance measured is a maximum absorbance at a given wavelength or over a wavelength range;

  如果规定最大吸收波长或波长范围，可直接对供试品溶液进行测定。

- after carrying out a chemical reaction that forms, with the impurity, a substance that absorbs at a wavelength where the substance to be examined is transparent, a maximum value at the given wavelength being prescribed.

  在进行化学反应或显色反应后，杂质在规定波长处有吸收，而主成分无吸收，给出规定波长处的最大吸光值。

For measurements in the ultraviolet region, it is advisable to avoid measuring at wavelengths below 230 nm as more interferences and more stray light are observed in this region.

对于紫外区的测量，最好避免测量波长低于 230nm，因为在该区域会观察到更多的干扰和更多的杂散光。

It is important to describe precisely the operational conditions to be observed, in particular the preparation of solutions prepared by successive dilutions.

准确描述操作条件非常重要，特别是通过连续稀释的方式制备溶液时。

II.7.8. Related substances 有关物质

The policy on control of impurities is described in general chapter 5.10. Control of impurities in substances for pharmaceutical use and in the general monograph Substances for pharmaceutical use (2034). Monographs should be elaborated accordingly. Monographs are designed to take account of substances used in approved medicinal products in member states and should provide adequate control of all impurities occurring in these substances, insofar as the necessary information and samples (substance and impurities) are available from the manufacturers. Such impurities are controlled in a test for related substances and any other individual test for impurities (e.g. “Impurity X” or “Enantiomeric purity”). Where the required information and samples are not provided for a substance synthesised by a given method, the monograph will not necessarily cover the corresponding impurity profile.

（欧洲药典）通则 5.10《药用物质中杂质的控制》和总论《药用物质》（2034）中阐述了杂质的控制策略。各论的也应作相应的阐述。各论的设计应考虑成员国已批准的药物制剂中使用的物质并应充分控制这些物质中出现的所有杂质。可以从生产商处获得必要的信息和样品（包括主成分和杂质）。在检查项目中以有关物质项目和其他杂质的个别试验项目（例如“杂

质 X”或“对映体纯度”）对这些杂质进行控制。如果没有为用特定方法合成的物质提供需要的信息和样品，则各论中不一定涵盖相应的杂质情况。

The provisions for related substances in the general monograph Substances for pharmaceutical use (2034) and general chapter 5.10 apply to all active substances and excipients, unless otherwise stated therein.

除非另有说明，（欧洲药典）总论《药用物质》（2034）和通则 5.10 中对于有关物质的条款适用于所有活性物质及辅料。

If an exception is to be made for a particular substance normally covered by these provisions, the following statement is included in the specific monograph: “The thresholds indicated under Related substances (Table 2034.-1) in the general monograph Substances for pharmaceutical use (2034) do not apply”. It is recommended to provide the reason for the deviation in a footnote during the Pharmeuropa stage. This explanation will be transferred to the EDQM Knowledge Database once the monograph is published in the Ph. Eur.

如果某一物质超出本规定通常适用的情况，应在其各论中包含如下表述：总论《药用物质》（2034）中有关物质（表 2034-1）中规定的限值不适用于本品。建议药典各论起草阶段，在脚注中提供不符合的原因。当欧洲药典收载该各论时，该解释将转移至 EDQM 知识数据库中。

Monographs should include acceptance criteria for:

各论中应包括以下限度：

- each specified impurity;

  单个特定杂质；

- unspecified impurities (previously referred to as “any other impurities”), normally set at the identification threshold;

  非特定杂质（此前被称为“任意其他杂质”），通常的限度为鉴定水平；

- the total of impurities.

  总杂质。

Impurities to be controlled include intermediates and by-products of synthesis, co-extracted substances in products of natural origin and degradation products. Monographs on organic chemicals usually have a test entitled “Related substances” (or a test with equivalent purpose under a different title), designed to control organic impurities. Where applicable, inorganic impurities are usually covered by other tests. Residual solvents are covered by specific provisions [see below and in general chapter 5.4. Control of residual solvents and the general monograph Substances for pharmaceutical use (2034)].

需要控制的杂质包括中间体和合成的副产物、天然来源产品中的共提物和降解产物。有机化学药物的各论中通常对于杂质的控制项目称为“有关物质”（或不同名称但功能相同的试验）。在适用的情况下，无机杂质在其他项目下进行。残留溶剂有特定的规定[参加下文、附录 5.4《残留溶剂控制》及总论《药用物质》（2034）的规定]。

DNA-reactive (mutagenic) impurities. ICH guideline M7 on assessment and control of DNA reactive (mutagenic) impurities in pharmaceuticals to limit potential carcinogenic risk (EMA/CHMP/ICH/83812/2013) entered into force on 1 January 2016.

DNA-反应（致突变）杂质。ICH 指导原则 M7《评估和控制药物中的 DNA 活性（致突变）杂质以限制潜在的致癌风险》（EMA/CHMP/ICH/83812/2013）于 2016 年 1 月 1 日生效。

The following pragmatic approach is in line with the ICH M7 guideline and should be followed when elaborating or revising monographs related to substances for human use. A DNA-reactive impurity is covered in the individual monograph only where there is study data demonstrating mutagenicity of the impurity by a recognised toxicity test. The existence of structural alerts alone is considered insufficient to trigger follow-up measures. Following a decision by the Ph. Eur. Commission (November 2016), DNA-reactive impurities should be addressed in individual monographs in:

在起草或修订与人用药相关的各论时，实际使用的方法应符合 ICH M7 准则。只有当通过公认的毒性试验获得的研究数据证明该杂质具有致突变性的情况下，才会在该各论中涉及 DNA-反应杂质。仅仅存在警示结构被认为不足以引发后续的控制措施。在欧洲药典委员会做出决定后（2016 年 11 月），DNA-反应性杂质被认为是一种新的方法。DNA-反应杂质应在个别各论中描述：

_ the PRODUCTION section, by a statement, when no specific test or limit is known to the GoE at the time of elaboration/revision of a monograph or when the technique is so special that it is not available to a majority of users;

如果在制定/修订各论时，专家组不知道具体的测试，或者该技术非常特殊，以至于大部分用户无法使用时，则应在“生产”部分加上说明；

_ the TESTS section, when the analytical procedure and the limit are known and the technique is widespread.

当测试方法和限度值是已知的，并且该技术被广泛应用时，该方法会体现在测试部分。

Additional information and requirements for specific types of DNA-reactive impurities is provided in the general monograph Substances for pharmaceutical use (2034).

特定类型的 DNA-反应杂质的更多信息和要求，参见（欧洲药典）总论《药用物质》（2034）。

If a new synthetic route is used that may give rise to different DNA-reactive impurities or to higher levels of previously recognised ones, the evaluation by a Competent Authority should be used as the basis for the impurity in question.

如果应用新的合成路径可能导致不同的 DNA-反应杂质，或产生更高水平的已知杂质，则应将主管部门的评估作为有关杂质的依据。

If an issue concerning a DNA-reactive impurity is raised by a Competent Authority (notably for revision of a monograph or in comments on a Pharmeuropa draft), this will be dealt with on the basis of data provided to the Ph. Eur. Commission by the Competent Authority.

如果主管当局提出有关 DNA-反应杂质的问题（特别是对各论的修订或对药典草案的评论），

应当依据主管当局提供给欧洲药典委员会的数据进行处理。

Control of impurities. The most common and preferred method for controlling organic impurities is LC; GC or CE may be the preferred method in some instances. Although there are still some monographs that prescribe TLC, this technique should be reserved for controlling specific impurities that cannot conveniently be controlled by LC or GC. Existing TLC tests that do not follow this recommendation will be replaced gradually as soon as information on suitable LC or GC tests becomes available.

杂质控制。液相色谱法（LC）是控制有机杂质最常用也是首选的方法；在有些情况下，气相色谱法（GC）和毛细管电泳法（CE）是更合适的方法。尽管仍有部分各论采用 TLC 方法，但该项技术应保留用于不能被 LC 或 GC 方法控制的特定杂质。一旦有了合适的 LC 或 GC 方法，不遵循这一建议的现有的 TLC 测试将逐渐被取代。

Where the counter-ion of an active substance is formed from a lower organic acid, a test for related substances of the organic moiety is usually not considered necessary (e.g. magnesium lactate used as a source of magnesium).

当活性物质的反离子是由低价有机酸形成的，通常认为不需要对有机部分的有关物质进行测试（例如 用作镁来源的乳酸镁）。

Monographs frequently have to be designed to cover different impurity profiles because of the use of different synthetic routes and purification procedures by manufacturers. The usual practice is to include a general LC test, supplemented where necessary by other tests (LC, GC, CE, TLC or other techniques) for specific impurities. However, it is becoming increasingly impractical in some cases to design a single general test; in such cases, more than one general test is included and the scope of the different tests is defined in the tests themselves with a cross-reference in the IMPURITIES section.

由于不同的生产商采用不同的合成路径和精制工艺，因此各论通常需要设计包含不同的杂质概况。通常的做法是包括一个通用的 LC 方法，在必要时通过其他的测试方法（LC，GC，CE，TLC 或其他技术手段）对特殊杂质进行控制。然而，在某些情况下，设计一个单独的通用方法变得越来越不现实；在这种情况下，需要包含一个以上的通用方法，不同方法的测试范围应当在各自的测试中明确，并在“杂质”部分交叉引用。

Monographs cover a number of specified impurities listed in the IMPURITIES section. Specified impurities are those that occur in current batches of the substances used in approved products and for which an individual acceptance criterion is provided. Wherever feasible, monographs also have an acceptance criterion for other impurities (at the identification threshold for the substance) and a limit for the total of impurities (or a limit for the total of impurities other than a number of identified specified impurities) above the reporting threshold. The acceptance criterion for specified impurities may be set at the identification threshold for the substance.

各论的杂质部分包含了一些特定杂质。特定杂质是指在已批准药品中所用的当前批次物料中存在的，并且提供了单独的可接受标准的杂质。如果可行，各论中也应包含其他杂质的可接受标准（物质的鉴定限度）和超过鉴定限度的杂质总量限度（或杂质总量限度，非特定杂质含量）。对特定杂质的可接受标准可以设定为该物质的鉴定限度。

The acceptance criteria for specified impurities take account of both:

特定杂质的可接受标准应当考虑以下内容：

- approved limits;

  已批准的限度；

- recent batch data and stability data, with the acceptance criteria being set to take account of routine production conditions; data is provided by the manufacturer for typical batches and verified experimentally during elaboration of the monograph on at least three batches.

  最近批次数据和稳定性数据，可接受标准的建立应考虑常规生产条件；生产商提供的典型批次的数据，并在各论起草制定中经过至少三个批次的确认试验。

If several approved limits exist, the highest is taken.

如果存在多个已经批准的限度，则采用最严限度。

When a monograph describes the salt form of the substance, then, for the purpose of calculation and specification setting and unless otherwise prescribed, the impurity is assumed to be present in the same salt form.

当各论中描述的物质以盐的形式存在，为了计算和标准设定的目的，除非有其他规定，否则假定杂质以相同的盐的形式存在。

All decisions on impurity acceptance criteria should be based on the real impurity content (meaning after application of correction factors (CFs), where applicable) in representative batches examined.

所有关于杂质可接受标准的决定都应基于代表性批次的杂质实际含量（如适用，使用校正因子（CFs）校正后）的测定。

Impurities must be specified and located appropriately in the chromatogram if the reported batch values for an impurity are:

如果报告的批次的杂质数值符合以下要求，则杂质必须指定并在色谱图中适当定位：

- above the applicable limit for unspecified impurities before correction and cross this limit downwards when corrected (overestimation, CF＜1）;or

  校正前超过未指定杂质的适用限度，校正后向下超过限度（被高估，CF＜1）；或

- below the limit for unspecified impurities before correction and cross this limit upwards when corrected (underestimation, CF>1).

  校正前低于未指定杂质的适用限度，校正后向上超过限度（被低估，CF>1）。

Usually, no correction factor will be given if the reported batch values for an impurity are below the applicable limit for unspecified impurities before correction and below the reporting threshold (disregard limit) after correction.

通常，如果某一杂报告批结果在校正前小于未指定杂质适用的限度，校正后低于报告限（可忽略限度），则不会给出校正因子。

In any case, CFs between 0.8 and 1.25 (corresponding to response factors of 1.2-0.8) are not given in monographs. Additional information on the indication of CFs is given in part II.7.8.2.b.

任何情况下，如果校正因子（CFs）在 0.8～1.25（相应的响应因子 1.2～0.8）之间，可不列入各论。关于 CFs 更多的信息可以参见本指南 II.7.8.2.b 章节。

Response and correction factors. According to general chapter 2.2.46. Chromatographic separation techniques, the relative detector response factor (commonly referred to as the “response factor”) expresses the sensitivity of a detector for a given substance relative to a standard substance. The correction factor given in the monograph is the reciprocal value of the response factor.

响应因子与校正因子。依据（欧洲药典）通则 2.2.46《色谱分离技术》，相对检测响应因子（通常指响应因子）表示检测器对给定物质相对于标准物质的灵敏性。各论中给出的校正因子是响应因子的倒数。

The response factor can be determined by preparing solutions of defined concentrations of the impurity and the substance to be examined and measuring them by LC/UV at a given wavelength and flow rate. The concentration of the impurity and that of the substance to be examined should be of the same order of magnitude and the measurement should be carried out using a calibration curve determined at several points around the concentration which corresponds to the acceptance criterion of the impurity. For the calculation, the mean of the area ratios over the whole range of linearity or the ratio of the slopes of the respective linearity regression equations may be used. The response factor can be calculated using the following formula:

响应因子可以通过配制规定浓度的杂质和待测物质溶液，并通过 LC/UV 在规定波长和流速条件下测定获得。杂质和待测物浓度应处于同一数量级并用标准曲线法测定，标准曲线点为杂质的可接受标准对应的浓度附近的浓度点。可以使用整个线性范围内的面积比的平均值或各线性回归方程的斜率比计算。响应因子可以通过以下公式计算获得：

$$RRF = \frac{A_i}{A_s} \times \frac{C_s}{C_i}$$

RRF = (relative) response factor;

RRF=（相对）响应因子

Ai = area of the peak due to the impurity;

Ai=杂质峰面积

As = area of the peak due to the substance to be examined;

As=待测物峰面积

Cs = concentration of the substance to be examined in milligrams per millilitre;

Cs=待测物浓度（mg/ml）

Ci = concentration of the impurity in milligrams per millilitre.

Ci=杂质浓度（mg/ml）

It is also important to consider the form (base/acid or salt) of both the impurity and the substance to be examined used when determining the response factor and to apply an additional correction for the molecular mass ratio when they are present in different forms. This correction can be done by ensuring that Ci is expressed with respect to the same form as the substance to be examined (i.e. as base/acid or salt) provided the impurity can actually be present in that form.

在确定响应因子时考虑杂质和待测物质的形式（碱/酸，或成盐）也很重要，并在它们以不同形式存在时依据分子量比值进行额外校正。可以通过确保 Ci（杂质浓度）表示为与待测物相同的形式（例如作为碱/酸，或成盐形式）来完成校正，前提是该杂质实际上可以以该形式存在。

Preferably, the response factor should be determined in two laboratories using the same protocol. If different UV-Vis detector types (diode array detector (DAD) and variable wavelength detector (VWD)) are available, these may also be considered for this measurement.

响应因子应在两个实验室使用相同的方案确定。如果有不同的紫外-可见检测器类型（二极管阵列检测器（DAD）和可变波长检测器（VWD）），也可以考虑用于该项测量。

The weighings of impurity and substance to be examined should both be corrected for their respective purity. If the available amount of impurity does not allow any experimental determination, values from the certificate of analysis may be used. If enough material is available, the chromatographic purity and water/solvent content of the impurity and the substance to be examined should be determined beforehand. A provisional value might be assigned on the basis of the following formula:

杂质和待测物的称量值应当依据各自的纯度校正。如果杂质的可用量不能满足试验测定，则可以使用分析报告中的数值。如果可以获得足够的物料，应事前确定杂质和待测物质的色谱纯度和水/溶剂含量。可以用以下公式对临时值赋值：

$$content(\%) = [100 - (water + solvents)] \times \frac{chromatographic\ purity\ (\%)}{100}$$

含量（%）=[100-（水分+溶剂）]×色谱纯度（%）/100

where the chromatographic purity is determined by normalisation or using a dilution of the test solution or of a solution of the impurity.

色谱纯度通过归一化或使用供试品或杂质溶液的稀释液来测定。

When only a small amount of the impurity is available, analytical procedures with low sample amounts may be preferred (e.g. thermogravimetric analysis for water/solvents, coulometry for water and LC to estimate purity by injecting a concentrated solution of the impurity). Suitable alternative approaches such as a combination of qNMR and LC data or a comparison of LC-UV and LC-CAD may be employed.

当只有少量杂质可使用，最好使用样品量少的测定方法（例如：水/溶剂的热重分析，库伦法测定水分和通过注入杂质的浓溶液的 LC 法）。可以采用适当的替代方法，如结合 qNMR 与 LC 数据，或比较 LC-UV 和 LC-CAD。

Separation methods. For pharmacopoeial purposes, the objective of a purity test using a separation method will usually be the control of impurities derived from one or more known manufacturing processes and decomposition routes. However, the experimental conditions, especially the detection system, are chosen specifically so as not to make the test unnecessarily narrow in scope. Chromatographic purity tests may often be the best means of providing a general screening of organic impurities derived from new methods of manufacture or accidental contamination. It may be advantageous to supplement a chromatographic test with other chromatographic or non-chromatographic tests.

分离技术。药典项下杂质测定所用分离技术通常用于一个或多个生产工艺或降解途径的药品中杂质的质量控制。然而试验条件，特别是检测系统的选择，应避免使检测范围不必要的缩小。色谱纯度测试是源自新生产方法或意外污染的有机杂质最佳的一般筛选方法。通过其他色谱或非色谱测试补充色谱测试可能是有利的。

As mentioned in part II.6.8, a chromatographic system applied to purity testing may, when suitable, be applied also for identification.

如本指南 II.6.8 所提及的，适用时，应用于杂质检测的色谱体系也可以用于鉴别测试。

When a related substances test based on a chromatographic technique is carried out, a representative chromatogram is published with the monograph in Pharmeuropa. Although the chromatogram will not ultimately be published in the Ph. Eur., it will be transferred to the EDQM Knowledge Database.

当进行基于色谱技术的相关物质测定时，药典各论中会收载典型色谱图。尽管色谱图最终不会在欧洲药典中发补，但是该图谱会被转移到 EDQM 知识数据库中。

When a mixture of impurities with or without the substance to be examined is available as a reference substance (e.g. peak identification CRS, impurity mixture CRS or system suitability CRS), a representative chromatogram, if mentioned in the monograph, will be supplied with the reference substance.

当包含或不包含待测物的杂质混合物作为标准物质（例如峰鉴别标准品、杂质混合物标准品或系统适用性标准品）使用时，如果各论中涉及了，将与标准物质一起提供其典型图谱。

Monographs should provide a reliable means of locating the impurities used for the system suitability test (SST) and all specified impurities on the chromatogram. Identification of impurities at or below the limit for unspecified impurities is necessary if a correction factor is to be applied. In such cases, these impurities are listed as specified impurities.

各论应提供可靠的方法定位系统适用性测试（SST）中的杂质和色谱图中所有的特定杂质。如果要应用杂质校正因子，则有必要对等于或低于非特定杂质限度的杂质进行鉴别。在这种情况下，这些杂质应被列为特定杂质。

Peaks may be located using:

可以使用下列方法对峰进行定位：

- a reference standard or a reagent for each impurity;

  每个杂质的标准物质或试剂;

- a reference standard containing some or all of the impurities, (e.g. peak identification CRS, system suitability CRS).

  包含部分或全部杂质的标准物质（例如峰鉴别标准物质，系统适用性标准物质）。

Location by relative retention is not generally considered sufficient for pharmacopoeial purposes, especially for gradient elution. Where a reference standard containing one or several impurities, with or without the substance to be examined, is to be used, a sample of each specified impurity should be provided to the EDQM to enable the establishment of the reference standard.

对于药典的目的来说，相对保留时间通常被认为是不够的，尤其是梯度洗脱方法。当使用含有一个或多个杂质的标准物质，无论是否含有待测物质，都应向 EDQM 提供每个特定杂质的样品，以便于建立参考标准。

In general, relative retention is given to one decimal place. However, it is given to two decimal places where necessary to indicate the elution order of closely eluting peaks. The following general considerations apply to separation techniques:

通常情况下，相对保留（时间）需要保留至小数点后一位。但是在必要时为了表示相近洗脱峰的洗脱顺序，需要显示两位小数。以下需要考虑的内容适用于分离技术：

- high concentrations/loadings are normally used since the symmetry of the principal peak or shape of the spot is not critical in impurity testing, so long as there is no interference. When using an external standard in quantitative determinations, the response of the principal peak in the chromatogram obtained with the test solution does not need to be in the linear range of the detector;

  如果主峰的对称性或主斑点的形状在杂质测试中并不关键，只要没有干扰，应采用高浓度/高点样量。当使用外标法进行定量测试时，供试品溶液获得的色谱图中主峰的响应不需要在检测器的线性范围内；

- in general tests for related substances, the substance to be examined should not bechemically modified (e.g.derivatisation) before purity testing since the impurity pattern may be modified；

  在有关物质的一般测试中，被测物质在纯度测试前不应进行化学修饰（例如衍生化），否则杂质类型可能会发生改变；

- similarly, extraction of the free base or acid prior to impurity testing is to be avoided；

  同样的，应避免在杂质测试前萃取游离碱或游离酸；

- t_R of the principal peak is determined using the diluted test solution (to increase accuracy while avoiding saturation effects).

  使用稀释的供试品溶液确定主峰的保留时间（t_R）（提高准确度，同时避免饱和效应）。

II.7.8.1. Thin-layer chromatography (2.2.27) and high-performance thin-layer chromatography for herbal drugs and herbal drug preparations (2.8.25)

用于植物药和植物药制剂的薄层色谱法（2.2.27）和高效薄层色谱法（2.8.25）

TLC methods should only be used to control a specified impurity and where LC, GC or CE methods are not appropriate (usually due to a lack of a suitable detection system). More information on HPTLC can be found in the Technical guide for the elaboration of monographs on herbal drugs and herbal drug preparations.

只有在控制特定杂质和LC，GC或CE方法不适用（通常确实合适的测试系统）时才会采用薄层色谱法（TLC）。更多关于高效薄层色谱法（HPTLC）的信息参见植物药和植物药制剂质量标准的起草技术指南。

Commercially available pre-coated plates, described in general chapter 4.1.1. Reagents, are to be used; the trade name of the plate found to be suitable during the elaboration of the monograph is indicated in a footnote to the draft monograph and added to the EDQM Knowledge Database after the monograph is adopted. In addition to information on the coating material used (type of coating material, type of binder), general chapter 4.1.1. Reagents describes a suitability test procedure under TLC silica gel plate R. The monograph must describe the type of plate, including the particle size for HPTLC plates, and include a system suitability requirement. It is often the case that the substances that would be best suited for a SST will not be readily available individually, in which case a sample of the substance to be examined containing them as contaminants or even a deliberately spiked sample may then be prescribed. Permissible adjustments to the different parameters are indicated in general chapter 2.2.46. Chromatographic separation techniques.

使用通则4.1.1《试剂》中描述的市售预制薄层板。各论起草过程中适用的薄层板的商品名称应标注在各论草案的脚注中，之后在各论收载后该信息会被补充进EDQM知识数据库中。除了使用的涂层材料的信息（涂层材料的类型，粘合剂类型）外，通则4.1.1.《试剂》还描述了TLC硅胶板R的适用性测试方法。各论中应描述薄层板的类型（包括HPTLC薄层板的粒径大小）并包括系统适用性的要求。通常情况下，最适合系统适用性测试的组分不易单独获取，在这种情况下，可采用包含污染成分的待测物质，甚至是特意在样品中加标来进行制备。通则2.2.46《色谱分离技术》中说明了不同参数的允许调整范围。

If any pre-treatment is required or if the chromatography is carried out in unsaturated conditions for the satisfactory conduct of the test, then this information is included in the text of the monograph. This especially applies to the use of reverse-phase plates.

如果为了获得满意的测试需要进行预处理或在不饱和条件下进行色谱分析，这些信息应包括在各论的文本中。上述要求尤其适用于反相板的使用。

One or more dilutions of the substance to be examined will often prove adequate for reference purposes, provided the impurities to be compared exhibit a similar behaviour under the chosen chromatographic conditions. This implies that the spots to be compared must be sufficiently close in terms of their RF value to minimise errors introduced by different diffusion of the substances during their migration. Otherwise, reference solutions containing the specified impurities are to be employed. It may be necessary to instruct the analyst to disregard a spot – often due to the non-migrating counter-ion of a salt – remaining on the starting line.

如果要比较的杂质在所选色谱条件下表现出类似的行为，则待测物质的一次或多次稀释通常足以作为参考。这意味着需要比较的斑点在它们RF值方面必须足够接近，以尽量减少物质

在迁移过程中不同扩散所带来的误差。否则，应使用含有特定杂质的对照溶液。有必要指示分析人员不考虑留在原点的斑点-通常是由于盐的负离子未发生迁移造成的。

Summation of the responses exhibited by each individual spot is only acceptable when appropriate equipment is prescribed. It is not recommended to set a limit or limits for the concentration of impurities without a limit on their number, otherwise the total theoretical impurity level would be unacceptably high. This situation may be counteracted by limiting the impurities on two or more levels, allowing only a defined number to be at the higher level and the rest below the lower level. As examples, the test may specify that no contaminant may exceed a relative concentration of 1% and that only one may exceed 0.25%, or that no contaminant may exceed a relative concentration of 1%, only one contaminant above 0.5% and no more than four contaminants above 0.25%.

只有在规定了适当的设备的情况下，对每一个单独的斑点所表现的响应值进行总和才是可以被接受。不建议在不限制杂质数量的情况下，对杂质浓度设置一个或多个限值，否则总的理论杂质的水平将高到无法接受的水平。这种情况可以通过在两个或多个水平限制杂质，只允许规定数量的杂质在较高的水平，其余的杂质在较低的水平。例如，测试可以规定，任何杂质的相对浓度不得超过1%，只有一种可以超过0.25%，或者任何杂质的相对浓度不得超过1%，只有一种可以超过0.5%，超过0.25%的杂质不得超过4种。

II.7.8.2. Liquid chromatography (2.2.29) 液相色谱 (2.2.29)

Defining the appropriate chromatographic system will often be one of the major problems to be dealt with when developing a pharmacopoeial purity test based on chromatography. In LC, the matter is further complicated by the existence of numerous variants of stationary phases, especially amongst the chemically bonded reverse-phase materials for which not only brand-to-brand but occasionally also batch-to-batch variations occur, all of which can influence a given separation. Once the type of stationary phase tested has been found to show a satisfactory separation, it must be defined by selecting the appropriate reagent entry. Correspondence tables between the trade name of the LC columns and the description of the stationary phases are available on the Extranet, General Information for Experts section. Particle size (µm) is stated in the analytical procedure; for size-exclusion chromatography, particle size (µm) and pore size (nm) are stated. The trade name of the column(s) found to be suitable during the elaboration of the monograph is indicated in a footnote to the draft monograph and is transferred to the EDQM Knowledge Database after the monograph is adopted.

在开发基于色谱法的药典纯度测试时，确定适当的色谱系统是要处理的主要问题之一。在液相色谱中，由于存在许多不同的固定相，特别是在化学键合的反相材料，不仅品牌与品牌之间存在差异，而且偶尔也会发生批次与批次之间的差异，所有这些都可能影响特定的分离，使问题进一步复杂化。一旦发现测试所用的固定相类型获得满意的分离效果，就必须通过选择适当的洗脱试剂来定义该方法。可以在外部网站《专业部分的一般信息》获得液相色谱柱的商品名称与固定相的描述之间的对应表格。在测试方法中应标明粒径（µm），或分子排阻色谱的粒径（µm）和孔径（nm）。在各论起草过程中使用的色谱柱的商品名应以脚注的方式标注在各论草案中，在各论收载之后该信息会转移到EDQM知识数据库中。

The following are given when describing the chromatographic system: the column dimensions (length and internal diameter), nature of the stationary phase (as detailed previously) including any steps to prepare or pre-treat it, composition and flow rate of the mobile phase including gradient programme (if any), column and autosampler temperature (if differing from room temperature or especially if thermostated), method of injection (if important), injection volume and method of detection.

在描述色谱条件时，需要给出以下信息：色谱柱尺寸（柱长和内径），固定相性质（如前文所述），包括任何制备或预处理的步骤，流动相的组分和流速，包括梯度程序（如果有），色谱柱和自动进样器温度（如果与室温不同或特别是需要恒温时），进样方法（如为重要信息），进样体积和检测方法。

If a pre-column is deemed useful during the elaboration of the monograph and the validation data has been obtained using the pre-column, its use is normally stated in the monograph.

如果在起草各论的过程中认为预柱是有必要的，并且验证数据是通过使用预柱获得的，通常会在各论中说明预柱的用途。

Depending on the detection wavelength selected, the analyst should choose a suitable grade of solvent when preparing the mobile phase. The following guidance applies to the most frequently used solvents, methanol and acetonitrile. If water is used as a component of the mobile phase, water for chromatography R should be used.

依据选定的检测波长，分析人员在配制流动相时应当选择适当级别的溶剂。以下指南适用于最常用的溶剂，甲醇和乙腈。如果使用水作为流动相的一个组分，应当使用色谱用水R。

波长范围	乙腈级别	甲醇级别
$\lambda \geq 250$ nm	R级乙腈	R级甲醇
220 nm $\leq \lambda < 250$ nm	色谱级乙腈	R1级甲醇
$\lambda < 220$ nm	R1级乙腈	R2级甲醇

Permissible adjustments to the different parameters are indicated in general chapter 2.2.46. Chromatographic separation techniques.

在通则2.2.46《色谱分离技术》中，描述了不同参数的可允许的调整范围。

Wherever possible, test and reference solutions are prepared using the mobile phase as the solvent in order to minimise peak anomalies.

尽量使用流动相作为溶剂配制待测溶液和对照溶液，以最大程度的减少峰异常，。

Unlike solutions for quantitative use, the quantities prescribed in reference solutions for qualitative use only are described without an extra decimal place.

与定量使用的溶液不同，仅用于定性使用的对照溶液中规定的数量没有额外的小数点要求。

Since many active substances are synthesised by a number of synthetic routes, the list of potential impurities to be limited may be large and the analytical challenge to separate them is great. For the sake of robustness and reproducibility, isocratic elution is to be preferred when setting up a pharmacopoeial procedure. However, because isocratic liquid chromatographic methods may not be sufficiently selective, there is an increasing need to employ gradient methods.

由于许多活性物质是通过多种合成途径合成的，因此潜在杂质的数量可能很大，分离它们的

分析挑战也很大。为了（分析方法的）稳健性和再现性，在建立药典方法时，首选等度洗脱方法。然而，由于等度洗脱的液相色谱方法可能没有足够的分离度，因此越来越需求使用梯度洗脱方法。

When a gradient system is described, all necessary parameters must be clearly given (composition of mobile phases, equilibrium conditions, gradient conditions (linear or step), etc.). In general, the return to the initial conditions and re-equilibration are not prescribed in monographs since this is considered to be instrument specific. Should this information be considered important (e.g. ion-exchange chromatography), it may be added as a note to the draft monograph and transferred later to the EDQM Knowledge Database.

当描述梯度洗脱时，所有必要的参数（流动相组成，平衡条件，梯度条件（线性的或步骤）等）都应明确给出。一般情况下，各论中没有规定恢复初始条件和重新平衡，因为这被认为是对于仪器的要求。如果这些被认为是重要信息（例如离子交换色谱）可以作为注释列入各论草案中，之后转载至EDQM知识数据库中。

For gradient elution in LC, an important parameter to be considered is the volume between the solvent mixing chamber and the head of the column. This volume is referred to as the dwell volume, “D” (other terms employed include effective system delay volume, dead volume and delay volume). The dwell volume is dependent on the configurations of the pumping system including the dimensions of the capillary tubing, the solvent mixing chamber and the injection loop. Large differences in dwell volume from one pumping system to another will result in differences in elution of peaks. The greatest effect of differing dwell volumes on retention times is for those substances that are not strongly retained. Thus, gradient systems should be designed with an initial isocratic phase so that analytes do not elute too close to the injection peak, making it possible to correct for marked differences in dwell volume between different gradient pumping systems. The minimum time for the initial isocratic step will depend on the dwell volume of the system and will allow equilibration of the system after sample injection. When the initial validation has been performed without an initial isocratic step, it may not be necessary to revalidate a procedure to which an isocratic step has been added if analytes do not elute too close to the injection peak. The dwell volume of the pumping system employed to develop the procedure should be equal to or less than 1.0 mL. If the procedure is developed using a system with a dwell volume greater than 1.0 mL, then a suitable initial isocratic step is essential. Experts’ reports should indicate the dwell volume of the instrument used for their experimental work. This dwell volume will be stated in a footnote in the draft text and will be transferred to the EDQM Knowledge Database after the monograph is adopted. A method for determining the dwell volume is provided in general chapter 2.2.46. Chromatographic separation techniques.

液相色谱中的梯度洗脱方法中，需要考虑的一个重要的参数是溶剂混合腔与柱头之间的体积。该体积被称为滞留体积“D”，其他术语包括有效延迟体积，死体积和延迟体积。滞留体积取决于泵系统的配置，包括毛细管、溶剂混合腔和进样环的体积。不同泵系统在滞留体积上的巨大差异会导致峰洗脱的差异。在保留时间上，不同滞留体积对保留时间的最大影响在于那些没有很强保留的物质。因此，梯度程序应设计一个初始等度步骤，以便分析物不会太接近溶剂峰，从而有可能纠正不同梯度泵系统之间的显著滞留体积差异。初始等度步骤的最短时间取决于系统的滞留体积，并在进样后允许进行系统平衡。当首次验证是在没有初始等度步骤的情况下进行时，如果分析物洗脱不太接近溶剂峰，则可能不需要重新验证一个增加等度步骤的程序。用于开发该方法时使用的泵系统的滞留体积应小于等于1.0mL。如果开发方法使用的系统的滞留体积大于1.0mL，则适宜的初始等度步骤是必要的。专家的报告应说明用于试验工作的仪器的滞留体积。滞留体积应标注在草案的脚注文本中，各论收载后，该

信息将被转载至EDQM知识数据库中。通则2.2.46《色谱分离技术》中提供了测定滞留体积的方法。

II.7.8.2.a. System suitability criteria 系统适用性标准

One or more system suitability criteria are to be included in the test. Requirements given in general chapter 2.2.46. Chromatographic separation techniques are also applicable.

测试中应包括一项或多项系统适用性标准。通则2.2.46《色谱分离技术》中给出的要求是适用的。

Separation capacity. This criterion is necessary when separation techniques are employed for assays and tests for related substances. The following approaches, most of which require the separation or partial separation of a critical pair, are acceptable for a SST for selectivity:

分离能力：当分离技术应用于含量测定和有关物质检查时，该标准是必要的。以下方法（其中大部分需要分离或部分关键组分的分离）对于系统适用性测试（SST）的选择性是可接受的：

- Resolution. As calculated by the formula given in general chapter 2.2.46. Chromatographic separation techniques using two closely eluting peaks (critical pair). In cases where several closely eluting impurities are present, it may be useful to describe more than one resolution requirement, particularly in gradient systems. The resolution test described should ensure that all the impurities controlled by the procedure and not just the critical pair are separated from each other and from the principal peak. Peaks of different heights may be used to calculate the resolution provided the detector is not saturated.

  分离度：采用紧密相邻的两个洗脱峰（关键组分），使用通则 2.2.46《色谱分离技术》中给出的公式计算。在存在几种紧密相邻的杂质的情况下，描述一种以上分离度要求是有用的，特别是在梯度洗脱系统中。描述的分离度测试应确保方法可以控制所有杂质，而不仅仅是关键组分之间的分离以及与主峰之间的分离。如果检测器显示色谱柱不过载的情况下，可以用不同高度的色谱峰来计算分离度。

- **Peak-to-valley ratio**. This can be employed when complete separation between two adjacent peaks cannot be achieved (i.e. when the resolution is less than 1.5). The minimum requirement for peak-to-valley ratio should not be less than 1.5. Better separation is often necessary to ensure a meaningful integration of impurity peaks. When the quantitative composition of a reference standard used in this test changes (replacement batch), it is necessary to check whether the SST requirements need to be adjusted.

  峰谷比：当无法实现两个相邻峰之间完全分离（即分离度小于 1.5）时，可以使用这种方法。峰谷比的最低要求不应低于 1.5。通常需要更好的分离来确保杂质峰有意义的积分。当本试验中使用的标准物质定量组分发生变化（更换批次）时，有必要检查是否需要调整系统适用性试验（SST）要求。

When gradient elution is described, describing a system suitability requirement for each critical gradient step is desirable.

当描述梯度洗脱时，需要描述每个关键梯度步骤的系统适用性要求。

In situ degradation such as oxidation, hydrolysis, Z-E isomerisation or ring closure offers an alternative approach for defining the suitability of the system, provided that the solution of the substance can be degraded, in mild "stress" conditions within a reasonably short time, to produce decomposition products. The peaks of these products can then be used to determine a resolution or a peak-to-valley ratio. This may be a useful alternative to using impurity reference standards.

原位降解（例如氧化，水解，Z-E异构化或闭环）为确定系统的适用性提供了另一种方法，前提条件是物质的溶液可以在适当的较短时间内在温和的“压力”条件下可以降解并产生降解产物。之后可以使用这些降解产物峰来确定分离度或峰谷比。这是需要使用杂质标准物质的一种实用的替代方法。

In exceptional cases, a chromatogram of an impure or preferably "spiked" substance can also be employed to define the system. In this case, a chromatogram is usually supplied with the reference substance (for system suitability or for peak identification) or the peak identification is described in the text of the test for related substances (e.g. when only one impurity is to be identified).

特殊情况下，也可以使用不纯的物质或加标物质的色谱图来定义系统。在这种情况下，色谱图通常与标准物质（用于系统适用性或峰鉴别）一起提供，或在有关物质测试（例如，当仅定义一种杂质时）的文本中描述峰鉴别。

The use of a spiked (or impure) substance requires procurement of sufficient material to establish the reference substance used and, in the future, replacement of the SST material with material exhibiting the same characteristics.

使用加标（或不纯）物质需要采购足够的物料以确定所使用的标准物质，并在将来使用表现相同特性的物料代替系统适用性测试所用物料。

It should be noted that retention times or relative retention values are given only for information and do not constitute alternative system suitability criteria.

需要注意的是保留时间或相对保留值仅供参考，并不构成替代系统适用性标准。

Sensitivity. The disregard limit/reporting threshold serves a dual purpose:

灵敏度：忽略限/报告限提供双重目的：

- decision criterion for whether a peak area or a corrected peak area of an impurity is to be included in the total of impurities;

  是否将一个杂质的峰面积或校正峰面积计入杂质总量的判断标准；

- general criterion for determining compliance of the actual chromatographic system with the requirement of general chapter 2.2.46. Chromatographic separation techniques (signal-to-noise (S/N) ratio ≥ 10 at the disregard limit/reporting threshold).

  确定实际色谱系统是否符合通则 2.2.46《色谱分离技术》要求（忽略限/报告阈值的信噪比（S/N）≥10）的一般标准。

Typically, the disregard limit for substances covered by a monograph is set in accordance with the reporting threshold given in Table 2034.-1 (see Substances for pharmaceutical use (2034)). However, disregard limits are only described when the comparative style is used for the related substances test; new and revised monographs should be written in the quantitative style and include a reporting threshold. This threshold helps compensate for differences in sensitivity that can be observed when different analytical systems are being employed.

通常，依据表2034-1（参见药用物质（2034））中给出的报告阈值，设置各论涵盖物质的忽略限。然而，只有在使用比较测试方式进行有关物质测试时，才描述忽略限。新起草和修订的各论应以定量的形式描述，并包含报告阈值。该阈值有助于弥补在使用不同分析系统时观察到的灵敏度的差异。

When the normalisation procedure is used for quantitation, a reporting threshold is always included in the test.

当采用归一化法定量分析时，测试中应始终包括报告阈值。

When external standardisation is used, if several impurities are limited and a limit for total impurities is prescribed, a reporting threshold is included in the test. When only one impurity is limited, no reporting threshold is included, but if the sensitivity is borderline, a minimum S/N requirement may be added to the monograph.

当使用外标法时，如果规定了多个杂质及杂质总量的限值，则测试中应包括报告阈值。当只规定一种杂质的限值时，可以不包括报告阈值，但是如果灵敏度处于临界值，各论中应增加最小S/N的要求。

For specified impurities with CFs > 1.25 (i.e. response factors < 0.8), the peak should be quantifiable not only at its limit, but also down to the disregard limit/reporting threshold, which is important for determining of the sum of impurities. Therefore, if the general signal-to-noise requirement of 10 is not applicable, it may be necessary to add a specific sensitivity criterion (S/N) for this impurity.

校正因子（CFs）>1.25（即响应因子<0.8）的特定杂质，该峰不仅应该在其限值处可以定量，而且还应该在其下降到忽略限/报告阈值处也可以定量，这对于测定杂质总量很重要。因此，如果一般的信噪比要求10，在此就不适用，则可能需要为该杂质增加一个特定的灵敏度标准（S/N）。

Example: impurity X is specified at 0.15% with a correction factor of 5 and a general disregard limit/reporting threshold at 0.05%. For the impurity X under consideration, the sensitivity of the procedure is sufficient if:

举例：杂质X校正因子为5，限度规定为0.15%，通用的忽略限/报告阈值为0.05%。对于杂质X，如果满足以下条件，方法的灵敏度就足够了：

- （1）a S/N ratio of minimum 10 is obtained with a 0.05% (relative to the test solution) solution of impurity X, when impurity X is available as a reagent/CRS and used as external standard; or

  （1）当杂质 X 可获得，作为试剂/标准物质被使用时，使用浓度为 0.05%（相对于供试品溶液浓度）的杂质 X 溶液获得最小为 10 的 S/N 值；

- (2) a S/N ratio of minimum 50 (10 x 5 for the correction factor) is obtained with a 0.05% solution of the active substance when impurity X is not available.

  当杂质 X 不可获得时，使用 0.05%的活性物质的溶液获得信噪比至少为 50（10×5 为校正因子）。

Option (2) is preferred when only limited amounts of the isolated impurity are available and the correction factor of the specified impurity is between 0.2 and 5. Outside this range, it is preferable to use the impurity as external standard to avoid the additional uncertainty introduced by the multiplication factor. In the case of option (2), since the correction factor of impurity X is 5 (i.e. the response factor is 0.2) and a dilution of the test solution is used for the quantitation, it is recommended to verify the sensitivity of the procedure during its validation. The S/N ratio of the impurity peak at the reporting threshold should be at least 10 to be quantifiable. To take account of different sensitivities of equipment used, a minimum S/N ratio should be described in monographs where the observed S/N of the impurity peak is not higher than 50 at the reporting threshold. The introduced S/N ratio requirement should be at least 10 times the correction factor (e. g. correction factor is 4, then S/N requirement should be at least 40).

当只能得到有限数量的分离杂质，并且指定杂质的修正系数在0.2~5之间的情况下，最好选择选项（2）。在此范围之外时，最好使用杂质作为外标以避免倍增因子引入额外的不确定度。在选项2的情况下，由于杂质X的校正因子是5（即响应因子为0.2），并且使用供试品溶液的稀释液进行定量，因此建议在验证阶段确认该方法的灵敏性。杂质峰在报告阈值处的S/N值至少为10，才能进行定量。考虑到所用仪器的不同的灵敏度，当观察到的杂质峰S/N在报告阈值处不高于50时，应在各论中描述最小S/N值。采用的S/N值要求至少应为校正因子的10倍（例如校正因子为4，则S/N要求应为至少为40）。

Example 1: Rosuvastatin calcium: Impurity C, correction factor 1.4, limit 0.8%, reporting threshold 0.05%, quantified using a dilution of the test solution of 0.2% (ref. sol. (b)).

例1：瑞舒伐他汀钙产品：杂质C，校正因子为1.4，限度为0.8%，报告限为0.05%，使用浓度为0.2%的供试品溶液稀释液（对照溶液（b））进行定量。

➔ *S/N of impurity C is 55 at the reporting threshold (minimum requirement of 10 to be quantifiable, but a S/N minimum 50 should be obtained to take account of the sensitivity of different equipment);*

在报告限杂质 C 的 S/N 值为 55（最低要求为 10 时可以定量，但是考虑到不同仪器的灵敏度，S/N 值最低应为 50）；

➔ *S/N of principal peak in ref. sol. (b) is 361, i.e. ≈ 90 at the reporting threshold of 0.05% (minimum requirement at the reporting threshold: 10 × 1.4 (CF) = 14).*

对照溶液（b）中主峰的 S/N 值为 361，即在 0.05% 报告限约为 90（报告限最低要求：10×1.4（校正因子）=14）。

Conclusion: the procedure is very sensitive so a minimum S/N is not required in the monograph.

结论：该分析方法足够灵敏，因此各论中不需要描述最小S/N值。

Example 2: Correctoprolol (theoretical case): Impurity A, correction factor 2.2, limit 0.2%, reporting threshold 0.05%, quantified using a dilution of the test solution of 0.1% (ref. sol. (b)).

例2：Correctoprolol（理论情况）：杂质A，校正因子2.2，限度0.2%，报告限0.05%，使用浓度为0.1%的供试品溶液稀释液（对照溶液（b））进行定量。

➔ *S/N of impurity A is 35 at the reporting threshold (minimum requirement of 10 to be quantifiable, but a S/N minimum 50 should be obtained to take account of the sensitivity of different equipment)*

报告限杂质A的S/N值为35（最低要求为10时可以定量，但是考虑到不同仪器的灵敏度，S/N值最低应为50）

➔ *S/N of principal peak in ref. sol. (b) is 154, i.e. 77 at the reporting threshold of 0.05% (minimum requirement at the reporting threshold 10 × 2.2 (CF) = 22)。*

对照溶液（b）中主峰的S/N值为154，即在0.05%报告限约为77（报告限处最低要求：10×2.2（校正因子）=22）。

Conclusion: based on these results, the sensitivity is sufficient but the minimum requirement might not be met if less sensitive equipment is used; the recommendation is to include in the monograph a minimum requirement for S/N of 44 for reference solution (b) (22 × 2 since ref. sol. (b) at 0.10%).

结论：基于上述结果，灵敏度是足够的，但是如果使用低灵敏度的仪器，最低要求可能无法满足，建议在各论中包含对照溶液（b）S/N的最低要求为44（44源自参考溶液（b）在浓度为0.10%的报告限的最低要求）。

For tests for impurities which are limited at ppm level (e.g. DNA-reactive impurities), the SST may include a minimum S/N ratio requirement, such as S/N minimum 10 at 50% of the stated limit for quantitative tests and S/N minimum 10 at the stated limit for limit tests.

对于限值为ppm级别的杂质（例如DNA-反应杂质）的检测，系统适用性测试可包括最小S/N值要求，例如定量测试时，在规定的限值的50%处S/N值最小为10，对于限度测试，在规定限度处S/N值最小为10。

Repeatability. In LC with UV detection, it is commonly accepted that the relative standard deviation of the peak area obtained on a minimum of three injections of a reference solution corresponding to 0.1% of the test solution is not more than 5.0%.

重复性：带紫外检测器的液相中，通常可接受的是供试品溶液浓度的0.1%的对照溶液最少进样3次获得的峰面积的相对标准偏差不超过5.0%。

II.7.8.2.b. Quantitation 定量测试

Quantitation is required for limits applied to specified impurities, unspecified impurities and total impurities. It is most commonly achieved using an external standard and less commonly by the normalisation procedure. The use of the normalisation procedure is discouraged because linearity problems may be observed.

对于特定杂质、未指定杂质和杂质总量的限值要求进行定量。最常见的是使用外标法进行测定，归一法比较少见。考虑到线性问题，不鼓励使用归一化方法。

External standard. A dilution of the test solution/substance to be examined is used, unless there is a large difference in the detector response of a specified (or exceptionally an unspecified) impurity that necessitates the use of a specific external standard, which may be:

外标法：可使用供试品溶液/待测物质的稀释液，除非特定杂质（或者特别是未指定杂质）的检测器响应有很大的差异需要使用特定的外部校准，可以使用以下方案：

- a solution of the impurity, normally in the form of a reference standard (preferred option);

  杂质溶液，通常是以标准物质的形式存在（首选方案）；

- a solution of the substance to be examined containing a known amount of the impurity.

  包含已知量的杂质的待测物质的溶液。

Where a dilution of the substance to be examined is used as the external standard, experts should determine CFs for the impurities, which are indicated in monographs only if they are outside a range of 0.8-1.25 (i.e. the corresponding response factors are outside a range of 0.8-1.2) and considered relevant in light of the batch results (see part II.7.8). CFs are normally given to only one decimal place. The "whole" substance (active moiety, counter-ion and solvate) is taken into account (e.g. Donepezil hydrochloride monohydrate (3067): "Calculation of percentage content: for each impurity, use the concentration of donepezil hydrochloride monohydrate in reference solution (a)").

当使用待测物质稀释液作为外标时，专家需要定义杂质的校正因子（CFs），并且只有在校正因子在0.8~1.25范围外（即响应因子在0.8-1.2范围外时）时需要在各论中载明，并依据批次结果考虑相关性（见II.7.8部分）。校正因子通常只给出一位小数。需要考虑全部物质（活性组分、反离子和溶剂）（例如盐酸多奈哌齐一水合物（3067）："使用盐酸多奈哌齐一水合物对照溶液（a）的浓度计算每一个杂质的百分含量"）。

It is recommended not to apply CFs of less than 0.2 or greater than 5 for specified impurities, but to use external standards in these cases where possible.

建议对于特定杂质，不要使用低于0.2或高于5的校正因子，如果可能，应使用外标法计算。

In order to take account of different responses, it is possible to use a wavelength that is different from the default wavelength for the control of particular impurities. It is understood that the test and the reference solutions are recorded at the same wavelength unless otherwise prescribed.

为了考虑不同的响应，可以使用不同于默认波长的波长来控制特定杂质。除非另有规定，否则应在相同的波长下记录供试品溶液和对照溶液。

The acceptance criteria for related substances tests may be expressed either in terms of comparison of peak areas (the historically used "comparative test style") or as numerical values (the "quantitative test style" that is preferred for new texts or major revisions).

有关物质测试的可接受标准可以用峰面积对比（历史上用比较测试的方式）表示，或用数值（新文本或主要修订应首选的"定量测试类型"）表示。

Based on the requirements of the general monograph Substances for pharmaceutical use (2034):

基于总论《药用物质》（2034）的要求：

- in monographs using the comparative style (acceptance criteria expressed as a comparison of peak areas), a disregard limit is usually set with reference to a dilution of the test solution;

  在使用比较方式（以峰面积的比较作为可接受标准）的各论中，忽略限的设置通常参照供试品溶液的稀释液；

- in monographs referring to numerical values for acceptance criteria, a reporting threshold is defined as a numerical value (%).

  在涉及接受标准为数值的各论中，报告阈值定义为数值（%）。

Normalisation procedure. Quantitation by (area) normalisation requires that all the solutes are known to be eluted and detected, preferably with uniform response factors, and that the detector response is linear up to about 120% of the concentrations employed. This must be validated.

归一法测试：通过（面积）归一法进行定量的方法要求所有已知溶质都已经被洗脱并被检测，最好具有一致的响应因子，且检测器响应线性可达所用浓度的120%左右。这必须经过验证。

As indicated in general chapter 2.2.46. Chromatographic separation techniques, peaks due to solvents or reagents or arising from the mobile phase or the sample matrix, and those at or below the reporting threshold, are excluded before calculating the percentage content of a substance by normalisation. An additional reference solution is prescribed to determine the reporting threshold. The corresponding numerical value (%) is stated in the monograph.

就如通则2.2.46《色谱分离技术》中所描述的，在通过归一法测定物质百分含量之前应排除溶剂、试剂、流动相或样品基质产生的色谱峰，以及那些在报告阈值或低于报告阈值的色谱峰。规定了一个额外的对照溶液确定报告阈值。在各论中明确了相应的数值（%）。

II.7.8.3. Gas chromatography (2.2.28) 气相色谱 (2.2.28)

The difficulties encountered when defining the appropriate chromatographic system in GC purity tests are similar to those mentioned under LC (part II.7.8.2), although the emphasis may be elsewhere. The experimental details to be described in a pharmacopoeial test must, therefore, also be worded as an example so that the chromatographic parameters can be varied to obtain the required performance. Once the type of stationary phase tested has been found to show a satisfactory separation, it must be defined by selecting the appropriate reagent entry (4.1.1). Correspondence tables between the trade name of the GC columns and the reagent stationary phase description are available on the Extranet, General Information for Experts section. The film thickness (in µm, capillary columns) or the particle size (in µm, packed columns, in older procedures) is given after the reagent name. The trade name of the column(s) found to be suitable during elaboration of the monograph is indicated in a footnote to the draft monograph and is transferred to the EDQM Knowledge Database after the monograph is adopted.

在气相色谱纯度测试中确定适当色谱体系时遇到的困难与LC(第二部分7.8.2)中提到的困难类似，尽管重点可能在其他地方。因此药典测试中所描述的试验细节应当作为一个例子表述，

以便改变色谱参数以获得所需要的性能。一旦发现测试的固定相能够获得令人满意的分离效果，必须选择适当的试剂（4.1.1）来定义该方法。可以在外部网站《专业部分的一般信息》获得气相色谱柱的商品名与固定相的描述之间的对应表格。薄膜厚度（毛细管柱，以μm为单位）或粒径（以μm为单位，填充柱在旧的程序中）在试剂名称后面给出。在起草各论过程中找到的合适的色谱柱的商品名应以脚注的形式标注在各论草案中，之后在各论收载后该信息转移至EDQM知识数据库中。

The chromatographic system must be described in essentially the same way as for LC, with the appropriate adjustments made (temperature programme (if any) instead of elution programme, injection port and detector temperatures, etc.). The use of packed columns should be avoided. Permissible adjustments of the different parameters are provided in general chapter 2.2.46. Chromatographic separation techniques

应当以与液相色谱基本相同的方式描述（气相）色谱系统，可以进行适当的调整（以温度程序（如有）替代洗脱程序，进样口和检测器温度等）。应避免使用填充柱。通则2.2.46《色谱分析技术》中提供了可允许调整的不同参数。

For reasons of robustness and reproducibility, isothermal operating conditions are preferred. Quantitation is usually based on an internal standard technique or on the (area) normalisation procedure. The same limitations concerning summation of peak responses as mentioned for LC apply here.

出于耐用性和重现性的要求，应优先选择等温操作条件。通常基于内标法或（面积）归一法进行定量。液相色谱中提到的峰响应总和的限值同样适用于此处。

For the expression of acceptance criteria, the principles defined in part II.7.8.2.b for LC are to be applied.

对于可接受标准的表述，应采用章节II.7.8.2.b部分对液相色谱定义的原则。

II.7.8.4. Capillary electrophoresis (CE) (2.2.47) 毛细管电泳法 (CE) (2.2.47)

CE is increasingly employed to separate and control a large number of impurities of vastly different polarities. It is also suitable for controlling the content of the unwanted enantiomer in chiral therapeutic substances. The problem encountered in reverse-phase LC of varying performance from different stationary phases is avoided if the separation is conducted in a fused-silica capillary.

毛细管电泳法越来越多的用于分离和控制极性差异很大的杂质。它也适用于控制手性治疗物质中不需要的异构体的含量。如果在熔融的石英毛细管中进行分离，则可以避免在反相液相色谱中遇到的由于不同固定相性能不同的问题。

Joule heating occurs during a run. To obtain satisfactory reproducibility, a defined temperature is maintained using a thermostat; for instruments without a thermostat, a low voltage should be used.

在运行过程中会产生焦耳热。为了获得满意的测试重现性，需要使用恒温器保持规定的温度，对于没有恒温器的仪器，应当使用低电压。

The limit of detection is adversely affected by the small injection volume and the small detection pathway in the capillary, even when stacking techniques are applied. For the control of impurities or assays, it is recommended to use an internal standard to achieve appropriate precision. Otherwise, the guidance for the use of this technique is similar to that given previously for LC.

即使应用了浓缩技术，检测限也会受到小进样量和小的检测光程的不利影响。对于杂质或含量的控制，建议使用内标法以达到适当的精密度。除此之外，该技术的应用指南类似于之前给出的液相色谱。

For chiral analysis, a chiral reagent is added to the running buffer. The chiral reagent should be carefully described in the monograph or as a reagent, particularly for cyclodextrin derivatives. Since many of the cyclodextrin derivatives are randomly substituted, it is important to give the exact or average degree and location of substitution. More than one batch of the cyclodextrin derivative should be used for the validation of the analytical procedure.

在手性分析中，向操作缓冲液中加入手性试剂。在各论中或试剂项下应详细描述手性试剂，特别是对于环糊精类衍生物。由于许多环糊精类衍生物是随机取代的，因此给出准确的或平均取代度以及取代的位置是非常重要的。应使用一批以上的环糊精衍生物进行分析方法的验证。

Experimental parameters to be considered for inclusion in the monograph：

应考虑纳入各论的试验参数：

- instrumental parameters: voltage, polarity, temperature, capillary size (diameter and length –total and effective – to the detector);

  仪器参数：电压，电极，温度，毛细管规格（直径和有效长度—进样端至检测器间的距离）；

- coating material of the capillary (where applicable)；

  毛细管涂布材料（如适用）；

- buffer: pH, molarity, composition;

  缓冲液：pH，摩尔浓度，成分；

- sample solvent;

  样品溶剂；

- separation: pole outlet, voltage (U), current (I);

  分离：直流电源，电压(U)，电流（I）；

- injection: time (t), voltage (U) for electro kinetic injection or pressure difference Δp for hydrodynamic injection;

  进样：进样的时间（t）和电动进样电压（U），或流体动力进样的压差Δp；

- detection: wavelength, instrumentation;

  检测器：波长，仪表；

- temperature;

  温度；

- shelf life of solutions;

溶液的有效期；

- rinsing procedures (time, reagents, Δp) needed to stabilise the migration times and the resolution of the peaks:

  稳定迁移时间和峰分离度所需的冲洗程序（时间，试剂，压差）；

  ○ pre-conditioning of a new capillary;

  新毛细管的预处理；

  ○ pre-conditioning of the capillary before a series of measurements;

  在一系列测试前对毛细管进行的预处理；

  ○ between-run rinsing.

  运行期间的冲洗。

The following information is provided in a footnote and transferred to the EDQM Knowledge Database after the monograph is adopted:

以下信息应在脚注中提供，并在各论收载后转移至EDQM知识数据库中：

- if a coated capillary is used, the trade name of the capillary found suitable during the elaboration of the monograph;

  如果应用的有涂布的毛细管，在各论的起草过程中找到的合适的毛细管的商品名；

- for chiral separations, the trade name of the chiral reagent (cyclodextrin or other) found to be suitable during the elaboration of the monograph.

  对于手性分离，在各论起草过程中发现的合适的手性试剂（环糊精或其他）的商品名。

In order to minimise the electro-osmotic flow signal, test and reference solutions are, wherever possible, prepared using water for chromatography R or the running buffer as the solvent.

为了尽量减少电渗流信号，如可能，尽量使用色谱用水或毛细管电泳运行用缓冲液作为溶剂制备供试品溶液和对照溶液。

II.7.9. Readily carbonisable substances 易炭化物

The value of this non-specific test has greatly diminished through the introduction of chromatographic tests providing more information on organic impurities. A test for readily carbonisable substances is often highly sensitive, which can be a major advantage if this is required. However, it should be noted that those impurities that produce a coloration under the conditions of the test will often respond equally well to a test for colour in simple aqueous or alcoholic solution, and in such cases unnecessary duplication is to be avoided.

自从引入可提供更多有机杂质信息的色谱方法后，此项非专属性的检查方法的价值已经大大降低了。易碳化物质的测试通常非常敏感，如果需要，这可能是一个主要优势。然而，应该注意的是，在测试条件下产生颜色的那些杂质通常对简单的水溶液或醇溶液中的颜色测试反应同样良好，在这种情况下，应避免不必要的重复试验。

If, during the elaboration of a monograph, it appears that impurities may be present that are not accounted for by other tests, then this test is carried out and, if appropriate, included in the monograph.

如果在各论的制定过程中，可能存在其它测试无法说明的杂质，应当执行易炭化物的测试，如适用，各论中应包含该项目的测试。

II.7.10. Foreign anions and/or cations 外来阴离子和/或阳离子

Since strong inorganic acids and bases are widely used in synthesis, the contents of foreign anions and/or cations in a substance can be indicative of the extent to which it has been purified. They can also reveal whether contamination with closely related substances has taken place. At the same time, impurities that are typically ionic can often be removed from poorly water-soluble substances by treatment with water without necessarily removing the organic impurities. As a result, tests for anions and cations cannot replace a test for related substances in organic substances but they may constitute a useful supplement for water-soluble organic substances. For inorganic substances, which are usually prepared from other inorganics, a much broader range of tests for foreign ions must be considered.

由于在药物合成过程中广泛使用无机强酸和强碱，因此外来阴离子和/或阳离子的含量可以表征该药物的纯化程度。它们还可以揭示是否发生了密切相关物质的污染。同时，通常是离子型的杂质可以通过用水处理从水溶性差的物质中去除，而不必去除有机杂质。因此，阴离子和阳离子测试不能取代有机物质中有关物质的测试，但它们可以作为水溶性有机物质的有用补充。对于通常由其他无机物制备的无机物质，必须考虑对外来离子进行更广泛的测试。

When considering the introduction of tests for foreign anions in organic substances, a single test, either for chlorides, sulfates or – less commonly – nitrates, will usually suffice, even if several could theoretically be present. The test is then to be carried out on the most abundant anion. When a test for chlorides is considered (up to 0.10%) a limit test should be used instead of titration.

当考虑在有机药物中引入外来阴离子检查项目时，即使理论上可能存在多个阴离子时，通常检查一种离子，比如氯化物、硫酸盐或者不常见的硝酸盐就足够了。然后对含量最高的阴离子进行检查。当考虑对氯化物进行测试（上限为0.10%）时，应使用限度测试替代滴定法。

Certain cations must be stringently limited because of their toxicity or catalytic activity. These are treated separately in part II.7.11. In organic substances, the majority of cations are adequately controlled via a determination of sulfated ash, unless there are special reasons for limiting their presence, either individually or in smaller groups (see part II.7.18).

由于某些阳离子具有毒性或者催化活性，必须对这些离子进行严格的限度检查。这些内容在II.7.11部分单独描述。对于有机物质，除非有特殊原因需要限制其以单个或以很小组分群形式存在以外，通用的方法是通过硫酸灰分(见II.7.18部分)测定进行阳离子控制。

II.7.11. Elemental Impurities 元素杂质

Since the scope of the ICH guideline covers all medicinal products for human use on the market, a cross-reference to general chapter 5.20 (linked to the ICH Q3D guideline) has been introduced in general monograph Pharmaceutical preparations (2619), rendering the guideline mandatory.

由于ICH指导原则的范围涵盖了市场上全部人用医药产品，因此在总论《药物制剂》（2619）中引用了对通则5.20（链接到ICHQ3D指导原则）的交叉引用，使该指南成为强制

性要求。

Since the 9th Edition of the Ph. Eur., all the tests for heavy metals (2.4.8) have been deleted from individual monographs on substances for both human and veterinary use. As of the 11th Edition, tests for heavy metals will also be deleted from individual monographs on substances for veterinary use only. In both cases, no such test will be included in new monographs. For products within the scope of ICH Q3D, users are expected to apply the guidance laid down in the guideline, and analytical procedures may be developed with the help of general chapter 2.4.20. Determination of elemental impurities.

从欧洲药典第9版开始，所有关于重金属（2.4.8）的检测均从有关人用和兽用均可使用的物质的各论中删除。从第11版起，重金属的检测也将从仅兽用物质的各论中删除。在这两种情况下，新的各论中都不会包含该项测试。对于 ICH Q3D 范围内的产品，希望用户应应用指南中规定的指导原则，并在通则 2.4.20 《元素杂质的测定》的帮助下建立分析方法。

A different policy is applied for monographs that describe specific tests for elemental impurities. It is decided on a case-by-case basis if tests are kept for these monographs, particularly for those on excipients of natural origin.

对描述元素杂质特定测试的各论适用不同的策略。各论（特别是关于天然来源的赋形剂中是否保留该测试应依据具体情况决定。

II.7.12. Loss on drying (2.2.32)干燥失重 (2.2.32)

It should be noted that the loss on drying test covers both water and other substances that are volatile at the prescribed drying temperature.

需要注意的是，干燥失重测试包括水和在规定的干燥温度下易挥发的其他物质。

Generally, only an upper limit for loss on drying is given. If the substance is defined as a hydrate (or solvate), upper and lower limits are indicated. Drying is carried out to constant mass, unless a drying time is specified in the monograph. However, it should be noted that any indicated drying time may not necessarily lead to a dry substance. When a drying time is prescribed, adequate validation data must be provided. Where the drying temperature is indicated using a single value, a tolerance of ± 2 °C is understood. For temperatures higher than 105 °C, a greater tolerance has to be indicated in the monograph.

一般来讲，干燥失重项目仅给出标准上限。如果该药物是水合物（或溶剂化产物），会给出上限和下限。除非在各论中明确规定干燥时间，否则干燥是指干燥至恒重。然而需要注意的是任何指定的干燥时间不一定可以获得干燥的物质。规定干燥时间时，必须提供充足的验证数据。当干燥温度使用单一数值时，可以理解为干燥温度在±2℃范围内波动。如果干燥温度高于105℃，各论中应当给出更大的温度允许范围。

Based on agreements reached in the Pharmacopoeial Discussion Group (PDG), 105 °C is generally prescribed for chemicals as the temperature of choice for this test..

根据药典讨论组（PDG）达成的协议，化学品通常采用105℃作为该项测试选择的温度。

General chapter 2.2.32. Loss on drying includes four sets of standard conditions that are referred to in monographs using conventional expressions:

通则2.2.32《干燥失重》包括四组设置的标准条件，各论中采用下列常规的表达方式：

a）“in a desiccator” (over 100 g of molecular sieve R at atmospheric or reduced pressure and at room temperature);

a）“在干燥器中”（在大气压或减压及室温条件下，超过100g分子筛）；

b）“in vacuo” (over molecular sieve R at a pressure not exceeding 2.5 kPa at room temperature);

b）“在真空中”（在室温下，压力不超过2.5KPa，使用分子筛）；

c）“in vacuo within a specified temperature range” (over molecular sieve R at a pressure not exceeding 2.5 kPa within the temperature range specified in the monograph) [NOTE: the drying capacity of desiccants decreases when the temperature increases];

c）“在给定的温度范围内真空干燥” 在各论规定的温度范围内，在不超过2.5 kPa的压力下使用分子筛R）[注：干燥剂的干燥能力随温度升高而降低]；

d）“in an oven within a specified temperature range” (the preferred specified temperature is 105 °C, for harmonisation with the Japanese and US pharmacopoeias, with an implied tolerance of ± 2 °C).

d）“在指定温度范围内的烘箱中”（首选的指定温度为105°C，与日本和美国药典保持一致，意味着为波动范围为±2°C）。

If other conditions are used, in particular lower pressures (e.g. for antibiotics), these are described in the monograph. A molecular sieve 0.5 nm is the preferred drying agent.

如果使用其他条件，特别是使用低压（例如抗生素），各论中应对此进行描述。0.5nm的分子筛是首选的干燥剂。

Limits below 10% should be given to two significant figures and limits of 10% or greater to three significant figures. The sample size is chosen to give a difference of 5-50 mg before/after drying and is given to four significant figures.

干燥失重的限度低于10%时，应给出两位有效数字。当干燥失重的限度为 10%或更高时，应给出三位有效数字。选择的样品量应能使干燥前后的重量差异为 5~50mg，样品重量采用四位有效数字表示。

The test can be carried out on a semi-micro scale, in which case the accuracy with which the test sample is to be weighed should be specified accordingly.

采用半微量试验进行干燥失重检查，应规定样品的称样量及相应的准确度。

Method d) is to be preferred when the product is sufficiently stable at 105 °C. Otherwise, method b) or c) is usually applied. It is important to remember, however, that organic solvents are not always easily removed (e.g. organic solvents in colchicine).

当药品在 105°C足够稳定时，优先采用方法d）。否则通常使用方法b）或方法c）。不管怎

样，必须牢记的是，有机溶剂并不总是容易除去（比如秋水仙碱中的有机溶剂）。

II.7.13. Thermogravimetry (2.2.34) 热重量法 (2.2.34)

This method can be used to determine loss on drying when the amount of substance has to be restricted, to reduce analyst exposure to toxic substances (e.g. vincristine sulfate and vinblastine sulfate) or if the substance is only available in limited quantities.

当样品量受到限制，比如为减少有毒物质对分析人员的暴露量（比如硫酸长春新碱及硫酸长春碱)或者样品数量有限时，可采用热重法测定药品的干燥失重。

II.7.14. Semi-micro determination of water (2.5.12) – volumetric Karl-Fischer半微量水分测定法 (2.5.12) – 卡尔费休法

The commercial name of the titrant and the solvent used during elaboration of the monograph should be indicated in a footnote to the monograph; it will be transferred to the EDQM Knowledge Database after the monograph is adopted.

在各论起草过程中使用的滴定剂和溶剂的商品名应在各论的脚注中注明，在各论被收载后，该信息被转入EDQM知识数据库中。

Limits below 10% should be given to two significant figures and limits of 10% or greater to three significant figures. If water content is less than 0.5%, it is recommended to switch to micro determination of water. The sample size is chosen to obtain a titration volume of about 1 mL and should be given to three significant figures; it may be necessary to lower the strength of the titrant when testing samples with low water content.

水分的限度低于 10%时，应给出两位有效数字，当限度为 10%或更高时，应给出三位有效数字。如果含水量小于0.5%，建议改用微量水分测定。选择的样品量应能消耗约 1ml 的滴定液，样品重量用三位有效数字表示。在测试含水量低的样品时，可能需要降低滴定剂的浓度。

In the case of well-defined hydrates, water content is specified as a range, whereas a maximum content is generally prescribed for products containing variable quantities of water. When more than one form is identified, a cross-reference to the water test is placed in the IDENTIFICATION section of the monograph.

在明确定义为水合物的情况下，含水量为一个范围，而对于含水量可变的产品，通常规定最大含水量。当识别出不止一种（含水）形式时，对含水量测试的交叉引用放在各论的鉴别部分。

II.7.15. Micro determination of water (2.5.32) – coulometric Karl-Fischer

微量水分测定法 (2.5.32) – 库伦法

No detailed description for the composition of the electrolyte (anolyte and catholyte) reagent is given in this general chapter since almost all laboratories use commercially available, ready-to-use reagents.

因为几乎所有的实验室都采用市售即用的商品化试剂，所以在该通则中没有给出电解液(阳极电解液和阴极电解液)的详细组成。

The commercial name of the titrant (electrolyte reagent) used during elaboration of the monograph should be indicated in a footnote to the monograph; it will be transferred to the EDQM Knowledge Database after the monograph is adopted.

各论起草过程中使用的滴定剂（电解液试剂）的商品名应在各论的脚注中注明，各论被收载后，该信息将转入EDQM知识数据库中。

The method of sample preparation must be described. If dissolution in a water-free solvent is necessary, the solvent and the volume must be given. When the oven technique is used to release the water from the sample, the heating temperature is stated in the monograph. The selected gas and gas flow rate are indicated in a footnote and transferred to the EDQM Knowledge Database. The heating time may also be indicated, depending on the instrument used. The direct introduction of solid material in the reaction vessel should only be prescribed in exceptional cases (e.g. no suitable solvent found, degradation of the substance upon heating).

样品的制备过程必须描述。如果样品需要溶解在无水溶剂中，则必须给出溶剂名称和体积。当使用烘箱从样品中去除水分时，各论中应注明加热温度。所选择的气体和气体流速应在脚注中注明，并在之后转入EDQM知识数据库中。加热时间也可根据所使用的仪器进行注明。只有在特殊情况下才应规定在反应容器中直接引入固体材料（例如，没有找到合适的溶剂，加热后物质降解）。

Limits should be expressed to two significant figures. In the case of well-defined hydrates, water content is specified as a range, whereas a maximum content is generally prescribed for products containing variable quantities of water. When more than one form is identified, a cross-reference to the water test is placed in the IDENTIFICATION section of the monograph.

限度应表述为两位有效数字。在明确定义为水合物的情况下，含水量为一个范围，而对于含水量可变的产品，通常规定最大含水量。当鉴别出不止一种（含水）形式时，对含水量测试的交叉引用放在各论的鉴别部分。

The sample size is normally chosen to have a water content of 100 µg to 10 mg. Titrations down to 10 µg are prescribed only where the water content is very low or the sample size is limited by the cost of the substance. The calculation is based on the maximum value as stated in the monograph. The sample size should be stated to three significant figures.

选择的样品量中应有100µg~10mg水。只有当药物中的水分非常低或者由于药物的价格昂贵限制了样品的使用时，才考虑规定滴定样品中含水量低至10µg。计算应基于各论中描述的最大值。应采用三位有效数字表述称样量。

II.7.16. Gas chromatographic determination of water

气相色谱法测定水分

This method, using a thermal conductivity detector (TCD), may also be used for the determination of water.

使用热导检测器（TCD）的气相色谱法也可用于水分的测定。

II.7.17. Determination of water by distillation (2.2.13)

共沸蒸馏法测定水分（2.2.13）

This method is used mainly for herbal drugs. It is applicable to a quantity of substance capable of yielding 2-3 mL of water.

该方法主要用于草药。适用于可蒸馏出2~3ml水的样品。

II.7.18. Sulfated ash (2.4.14) 硫酸灰分（2.4.14）

This test is usually intended for the determination of total foreign cations present in organic substances and in those inorganic substances which themselves are volatilised under the conditions of the test. Due to the resulting high bias, the test will be of little value as a purity requirement for the majority of inorganic salts of organic substances.

本法通常用于测定有机药物中的外来阳离子总量以及在试验条件下自身具有挥发性的无机物质中存在的总外来阳离子量。由于产生的高偏差，该测试对于大多数有机物质中无机盐的纯度要求几乎没有价值。

The limit in a test for sulfated ash is usually set at 0.1%, unless otherwise justified. The amount of substance prescribed for the test must be such that a residue corresponding to the limit will not be less than 1 mg (calculated by mass difference) and the prescribed mass of substance is then given to the appropriate number of significant figures (1.0 g). If the substance tested contains fluorine, the monograph should describe the use of a platinum crucible.

除非另有规定，硫酸灰分的限度一般为0.1%。该测试规定的供试品的用量必须使对应于限值的残留量不小于1mg（按照质量差值计算），规定的称样量应有适当的有效数字（1.0g）。如果待测物含有氟，各论中应当描述使用铂坩埚。

II.7.19. Residue on evaporation 不挥发物

The amount of a liquid material prescribed for the test is such that a residue corresponding to the limit will weigh at least 1.0 mg. The appropriate mass or volume of the substance will normally be in the range of 10-100 g (or mL).

该测试规定的液体样品的用量必须使对应于限值的残留量至少为1.0mg。药物称样量或体积一般为10~100g（ml）范围内。

II.7.20. Residual solvents (2.4.24) 残留溶剂（2.4.24）

Control of residual solvents is covered in general chapter 5.4. Residual solvents and in the general monograph Substances for pharmaceutical use (2034), which apply the ICH Q3C guideline. A procedure included in general chapter 2.4.24 must be validated if it is quantitatively applied to control residual solvents in a substance. Suitable validated procedures may be used instead of those described in general chapter 2.4.24.

通则5.4《残留溶剂》以及总论《药用物质》(2034)提供了对残留溶剂的控制，并依据ICHQ3C的指导原则。通则2.4.24中包含的方法如果用于定量控制药物中的残留溶剂，则必须进行验证。可以使用适当的经过验证的方法替代通则2.4.24中描述的方法。

A test for a Class 1 solvent is included in the monograph if it is potentially present in an approved product.

如果一类溶剂可能存在于已批准的产品中，则应在各论中对其进行测试。

Tests for Class 2 solvents are not included in monographs since the limit may be set using option 2 of general chapter 5.4. Residual solvents, whereby all the ingredients in a medicinal product are taken into account.

第二类溶剂的残留量测试不包括在各论中，因为可以按照通则5.4《残留溶剂》中的方法2进行限度设定，且制剂中各组分的残留溶剂均应被涵盖。

A test for a Class 3 solvent is included if it is potentially present in an approved product at a level higher than 0.5%, otherwise a test for loss on drying is generally prescribed.

如果在已批准的产品中可能存在高于0.5%的第三类溶剂的残留，应对第三类溶剂的残留进行控制，否则通常规定进行干燥失重测试。

Where a quantitative determination of a residual solvent is carried out and a test for loss on drying is not carried out, the content of residual solvent is taken into account when calculating the assay content of the substance, the specific optical rotation and the specific absorbance.

定量检测残留溶剂但未进行干燥失重检测时，在计算药物含量、比旋度和吸收系数时应当考虑残留溶剂的含量。

II.7.21. Bacterial endotoxins 细菌内毒素

When a substance for pharmaceutical use is intended for injection or irrigation, the substance has to comply with the test for bacterial endotoxins. Guidance on how to establish limits is given in general text 5.1.10. Guidelines for using the test for bacterial endotoxins. In principle, the test is no longer added to new monographs. Compliance with the test is requested via the general monograph Substances for pharmaceutical use (2034). A test is included only where a specific procedure has to be described (e.g. if a specific sample preparation has to be used or if a specific method of general chapter 2.6.14 has to be applied). If a test is included in the monograph, no limit is given.

当药用物质用于注射或冲洗液时，该物质必须符合细菌内毒素的测试。通则5.1.10《细菌内毒素测试的指南》的通用表格中给出了建立限度的指导原则。原则上，该项测试不需要增加到新的各论中。应当符合总论《药用物质》（2034）中要求的测试。只有需要描述特定方法时，（各论中）应当包括该项测试（例如，必须使用特定的样品制备方法，或应用各论2.6.14中的特定方法）。如果各论中包括该项测试，则不必给出限度。

For monographs under revision, the decision whether or not to delete the test and/or the limit is made on a case-by-case basis.

对于正在修订的各论，是否删除该项测试和/或限度取决于具体情况。

During the elaboration and, if applicable, revision of a monograph, data are gathered and examined in order to decide whether there is a need to give a specific sample preparation procedure in the individual monograph or whether it can be considered that the topic of bacterial endotoxins is adequately covered by the general monograph Substances for pharmaceutical use (2034). These data include but are not limited to: validation of the bacterial endotoxin test, batch data and demonstration of absence of interference of the substance with the test.

在各论的起草和修订（如适用）的过程中，为了决定各论中是否需要给出特定的样品制备过程或是否可以认为细菌内毒素的要求已充分涵盖在总论《药用物质》（2034）中，应对数据进行收集和检查。这些数据包括但不限于：细菌内毒素测试的验证，批数据和该物质对测试没有干扰的证明。

If a test for pyrogens is replaced by a test for bacterial endotoxins, the decision concerning whether to include a test in the monograph follows the considerations described above. The information on the replacement of the testing procedures is given in the EDQM Knowledge Database.

如果热原测试被细菌内毒素测试取代，关于是否在各论中包括该测试的决定应依据上述考量。EDQM 知识数据库中给出了该测试方法替代的信息。