欧洲药典-澄清度检测规定

欧洲药典：

Clarity and degree of opalescence of liquids

VISUAL METHOD 一般方法

Using identical test-tubes of colourless, transparent, neutral glass with a flat base and an internal diameter of 15-25 mm, compare the liquid to be examined with a reference suspension freshly prepared as described below, the depth of the layer being 40 mm. Compare the solutions in diffused daylight 5 min after preparation of the reference suspension, viewing vertically against a black background. The diffusion of light must be such that reference suspension I can readily be distinguished from water R, and that reference suspension II can readily be distinguished from reference suspension I.

在内径 15～25mm，平底，无色、透明、中性玻璃管中，加入等量的供试溶液与浊度标准液，使液位的深度都为 40mm，按如下所述方法进行比较。浊度标准液制备 5 分钟后，以色散自然光照射浊度标准溶液和供试溶液，在黑色背景下从垂直方向观察、比较澄清度或浑浊程度。色散自然光必须较容易区分浊度标准溶液Ⅰ与水，浊度标准溶液Ⅱ与浊度标准溶液Ⅰ

A liquid is considered clear if its clarity is the same as that of water R or of the solvent used when examined under the conditions described above, or if its opalescence is not more pronounced than that of reference suspension I.

如果供试溶液的澄清、透明程度与水相同，或者与所用溶剂相同，或者其澄清度不超过Ⅰ号浊度标准溶液，那么可判定该溶液为澄清。

Hydrazine sulfate solution. Dissolve 1.0 g of hydrazine sulfate R in water R and dilute to 100.0 mL with the same solvent. Allow to stand for 4-6 h.

硫酸肼溶液：取 1.0g 硫酸肼溶于水，加水稀释至 100.0ml，静置 4～6 小时。

Hexamethylenetetramine solution. In a 100 mL ground-glass-stoppered flask, dissolve 2.5 g of hexamethylenetetramine R in 25.0 mL of water R.

乌洛托品（六亚甲基四胺）溶液： 在 100ml 容量瓶中，以 25.0ml 水溶解 2.5g 乌洛托品。

Primary opalescent suspension (formazin suspension).

To the examethylenetetramine solution in the flask add 25.0 mL of the hydrazine sulfate solution. Mix and allow to stand for 24 h. This suspension is stable for 2 months, provided it is stored in a glass container free from surface defects. The suspension must not adhere to the glass and must be well mixed before use.

浊度标准贮备液：在存放乌洛托品溶液的 100ml 容量瓶中，加 25.0ml 的硫酸肼溶液。混合，静置 24 小时，贮存在无表面要求的玻璃容器中，可在 2 个月内使用。该浊度液不得黏附玻璃，用前必须充分摇匀。

Standard of opalescence. Dilute 15.0 mL of the primary opalescent suspension to 1000.0 mL with water R. This suspension is freshly prepared and may be stored for up to 24 h.

浊度标准原液：取浊度标准贮备液 15ml，加水稀释、定容至 1000ml。该液临用前制备，至多保存 24 小时。

Reference suspensions. Prepare the reference suspensions according to Table 2.2.1.-1. Mix and shake before use.

浊度标准液：由浊度标准原液与水按表 1-1 配制,即得。本液应临用前配制。

Table 1.-1

Turbidity standard. The formazin suspension prepared by mixing equal volumes of the hydrazine sulfate solution and the hexamethylenetetramine solution is defined as a 4000 NTU (nephelometric turbidity units) primary reference standard. Reference suspensions I, II, III and IV have values of 3 NTU, 6 NTU, 18 NTU and 30 NTU respectively. Stabilised formazin suspensions that can be used to prepare stable, diluted turbidity standards are available commercially and may be used after comparison with the standards prepared as described.

浊度标准：乳光悬浊贮备液[硫酸肼溶液和乌洛托品（六亚甲基四胺）溶液以等量体积混合]定为4000NTU（比浊测定法的浊度单位）储备液对照标准.浊度标准液 I, II, III 和 IV 相应的 NTU 值分别是 3 NTU, 6 NTU, 18 NTU 和 30 NTU。稳定的乳光悬浊贮备液可用于稀释制备浊度标准，具有现实的商业价值，也可以与上述的标准化制备进行较。

Formazin has several desirable characteristics that make it an excellent turbidity standard. It can be reproducibly prepared from assayed raw materials. The physical characteristics make it a desirable light-scatter calibration standard. The formazin polymer consists of chains of different lengths, which fold into random configurations. This results in a wide assay of particle shapes and sizes, which analytically fits the possibility of different particle sizes and shapes that are found in the real samples. Due to formazin’s reproducibility, scattering characteristics and traceability, instrument calibration algorithms and performance criteria are mostly based on this standard.

因福马尔肼具有一些我们所希望的特性，所以它是一种非常优良的浊度标准物。它可以从被测原料中反复制备。具有所想要的光闪射校正标准化的物理特性。福马尔肼聚合物由不同长度的链组成，他们可以折成各种形状，应此可以分析不同大小和形状的粒子。这一特性使得我们可以对现

实样品中所具有的不同大小及性状的粒子进行测定。由于。福马尔肼具有可重复性、光散射性、可描绘性、仪器校准可算和操作标准化的特性，使其成为了浊度标准物。

instrumental methods Introduction

仪器方法简介

The degree of opalescence may also be determined by instrumental measurement of the light absorbed or scattered on account of submicroscopic optical density inhomogeneities of opalescent solutions and suspensions. 2 such techniques are nephelometry and turbidimetry. For turbidity measurement of coloured samples, ratio turbidimetry and nephelometry with ratio selection are used.

该仪器是根据浑浊液和悬浊液亚显微镜光密度的不均一性来测量光的吸收或光的散射，即散射测浊法和透射测浊法。对于有色样品的浊度测试法，要用到比率透射比浊法和可选择比率的散射比浊法。

The light scattering effect of suspended particles can be measured by observation of either the transmitted light (turbidimetry) or the scattered light (nephelometry). Ratio turbidimetry combines the principles of both nephelometry and turbidimetry. Turbidimetry and nephelometry are useful for the measurement of slightly opalescent suspensions. Reference suspensions produced under well-defined conditions must be used. For quantitative measurements, the construction of calibration curves is essential, since the relationship between the optical properties of the suspension and the concentration of the dispersed phase is at best semi-empirical.

通过投射光（投射比浊法）或散射光（散射比浊法）来测量混悬粒子的光散射效能。浊度比率结合了透射比浊法和散射比浊法二者的原理。透射比浊法和散射比浊法用于测量具有轻微乳光的混

悬液。必须使用在的条件下制得的标准混悬液。因为混悬液的光学性质与分散相的浓度之间的关系多是一个半经验值，所以定量测定主要使用标准曲线法。

The determination of opalescence of colored liquids is done with ratio turbidimeters or nephelometers with ratio selection, since color provides a negative interference, attenuating both incident and scattered light and lowering the turbidity value. The effect is so great for even moderately colored samples that conventional nephelometers cannot be used.

因为溶液颜色会产生负干扰，衰减入射光和散射光并降低浊度值，用比率透射浊度法和可选择比率的散射浊度法测定有色溶液的乳光。对于正好适度的有色样品，效果非常好，以至于常规的浊度仪不再使用。

The instrumental assessment of clarity and opalescence provides a more discriminatory test that does not depend on the visual acuity of the analyst. Numerical results are more useful for quality monitoring and process control, especially in stability studies. For example, previous numerical data on stability can be projected to determine whether a given batch of dosage formulation or active pharmaceutical ingredient will exceed shelf-life limits prior to the expiry date.

用仪器来判断澄清度和乳光，试验所提供的分辨能力更强，不再依靠分析者的视觉敏锐性来判断。对于定性监控和过程控制，特别是稳定性研究，数字化结果更有用。例如，之前所得的关于稳定性的数字化资料用于判断一个给定批号的剂量成分或活性药物组分是否超过了贮存期限或者没过有效期。

Nephelometry

When a suspension is viewed at right angles to the direction of the incident light, the system appears opalescent due to the reflection of light from the particles of the suspension (Tyndall effect). A certain portion of the light beam entering a turbid liquid is transmitted, another portion is absorbed and the remaining portion is scattered by the suspended particles. If measurement is made at 90° to the light beam, the light scattered by the suspended particles can be used for the determination of their concentration, provided the number and size of particles influencing the scattering remain constant. The reference suspension must maintain a constant degree of turbidity and the sample and reference suspensions must be prepared under identical conditions. The Tyndall effect depends upon both the number of particles and their size. Nephelometric measurements are more reliable in low turbidity ranges, where there is a linear relationship between

nephelometric turbidity unit (NTU) values and relative detector signals. As the degree of turbidity increases, not all the particles are exposed to the incident light and the scattered radiation of other particles is hindered on its way to the detector. The maximum nephelometric values at which reliable measurements can be made lie in the range of 1750-2000 NTU. Linearity must be demonstrated by constructing a calibration curve using at least 4 concentrations.

散射比浊法当混悬液在垂直于入射光的方向观察，因混悬液粒子产生的反射，系统出现乳光 (丁达尔效应)..。进入一个浑浊液的光束，一部分被透过，一部分被吸收，剩余部分被悬浊粒子散射。如果在与光束 90°的方向检测，假如粒子数量和大小对散射的影响维持常数，可以用悬浊粒子的光散射来测定他们的浓度。照溶液的浊度必须保持不变，并且样品和对照混悬液在一样的条件下

制备。丁达尔效应)依赖于粒子的大小和数量。在低浊度范围，光散射浊度法更可靠，散射法浊度单位值和有关检测器信号成线性。随浊浊度的增加，不是所有的粒子都能暴露在入射光下的，并且在到达检测器的途径中，其他粒子的散射光被阻碍。一个可靠的测量所能测量的大散射浊度值是 1750-2000 NTU。必须用至少 4 个浓度构建标准曲线来证明线性。

Turbidimetry

The optical property expressed as turbidity is the interaction between light and suspended particles in liquid. This is an expression of the optical property that causes light to be scattered and absorbed rather than transmitted in a straight line through the sample. The quantity of solid material in suspension can be determined by the measurement of the transmitted light. A linear relationship between turbidity and concentration is obtained when the particle sizes are uniform and homogeneous in the suspension. This is true only in very dilute suspensions containing small particles. Linearity between turbidity and concentration must be established by constructing a calibration curve using at least 4 concentrations.

透射浊度法在液体中悬浊粒子和光之间存在相关性，这一光学特性表示为浊度。表示的是光在直线方向上发生的散射和吸收，而不是光直线通过样品的透射光学特性，通过测量透射光来测定混悬液中固体物质的量。当混悬液中粒子的大小均一且性质相同，可获得浊度和浓度之间的线性关系。仅仅在很稀的含有少量粒子的混悬液中，才可实现线性。必须使用至少 4 个浓度构建标准曲线来证明浊度和浓度间呈线性。

Ratio Turbidimetry

In ratio turbidimetry the relationship of the transmission measurement to the 90° scattered light measurement is determined. This procedure compensates for the light

that is diminished by the colour of the sample. The influence of the colour of the sample may also be eliminated by using an infrared light-emitting diode (IR LED) at 860 nm as the light source of the instrument. The instrument's photodiode detectors receive and measure scattered light at a 90° angle from the sample as well as measuring the forward scatter (light reflected) in front of the sample along with the measurement of light transmitted directly through the sample. The measuring results are given in NTU(ratio) and are obtained by calculating the ratio of the 90° angle scattered light measured to the sum of the components of forward scattered and transmitted light values. In ratio turbidimetry the influence of stray light becomes negligible.

Nephelometers are used for measurements ofthedegreeofopalescenceof；比率透射比浊法测定的是透视光的测量和 90°方向上；

Table 2.2.1.-2

INSTRUMENTAL DETERMINATION OF OPALESCENCE

乳光的仪器测定

Requirements in monographs are expressed in terms of the visual examination method with the defined reference suspensions. Instrumental methods may also be used for determining compliance with monograph requirements once the suitability of the instrument as described below has been established and calibration with reference suspensions I-IV and with water R or the solvent used has been performed.

乳光的仪器测定在用准确的参比混悬液定义可见方法时已表明了要求。一旦后面所规定的建立了仪器的适应性，并用参比混悬液 I-IV 和水或使用的溶剂进行校正，文中的方法也使用于仪器校正。

Apparatus. Ratio turbidimeters or nephelometers with selectable ratio application use as light source a tungsten lamp with spectral sensitivity at about 550 nm operating at a filament colour temperature of 2700 K, or IR LED having an emission maximum at 860 nm with a 60 nm spectral bandwidth. Other suitable light sources may also be used. Silicon photodiodes and photomultipliers are commonly used as detectors and record changes in light scattered or transmitted by the sample. The light scattered at 90 ± 2.5° is detected by

the primary detector. Other detectors are those to detect back and forward scatter as well as transmitted light. The instruments used are calibrated against standards of known turbidity and are capable of automatic determination of turbidity. The test results expressed in NTU units are obtained directly from the instrument and compared to the specifications in the individual monographs.

仪器：使用可选择的比率浊度计和浊度计时，用钨灯作光源，在 2700K 的谱线标记温度时，钨灯在大约 550nm 处有特殊选择性，或者用在 860nm 处有大发射并且有 60nm 光谱宽度的红外发光二级管。也可以使用其他合适的光源。常用硅制光电二极管和光电倍增管作检测器，并记录因样品产生的光散射或光透射的改变。主要检测器检测在 90 ± 2.5°方向上的光散射。其他的检测器检测朝后和朝前的光散射，就像测光透射一样。使用的仪器用已知浊度的标准溶液来校正，并能够自动测定浊度。从仪器上直接获得用 NTU 单位表示的测定结果，并且，在个别文中与规定进行比较。

Instruments complying with the following specifications are suitable.

根据后面的说明使用仪器

— Measuring units: NTU. NTU is based on the turbidity of a primary reference standard of formazin. FTU (Formazin Turbidity Units) or FNU (Formazin Nephelometry Units) are also used, and are equivalent to NTU in low regions (up to 40 NTU). These units are used in all 3 instrumental methods (nephelometry, turbidimetry and ratio turbidimetry).

— 测量单位：NTU，NTU 根据的是福尔马肼标准储备液的浊度。液使用 FTU（福尔马肼浊度单位）或 FNU（福尔马肼散射测浊法单位）单位，在低浊度范围内等于 NTU（大于 40NTU）。这些单位在散射测浊法、浊度法、比率浊度法，三种仪器方法中均可使用。

— Measuring range: 0.01-1100 NTU.

— 测量范围：0.01-1100NTU

— Resolution: 0.01 NTU within the range of 0-10 NTU, 0.1 NTU within the range of 10-100 NTU, and 1 NTU for the range > 100 NTU. The instrument is calibrated and controlled with reference standards of formazin.

— 分辨率：在 0-10NTU 范围内分辨率为 0.01NTU，在 10-100NTU 范围内分辨率为 0.1NTU，在>100NTU 范围内分辨率为 1NTU。用福尔马肼的参比标准校正和控制仪器。

— Accuracy: 0-10 NTU: ± (2 per cent of reading + 0.01) NTU. 10-1000 NTU: ± 5 percent.

— 度：0-10 NTU±（2%测量读数+0.01）NTU，10-1000 NTU: ± 5%

— Repeatability: 0-10 NTU: ± 0.01 NTU. 10-1000 NTU: ± 2 per cent of the measured value.

— 重复性：0-10 NTU± 0.01 NTU，10-1000 NTU± 2%的测量值

— Calibration: with 4 reference suspensions of formazin in the range of interest.

Reference suspensions described in this chapter or suitable reference standards calibrated against the primary reference suspensions may be used.

— 校正：用在感兴趣范围内的 4 中福尔马肼参比混悬液。可以用按本章规定的参比混悬液或合适的相对于参比混悬液储备液标有刻度的参比标准来校正。

— Stray light: this is a significant source of error in low level turbidimetric measurement;

stray light reaches the detector of an optical system, but does not come from the sample; < 0.15 NTU for the range 0-10 NTU, < 0.5 NTU for the range 10-1000 NTU.

— 杂散光：在低水平的浊度测定中，杂散光是主要的误差来源。杂散光就是能到达光学系统的检测器，但不是由于样品而产生的光。0-10 NTU 的范围内杂散光< 0.15 NTU，10-100NTU 的范围内杂散光< 0.5 NTU。

Instruments complying with the above characteristics and verified using the reference suspensions described under Visual method may be used instead of visual examination for determination of compliance with monograph requirements.

符合上面的特性，并用在可见方法下规定的参比混悬液进行校正的仪器，在这范围内，这些仪器可替代可视检查，这些检查和文中要求一致。

Instruments with range or resolution, accuracy and repeatability capabilities other than those mentioned above may be used provided they are sufficiently validated and are capable for the intended use. The test methodology for the specific substance/product to be analysed must also be validated to demonstrate its analytical capability. The instrument and methodology should be consistent with the attributes of the product to be tested.

所提供的仪器的使用范围、分辨率、准确度、重复性、容量及其它上面提到的参数，这些是十分有效的并能够预期使用。对于分析特殊的物质/产品，也必须进行试验方法学验证来说明其分析能力。仪器和方法学应该和测试样品的特性一致。

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