

MHRA GMP Data Integrity Definitions and Guidance for Industry March 2015

MHRA GMP 数据完整性定义和行业指导原则 2015 年 3 月

简述:

Data integrity is fundamental in a pharmaceutical quality system which ensures that medicines are of the required quality. This document provides MHRA guidance on GMP data integrity expectations for the pharmaceutical industry. This guidance is intended to complement existing EU GMP relating to active substances and dosage forms, and should be read in conjunction with national medicines legislation and the GMP standards published in Eudralex volume 4.

数据完整性是制药质量体系确保药品质量的基石。本文提供了 MHRA 对制药行业 GMP 数据完整性方面的指导原则。本指导原则旨在对现有欧盟有关原料药和药物制剂的 GMP 进行补充说明，需结合国家药品法规及颁布在 Eudralex 第四册内的 GMP 标准进行阅读理解。

The data governance system should be integral to the pharmaceutical quality system described in EU GMP chapter 1. The effort and resource assigned to data governance should be commensurate with the risk to product quality, and should also be balanced with other quality assurance resource demands. As such, manufacturers and analytical laboratories are not expected to implement a forensic approach to data checking on a routine basis, but instead design and operate a system which provides an acceptable state of control based on the data integrity risk, and which is fully documented with supporting rationale.

数据管理体系应该与欧盟 EU GMP 第一章所述的质量体系结合在一起。投入到数据管理的精力和资源应与其产品的风险等级相对应，同时还应该权衡其他质量保证工作的资源需求。因此，生产者和分析实验室并不是要刻板地进行常规的数据核对，而是要设计出并运行一套管理体系，来控制数据完整性的风险，而且详细记录这个体系合理性的支持依据。

Data integrity requirements apply equally to manual (paper) and electronic data. Manufacturers and analytical laboratories should be aware that reverting from automated / computerised to manual / paper-based systems will not in itself remove the need for data integrity controls. This may also constitute a failure to comply with Article 23 of Directive 2001/83/EC, which requires an authorisation holder to take account of scientific and technical progress and enable the medicinal product to be manufactured and checked by means of generally accepted scientific methods.

手工（纸质）数据和电子数据在数据完整性方面的要求是一致的。生产者和分析实验室要意识到，从自动化/电脑系统回归到手工（纸质）记录的做法，并不能减少对数据完整性进行控制的要求。这反而会造成对条款 2001/83/EC 第 23 条的不符合，该条款要求企业根据科学和技术发展的状况，采用普遍接受的科学的方法进行药品生产和检验。

Throughout this guidance, associated definitions are shown as [hyperlinks](#).

本指导原则所涉及的相关定义可以点下面的链接。

Establishing data criticality and inherent integrity risk:

建立数据的关键程度和内在的完整性风险:

In addition to an overarching [data governance](#) system, which should include relevant policies and staff training in the importance of [data integrity](#), consideration should be given to the organisational (e.g. procedures) and technical (e.g. computer system access) controls applied to different areas of the quality system. The degree of effort and resource applied to the organisational and technical control of [data lifecycle](#) elements should be commensurate with its criticality in terms of impact to product quality attributes.

仅仅靠一个总体的数据管理体系是不够的，虽然已包括了对数据完整性至关重要的相应的方针和人员培训，还应该考虑在不同的质量体系领域采用组织性的控制手段（如操作程序）和技术控制手段（如计算机系统

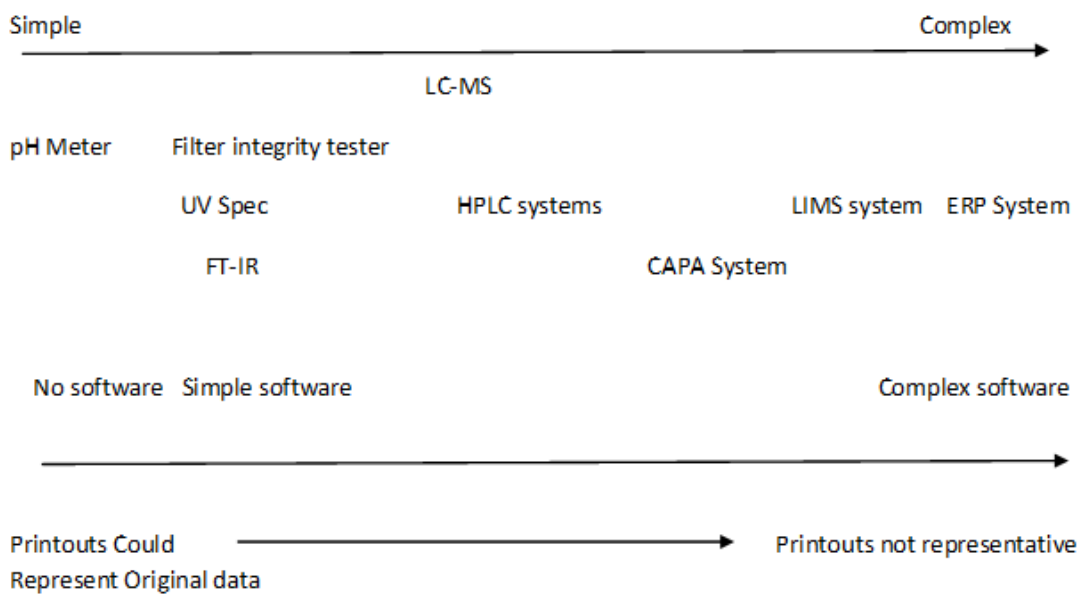
访问权限)。对数据生命周期中的各要素的组织性控制的和技术型控制的程度及投入的资源，要与该数据对产品属性的影响程度相对应。

Data may be generated by (i) a paper-based record of a manual observation, or (ii) in terms of equipment, a spectrum of simple machines through to complex highly configurable computerised systems. The inherent risks to data integrity may differ depending upon the degree to which data (or the system generating or using the data) can be configured, and therefore potentially manipulated (see figure 1)

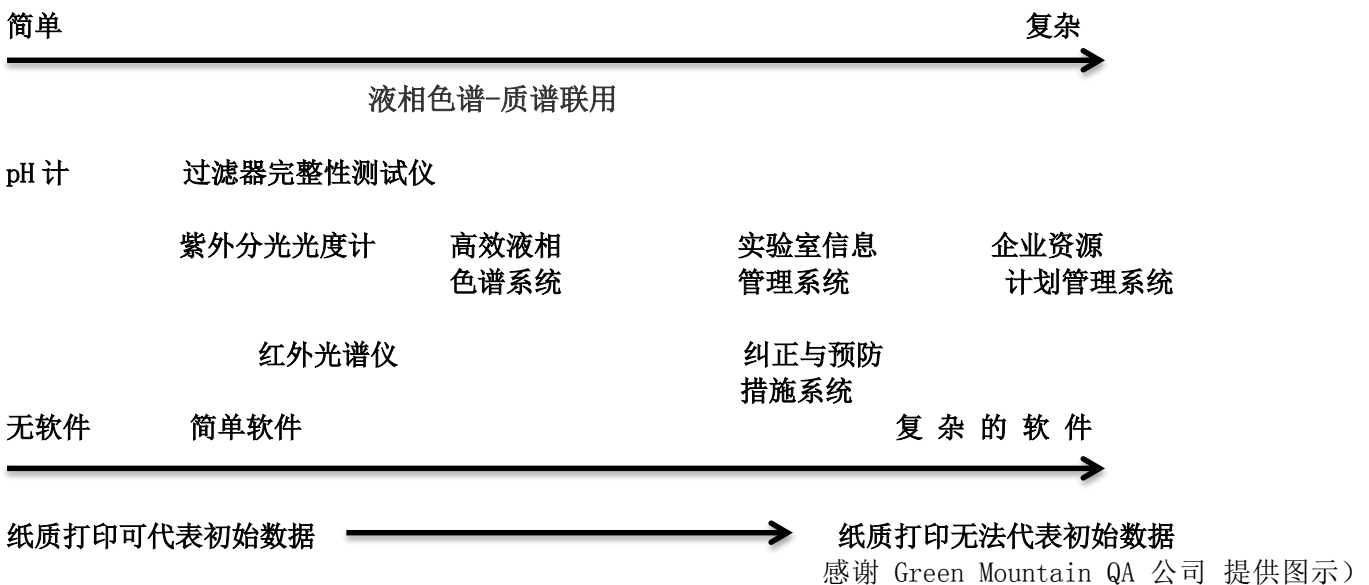
数据可由以下几种情况产生：（1）人工观测后进行的纸质记录，（2）从一些仪器得来，从简单的设备直至那些复杂的高度配置的计算机系统而产生的图谱。数据完整性的内在风险也因此而有所不同，这取决于数据（或者是系统生成的或使用的数据）的可配置的程度及由此而被造假的可能性程度（见图1）。

Figure 1: Diagram to illustrate the spectrum of simple machine (left) to complex computerised system (right), and relevance of printouts as ‘original data’

图 1: 图示列举了简单设备图谱（左）到复杂的计算机化系统图谱（右），及将打印数据作为“初始数据”的对应关系



(diagram acknowledgement: Green Mountain QA LLC)



感谢 Green Mountain QA 公司 提供图示)

With reference to figure 1 above, simple systems (such as pH meters and balances) may only require calibration, whereas complex systems require ‘validation for intended purpose’. Validation effort increases from left to right in the diagram above. However, it is common for companies to overlook systems of apparent lower complexity. Within these systems it may be possible to manipulate data or repeat testing to achieve a desired outcome with limited opportunity of detection (e.g. stand-alone systems with a user configurable output such as FT-IR, UV spectrophotometers). 参考图 1，简单系统（诸如 pH 计和天平）可能只需要校准，而复杂的系统需要“对预期用途进行验证”。验证活动在上图中从左到右相应加强。但是，企业常常容易忽视一些貌似并不复杂的系统。在此类系统中，有可能通过人为处理数据或重复检测以获取期望的结果，并且不容易被发现（例如带有用户可配置输出功能单机版设备，如红外光谱仪，紫外分光光度计）。

Designing systems to assure data quality and integrity 系统化设计以确保数据质量和完整性

Systems should be designed in a way that encourages compliance with the principles of data integrity. Examples include:

系统的设计应遵循数据完整性的原则
示例包括以下：

- Access to clocks for recording timed events
对记录事件时间的计时器进行权限控制
- Accessibility of batch records at locations where activities take place so that ad hoc data recording and later transcription to official records is not necessary
将记录放置在生产现场，避免不必要的临时记录数据然后事后誊成正式记录
- Control over blank paper templates for data recording
对用于数据记录的纸质空白模板进行控制
- User access rights which prevent (or audit trail) data amendments
用户权限控制以防止（或审计追踪）数据篡改
- Automated data capture or printers attached to equipment such as balances
采用数据自动采集方式或将打印机连接到设备，例如天平
- Proximity of printers to relevant activities
打印机设置在靠近相关活动的位置
- Access to sampling points (e.g. for water systems)
取样位置所在区域（例如水系统的取样位置）的权限控制
- Access to raw data for staff performing data checking activities.
员工进行数据核对时，对进入原始数据进行权限控制

The use of scribes to record activity on behalf of another operator should be considered ‘exceptional’, and only take place where:

用记录员替另一个操作人员进行记录是“特例/非常规流程”，仅在以下情况下采用：

- The act of recording places the product or activity at risk e.g. documenting line interventions by sterile operators.
记录活动会使产品或活动有风险，例如无菌操作人员记录生产线的干扰活动
- To accommodate cultural or staff literacy / language limitations, for instance where an activity is performed by an operator, but witnessed and recorded by a Supervisor or Officer.
用于解决文化或员工书写/语言能力不足，例如由主管或办公室人员见证并记录另一操作员工的操作。

In both situations, the supervisory recording must be contemporaneous with the task being performed, and must identify both the person performing the observed task and the person completing the record. The person performing the observed task should countersign the record wherever possible, although it is accepted that this countersigning step will be retrospective. The process for supervisory (scribe) documentation completion should be described in an approved procedure, which should also specify the activities to which the process applies.

在这两种情况下，监督者的笔录必须是实时记录，并且明确标明操作的人和记录的人。虽然大家都能接受加签或者会签可以是事后补签，但是操作者还是尽可能的及时加签或者会签操作记录。应在批准的规程中规定监督者笔录的方式完成该记录，并明确该流程的适用范围。

Term 术语	Definition 定义	Expectation / guidance (where relevant) 相关要求/指导原则
<p>Data 数据</p>	<p>Information derived or obtained from <u>raw data</u> 由原始数据衍生或取得的信息 (e.g. a reported analytical result) (例如报告的分析结果)</p>	<p>Data must be: 数据必须符合以下原则:</p> <p>A - attributable to the person generating the data 可追溯至数据由谁生成</p> <p>L – legible and permanent 清晰并持久</p> <p>C – contemporaneous 同步</p> <p>O – <u>original</u> (or ‘true copy’) 初始 (或正确的副本)</p> <p>A – accurate 准确</p>
<p>Raw data 原始数据</p>	<p><u>Original records</u> and documentation, retained in the format in which they were originally generated (i.e. paper or electronic), or as a ‘true copy’. Raw data must be contemporaneously and accurately recorded by permanent means. In the case of basic electronic equipment which does not store electronic data, or provides only a printed data output (e.g. balance or pH meter), the printout constitutes the raw data. 初始的记录和文档，以初始生成的格式（即纸质或电子形式）或以“正确的副本”进行保留。原始数据必须以能永久保存的形式同步并准确地记录。对于一些不能存储电子数据或仅有数据打印输出的简单电子设备（例如天平或 pH 计），打印数据构成原始数据</p>	<p>Raw data must: 原始数据必须:</p> <ul style="list-style-type: none"> • Be legible and accessible throughout the <u>data lifecycle</u>. 在整个数据生命周期过程中都清晰可辨并能够及时获取 • Permit the full reconstruction of the activities resulting in the generation of the data 允许完全重现数据生成的活动

In the following definitions, the term 'data' includes raw data.

在以下定义中，术语“数据”包括原始数据

<p>Metadata: 元数据</p>	<p>Metadata is data that describe the attributes of other data, and provide context and meaning. Typically, these are data that describe the structure, data elements, inter-relationships and other characteristics of data. It also permits data to be attributable to an individual. 元数据是描述其它数据的特性，并提供背景信息和含义的数据。通常，元数据用于描述数据结构，数据要素，数据的内在关系和其它特征。它还允许数据可被追踪至产生数据的个体。</p>	<p>Example: data (bold text) 3.5 and metadata, giving context and meaning, (italic text) are: <i>sodium chloride batch 1234, 3.5mg. J Smith 01/07/14</i> 例如：数据（黑体） 3.5 和元数据给出了背景信息和含义，（斜体） <i>氯化钠批号 1234， 3.5mg. J Smith 01/07/14</i></p> <p>Metadata forms an integral part of the original record. Without metadata, the data has no meaning. 元数据与初始记录密不可分，如果没有元数据，则该数据是无意义的。</p>
<p>Data Integrity 数据完整性</p>	<p>The extent to which all data are complete, consistent and accurate throughout the <u>data lifecycle</u>. 数据完整性的范畴包括所有数据在整个<u>数据生命周期</u>中的全面性，一致性和准确性的程度。</p>	<p>Data integrity arrangements must ensure that the accuracy, completeness, content and meaning of data is retained throughout the data lifecycle. 数据完整性的设置必须在整个数据生命周期中，保持数据的准确，完全，以及内容和含义。</p>
<p>Data governance 数据管理</p>	<p>The sum total of arrangements to ensure that data, irrespective of the format in which it is generated, is recorded, processed, retained and used to ensure a complete, consistent and accurate record throughout the <u>data lifecycle</u>. 指所有约定的总成：不论数据的生成格式、记录方式、处理过程、保留和使用的方式，这些约定确保了整个<u>数据生命周期</u>过程中记录的全局性、一致性和准确性</p>	<p>Data governance should address data ownership throughout the lifecycle, and consider the design, operation and monitoring of processes / systems in order to comply with the principles of <u>data integrity</u> including control over intentional and unintentional changes to information. 数据管理应界定数据在整个生命周期中的归属问题，并考虑对流程/系统的设计、运行和监控，以便符合<u>数据完整性</u>原则，包括全面控制有意或无意的的信息修改。</p> <p>Data Governance systems should include staff training in the importance of data integrity principles and the creation of a working</p>

		<p>environment that encourages an open reporting culture for errors, omissions and aberrant results. 数据管理体系应该包括针对数据完整性原则的重要性对员工进行培训，以及营造一种企业文化，鼓励公开报告错误、数据遗漏和异常结果。</p> <p>Senior management is responsible for the implementation of systems and procedures to minimise the potential risk to data integrity, and for identifying the residual risk, using the principles of ICH Q9. Contract Givers should perform a similar review as part of their vendor assurance programme 高级管理团队负责系统和规程的实施，以降低潜在的数据完整性风险，并运用 ICH Q9 风险管理原则，识别剩余风险。有合同外包的企业，委托方应进行类似的审核，作为供应商管理项目的一部分。</p>
<p>Data Lifecycle 数据生命周期</p>	<p>All phases in the life of the <u>data</u> (including <u>raw data</u>) from initial generation and recording through processing (including transformation or migration), use, <u>data retention</u>, <u>archive</u> / retrieval and destruction. <u>数据</u>(包括原始数据) 生命周期的的各个阶段，包括数据的初始生成和记录、处理（包括转换和迁移）、使用、<u>数据保留</u>，<u>归档</u>/调取和销毁。</p>	<p>The procedures for destruction of data should consider data criticality and legislative retention requirements. Archival arrangements should be in place for long term retention (in some cases, periods up to 30 years) for records such as batch documents, marketing authorisation application data, traceability data for human-derived starting materials (not an exhaustive list). Additionally, at least 2 years of data must be retrievable in a timely manner for the purposes of regulatory inspection 销毁数据的规程应该考虑数据的关键性和法规对数据保留的要求。对需要长期保留的记录应进行归档（在某些情况下，保存期长达 30 年），例如批次文件，上市许可申请数据，来源于人体的起始原料的可追溯数据（不是详尽的清单）。此外，必须能够及时调取至少最近 2 年的数据，以满足法规部门检查的目的。</p>
<p>Primary Record 基准记录</p>	<p>The record which takes primacy in cases where <u>data</u> collected or retained concurrently by more than one method fail to concur. 当采用多于一种方法同步收集或保留的<u>数据</u>发生不一致时，该记录作为首要判断依据。</p>	<p>In situations where the same information is recorded concurrently by more than one system, the data owner should define which system generates and retains the primary record, in case of discrepancy. The 'primary record' attribute should be defined in the quality system, and should not be changed on a case by case basis. 当相同信息同步被多于一个系统进行记录时，数据拥有者应界定由哪</p>

		<p>个系统生成并保留的数据为基准记录，以防数据出现不一致时可以进行判决。“基准记录”的属性应在质量体系中进行明确定义，并且不得因个例而变化。</p> <p>Risk management principles should be used to ensure that the assigned ‘primary record’ provides the greatest accuracy, completeness, content and meaning. For instance, it is not appropriate for low-resolution or static (printed / manual) data to be designated as a primary record in preference to high resolution or dynamic (electronic) data. All data should be considered when performing a risk based investigation into data anomalies (e.g. out of specification results)</p> <p>应运用风险管理原则确保被指定为“基准记录”的记录在最大程度上保持其准确性，完全性、和内容与含义。例如：低分辨率或静态的（打印/人工记录）数据优先于高分辨率或动态（电子）数据设计作为基准记录是不合适的。所有数据都应考虑到被作为异常数据进行基于风险的调查的情况（例如：超标结果）</p>
<p>Original record / True Copy: 初始记录/正确的副本</p>	<p>Original record: <u>Data</u> as the file or format in which it was originally generated, preserving the <u>integrity</u> (accuracy, completeness, content and meaning) of the record, e.g. original paper record of manual observation, or electronic raw data file from a computerised system</p> <p>初始记录：<u>数据</u>作为文件或以初始生成的格式，维持记录的<u>完整性</u>（准确性、全面性、内容与含义）。例如，纸质的人工观测初始记录，或计算机系统的初始电子数据文件。</p> <p>True Copy: An exact verified copy of an original record. 正确的副本：经确认与初始记录完全相同的复制件。</p> <p>Data may be static (e.g. a ‘fixed’ record such as paper or pdf) or dynamic (e.g. an electronic record which the user / reviewer can interact with).</p>	<p>Original records and true copies must preserve the integrity (accuracy, completeness, content and meaning) of the record. Exact (true) copies of original records may be retained in place of the original record (e.g. scan of a paper record), provided that a documented system is in place to verify and record the integrity of the copy.</p> <p>初始记录和正确的副本必须维持记录的完整性（准确性、完全性、内容与含义）。初始记录完全正确的复制件可以和初始记录放置在一起（例如纸质记录的扫描件），并建立文件记录体系来核对和记录复制记录的完整性</p> <p>It is conceivable for <u>raw data</u> generated by electronic means to be retained in an acceptable paper or pdf format, where it can be justified that a static record maintains the integrity of the original data. However, the data retention process must be shown to include verified copies of all raw data, <u>metadata</u>, relevant <u>audit trail</u> and result files, software / system configuration settings specific to each analytical</p>

	<p>数据可以静态的（例如：象纸质或 pdf 格式的“固态”记录），或动态的（例如：用户/审阅者可以与之互动的电子记录）。</p> <p>Example 1: a group of still images (photographs – the static ‘paper copy’ example) may not provide the full content and meaning of the same event as a recorded moving image (video – the dynamic ‘electronic record’ example). 例1：一组静止的图像（照片- 静态的“纸质复印件”范例）对于记录同一事件，不能象动态的影像（录像-动态的“电子记录”范例）那样提供全部的内容和含义</p> <p>Example 2: once printed or converted to static .pdfs, chromatography records lose the capability of being reprocessed and do not enable more detailed viewing of baselines or any hidden fields. By comparison, the same dynamic electronic records in database format provides the ability to track, trend, and query data, allowing the reviewer (with proper access permissions) to reprocess, view hidden fields, and expand the baseline to view the integration more clearly. 例 2：色谱图一旦打印或转换成静态的 pdf 文件，就无法重复计算，以及进一步被详细查看基线或任何隐藏区域的功能。相比之下，同样的以数据库形式记录的动态电子记录提供了数据被溯源，被追踪和查询的功能，允许审阅者（拥有适当的登录权限）进行重复计算，查看隐藏区域，以及扩展基线来更清晰地查看积分情况。</p>	<p>run*, and all data processing runs (including methods and audit trails) necessary for reconstruction of a given raw data set. It would also require a documented means to verify that the printed records were an accurate representation. This approach is likely to be onerous in its administration to enable a GMP compliant record. 当静态记录能保证原始数据的完整和真实时，由电子方式生成的原始数据采用纸质或 PDF 格式进行保留是可以接受的。但是数据保留流程必须体现以下各个内容：包括核对过的所有原始数据、元数据、相应审计追踪（系统日志）和结果文档，针对每一次分析测试运行的软件/系统配置，以及对一套给定原始数据进行复原所必须的所有数据处理运行过程（包括方法和审计追踪）。还需要一个书面的方式来确认打印记录是准确的再现。这种方法可能在实现记录符合 GMP 要求的管理上比较繁琐。</p> <p>Many electronic records are important to retain in their dynamic (electronic) format, to enable interaction with the data. Data must be retained in a dynamic form where this is critical to its integrity or later verification. This should be justified based on risk. 很多电子数据为了能对数据进行后期操作而以动态格式（电子的）保留是很重要的。当数据的真实完整或后期确认是非常关键时，必须以动态格式保留。这应该进行基于风险地判断。</p> <p>* Computerized system configuration settings should be defined, tested and ‘locked’ and protected from unauthorised access as part of computer system validation. Only those variable settings which relate to an analytical run would be considered as electronic raw data 计算机系统的配置参数设定应进行定义，测试，“锁定”并可以防止非授权进入，是计算机系统验证的一部分。只有那些关于一次分析操作的可变参数的设定才被认作是电子原始数据。</p>
<p>Computer system transactions:</p>	<p>A computer system transaction is a single operation or sequence of operations performed as a single logical ‘unit of work’. The operation(s) that make up a transaction are not</p>	<p>Computer systems should be designed to ensure that the execution of critical operations are recorded contemporaneously by the user and are not combined into a single computer system transaction with other</p>

<p>计算机系统处理</p>	<p>saved as a permanent record on durable storage until the user commits the transaction through a deliberate act (e.g. pressing a save button), or until the system forces the saving of data.</p> <p>计算机系统的处理是一个单一操作或作为一个单一逻辑“工作单元”的系列操作。这些运作组成了一次处理，直到用户通过一个仔细考虑后的操作（例如按下保存键）对这个处理认可后，或直至系统强制存储数据时，它们才被作为可以长期存储的永久记录保存下来。</p> <p><u>The metadata</u> (i.e., user name, date, and time) is not captured in the system <u>audit trail</u> until the user commits the transaction.</p> <p>直到用户认可了此处理后，<u>元数据</u>（指，用户名，日期和时间）才被保留在系统<u>审计追踪</u>中。</p> <p>In Manufacturing Execution Systems (MES), an electronic signature is often required by the system in order for the record to be saved and become permanent.</p> <p>在制造执行系统 MES，系统通常要求一个电子签名来使记录得以存储，并永久保留。</p>	<p>operations. A critical processing step is a parameter that must be within an appropriate limit, range, or distribution to ensure the desired product quality. These should be reflected in the process control strategy.</p> <p>计算机系统设计应确保用户对关键操作进行同步记录，并且不得与其它操作合并成一个单一的计算机系统处理。关键工艺步骤是指某个参数必须在合适的限度，范围，分布之内，以确保预期的产品质量。这些必须体现在过程控制策略中。</p> <p>Examples of 'units of work': “单元操作”的例子</p> <ul style="list-style-type: none"> • Weighing of individual materials 对单个物料的称量 • Entry of process critical manufacturing / analytical parameters 输入生产/分析过程关键参数 • Verification of the identity of each component or material that will be used in a batch 用于一批生产中每个部件或物料标识信息的核对 • Verification of the addition of each individual raw material to a batch (e.g. when the sequence of addition is considered critical to process control – see figure 2) 每批生产中对每个初始物料的添加过程的核对（例如：当加料顺序对工艺控制有关键影响时-参见图 2） • Addition of multiple pre-weighed raw materials to bulk vessel when required as a single manufacturing step (e.g. when the sequence of addition is not considered critical to process control – see figure 3) 向大罐中加入多个预先称量好的初始物料需要作为一个生产步骤时（例如：加料顺序对工艺控制没有关键影响时 - 参见图 3）
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Figure 2: Logical design permitting contemporaneous recording of addition of a single material in a manufacturing ‘unit of work’. This record is permanently recorded(step2),with audit trail, before progressing to next ‘unit of work’.

图 2：允许在一个制造“工作单元”中同步记录单一物料加入步骤的逻辑设计。在处理下一个“工作单元”之前，这个记录会被永久记录（步骤 2）并伴有审计追踪。

允许操作者和复核者同步记录物料加入过程

Allows for contemporaneous recording of the material addition by the operator and verifier.

Material Additions		
Step	Instructions	Data
1.	Scan barcode of material ABC123.	ABC123 <Barcode>
2.	Add material ABC123 to the blender.	Operator Signature Verifier Signature

Next Step →

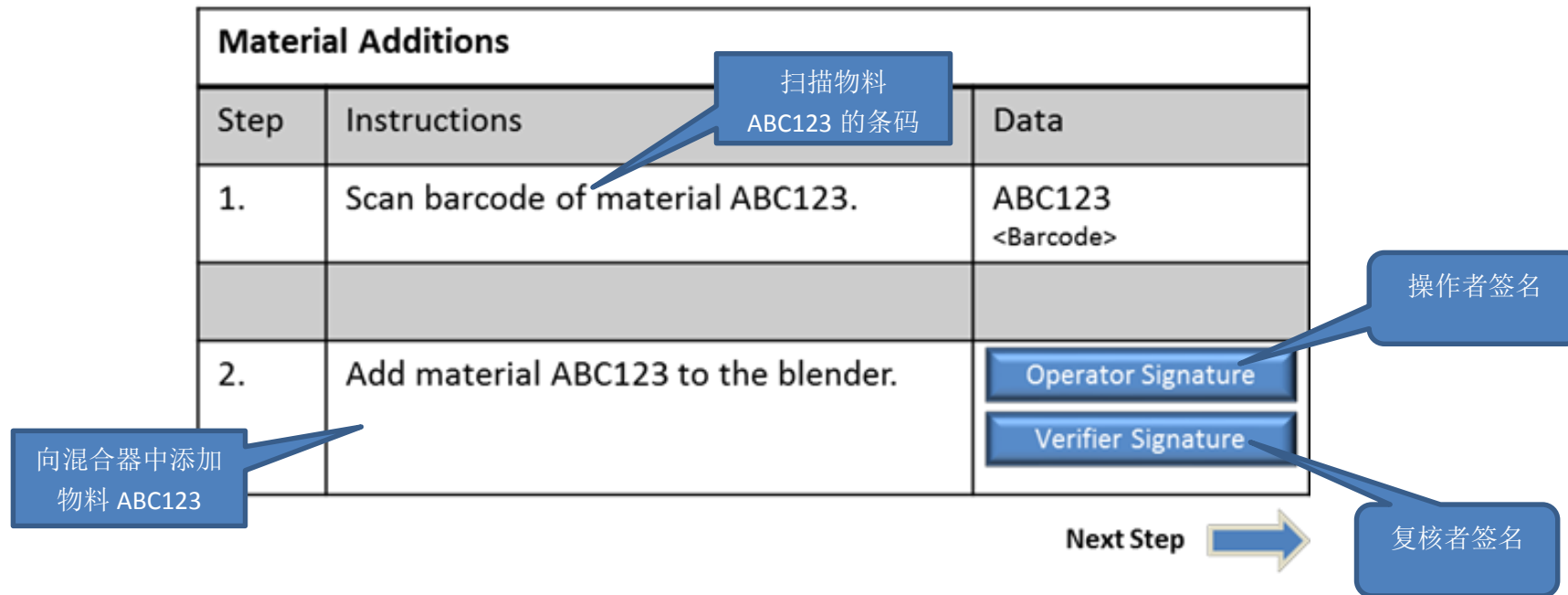


Figure 3: Logical design permitting the addition of multiple materials in a manufacturing ‘unit of work’ before committing the record to durable media. Steps 1,3 and5 are contemporaneous entries (bar code),but are not permanently recorded with audit trail until step6.

图 3：允许在记录提交给持久介质（durable media）前，在一个制造“工作单元”中加入多种物料的逻辑设计。步骤 1，3，5 是同时输入的（条形码），但在步骤 6 执行前，并没有被永久性记录及生成相应的审计追踪。

不允许操作者和复核者同时记录物料的添加。

Does not allow for contemporaneous recording of the material addition by the operator and verifier.

Material Additions		
Step	Instructions	Data
1.	Scan barcode of material ABC123.	ABC123 <Barcode>
2.	Add material ABC123 to the blender.	
3.	Scan barcode of material DEF456.	DEF456 <Barcode>
4.	Add material DEF456 to the blender.	
5.	Scan barcode of material GHI789.	GHI789 <Barcode>
6.	Add material GHI789 to the blender.	Operator Signature Verifier Signature

扫描物料 ABC123 的条码

向混合器中添加物料 ABC123

操作者签名

复核者签名

Next Step → i

<p>Audit Trail 审计追踪</p>	<p>GMP audit trails are <u>metadata</u> that are a record of GMP critical information (for example the change or deletion of GMP relevant <u>data</u>), which permit the reconstruction of GMP activities. GMP 审计追踪是元数据，记录了可以再现该 GMP 活动的 GMP 关键信息（例如对于 GMP 相关<u>数据</u>的修改和删除），</p>	<p>Where computerized systems are used to capture, process, report or store raw data electronically, system design should always provide for the retention of full audit trails to show all changes to the data while retaining previous and original data. It should be possible to associate all changes to data with the persons making those changes, and changes should be time stamped and a reason given. Users should not have the ability to amend or switch off the audit trail. 当计算机化系统用于电子化采集、处理、报告或储存原始数据时，系统设计应始终提供具有保留全套审计追踪的功能来显示对以前保留的数据和初始数据的所有更改情况。数据的所有改变应该可以关联到数据修改者，应记录更改的时间并给出原因。用户应该没有权限修改或关闭审计追踪功能。</p> <p>The relevance of data retained in audit trails should be considered by the company to permit robust data review/ verification. The items included in audit trail should be those of relevance to permit reconstruction of the process or activity. It is not necessary for audit trail review to include every system activity(e.g. user log on/off, keystrokes etc.),and maybe achieved by review of designed and validated system reports. 公司应该考虑到保留在审计追踪中数据的相关性，以便进行可靠的数据审核/确认。包含在审计追踪中的条目应该是允许过程或活动再现的那些相关信息。审计追踪的审核没有必要包括囊括所有系统活动（例如用户的登录和退出，键盘输入等），可以通过系统审核设计报告和系统验证报告来达到目的。</p>
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<p>Audit trail (Continuoue) 审计追踪 (续)</p>		<p>Audit trail review should be part of the routine data review /approval process, usually performed by the operational area which has generated the data (e.g. laboratory).There should be evidence available to confirm that a review of the relevant audit trail has taken place. When designing a system for review of audit trails, this maybe limited to those with GMP relevance(e.g. relating to data creation, processing, modification and deletion etc).Audit trails maybe reviewed as a list of relevant data, or by a validated ‘exception reporting’ process.QA should also review a sample of relevant audit trails, raw data and metadata as part of self-inspection to ensure on-going compliance with the data governance policy/procedures.</p> <p>审计追踪的审核应该是日常数据审核/批准的流程的一部分，通常在产生数据的操作区域（例如实验室）进行审查。应具有有效的证据以确认相关审计追踪的审核已经实施。当设计一个用于审计追踪审核的系统时，应尽量把它限定在与 GMP 相关的范畴内（例如，与数据产生、处理、修改和删除等相关）。可以将审计追踪作为一个相关数据列表进行审核，或由一个经过验证的异常报告流程执行审核。为了确保持续符合数据管理政策与规程，QA 在自检过程应该抽样审核相关审计追踪，原始数据和元数据。</p> <p>If no audit trailed system exists, a paper based audit trail to demonstrate changes to data will be permitted until a fully audit trailed (integrated system or independent audit software using a validated interface) system becomes available. These hybrid systems are currently permitted, where they achieve equivalence to integrated audit trail described in Annex 11 of the GMP Guide. If such equivalence cannot be demonstrated, it is expected that facilities should upgrade to an audit trailed system by the end of 2017.</p> <p>如果没有现成的带审计追踪功能的系统，在采用能充分执行审计追踪的系统前（集成系统或使用验证过的界面连接的独立审计软件），允许采用纸质的审计追踪来说明数据的修改。如果能达到 GMP 指南附录 11 所要求的集成审计跟踪的等同效果，这些混合审计追踪系统目前是允许的。如果不能证明其等效性，那么在 2017 年底前企业应升级到使用一个带审计追踪功能的系统。</p>
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<p>Data Review 数据审核</p>		<p>There should be a procedure which describes the process for the review and approval of data, including raw data. Data review must also include a review of relevant metadata, including audit trail. 应该建立规程，描述包括原始数据在内的数据审核和批准流程。数据的审核必须包括相关元数据及其审计追踪的审核。</p> <p>Data review must be documented. 数据审核必须记录。</p> <p>A procedure should describe the actions to be taken if data review identifies an error or omission. This procedure should enable data corrections or clarifications to be made in a GMP compliant manner, providing visibility of the original record, and audit trailed traceability of the correction, using ALCOA principles (see 'data' definition). 该规程应描述如果数据审核发现错误或遗漏时所需采取的行动。此规程应促使以符合 GMP 要求的方式进行数据更正或澄清说明，确保初始记录的清晰可见性，纠正过程有审计追踪确保可追溯性，并使用 ALCOA 原则（参见“数据”的定义）。</p>
<p>Computerised system user access / system administrator roles 计算机系统的用户访问权限/系统管理员角色</p>		<p>Full use should be made of access levels to ensure that people have access only to functionality that is appropriate for their job role. Facilities must be able to demonstrate the access levels granted to individual staff members and ensure that historical information regarding user access level is available. 要充分利用设置访问权限级别来保证员工只能访问与他们的工作角色相适应的功能区。企业必须能证明给个体用户设置了访问权限级别，并保证可以获取用户访问权限的历史信息。</p> <p>Shared logins or generic user access should not be used. Where the computerised system design supports individual user access, this function must be used. This may require the purchase of additional licences. 不应使用共享登录账号和密码或无权限级别区分的登入方式。当计算机系统的设计支持单个用户访问权限时，该功能必须被使用。这可能需要购买额外的许可证。</p>

It is acknowledged that some computerised systems support only a single user login or limited numbers of user logins. Where alternative computerised systems have the ability to provide the required number of unique logins, facilities should upgrade to an appropriate system by the end of 2017. Where no suitable alternative computerised system is available, a paper based method of providing traceability will be permitted. The lack of suitability of alternative systems should be justified based on a review of system design, and documented.

众所周知,一些计算机化系统只支持单用户登录或有限数量的用户登录。当有其他替代的计算机化系统能提供所需数量的唯一登录时,企业应在2017年底前升级到该适当的系统。如果没有其它合适的替代计算机化系统,允许使用具有可追溯性的纸质记录方法。应通过对系统设计的审核来证明缺乏合适的替代系统的理由是合理的,并进行相应记录。

System administrator access should be restricted to the minimum number of people possible taking account of the size and nature of the organisation. The generic system administrator account should not be available for use. Personnel with system administrator access should log in under unique log-ins that allow actions in the audit trail(s) to be attributed to a specific individual.

根据组织的规模和性质,尽可能将系统管理员权限的数量限制到最少。不能采用无法区分身份的系统管理员帐户。担任系统管理员的人员登入系统时应采用唯一的登录帐号,以便审计追踪能追踪到特定个人。

System Administrator rights (permitting activities such as data deletion, database amendment or system configuration changes) should not be assigned to individuals with a direct interest in the data (data generation, data review or approval). Where this is unavoidable in the organisational structure, a similar level of control may be achieved by the use of dual user accounts with different privileges. All changes performed under system administrator access must be visible to, and approved within, the quality system.

不得将系统管理员权限(授权的操作,如数据删除、数据库修改或系统配置的修改)分配给数据(数据生成、数据审核或批准)的直接利益方。当由于组织结

		<p>构原因不可避免时，可采用不同权限的双用户帐户来实现同等水平的控制。使用系统管理员权限进行的所有更改必须在质量体系中被监督和批准。</p>
<p>Computerised system user access / system administrator roles (continued) 计算机化系统的用户权限/系统管理员的角色(接上文)</p>		<p>The individual should log in using the account with the appropriate access rights for the given task e.g. a laboratory manager performing data checking should not log in as system administrator where a more appropriate level of access exists for that task. 用户应使用与实施任务相适应的访问权限进行账户登录, 例如, 当已有一个更合适的访问权限存在时, 实验室经理在进行数据复核时不应以系统管理员的账户登录。</p>
<p>Data retention 数据保留</p>		<p>Raw data (or a true copy thereof) generated in paper format may be retained for example by scanning, provided that there is a process in place to ensure that the copy is verified to ensure its completeness. 如果已经建立流程来确保对复印件进行核对其完全性的话, 那么纸质的原始数据(或它的正确副本)可以通过例如扫描的方式来保存。</p> <p>Data retention may be classified as archive or backup 数据保留可以分为归档和备份</p> <p>Data and document retention arrangements should ensure the protection of records from deliberate or inadvertent alteration or loss. 数据和文件的保留方式应能确保记录不被蓄意或无意的更改或丢失</p> <p>Secure controls must be in place to ensure the data integrity of the record throughout the retention period, and validated where appropriate. 必须建立安全控制措施, 确保在保留期间内记录的数据完整性, 适当时进行验证。</p> <p>Where data and document retention is contracted to a third party, particular attention should be paid to understanding the ownership and retrieval of data held under this arrangement. The physical location in which the data is held, including</p>

		<p>impact of any laws applicable to that geographic location should also be considered. The responsibilities of the contract giver and acceptor must be defined in a contract as described in Chapter 7 of the GMP Guide</p> <p>当采用第三方外包服务的方式保留数据和文件时，应特别注意了解在这种协议下数据的所有权和取回方法。应考虑存放这些数据的实际位置，包括任何适用于那个地理位置的法规影响。委托方和受托方的职责必须根据 GMP 规范第 7 章中的要求在合同中明确定义。</p>
Archive 归档	<p>Long term, permanent retention of completed data and relevant metadata in its final form for the purposes of reconstruction of the process or activity.</p> <p>为了能重现过程或活动的目的，对完整的数据和相关元数据以最终格式进行长期,永久的保留。</p>	<p>Archive records should be locked such that they cannot be altered or deleted without detection and audit trail.</p> <p>归档记录应被锁定，以免记录的更改或删除未被察觉和没有审计追踪记录。</p> <p>The archive arrangements must be designed to permit recovery and readability of the data and metadata throughout the required retention period.</p> <p>归档方式的设计必须允许在整个要求的保留期限内能够进行数据和元数据的恢复和读取。</p>
Backup 备份	<p>A copy of current (editable) data, metadata and system configuration settings (variable settings which relate to an analytical run) maintained for the purpose of disaster recovery.</p> <p>为了灾难性破坏后恢复数据的目的而复制一份现有的（可编辑得）数据，元数据和系统设置（与一次分析运行相关的可变参数设置）并维护</p>	<p>Backup and recovery processes must be validated.</p> <p>备份和恢复流程必须经过验证</p>
File structure 文件结构		<p>File structure has a significant impact on the inherent data integrity risks. The ability to manipulate or delete flat files requires a higher level of logical and procedural control over data generation, review and storage.</p> <p>文件结构对其内在的数据完整性风险有显著的影响。由于单层文件可能被篡改和删除, 需要制定一个更高层次的逻辑和程序控制手段, 控制数据的生成, 审核和储存过程。</p>

<p>Flat files: 单层文件</p>	<p>A 'flat file' is an individual record which may not carry with it all relevant metadata (e.g. pdf, dat, doc). 单层文件是没有携带任何相关元数据的一个单独记录(例如: pdf, dat, dot)</p>	<p>Flat files may carry basic metadata relating to file creation and date of last amendment, but cannot audit trail the type and sequence of amendments. When creating flat file reports from electronic data, the metadata and audit trails relating to the generation of the raw data is also lost, unless these are retained as a 'true copy'. 单层文件可能携带与文件创建和数据最后一次修改日期相关的基础元数据，但不能审计追踪历次修改的类型和顺序。当由电子数据创建单层文件报告时，生成原始数据的相关的元数据和审计追踪也会丢失，除非这些信息已被保存为“正确的副本”。</p> <p>Consideration also needs to be given to the 'dynamic' nature of the data, where appropriate (see 'true copy' definition) 适当时（见“正确的副本”的定义），也需要考虑数据的“动态”性质</p> <p>There is an inherently greater data integrity risk with flat files (e.g. when compared to data contained within a relational database), in that these are easier to manipulate and delete as a single file. 单层文件有很大的内在的数据完整性风险（例如：相比与包含在关系型数据库中的数据时），是由于单层文件很容易被作为一个单个文件进行篡改和删除。</p>
<p>Relational database: 关系型数据库</p>	<p>A relational database stores different components of associated data and metadata in different places. Each individual record is created and retrieved by compiling the data and metadata for review. 关系型数据库在不同的地方存放与数据和元数据相关的不同要素。每个单独记录的创建和恢复都通过收集数据和元数据来完成，以供审核。</p>	<p>This file structure is inherently more secure, as the data is held in a large file format which preserves the relationship between data and metadata. This is more resilient to attempts to selectively delete, amend or recreate data and the metadata trail of actions, compared to a flat file system. 这个文件结构自然更具安全性，因为数据以一个很大的文件格式保存，可以保留数据与元数据的关系。相比于单层文件系统，更能复原那些企图进行选择性的删除，修改或重新创造数据和元数据痕迹的操作。</p> <p>Retrieval of information from a relational database requires a database search tool, or the original application which created the record. 从关系型数据库调取信息，需要使用一个数据库搜索工具，或创建记录的初始应用。</p>

<p>Validation - for intended purpose (See also Annex 15 and GAMP 5) 验证-为了预定目的 (参考附录 15 和 GAMP5)</p>		<p>Computerised systems should comply with the requirements of EU GMP Annex 11 and be validated for their intended purpose. This requires an understanding of the computerised system's function within a process. For this reason, the acceptance of vendor-supplied validation data in isolation of system configuration and intended use is not acceptable. In isolation from the intended process or end user IT infrastructure, vendor testing is likely to be limited to functional verification only, and may not fulfil the requirements for performance qualification.</p> <p>计算机化系统应符合 EU GMP 附录 11 的要求，并需验证其符合预期的用途。这就需要充分理解计算机化系统在一个流程中的功能。因为这个原因，采纳供应商提供的独立于系统配置和预期用途的验证数据是不被接受的。离开了预期流程或最终用户的 IT 基础设施，供应商测试只局限于功能性测试，可能不能满足性能确认的要求。</p> <p>For example - validation of computerised system audit trail 例如- 验证计算机化系统的审计追踪功能</p> <p>A custom report generated from a relational database may be used as a GMP system audit trail. SOPs should be drafted during OQ to describe the process for audit trail verification, including definition of the data to be reviewed. 'Validation for intended use' would include testing during PQ to confirm that the required data is correctly extracted by the custom report, and presented in a manner which is aligned with the data review process described in the SOP.</p> <p>关系型数据库产生的定制报告可以被用作 GMP 系统的审计追踪。在运行确认阶段应编写 SOP 描述审计追踪被确认的过程，包括对被审核数据的定义。“符合预期用途的验证”应包含在性能确认阶段进行的测试，用来确认所需的数据已经由定制报告正确获取，并且表现方式和标准操作规程中描述的数据审核流程一致。</p>
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Revision 版本	Publication Month 公布月份	Reason for changes 修改原因
Revision 1 版本 1	January 2015 2015年1月	None. First issue. 第一版
Revision 1.1 版本1.1	March 2015 2015年3月	Added clarifications in response to stakeholder questions. 针对利益相关方的问题，加入解释