计算机化的实验室数据收集系统的验证和确认

Validation and Qualification of Computerized Laboratory Data Acquisition Systems

PDA 技术报告 No. 31

Technical Report No. 31 PDA

1. Objective 目的

The purpose of this article is to provide guidance to laboratory scientists, technicians and managers responsible for the implementation, testing, control and usage of Laboratory Data Acquisition Systems (LDAS) used within a GMP, GLP, and GCP regulated environment.

本文为实验室科学家、技术员以及管理者提供了在 GMP, GLP 和 GCP 规范化环境下使用的 LDAS 的执行、测试、控制和用途方面的指南。

2. Scope 范围

This article specifically addresses computerized LDAS within a regulated environment. This guidance is also applicable to systems considered critical to the operations of a company, department or function regardless of the system's regulatory impact. The scope of this article excludes the typical Laboratory Information Management System (LIMS). The fundamental difference between a LIMS and an LDAS system is that the LDAS has a laboratory instrument as its primary focus, such as a computerized HPLC, whereas a LIMS, though instruments may be attached, has the management of data as its primary focus. The guiding key practices for testing and controlling an LDAS are similar to those for testing and controlling a LIMS;[-1] the fundamental differences lie in the application of these key practices.

本文仅涉及在规范化环境下的计算机化的 LDAS。本指南同样适用于那些被视为对公司、部门或团体的运作起关键作用的系统，无论这些系统是否在规范化的体系内。本文的范围不包括典型的 LIMS（实验室信息管理系统）。LIMS 和 LDAS 最基本的区别在于 LDAS 优先考虑实验室仪器，比如计算机化的 HPLC；而 LIMS 虽然也和仪器有关联，但它主要考虑的是数据的管理。LDAS 测试和控制的关键实践指南和 LIMS 类似，基本区别在于其应用。

3. Overview of Validation Concepts 一些验证概念的综述

The testing, calibration and control of laboratory systems are not new concepts.

Instruments are usually calibrated (i.e. tested) prior to their use in an experiment. Likewise, controls are typically utilized to ensure that the instrument remains in calibration thus assuring the on-going quality of the data. It is the *extent* of testing and control *and* the amount of subsequent documentation required, especially within the regulated environment, which has changed dramatically over the past years.

实验室系统的测试、校准和控制并不是什么新鲜的概念。仪器一般在实验使用前进行校准（比如检测）。同样，控制一般用于确保仪器始终住处校准状态以保证数据的持续性质量。这是测试和控制的范围以及后续文档的数量所需要的，特别是在规范化的环境中，在过去几年里已经发生了巨大的变化。

Several years ago, validation was a term inappropriately applied only to the documented testing of a system. This testing verified the proper functioning of the system. Procedures for maintaining the system in this "validated" state assured the scientist that the system was under control and produced consistent and reliable results.

几年前，验证只是不恰当地应用于系统的文件化测试的一个术语。这种测试确认了系统可以正常运转。用于维持系统在已验证状态的规程使科学家确信系统在控制中并可以产生稳定的和可靠的结果。

As a result of regulatory concerns, the testing and control of a system is now a larger process. Validation involves the documented assurance that a system has been defined, designed, developed and delivered in a manner consistent with its intended purpose. It should include processes that address on-going support, control, and the retirement of the system.

由于涉及到法规问题， 系统的测试和控制现在是一个更大的过程。验证为系统符合其预期用途的定义、设计、开发和交付方式提供了文件化保证。它应包括处理系统持续性支持、控制和退役的全过程。

The process applied to the control of these systems is called "Validation" and a definition often used is:

应用于这些系统控制的过程称为"验证"，一般使用的定义为：

"Establishing documented evidence that provides a high degree of assurance that a specific process will consistently produce a product meeting its predetermined specifications and quality attributes."(FDA: General Principles of Process

Validation,1987).

"建立书面的证明，以充分保证某个特定的工艺可以稳定地生产出符合预定规格和质量标准的产品"（FDA 工艺验证一般原则 1987）

Which systems should be validated? Any system that is used to create, modify, maintain, archive, retrieve, or transmit data[2] intended for submission to a regulatory agency must be validated. Recent regulatory inspections indicate that the validation concept is broadening to include any system that may impact a regulatory decision including electronic Standard Operating Procedure (SOP) systems, report tracking systems, etc., but these issues are outside of the scope of this article.

哪些系统应当被验证？用于向法规机构提交的数据的创建、修改、维护、归档、检索或传输的系统都必须验证。最近的法规检查表明，验证的概念被扩大到影响到法规决策的任何系统，包括电子操作规程系统、报告追踪系统等等，但这些问题已经不在本文的范围以内。

Validation is mandatory within a GMP/GLP regulated environment. However, determining which systems require validation, and how much testing to perform and associated documentation to retain, is sometimes problematic. Since validation is an assurance process it is also applicable to those systems considered important to the operations of any business. Thus, the key practices set forth in this article may be applied to systems within a non-GMP/GLP regulated environment but considered important enough to justify the resource expenditures inherent in the validation process.

在 GMP/GLP 规范化的环境中，验证是强制的。然而，决定哪些系统需要验证，需要做多少测试以及保留多少文档，有时却是有疑问的。因为验证是一种保证过程，它同样适用于任何重要的商业操作。因此，本文中的关键规范可以被用于非 GMP/GLP 规范化环境中但认为是重要的，足以证明验证过程本身花费的资源是正确的系统。

What follows is a brief overview of validation concepts. Numerous articles and books have been written describing these practices indetail.[3-5]

下面的是一些验证概念的简要概述。许多文章和书籍都已经详细描述过这些实践活动。

3.1 Suggested Practices 一些推荐的实践活动

The following key practices are recommended to help identify and control all computer validation efforts within your business.

下面推荐的实践可以帮助识别和控制你公司内的所有计算机验证工作。

Inventory: An inventory should be created of all computer systems being used within the appropriate business area (company, department etc.). It should be a dynamic inventory representing at any point in time all systems currently in use. A regulatory inspector often asks for this inventory as one currently in use. A regulatory inspector often asks for this inventory as one of the first questions during an inspection.

清单： 应为在合适商业区域（公司、部门等）内使用的所有计算机系统创建一份清单。这份清单应该时动态的，能够实时显示任何时间点使用的所有系统。法规部门的检查员通常会要求提供这样一份清单，这也通常是检查员提出的第一个问题。

System Assessment: The assessment of each computer system within the inventory should be based on its impact to regulatory submissions, product, and the system's criticality to the efficient functioning of the business. The need for validation should be based upon this risk assessment.

系统评估：清单内的每一个计算机系统的评估应基于系统对注册申报、产品和系统对公司高效运转关键性的影响。验证的需求应基于这种风险评估。

Validation Master Plan: The Validation Master Plan is a direct result of the inventory system assessment. It is a document that lists and prioritizes the computer systems/applications to be validated and associated responsibilities and timelines. In the list there may be systems that are identified as candidates for replacement, reengineering, or retirement. Justification for not validating a system should be documented.

验证主计划：验证主计划是库存系统评估的直接结果。它列出了待验证计算机系统和应用程序并进行排序，并且包括相关的职责和时间轴。在这份清单里，也可以包括用于替换、重建或退役的候选系统。如果系统不验证，需要正当的理由并被记录归档。

Validation Teams: Some companies have a fairly high-level management team responsible for approving the Validation Master Plan. The team should represent the user departments, Quality Assurance, and any other relevant areas. In addition, dependent on the scope of the validation, each validation project should have a team comprised of the appropriate user, Information Technology and Quality Assurance resources. Representation from these areas will ensure that knowledgeable personnel have placed a proper focus on the validation effort and that all critical aspects of the system have been documented, tested, and controlled.

验证小组：一些公司有相当高层次的管理小组负责批准验证主计划。该小组应代表用户部门、QA 部门和其他相关部门。另外，根据验证的范围，每一个验证项目均应成立验证小组，并配置合适的用户、IT 和 QA 资源。这些部门的代表将确保具备相关知识的人员在验证工作中关注合适的点并保证系统所有的关键点均已记录、测试和控制。

3.2 Validation Related Activities 验证相关活动

As mentioned above, validation is a process that impacts the acquisition, implementation and retirement phases of a computer system. Although the control mechanisms required during these phases have been well documented in other articles, a brief review has been included for those not familiar with this information. Keep in mind that all documentation should be appropriately approved, version controlled and archived.

如上所述，验证是一个影响到计算机系统收集、执行和退役阶段的过程。尽管在其他文章中已经很好收录了这些阶段中的控制机制，但本文包括了这些信息的其他一些简要回顾。值得注意的是，所有文件都应被恰当的批准、版本控制和归档。

3.2.1 System Definition Phase 系统定义阶段:

A Requirements Document should be developed which describes the system as it will be used within the laboratory. It should include the purpose of the system, the desired functions, necessary security and access requirements, and external connections (i.e. instruments, networks, other computers etc.). It should also include any requirements for compatibility with existing or future equipment and computing architectures.

应开发一份即将用于实验室系统的需求描述文件。该文件应包括系统的目的、期望的功能、必要的安全和访问要求和一些外部接线（比如仪器、网络、其他电脑等等）。同样应包括任何和现存或将来设备和计算架构兼容性的需求。

3.2.2 Acquisition Phase 收集阶段：

A Supplier Assessment may be included as part of the acquisition phase. This is ideally accomplished via a "Supplier Audit",[6] a scheduled visit at the supplier's place of business to assess their quality practices used for system development and support. Auditing is also applicable for in-house developed systems. A 'Request for Information' may be used as a preliminary assessment tool to eliminate a prospective supplier if multiple suppliers are being considered.

供应商的评估可以作为收集阶段的一部分包括在内。在理想情况下可以通过“供应商审计”完成，通过预定的对供应商公司现场的访问来评价他们用于系统开发和支持的质量规范。如果考虑多个供应商，可以使用“信息调查表”作为初步评估工具以筛选出预期的供应商。

In either case, the supplier assessment should minimally address the following:

无论哪种情况，供应商审计应至少包括以下内容：

1. Business Related 商业相关
    - Financial stability 财政稳定性
    - Organizational structure 组织架构
    - Product focus and strategies 产品焦点
    - Employee credentials and training 员工文凭和培训
2. Development Related 开发相关
    - Development methodologies 方法学开发
    - Software quality assurance practices 软件质量保证规范
    - Change control Procedures 变更控制程序
    - Configuration Management Procedures 配置管理程序
    - Personnel Training Procedures 人员培训程序
    - User and Support documentation 用户和支持文件
    - Testing Procedures 测试程序
    - Technical Review practices 技术回顾规范
    - Security Procedures 安全程序
3. Ongoing Support 持续性支持
    - Security 安全
    - Maintenance and Change Control 维护保养和变更控制
    - Customer Support 客户支持
    - Documentation Management 文件管理
    - Backup and Recovery 备份和恢复
    - Operations 操作
    - Training 培训

- Disaster Recovery 灾难性恢复

Key deliverables from the Supplier Audit are the Audit Report, the supplier's response to audit findings, and the client's 'rating' of the supplier. In addition, the Design Specifications and Statement of Source Code Availability should also be delivered.

供应商审计中关键的交付物是审计报告、供应商对审计中发现问题的响应以及客户对供应商等级的评定。另外，设计标准和源代码可获得性声明同样也应交付。

The Design Specifications is a highly technical document used by the developers to translate the Requirement Specifications into actual development practice.

技术标准是一份高技术含量的文件，开发者可以使用它将需求标准转化为实际的开发规范。

The Statement of Source Code Availability should ideally indicate that the source code for the software has been deposited in an escrow account so that it is available regardless of adverse business situations. It may also state that the source code is available for inspection at the supplier's site. This statement is not necessary if the code will be maintained by the client or was developed in-house.

源代码可获得性声明应明确指出软件的源代码应已由第三方托管以便无论出现恶劣的商业状况它均可获得。同样它可以规定源代码可以因检查的需要从供应商处获得。如果代码由客户维护或内部开发，则这份声明是不必要的。

3.2.3 Implementation/Testing Phase 执行/测试阶段：

A plan of action should first be developed which outlines the testing activities to be performed, expected results and control issues during this phase. This document is typically entitled the "Test Plan". Recommended sections of this document include:

首先需要开发一份行动计划，在这份计划中应概述下待进行的活动、期望的结果和这个阶段中的问题控制。这份文件一般以"测试计划"作为标题。文件包括的内容建议如下：

- Introduction and overview of the system 系统的介绍和概况
- Identification of system components to be tested 待测试系统组件的识

别

- Testing procedures 测试程序
- Responsibilities 职责
- Expected results and criteria for acceptance 期望的结果和可接受标准
- Approvals 批准

The testing (Qualification) procedures identified within the Test Plan are divided into three ‘‘qualification’’ categories. Some companies accomplish each category at different times with a separate test protocol for each, while other companies design an overview ’’Systems Qualification’’ document with each type of testing as a subsection.

测试（确认）程序在测试计划中定义并被划分为 3 个“确认”类别。一些公司对每一个类别均有一个单独的测试方案并在不同的时间内完成，而其他一些公司则设计一份“系统确认”概况文件包含了所有类型并分段测试。

It is important that each qualification be accomplished regardless of whether it is under one or multiple testing protocols.

重要的是每一项确认均要完成无论是一份或多份测试方案。

Installation Qualification (IQ): Tests and documents whether the entire system (i.e. hardware, application and system software) has been installed correctly at the user site.

安装确认（IQ）：测试并记录整个系统（比如硬件、应用和系统软件）是否被正确安装到用户现场。

Operational Qualification (OQ): Tests and documents whether *each component* of the system (i.e. hardware and application software) performs as intended throughout its expected operational ranges.

运行确认（OQ）：测试并记录系统的每一个组件（比如硬件、应用软件）是否按要求始终在其预期的运行范围内运行。

Performance Qualification (PQ): Tests and documents whether the *entire system* (i.e. hardware, application software and associated instruments) performs as intended throughout its expected operational ranges. It is recommended that user involvement should be included in PQ and, if feasible,

an actual sample or product be utilized.

性能确认（PQ）：记录并测试整个系统（比如硬件、应用软件和相应的仪器）是否按要求始终在其预期的运行范围内运行。建议用户应参与 PQ，如果可行，可以使用实际的样品和产品。

Linkage and traceability (via referencing) between the requirements, design, and testing documents is a good engineering practice and has become an expectation of some regulatory inspectors.

使需求、设计和测试文件关联并具有可追溯性（通过引用）是一个良好的工程规范并且已成为一些法规检查员的期望要求。

A "Validation Test Summary Report" should be developed upon completion of the qualification and be retained as part of the overall validation documentation. This summary should be a high level document targeted to upper management describing the results of the qualification effort and identifying any problem areas or issues and the irresolution.

在确认完成的基础上开发一份"验证测试总结报告"并作为总体验证文档的一部分。这份总结应是一份面向高级管理层的高水平文件，在这份文件里描述了确认工作的结果并识别任何问题领域或争议点以及迟疑点。

3.2.4 Miscellaneous Activities 其他活动：

Training: User training should be accomplished as soon as possible after the system has been installed. This is particularly important for those users who will be participating in the qualification testing. In addition, a process should be implemented and documented for on-going training for the initial system, for updates to the system, and for new employees. The training should be documented within employee training records.

培训：用户的培训应尽可能在系统完成安装后尽快完成。这对于参与确认测试的用户尤其重要。另外，应对初始系统、升级后的系统以及新员工进行持续性培训并记录归档。这些培训应收录到员工的培训记录中去。

Change Control: A process should be implemented to manage any changes that impact the computer system. This is to ensure that the system remains in a validated state. Any circumstance that may impact the system should be

documented and assessed for potential affects on data, system reliability, and documentation. Additional testing may result from this assessment. All testing and change control documents should be appropriately approved and archived.

变更控制：应执行管理任何影响到计算机系统的变更的程序。这是为了保证系统始终维持在已验证的状态。任何影响到系统的情况都应记录并评估其对数据、系统可靠性以及文档的潜在影响。所有测试和变更控制文件应经恰当的批准并归档。

Standard Operating Procedures (SOPs): SOPs should be developed for all aspects of the validation process, user training, system maintenance, change control, documentation archival, periodic review, and for any other process which may impact the proper functioning and use of the regulated system. A good rule of thumb for determining what needs to be documented as a procedure is any activity that is a stepwise, repetitive process that requires consistency (e.g., back-up, restore, startup, and shutdown).

标准操作规程（SOP）：应开发涉及到验证工艺、用户培训、系统维护保养、变更控制、文件档案、周期回顾以及其他影响到规范化的系统运作的工艺的所有方面的标准操作规程。一个决定哪些需要写成规程的良好经验法则可以是任何阶梯式的、重复的并要求一致性的过程的活动。（比如：备份、恢复、启动和关闭）。

4. Fundamental LDAS Concepts and Attributes LDAS 基本概念和特性

In general, a computerized Laboratory Data Acquisition System is a tool to aid in the decision making process of the product quality, based upon the physical and/or chemical characteristic for the analyzed sample.

一般来说，计算机化的 LDAS 是作为一种工具来帮助产品质量的决策过程，此过程基于被分析样品的物理和/或化学特性。

The following concepts and attributes will facilitate a better understanding of your LDAS and assist you applying the validation process to the appropriate level of detail.

下面的一些概念和特性可以帮助你更容易理解 LDAS 并协助你在应用验证的过程中达到合适的细节水平。

4.1 Concept#1: Common Characteristics May Be Used to Classify the Majority of Computerized Laboratory Data Acquisition Systems

概念#1：可用来分级大多数计算机化的 LDAS 的普遍特征。

Lab Systems vary in complexity, function, and scope of use. Therefore, not all systems will fall easily within these characteristics. The word ‘‘System’’ includes the computer hardware, software and associated instrumentation and equipment (such as an Analog to Digital (A/D) Interface), as well as, the external physical wiring.

实验室系统在使用的复杂性、功能和范围存在着多样化。因此，不是所有系统都能简单的对应上这些特征。“系统”这个词包括了计算机硬件、软件和相关联的仪表和设备（比如一个模拟/数字（A/D）转换信号接口）以及外部的物理接线。

A typical computerized ‘Laboratory Data Acquisition System’’ (LDAS) has the following characteristics:

典型的计算机化的 LDAS 有如下一些特征：

The system is designed to measure the chemical or physical property of a sample being analyzed.

系统是被设计用来测量被分析样品的化学或物理性质。

The system is associated with a sensor component that is capable of measuring the chemical or physical activity of a sample. The typical final output of the sensor is an analog signal. In some instances, it may be possible to segregate the LDAS from the sensor component for validation purposes.

系统配置有一个传感器组件，可以测量样品的物理或化学活性。传感器典型的最终输出是模拟信号。某些情况下，可能因为验证的需要将传感器组件从 LDAS 上分离出来。

The system is associated with an analog to digital converter component (A/D) that is capable of converting the analog output from the sensor into a digital format.

系统配置有一个数字信号转换器组件，可以将传感器输出的模拟信号转换为数字信号。

The system has a user interface that is capable of printing, exporting, or displaying the output from the A/D component.

系统有用户界面，可以将 A/D 组件的输出打印、导出或显示出来。

The system includes an application program or software to handle the data processing and the interactions or coordination of the above components.

系统包含一个应用程序或软件用来处理数据的加工和上述组件的交互或协调。

Additional characteristics that distinguish an LDAS from other computer systems are

the location of the system (typically within a laboratory environment) and the type of samples being analyzed. These samples can typically be categorized as raw material, in-process, and finished product samples. The system should be operated by a person with a technical background or a person that has been trained and qualified in using the system. Furthermore, the use of the system is usually governed by documented procedure.

其他一些区分 LDAS 和其他计算机系统的特征包括系统的位置（典型的位于实验室环境）和被分析样品的类型。这些样品典型地分为原料、中间品和成品样品。系统的操作那个应由有技术背景的人或已完成培训并认证通过的人员进行。此外，系统的使用应遵循书面的操作规程。

4.2 Concept#2: An LDAS May Be Classified According to Its Attributes of Configurability, Complexity, and Data Integrity

概念#2：LDAS 可能根据其可配置性、复杂性和数据的完整性进行分类。

The LDAS classification concept is important for justifying the extent of the validation effort. This classification will determine how a LDAS system should be validated or qualified by providing a tool for assessing the data integrity and security factors of a LDAS system.

LDAS 分类概念对于判断验证工作的程度是十分重要的。这种分类将决定 LDAS 系统应如何通过工具或对数据完整性和 LDAS 系统安全因素的评价来进行验证或认证。

Typically, the data integrity and security of a LDAS can be related to the integrity and security of the application program or software because the application program or software has a major role in processing and handling the data.

通常地，LDAS 数据的完整性和安全性和其应用程序或软件的完整性和安全性有关，因为应用程序或软件在数据的加工和处理中起了重要作用。

Classification is based upon the assessment of the LDAS complexity, the interaction between the LDAS components; the equipment, the sensor, the A/D, the user interface, and the integrity and security of the application program (i.e. software)

LDAS 的分类是基于对 LDAS 的复杂性、LDAS 组件间的交互、设备、传感器、A/D、用户界面、应用程序（如软件）的安全性和完整性的评价

System Attributes 系统特性
4.2 CLASSIFYING LDAS COMPLEXITY&SECURITY LDAS 分类，基于复杂性和安全性
4.2.1 Software Configurability 软件的可配置性 ： Configurable @instrument level 可配置-仪器水平 Configurable @server level 可配置-服务器水平 Frequency of configuration 配置的频率 Configuration security 配置的安全性
4.2.2 System Complexity 系统复杂性: Sequential or multitasking 序列的或多任务的 Monitor or control 监测或控制 Program location 程序位置
4.2.3 Data Integrity 数据完整性: Data storage—analog 数据存储-模拟 Data storage—digital 数据存储-数字 Data storage—process 数据存储-过程 Data storage—final 数据存储-最终 Output data 输出数据
4.3 CONTROL MANAGEMENT PROCESSES 控制管理程序 Vendor assessment 供应商评估 Vendor support (*my addition—SB*) 供应商支持（额外的服务预订） Source code control 源代码控制 Updated, as-built system definition 升级、系统竣工定义 Validation plan 验证计划 Completion of IQ,OQ,PQ IQ、OQ、PQ 的完成 SOP's—operational SOP-操作 SOP's—admin/maint SOP-管理/维修 Current training procedures &records 现行的培训规程和记录

4.3 Attribute#1: Configurability *of the Application Program or Software—Configurable or Non-Configurable*

*特性**#1**：应用程序或软件的可配置性-可配置或不可配置*

"Configurable" means that the program behavior can be changed by setting(configuring) the program variables or parameters. This excludes the Analyst variable/parameters configuration, which should have been addressed during the analytical method validation. If the program cannot be configured, then the program behavior is more predictable than those programs that can be configured. Therefore, the data integrity of the LDAS equipped with a non-configurable program is more easily assured than the LDAS equipped with a configurable program.

"可配置"意味着程序行为可以通过设定（配置）程序变量或参数来改变程序行为。这不包括分析员变量或参数配置，其应在分析方法验证中涉及。如果程序不能被配置，其程序行为比可配置的程序行为更加可以预测。因此，配置有不可配置程序的 LDAS 的数据完整性更加能够保证。

Factors impacting the control of a configurable system include:

影响可配置系统控制的因素包括：

Frequency of setting the program's configuration: Is the program only configured once or does the program's configuration have to be performed and set whenever the LDAS is used. Control for a "once configured" LDAS is easier than for the LDAS that needs to be configured every time the system is used.

程序配置设定的频率：程序是否只需配置一次或程序的配置必须每次使用都需进行？"一次性配置"的 LDAS 的控制比每次使用都需设定配置的更加容易些。

Security of the program's configuration: Can the program's configuration be directly accessed or modified by any user or is access to the LDAS program's configuration restricted to only authorized people (e.g., system's administrator)? The control required for the "limited access" LDAS configuration program is less than that required by LDAS equipped with a configuration program that can be accessed by any individual.

程序配置的安全性：程序的配置是否可以由任何用户访问或修改，或者访问 LDAS 程序配置受到限制，只能由得到授权的人（比如系统管理员）访问？"受限访问"的 LDAS

配置程序的控制要求比可由任何个人访问的 LDAS 配置程序要少。

Some systems have more than one configuration access method. A system may have a broad scope configuration, accessible by limited personnel in addition to “work related” configurations accessed by individual scientists. In this instance, you should treat the LDAS the same as a LDAS that can be configured by any individual.

一些系统有多个配置访问方式。系统可能有广泛的配置，除了个别科学家可以访问工作相关的配置，还可以由一些限定的人员访问。在此情况下，你必须按可被任何人配置的 LDAS 系统来处理。

System Attributes **系统特性**	**Validation Considerations—Not all-inclusive(examples only)** 验证考虑点-并非包括所有情况（只用来做样本）
Attribute#1: CONFIGURABILITY 特性#1： 可配置性	
1.1 Frequency of Configuration 配置频率	If configured often: 如果经常配置 SOP, checklist, log, performed by& reviewed by signatures SOP、检查单、日志、实施人和复核人签名 If configured seldom: 如果很少配置 Change control with associated impact assessment 变更控制并对相关变更影响进行评价
1.2 Security of Configuration 配置安全性	Configured by any user: 任何人都可配置 Operator/ user training 操作人/使用人培训 Record configuration before& after user changes 记录在用户变更之前和之后的配置 Configured by system administrator only: 只能系统管理员配置 Challenged by multiple level security passwords. 用多级安全密码挑战
Attribute#2: SYSTEM COMPLEXITY 特性#2： 系统复杂性	
2.1 Simultaneous or Sequential Tasking 同步或序列任务	Simultaneous (multitasking):同步（多任务处理） Test environment separate from production system. 独立于生产系统的测试环境 Test under simulated multitasking conditions to insure compatibility of

	all components. 模拟多任务条件进行测试以确保所有组件的兼容性 Test system loading—verify response time not impacted 测试系统加载-确认没有影响相应时间 Sequential:序列 Verify sequence of operations is consistent with sequence chart/ steps or timing diagrams. 确认操作的序列符合序列图/步骤或时序图
2.2. Monitor or Control 监测或控制	Monitor only: 只监测 Verify sensor types, locations, connections 确认传感器类型、位置和连接 Calibration—sensor and instrument 校准-传感器和仪表 Simulate or force sensor inputs 模拟或压力传感器输入 Display or print monitored values 显示或打印的监测值 Control& monitor-(Same as Monitor Only plus the following:) 控制和监测（和监测一样并加上以下内容）: Verify types, locations& connections of controlled devices 确认控制装置的类型、位置和连接 Verify control sequences, steps, events 确认控制序列、步骤和事件
2.3 Program Embedded or Non-embedded 内嵌式程序或非内嵌式程序	Embedded program:内嵌式程序 IQ of program version or EPROM in local equipment 程序版本或设备上 EPROM 的 IQ Backup disk or tape of executable source 备份磁盘或可执行源代码的磁带 Procedure for program reload and reconfigure 程序重新加载和重新配置的规程 Battery backup or UPS 电源备份或 UPS

	Non-embedded program: 非内嵌式程序 Host computer backup and disaster recovery procedures 主机备份和灾难性恢复程序 Network& application security 网络和应用安全 IQ hardware configuration and application program version 硬件配置和应用程序版本的 IQ Compatibility of multiple applications on server 服务器上多种应用的兼容性 Response time through local or wide area network 通过局域网或广域网的响应时间
Attribute#3: DATA INTEGRITY 特性#3： 数据完整性	
3.1 Single Process or Multiple-process Data **单流程或多流程数据**	Process data one time only: 数据只处理一次 Equivalent results from other instrumentation **其他仪器的等价结果** Repeatable results from second sample, same source **相同的来源，第二个样品可重复的结果** Re-processing capability: 再处理能力 Repeatable results with same setup parameters 相同设定参数下的可重复的结果 Acceptable results from re-process data with parameter variation **不同参数下的再处理数据的可接受结果** Availability of procedures to assess when re-processing is needed and acceptable **评价再处理何时需要并可接受的规程的有效性** Modifiable parameters should be under procedural or system control **可修改的参数应在程序或系统的控制下**
3.2 Temporary or Permanent	Temporary data storage: 临时数据储存

Data Storage **临时和永久数据存储**	Battery backup– power disruption test 电池备份-电源中断测试 Hard copy or screen print procedure for volatile data 易变数据的硬拷贝或屏幕打印程序 Permanent data storage: 永久数据储存 Stored data down- load to external storage media **存储出数据-载入到外部存储介质** External storage media backup (disk,tape,...) 外部存储介质备份（磁碟、磁带）

4.4 Attribute#2: System Complexity

特性**#2**：系统复杂性

A LDAS that is required to perform multiple tasks is considered to be more complex and difficult to control than a LDAS that performs a single task. Program control is typically easier for a single task LDAS than for a multiple task LDAS program since the program is typically simpler.

多任务处理的 LDAS 被认为比单任务处理的 LDAS 更复杂和更难控制。单任务的 LDAS 的程序控制一般比多任务的 LDAS 更容易，因为其程序一般更简单。

Simultaneous or Sequential Tasking 同步或序列任务处理

Are multiple tasks performed simultaneously (multitasking) or in a sequential manner? Generally, the application program for a LDAS with multiple tasks performed sequentially is less complicated than an LDAS application program that must perform the multiple tasks simultaneously. For all multitasking application programs, you need to address the size of the system's data buffer, the timing and coordination of system's resources needed for the coordination of data input, process, and output. Some LDAS are capable of performing both sequential and simultaneous multiple task modes; in this case the LDAS system should be considered to be simultaneous multitasking.

多个任务是同步进行（多任务处理）或是按照序列进行？一般来说，按照序列来处理任务的 LDAS 应用程序比同步处理多个任务的简单一些。对于所有的多任务处理应用程序，你需要解决系统数据缓存区空间大小、数据输入、处理、输出所需要的系统资源的时序安排

和协调处理。一些 LDAS 可以同时进行序列和同步处理多任务模式，这种情况下，LDAS 须以同步多任务处理模式考虑。

The role of the program in Monitoring and Controlling the laboratory equipment

应用程序在实验室设备监测和控制中的作用

A program that actively controls and monitors the lab equipment is typically more complicated than a program that plays the passive role of just receiving and processing data from the equipment.

主动控制和监测实验室设备的程序一般比被动式接受和处理来自设备的数据的程序要更加复杂。

The Application Program or Software: Embedded or Non-Embedded in The Equipment

应用程序或软件：嵌入式或非嵌入式

'Embedded'' means that the program cannot be changed by the user. The program can only be changed if it's accompanied by a physical hardware change. The typical embedded program is supplied in the form of a ROM chip (e.g., EPROM) placed (or embedded) in the equipment hardware. Since the application program is embedded, it is more difficult for a user to make changes to the program. Therefore, the difficulty in changing the program gives better assurance to program integrity, which translates to better assurance of data integrity. For a non-embedded program, it is also important to consider where the non-embedded program resides, whether it's on a local hard disk or on a server. Typically, programs located on the server are more secure than programs located on a local hard disk.

"内嵌式"意为程序不可被用户修改。这类程序只有随着物理的硬件改变而被修改。典型地内嵌式程序是以 ROM 芯片形式（比如 EPROM）安置在（或内嵌在）设备的硬件中。因为应用程式是内嵌的，所以它更难被修改。因此，可以更好保证程序的完整性，也意味着可以更好保证数据的完整性。对于非内嵌程序，同样需要考虑它的位置，是否在本地硬盘或在服务器。一般来说位于服务器的程序更安全。

4.5 Attribute#3: Data Integrity— *Data Storage or No Data Storage and Single Processing or Multiple Processing.*

4.5 特性#3：数据完整性-数据存储或无数据存储以及单处理或多重处理

In this concept paper, the data will be categorized as follows (see also Diagram No.1):

在这篇概念性的文章中，数据按以下进行分类（也可参看图表 1）：

Analog Data: This is the data that comes from the lab equipment analog detector or sensor.

模拟数据：这种数据来自于实验室设备模拟检测器或传感器

Digitized Data: This is the data after being digitized by the LDAS analog to digital Converter.

数字数据：这种数据由 LDAS 模拟/数字转换器数字化产生

Processed Data: This is the digitized data processed by the data process parameters.

经处理的数据：这是由数据工艺参数进行处理后的数字化数据

Final Data: This is the final processed data, representing the LDAS analysis result.

最终数据：这是最后的处理数据，代表着 LDAS 分析结果

The processing and integrity of data from the beginning of data creation to the final output is considered to be critical for every LDAS. Process parameters must be available or accessible for processed data. Hence, the validation and/or qualification of a LDAS system should address the data integrity issue during input, processing, and output of the LDAS data.

从数据开始创建到最后的数据输出，其处理过程和完整性对于每一个 LDAS 来说都是非常关键的。数据工艺参数对经处理的数据必须有效或可访问。因此，LDAS 系统的验证和/或确认应涉及到 LDAS 数据在输入、处理和输出时候的完整性。

Consideration should also be given to the LDAS data processing capability. Some LDAS are capable of performing data processing onetime only (data processing is a one-time event). That is, once the data output is produced, the data output cannot be re-generated by the LDAS. For these LDAS the sample must be re-analyzed by the lab equipment again to produce another data output (repeat testing). Other LDAS may have the capability of re-processing data several times. That is, data can be re-processed utilizing a different set of parameters. Data integrity issues are more important on an LDAS that is capable of reprocessing data.

同时应注意 LDAS 的数据处理能力。一些 LDAS 只能处理数据一次（数据处理是

一种一次性时间），也就是说，一旦生成数据输出，那么数据输出就不可以再被 LDAS 重新生成。对于这些 LDAS 系统，样品需要被其他实验室仪器再分析一遍以获得其他数据输出（重复测试）。其他的 LDAS 系统可以再处理数据若干次，即可以利用不同组参数重新处理数据。对于可以再处理数据的 LDAS 系统来说，数据的完整性问题更加重要。

Consideration should be given to an LDAS capable of storing data (raw and/or processed) and to whether this stored data is temporary or permanent.

要考虑带数据储存（原始的或经处理的）的 LDAS 系统，其储存的数据是临时的或者是永久的。

Diagram No.1: A Simplified Data Flow Diagram for a LDAS:

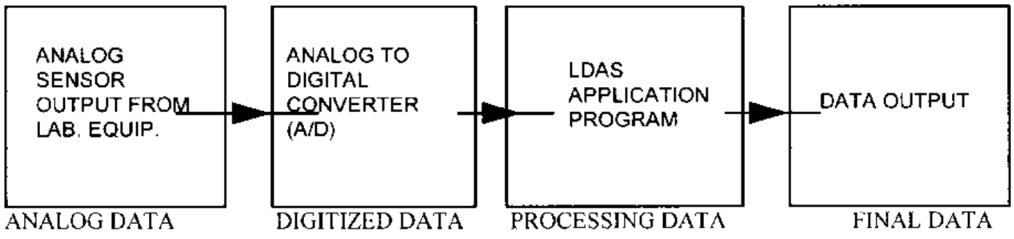

图 表 1 ： LDAS 简 化 数 据 流 程 表

5. **Control Management Processes 控制管理程序**

The control management processes are the processes that provide the evidence that the LDAS system was validated or qualified and that it is operated in a controlled manner.

控制管理程序是为了证明 LDAS 系统是经验证的或通过认证的并且按受控的方式进行操作。

5.1 Relating the LDAS Classification Concepts to the LDAS Validation Effort

LDAS 分类概念和 LDAS 验证工作的联系

A brief review of validation principles was provided earlier in this article. These principles will now be applied to a typical LDAS while illustrating the impact of the LDAS classification concepts on the validation deliverables.

前文已经简单的回顾了其验证原则。当阐明 LDAS 分类概念对验证交付物的影响时，这些原则现在将被应用到一个典型的 LDAS。

**Denotes document or task(s) that are required regardless of the extent of the validation effort implied by the application of the LDAS Classification Concepts.*

*带*符号表示无论 LDAS 分类概念的应用所意指的验证到何种程度都需要的文件或任务*

5.1.1 Validation Plan 验证计划:

This document describes the tasks, timelines, and responsibilities for validating an LDAS. For a complex LDAS, it is recommended that this document include where the LDAS application program is configurable, a description of multitasking capabilities, and where the LDAS data will be located etc.

在这份文件描述了验证 LDAS 中的任务、时间线和职责。对于复杂的 LDAS 系统，建议文件中应描述清楚 LDAS 应用程序那里可以配置、多任务处理的性能和 LDAS 数据位于哪里等等。

5.1.2 *System Description 系统描述:

The document should describe the LDAS function and purpose, and the type of chemical and/or physical analysis performed by the LDAS. The document should also discuss the hardware and software elements of the LDAS. The extent of the description of how an LDAS accomplishes its functionality will be based on the complexity of the LDAS. This document is not just for purchased systems; it should also be prepared for in-house or custom developed LDAS systems. The document should discuss any requirements based on the LDAS classification. The impact of the LDAS classification concepts should be considered as follows:

文件中应描述 LDAS 系统的功能和用途，以及所进行的物理/化学分析的类型。在文中同样需要讨论 LDAS 的硬件和软件元素。LDAS 系统如何达到其功能的描述程度基于 LDAS 系统的复杂性。这份文件不仅仅针对购买的系统，同样适用于内部或定制开发的 LDAS 系统。基本 LDAS 的分类，在文中必须讨论对 LDAS 的任何需求.LDAS 的分类概念影响应考虑以下几点：

The LDAS application program configurability: whether the configurability needs to be performed by an end-user or administrator, whether the configuration needs to be performed each time the LDAS is used, or whether the configuration only needs to be

performed once.

LDAS 应用程序可配置性：其配置性是否由终端用户或管理员进行设置，其配置是否在 LDAS 每次使用都需进行，或只需进行一次。

The LDAS application program location and security: whether it resides on the local drive or a network drive.

LDAS 应用程序的位置和安全性：应用程序位于本地驱动器或在网络驱动器上

The LDAS complexity: whether the LDAS is required to control the lab equipment or not, whether the LDAS functionality is single or multitasking, and whether the LDAS application program is embedded or not.

LDAS 系统的复杂性：LDAS 系统是否控制实验室仪器，LDAS 系统功能是单任务处理或多任务处理，LDAS 应用程序是内嵌式还是非内嵌式

The LDAS data integrity: whether the LDAS is required to store data or not, whether the data is processed more than once, and the location of the data reprocessing. The document should also discuss the LDAS capability of generating data, the security of the data, and the storage of data.

LDAS 数据的完整性：LDAS 是否储存数据，数据是否被处理多次，再处理数据的位置在哪。文件同样需要讨论 LDAS 数据生成、数据的安全性以及数据存储的能力。

5.1.3 * Installation Qualification (IQ) 安装确认:

This document describes how the LDAS should be installed, including the necessary verification of the LDAS environment, condition, and other requirements (e.g., physical security and power conditioning requirements). The impact of the LDAS classification concepts should also be considered as follows:

IQ 文件中描述了 LDAS 应被如何安装，包括确认 LDAS 安装环境、条件和其他要求（比如物理安全和电力调节要求）。LDAS 分类概念的影响应考虑以下几点：

For LDAS that control lab equipment, the document should verify the connection from the lab equipment to the computer system. If the equipment control is configurable, verification of the configuration installation should also be performed.

用以控制实验室设备的 LDAS，文件中应确认计算机系统和实验室设备之间的连接。如果设备控制是可配置的，则也应进行配置安装的确认

For LDAS with a non-embedded application software, verify the appropriate software

installation.

非内嵌程序的 LDAS，确认其软件已被合适的安装

For LDAS with a configurable application program, verify the required configuration setting of the program (e.g., default values for the LDAS operation).

可配置应用程序的 LDAS，确认程序按要求的配置进行设置（比如：LDAS 运行的默认值）

For LDAS with data storage capability, verify the installation and existence of the data storage equipment.

带数据储存的 LDAS，确认数据储存装置已被安装

*Calibration: Should be performed for any LDAS system that requires calibration.

*校准： 如 LDAS 系统需要校准，则应进行

It is recommended that a generic IQ checklist be developed to facilitate the factors to be considered for installing a LDAS.

建议开发一个通用的 IQ 检查表使 LDAS 安装时需考虑的因素更简单。

5.1.4 Operational Qualification(OQ) 运行确认:

This document describes how the individual LDAS components should be qualified. The impact of the LDAS classification concepts on the operational qualification should be considered as follows:

OQ 文件中描述了 LDAS 单个组件是如何被认证的。LDAS 分类概念在运行确认中的影响应考虑以下几点：

For LDAS that controls the operation of attached lab equipment, you should verify the proper functions and controls of the lab equipment.

对于控制实验室设备运行的 LDAS，你应确认其合适的实验室设备合适的功能和控制。

For LDAS that is capable of multitasking, you should verify that each critical task is capable of being performed simultaneously by the LDAS.

对于多任务处理的 LDAS，你应确认 LDAS 有能力同时处理每一个关键任务。

For LDAS with an application program that is configurable, you should verify that the desired configuration parameters function as expected (e.g., boundary values). The functionality of LDAS configurable parameters set by the analyst should be verified as part of the LDAS configuration. The range of the acceptable settings for a specific

analytical method will be qualified as part of the analytical method validation, whilst the range of acceptable parameters should be qualified as part of the LDAS qualification.

对于应用程序可配置的 LDAS，你应确认期望的配置参数功能符合预期（比如临界值）。由分析员设置的 LDAS 的功能性可配置参数应当作为 LDAS 配置的一部分被确认。特定分析方法的可接受设置的范围应当作为分析方法验证的一部分被认证，同时可接受参数的范围也应作为 LDAS 确认的一部分被认证。

For LDAS capable of processing data several times, you should verify that this functionality works according to the expected results.

对于可以多次处理数据的 LDAS， 你应按照预期的结果确认这种功能性工作。

For LDAS capable of storing data, you should verify that the system is capable of storing and retrieving the data accurately and reliably.

对于可以储存数据的 LDAS，你应确认系统可以准确地和可靠地储存和检索数据。

Verify the LDAS logical security (i.e., data and application program security).

确认 LDAS 系统的逻辑安全（比如数据和应用程序的安全性）。

5.1.5 *Performance Qualification 性能确认:

This document describes how the LDAS should perform while analyzing the sample's physical and/or chemical characteristics. The document should contain the test cases that challenge the LDAS in the production environment. The impact of the LDAS classification concepts should be considered as follows:

PQ 文件中描述了 LDAS 在分析样品的物理和/或化学特征时是应如何工作的。该文件应包含 LDAS 在生产环境的挑战测试案例。LDAS 分类概念的影响应考虑以下几个方面：

For LDAS capable of performing sequential multitasking, you should verify that the sequences required during the usage of the equipment work according to expected results.

对于可以进行序列多任务处理的 LDAS 系统，你应确认在设备工作使用中所要求的序列符合预期的结果。

For LDAS capable of performing simultaneous multitasking, you should prepare and verify a scenario matrix of possible simultaneous multitasking sessions. For LDAS capable of data storage, you should include the verification of accurate data storage

and retrieval capability.

对于可以进行同步多任务处理的 LDAS 系统，你应根据可能同步多任务处理的对象，制作一份矩阵确认方案并加以确认。而对于可以数据储存的 LDAS 系统，你的确认应包括数据储存的准确性以及检索的性能。

5.1.6 System Operational Procedure and Validation Maintenance 系统操作规程和验证维护:

The documents prepared in this section indicate how the LDAS should be operated and supported so that the validation status of the LDAS is maintained. It is noted that there are several methods for preparing written procedures, i.e., the procedures mentioned in this section can be unified into one procedure, or split into more than one procedure. It is up to each company to determine how the procedures should be prepared. It should also be noted that the style and level of details for preparing a procedure might vary from company to company, as well as from one LDAS to another LDAS.

这份文件指明了 LDAS 应被如何操作和支持，以便维持其验证状态。要注意起草书面规程有很多方法，比如本章节提及的规程都可以统一到一份规程中或分成若干份规程。这取决于公司对规程起草的规定。同样需要注意的是，起草规程的风格和细节水平每个公司都可能不一样，正如每一个 LDAS 的规程也是都不一样。

5.1.6.1 *Analysis Procedures: Written procedures to be used by the user for accomplishing the LDAS task of analyzing the chemical and/or physical properties of a sample. These procedures should be prepared regardless of the LDAS classification. The impact of the LDAS classification concepts should also be considered as follows:

分析规程：用户使用书面的规程来完成 LDAS 分析样品化学和/或物理属性的任务。无论 LDAS 属于哪类，这些规程都应被起草。LDAS 分类概念的影响应考虑以下几个方面：

For LDAS that control the operation of attached lab equipment, the written procedure should indicate the accepted steps or methods in controlling the lab equipment operation.

对于控制实验室设备运行的 LDAS 系统，在书面的规程中应指出控制实验室设备运行的可接受步骤或方法。

For LDAS capable of multitasking, the written procedure should indicate the

accepted steps and limitations in performing the multitasking functions. The procedure should also indicate any LDAS functionalities that should not be used.

对于可以多任务处理的 LDAS，在书面的规程中应指出进行多任务处理功能的可接受步骤和限制因素。同样还需要指出任何不应被使用的 LDAS 功能。

For LDAS with a configurable application program, the written procedure should indicate the accepted configuration parameter(s). Consider also including the configurations that cannot be used. In addition, if the configuration can only be performed by a LDAS Administrator, then consider the need for preparing a separate configuration procedure for the LDAS Administrator.

对于具有可配置性应用程序的 LDAS 系统，在书面的规程中应指出可接受的配置参数。应考虑不能被使用的参数。另外，如果配置只可以被 LDAS 管理员设定，那么需要考虑为 LDAS 管理员准备一份单独的配置管理规程。

For LDAS capable of processing data several times, the written procedure should indicate how this function can be used and the accepted cases when the re-processed data is acceptable.

对于可以多次处理数据的 LDAS 系统，书面的规程中应指出这种功能应如何被使用以及再处理的数据可接受时的系统可接受的情况。

For LDAS capable of storing data, the written procedure should indicate how this task should be accomplished. Consider the need for preparing a raw data definition, file naming convention for storing data, as well as the rules for storing (including backups), for retrieving, and for transferring data for archival purpose, and the time period for data retention. The need to prepare a written procedure for data audit (e.g., the system's audit trail) should also be considered.

对于可以储存数据的 LDAS，书面的规程中应指出这项任务应如何被完成。需要考虑到原数据的识别、储存数据的文件命名约定，还需要考虑到储存的规则（包括备份）、检索规则以及归档数据规则和数据保留时间周期的规则。同样还需要考虑要有一份规程针对数据的审计（比如系统的审计追踪）。

5.1.6.2 Operation Procedures: Written procedures to ensure that the LDAS system operates as expected.

操作规程：书面的操作规程以保证 LDAS 系统如预期运行

*Written Calibration procedure for LDAS requiring calibration. Procedure should indicate the frequency of calibration, steps for calibrating, and the acceptable calibration result.

*在需校准 LDAS 系统的书面校准规程中应指出校准的频率、校准的步骤和可接受的校准结果。

Written Preventative Maintenance procedure for LDAS.

书面的 LDAS 系统预防性维护保养规程

The impact of the LDAS classification on this procedure is as follows:

LDAS 在规程中的分类影响如下：

For LDAS capable of data storage, you should consider the need for the periodic checking of data storage media integrity (e.g., periodic check of backup tapes).

对于可以数据存储的 LDAS 系统，你应考虑数据储存介质完整性的定期检查的需要（比如定期检查备份磁带）。

For LDAS attached to lab equipment, you should consider the need for the periodic checking of lab equipment connections.

对于连接实验室设备的 LDAS 系统，你应考虑实验室设备连接定期检查的需要。

* A written Change Control procedure for LDAS is required. The procedure should evaluate the impact of the changes, and if necessary, document the test(s) to verify the impact of the changes on the LDAS performance. The impact of the LDAS classification on this procedure are as follows:

需要有书面的 LDAS 变更控制规程。该规程应评估变更的影响，并且如果需要的话，记录确认变更对 LDAS 系统性能的各种测试。规程中 LDAS 分类的影响包括：

*An Equipment Log Book should be provided for all types of LDAS. The purpose is to record the usage, problems, calibrations, and maintenance of the equipment. Additionally, the logbook can be used to record system error messages, upgrades, maintenance and repairs.

所有类型的 LDAS 应当有设备日志，用以记录设备的使用、问题、校准和维护保养。此外，日志还可以记录系统的错误信息、升级、维护和修理。

A Written Periodic Review procedure to assess the validation status of LDAS is recommended. The periodic review may include the review of (if applicable): the LDAS

Equipment Logbook, Change Control records, training records as well as the system's documentation.

建议有书面的定期回顾规程以评估 LDAS 系统的验证状态。定期的回顾包括以下内容的回顾（如适用）：LDAS 设备日志、变更控制记录、培训记录和系统文档。

Also, if applicable, the following should be included in the periodic review: stored data integrity, data backup integrity, and audit trail integrity.

如需要的话，同样需要定期回顾以下内容：存储数据的完整性、数据备份的完整性和审计追踪的完整性。

5.1.6.3 Other Validation-related Issues 其他验证相关问题:

- *Training: Documentation of training adequacy is required for any type of LDAS and for all level of LDAS users (i.e., including, if applicable, LDAS System Administrator)

*培训：对于所有类型所有水平的 LDAS 系统都应有足够的培训文档（例如，如适合包括 LDAS 系统管理员）

- Supplier Assessment: It is recommended that Supplier Assessment be considered for LDAS application programs that are deemed critical. The complexity of LDAS determines the depth of a supplier assessment. The assessment is also recommended for suppliers (in-house or external) that develop customized LDAS.

  供应商评估：建议考虑对关键 LDAS 应用程序供应商进行评估。LDAS 的复杂性决定了供应商评估的深度。同样也建议对开发用户定制的 LDAS 供应商（内部或外部的）进行评估

- Source code availability or the capability to access the source code is a must for a custom or in-house developed LDAS

  源代码的有效性或源代码的可读性对于定制的或内部开发的 LDAS 是必须的。

6. Execution and Other Administrative Issues 执行和其他管理问题

6.1 Pre-Validation Activities 预验证活动

Prior to executing a LDAS validation, it is recommended that the following activities or tasks be performed.

在 LDAS 验证执行前，建议先进行以下活动或任务：

6.1.1 Inventory of Laboratory Systems 实验室系统的清单:

The purpose of the inventory list is to aid a Lab Manager in identifying all the available lab systems at their respective site (a site in this case can be defined as a company, a group of laboratories, or a laboratory). The inventory list will ensure that no LDAS is overlooked. To a Quality Auditor, the inventory list can serve as a preliminary indicator that the site has control over their lab equipment. This inventory list can also help the Quality Auditor in orienting themselves with the site, the type of testing accomplished, the type of samples, etc. This list should be updated on a periodic basis.

列出实验室仪器库存清单的目的是帮助实验室管理员在相应的位置找到实验室系统（这里的位置可以定义为公司、实验室团队或单个实验室）。清单可以保证没有 LDAS 会被忽略。而对于质量审计员来说，清单的有无是实验室现场设备是否在控制中的初步的指示器。库存清单同样可以帮助质量审计员

It is recommended that the inventory list, at the minimum, contains the following information:

建议库存清单至少要包括以下信息:

- The identification or name of the equipment (including model number, serial number, installation date, application version number, supplier, and departments served).

  设备名称或识别信息（包括型号、编号、安装日期、应用程序版本号、供应商和使用部门）

- The location of the equipment.

  设备位置

- The identity of the "system owner". This is the person who is responsible for assuring that the system documentation is available or, depending on how the lab operates, this person can identify the person(s) responsible for the system's documentation (e.g., meteorology person responsible for the system's calibration).

  系统所有者身份。系统所有者应负责确保系统文档的有效性或基于实验室的实际规定，系统所有者可以确定谁为系统文档负责（比如气象学家负责系统的校验）

- The validation status of the equipment. This may include the prioritization of

systems to be validated based on the risk assessment and the assignment of responsibilities for validation and approval.

设备的验证状态。这可能包括系统基于风险的验证优先级和验证和批准职责的分配

6.1.2 Policies for the Administration of Laboratory System Validation: 实验室系统验证管理方针

The site should have written computer system validation policies and philosophies addressing the conduct of LDAS validations. The implementation of any applicable LDAS classification concepts introduced in this paper can also be included in the policy. A typical validation policy discusses the following:

这部分为描述计算机系统验证方针和进行 LDAS 验证所涉及的观点。本文所述的 LDAS 分类概念也可以包括在方针中。典型的验证方案讨论如下：

- The purpose or objective of performing the computer system validation, the scope of the validation, and the method of performing the validation.

  计算机验证的目的或目标，验证的范围和验证使用的方法

- The description and purpose of the validation document deliverables. The deliverables may include the following:

  验证交付文件的描述和用途。交付物可能包括：

  1. System Specific Validation Plan, which may define the overall plan for validating a LDAS system.

     系统具体验证计划，定义了 LDAS 系统所有的验证计划

  2. System Description, which may define the functionality and purpose of the LDAS system (e.g., the deliverable can be in the form of Functional Requirements and Design Specification Documents).

     系统描述，定义了 LDAS 系统的功能和用途（比如, 交付文件可以以功能需求和设计标准文件（FRDSD）的形式）

  3. System Development Life Cycle (SDLC) documentation requirement for a custom developed LDAS. This may include the requirements for performing prototyping documentation and documentation of the source code, source code availability, source code structural testing documentation, as well as other testing documentation during the development stage.

为用户定制而开发的 LDAS 对系统开发生命周期（SDLC）文件材料的要求。包括原型测试文件、源代码文件、源代码有效性、源代码架构测试文件和其他开发阶段的测试文件

4. The LDAS Qualification testing requirement policies, which may consist of Installation Qualification, Operation Qualification, and Performance Qualification, as well as the policies for reporting the qualification test results.
LDAS 确认测试需求方针，由安装确认、运行确认和性能确认组成，同样也包括确认测试结果报告的方针
5. Additional supporting documentation for the controlled operation of the LDAS and for maintaining the LDAS validated status may include the written operational procedures, calibration procedures, change control procedures, backup/archives and retrieval/recovery procedures, error logs and audit trail procedures, equipment log procedures, and periodic review procedures. Additionally, site policies on the requirement of supplier management, user training (e.g., for the system administrator, end user, developer, and validator) can also be included.
LDAS 受控运行的额外支持性文件和维持 LDAS 已验证状态的文件包括书面的操作规程、校准规程、变更控制规程、备份/存档和检索/恢复规程、错误日志和审计追踪规程、设备日志规程和定期回顾规程。另外，供应商管理以及用户培训的方针部分（比如对管理员、终端用户、开发者和验证者）同样应包括在内。

- The corporate procedures applicable to possible scenarios during the validation execution should also be included in the site policies. This may include the procedures to handle deviations during the validation execution and changes to the qualification test protocols or other validation documents.
在这部分方针内同样应包括公司针对在验证实施过程中各种可能发生的情况而制定的合适的规程。包括验证过程中的偏差以及确认测试方案或其他验证文件变更的处理。

7. Other Issues 其他问题

7.1 Control of the Documentation[7] *文件控制*

The documentation associated with the entire validation process is the only proof that the system has been tested and that its acquisition, implementation and usage are under control. It is therefore imperative that the documentation is developed, modified and maintained in a controlled manner and, if appropriate, meets the expectations of a regulated environment.

验证全过程中相应的文件时系统已被测试并且其收集、执行和用途受控的唯一证明。因此，文件的开发、修订和维护必须已受控的方式进行而且如何适用的话，应符合规范化环境的预期要求。

7.1.1 Version Control: 版本控制

Documents should have a version number assigned. A standardized process should be implemented for the proper construction and control of version numbers. A modification history is useful if included as part of the document. This should include version number, author and date of update. It may also include a brief summary of changes.

文件应分配版本号。版本号的建立和控制应使用标准化的程序。修订历史是有用的应作为文件的一部分，里面应包括版本号、作者和升版日期，也应包括简要的变更说明。

7.1.2 Manual Entries: 手工输入

All hand written entries or changes to any document, including validation plans, should be in black ink accompanied by the initials of the person making the entries and the date of the entry. Modifications or deletions should be crossed out with a single line so as not to obscure the original entry.

在任何文件包括验证计划中所有手写的输入或修改都应使用黑色墨水笔书写并签名（缩写）和输入日期。修订或删除的内容使用单线划掉以使原来的内容清晰可见。

7.1.3 Approvals: 批准

Approval of test protocols (prior to execution) and the approval of test results and the summary report should be at the department head level. Since it is possible that upper management may not understand the details of the test plan and the testing details, it is suggested that a review be first accomplished, and signed off, by internal QA people, Information Technology personnel, and users who have been trained on the system.

测试方案的批准（执行前）和测试结果和总结报告的批准应由部门负责人级别进行。因为高级管理层可能不了解测试计划细节和测试的具体情况，所以建议首先由内部 QA、IT 和经过培训的用户进行复核并签署通过。

7.1.4 Archival: 存档

All validation related documentation should be archived. An archive should conform to the following conditions controlled by Standard Operating Procedures (SOPs) (summarized from GLPs):[8]

所有验证相关的文件都应被归档。归档应符合 SOP 中的控制条件（从 GLP 总结）：

—Allow orderly storage and expedient retrieval. 应有序的保存和方便检索

—Conditions of storage shall minimize deterioration of the documents in accordance with the requirements for the time period of their retention and the nature of the documents.

根据文件保留期限和文件本身性质的要求，尽可能降低文件储存的不利因素

—An individual shall be identified as responsible for the archives.

规定专人负责存档

—Only authorized personnel shall enter the archives.

只有得到授权的人才能接触到档案

—Material retained or referred to in the archives shall be indexed to permit expedient retrieval.

档案中保存或引用文件材料的应编入索引以利于检索

7.2 Multitasking Instrumentation 多任务处理测试仪器

The increased sophistication and multitasking capabilities of LDAS and their associated sample preparation and management functions are leading to the establishment of new operating paradigms. The use of multitasking LDAS is changing the laboratory organization from one in which multiple individuals perform single tests on multiple instruments to one where a single individual performs multiple tests using a single instrument. This change has created additional considerations in validating LDAS. These include instrument versus process validation, equipment management and integration of batch and real-time testing.

LDAS 复杂和多任务处理能力的增加以及其相关的样品准备以及管理功能正产生新的操作模式。多任务处理 LDAS 的使用正改变着实验室的机制，由多个个体用多个仪器从事单个测试向单个个体使用单个仪器从事多个测试任务转变。这种转变导致了 LDAS 验证需要考虑更多的因素。包括仪器方面的工艺验证、设备管理和批检测以及实时检测的整合。

7.2.1 Instrument versus Process Validation: Additional Considerations Due to Potential Interactions Between Test Procedures:

仪器方面的工艺验证：由测试规程间潜在的相互作用引起的额外考虑

In the single instrument/single test environment, the focus of validation is on the specific instrument/assay combination. Multitasking LDAS offer two features that increase validation complexity. First, and most obvious, is the ability to perform multiple tests on a single sample. The second is the ability to define test requirements for each sample in a multi-sample run. This introduces the need to validate a process rather than a single instrument/test combination. The validator must now be concerned with test interactions, test management and time constraints. Worst case testing should be added to ensure data accuracy under all conditions.

在单个仪器/单个测试环境中，验证所关注的焦点在特定的仪器/多指标分析。多任务处理的 LDAS 的两点特性使得验证的复杂性增加。首先，并且是最明显的一点，是进行对单个样品进行多项测试的能力。其次是在多样品测试运行中，对每一个样品的测试要求识别能力。这些说明了需要的是验证一个过程而不是验证单个的仪器或多个测试指标。验证者必须关注测试的相互作用、测试管理和时间限制。应进行最差情况测试以保证在所有条件下的数据准确性。

- **Test Interactions**—Testing should demonstrate that the LDAS manages the sample preparation and analysis process such that:

测试相互作用-测试应能证明 LDAS 系统可以按如下管理样品配制和分析过程：

• Instrument set-up and preparation are adequate to eliminate residues left from prior samples, controls and/or reagents.

仪器的装配和准备可以充分的将上批的样品、控制元件和/或试剂的残留消除掉。

• Test requirements are sample specific.

测试符合样品的特性

• No test parameters are transferred from one sample to the next.

上一个的样品测试参数不会转移到下个。

• **Time Constraints**— Testing is required that demonstrates the ability of the LDAS to correctly manage time-based requirements at both the sample and process levels. Typical time requirements include retention times, integration periods, sample hold times and wash times.

时间限制-测试应可以证明 LDAS 系统可以在样品和过程水平正确的管理基于时间的要求。典型的时间要求包括保留时间、积分时间、样品保持时间和洗出时间

• **Test Management**— Validation should prove that testing can be conducted in planned sequences and that specific test requirements can be defined for each sample. Evaluation of individual tests should include correct management of reagents and controls.

测试管理-验证应证明测试可以按照设计的序列进行并且可以为每一个样品设定特定的测试需求。单个测试的评价应包括试剂和控制元件的正确管理。

• **Worst Case Testing**—Testing that combines the most stringent challenges from above should be conducted.

最差情况测试-应结合上述需求中最严厉的挑战进行测试。

7.2.2 Equipment Validation: Issues Related to the Control and Maintenance of Support Equipment: The ability of the LDAS to interact with support equipment should be considered when developing a validation plan. This interaction means that a Configuration Management Program to control changes to, and maintenance of, critical components should be developed and verified.

设备验证：支持性设备的控制和维护相关问题：开发验证计划时应考虑 LDAS 的能力和支持性设备的交互作用。这里的交互作用指应开发并确认配置管理程序以控制关键组件的变更以及维护保养。

• **Support Equipment Maintenance**— Qualification of automated sample preparation equipment, reagent dispensers and sampling devices should verify that they can handle functional changes such as volumes, pressures

and times that are required for each test performed by an instrument. It should also prove that the equipment can handle changes in requirements from sample to sample. Interaction testing that includes communication failures is required if the LDAS controls or interacts with the support equipment.

支持性设备的维护保养-自动化样品配制设备、试剂分配器和进样装置的验证应确认其可以处理一些功能性的改变，比如同台仪器进行的每项测试所要求的体积、压力和时间。必须证明设备可以样品到样品中的需求改变。如果 LDAS 系统控制或与支持性设备交互的话，那么交互作用的测试应包含通讯失效的测试。

- **Configuration Management—** Critical portions of the LDAS should be identified and procedures for their maintenance should be developed and verified. Testing should prove that maintenance procedures are adequate to ensure continued function of the LDAS and support equipment.

  配置管理-应识别 LDAS 关键部分，其维护保养规程应被开发并进行确认。测试应证明维护保养程序足够充分，以保证 LDAS 和支持性设备的持续功能。

7.2.3 Integration of Batch and Real-time Testing: Evaluation of the Significance of Test Interruptions: Some LDAS have the additional capability of interrupting a test run to test another sample or set of samples. This feature provides the ability to combine batch and real-time testing on one instrument. Laboratories can now be organized based on lab function rather than manufacturing process support. This capability creates a dilemma by increasing both lab efficiency and validation complexity. The LDAS should provide a method for interrupting the test in progress while temporarily storing its status and data. It should then allow initiation of a new test or set of tests, control that test and revert to the original run upon completion of the interrupt. Additional testing is required to prove that the interruption has no impact on the quality of data collected for either set of samples.

批测试和实时测试整合：有些 LDAS 系统可以中断检测过程并进行另外一份或一组样品的检测。这种特性提供了在同一台仪器上结合批测试和实时测试的能力。但这往往提高实验室效率的同时也增加了验证的复杂程度。此 LDAS 应提

供当中断正在进行测试并临时保存状态和数据的方法，然后允许进行一个或一组新的测试，控制测试并回到并完成原先中断的测试。对于额外进行的测试需要证明中断不会对任一样品收集的数据产生影响。

• **Test Management**— Testing is required to verify that the LDAS is capable of managing the interruption process and controlling the testing of each set of samples.

测试管理-有必要测试并确认 LDAS 系统有能力管理中断过程和控制每一组样品的检测。

• **Interruption Times**—Testing should include determination of the maximum interrupt period for each test and verify that either the LDAS or the manual procedures will correctly manage the interruption.

中断时间-测试应包括每一项测试最大的中断周期的证明并确认 LDAS 或是手动程序都可以正确的管理中断。

• **Number of Interrupts Allowed**—Testing should demonstrate that either the LDAS or manual procedures will control the interruption process to prevent exceeding the allowed number of interrupts.

允许的中断数量-测试应证明 LDAS 或者是手动程序都可以控制中断过程并防止超出允许的中断数量

• **Data Storage—**Test cases should challenge the ability of the LDAS to store and recover data from the interrupted test. This test should involve the largest expected amount of data.

数据储存-测试案例应挑战 LDAS 在中断测试中储存和恢复数据的能力。这项测试涵盖了最大期望的数据数量。

7.3 Single Versus Multiple Instrument Control

单仪器控制和多仪器控制

LDAS that provide the capability for networking multiple instruments have a major impact on validation requirements. The management of multiple instruments moves validation to a multi-process level. First, the individual instrument should be tested to ensure the validity of data processing by the LDAS. The network configuration should then be tested to assure that

simultaneous operation of instruments has no impact on data integrity.

通过网络控制多台仪器的 LDAS 系统在验证方面有着更多的要求。多仪器的管理将验证提升到一个多进程的水平。首先，应测试单个的仪器以确保 LDAS 处理数据的有效性。然后应测试网络配置以保证同时进行的仪器操作对数据的完整性没有影响。

- **Configuration Management**— Testing described above should be augmented with tests to ensure adequate network configuration management procedures are in place.

  配置管理-应增加上述的测试以确保充足的网络配置管理规程在合适的位置。

- **Instrument Integration**—Test cases should be developed that prove that the LDAS can successfully manage the assigned instruments in all anticipated configurations. Testing should include simultaneous operation of similar instruments to prove that data processing is managed at the sample/instrument/test level.

  仪器集成-开发的测试案例应证明 LDAS 可以成功的管理指定的仪器，包括所有预期的配置。测试还应包括类似仪器的同时操作以证明数据处理可以在样品/仪器/测试水平管理之下。

- **Network Operations** —Testing should confirm that the network hardware and software can successfully handle current and planned laboratory output. Recommended testing includes stress testing under expected worst case conditions (e.g. multiple instruments operating simultaneously).

  网络操作-测试应确认网络硬件和软件可以解决当前的以及计划的实验室输出。建议的测试包括预期最差情况下的压力测试（比如同时多台仪器运行）

- **System Capacity Analysis —**The ability of system memory, processing and data storage capabilities to handle expected data volumes should be tested.

系统能力分析-应测试系统内存能力，处理预期数据量时的数据处理和分析能力。

• **Data Transfer**—Testing should also include the evaluation of data transfer between instruments and the network. Testing should include correct handling of communications and system failures, and the condition or status of the data in the event of a failure.

数据传输-测试还应包括仪器和网络间数据传输的评估。测试应包括正确的通讯处理和系统故障，以及发生故障时数据的状况或状态。

7.4 Difficulties Inherent to the Control and Testing of Lab Systems

实验室系统控制和测试一些难点

7.4.1 Defining Validation/Control of System Components: It is sometimes difficult to determine which parts of a lab system should be validated and which parts should be simply controlled. It is useful to construct a diagram that illustrates the entire system and its related components. You should determine which components can have input and output verified via documented controls and which components will be difficult to verify or whose data is too voluminous to verify. The components that cannot be verified at run-time should be tested.

定义系统组件的验证/控制：有时很难决定实验室系统哪些部分应该被验证，哪些部分只需要简单的受控。有必要建立一份图表来阐明整个系统和相关的组件。应决定哪些组件只需要确认输入和输出并经文件化的控制，哪些组件可能较难确认或其数据太多而无法确认。无法在运行时确认的组件应进行测试。

7.4.2 Outside Maintenance Control: Since lab data acquisition systems are typically made up of multiple components (e.g. computer hardware, software, instruments etc.) it can be difficult to track and control on-going maintenance. It is important that processes be implemented to document any work done on a system component and to assess its impact on the validated state of the system and the integrity of the data.

外部维护控制：因为实验室数据采集系统一般由多个组件组成（比如计算机硬件、软件、仪器等），所以可能很难追踪并控制持续的维护。重要的是，对系统组件进行的任何工作都应被记录并且评估对系统验证状态以及数据

完整性的影响。

7.4.3 Environment: Lab systems may sometimes be placed in hostile environments. The supplier should be contacted and asked about any special precautions and maintenance issues that may impact these systems. “Monitoring processes” should be implemented to assure the environment does not change from the environment within which the system was validated. If a change does occur, the system may require re-testing.

环境：实验室系统可能有时会被放在一个不利的环境中。应联系供应商并询问可能会影响这些系统的任何特殊规定的注意事项和维护问题。应进行“过程监测”以确保系统所处的环境和系统验证时的环境没有变化。如果发生了变化，那么需要重新测试系统。

7.4.4 Security and Access Control: From a regulatory standpoint, laboratory systems are notoriously known for their inadequate security and access control. If the data is critical then proper system security is required to prevent unauthorized use of the system. If a system that lacks adequate security should be used, then appropriate written security procedures should be implemented with careful consideration of facility security to prevent physical access to the system. For example, if the LDAS consists of a client/server network type of system, the server should be located in room accessible only to authorized personnel.

安全和访问控制：从法规的角度来说，实验室系统普遍存在着安全性和访问控制措施不充分的问题。如果数据时关键的，那么应该有合适的系统安全措施以防止未经授权的人使用系统。如果系统缺少足够的安全措施，那么使用该系统应当遵守合适的书面安全规程，该规程应当详细考虑了采用安全设施以从物理上阻止访问系统。比如，如果 LDAS 系统由客户端和服务器这种网络类型组成，那么服务器应安装于只允许授权人员进入的房间。

7.5 Regulatory Expectations 法规的期望要求

You should validate systems having a direct impact on the quality of data being submitted to a regulatory agency. In practice, this principle is occasionally

broadened by regulatory inspectors to include systems that indirectly impact regulatory data and decisions (e.g. electronic SOP systems and report tracking systems). It is advisable to seek the advice of an internal Quality Assurance group if you are unsure whether a system has direct or indirect impact.

应当对需要提交法规机构的质量数据有着直接影响的系统进行验证。实际上，这条原则有时候被官方检查员扩大到非直接影响法规数据和决定的系统上（比如电子 SOP 系统和报告追踪系统）。最好可以得到公司内质量保证部门的建议，如果你不确定系统是否有着直接或间接的影响。

8. Examples of Laboratory System Validation 实验室系统验证实例

8.1 pH Meters: Example of System Requiring Only Qualification

PH 计：只需确认的系统实例

For a single task, non-configurable LDAS such as a pH meter where the program behavior is very predictable, and data integrity is not an issue, the requirements for validation is minimal. Each of the following issues should be addressed, but because of the simplicity of the system, they could be addressed in the equipment log or in a single document rather than in multiple documents.

对个单个任务来说，不可配置的 LDAS 系统比如 pH 计这种程序行为完全可以预测的，数据的完整性不是问题，验证的需求程度是极小的。下面列出的问题应当被处理，但由于系统的简单性，他们可以包含在设备的使用日志或一份单个记录，而不是多份记录中。

8.1.1 Validation Plan: Though a validation plan is not necessary for such a simple LDAS as a pH meter, it can be useful as a project plan for the process.

验证计划：尽管对于简单的 LDAS 系统比如 pH 计来说，验证计划并不是必须的，但是它作为过程的项目计划还是很有用的。

8.1.2 System Description: For a very simple LDAS system like a pH meter, this section will be very brief as it need only describe the function and the purpose of the equipment.

系统描述：对于非常简单的 LDAS 系统，比如 pH 计，这部分可以非常简短只需要描述下设备的功能以及用途即可。

8.1.3 Installation Qualification: This section will describe very briefly how the pH

meter will be installed, including any necessary environmental concerns such as temperature. Upon arrival of the instrument, the user needs to confirm that the shipment matches what was ordered, and that all appropriate documentation has been received. The pH meter can then be set-up in an appropriate place following the installation directions provided by the manufacturer. Care should be taken to follow any necessary procedures and precautions concerning the conditioning, cleaning and storage of the electrode.

安装确认：这部分将简短描述了 pH 计如何被安装，包括任何需要关注的环境点，比如温度。在仪器到达时，用户需要确认到货和订单一致，并且所有相关的文件都已经收到。PH 计按照供应商提供的安装指南在合适的地点安装，注意电极的调试、清洁和储存应遵从相关规程以及注意事项。

8.1.4 Performance Qualification: This section should briefly describe how the system should perform in analyzing samples.

性能确认：这部分应简明的描述系统应如何完成样品的分析。

8.1.5 System Operational Procedure and Validation Maintenance: The working of the instrument should be verified prior to each use through the use of standard buffer solutions. An equipment logbook should be established containing all appropriate information including; the make and model number of the pH meter, the date it was received and placed into service as well as any maintenance or service. Standardization is defined as a comparison with a standard of known or accepted value. The equipment needs to be standardized before each use according to the procedures outlined in the manufacturer's manual. This standardization needs to be performed using appropriate, purchased calibration buffers. Care should be taken to ensure that the calibration buffers are within their expiration date and stored according to manufacturer's recommendations. According to regulations, calibration activities should be recorded. This information can be placed in the logbook established for the given pH meter or placed directly into the study data. There should be Standard Operating Procedures (SOPs) that contain sufficient detail for performing the procedures as required. As with any regulated data, all applicable Standard Operating Procedures, equipment manuals, supplier supplied operating

instructions and records of standardization need to be maintained in a dedicated archive.

系统操作规程和验证的维护：在设备工作前，可以通过使用标准缓冲溶液来进行确认。在设备的日志中应包含所有适当的信息，包括pH计制造编号和型号、仪器接收日期和投入使用日期以及任何维护或检修日期。定义的标准需要和已知的或已接受的标准值进行对照。应按照制造商手册中的程序在每次使用前标准化设备。标准化时需要合适的市售标定缓冲液。要注意标定缓冲液应在有效期内并按制造商的建议条件储存。按照法规的要求，校准活动应被记录。这些信息可以放入 pH 计的使用日志或直接写进检验记录中。在 SOP 应包含足够的操作细节以指导操作。所有涉及到规范化数据的相关 SOP、设备手册、供应商提供的操作说明和标准化的记录都应进行合适的归档。

8.2 HPLC With Chromatographic Software: Example of System Requiring Validation

带色谱软件的 HPLC：需验证系统的实例

All GMP/GLP regulations and quality standards mandate that equipment needs to be of suitable design, well maintained, and calibrated. An analytical instrument system consists of the instrument hardware, as well as the associated computer hardware, firmware and software. Most computerized HPLC systems consist of an HPLC instrument including an auto sampler, a pump, column, a column thermostat, detector, and the computer with its associated hardware, firmware and software for controlling experiments and managing the resulting data. As an entire package, the computerized HPLC system requires validation. There is some debate as to the value of a full-fledged validation effort for an HPLC system that is purchased from a supplier and that has extensive control mechanisms such as standard curves and quality control samples that indicate system malfunction. However, there is also a body of FDA 483 evidence indicating that fully documented validation efforts are necessary.[9]

所有 GMP/GLP 法规和质量标准均要求设备应进行合理的设计、良好的维护以及校准。分析仪器系统由仪器硬件以及关联的计算机硬件、固件和软件组成。多数计算机化的 HPLC 系统由包含了自动进样器、泵、色谱柱、柱温箱、检测器的 HPLC 仪器和关联相关硬件、固件和软件计算机组成，计算机软件用来控制实验和管理结果数据。作为完整的验证包，计算机化的 HPLC 系统需要进行验证。对于从供应商购买并且有丰富的控制机制（如标准曲

线和用于指示系统故障的质量控制样品）的 HPLC 系统，其成熟验证工作的具体内容还有一些争议。然而，许多 FDA 483 都指出完整的文件化验证工作是必须的。

An HPLC with chromatographic software is an example of a configurable LDAS in which every user accesses the configuration program. An HPLC system is often multitasking and actively controls and monitors the system. Chromatographic software is often capable of re-processing the data multiple times. Because of the complexity of the typical HPLC with chromatographic software system, the classification and factorial analysis of these systems dictates a very thorough validation effort. The equipment verification and validation process begins before the design phase and lasts until the product is retired, in other words, through the entire life cycle of the product. This commitment requires resource allocation to complete all of the necessary requirements to achieve and maintain a state of validation.

带色谱分析软件的 HPLC 是一个典型的可配置 LDAS 实例，每一个使用者都可接触到配置程序。HPLC 系统经常进行多任务分析并且积极的控制以及监测整个系统。色谱分析软件常可以再处理数据很多次。由于典型的带色谱分析软件 HPLC 系统的复杂性，对这些系统进行分组和因素分析将可以使验证工作更加周密。设备确认和验证过程在设计阶段前开始并持续至产品退役，换句话来说，应贯穿产品的整个生命周期。这需要有足够的资源分配来完成所有必要的需求以达到并维持验证状态。

8.2.1 Validation Plan: Because of the complexity of the typical HPLC system, a validation plan should be prepared that describes the requirements and responsibilities for validating the system. This document will serve as the project plan for the validation efforts.

验证计划：由于典型 HPLC 系统的复杂性，应起草验证计划并描述验证系统中的需求和职责。这份文件也将作为验证工作的项目计划。

8.2.2 System Description: Before the purchase decision is made, the Functional Requirements document should be written, describing the types of analysis and the performance required of the instrument. This document specifies the minimal functional requirements of the instrument to be purchased. For example, will the HPLC be used for only one type of analysis, or will the instrument be required for many different analyses of varying complexity?

系统描述：在决定采购前，应起草功能需求文件，描述分析的类型以及仪器性能的要求。这份文件指明了仪器的最低功能要求。比如 HPLC 是否只用于一种类型的分析，或者仪器需要进行不同复杂程度的多种分析吗？

Although the regulatory requirement for such documentation could be questioned, there are definite business reasons for this exercise. The Functional Requirement Document forms the basis to which instrument performance (system qualification) will later be compared. For in-house or custom developed systems, this document can also contain the Design Specification. This document should discuss the impact of the LDAS classification (i.e. configurability, complexity, data integrity, data security and data storage).

尽管文件中关于法规方面的需求可能会被质疑，但文件中的商业上的原因都很明确。功能需求文件构成了仪器性能（系统确认）对比的基础。对于内部或定制开发的系统，这份文件同样包含了设计标准。这份文件应对 LDAS 的分类影响进行讨论（比如可配置性、复杂性、数据完整性、数据安全和数据存储）。

For an instrument that will be purchased, the requirements specification is prepared based on the requirements of the laboratory with the assistance of product information obtained from suppliers. Environmental and safety requirements and concerns need to be examined at this time (e.g. does a new LC/MS/MS require a new power supply or additional space for diffusion pumps.)

对于购买的仪器，需求标准应基于实验室需求起草，并且应从供应商处获得产品信息的协助。环境和安全需求以及关注点需要在此时检查（比如，新的 LC/MS/MS 是否需要新的电源或额外的空间以放置扩散泵？）

Consideration should be given to any existing data systems and how the new system will interface with the processes already operating within the laboratory. For example, an HPLC in a Drug Metabolism laboratory used for the analysis of samples for pharmacokinetic analysis needs to interface with the available pharmacokinetic software packages. Consideration should be given to the software's ability to export the data in a format that can be used by other software packages and retrieved in the future.

应考虑任何现存的数据系统以及新系统将如何接入实验室内已经运行的进程。比如，在药物代谢实验室用于药动学分析的 HPLC 需要接入可用的药动学软件包。应考虑软件数据

输出能力，其格式应可以被其他软件使用并在将来可以恢复。

Documentation should address the configurability of the program. Will the user configure the instrument through the use of macros? For example, an HPLC with a mass spectrometer as a detector where user written macros control the mass spectrometer acquisition parameters and may even control whether the LC effluent is diverted to waste or to the mass spectrometer. These macros will require their own ”validation” to document their creation, function, and control. The user should be careful in the use of macros, especially when there is a system upgrade (i.e. do they still function correctly?).

文件中应注意程序的可配置性。用户配置仪器是否都通过使用宏命令？比如，一台将质谱仪作为检测器的 HPLC，用户通过写入宏命令来控制质谱仪采集参数，甚至可以控制液相流出物是进入质谱仪还是作为废液排出。这些宏命令本身需要验证，记录他们的创建、功能和控制。当用户使用宏时应特别小心，尤其是当系统升级后（比如宏命令功能是否还依然正确）。

For purchased instruments, the supplier needs to be evaluated and qualified. It is the responsibility of the user to demonstrate that the entire system, including the software, is validated. The user should determine that the instrument was developed following recognized quality and technical standards. To determine this, the quality systems of the supplier need to be evaluated according to an established supplier assessment program. This program should include an evaluation of the training given to the vendors employees as well as looking at the quality processes and programs of the supplier. If a supplier is unable or unwilling to supply all of the necessary information, an alternate supplier may need to be considered. If another supplier cannot be found, the user may have to perform more extensive testing of the system.

对于市售仪器，需要对供应商进行评估和认证。用户有责任确认整个系统包括软件都已经完成验证。用户应证明仪器的开发遵循经认可的质量和技术标准。为了证明这一点，供应商的质量系统需要根据已建立的供应商评估程序进行评估。这套评估程序应包括供应商员工培训和查看供应商质量流程和程序的评价。如果供应商无法或不愿意提供所有必要的信息，那么就需要考虑备用的供应商。如果找不到其他供应商，那么用户不得不对系统进行大量的测试。

8.2.3 Installation Qualification: The installation qualification document should

describe how the HPLC system will be installed. The installation qualification (IQ) is performed in conjunction with the service representative who is installing the instrument. This phase includes a verification that the correct equipment was shipped and installed correctly and that all of the documentation is complete. Verification of the configuration installation should be performed as well as installation of any appropriate software and any data storage devices. It is important that the supplier provides adequate documentation to enable the system to be operated safely and efficiently.

安装确认：安装确认文件应描述 HPLC 系统将如何被安装。应和系统安装代表共同进行安装确认。这阶段包括了确认到货的仪器是正确的，并且被正确的安装以及所有的文件资料是完整的。确认合适的软件和数据储存装置以及相关配置均被正确的安装。重要的是，供应商因提供充分的文件资料以使系统可以安全高效的运行。

8.2.4 Operation Qualification: The operational qualification document should describe how the HPLC system components should be qualified. The LDAS classification of the HPLC system will determine the aspects of the system functionality that need to be verified. Instrument testing can evaluate each module of the instrument individually, or the entire instrument can be evaluated as a unit. Because of the interdependencies of the individual components, the evaluation of the instrument as a whole unit is preferable, though the testing of the individual modules is valuable in determining which specific components were involved when a problem is detected. The performance precision of an individual module is more important than the accuracy, except when methods are transferred between instruments or laboratories.

运行确认：运行确认文件应描述 HPLC 系统组件应如何通过认证的。HPLC 在 LDAS 的分类将决定系统需要进行确认的功能性方面。仪器测试应单独的评价每一个仪器模块，或者所有仪器作为整体被评价。由于单独组件之间的相关性，仪器作为整体进行评价更为可取，尽管单独的组件测试在系统故障发生时，判断是哪个组件有关是非常有意义的。单个模块的性能精密度比准确度更重要，除非方法在仪器之间或实验室之间转移。

For an HPLC method with peak identification based upon retention time, differences in instrumentation causing differences in temperature, flow rate, gradient mixture, etc. may effect the absolute and /or relative retention times. The operational qualification (OQ) needs to be performed and documented by the users of the system. The operation of the

system through the full range of possible values for any of the configurable parameters of the system needs to be verified. The user and/or the supplier need to demonstrate that any software and hardware work correctly, performing all of the possible tasks through all the anticipated operating ranges.

对于峰鉴别基于保留时间的 HPLC 方法，不同仪器有着不同的温度、流速、梯度等，可能会影响绝对和/或相对保留时间。应对用户的系统进行确认并记录。应确认系统在任何可配置参数的全量程范围内的运行。用户和/或供应商需要证明所有软件和硬件正确工作，在所有预期操作范围内进行所有可能的任务。

The operation of all user configurable functions need to be verified, as well as the data processing and data storage functions. The system should be evaluated according to the procedures for which it will be used. There may be functions that will not be used, but unless they can be disabled, their performance should be verified.

应确认所有用户可配置的功能操作，包括数据处理和数据储存功能。系统应根据使用的规程进行评价。可能系统有些功能不会使用，但是至少他们可以关闭，否则他们的性能仍然需要进行确认。

8.2.5 Performance Qualification: The performance of the instrument is compared to the requirements specification and known standards are run to verify the performance of the hardware and the software during all possible operation scenarios. Reference data files and procedures should be stored so the tests can be routinely run and the operation of the instrument verified later against the known data. The functioning of the system during actual user applications needs to be evaluated. This must also address the issue of system configurability and ensure that the appropriate parameters are functioning.

性能确认：确认系统硬件和软件在所有可能运行情况下的性能并和需求标准和已知的标准进行比较来确认仪器的性能。参考的数据文件和规程应储存以便测试可以定期的进行并且以后进行的仪器运行数据可以和先前的进行比较。应评价系统在用户实际应用中的运行情况。这同样必须处理系统可配置性的问题并且确保使用合适的参数。

8.2.6 System Operational Procedure and Validation Maintenance: The documentation prepared needs to include the procedures that need to be followed during the day-to-day operation of the HPLC system. Standard procedures need to be created that document, for the individual system, any file naming conventions as well as any

general operational procedures.

系统操作规程以及验证的维护：制定的文件应包括应遵守的日常 HPLC 系统操作规程。为每一个单独的系统创建标准操作规程，包括任何文件命名的约定，也可以使用通用的操作规程。

The performance of HPLC equipment is routinely defined during the method validation and includes analysis of system linearity over the anticipated concentration range. The system precision is determined by the examination of initial quality control samples and during the daily analysis of samples. These procedures need to be documented to enable all system users to consistently apply these principles. A laboratory should establish guidelines for establishing the anticipated concentration range for a given method and the procedures to be followed for samples that are out of the range of calibration standards.

HPLC 仪器的性能通常在方法验证中规定，包括系统分析在预期浓度范围内的线性。系统的精密度可以通过初始的质量控制样品和日常分析样品来决定。这些程序需要进行记录以使所有系统用户可以方便的应用这些原则。实验室应有给定方法的预期浓度范围的建立的指南，并且应有超出校准标准范围样品所应遵从的程序。

Quality control samples should be interspersed among the actual samples throughout the run. The procedures for the preparation of the quality control samples, the frequency for the running of these samples and the acceptance criteria, as well as the procedures to be followed when these samples are out of range, should be documented in SOPs.

在进行分析时，质量控制样品应穿插在实际的样品中。质量控制样品的配制程序、上述样品的运行频率以及可接受标准、以及样品超出范围所应遵从的程序都应在 SOP 中进行规定。

Any training given to users of a system should be documented in the individual training records.

系统用户的培训应记录在单独的培训记录中。

To ensure the ongoing performance of the instrument, the users need to develop, document, and implement operational, preventive maintenance and calibration procedures as well as change control procedures. For an HPLC system where the system controls the HPLC as well as allowing the analysis of the chromatographic data, written

procedures are needed to describe the operation of the equipment and the chromatography software, including any functions that should not be used. As with many chromatography systems, if the system is configurable, procedures need to be established as to who can perform the configuration changes and what parameters are allowable. Written change control procedures need to be established. Often, maintenance schedules and procedures are recommended by the supplier in their documentation that can often be performed by service technicians.

为了确保仪器的持续性能，用户应当开发、正式成文以及实施仪器的操作、预防性维护和校准程序以及变更控制程序。对于允许色谱数据分析的 HPLC 系统，书面的规程需要描述仪器和色谱软件的操作，包括不需要使用的功能。对于许多色谱系统，如果系统是可配置的，规程中同样需要说明谁可以改变设置并且哪些参数是允许的。应建立书面的变更控制程序。通常，维护的频率和程序由供应商在其服务技术人员实施的文件中提供。

Instrument failures, and the corrective action taken, must be documented. Care should be taken to document completely the service performed during scheduled and non-scheduled service calls. There are cases where equipment hardware repairs have resulted in upgrades to firmware resulting in system changes.

仪器故障以及实施的纠正措施应当记录。应注意完整的记录定期和非定期的维护活动。有些情况下是因为设备硬件维修和固件升级而引起的系统变更。

Calibration procedures also need to be established and documented. Many types of equipment have built in calibration routines, e.g. UV detectors. Any chemical tests used for the calibration testing should either be traceable to national standards or be of known stability. Part of this process should include the generation of logbooks for recording all instrument activities.

同样需要建立校准程序并记录归档。许多类型设备已经建立了日常校准工作，比如 UV 检测器。任何用来校准测试的化学试剂均应可以追溯到国家标准或已知的稳定性。这部分流程还应包括建立日志来记录所有仪器活动。

Changes to the computerized system (whether hardware or software) need to follow set procedures and be documented. Some changes may require re-qualification of some aspects of the system and these should be performed and documented. The extent of the re-qualification efforts will depend upon the type of change and the extent of the

information shipped by the supplier with the upgraded hardware or software.

计算机化系统的变更(无论是硬件或软件)都应按照既定的规程进行并且需要记录归档。某些变更可能需要重新确认系统的某些方面并且这些都应被记录归档。再确认工作的程度基于变更的类型以及供应商对更新的硬件或软件所提供信息程度。

Before the system is put back into service for routine analysis, performance qualification (PQ) is required. A procedure for the periodic review of the validation status of the HPLC system should also be established. This review should include a review of all records and log books as well as a review of the stored data integrity, data backup integrity and the audit trail integrity.

在系统再次投入日常分析使用之前，需要进行性能确认（PQ）。同样需要建立规程以定期回顾 HPLC 系统的验证状态。回顾内容应包括所有记录和所有日志的回顾，以及存储数据的完整性、数据备份的完整性以及审计追踪完整性的回顾。

All laboratories need to maintain in a dedicated archive all records and data. Therefore, all validation documents including supplier supplied documentation (e.g. shipping records, equipment manuals and user manuals), all user generated documentation and records, training records, standard operating procedures and equipment logs need to be archived.

所有实验室应建立专门的档案室来管理所有记录和数据。因此，所有验证文档包括供应商提供的文件材料（比如发货记录、设备手册和用户手册）、所有用户制定的文档和记录、培训记录、标准操作规程和设备使用日志均应归档。

9. Glossary 术语

A/D: Analog to Digital Converter

A/D: 模拟转数字转化器

LDAS: Abbreviation for computerized Laboratory Data Acquisition System

LDAS：计算机化实验室数据采集系统的缩写

Raw data means any laboratory worksheets, records, memoranda, notes, or exact copies thereof, that are the result of original observations and activities of a NonClinical laboratory study and are necessary for the reconstruction and evaluation of the report of that study. In the event that exact transcripts of raw data have been prepared (e.g., tapes which have been transcribed verbatim, dated, and verified accurate by signature), the

exact copy or exact transcript may be substituted for the original source as raw data. Raw data may include photographs, microfilm or microfiche copies, computer printouts, magnetic media, including dictated observations, and recorded data from automated instruments. (From the GLP CFR 21, section 58.3)

原始数据意为实验室工作表、记录、备忘录、笔记或确切的副本拷贝件（非临床实验室研究的原始观察结果和活动并且是研究报告的重组和再评价必需物）。如果已准备了准确的原始数据的副本（比如逐字转录的磁带并签名和签日期确认准确性），那么此拷贝或副本也是可以取代原始来源作为原始数据。原始数据可能包括照片、微缩胶卷或微缩胶片的复印件、计算机打印输出、磁性介质，包括口述的观察结果和从自动仪器上记录的结果（来自GLP CFR 21,58.3 章）。

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