增加以下内容：

〈1058〉分析仪器确认

介绍

大量的试验室设备、仪器、分析计算机系统，从简单的氮蒸汽到复杂的多功能技术（见仪器目录）应用在制药工业中，这些用于获取数据，以确信产品是适于预期使用。分析的目标是经常性获得可靠的，有效的和适用于检测目的的数据。根据使用情况，使用者对验证程序，校准仪器，运行额外的仪器检查，例如系统适用性试验和对过程中的质量控制检查样品的分析，用于确保获取数据的可靠性。随着复杂和自动化分析仪器的增多，摆在使用者面前的是，对确认仪器资格性的需求也随之增加。

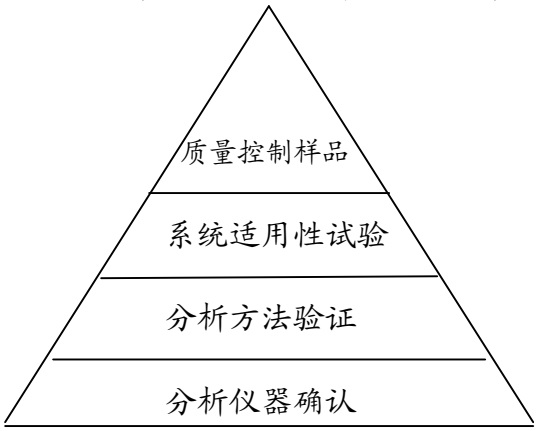
目前，分析仪器确认（AIQ）不像方法验证和系统适用性试验，有专门的指导或流程。观点争执于仪器确认和校准流程和执行者的作用和责任。因此，仪器确认有很多不同的方式，这样就需要了大量的资源，产生多种不同的文件。本章对 AIQ 进行了科学的探讨，并把 AIQ 作为获得可靠而一致数据的一个主要因素。注意，确认过程的严谨性取决于仪器设施的复杂和预期目的。其过程着重于在从分析仪器获得可靠数据的总体过程中

验证和确认

本章中，词语“验证”用于生产过程，分析步骤，软件操作。词语“确认”用于仪器。因此，短语“分析仪器确认”（AIQ）用于确保仪器适用于预期应用的过程。

数据质量的组成部分

在可靠和一致性数据（质量数据）产生的过程中，有四个关键要素。图一用质量三角形的层叠形式描述了这些组成部分。每一层都在总体质量中。分析仪器确认组成了获得质量数据的基础。其他产生质量数据的必要的组成部分包括分析方法验证，系统适用性试验，质量控制检查样品。这些质量组成部分演示如下：



图一 数据质量的组成部分

分析仪器确认

AIQ 是收集仪器可以适用于预期目的文字信息。在分析中，使用已确认的仪器有助于提高生成数据可靠性的信任度。

分析方法验证

分析方法验证是收集分析步骤可以适用于预期目的文字信息。用已确认的分析仪器来进行的验证过程可以让人相信其过程能够的出可被接受质量的测试数据。在总体信息章节 compendial 方法验证〈1225〉中可以找到关于 compendial 方法验证的附加指导。

系统适用性试验

系统适用性试验证明系统是根据试验开始的标准进行的。这些检测紧跟着样品分析，以保证系统运行在检测的时间里是被接受的。USP 总章色谱〈621〉中有与色谱系统有关的系统适用性的更细节的讨论。

质量控制检查样品

很多分析试验采用参照物和/或校正标准物在已标化的仪器中进行试验。一些分析试验需要质量控制检查样品来提供过程中或进行中的试验适用性能的保证。在这个角度上，AIQ 和分析方法确认在分析试验开始之前对分析质量有帮助。系统适用性试验和质量控制检查有助于在样品分析刚刚开始之前或过程中确认分析结果的质量。

分析仪器确认过程

以下部分对 AIQ 过程进行细化。其他三个有关分析数据质量的组成部分——分析方法验证，系统适用性试验，质量控制检查样品——不再这一章节的包含之列。

确认阶段

仪器确认不是一个单一的持续过程，而相反，源于几个分离的活动。为了方便，这些活动可分成四个阶段：设计确认（DQ），安装确认（IQ），运行确认（OQ），性能确认（PQ）。

某些 AIQ 活动包含不只一个确认过程，分析试验有可能在不只一个阶段进行 AIQ（见表一），然而，在很多时候进行 AIQ 需要专门的指令，例如，安装确认必须第一个出现以保证开始其他确认活动。AIQ 活动应被规定和记录。

表一 分析仪器确认的每个阶段的周期、适用情况、工作*

DQ	IQ		OQ		PQ
周期和适用情况					
在仪器新型号购买之前	每台仪器安装时(新的，就的或已有但未确认的仪器)		安装或仪器大修之后		每台仪器按规定的间隔具有周期性
工作内容					
制造商 DQ 保证	描述	→ ←	固定参数		预防性维修和保养
制造商提供充分可用性的保证	仪器运输				
仪器适于在实验室使用	集成和安装的有效和便利	→ ←	环境		
	网络和数据	→	可靠的数据存贮、备		

	存储	←	份、获取		
	安装证明	→ ←	仪器功能检测	→ ←	运行检查

*每个阶段的工作内容可根据下表进行。然而，某些情况，有更适当的去进行或和其他阶段的可供操作的工作集合在一起。这种覆盖不只一个确认阶段的工作在表中用双箭头连接。如果在给出阶段进行的工作在其他阶段进行，在工作列出的阶段不必再重复。进行工作远比工作在哪个阶段进行更重要。

DQ

DQ 是对以下活动作文字收集，那就是对仪器功能和运行技术要求，和销售商选择标准的明确，这些都基于仪器的预期目的。DQ 不仅要仪器开发商和制造商进行还要使用者进行。制造商对机器设计和维修保养信息负主要责任。这些信息包括描述分析仪器是怎样制作的（设计说明书，功能需求等）及其在给使用者安装之前如何测试。然而，使用者应明确商用（COTS）仪器应适用于预期使用，制造商采取质量体系以提供可靠的设备。使用者应该明确制造商所能提供安装服务和培训的能力，使用者与制造商前期沟通可帮助使用者的明确。

IQ

IQ 是对以下必要的活动作文字收集，即仪器按设计和规定运输，并在选定的环境中适当的安装，环境可适用于仪器。IQ 确认应用于新的，或二手的或任何已存在但之前没有做确认的仪器。IQ 相关的部分也应用于确认过的但移位至另一个地点，或因为其他原因需要再进行安装确认的仪器，例如长期闲置的仪器。IQ 相关的典型活动和文字资料如下

描述——提供仪器的描述或仪器组成部分的收集。包括制造商，型号，序列号，软件版本，地点。可使用恰当的图标和流线图。

仪器运输——明确已有仪器、软件、手册、备件和其他订购单明确的仪器附件，这些都未被损坏。对于二手的或是已有的仪器，应有手册和文字资料。

效用性/便利性/环境——证明满意的安装地点应与制造商提供的环境需求匹配。

集成和安装——集成和安装仪器，运行初步诊断和测试。集成和安装应有制造商、供应商，专门工程师或者确认过的内部职员进行。制造商安装试验和指导为决定仪器的接受度提供有价值的基本参考。在集成和安装过程中观察到的任何非常规事件都应记录。然而，从制造商或供应商处购买的安装包应补充到使用者特定的规范中。

网络和数据存储——一些分析系统需要使用者在安装地点提供网络连接和数据存储功能。需要时，连接仪器至网络，并检查其功能。

安装验证——安装之后进行仪器的初始诊断和检查

OQ

在成功完成 IQ 之后，仪器已准备好进行 OQ 测试。OQ 是对必要活动的文字资料收集，这些活动可证明仪器根据运行说明在所选条件下运行。在 IQ 阶段测定活动有以下测定数据组成。

固定参数——这些测定测量仪器的固定不变的参数，如长度，高度，重量，输入电压，可接受压力，负荷。如果制造商提供的数据的说明可令使用者满意，测试可免除。然而，如果使用者想证明参数，测试应在使用场地进行。固定参数不会改变仪器的寿命，因此，不需要再测定。注意：测试应在 IQ 阶段进行（见表一）；如果这样，固定参数在 OQ 阶段不需要再测定。

数据存储、备份和获取的保密性——当适用时，根据给出的步骤在使用地点测试保密数据功能如存储，备份，审查跟踪，获取。

仪器功能测试——使用者需要的仪器功能应测试，以证明仪器可以象制造商预期的那样工作。当判定这些参数的技术，或设计评价被测参数的试验时，制造商提供的信息是有用的。使用者，或已认可的设计人员，应进行这些试验已证明仪器在使用环境中符合制造商或使用者的技术要求。

仪器能承受的 OQ 测试的范围取决于其预期使用。因此，在本章中任何仪器和设备都没有专门的 OQ 试验。

常规的分析试验不能组成 OQ 测试。OQ 测试需要专门设计以证明仪器在使用环境中根据技术要求运行的，不需要在规定的间隔时间内重复试验。然而，当仪器有重大维修和改变，相关 OQ 和/或 PQ 测试应被重复，以证明是否仪器能继续令人满意的运行。如果仪器被移动到另外的位置，应对作其组成进行评估，如果需要的话，OQ 测试应重复。

OQ 测试可以部分或整体进行。如果系统的组成部分进行变更，而没有进行确认，系统的单个组成部分进行模块测试，可使这种改变更方便。整个系统的全部测试，当然也被接受。

PQ

PQ 是对必要活动的文字收集，这些活动用以证明仪器在使用者的技术要求之下可持续运行，并可适用于预期使用。在 IQ/OQ 完成之后，仪器的为预期目的的持续的适用性可通过 PQ 验证证明，PQ 阶段可包括以下参数。

性能检查——建立一种或一系列试验来证明仪器的运行，根据预期使用目的是可接受的。PQ 测试通常基于仪器在安装地点的常规运行，由分析已知化合物或标准品组成。试验应在优良技术的基础上进行，并反映仪器总体的预期使用目的。一些与测试同时进行的系统适用性试验或质量控制检查，有助于证明仪器是正常运行的。PQ 测试和 OQ 测试中进行的试验相似，但所需要的结果的技术说明是不同的。尽管如此，PQ 测试得出的技术说明仍可证明，仪器的运行是按照预期目的进行的，而且是毫无困难的。对于 OQ 测试来讲，PQ 测试可以整体也可以部分进行。

测试的频率根据仪器的耐用性和进行试验的关键程度来判断。试验可以是不定期的，例如，每次仪器使用的时候，试验也可以按规律周期定期进行。仪器的使用情况可影响上述决定。每次仪器使用的时候重复同样的 PQ 测试是有用的，因此，应编辑仪器的运行历史。或者，仪器可被并入一个综合支持系统去证明他被确认。一些跟检查样品同时进行的系统适用性试验或质量控制检查也能表明仪器正常运行。

预防性保养和维修——当仪器不能按照 PQ 测试技术要求运行，仪器需要保养和维修。周期性的预防性保养适用于很多仪器。相关的 PQ 测试在必要的保养或维修之后应被重复，以证明仪器已被确认。

操作，校准，维修，改变控制的操作方法——建立仪器维修和校准的操作方法。每次保养和校准行为应被记录。

作用和责任

使用者

使用者最终应对仪器的使用和数据负责任。使用者组群包括检验员，他们的监督者，仪器专家，组织机构管理者。使用者应经常进行仪器使用的培训，培训记录应按要求予以保留。

使用者有责任对仪器进行确认，因为他们在仪器使用上经过培训并具有专业知识，这使他们能设计成功的确认（AIQ）试验和技术说明，他们是最佳人选。因此，设备制造商和供应商，验证专家，质量保证人员（QA）应按需提出建议和帮助，但最终确认仪器的职责应在使用者身上。使用者也应通过定期执行 PQ 来在确认基础上对仪器进行保养。

质量小组

在 AIQ 过程中质量小组的作用和其他规律性活动相同。质量部门人员有责任确认 AIQ 过程应配合需求，并且可以被操作，同时仪器的预期使用可以被有效的和记录的数据支持。

制造商

制造商和开发商在设计仪器时有责任进行 DQ 确认。他们同样要为生产和仪器集成时相关过程的验证负责任。制造商应在安装给使用者之前测试集成的仪器。最后，希望制造商和供应商能在产品售出后通知所有已知使用者有关发现的硬件的缺陷，并提供使用者培训，服务，维修，安装支持，并有必要邀请使用者审查。

软件确认

分析工作中的软件使用一般分成三种，固件；仪器控制，数据获取和控制软件；外置软件。虽然软件确认不是本章的主要问题，但是以下所表述的部分仍属于分析仪器确认的范围里。

固件

计算机化的分析仪器将低级软件（固件）包含在整体之中。如果没有正确的操作固件，这样的仪器不能使用，使用者也不能改变固件的设置和功能。因此，固件被视为仪器本身的一部分。事实上，硬件确认如果没有固件的运行也是不可能实现的。因此，当硬件（也就是分析仪器）在使用场所被确认的时候，其集成的固件也必定通过了确认。根本不需要单独确认安装的固件。无论何时只要有可能，固件形式应作为 IQ 的一部分被记录。固件形式的任何改变都应通过仪器的改变控制来进行追踪。（可见后面的改变控制）

仪器控制，数据获取和运行软件

如见，很多计算机化的仪器都通过连接电脑而安装了仪器控制，数据获取和运行软件。仪器的运行可通过操作软件来进行，而在仪器上操作的控制则很少了。数据获取和之后的计算也必须通过软件运行。因此，软件和硬件功能相互作用，对得到分析结果都是关键的。

制造商应执行 DQ，并验证软件，提供使用者验证的总结。在使用地点，包含仪器整体和软件系统的全部确认，比软件单独验证更为有效。因此，使用者根据 AIQ 过程通过确认仪器来确认有关仪器控制，数据获取和运行的软件。

外置软件

验证外置软件的官方指导，例如 LIMS，是可采用的。验证过程通过软件开发商发布，开发商也应说明适于软件的开发模块。确认按计划的一系列活动开始，并通过开发周期的不同阶段实行。

改变控制

当制造商增加新特性和改正已知缺陷的时候，不可避免改变仪器包括软件。然而，执行所有的改变不一定会总是给使用者带来好处。因此，使用者应采用有用或必要的改变，并且评估改变的效果，去决定所需的再确认。改变控制过程就是作这些。

改变控制可按照 DQ/IQ/OQ/PQ 分类进行。对于 DQ，评估改变的参数，决定是否

需要许可进行执行。如果必须进行改变，在 IQ 阶段安装所改变的系统。评估存在的 OQ，PQ 测试所需的修订，缺陷，和作为安装改变的结果增加的东西。当改变需要将增加，减少或修订放到 OQ 或 PQ 测试中，按照以下该书的方式进行。

OQ——对于改变而言，修订 OQ 测试是必要的。运行和改变有关的测试。证明仪器在改变安装之后的有效使用。

PQ——对于改变而言，修订 PQ 测试是必要的。如果在 OQ 阶段类似的测试没有运行，在改变安装之后执行 PQ 测试。以后，要求执行修订过的 PQ 测试。

如果固件，仪器控制，数据获取，运行软件进行改变，改变控制通过被影响的仪器的 DQ/IQ/OQ/PQ 进行。外置软件的改变控制需要在使用地点进行改变功能的测试。

AIQ 文字资料

通过仪器确认获得的文件应以容易接近的态度保存。当一个种类的多个仪器存在时，所有仪器共同的文件和单个仪器单独的文件应分开保存。当改变控制时，附加的文件增加到验证过程文件中，所有模式的文件都应适当的保存，以期获得适当的保护和获取。

仪器目录

标准的现代实验室包括一套仪器设备，简单到氮蒸汽，复杂到自动化仪器。因此，采用一套单一的规程去验证这些互不相同的仪器是不科学且不恰当的。使用者最有能力建立仪器所需确认层次。在所需最基本的层次，将仪器目录分为三组是很方便的：A，B，C,正如如下所说。每一组仪器都有举例。注意这里提供的仪器列表仅仅为了举例，并不详尽。在使用场所没有提供一个确切的目录。此目录应该由使用者根据自己特殊的仪器或器具来确定。

仪器的明确划分应该由使用者根据其所需来进行。根据每个使用者的需要，同样的仪器可以适当的分成一个使用人一组或是不同的使用人不同的组。因此，高度鼓励使用者进行仔细的选择。

A 组

A 组包括没有测量功能或常规校准需求的标准设备，制造商基本功能的技术要求可被使用者接受。A 组设备对使用者需求的一致性可以通过操作时的视觉观察来证明和记录。本组的仪器如氮蒸汽，磁力搅拌器，蜗旋混和器，离心机。

B 组

B 组包括提供测定值的标准仪器和设备，仪器可通过需要校准的物理参数控制（温度，压力，流速），使用者的需求应基本上与制造商提供的功能和操作限制的技术要求一致。B 组仪器或设备与使用者需要的一致性可根据仪器或设备的标准操作规程来确定，并在 IQ/OQ 阶段记录。本组仪器有天平，熔点仪，光显微镜，ph 计，可变移液器,折射计，温度计，滴定计，粘度计。本组设备有煤油炉，干燥器，电冰箱，水浴锅，泵，稀释计

C 组

C 组包括仪器和计算机分析系统，使用者对功能，操作和运行的限制需求在分析使用时都是特定的。C 组仪器对使用需求的一致性有特定功能功能测试和运行测试决定。安装这些仪器需要复杂的操作，需要专家的帮助。一个完整的确认过程，如在这个文件中提到的，需要应用到这些仪器上。本组仪器如下：

原子吸收光谱计

示差扫描量热计

溶出仪

电子显微镜
火焰吸收光度计
高压液相仪
质谱
微孔板检测器
热重分析仪
X-射线荧光光谱仪
X 光粉末衍射仪
密度计
二极管阵列检测器
元素分析仪
气相色谱仪
红外光谱仪
近红外光谱仪
拉曼光谱仪
紫外光谱仪
诱导配对等离子发射光谱仪

Add the following:

■〈1058〉 Analytical Instrument Qualification

INTRODUCTION

A large variety of laboratory equipment, instruments, and computerized analytical systems, ranging from simple nitrogen evaporators to complex multiple-function technologies (see *Instrument Categories*), are used in the pharmaceutical industry to acquire data to help ensure that products are suitable for their intended use. An analyst's objective is to consistently obtain reliable and valid data suitable for the intended purpose. Depending on the applications, users validate their procedures, calibrate their instruments, and perform additional instrument checks, such as system suitability tests and analysis of in-process quality control check samples to help ensure that the acquired data are reliable. With the increasing sophistication and automation of analytical instruments, an increasing demand has been placed on users to qualify their instruments.

Unlike method validation and system suitability activities, analytical instrument qualification (AIQ) currently has no specific guidance or procedures. Competing opinions exist regarding instrument qualification and validation procedures and the roles and responsibilities of those who perform them. Consequently, various approaches have been used for instrument qualification, approaches that require varying amounts of resources and generate widely differing amounts of documentation. This chapter provides a scientific approach to AIQ and considers AIQ as one of the major components required for generating reliable and consistent data. Note that the amount of rigor applied to the qualification process will depend on the complexity and intended use of the instrumentation. This approach emphasizes AIQ's place in the overall process of obtaining reliable data from analytical instruments.

Validation versus Qualification

In this chapter, the term validation is used for manufacturing processes, analytical procedures, and software procedures and the term qualification is used for instruments. Thus, the phrase “analytical instrument qualification” (AIQ) is used for the process of ensuring that an instrument is suitable for its intended application.

COMPONENTS OF DATA QUALITY

There are four critical components involved in the generation of reliable and consistent data (quality data). *Figure 1* shows these components as layered activities within a quality triangle. Each layer adds to the overall quality. Analytical instrument qualification forms the base for generating quality data. The other components essential for generating quality data are analytical method validation, system suitability tests, and quality control check samples. These quality components are described below.

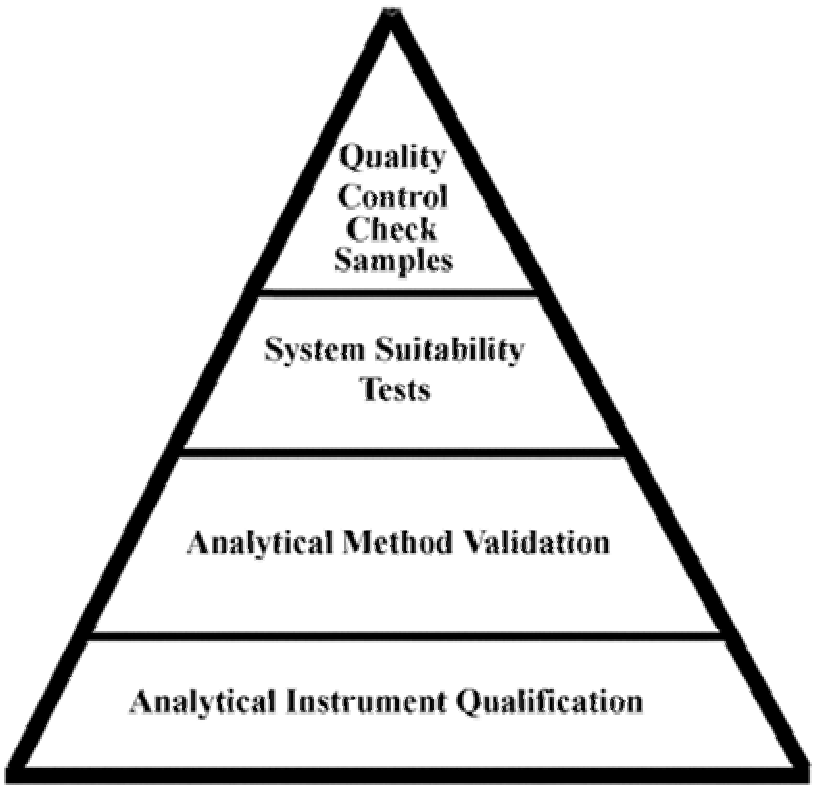


Figure 1. Components of data quality.

Analytical Instrument Qualification

AIQ is the collection of documented evidence that an instrument performs suitably for its intended purpose. Use of a qualified instrument in analyses contributes to confidence in the validity of generated data.

Analytical Method Validation

Analytical method validation is the collection of documented evidence that an analytical procedure is suitable for its intended use. Use of a validated procedure with qualified analytical instruments provides confidence that the procedure will generate test data of acceptable quality. Additional guidance on validation of compendial procedures may be found in the general information chapter *Validation of Compendial Procedures* 〈1225〉.

System Suitability Tests

System suitability tests verify that the system will perform in accordance with the criteria set forth in the procedure. These tests are performed along with the sample analyses to ensure that the system's performance is acceptable at the time of the test. USP general chapter *Chromatography* 〈621〉 presents a more detailed discussion of system suitability tests as related to chromatographic systems.

Quality Control Check Samples

Many analysts carry out their tests on instruments standardized using reference materials and/or calibration standards. Some analyses also require the inclusion of quality control check samples to provide an in-process or ongoing assurance of the test's suitable performance. In this manner, AIQ and analytical method validation contribute to the quality of analysis *before* analysts conduct the tests. System suitability tests and quality control checks help ensure the quality of analytical results *immediately before* or *during* sample analysis.

ANAYLTICAL INSTRUMENT QUALIFICATION PROCESS

The following sections address in detail the AIQ process. The other three components of building quality into analytical data—analytical method validation, system suitability tests, and quality control check samples—are not within the scope of this chapter.

Qualification Phases

Instrument qualification is not a single continuous process, but instead results from several discrete activities. For convenience, these activities can be grouped into four phases: design qualification (DQ), installation qualification (IQ), operational qualification (OQ), and performance qualification (PQ). Some AIQ activities cover more than one qualification phase, and analysts potentially could perform them during more than one of the phases (see *Table 1*). However, in many instances there is need for specific order to the AIQ activities; for example, installation qualification must occur first in order to initiate other qualification activities. The AIQ activities will be defined and documented.

Table 1. Timing, Applicability, and Activities for Each Phase of Analytical Instrument Qualification

Design Qualification	Installation Qualification		Operational Qualification		Performance Qualification
Timing and Applicability					
Prior to purchase of a new model of instrument	**At installation of each instrument (new, old, or existing unqualified)**		**After installation or major repair of each instrument**		**Periodically at specified intervals for each instrument**
Activities					
Assurance of manufacturer's DQ	**Description**	⇆	**Fixed parameters**		**Preventive maintenance and repairs**
Assurance of adequate support availability	**Instrument delivery**				**Establish practices to address operation,**

Design Qualification	Installation Qualification		Operational Qualification		Performance Qualification
from manufacturer					**calibration, maintenance, and change control**
Instrument's fitness for use in laboratory	**Utilities/facility Assembly and installation**	⇆	**Environment**		
	Network and data storage	⇆	**Secure data storage, backup, and archive**		
	Installation verification	⇆	**Instrument function tests**	⇆	**Performance checks**

*** Activities under each phase are usually performed as given in the table. However, in some cases, it may be more appropriate to perform or combine a given activity with another phase. Such activities spanning more than one qualification phase are shown as connected by double arrows. If an activity listed under a given phase is performed under another phase, it is not necessary to repeat the activity under the phase where the activity is listed. Performing the activity is far more important than the phase under which the activity is performed.**

DESIGN QUALIFICATION

Design qualification (DQ) is the documented collection of activities that define the functional and operational specifications of the instrument and criteria for selection of the vendor, based on the intended purpose of the instrument. Design qualification (DQ) may be performed not only by the instrument developer or manufacturer but also may be performed by the user. The manufacturer is generally responsible for robust design and maintaining information describing how the analytical instrument is manufactured (design specifications, functional requirements, etc.) and tested before shipment to users. Nonetheless, the user should ensure that commercial off-the-shelf (COTS) instruments are suitable for their intended application and that the manufacturer has adopted a quality system that provides for reliable

equipment. Users should also determine the manufacturer's capability for support installation, services, and training. This determination might be aided by the user's previous interaction with the manufacturer.

INSTALLATION QUALIFICATION

Installation qualification (IQ) is the documented collection of activities necessary to establish that an instrument is delivered as designed and specified, and is properly installed in the selected environment, and that this environment is suitable for the instrument. IQ applies to an instrument that is new or was pre-owned, or to any instrument that exists on site but has not been previously qualified. Relevant parts of IQ would also apply to a qualified instrument that has been transported to another location or is being reinstalled for other reasons, such as prolonged storage. The activities and documentation typically associated with IQ are as follows.

Description— Provide a description of the instrument or the collection of instrument components, including its manufacturer, model, serial number, software version, and location. Use drawings and flow charts where appropriate.

Instrument Delivery— Ensure that the instrument, software, manuals, supplies, and any other instrument accessories arrive as specified in the purchase order and that they are undamaged. For a pre-owned or existing instrument, manuals and documentation should be obtained.

Utilities/Facility/Environment— Verify that the installation site satisfactorily meets manufacturer-specified environmental requirements.

Assembly and Installation— Assemble and install the instrument, and perform any preliminary diagnostics and testing. Assembly and installation may be done by the manufacturer, vendor, specialized engineers, or qualified in-house personnel. Manufacturer-established installation tests and guides provide a valuable baseline reference for determining instrument acceptance. Any abnormal event observed during assembly and installation merits documenting.

Installation packages purchased from the manufacturer or the vendor may, however, need to be supplemented with user-specific criteria.

Network and Data Storage— Some analytical systems require users to provide network connections and data storage capabilities at the installation site. When required, connect the instrument to the network, and check its functionality.

Installation Verification— Perform the initial diagnostics and testing of the instrument after installation.

OPERATIONAL QUALIFICATION

After a successful IQ, the instrument is ready for OQ testing. Operational qualification (OQ) is the documented collection of activities necessary to demonstrate that an instrument will function according to its operational specification in the selected environment. Testing activities in the OQ phase may consist of these test parameters.

Fixed Parameters— These tests measure the instrument's nonchanging parameters such as length, height, weight, voltage inputs, acceptable pressures, and loads. If the manufacturer-supplied specifications for these parameters satisfy the user, the test requirements may be waived. However, if the user wants to confirm the parameters, testing can be performed at the user's site. Fixed parameters do not change over the life of the instrument, and therefore never need redetermination. [NOTE—These tests could also be performed during the IQ phase (see *Table 1*); if so, fixed parameters need not be redetermined as part of OQ testing.]

Secure Data Storage, Backup, and Archiving— When applicable, test secure data handling such as storage, backup, audit trails, and archiving at the user's site according to written procedures.

Instrument Function Tests— Instrument functions required by the user should be tested to verify that the instrument operates as intended by the manufacturer. Manufacturer-supplied information is useful in identifying specifications for these parameters and in designing tests to evaluate the

identified parameters. Users, or their qualified designees, should perform these tests to verify that the instrument meets manufacturer or user specifications in the user's environment.

The extent of OQ testing that an instrument undergoes depends on its intended applications. Therefore, no specific OQ tests for any instrument or application are offered in this chapter.

Routine analytical tests do not constitute OQ testing. OQ tests are specifically designed to verify the instrument's operation according to specifications in the user's environment, and repeating the testing at regular intervals may not be required. However, when the instrument undergoes major repairs or modifications, relevant OQ and/or PQ tests should be repeated to verify whether the instrument continues to operate satisfactorily. If an instrument is moved to another location, an assessment should be made of what, if any, OQ test should be repeated.

OQ tests can be modular or holistic. Modular testing of individual components of a system may facilitate interchanging of such components without requalification. Holistic tests, which involve the entire system, are also acceptable.

PERFORMANCE QUALIFICATION

Performance qualification (PQ) is the documented collection of activities necessary to demonstrate that an instrument consistently performs according to the specifications defined by the user, and is appropriate for the intended use. After IQ and OQ have been performed, the instrument's continued suitability for its intended use is demonstrated through performance qualification. The PQ phase may include the following parameters.

Performance Checks— Set up a test or series of tests to verify the acceptable performance of the instrument for its intended use. PQ tests are usually based on the instrument's typical on-site applications and may consist of analyzing known components or standards. The tests should be based on good science and reflect the general intended use of the instrument. Some system suitability

tests or quality control checks that are performed concurrently with the test samples can be used to demonstrate that the instrument is performing suitably. PQ tests may resemble those performed during OQ, but the specifications for their results may be set differently if required. Nevertheless, user specifications for PQ tests should demonstrate trouble-free instrument operation for the intended applications. As is the case with OQ testing, PQ tests may be modular or holistic.

Testing frequency depends on the ruggedness of the instrument and the criticality of the tests performed. Testing may be unscheduled—for example, each time the instrument is used. It may also be scheduled for regular intervals. Experience with the instrument can influence this decision. It may be useful to repeat the same PQ tests each time the instrument is used so that a history of the instrument's performance can be compiled. Alternatively, the instrument may be incorporated into an integrated support system to assure that it remains continually qualified. Some system suitability tests or quality control checks that are performed concurrently with the test samples also imply that the instrument is performing suitably.

Preventive Maintenance and Repairs— When an instrument fails to meet PQ test specifications, it requires maintenance or repair. A periodic preventive maintenance may also be recommended for many instruments. The relevant PQ test(s) should be repeated after the needed maintenance or repair to ensure that the instrument remains qualified.

Practices for Operation, Calibration, Maintenance, and Change Control— Establish practices to maintain and calibrate the instrument. Each maintenance and calibration activity should be documented.

ROLES AND RESPONSIBILITIES

Users

Users are ultimately responsible for instrument operations and data quality. The user's group encompasses analysts, their supervisors, instrument

specialists, and organization management. Users should be adequately trained in the instrument's use, and their training records should be maintained as required by the regulations.

Users should also be responsible for qualifying their instruments because their training and expertise in the use of instruments make them the best-qualified group to design the instrument test(s) and specification(s) necessary for successful AIQ. Consultants, equipment manufacturer or vendors, validation specialists, and quality assurance (QA) personnel can advise and assist as needed, but the final responsibility for qualifying instruments lies with the users. The users must also maintain the instrument in a qualified state by routinely performing PQ.

Quality Unit

The role of the Quality Unit in AIQ remains the same as for any other regulated activity. Quality personnel are responsible for assuring that the AIQ process meets compliance requirements, that processes are being followed, and that the intended use of the equipment is supported by valid and documented data.

Manufacturers

Manufacturers and developers are responsible for DQ when designing the instrument. They are also responsible for validation of relevant processes used in manufacturing and assembly of the instrument. Manufacturers should test the assembled instruments before shipping them to users.

Finally, it is desirable that manufacturers and vendors should notify all known users about hardware defects discovered after a product's release; offer user training, service, repair, and installation support; and invite user audits as necessary.

SOFTWARE VALIDATION

Software used for analytical work can be classified into three categories: firmware; instrument control, data acquisition, and processing software; and stand-alone software. Although software validation is not the primary focus of

this chapter, the following sections describe in which cases this activity is under the scope of the analytical instrument qualification.

Firmware

Computerized analytical instruments contain integrated chips with low-level software (firmware). Such instruments will not function without properly operating firmware, and users generally cannot alter firmware design or function. Firmware is therefore considered a component of the instrument itself. Indeed, the qualification of hardware is not possible without operating it via its firmware. Thus, when the hardware (that is, the analytical instrument) is qualified at the user's site, the integrated firmware is also essentially qualified. No separate on-site qualification of the firmware is needed. Whenever possible, the firmware version should be recorded as part of the IQ activities. Any changes made to firmware versions should be tracked through change control of the instrument (see *Change Control,* below).

Instrument Control, Data Acquisition, and Processing Software

Software for instrument control, data acquisition, and processing for many of today's computerized instruments is loaded on a computer connected to the instrument. Operation of the instrument is then controlled via the software, leaving fewer operating controls on the instrument. Also, the software is needed for data acquisition and postacquisition calculations. Thus, both hardware and software, their functions inextricably intertwined, are critical to providing analytical results.

The manufacturer should perform DQ, validate this software, and provide users with a summary of validation. At the user site, holistic qualification, which involves the entire instrument and software system, is more efficient than modular validation of the software alone. Thus, the user qualifies the instrument control, data acquisition, and processing software by qualifying the instrument according to the AIQ process.

Stand-Alone Software

An authoritative guide for validating stand-alone software, such as LIMS, is available.[1] The validation process is administered by the software developer, who also specifies the development model appropriate for the software. Validation takes place in a series of activities planned and executed through various stages of the development cycle.

CHANGE CONTROL

Changes to instruments, including software, become inevitable as manufacturers add new features and correct known defects. However, implementing all such changes may not always benefit users. Users should therefore adopt changes they deem useful or necessary and should also assess the effects of changes to determine what, if any, requalification is required. The change control process enables them to do this.

Change control may follow the DQ/IQ/OQ/PQ classification process. For DQ, evaluate the changed parameters, and determine whether need for the change warrants implementing it. If implementation of the change is needed, install the changes to the system during IQ. Evaluate which of the existing OQ and PQ tests need revision, deletion, or addition as a result of the installed change. Where the change calls for additions, deletions, or revisions to the OQ or PQ tests, follow the procedure outlined below.

Operational Qualification— Revise OQ tests as necessitated by the change. Perform the relevant tests affected by the change. This ensures the instrument's effective operation after the change is installed.

Performance Qualification— Revise PQ tests as necessitated by the change. Perform the PQ testing after installation of the change if similar testing is not already performed during OQ. In the future, perform the revised PQ testing.

For changes to firmware and to software for instrument control, data acquisition, and processing, change control is performed through DQ/IQ/OQ/PQ of the affected instrument. Change control for stand-alone software requires user-site testing of changed functionality.

AIQ DOCUMENTATION

Documents obtained during instrument qualification should be retained in an accessible manner. Where multiple instruments of one kind exist, documents common to all instruments and documents specific to an instrument may be stored separately. During change control, additional documents may supplement those obtained during the qualification process, and both sets of documents should be retained and maintained in a suitable manner that allows for appropriate protection and access.

INSTRUMENT CATEGORIES

Modern laboratories typically include a suite of instruments and equipment varying from simple nitrogen evaporators to complex automated instruments. Therefore, applying a single set of principles to qualifying such dissimilar instruments would be scientifically inappropriate. Users are most capable of establishing the level of qualification needed for an instrument. On the basis of the level needed, it is convenient to categorize instruments into three groups: A, B, and C, as defined below. Examples of instruments in each group are provided. Note that the list of instruments provided here is for illustration only and is not meant to be exhaustive. It does not provide the exact category for an instrument at a user site. That category should be determined by users for their specific instruments or applications.

The exact grouping of an instrument must be determined by users for their specific requirements. Depending on individual user requirements, the same instrument may appropriately fall into one group for one user and another group for another user. Therefore, a careful selection of groups by users is highly encouraged.

Group A

Group A includes standard equipment with no measurement capability or usual requirement for calibration, where the manufacturer's specification of

basic functionality is accepted as user requirements. Conformance of Group A equipment with user requirements may be verified and documented through visual observation of its operation. Examples of equipment in this group are nitrogen evaporators, magnetic stirrers, vortex mixers, and centrifuges.

Group B

Group B includes standard equipment and instruments providing measured values as well as equipment controlling physical parameters (such as temperature, pressure, or flow) that need calibration, where the user requirements are typically the same as the manufacturer's specification of functionality and operational limits. Conformance of Group B instruments or equipment to user requirements is determined according to the standard operating procedures for the instrument or equipment, and documented during IQ and OQ. Examples of instruments in this group are balances, melting point apparatus, light microscopes, pH meters, variable pipets, refractometers, thermometers, titrators, and viscosimeters. Examples of equipment in this group are muffle furnaces, ovens, refrigerator-freezers, water baths, pumps, and dilutors.

Group C

Group C includes instruments and computerized analytical systems, where user requirements for functionality, operational, and performance limits are specific for the analytical application. Conformance of Group C instruments to user requirements is determined by specific function tests and performance tests. Installing these instruments can be a complicated undertaking and may require the assistance of specialists. A full qualification process, as outlined in this document, should apply to these instruments. Examples of instruments in this group include the following:

- atomic absorption spectrometers
- differential scanning calorimeters
- dissolution apparatus

- electron microscopes
- flame absorption spectrometers
- high-pressure liquid chromatographs
- mass spectrometers
- microplate readers
- thermal gravimetric analyzers
- X-ray fluorescence spectrometers
- X-ray powder diffractometers
- densitometers
- diode-array detectors
- elemental analyzers
- gas chromatographs
- IR spectrometers
- near-IR spectrometers
- Raman spectrometers
- UV/Vis spectrometers
- inductively coupled plasma-emission spectrometers

■ *1S (USP31)*

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[1] *General Principles of Software Validation: Final Guidance for Industry and FDA Staff,* U.S. Department of Health and Human Services, Food and Drug Administration, Rockville, MD, January 11, 2002. http://www.fda.gov/cdrh/comp/guidance/938.html (accessed September 2004).

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Expert Committee : (GC05) General Chapters 05

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Phone Number : 1-301-816-8319

- near-IR spectrometers
- Raman spectrometers
- UV/Vis spectrometers
- inductively coupled plasma-emission spectrometers

■ *1S (USP31)*

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[1] *General Principles of Software Validation: Final Guidance for Industry and FDA Staff,* U.S. Department of Health and Human Services, Food and Drug Administration, Rockville, MD, January 11, 2002. http://www.fda.gov/cdrh/comp/guidance/938.html (accessed September 2004).

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