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Analytical Instrument Validation According to Food Safety Management System (ISO 22000)

Technical Report vol.13

1. Background of the Birth of ISO 22000

Food safety and the peace of mind associated with food safety are important factors in our ability to engage in social living. Up until more than half a century ago, food production and consumption was conducted by limited means within limited geographical regions, but with improvements in division of labor and efficiencies, or in other words, globalization, troublesome incidents attributable to this food supply configuration began to occur. These incidents had the effect of raising concerns about food safety among consumers, and at the same time, it became widely recognized that "securing the safety of food was not only the responsibility of enterprises involved in food production, but that enterprises and organizations(*1) involved in the entire food chain each had a role to play in achieving this objective." With this background, ISO 22000(*2) was issued as an international standard in September, 2005.

(*1) ISO 22000 applies to all enterprises and organizations that directly impact the food chain, including feed producers, primary product producers (farms, fisheries, livestock producers), food manufacturers, retailers, restaurateurs and caterers, cleaning / washing / sterilization / disinfection service providers, transport and storage, as well as delivery services. In addition, the standard also applies to enterprises and organizations that are indirectly involved in the food chain, including equipment suppliers, cleaning agent and sterilization and disinfectant suppliers, packaging material suppliers, and suppliers of materials that come into contact with food products.

(*2) The formal name is ISO 22000:2005 Food Safety Management System - Requirements for any Organization in the Food Chain. Also abbreviated as FSMS.

2. Relationship Between ISO 22000 and HACCP(*3)

It is said that ISO22000 is based on HACCP. The concept of HACCP arose in the process of developing safe space food during NASA's planning for the Apollo project. Afterwards, it became the start of international standardization effort undertaken by the Codex Alimentarius Commission(*4), adopting it as the Codex HACCP Guidelines in 1993. This was received by the international community to the extent that every country in the world began to incorporate the HACCP into their respective laws. The HACCP consists of 12 steps and 7 principles, of which the most well known are "Principle 1: Hazard(*5) Analysis" and "Principle 2: Critical Control Points", the initials of which comprise the acronym for this food safety standard. The commonality between ISO 22000 and HACCP is underscored by the inclusion of Appendix B "Cross references between HACCP and ISO 22000:2005", at the end of the ISO 22000 document.
Due to the inherent shortcomings of the HACCP, which focuses primarily on the manufacturing process and which is adapted by limiting the targeted products according to the country, applicability of ISO 22000 is much wider since it addresses every food product in the overall food chain.

(*3) HACCP: Hazard Analysis and Critical Control Points
(*4) The implementation organization established in 1962 by the FAO (Food and Agriculture Organization of the United Nations) and WHO (World Health Organization) to develop food standards and guidelines under the Joint FAO/WHO Standards Program with the aim of protecting the health of consumers and ensuring fair trade practices.
(*5) Hazard refers to a harm factor, and can be classified as a "biological hazard (e.g. viruses, parasites, etc.)", "chemical hazard (e.g. pesticides, toxic elements, food additives)", and "physical hazard (e.g. metals, glass, plastics)".

3. Relationship Between ISO 22000 and ISO 9001(*6)

ISO 22000 is said to incorporate the concepts of both HACCP and ISO 9001. ISO 9001 is management system for product safety, while ISO 22000 is a management system for food safety. However, looking at ISO 22000, the commonality between ISO 22000 and ISO 9001 is underscored by the inclusion of Appendix A "Cross references between ISO 22000:2005 and ISO 9001:2000", at the end of the ISO 22000 document. For example, in addition to the ISO 9001 concepts of "top management participation" and "continuous improvement" being incorporated into ISO 22000, the overall composition is similar, such that it is considered to be aligned with and compatible with ISO 9001. However, there are great differences between the two with respect to the requirements elucidated in Clauses 7 and 8, with Clause 7 of ISO 22000 corresponding to HACCP.
After introducing the ISO-9001 management system, the ISO 22000 could not be introduced without examination, but the ISO 22000 system could be introduced without the introduction of ISO 9001. However, ISO 9001 concepts in the construction of an ISO 22000 system with would certainly enhance the possibility of its successful introduction.

(*6) The formal name is ISO9001:2000 Quality Management Systems - Requirements.

4. Introduction of ISO 22000 System

As explained above, ISO 22000 can be considered a risk management system based on the HACCP "food safety management tool" and ISO 9001 "continuous improvement system".
In the basic plan(*7) of Japan's Ministry of Agriculture, Forestry and Fisheries, the mention of disseminating and cultivating food safety management systems (ISO 22000) among the "measures for securing a stable food supply" foretell future advances in the introduction of ISO 22000 systems. Here it should be noted that ISO 22000 pertains to certification of enterprises and organizations, distinguishing it from the JAS system(*8), which certifies individual products.

(*7) Agricultural guidelines for actualizing the principles stipulated in the fundamental plan governing foods, agriculture and farming communities, and this fundamental plan submitted by the cabinet council in March, 2005.
(*8) JAS (Japan Agricultural Standards): JAS standard system based on the Law Concerning Standardization and Proper Labeling of Agricultural and Forestry Products

5. ISO 2000 Requirements with Respect to Analytical Instruments

Here, we will consider the relationship between food analysis business-related ISO 22000 and analytical instruments. The objective is to provide consistently reliable data for the individuals involved in analysis. Furthermore, there must be on-going evaluation of the performance of the instrument being used, as well as validation of analytical conditions and analysis procedures in order to ensure the quality of generated data.

There are many requirements related to measurement devices found in ISO 22000. Here we will focus on those of sub-clause "8.3 Control of Monitoring and Measuring."

Below are the requirements excerpted from this sub-clause<Note> (*9) (*10).

<Note> The contents taken from ISO22000:2005 are reproduced with the permission of the International Organization for Standardization, ISO. This standard can be obtained from any ISO member (Japanese Standards Association: http://www.jsa.or.jp) and from the Web site of the ISO Central Secretariat at the following address: http://www.iso.org. Copyright remains with ISO.

8.3 Control of monitoring and measuring

The organization shall provide evidence that the specified monitoring and measuring methods and equipment are adequate to ensure the performance of the monitoring and measuring procedures.

Where necessary to ensure valid results, the measuring equipment and methods used

a) shall be calibrated or verified at specified intervals, or prior to use, against measurement standards traceable to international or national measurement standards; where no such standards exist, the basis used for calibration or verification shall be recorded,

b) shall be adjusted or re-adjusted as necessary,

c) shall be identified to enable the calibration status to be determined,

d) shall be safeguarded from adjustments that would invalidate the measurement results, and

e) shall be protected from damage and deterioration.

Records of the results of calibration and verification shall be maintained.

In addition, the organization shall assess the validity of the previous measurement results when the equipment or process is found not to conform to requirements. If the measuring equipment is nonconforming, the organization shall take action appropriate for the equipment and any product affected. Records of such assessment and resulting actions shall be maintained.

When used in the monitoring and measurement of specified requirements, the ability of computer software to satisfy the intended application shall be confirmed. This shall be undertaken prior to initial use and shall be reconfirmed as necessary.

With respect to management of the analytical equipment, the general focus tends to be limited to the hardware. However, as specified above, the software(*11) as well as the hardware must be validated according to ISO 22000.

(*9) Here, it is loosely translated from "control of analytical instruments". Since ISO 22000 is not translated from the JIS standard as in the case of ISO 9001, the original English (or French) is the formal standard.

(*10) Sub-clause 8.3 is approximately the same as sub-clause 7.6 "Control of Monitoring and Measuring Devices" of ISO 9001.

(*11) In the case of ISO 9001, a similar requirement for software is specified for ISO9001 in sub-clause 7.6.

6. Computer System

Relevant to this discussion, an analytical instrument such as an LCMS system consists of the LCMS instrument and a computer, and this computer has software installed on it. The typical analysis flow using an LCMS system would be as follows.

Establish communication between the LCMS unit and the computer → set the analytical conditions using the computer → start analysis → analysis is carried out by the LCMS unit according to the analytical conditions set via the computer, and data are generated → the generated data are transmitted to the computer, where post-analysis and data output are conducted → data is then controlled by the computer

Thus, the LCMS unit and the computer have an inseparable relationship, and should be considered as a single entity comprising a system, which could be referred to as a "Computer System"(*12).

(*12) Analytical instrument could be referred to as a computer system in this Technical Report.

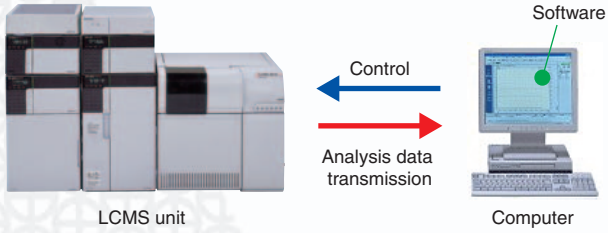


Fig. 1: Computer System

7. Validation of Analytical Equipment

The software which runs on the computer system is constantly being upgraded, and the broadening of its possibilities and application range never ceases. And this also pertains to the software directly related to the analytical instrument. For example, there may be any

number of ways, operationally, to set analytical parameters and analyze and control data. Therefore, some sort of validation is also required for the computer system. Computer system validation (analytical system validation) refers to verification that the system can fulfill the intended analysis objective, or in other words, verification operations related to accumulating objective evidence that the system can generate data with consistent reliability. Moreover, after the start of operations with the system, its state of validation must be maintained all the way up to the point of its disposal. In other words, validation is required throughout the life cycle of the system.

8. Performing Analytical System Validation According to ISO 22000

Now, the question is how to conduct validation of an analytical system according to ISO 22000. To illustrate this, we envision a model flow of the analytical system from purchase consideration to installation and operation, as shown below.

Model Flow

- Based on a survey of market demands for the analytical instrument, the instrument manufacturer designs, develops, manufactures and conducts validation certification of the instrument, and then engages in sales activities.
- On the other hand, in the department to which the user belongs, a new equipment introduction plan is presented, and consideration of the instrument purchase begins.
- The analytical instrument manufacturer suggests the most suitable instrument among its products based on the user's requirements specifications, and after completion of the sales contract, transfers that equipment to the user.
- After validating the equipment for the intended purpose, the user places the equipment into service.

The following flow chart illustrates the introduction and placement into service of the analytical equipment according to the envisioned model.

<Introduction and Placement into Service of Analytical Equipment : Flow Chart>

[User]
Clarifies testing and inspection to be conducted with respect to production and shipping of its own product, and develops a validation plan.

↓

[User]
Drafts a requirements specification document for the equipment, and presents it to the analytical equipment manufacturer (hereafter, "Vendor").

↓

[Vendor]
Verifies requirements specifications and suggests most suitable equipment for User.

↓

[User]
Examines the equipment and evaluates the Vendor.

↓

[User / Vendor]
User and Vendor enter into a contract.

↓

[Vendor]
Delivers the equipment to the User.

↓

[User]
Conducts acceptance evaluation of purchased equipment based on previously determined inspection plan.

[Vendor]
Provides service (IQ, OQ operations) if requested, based on the contract(*13).

↓

[User]
Completes validation of the equipment for the intended analysis, and begins regular operation.

↓

[User]
Conducts testing and inspection for production and shipping of its own products using the purchased equipment.

↓

[User]
Performs maintenance and repairs of the equipment.

[Vendor]
Provides service (maintenance, repairs) if requested, based on the contract(*13).

↓

[User]
Performs periodic qualification evaluation of the equipment.

[Vendor]
Provides service (OQ operations) if requested, based on the contract(*13).

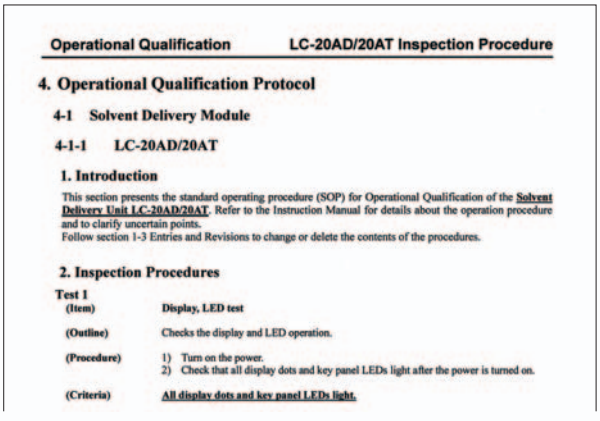
(*13) When commissioning an outside vendor to conduct IQ/OQ operations and maintenance work, it is advisable to ensure that the outside service company (or department providing the service) is certified according to ISO 9001. Here, IQ indicates Installation Qualification, OQ indicates Operational Qualification.

As is understood from the above flow chart, qualification evaluations such as IQ and OQ are only a part of validation, and conducting IQ and OQ does not constitute completion of validation. With respect to evaluation of software, there is a limit to the range of evaluation that can be conducted during verification at the installation site. In order to conduct a more certain evaluation, careful confirmation of the software specifications and inspection of the vendor (evaluation of development system and quality assurance system, etc. of the analytical equipment manufacturer) are carried out during pre-purchase consideration. In addition to this, conducting verification of a high-risk item upon delivery makes it possible to perform software evaluation more efficiently.

9. Actual Analytical Instrument Validation

For an analytical instrument taking the form of a system like an LCMS, the system is evaluated as a whole after each unit is first evaluated individually. Here, taking the LCMS-2010EV single quadrupole LCMS system as an example, we introduce one each of the evaluation procedures for the LCMSsolution software, the solvent delivery pump and the mass spectrometer.

<Test Item> LCMSsolution Software Alteration Check
[Outline]
Conducts the alteration check to verify that the program has not been altered.
[Procedure]
(1) Open LCMSsolution.
(2) Run the program alteration check.
[Criteria Example]
"Not altered" is displayed for all verification items.



Operational Qualification LC-20AD/20AT Inspection Procedure

4. Operational Qualification Protocol

4-1 Solvent Delivery Module

4-1-1 LC-20AD/20AT

1. Introduction

This section presents the standard operating procedure (SOP) for Operational Qualification of the Solvent Delivery Unit LC-20AD/20AT. Refer to the Instruction Manual for details about the operation procedure and to clarify uncertain points.
Follow section 1-3 Entries and Revisions to change or delete the contents of the procedures.

2. Inspection Procedures

Test 1

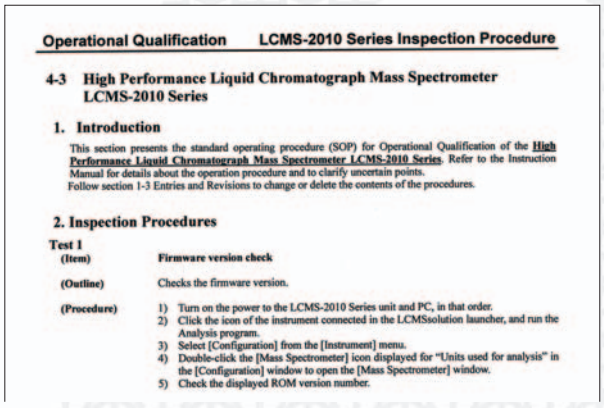
(Item)	Display, LED test
(Outline)	Checks the display and LED operation.
(Procedure)	1) Turn on the power. 2) Check that all display dots and key panel LEDs light after the power is turned on.
(Criteria)	All display dots and key panel LEDs light.

Fig. 2: LC-20AD OQ Text Example

<Test Item> LC-20AD Solvent Delivery Stability Test
[Outline]
Checks that the pump pulsation is within the specified range.
[Procedure]
(1) Connect a resistor tube to the pump outlet.
(2) Replace the mobile phase in the flow line with water, and begin pumping.
(3) Use the "PULSE CHECK" function to obtain the pressure fluctuation value.
[Criteria Example]
Pulsation: ≤0.20 MPa

<Test Item> LCMS-2010EV Autotuning Test
[Outline]
Verifies that autotuning is conducted properly for the mass spectrometer.
[Procedure]
(1) Open the LCMSsolution Autotuning window.
(2) Run Autotuning.
[Criteria Example]
Detector voltage remains with the range of -7 to -2.5 kV.
(Other criteria items omitted.)

The IQ and OQ must be executed in the way that was previously established in the requirements specifications. Therefore, if the IQOQ operations are to be outsourced, the procedures must be arranged beforehand.



Operational Qualification LCMS-2010 Series Inspection Procedure

4-3 High Performance Liquid Chromatograph Mass Spectrometer LCMS-2010 Series

1. Introduction

This section presents the standard operating procedure (SOP) for Operational Qualification of the High Performance Liquid Chromatograph Mass Spectrometer LCMS-2010 Series. Refer to the Instruction Manual for details about the operation procedure and to clarify uncertain points.
Follow section 1-3 Entries and Revisions to change or delete the contents of the procedures.

2. Inspection Procedures

Test 1

(Item) Firmware version check

(Outline) Checks the firmware version.

(Procedure)
1) Turn on the power to the LCMS-2010 Series unit and PC, in that order.
2) Click the icon of the instrument connected in the LCMSsolution launcher, and run the Analysis program.
3) Select [Configuration] from the [Instrument] menu.
4) Double-click the [Mass Spectrometer] icon displayed for "Units used for analysis" in the [Configuration] window to open the [Mass Spectrometer] window.
5) Check the displayed ROM version number.

Fig. 3: LCMS-2010EV OQ Text Example

Fig. 4: LCMS-2010EV System

Citations and References

* ISO 22000 : 2005 Food safety management systems – Requirements for any organization in the food chain (2005)
* ISO 9000 : 2005 Quality management systems – Fundamentals and vocabulary (2005)
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* ISO/IEC017025 : 2005 General requirements for the competence of testing and calibration laboratories (2005)
* ISPE/GAMP Forum: GAMP4, Good Automated Manufacturing Practice Guide for Validation of Automated Systems in Pharmaceutical Manufacture (2002)
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* Bilingual ISO 22000:2005 Food Safety Management Systems – Requirements for organizations throughout the food chain, Japanese Standards Association (2007)
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* Shigenobu Ikedo: Understands well how to interpret and make the best use of ISO22000, The Nikkan Kogyo Shimbun, Ltd. (2006)
* Tomio Yada: Guideline for Construction and Running of ISO22000 Food Safety Management Systems, Union of Japanese Scientists and Engineers (2006)

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