Levels of instrument control with chromatography data systems and the implications for compliance

Application Note

Introduction

The extent to which chromatography data systems have control over instruments can be decisive when laboratories must comply to regulations such as 21 CFR Part 11.

Most manufacturers offer data systems that provide complete or near-complete control of their own instruments. The data systems are able to create complete sets of raw and meta data, and good documentation. The data systems are also able to do error reporting and handling, sufficient enough to verify that the analyses were completed without technical failures. There is often some level of diagnostics, which are sometimes online and in real-time.

However, when these data systems offer control of other vendor's instruments—developed by sharing control codes or by reverse-engineering—the level of control often falls drastically.

This note describes various levels of instrument control, and provides a checklist for evaluating the capability of instrument control and data handling software.

Four levels of control

Instrument control can be implemented at different levels of complexity. The levels of control can access various instrument parameters and also influence the level of meta data collected and stored for compliance to 21 CFR Part 11. More advanced levels of instrument control provide diagnostics and feedback for better instrument service and ensure compliance to 21 CFR Part 11 requirements.

Level 1

This level of instrument control is the simplest whereby parameters are set manually on a panel or through a control module, and the signal is recorded by an analog-to-digital converter. This type of operation is sometimes the only way to integrate instruments from different manufacturers into one data and control system, or to incorporate older instrumentation that is not supported on a new data system. Since the instrument setpoints reside on the instrument or separate controller, it is not possible to capture them in data files or even make a printout of the settings. In this case, the analyst must record the settings by hand in a notebook. This approach is less satisfactory in a regulated lab, where meta data (instrument settings and parameters used to generate raw data) must be recorded so that raw data can be reproduced in exactly the same manner for review during audits.

Some analog-to-digital converters cannot receive binary coded decimal (BCD) information from autosamplers. In this case, it is impossible to link injections to sample name or sample ID. This makes it impossible to create an audit trail.

Level 2

In level 2 control, basic instrument parameters such as flow rate, wavelength, column or oven temperature, and solvent composition can be sent from controller to instrument.

Some instrument manufacturers share control codes with software vendors so that the software can set these basic parameters. In some cases, the codes are not shared, and the software manufacturer obtains the codes by reverse engineering. In this process, the codes are captured by analyzing the output of the instrument during operation.

Level of Control	Parameters Controlled	Compliance with 21 CFR Part 11
Level 1 Parameter set up on instrument, synchronization using external contacts to start and stop analyses, analog signal acquisition	Start/Stop (no digital instrument control or data acquisition)	*Metadata*: Instrument parameters must be documented manually *Device Checks*: Positive ID of sample vials may not be available (using bar codes or BCD input)
Level 2 Basic digital instrument control through LAN, RS232 or GPIB	Basic instrument parameters such as flow rate of LC pump or wavelength of LC detector	*Audit Trail*: Typically no instrument error information available, additional inspections are required to determine the validity of the measurements *Validation*: Difficult to support and validate if reverse-engineered
Level 3 Full digital instrument control through LAN, RS232 or GPIB	All control parameters, including injector program and method sequencing, wavelength calibration, and error recording	*Audit Trail and Metadata*: Full documentation of instrument parameters used to generate a result
Level 4 Advanced functionality	Handshake protocol between controller and device (provides active acknowledgment of correct receipt), self-diagnostics and early maintenance feedback (EMF), automatic tracking of serial and product numbers, electronic instrument logbook, supports advanced tagging of components such as column ID tags, instrument performs real-time data acquisition and synchronization independent of the computer	Advanced error detection and prevention *Validation*: facilitates the execution of instrument qualification and preventive maintenance, qualifies for device checks required by the rule, guaranteed and reproducible execution of data acquisition independent of the current data system load (facilitates the qualification of data integrity and traceability)

Table 1
The four levels of instrument control showing the corresponding parameters and degree of compliance

Because the manufacturer of the instrument may not be aware of or responsible for the implementation of the reverse-engineered code, updates to instrument firmware made during normal maintenance may result in the data and control software no longer functioning correctly with the instrument. Further, new modules that become available from the instrument manufacturer may not be supported on the software at the time of introduction and there may be a considerable delay until they become supported. Therefore it is always best practice to obtain officially supported software, either from a source that shares codes with the manufacturer of the instrument, or from the instrument manufacturer themselves, because they ensure that the firmware work with the software during the test phase of software development. Always check with the software vendor to make sure that the control codes are officially supported by the instrument manufacturer.

Error handling, diagnostics and automatic logging are not typically available at level 2 of instrument control. These features are often important for high-productivity labs to ensure maximum uptime and quick intervention when instruments need maintenance.

Level 3
Most instrument manufacturers are able to provide full instrument control for their own systems. This makes it possible to collect raw and meta data for good documentation and for an audit trail.

Error reporting and error handling can be quite sophisticated at this level, with shutdown-on-error protocols and electronic logging of error conditions. Diagnostics may or may not be available at this level, depending on how the instrument–software communication is designed. Generally, real-time diagnostics require direct instrument communication with the software. If the control is accomplished through an indirect buffering system, the diagnostics may only be of limited use as the feedback and handshaking is not available to the software.

Level 3 control may also include the function of early maintenance feedback. EMF was first used by the aeronautics industry whereby parts on aircraft are replaced on a routine maintenance schedule based on their expected optimum life. In this way, parts are exchanged before they are likely to fail. This ensures that the aircraft is always at peak maintenance during every day when it is in service. This maintenance scheme has been adapted for instruments—the user enters parameters for replacement of pump seals, detector lamps, and other parts based on their optimum lifetime for a particular set of assay conditions (that means for example, more frequently for seals when using high salt concentrations or high pH.)

This level of control also can provide tracking of module serial number and firmware revisions. This is a useful function not only for lab-wide maintenance, but also for documentation and function checks required by regulatory agencies.

Level 4

In level 4, all communications, including command transfers, are performed using a handshake. A handshake requires that the receiver of a data record must actively acknowledge receipt. For example, the controller sends a command such as *Start* to the device, the device interprets the command and acknowledges with *Okay, Start*. If the device is unable to execute the command, it sends a negative receipt such as *Not Okay, No Start* back to the controller. This system prevents situations in which the controller records a command as having been sent, but it has never been properly received or executed by the device.

For regulated labs, this additional capability makes it possible to track and document the proper functioning of instruments during analyses.

Communication interfaces

Communication through GPIB

GPIB is a parallel communication interface that can connect up to 15 devices on a common bus. All communications, including commands and data, use a hardware handshake for every byte (8 bits.) All devices connected to the bus participate in that handshake. As a result, every device on the bus can influence the ongoing communication and can cause severe communications problems such as hang-ups or data corruption. The cause can be as simple as a hardware failure of a printer on the bus or a firmware error in one of the devices. And, it can be difficult to implement power-up or down of instrument. GPIB interfaces are also limited to a distance of two meters from the controller device. Therefore, GPIB can be inconvenient to implement in the lab because of space constraints.

Communication through LAN

Local area network or LAN communication uses the transmission protocol TCP/IP. This protocol breaks the information being transmitted into packets, which can be checked for errors with a redundancy mechanism such as checksum. Checksum, unlike handshaking, is a running

	Speed	Error Detection	Remote Monitoring	Number of Devices	Power-down for idle Instruments	Qualification Requirements
GPIB	Fast enough for high-speed data acquisition	Bidirectional information can be sent, allowing for device checks according to 21 CFR Part 11	Monitoring instruments from remote devices requires extra instrument controller	Limited to a maximum of 15 devices on one bus	Power-down protocols can be problematic	Instrument controller must have operation qualification
LAN	Fast enough for high-speed data acquisition	Error detection and correction is built in checksum protocols, for data integrity according to 21 CFR Part 11	Remote status information is available without extra instrument controller	Unlimited	Power-down protocols are supported	Controller need not be next to instrument, controller is part of system and covered by system qualification

Table 2
Comparison of GPIB and LAN communication

total of all transmitted bytes attached to the packet and is used by the recipient to recalculate and compare with the original checksum. If there is a mismatch, retransmission is requested. This method of communication guarantees error-free data transfer and is excellent for implementing device checks and system checks such as those mandated by 21 CFR Part 11. TCP/IP communication is unaffected by idle instruments on the LAN and supports power-down of instruments that are not in use.

Instrument control checklist

This checklist allows you to analyze competitive control and data handling systems for remote status, firmware support, spectral data handling, error trapping and audit-trail requirements.

- ❑ LAN-based instrument control through industry-standard TCP/IP.
- ❑ Instrument connected through standard cables (RJ45) or network cabling (industry standards).
- ❑ Information about sample, pump and autosampler, Status of detector, lamp and heated column.
- ❑ Monitor all signals A, B, C, D, E, snapshot or real-time and spectra.
- ❑ Set instrument parameters remotely. Export real-time plot of signal data. Execute CP macro remotely to operate instrument.
- ❑ Display of instrument parameters and modules in color graphical windows for easy status recognition.
- ❑ Automatically export module serial numbers (meta data) and column data (TAG system).
- ❑ Acquire independent signals (A or B, or C...) instead of all signals.
- ❑ Create a list of all connected modules, with each module's firmware revision and serial number.
- ❑ Support new modules when hardware is introduced. Test and support for firmware upgrades.
- ❑ Record autosampler information continuously in electronic logbooks for data traceability and integrity.
- ❑ Track who, what, when and why for activities during instrument setup or parameters changes in audit trail.
- ❑ Audit trail information, including instrument ID and column information (admin-defined ID, automatic column and instrument usage tracking) according to predicate rules.
- ❑ Automated IQ/OQ protocols for instrument modules.
- ❑ Early maintenance feedback (EMF) to facilitate preventive repairs.
- ❑ EMF with step-by-step diagnosis to lead to problem and confirmation.
- ❑ Multimedia repair procedures built into software.
- ❑ Acquisition and storage of signal and spectral data to 21 CFR Part 11.
- ❑ Storage in database of peak purity data, spectral scans and isoplots.
- ❑ Acquisition of fluorescence scans with varied excitation and emission wavelengths to give three-dimensional characterization of sample.
- ❑ Extraction of signals from spectral data to determine optimum detection wavelength for each peak.
- ❑ Spectral library searches to obtain qualitative identification.

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