# The Quality Imperative: SAS Institute's Commitment to Quality

A corporate statement of SAS' commitment to product quality, service quality, and customer satisfaction

## Appendix 1: Regulated Industry Issues

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## Introduction

SAS is not a publicly traded company. However, many large customers rely on SAS to enable their compliance with regulatory requirements. SAS Legal Services, in conjunction with teams providing solutions for regulated industries, continuously monitor regulatory affairs worldwide. This appendix answers commonly asked questions from regulated customers, including those from the pharmaceutical and other industries.

Note that the FDA does not certify software tool vendors. We consider SAS a tool: our customers need to validate systems that they build with SAS, but they do not need to validate SAS software. SAS is developed using a controlled process that consists of distinct development phases. Quality control activities are performed during various phases to make sure that quality is built into the software. SAS understands FDA requirements for computerized system validation and can identify existing practices and procedures that conform to FDA expectations. SAS also understands the FDA-regulated industry's motivation to assess technology providers like SAS. Some validation methods for SAS procedures (PROCs) that are used extensively by pharmaceutical companies, as well as other SAS components such as actions or other routines, are covered in the section **Validating an Analytical Component**. The methods described might be useful in designing test cases to validate programs or applications that are built using SAS components. Companies must develop their own validation process for any tools that they use. For further details, see The **SAS Software Development Life Cycle** section in this paper, as well as the "Life Sciences" section on the Customer Success website (**sas.com/customers**).

Customers have inquired whether source code is available for an FDA audit if required for compliance needs. SAS would allow the FDA to examine relevant portions of the source code on a secure machine at SAS headquarters pursuant to appropriate confidentiality agreements.

## ISO 9001 Certification

The SAS entities with ISO 9001 certification as of this document's publication date are listed below. The list below has the potential to be incomplete, as new entities may have achieved certification since this paper's publication. To obtain a complete and updated copy of all valid certificates received by SAS, send email to **qualitypaper@sas.com**.

- SAS UK (SAS Software Ltd.) A complete and updated list of certificates obtained by SAS UK can be found here: **https://www.sas.com/en_gb/company-information/profile.html#compliant**
- SAS R&D Scotland (SAS Software Ltd. T/A SAS R&D Scotland)
- SAS Institute Australia Pty Ltd.
- SAS Italy (SAS Institute SRL)
- SAS Poland (SAS Institute Sp. zo.o)
- SAS Spain (SAS Institute, S.A.U.)

## ISO 27001 Certification

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- SAS UK (SAS Software Ltd.) A complete and updated list of certificates obtained by SAS UK can be found here: **https://www.sas.com/en_gb/company-information/profile.html#compliant**
- SAS Event Stream Processing R&D
- SAS R&D Scotland (SAS Software Ltd. T/A SAS R&D Scotland)
- SAS Italy (SAS Institute SRL)
- SAS Spain (SAS Institute, S.A.U.)
- SAS Institute Peru S.A.C.
- SAS Institute Australia Pty Ltd.
- SAS Portugal (SAS Institute, S.A.U.)

## Complying with Title 21 CFR Part 11

The United States regulation known as Title 21 CFR Part 11 (**http://www.ecfr.gov/cgi-bin/text-idx?SID=ea01d0a91871a45dca2497b337f677c4&mc=true&node=pt21.1.11&rgn=div5**), or the "Electronic Records; Electronic Signatures" rule, provides information about what constitutes trustworthy and reliable electronic records and electronic signatures. Many of our customers who are regulated by the United States Food and Drug Administration (FDA) are required to comply with this rule, which sets forth the criteria under which the FDA considers electronic records and electronic signatures to be trustworthy, reliable, and generally equivalent to paper records. CFR Title 21 serves as the predicate rule and has been in force for some time. Although the requirements of CFR Title 21 were originally written for the paper record, CFR Title 21 now explicitly applies to electronic records and signatures as well.

Part 11 does not outline details such as whether a record or signature is required, who signs it, and so on, because this is determined by the underlying predicate rules. Predicate rules are the rules that are set forth by the Federal Food, Drug, and Cosmetic (FD&C) Act, Public Health Service (PHS) Act, and FDA regulations. Part 11 governs the treatment of these records and signatures that fall under predicate rules when they are created and maintained electronically.

The FDA has issued industry guidance for the use of electronic health record data in clinical investigations (**https://www.fda.gov/media/97567/download**). In issuing such guidance, the FDA sought to assist sponsors, clinical investigators, and other interested parties in using electronic health records (EHRs) in clinical trials. This guidance clarifies recommendations on applying Part 11 electronic records regulations to electronic data capture (EDC) systems. Among other things, the FDA provides guidance on the use of interoperable or fully integrated electronic health records (EHR) and EDC systems, appropriate validation methods, recordkeeping requirements, and the use of certified and noncertified EHR technology. However, we recognize that this guidance provides nonbinding recommendations and that certain specifications may change. Therefore, we continue to monitor FDA regulations and guidelines that pertain to SAS or to customers using SAS software.

SAS technologies provide the capability to use SAS and implement SAS solutions in a way that is compliant with 21 CFR Part 11. We provide tools to help customers build a Part 11 compliant application. Compliance with this regulation ultimately depends on how your application or the SAS solution is installed and used, how users are trained, and other factors. Customers need to use SAS according to the system requirements, install it according to the installation instructions, and use the DATA step and each procedure or solution according to the user documentation.

Although SAS includes features that enable users to comply with 21 CFR Part 11, simply using SAS software or any of SAS' solutions will not automatically render a user compliant. All elements must be present in a proper environment to be 21 CFR Part 11 compliant, including adherence to compliant standard operating procedures. Users should refer to the predicate rule or consult the FDA or its guidance documents to determine whether their system is in compliance with regulatory expectations.

SAS customers can use SAS products to build data collection, analysis, and other systems that can be used in compliance with Part 11. They can also use programming languages such as the Java Programming Language, C#, and Visual Basic. We enable these clients to access SAS using the Integration Technologies API. Developers of such systems would need to determine which features are needed for the system that they are designing and then build the appropriate checks into the system. Such features could include audit trails, security checks, and electronic signatures.

Regarding audit trails and integrity constraints, the audit trail feature of Base SAS has the essential elements to address and enable the controls and procedures for a 21 CFR Part 11 audit trail. For more information about audit trails and integrity constraints, see the paper "Integrity Constraints and Audit Trails Working Together" (**http://www2.sas.com/proceedings/sugi25/25/aa/25p008.pdf**).

The FDA accepts a SAS transport format as a method for accepting and archiving data sets. The SAS transport format is an open format, has a free viewer, is used extensively in the industry, and has long-term support. Other software vendors can write transport format using the specifications described on the FDA and SAS Technology web page.

The FDA now requires all new CDER and CBER study submissions to use industry standard data structures (**http://www.fda.gov/ForIndustry/DataStandards/default.htm**). The FDA requires the CDISC Study Data Tabulation Model (STDM), Standard for Exchange of Nonclinical Data (SEND), and Analysis Data Model (ADaM) for exchanging electronic data and report-ready tables. See the **CDISC** section for more information about how SAS supports CDISC.

SAS addresses revision control with SAS tools, applications, procedures, and custom application interfaces (APIs or engines). SAS also interfaces well with other revision control software or filing systems such as Documentum. Custom engines for interfacing with clinical data management and electronic data capture systems (Medidata Rave is one example) have been developed. SAS/ACCESS can also be used to obtain repetitive versions of data from a Laboratory Information Management System (LIMS) or Clinical Data Management System (CDMS). The COMPARE and CONTENTS procedures can be used to monitor changes or revisions regarding content in data. Functionalities such as data integrity constraints and audit trails can be enabled to assist in this process. All this

functionality is supported by the SAS Life Science Analytics Framework that provides a real-time assessment of metadata structure and revisions,or through data management solutions such as SAS Data Preparation.

SAS has developed a 21 CFR Part 11 enabling technology known as SAS Life Science Analytics Framework. (See **https://www.sas.com/en_us/software/life-science-analytics-framework.html**) SAS Life Science Analytics Framework software was designed and introduced to specifically address the issues associated with 21 CFR Part 11 and the FDA's Guidance for Industry. The software provides these capabilities while offering an enhanced operating environment for managing clinical data, programs, logs, documents, and reports. Careful consideration was given to the intended performance with respect to data warehousing, analysis and reporting, electronic submissions, and related e-signature requirements. Application of both process and quality management has enabled the software to meet the intended requirements of the system's 21 CFR Part 11 functionality.

The Health and Life Sciences (HLS) R&D organization follows the SAS software development process. To meet the needs of their FDA-regulated customers, they have implemented an additional Quality Management System (QMS) to govern their software development. HLS R&D might use additional tools that are not generally used by SAS R&D but that are validated for use through the HLS QMS.

## CDISC

SAS has been an active supporter and platinum member of the Clinical Data Interchange Standards Consortium (CDISC) since 2000 with both resource and administrative support. For details, see **http://www.cdisc.org/**. SAS views the FDA's adoption and requirement of the Study Data Tabulation Model (SDTM), Standard for Exchange of Nonclinical Data (SEND), Analysis Data Model (ADaM), Define-XML, and other CDISC data standards for the electronic Common Technical Document (eCTD) as very significant events. We recognize the value that data standards give the industry in providing the key elements for improving global public health. Implementing and applying the CDISC standard in commonly used pharmaceutical industry software makes it possible for both product sponsors and regulatory authorities to benefit from the value of standard data structure and elements.

SAS provides standard processes within its production software to facilitate using SDTM, SEND, and ADaM data models, Define-XML, Dataset-XML, Operational Data Modeling (ODM), and laboratory data (LAB). See the SAS statement on CDISC support at **http://www.sas.com/en_us/industry/life-sciences/sas-cdisc.html** for more information.

## HIPAA and HITECH

The health care reforms made by Title II of the Health Insurance Portability and Accountability Act of 1996 (HIPAA) and the Health Information Technology for Economic and Clinical Health (HITECH) Act of 2009 provide federal protections for the privacy and security of individually identifiable health information. The United States Department of Health and Human Services has issued regulations governing HIPAA/HITECH that require health care organizations and other covered entities, as well as their business associates, to meet certain minimum standards of privacy and security with respect to health care data and databases. These regulations also direct how such data and databases are to be stored, viewed, accessed, and shared. SAS software includes security and other built-in features that customers can use to implement HIPAA/HITECH-compliant applications, though each customer must assess its specific needs in the context of its own computing environment. See "SAS Software Security Framework: Engineering Secure Products" (**http://www.sas.com/content/dam/SAS/en_us/doc/whitepaper1/sas-software-security-framework-107607.pdf**) for an overview. SAS is available to assist with HIPAA/HITECH compliance issues related to the use of SAS technologies and solutions.

## Sarbanes-Oxley Compliance

Satisfying the various requirements of the Sarbanes-Oxley Act generally requires management of data, processes, and technologies to ensure appropriate internal controls associated with financial risk. Compliance with SOX often involves a review of multiple systems and application of software tools and technologies that, among other things, must address configuration and change management, business process management, and documents and records management. SAS software can help customers achieve SOX compliance, though each customer must assess its specific needs in the context of its own computing environment.

## U.S. Government Configuration Baseline

As a vendor of desktop software products to the U.S. Federal Government, SAS validates, through our release management process, that our desktop software products on the Microsoft Windows platform comply with the U.S. Government Configuration Baseline, formerly known as the Federal Desktop Core Configuration (FDCC). R&D validates the software and archives the validation reports as a part of due diligence before releasing the software.

## Statement on Auditing Standards No. 70

Service Organization Control (SOC) and SysTrust certifications apply only to SAS hosting services. Learn more by visiting the SAS Trust Center (**https://www.sas.com/en_us/trust-center/sas-trust-compliance.html**).

**Release Information**

The version of this paper is January 2022.

Unless otherwise indicated, this document relates only to SAS 9.4, SAS Viya, and the products that are available with SAS 9.4 and SAS Viya. It also relates to services from the date of this paper forward. Quality processes are continually evolving. Therefore, SAS reserves the right to modify the processes described in this document at any time. If you are using SAS 9.4 and SAS Viya and have questions about processes in those releases, send email to **qualitypaper@sas.com.**