21 CFR Part 11

Software Platforms

Background

Any organization that, as part of fulfilling FDA requirements or statutes, chooses to maintain or submit electronic records, is subject to Part 11 in title 21 of the FDA's regulations. 21 CFR Part 11 applies to electronic records that are "created, modified, maintained, archived, retrieved, or transmitted under any records requirements set forth in FDA regulations." Software systems seeking to comply with GxP and that create, update, store, retrieve or transmit electronic records for use in submission to the FDA therefore need to be compliant with 21 CFR Part 11.

Note: Depending on the geography of intended use, the software system will also need to be compliant with EU Annex 11, Brazil GMP and other related guidelines. This document focuses on 21 CFR Part 11.

There are two sections to 21 CFR Part 11: Electronic Records and Electronic Signatures.

1. Electronic Records

Including, but not limited to (for closed systems):

a. Validation of systems to ensure its intended use and accuracy, and the ability to discern invalid or altered records.
b. Ability to generate complete and accurate records in paper and electronic form suitable for inspection and review by the FDA.
c. Ability to retrieve records throughout the retention period.
d. Limiting system access to authorized individuals.
e. Use of audit trails to record the date and time of operator entries that create, modify or delete records.
f. Use of system checks to enforce only permitted sequences of steps, if appropriate.
g. Use of system checks to ensure only authorized access to system, signatures, etc.
h. System checks to ensure data input validity.
i. Determination that operators who develop, maintain or use electronic records have the necessary background and training to perform the necessary tasks assigned to them.
j. The establishment of written policies that ensure individuals accountable for actions initiated under their electronic signatures.
k. Controls over distribution of, access to, and use of documentation for system operation and maintenance.
l. Revision and change control to document modifications to systems documentation.
m. Signed electronic records to contain the printed name of the signer, the date and time of signature execution, and the meaning (such as review, approval, responsibility and author-ship) of the signature.

2. Electronic Signatures

Including, but not limited to :

a. Each electronic signature is unique to an individual.
b. Before an organization assigns or makes the electronic signature of an individual official, the organization will verify the identity of the individual.
c. Persons using electronic signature certify to the agency that their electronic signatures are intended to be the legally binding equivalent of their handwritten counterparts.
d. Electronic signatures not based on biometrics shall employ two distinct identification components, such as identification code and password.
e. Persons who use electronic signatures based on identification codes and passwords shall employ controls to ensure their integrity.

Compliance

There are two aspects to compliance of a software system to 21 CFR Part 11 guidelines.

1. Software System Compliance

Responsibility of the developers of the software system.

2. Organizational Compliance

Responsibility of the developers of the software system.

For example, providing the ability to obtain audit trails for a given operation is an example of Software System Compliance, whereas ensuring that only authorized individuals have access to the software system is an example of Organizational Compliance.

Software System Compliance requires carefully documenting each element of a software system as it pertains to electronic records, and examining this element against each part of 21 CFR Part 11 to ensure compliance. For example, Software System Compliance for Validation (Under Electronic Records, a. above) will require generating test cases corresponding to all envisioned types of usage, and ensuring that the output of the system generates accurate and repeatable electronic records.

How Strand Can Help

Our background as it pertains to 21 CFR Part 11, along with key clientele, is in the Table below. Strand specializes in developing software for genomics/ bioinformatics applications. Examples of our work with key pharma, diagnostics, reagent, instrument, and biotech companies is separately shared. Notably, we are an Illumina ICA Implementation Partner.

#	21 CFR Part 11 Chapter	Key Components	Relevant Strand Software Development Experience	Key Strand Differentiation
1	Electronic Signatures	Validation	• **V&V** (Verification and Validation), • **performance improvements**, and • **DHF documentation** For a 510(k) submission of bioinformatics software accompanying a medical device **Key Client**: An oncology kit manufacturing and sequencing instrument company with Revenue > $4bn	• V&V of bioinformatics pipelines • V&V of software accompanying precision medicine
2	Electronic Records & Electronic Signatures	Data Retention, Data Retrieval, Data Integrity, Access, Audit Trails, Operational and Device Checks, Control for Open Systems, Electronic Signatures, Controls for Identification Codes and Passwords	Cloud-based software platforms with **RBAC, Audit trails, Electronic Signatures**, and other key security elements to ensure integrity of **PHI** **Key Client**: Large Bay Area/Swiss based with Re	• Experience developing software for security in the context of PHI/non-PHI

A more detailed background is in the following section.

Sketch of project.

There are 3 parts to an envisioned project.

1. **Core Software Requirements**
   The functionality of the envisioned software, as well as the set of electronic records that it will store, enable the retrieval of, etc, for submission to the FDA.

2. **Checklist for Software System Compliance**
   Based on item 1, a checklist for compliance of the Software System to 21 CFR Part 11.

3. **FDA consultant advisory**
   Based on items 1 and 2, the estimated number of hours needed to consult with an FDA specialist on specific items of compliance.

Items 1, 2, and 3 comprise the majority of the work needed to build a software system that maintains electronic records in preparation for submission to the FDA.

Strand Background

Strand Life Sciences, founded in 2000, provides the following services to the major instrument, diagnostics, reagent, and pharma companies:

1. Develop, validate, and interpret data from omics assays
2. Develop, test, and deploy platforms for the interpretation of omics data
3. Design and validate NGS panels
4. Analyze and interpret omics data

In particular, Strand has extensive experience over the last 22 years building software and solutions for the analysis and interpretation of -omics data, incorporating large curated and public sourced databases empowering the reporting of clinical high throughput data, in both research and clinical settings, using core Java, Java/ Spring, C++, C#, .NET, Python etc. Key applications built by Strand follow.

- ### GeneSpring

  GeneSpring is a data analysis software for analyzing and interpreting data from genomics, proteomics, transcriptomics and metabolomics experiments, as well as to perform integrated analysis. GeneSpring has over 25,000 citations in Google Scholar.

- ### Mass Profiler

  Strand is rebuilding Mass Profiler Professional for Agilent with a revamped user experience. The Mass Profiler platform facilitates compound annotation and integrated pathway analysis of metabolomics and proteomics data.

- ### Strand NGS

  Strand NGS is an integrated platform that provides analysis, management and visualization tools for next-generation sequencing data. It supports extensive workflows for alignment, RNA-Seq, small RNA-Seq, DNA-Seq, Methyl-Seq, MeDIP-Seq, and ChIP-Seq experiments.

- ### StrandOmics

  StrandOmics, Strand's NGS variant classification-interpretation-reporting platform, combines bioinformatics algorithms, curated databases, visualization interfaces and reporting capabilities for clinical reporting of both rare inherited disorders as well as somatic tumor profiling tests in CAP- and HiPAA-certified settings.

- ### Strand's NLP engine

  Strand has a mature NLP based publication and literature processing engine, which can process full-text/ abstracts from PubMed or other sources and extract various biomedical concepts like genes, drugs and diseases present in the text and also the relationship between those concepts. Extracted information is stored in the backend database for efficient querying, and has been incorporated into Strand's multi-omic analytical platforms such as GeneSpring.

- ### Curation and annotation

  Strand has a team dedicated to curation for genomics in multiple disease categories. The team, comprised of scientists with Master's or PhD degree in the biological sciences, many with at least a year of international training, have helped build Strand's curated databases for interpretation of variants in cancer (somatic and germline) as well as rare inherited disorders (germline).

All curation is reviewed and clinical reporting carried out in a CAP lab setting. The team has generated several thousand reports so far. In addition, Strand has rendered variant/gene/disease curation and annotation services to various clients from the diagnostic/pharma sectors. This includes multi-omic data compilation from multiple sources (public and client's internal), followed by clean-up, metadata curation, data harmonization and organization.

Strand has extensive experience in customer-facing support scenarios including in the above examples, via dedicated call center teams to provide tele-support for these software products - such as the GeneSpring software, StrandNGS software, etc.

A few recommendations from some of our key customers are mentioned below:

a. "We were very impressed with the quality of work and timeliness; you're definitely our go-to for bioinformatics consulting." - Chris Edlund, Oncology Lead, Illumina

b. "Strand NGS RNA-Seq is tough to beat for painless data exploration, well thought out GUI and concise, highly functional toolset and statistic." - Roy Williams, Dir. of Bioinformatics, Aspen Neuroscience

c. "Communication has been very easy, and the Strand software team has been very independent, which has made working together smooth." - Paige Taylor, Software Development Team Lead, Invitae.

24+ YEARS OF EXPERIENCE

80,000+ Genetic Tests Reported

500+ Projects Executed for Genomics Majors Globally

Presence in **20+** Countries

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