How to Meet Compliance and Records Requirements of the US Food and Drug Administration

John Avellanet describes an 11-step strategy on how companies can implement effective document control to avoid falling foul of the US FDA.

Records prove compliance. So why did 271 pharmaceutical or medical technology companies in the past 14 months receive regulatory enforcement notices from the US Food and Drug Administration citing records-related failures such as "failure to maintain accurate, complete, and current records"[1] or "failure to retain all required records"[2]? Did the executives in these companies confuse standard operating procedures with FDA compliance?

SOPs are just written intents, nothing more. Without the records and documents to prove you actually followed your SOPs, your intent to comply is just that – an intent, not a result. This article describes a strategy companies can use to avoid receiving a 483 observation – so-called because 483 is the number of the form on which the FDA makes its observations – following a good manufacturing practice inspection.

The FDA is so concerned about executives continuing to misunderstand this basic precept – that records, not SOPs, prove compliance – that, at a conference in 2008, Deborah Autor, director of compliance at the FDA's Center for Drug Evaluation and Research, took the podium to offer three suggestions on the matter: "Train your employees on proper record handling, assure the reliability of the data reported in records, and emphasise that everyone in the company is responsible."

But PowerPoint training and team exhortations will not keep your company from being cited for "failure to document all activities as required"[3] or "failure to establish a procedure to maintain records"[4]. Crucial to compliance is a systematic approach that takes advantage of the tactics with which you are already familiar from your quality system – SOPs, policies, training and audits – and adds controls and boundaries to identify your proof and maintain it. In short, you need a records and document control strategy.

More than two hundred and seventy companies in the past 14 months received regulatory enforcement notices from the US FDA citing records-related failures

Strategy summary

To implement such a strategy quickly – especially if yours is a smaller company – start with a focus on the basics that tie in directly with FDA compliance. Over time, as the strategy is implemented and your controls mature, explore adding other business records more typical of a records management programme – material safety data sheets, contracts, and so on. At first, though, the immediate goal is being able to prove FDA compliance and your medicinal product's safety, efficacy, and quality.

For an FDA-oriented strategy, there are 11 steps that a company should take. The details and rationale of each step are discussed below.

To implement records and document control quickly start with a focus on the basics that tie in directly with FDA compliance

Step 1: Establish baseline knowledge

When I conduct workshops for companies on implementing this type of practical, FDA-compliant records retention and control programme, the first thing I do is ensure everyone is working from the same starting point. I take my records and information career experiences – including dealing with litigation, not just inspection – and distill this to the base elements necessary so my clients will avoid critical mistakes and hidden pitfalls.

To start, I give a very brief quiz designed solely to elicit attendee assumptions about records. The sooner these assumptions are out in the open, the faster they can be dealt with, and the more quickly we can drive to a common knowledge base. Take a look at the question below and think about how you would answer it.

Which of the following are records?

- an SOP draft;
- meeting minutes;
- someone's scribbled comments on a printout of the new drug development project plan;
- email;
- voicemail;
- an extra wet lab sample (for example, the study is complete);

Ensure everyone is working from the same starting point

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- all of the above; or
- none of the above.

If you answered "all of the above," you are right; every one of those is a record. This is why I tell attendees to avoid the pitfall of attempting a delineation between information, data, records and documents. Records contain information or data. Information can be in documents, images, sounds or countless other formats (including materials like blood or marketing displays). In the eyes of regulators and the courts, they are all records.

Inevitably, this realisation begets the next common pitfall: the argument that "well, if records prove compliance, then let us just keep everything". Look again at the list above and imagine how quickly your business would grind to a halt if you had to retain every voicemail, every SOP draft, every email and every piece of paper with an employee or onsite contractor's scribbled comment. Of course, when you keep everything, trying to find anything useful in the mountain of records becomes a Sisyphean task. Ultimately, the philosophy of "keep it all and let the lawyers sort it out" does not make good business or compliance sense.

It makes sense to establish a plan for what you have to retain, why and for how long

What does make sense is establishing a plan for what you have to retain, why you have to retain it and for how long. Setting a uniform knowledge base for each team member allows you to move forward making informed decisions.

To ensure that everyone is "working on the same page", you have a handful of options. If you have the money and the time, consider attending a records management conference. You can find these through the records management professional society, ARMA International (www.arma.org). Be cautious, though; most of these organisations do not deal with the nuances of FDA compliance or medicinal product litigation.

Another option is to hire an expert to conduct an onsite workshop for your management team or staff[5]. The least expensive option is to find a pre-recorded seminar on CD or via internet download, and then share it with your colleagues; search the internet for phrases such as "FDA records management" or "FDA records retention."

Step 2: Research retention requirements

Once your team agrees on what constitutes records along with other elements of records maintenance, it is time to research the specific regulatory requirements that apply to your organisation. To avoid becoming overwhelmed with this task, limit your research to the FDA regulations – good laboratory practices, good clinical practices, and/or current good manufacturing practices – relevant to your business activities.

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It is useful to have a list of various FDA record requirements, along with the records required by specific adjacent rules. For instance, if you are conducting or gathering data from clinical trials in the US, you need to also include requirements from the Health Insurance Portability and Accountability Act.

Identifying required records is not as simple as looking at a subsection in the applicable regulations. At minimum, you will also need to examine statutes relevant to your FDA-regulated business activities such as HIPAA or the FDA Amendments Act, and you will need to cull through all the guidance documents issued since the regulations were published (in the case of the GLPs, this would be all GLP-related guidance since 1987). For pharmaceutical and biotechnology companies, the FDA has expected compliance with the International Conference on Harmonisation since 2008, so you will also need to examine applicable ICH documents.

Another point to note about FDA records retention requirements is that they are not static. In addition to changes driven by the agency, your business activities also drive retention variability. A record from a nonclinical GLP study conducted today only needs to be kept for two years after the study is complete (21 CFR 58.195(b)). Unless, that is, you need that record to support a planned submission in 2019; in that case, you need to retain it at least until two years after the agency has approved your submission (for example, given current agency review timelines, expect to get rid of a record generated today sometime in 2023 or 2024).

The sooner you can define when you plan to submit your request to the agency and what you need to support your product development and commercialisation strategy, the faster it will be to clarify the records you need to prove compliance, safety and efficacy, and the easier it will be to identify and implement the records controls required. One control to establish as early on as possible is the functional or departmental group that "owns" a record.

Step 3: Begin crafting a records retention matrix

Record "ownership" should be covered when you establish your team's baseline knowledge

Record "ownership" is a complicated subject and should be covered when you establish your team's baseline knowledge. For now, assume that the "owner" of a record is the department or function that generates or approves it. Purchasing orders are owned by purchasing departments, lab notebooks by the laboratories, budgets by finance departments, and so on. This holds true

whether the record is on paper or in some other format. You need to establish who "owns" each set of records required under the regulations specific to your organisation.

To begin crafting a records retention matrix, take the information already gathered from the previous strategy steps – the types of records the FDA expects you to have and their regulatory retention – and then add your list of record owners. It may be easiest to assemble this information in a table that comprises initially at least three columns: record types, retention period and functional owner[6].

Do not get stuck quibbling over who owns specific documents such as calibration records for the high performance liquid chromatography versus the electron microscope. Instead, use broader groups such as "laboratory equipment calibration records" – and include the departmental group that is responsible for these records such as your product development laboratories. You may be accustomed with putting down as the responsible party the head of a function (director, research & development). However, this can be defined later on in your SOPs; for now, it is sufficient to simply state the functional area.

Step 4: Assess the environment and plan controls

Compliance missteps speak to an organisation's culture and the imprints they leave in their wake, the documents and records of everyday activities and decisions. To define the controls you need, you must assess your company's culture.

Culture and behaviour are intertwined. Without a supportive culture, behaviour falters; without compliance-mindful behaviour, culture regresses. You can have in place the best quality system and documentation rules possible, but, without abiding behaviour, you would be better off just preparing for the inevitable FDA 483 observations, warning letters and court cases.

In conducting records management audits, the following questions are among those that can help discern the underlying culture and individual attitudes:

- when was your record inventory last updated and verified?
- in cases where someone is unsure as to whether a record should be kept or thrown away, what is the usual decision taken?
- who is the person in charge of electronic records? and
- if a fellow scientist in the lab down the hall needs information from a study you conducted, how does she or he get it?

There are more questions to ask, but, for now, notice their pattern – none of them would result in a "yes" or "no" answer and they all avoid the possibility of a defensive answer (for example, none of them starts with "why"). The questions themselves are innocuous and fact-gathering; the responses speak to the culture.

If answers to these questions are similar to those below, you know you have a problem:

- "Record inventory? Do you mean what chemicals do we have?"
- "When we are not sure what to do with a record, we just keep it."
- "The people in charge of electronic records are supposed to be IT, but as you know they are tend not to keep on top of the matter," or "all that stuff on electronic records is right here in this drawer on these CDs"; and
- "Is the scientist down the hall that wants the information from my study in analytical chemistry or...quality control?"

The more cultural factors inhibit good compliance practices, the more controls you will need to establish and monitor. These controls should focus on ensuring information integrity, whether in paper or electronic form. Base your controls on a risk assessment of your environment, considering risks from missed signatures to computer viruses.

Make certain to address three common problems that lead to FDA 483 observations:

- uncontrolled changes (in materials, protocols, etc);
- equipment problems (including untrained or inexperienced personnel); and
- absence of contemporaneous results records.

In addition, be sure to identify controls you may already have that you can leverage, such as:

- inventory management systems;
- calibration and maintenance programmes;
- protocol and deviation approval SOPs; and
- internal quality audits.

Ensure that each control lines up with typical quality system controls, minimising redundancy and cost and further reinforcing your quality system.

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Step 5: Inventory information locations

The next step of the strategy is to conduct an inventory of where the records reside in your organisation. There are four ways to go about this:

- send out a questionnaire;
- conduct one-on-one interviews;
- undertake detailed audits of your network, offices and labs (and any other storage areas); or
- hire an outside expert to help you.

A combination of all four is the best way to obtain the information you need while containing risk and cost. The most expensive alternative is to simply outsource the inventory; the least expensive is to attempt it all yourself.

Tailor your approach based on the size of your company and its complexities. If you are in a start-up company with fewer than 20 people, conducting the inventory yourself is very viable. For virtual companies and mid-size organisations, it can be useful to attend a workshop on the matter and then have the workshop organiser help implement the rest of the programme, either directly or remotely. For large, multinational companies, it would be valuable to attend a few workshops to establish the baseline knowledge across various management teams, and then have the workshop organiser help put together a request-for-proposal to outsource the global inventory audit with local on-site teams.

Ensure your inventory is "as-is" – now is not the time to start moving records from one location to another. At the very least, identify what you have and do not have, where the records are (or ought to be) and in what format they exist.

Step 6: Complete the records matrix

With this information, you are ready to complete your records retention matrix, which was first discussed in Step 3. Populate the other columns in the table with the data gathered in the inventory. You will find that some records that represent your accountability under the regulations (for instance, clinical records) are not in your possession. This is true for most firms that outsource some aspects of their business functions, from outsourced clinical trials to payroll or personnel departments. For now, simply note what records are elsewhere (see Figure 1 for an example).

Figure 1. Example of a records retention matrix				
Record type	Retention period	Functional owner	Location	Format
Lab equipment calibration logs		R&D labs	R&D record storage room	paper
Clinical consent forms		Clinical project team – Product Alpha	ABC clinic	paper
Adverse event report raw data		Clinical project team – Product Alpha	ClinDATA company	electronic

The difficulties involved in handling records between outsourced suppliers and collaborative partners is complicated and should not be underestimated. The more your records network stretches across outside entities, the more you will need outside help to work with you and your legal counsel to define specific risks, tactics, and controls. When structuring supplier and partner contracts and quality systems records controls, you should keep in mind a simple rule: never put in place a control you are unwilling or unable to enforce[7].

Step 7: Draft records management policies and SOPs

You also need to write and implement a set of records management policies and SOPs that tie into your quality system (remember: records prove compliance). At the very least, consider one high-level, overarching "records and information management policy" and six SOPs that cover the following:

- retention requirements;
- records disposal;
- annual review;
- confidentiality, security and privacy;
- long-term archival; and
- litigation disposal-suspense.

Depending on the level of detail to which you aspire in your quality system, more SOPs can be added specific to the record types involved. Among the many SOPs I have seen were some that focused just on laboratory notebook distribution, some on transporting records to and from

long-term archival and some on computer equipment troubleshooting log handling. As you grow comfortable with your FDA-compliant records retention structure, you will be a better judge of what other SOPs you might need; for now, though, consider limiting yourself to just the high-level policy and the above list of six SOPs.

Your retention requirements SOP spells out items such as your records retention rules (does retention start after the record is created or after the business activity under which the record was generated is complete?), what needs to be retained (is it the approved SOP, the draft SOP, or both?) and who is allowed to make modifications to your records matrix versus who needs to review and approve such changes.

Records disposal is the records management profession's terminology for approved destruction of previously required records (for example, after keeping the nonclinical GLP-study record for two years, you decide not to pursue a submission and can now dispose of the record). Your records disposal SOP needs to cover who is allowed to make these decisions, what authorisation is required and so on.

The annual review SOP lays out the process personnel need to go through periodically to review their records – in their offices, network storage locations, computers etc – to ensure they are retaining appropriate records still in use while sending "closed" records off to long-term storage.

The SOP on confidentiality, security, and privacy can cover basic rules for the confidentiality of company records, the privacy of individual information (such as medical records) and the minimum security criteria expected – locked storage rooms or file cabinets, password protected network shares and so on.

The SOP on long-term archival should discuss how you store your records – whether in paper or other format – for the long-term. Remember that some records may move from a two-year retention period to a ten- or twelve-year period, and vice versa, depending on your business activities; clarify the process involved so that you do not accidentally keep something too long or mistakenly throw away something you needed to retain. If you are ever involved in litigation, be aware that accidental loss of records has resulted in multimillion dollar court fines.

Your SOP on litigation disposal-suspense needs to spell out when to stop destroying records, authorisations and how notification works.

Some of these SOPs can be purchased as templates over the internet. Do not just put your name and logo on the templates. Well crafted SOPs and policies tailored to your business are critical. Your records and document control SOPs will be some of the first documents scrutinised in any lawsuit, much less an FDA inspection. Getting outside help – along with your legal counsel's advice – will define your success and your liability.

Step 8: Implement and train

When it comes to implementation, you have two choices: either all at once or piece by piece. Personally, I tend to favour the "at one stroke" approach, expecting to improve and refine the programme over time. I have seen far too many piece-by-piece implementations waylaid in midstream as business priorities or executive sponsors changed over the course of a drawn-out attempt to establish a programme. If you have not been able to implement this type of programme (due to the size and complexity of your organisation) in less than a year, and preferably under 90-180 days, seek outside help.

As part of your implementation, you need to train your staff. To help you avoid potentially embarrassing situations, there are two important steps to implement. First, as part of any baseline knowledge workshop, have your records management expert work with you to "train-the-trainer" so you can conduct staff training yourself. Second, consider scheduling an annual review (see below) as soon as possible after training; make sure a mock review is part of your train-the-trainer training. The annual review is where you reinforce the programme rules and require personnel to demonstrate they understand their accountabilities and tasks.

Step 9: Revise current quality SOPs to reference records SOPs

As you implement the retention programme, you will need to initiate a change process to revise each of your quality systems SOPs (as appropriate) to integrate with the various retention rules and your records requirements programme. For each procedure, draw out the types of records generated as a result of following the SOP. For instance, your incoming materials inspection process may generate a signed or "quality checked" stamped bill of materials or packing slip; your training process might generate attendance sheets, a training outline or agenda, the training presentation slides, and the trainer's specific notes. Having a flowchart of each of your quality systems' procedures will greatly simplify your revisions.

A retention requirements SOP spells out items such as who is allowed to make modifications to your records matrix versus who needs to review and approve such changes

Well crafted SOPs and policies tailored to your business are critical

Consider scheduling an annual review as soon as possible after training staff in records requirement rules

If you are still insistent on adopting a piecemeal approach to implementation, note that this is the most common point at which efforts bog down.

Think of all the various tweaks and changes your colleagues would like to make to multiple SOPs. As soon as they hear you are going to be revising all the SOPs, expect the organisational politicking to commence; at its worst, your records retention efforts will be swept up into a big "let us revise all our SOPs" project. For this reason alone, consider implementing your programme all at once, adding the records references to any new quality SOPs currently under draft, but otherwise simply tackling your previous quality SOPs over time as part of your normal revision schedule.

Consider implementing your programme all at once

Step 10: Conduct an annual review

After you have implemented your records retention programme, and preferably immediately following training, conduct an organisation-wide records review. This is a supervised review of records conducted by all your employees to determine what records they have in their possession (no matter how thorough you think your inventory was, it is highly likely that you missed something). You will need a form for documenting that each employee reviewed their records, another form for listing what was sent off to archive, and, depending on your organisational controls, a summary form for each department or functional group. The first time you hold this review, it will take each employee at least one to three days (the longer they have been with the organisation, the longer it will take). Consider this first review as an annual review week; from that point forward, just a day or two a year will suffice.

I have referred to this as an "annual" review, but some practitioners suggest holding these quarterly or bi-annually. There is no "right" answer. My experience is that getting management and staff to agree to pause normal business once a year, for at least a day or two, is hard enough; trying to schedule a review every quarter calls for a level of authority and commitment that records retention does not generally command.

Step 11: Audit and report in your QSMR

The final step in our strategy is to incorporate a review of records and their controls into your internal quality audits. Flag problems for further scrutiny like missing signatures or out of order approvals (on a series of progressively timed activities); these are points FDA inspectors are trained to look for and so should you.

Incorporate a review of records and their controls into your internal quality audits

When you hold your quality systems management review (QSMR), review your records management and controls. In addition, ask the following questions: How are we doing on the records matrix? How are our record control SOPs holding up? Did we index all the records from that clinical site before we sent the boxes off to storage? What about the data backup tape? Have any new expectations from the FDA come out since last year?

Final thoughts

All of us create and manage a great deal of information every day, often without thinking about it: voicemails, emails, faxes, letters, notes, memos, calendars, maintenance logs, spreadsheets and so on. Some of that information is important, some is not. The FDA has defined what it expects to prove regulatory compliance. It is up to you to create this proof and maintain it.

It is up to you to create proof of regulatory compliance

If you cannot control your records, you cannot hope to convince regulators you have controlled the safety, efficacy and quality of your products.

Are you ready?

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