

# A Question of Time (and Date)

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**Accurate and precise time and date stamps are critical to ensuring integrity of the data and results generated by any computerized system used in any chromatography laboratory.**

## In the Real Paper World

When you write up your observations and notes in a traditional laboratory notebook there are a number of features that help to ensure data integrity. The notebook pages are sequentially numbered and they are all bound together so if a page is removed, it is immediately obvious. When recording observations in the notebook, the order of the write up is important and is enforced by the sequential or linear pagination of the notebook. The author signs and dates the recorded information and this is witnessed by a second person who signs and also dates when they reviewed the work. Note that it is not usual to time AND date signatures in a laboratory notebook.

## Working in an Electronic Environment

Converting from paper to electronic working, there is not the same linear sequence that occurs in the paper world as the records generated are based around the application software operation. The workflow of the computerized system will define the way that the software works but users can do many things within this. For example, a chromatography data system will set up the injection sequence for sample injection, acquire data from the chromatographic analysis and then process the data to produce results.<sup>1</sup> However, once data have been acquired, a user can review and process a chromatogram several times before a result is finally accepted. Owing to the speed of computers, there is a need to record BOTH the time and the date of any event in the system.

The files and results (both are electronic records) produced by a computerized system will not usually be arranged in the linear sequence seen in the laboratory notebook. If you are unlucky they will be stored in directory structures, which may mean you have to have file naming conventions to organize the data. If you are lucky the system is organized via a database and most of this work is done for you behind the scenes. To capture all creations, modifications and deletions to data there is an audit trail that acts as the mortar linking all the bricks together to build up the time sequence of events.

However, fundamental to the operation of the software application and the audit trail is an accurate and precise time and date stamp. Without this it will not be possible to

- link a time and date stamp to any electronic record. For example, file creation, records modification etc.
- build up a logical sequence of events
- establish the integrity of records and actions.

## Importance of Accurate Stamps

It cannot be overemphasized enough that an accurate and controlled time and date stamp is the cornerstone of data integrity within the laboratory and throughout the organization. Without it you have a situation where you cannot trust anything generated by any computer. ISO Standard 17799 on Information Management Security in section 9.7.3 discusses Clock Synchronization:<sup>2</sup>

*"The correct setting of computer clocks is important to ensure the accuracy of*

*audit logs, which may be required for investigations or as evidence in legal or disciplinary cases. Inaccurate audit logs may hinder such investigations and damage the credibility of such evidence.*

*Where a computer or communications device has the capability to operate a real-time clock, it should be set to an agreed standard, (e.g., Universal Coordinated Time (UCT) or local standard time).*

*As some clocks are known to drift with time, there should be a procedure that checks for and corrects any significant variation."*

This is not a pharmaceutical or healthcare regulation but a general standard for any computerized system operating in any organization. You do this because it's good business sense to do so.

## Computer Practices

Of course, there is a generally accepted view that when something is performed by a computer it must be true simply because the computer says so. Well sorry to be the bearer of bad news but things are a little different to what you believe. In 1990, the US Environmental Protection Agency (EPA) commissioned a report by Booz-Allen Hamilton<sup>3</sup> to evaluate the automated standards used in automated clinical laboratories in comparison to those used in environmental laboratories that reported data to the Agency. One of the working practices used in environmental laboratories quoted in the report was between 10 and 12 laboratories that used a technique known as "time travelling". Dubious is one of the words that you can use to describe this practice, fraudulent is

another. As we are concerned with time and date here, we'll focus on just a single feature — time travelling. Just like Doctor Who and his Tardis time machine, analysts found that they could also travel in time although it was limited to hours and minutes rather than millennia.

There are some EPA analyses where time is a critical issue: the sample must be taken and delivered to the laboratory within six hours. If the sample arrives after this time it must be rejected and a new one taken. However, for a laboratory with a LIMS used for sample reception, it is a relatively simple task for a system manager to change the clock back a few minutes. Now when the sample was received using the LIMS — lo and behold — the time of sample receipt was within the six hour time window allowed by the EPA. If inspected the computer says so and must, therefore, be right.

### 21 CFR 11 and FDA Guidance

The FDA is also interested in time stamps for the same reasons that ISO are: to ensure that any data and electronic records generated by a computerized system, such as a chromatography data system are trustworthy and reliable. Time stamps have been on the periphery of the regulation since the publication of 21 CFR 11 in 1997.<sup>4</sup> Originally in the preamble to the original regulation there was a note that time should be local to where the signer was. However, this gave rise to a little problem for systems working across time zones — it was technically impossible. The time stamp for data originates at the server where the data are stored rather than at the client where the data may be generated. If the server is located in a different country you get a different date and time stamp compared with where you are located.

In a draft Guidance issued in 2001,<sup>5</sup> the FDA changed their stance and stated that systems have to be implemented with a clear understanding of where the time stamp is located in a Part 11 Guidance specifically on time stamps. In 2003 in the Part 11 Scope and Application guidance the FDA stated as a footnote:

*“Although we withdrew the draft guidance on time stamps, our current thinking has not changed in that when using time stamps for systems that span different time zones, we do not expect you to record the signer's local time. When using time stamps, they should be implemented with a clear understanding of the time zone reference used. In such instances, system documentation should*

*explain time zone references as well as zone acronyms or other naming conventions.”<sup>6</sup>*

If time and date stamps are so fundamental to data integrity, you may ask the question, why is this not a fundamental part of the Part 11 regulation? When the FDA issues the new draft Part 11 — possibly sometime this year — perhaps

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### FDA Time Stamp Guidance

The FDA issued in March 2002 a draft guidance for industry on time stamps<sup>5</sup> and then withdrew it in February 2003. Notwithstanding the withdrawal, this guidance has good useful information and the key points and discussions for CDS applications are

- The time stamp needs to be accurate to “within a minute”; this is best interpreted as  $\pm 1$  minute.
- The location of the time stamp needs to be defined. For a system working on one site this is not an issue and is also pretty self-evident. However, for CDS that is operated across countries and time zones, this is critical. What happens if the network is down? How will local laboratories cope until the system is restored? What happens to the time stamp in these instances?

Knowing how the system handles times is the key issue here. In the final version of the Part 11 Scope and Application guidance there is a footnote that confirms that the FDA still wants the location of the time stamp to be defined.<sup>6</sup>

The guidance makes no reference to summer and winter daylight savings or to leap years. Typically these changes will be managed by the operating system, which requires an accurate time and date stamp setting and you may want to check that these have occurred the next working day after the event.

### Issues for Time and Date Stamps

Therefore, as it is fundamental to electronic record integrity regardless of the laboratory you are working in, we need to consider the following issues with time and date stamps:

- Accuracy of the time stamp

- Format of the time stamp
- Identification of the time zone and the impact of a chromatography data system working across different time zones.
- Unambiguous date format
- How is the time and date checked? This can be a combination of procedural and/or technical means. In addition, who is authorized to make changes to the

date and time and as a corollary who is not allowed to make changes to the time?

### Date Stamps and Their Format

If presented with a date of 05/09/04 what does this mean? Well it depends where in the world you are and what date format you use. You have three basic options:

1. 2005 September 4th (based on an ISO standard for date and time that starts with the largest part — the year and works down)
2. 5th September 2004, based on a European use of date formats
3. May 9th 2004, based on an American date format.

If you were planning on meeting “someone special” you could be waiting for a long time — or miss them altogether. So we need to use an unambiguous date format, especially in multinational companies where US and European chromatographers are working.

Personally, I prefer the US military date format which is DD MMM YYYY which means that there is no possibility of confusing the day and month as the month is spelt out: 04 SEP 2005. Another alternative when using a CDS is to implement windows long date formats in the operating system and/or software application. Here the date format is presented as September 04 2005. Regardless of your approach the time format needs to be documented in your user requirements specifications.<sup>1</sup>

### Stand-alone CDS Systems

Time stamps for stand-alone CDS systems are probably best set and maintained manually. Although there are technology options, they will be relatively expensive to implement on a number of individual workstations. Therefore, you'll need a manual procedure with records to show

## Questions of Quality

that the time stamp has been checked and maintained against a standard time source (e.g., speaking clock or another reliable time source). How often you will need to check the time stamp will vary. As a suggestion start on a monthly basis for the first six months then review how accurate the time stamp has been over this period and if you have needed to adjust the clock. You can then lessen the frequency if necessary on the basis of experience. You will need to maintain a log of who checked the computer clock, the computer time, the standard time and if any adjustment was made.

Being realistic and practical this is a waste of time (!) and resources especially when coupled with the need to manually back up individual systems. Ideally all stand-alone CDS systems should be networked to ensure that time stamps are maintained from a single source within the network.

### Networked CDS Systems

This is by far the easier and preferred option for setting and maintaining time stamps. Within your IT network a server provides the time stamps for all other servers and workstations. As a minimum each time a user logs on to the network from a workstation the time stamp is updated automatically. The operating system can also be set up to update the time stamp during the time that a workstation is logged on (e.g., hourly if required).

Trusted time sources are available to automatically check and correct the network clock; this can occur in a number of ways:

- Network Time Protocol (NTP) where the time server accesses a time source on the Internet
- Time sources from the National Observatories of some countries (e.g., US Naval Observatory has atomic clocks in Denver and Washington and there is the Frankfurt atomic clock for Europe and the UK has a time source at Rugby)
- Global Positioning Satellite (GPS) system can also provide a Universal Coordinated Time signal that can be used with the appropriate equipment to provide a check of server time.

The time signal is then interpreted by the operating system to the local time zone and any daylight saving that has been implemented.

Suggested checks of the time setting could be limited in these instances to seeing if daylight savings, if implemented,

have occurred every spring and autumn and if leap years have been incorporated every four years.

### Validation Issues

Some of the issues to be considered when validating a chromatography data system for time and date include

- Defining the time zone and format and date format in a user requirements specification (URS) or equivalent document. Include in this the time zone reference such as EST: Eastern Standard Time or GMT: Greenwich Mean Time.
- You should also note if the operating system is enabled for automatic summer and winter time daylight saving. There is a slight problem here for global systems operating between North America and Europe. Daylight saving is the same in the autumn when the clocks go back, however, there is a week's difference when they go forward. Europe goes forward at the end of March and North America does this a week later in early April. Check where the server is and if daylight saving has been enabled.
- The specifications for the system should state how the time is set and a procedure should say if it is checked either automatically via a trusted third party or by an operator. Even for clocks that are linked to trusted third parties, there needs to be an occasional check to ensure that all is in order but who can do this needs to be defined.
- For CDS systems operating over time zones you need to include a check of the time and date stamps from sites in different time zones. One aspect that can be forgotten is if the WAN or network is not available, the system can buffer data in the local A/D unit or data server. If this unit does not have a clock the buffered data will not have a time stamp until connection to the server is restored — you could get a nasty surprise when you look at the date and time stamps of this data.

### Summary

Time and date are important elements of data integrity for all chromatography laboratories, and having accurate and reliable date stamps will give confidence in data produced by a system.

### References

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