Data Integrity landscape of the Indian pharmaceutical industry

Laboratory systems have been scrutinized for rigorous Data Integrity audits in recent years. The warning letters and 483 citations issued to laboratories have been disproportionately large. Shimadzu recognizes its obligation to ensure the rich tradition of assisting their customers in achieving business excellence. Their world view of business includes not only providing the 'best in class' laboratory instruments and networks, but to also work very closely with their customers to address challenging industry issues such as Data integrity. In pursuit of that goal, Shimadzu recently conducted its 3rd Informatics User Forum, iForum 2016. It consisted of a series of conferences in the cities of Delhi, Ahmedabad, Bengaluru, Hyderabad and Mumbai. Over 750 delegates from over 120 companies attended. The conference theme was 'Laboratory Automation with Compliance'.

The core team

The core team of conference presenters consisted of Dr. Deepak Haldankar, a pharmaceutical industry consultant who has held senior management positions in several major Indian and Global pharmaceutical companies. Also included was Chinmoy Roy, a US FDA expert on Data Integrity and Computer Systems Validation. Chinmoy is a US pharmaceutical personnel with extensive Data Integrity implementation experience in the US. Rounding off the team was Caliber Technologies Pvt. Ltd., the manufacturer of Caliber LIMS. The Caliber team was headed by Caliber's CEO and President, Mr. Sekhar Surabhi.

Conference goals

The conference provided Shimadzu's customers the opportunity to meet and discuss their data integrity and computer system validation issues with industry experts. The experts stressed the importance of architecting and automating laboratory systems so as to reduce data integrity vulnerabilities. Attendees found the conference to be very informative. Some indicated that the conference sensitized them to the importance of considering data as one of their critical assets. Many attendees also left the conference with action plans to initiate and implement Data Integrity programs in their organizations.

Presentation highlights

The opening presentation set the theme for the conference by highlighting some of the recently issued warning letters on Data Integrity. It provided a broad overview of Data Integrity concepts and terms.

This was followed by a presentation that detailed the infrastructure that a company needs to build to demonstrate Data Integrity in their enterprise. A key recommendation during the conference was for companies to develop a 'Data integrity Assurance Plan'. This plan should at a minimum highlight the company's approach to assuring data integrity and principally address the following:

- Plan's scope
- Roles and responsibilities for ensuring data integrity
- Management's role and commitment
- Data background to include data lifecycle and data states
- Data governance
- Data management
- Design guidance to ensure designed systems take data integrity into design
- Validating systems for Data integrity
- Data integrity metrics and self-assessment for Data Integrity maturity model
- Monitoring programs such as internal audits, audit trail reviews

Subsequently, the Caliber LIMS team demonstrated their LIMS product. The demonstration focused on supporting the concepts of earlier presentations wherein a migration to a LIMS architecture was not only state-of-the-art but that it also provided the necessary technical controls to significantly enhance laboratory Data Integrity.

Recommendations for 'Laboratory of the Future'

Considering that laboratory systems have attracted stringent scrutiny from auditors, the recommendation is for Indian pharma companies to expeditiously upgrade their instruments with features such as role based access control and audit trail capabilities. Furthermore, to mitigate the data integrity concerns of the regulators, the presentations were geared towards highlighting the benefits of migrating towards a laboratory automation system based on a centralized database of a LIMS system. It would significantly contribute towards mitigating the data integrity concerns of the regulators and may result in faster audits with reduced propensity for warning letters.

Another recommendation was for inter-operability of instruments from several vendors, where instruments from multiple vendors exchange data via a communication network designed to internationally accepted design standards. The attendees were strongly advised against opting for laboratory instruments that had no inter-operability capabilities. In keeping with the 'continual improvement' requirement of ICH Q10, the experts advised that the companies from where the attendees hailed from should focus on their core business of drug manufacturing wherein they understand their sciences and manufacturing process and provide them the freedom to select instruments to meet their specific process needs. Under such a scenario they should have the ability to select the 'best of breed' instruments to meet their process requirements and should not be constrained by inter- operability concerns arising from the limited offerings of vendors.

The design of the automated laboratory of the future should focus on the following at a minimum:

1. Automatic electronic documentation of the system configuration
2. Automated instrument qualification along with capture of details of individuals performing the qualification along with date and time of the activity was performed with no potential for human manipulation
3. Automatic capture of raw data and metadata with automatic generation of checksum to detect any manipulations of data post data capture as per current draft guideline of FDA, WHO and EU.

Some key findings

The conference provided the experts an opportunity to interact with attendees during presentation sessions as well as on a one-on-one basis during the tea and lunch breaks. Here are some key observations of the experts.

Employee empowerment

The conference highlighted the need for C-level management is grappling with convincing themselves that empowering their employees in the decision making process would significantly reduce the propensity for Data Integrity issues. Dismantling the existing hierarchical management structure would significantly alleviate regulators' suspicions on the existence of data integrity issues in the company. The conference presenters also made some site visits of select pharma companies. The objective was to provide some onsite training and meet with C-level management and understand their management style. It was evident that in those companies where employees were empowered, they had no hesitation or inhibition in asking questions to seek clarifications on issues they were facing. We noticed that the presence of their supervisors and managers in the same room did not hinder them from asking their questions. We could also easily identify the supervisors since they were the ones taking down notes while allowing their direct reports a free hand in asking questions. In companies with a structured or tiered system of management, it was evident that attendees were reluctant to ask questions. Instead they crowded us after the training to ask us their questions and discuss their issues in private.

Employee training and re-training

With the mushrooming of training companies, some of whom even profess to sell the magical 'snake oil' to solve data integrity problems, it would be business savvy for management to screen the background of the trainers and their implementation experience on Data Integrity. Some training managers who also attended the conference, informed us that they readily agree to nominate their employees for trainings conducted by former FDA personnel. Many FDA personnel are only trained in a very thin slice of data integrity and typically do not have the background of presenting the vast sphere of Data Integrity. We also were informed by trainees that on their return

from training, their supervisors do not do any follow up and instead they strongly encourage them to resume their tasks they were involved with prior to the training. The potential benefits that are expected to accrue from such trainings are lost with such an approach.

No awareness of 'Code of Conduct' or 'Ethics Policy'

Some of the attendees stated that they were not aware of their company's 'Code of Conduct' or 'Ethics Policy'. They could not even recall if they were made aware of these during their onboarding. They even stated that their companies did not have any formal training or yearly retraining on Data Integrity. It is highly recommended that C-level management in every company address this issue on a priority basis, if they have not done so already.

cGMP data registry

Attendees from IT departments confirmed that their companies did not maintain a registry of servers which contained cGMP data along with their data owners, controlled access to that data etc. Our experts recommended that they pursue this issue with their senior management and proceed to establish such a registry as a first step towards gaining control of their cGMP data. They contended that they would take this back to their management as an action plan item.We urge C-level management to not let this go unheeded. Establishing this data registry is a 'quick gain' approach and would significantly enhance the company's commitment to gain control of their data in the eyes of the regulators.

Hands-off approach towards consultants

Some C-level executives mentioned that they hire consultants from outside with Data Integrity experience as recommended in some off the recent warning letters. However, even after doing so, they wondered why they continue to get warning letters. During my discussions with them, we traced it to their expectation that the consultants will address all the issues on their own. We recommended against such a blind trust in consultants and to instead adopt a more hands on approach by being involved with their activities, asking the consultant to justify their actions at every step and if needed to hire an additional independent consultant from another source to provide such an oversight. However, hiring an additional consultant should not absolve them of remaining closely involved in supervising the consultants.

Reluctance to upgrade systems

The Indian pharma industry management continues to consider system upgrades and system expansion as an expense instead of an investment in their business. They need to demonstrate foresight and consider voluntary upgrades instead of being forced to do so after they receive warning letters. It would be expedient for management to proactively upgrade systems. It is recommended that they work with their vendors to develop short term and long term plans for such system upgrades.

Recommendations for how to confidently face 'unannounced Audits'

Conference attendees also wanted to know how to successfully withstand unannounced audits by regulators. The importance of continuously operating in an 'ever ready for audit' manner was stressed. They were urged to lay greater stress on ensuring that their CAPA's were addressed in a timely manner. Conducting regular audit trail reviews and documenting the review results were also stressed. Another area that regulators frequently audit are internal audits and hence companies were advised to pay attention to conduct such audits regularly.

As an added plus, would be providing high visibility to data integrity issues at senior management meetings, frequent management walk downs on the manufacturing floor, attaining and demonstrating to regulators a company culture where individual employees were encouraged and incentivized to report data integrity issues, empowerment of employees and the dismantling of the proverbial culture of tiered and hierarchical management structure where the decision making is concentrated in the hands of a few etc.

In conclusion

For western pharma companies, India presents a huge potential for contract research and manufacturing operations. India's brain power, excellent education system, ability to communicate effectively in English continues to be a great attraction for these companies. To sustain this attraction, India needs to rapidly move towards the operational style of western companies wherein management is seen not as a controller but as a facilitator for their employees to realize their maximum potential in the delivery of their company's business goals. Towards that end, Indian pharma companies should initiate and undergo a transformational change wherein managements partner with their employees on an equal footing to deliver safe and cost effective pharmaceutical products for the western markets. Doing so would also strongly signal to the western world, India's commitment to deliver drugs that are safe thereby assuaging the existing notion that the Indian pharma industry is rampant with practices to defraud and deceive.an additional independent consultant from another source to provide such an oversight. However, hiring an additional consultant should not absolve them of remaining closely involved in supervising the consultants.

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