Dark Horse Consulting Group Inc. April 2020

Whitepaper

Get organised and get smart: The virtual audit
Ensuring quality and compliance during the current global pandemic

Executive summary

- Current global circumstances prevent all non-essential on-site activity, with immediate, far-reaching and consequent longer-term uncertainty
- The virtual audit is a structured, relatively lower cost, technology-driven solution capable of accommodating essential business requirements, even and especially for operations and supply chains with global reach
- Virtual auditing as an interim continuity strategy enables business-critical, third party oversight during this period of significant global and financial uncertainty, and prospectively defines focus for efficient, targeted on-site activity once travel restrictions are relaxed

Background

Amid ongoing, unprecedented global circumstances due to the worsening COVID-19 (coronavirus) pandemic, routine execution of standard onsite inspections and audits of facilities and systems is fundamentally prevented for an indeterminate duration. Broad jurisdictional alignment has been exemplified in multiple instances, including the FDA's decision to extend the curtailment of most foreign inspections through April and assess ex-U.S. mission-critical inspections on a case-by-case basis, along with MHRA's announcement on 31Mar2020 of the introduction of exceptional GMP flexibilities together with guidance that only essential Good Practice inspections of laboratories, clinical trials, manufacturing, distribution and pharmacovigilance will be conducted until further notice. Furthermore, MHRA announced the prioritisation of essential on-site inspections linked to the UK government's COVID-19 response or any other potential serious public health risk where the sites cannot be assessed remotely. The introduction of these measures clearly represents the use of mechanisms to address a very high likelihood of immediate, far-reaching and sustained consequences due to multiple factors including prevailing travel bans at global, national or organisational levels, oversubscribed airline travel availability for an extended period once travel restrictions are likely incrementally relaxed, for organisations whose progress is predicated on the positive outcomes of these activities.

A critical factor in the aligned, global decision by regulatory agencies to take this action means that responsibility resides with those with vendor oversight to do what is reasonably possible and to maximise technology to support continued development and/or manufacturing. Numerous additional measures have already been implemented as part of regulator's multi-pronged and risk-based approaches to ensuring the preservation of rigorous quality and compliance with applicable laws and regulations. Remote audits provide an alternative approach to the routine quality oversite necessary to ensure GXP compliance.

Strategic approach

This whitepaper outlines DHC's development and utilisation of a novel, alternative approach to site audit, detailing recommended strategies and tactics to facilitate the execution of all essential aspects a virtual audit, performed by our highly experienced auditors, with their usual level of scrutiny and rigor. While enabling and ensuring oversight of compliance and adherence to regulations, this offering represents a carefully devised solution, based on sequencing and timing that overcomes the critical impact of prevailing travel restrictions. It should be clearly understood that while this methodology enables new vendor onboarding, maintenance of adherence to audit schedules or the execution of a quality review, *the required, overall standard of expectation ultimately remains the same*. **Virtual activities, however thorough, should be considered an interim measure and cannot replace systematic and comprehensive on-site auditing once restrictions are lifted, since the ultimate position of the bar of quality that guarantees the safety of all patients has not changed, nor will it.**

Methodology

Strategically, the approach is split into two components as outlined below and utilises modified vendor assurance processes based on a Quality Risk Management (QRM) approach, triaged to determine

appropriateness on a case by case basis. For example, a new sterile product vendor at which an onsite audit has not previously been performed might not be deemed an appropriate candidate, however for an existing Drug Substance or raw material manufacturer with a demonstrable history of high quality and previous successful audits, this approach may be deemed suitable.

Prospective audits to onboard a supplier tend to be more heavily QMS-focused since there are no Batch Manufacturing Records (BMRs) to review at the time. Post-manufacturing audits are BMR-driven and offer the opportunity to retrospectively focus in particular on the manufacturing equipment used, review of ongoing stability programmes, etc. As such, a two-part strategy, with either an intense retrospective review of the first manufactured batch, or a prospective review of the next routine batch, would allow for an examination of all associated records to enable comprehensive, evidence-driven assessment.

For maintenance audits, a virtual audit taken as a Preventive Action will enable adherence to the vendor audit schedule. While the virtual audit is not an audit in the traditional sense, it will facilitate evidence-based assurance that systems and processes in place at the organisation under review are appropriate to the extent that they are and will continue to be fit for purpose until such time that an on-site audit can be performed. Investigations initiated 'for cause' must be assessed on a case-by-case basis. For initial, qualification audits, or due diligence, the necessity and methodology are acknowledged in the Purpose section of both the audit agenda and audit report.

It should be noted that any and all audit activities represent substantial human resource demands on the company being audited, especially during the current situation, and may represent a limitation on the utilisation of this approach. Such a decision should be determined as individual circumstances dictate.

Once suitability has been determined, the key requirements are to <u>get organised</u> and <u>utilise technology</u>.

The ability to efficiently and systematically review a substantial amount of documentation in a virtual environment can represent a significant challenge even in normal circumstances; compensation for the restrictive nature of a virtual approach requires systematic **preparation** and meticulous **organisation** in advance, together with the utilisation of appropriate **technology**. Even with comprehensive virtual access to facilities and systems, and while nothing can fully replicate on-site auditing, the proposed approach offers the ability to gain specific, focussed determinations relating to critical aspects of product manufacturing and its documentation.

Documentation

Access to a comprehensive body of documentation and evidence request list, housed in a secure e-document room is an absolute requirement for success, and in DHC's experience to date, this has been provided by the client. With this in mind, not all e-document rooms are created equal with respect to architecture, ease of navigation and speed of access, therefore careful consideration must be given to these requirements. DHC offers a highly secure, easily navigated virtual audit room where clients can safely deposit their Quality Management System (QMS) and technical documents for review. Preparation of the appropriate document library should be based on the advance requests that usually precede a normal audit, and include Site Master File, Quality Manual, Standard Operating Procedures, Policies, trending data (Environmental Monitoring, water, steam), facility layout, inventory log, E.g., For master and working cell banks, previous agency inspection reports (where available and appropriate), etc.

An alternate strategy is the client provision of temporary, read-only access to the e-QMS to facilitate review of SOPs and technical documents via their online system. Documentation review occurs remotely in conjunction with client representation present online at all times while the controlled space is accessed, allowing dialogue to occur in real time.

Once documents are uploaded to the secure e-room, one of two approaches can be taken:

1. An online document review is performed with questions recorded by the auditor. The questions are then provided to the auditee for response. This requires an iterative communication style with the vendor and may be suitable when human resources are limited.

2. A virtual e-meeting takes place between DHC and the client, attended by those who would normally be present during an on-site audit, with SMEs invited into the 'room' as necessary by the client's QA. Questions are posed and addressed as the meeting proceeds and QA provides required references and documents. This approach most faithfully mirrors the normal interaction during an audit and offers the opportunity to observe visual cues that would be evident during face to face interaction.

For large documents E.g., Autoclave IQ/OQ/PQ which are not typically available electronically due to their size, it is suggested that they are stored as encrypted, compressed files on a document portal equipped with secure, unique login and password credentials, capable of recording system access history. Where such tomes of information cannot be scanned in their entirety, it is recommended that focus is placed on key elements which are likely to be most impactful on quality, such as the summary reports, deviations, supporting SOPs. Furthermore, DHC has devised and tested additional strategies to enable documentation review.

The Virtual Tour

For facilities in which manufacturing remains ongoing, DHC utilises a proprietary toolkit to enable and document a virtual inspection of critical areas of the facility, maximising the 'virtual time on site' to observe and verify with the most intense focus placed on those aspects at highest likelihood of patient safety impact including (but not limited to) foci such as line assembly, laboratory and facility design, setup and operation, vial inspection of finished Drug Product, media fills, interventions etc. While it is fully appreciated that this cannot entirely replicate a live tour, the approach enables the identification of risks, issues and areas of concern that are the hallmarks of an inspection.

The virtual tour will be directed by a required areas list that describes, for example, the process of receiving and storing goods. The following areas will then be requested to be toured: receipt, inspection, unpacking, inventory management, quality control sampling, material release and material storage.

Auditor requests are then either uploaded to the secure e-document room or systematically reviewed in real time during virtual, online meetings, expedited by multiple client participants accessing the e-document repository. Additionally, the provision of a facility map that lists equipment present in each room, combined with a description of the unit operations and activities that occur in each area allows equipment and process information to be systematically identified, gathered and reviewed.

An onsite audit for a sterile product might typically take 3 days, with approximately half of that time used for observation within the facility during line setup or operation, and therefore the utility of the offering is heavily caveated such that eventually an on-site audit **must** ultimately occur, once current global travel restrictions have been lifted, at which point a supplementary, follow-up audit report based on onsite activities will be cross referenced against the original audit report generated by virtual activities.

Summary

In current circumstances, DHC's virtual audit offering represents a unique opportunity to enable a business-critical process to continue to occur. Virtual auditing may become more commonplace in certain specific cases in the adaptation to restriction. As in any audit or assessment process, the auditor is looking for a level of assurance that the required standards are being applied and adhered to by the organisation under scrutiny. Meticulous preparation is required in advance and confirmatory on-site auditing will still highly likely be required in most instances once travel restrictions are relaxed or lifted.