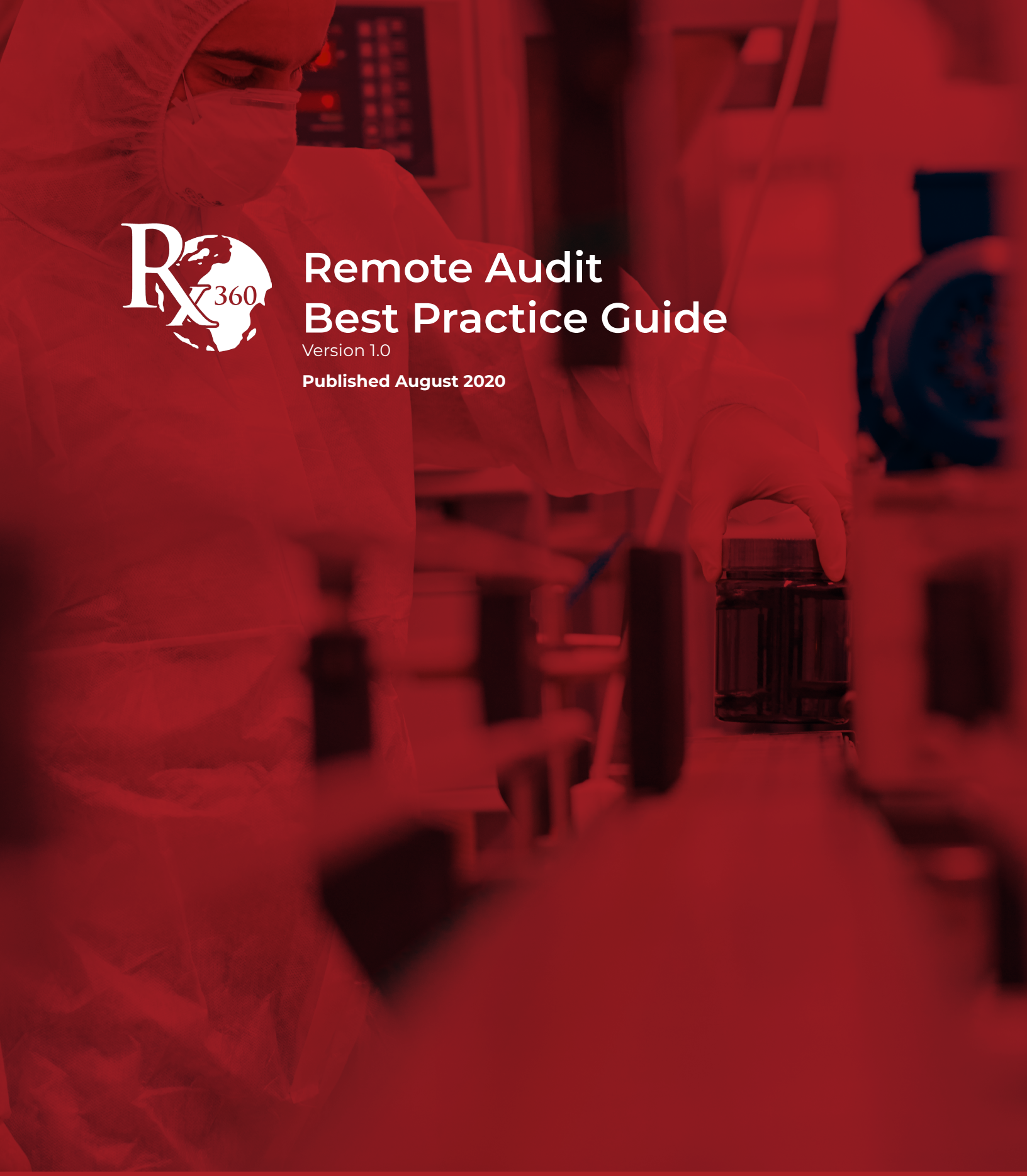

Remote Audit Best Practice Guide

Version 1.0

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Remote Audit Best Practice Guide

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SECTION ONE

Overview - Rx-360 Best Practice Guide for Remote Auditing

Through our member consortium, Rx-360 has developed a Version 1.0 Best Practice Guide for Remote Auditing. This initial version will present a foundation on best practices that the Rx-360 membership have utilized and observed, as well as processes that have been incorporated into the Rx-360 Audit Program.

This guide will be followed by versions that will focus on best practices for specific areas such as:

API
Supply Chain Security
Single Use Systems
Excipients
GMP / GMP Service Providers
GDP
Cell and Gene Therapy

This foundational guide will focus on definition of terms, types of remote auditing, IT capability, pre-audit surveying and a decision tree around deciding on a remote audit versus an onsite audit.

Remote auditing during the coronavirus pandemic of 2019 and 2020 has grown in its utility within the pharmaceutical industry. The processes involved with a remote audit will continue to evolve as the industry continues to adopt best practices. Being able to understand the growing bandwidth issues on both the pharmaceutical supplier side and the manufacturer side will position remote auditing to continue its growth and utilization for the long term.

SECTION TWO
Key Definitions of Terms

REMOTE AUDIT:
Remote audits leverage technology such as video teleconferencing and shared file folders to facilitate interviews and share documents and record, when an on-site audit is not viable or desired

VIRTUAL AUDIT:
As defined by ISO 19011 a virtual audit is a set of audit activities on a virtual environment. A virtual environment may be composed by digital and/or non-digital activities using technological assets (software, hardware, sensors, PLCs, automated devices) taking some or all decision(s) in the process(es).

ON-SITE AUDIT:
A supplier audit that is conducted on-site and in-person at auditee site. The audit is focused on a specific area identified by the pharmaceutical manufacturer or audit sponsor.

ICT:
Information and communication technologies utilized in remote audit models.

PRE-AUDIT INFORMATION AND SURVEY:
The establishment of why the audit is required. Determines the type, scope and objectives of the audit. Reasons may be to satisfy a regulatory requirement, a supplier qualification, defect/recall investigation or to gather data that justifies reduced analytical testing of a raw material upon future receipt. A pre-audit survey is a valuable tool that can be a major source of information if well constructed, comprehensive and used in a timely manner to collect, collate and analyze the responses.

SECTION THREE
Types of Remote Auditing

When deciding to conduct a remote audit as a primary audit process or a transition from a previously scheduled on-site audit, it is important to determine needs and capabilities in order to make the proper decision around which potential model to incorporate into your audit program.

As a first step, it's important to understand the benefits and challenges of remote auditing.

BENEFITS OF REMOTE AUDITS:

- Audits are allowed to take place when travel is not possible
- Audits in some cases can be done quickly and at less expense (no travel required) for urgent audit needs
- Flexible schedule: audit can be rescheduled easier than a traditional audit when there is an unexpected event without rebooking or incurring additional costs
- Auditor still can randomly request documents from auditee during remote audit

CHALLENGES TO REMOTE AUDITS:

- Limitations of QMS and GMP elements that can be covered due to offsite, such as plant tour, laboratory visit and other physical aspects (real time manufacturing process and physical security measures)
- May not be suitable for all audit types (such as API) due to manufacturing complexity
- Regulators may not view remote audits as a reasonable alternative
- Availability of communication portal to conduct the audit which may result in a multiple day audit versus a one-day onsite audit.

RX-360: TWO DISTINCT REMOTE AUDIT MODELS

THE FULL REMOTE MODEL:

- 100% Remote: The steps incorporated into this Full Remote Model are the same as described in the Hybrid Model but there will be 1 audit report after the completion of the remote audit. This model is conducted in one scheduled audit and done completely remote with no onsite component.

THE HYBRID MODEL (80% REMOTE AND 20% ONSITE):

80% Remote:

This portion of the Hybrid Model is based around the determination of what can be done remotely versus what cannot. Factors that go in this portion include the type of ICT being used, and elements within the audit scope that can't be transferred to the remote process.

Templated steps within this portion may include:

- Initial assessment to determine if the Hybrid Model fits the audit scope best and meets the needs of everyone involved (supplier/auditee and manufacturer/auditor). This can best be achieved by reviewing the on-site audit checklist or standard and determine

what may or may not be transferable to the remote model.

- Review and finalize scope of the audit.
- Determination an ICT that meets the needs of auditee and auditor. The ICT should act in a confidential manner and provide expected security as determined by auditee and auditor.
- Schedule and conduct a pre-audit meeting to review scope, selected ICT, and provide pre audit survey.
- Auditor requests materials such as SOP's, sample records, and other scope related documents to review independently of actual visual interview/audit.
- Auditor reviews documents and complies list of notes and questions prior to interactive online meeting.
- Auditor conducts remote audit online (personnel interview, request more documents, etc.)
- Based on document review and online visual interview, a draft audit report is completed and then finalized within 30 business days.

20% Onsite:

This portion of the Hybrid Model will include items as determined during the audit scope development which could not be completed via remote ICT.

Once the 20% onsite component of the Hybrid Model is complete, the audit sponsor or manufacturer will receive 2 audit reports. One report will detail the remote portion, and a second report will detail the onsite. Both sections will make up the full final audit report.

Although there may not be industry consensus on the use of this model, it is an option that can be considered if there is a special need requested by the audit sponsor.

With both models, CAPA identification and plans are developed and implemented as determined by audit observations.

Important items to consider as minimum requirements when conducting a remote audit include:

- IT capabilities at site based on geographic region and infrastructure
- Ensuring one consistent key point of contact at audit site
- Including regulatory oversight, licenses/registrations, inspection history, recalls, company profile, access to documents and size of location as part of your analysis
- As with an onsite audit, it is also important to fully understand the nature of the product being audited as well as its stage of development.
- There may be currently approved suppliers that would be good candidates for a remote audit. This may be determined by reviewing the quality history with the supplier (complaints, rejections, etc.) and audit history (any significant issues in past audits).

IT CAPABILITY IN REMOTE AUDITING

From a best practice standpoint, in April of 2020 the ISO 9001 Auditing Practice Group provided guidance on IT capability and remote audit realization. This guidance follows the process of determining whether a remote audit is the preferred method as well as post the agreement on which form of ICT will be used.

Ensuring Confidentiality and Security: The Practice Group discussed that post the ICT determination, measures to ensure confidentiality and security should also be revised and agreed upon by all parties involved with the audit. If the auditor intends to take screen shots copies of documents or other kind of records, he/she should ask for permission, either at opening meeting or when using ICT.

It's important when using ICT to interview individuals the audit team should record the name and function of the interviewed people and tell them what information is being retained. When conducting interviews remotely, the auditor will need to verify statements of fact against other evidence. These need to be asked and analyzed by the auditor. If they are sent via email, the auditor should ensure the level of confidentiality required for those documents. It's important to note that labor laws be reviewed in regards to recording employees.

Minimize Distractions: It is also important to ensure that there is no noise disturbing the communication. If the auditor is auditing remotely off site, they should ensure there are no interruptions nor disturbances. Similarly, when there are breaks, ensure the sound is muted and any camera switched off to ensure privacy. When using video for watching online live images of remote sites, it is important that the organization demonstrates veracity of images. If looking at images of a facility these can be compared with floor plans. Images of a geographical site that are observed can be compared with available satellite images or information available from Geographic Information Systems (GIS). The evidence and the way it was collected should be recorded.

Take Regular Breaks: In a remote audit it is important to allow for small breaks, typical of those that usually occur in an unplanned manner in an onsite audit. Being seated and using the screen continuously can be tiresome. Allowing for small intervals for stretching legs and reducing eye strains helps to enhance attention when receiving feedback. It is also acceptable for the auditor to inform the auditee when an interruption is required to read and analyze information that has been provided. This allows for increased understanding of the documentation and evidence that has been presented, and for determination of additional questions prior to reconvening the interview. If time is consumed on issues such as network downtime, unexpected interruptions or delays, accessibility problems or other ICT challenges, this time should not be counted as audit time. Provisions for ensuring audit time must be established.

PRE-AUDIT INFORMATION, SURVEYS, OR QUESTIONNAIRES:

When conducting a remote audit, preparation and the ability to review documents prior to visual and/or audio interviews is essential to the success and timeliness of the audit. Some examples of primary components of a pre-audit survey or questionnaire include:

General Company Information:

- Address, key point contacts, and geographic awareness
- List of material or products produced at audit site
- Are any materials or processes outsourced to another organization?
- Are there any documents that cannot or will not be shared during the audit?
- Will all documents reviewed be in English or the language of origin?
- Facility map or layout, including room classification

Personnel and Training Information:

- Does the audit site have training manuals and training programs in place for all employees?
- Are training records readily available?
- Does the supplier have established communicable disease processes for employee health screening and workplace exclusion where necessary?
- Gain an understanding of the breakdown of employees (regular vs temps/contractors) and whether the same curriculum would apply to an employee regardless of their employee status (e.g., regular vs temp/contractor)

Product Specific Production:

- How do you define an individual batch?
- Is this product manufactured by individual batches or is manufacturing continuous?
- Is the product manufactured in dedicated equipment?
- Is the original manufacturer name printed on each packaging unit?
- Schedule of product launches from the site
- A general process flow of the production process in order to understand what activities occur at the site.

Material Source – Product Specific:

- Are only non-biological origin materials used as raw materials during the manufacturing process?
- Is the product or any of its raw materials derived from GMOs (genetically modified organism)?

Residual Solvents and Elemental Impurities:

- Are solvents excluded from or consistently removed during the manufacturing process?

Cross Contamination Control:

- Which cross contaminations controls are in place?
- Are production materials handled and stored in a manner to prevent degradation, contamination and cross-contamination?
- What controls have been established to prevent cross contamination?

Regulatory:

- List of recent regulatory inspections at the site. If there were observations associated with the inspection, what is the current status of the corrective actions and are they completed as per the commitment?
- Please list regulatory correspondence impacting the site within the last five years (i.e. warning letters, CEP suspension, import alerts, etc.)
- Is the site registered with any government regulatory agency (FDA registration, GMP certification, etc.)?

Computerized Systems:

- Does the facility utilize computerized systems for managing GxP activities or data?
- Do computer systems that could impact quality have controls for operation, maintenance and prevention of unauthorized access?
- Do you document changes and deviations of validated systems?

Quality:

- What quality management system is utilized on site?
- Which Regulatory Initiatives does the site follow/comply with?

- Provide an organizational chart. Is the Quality department independent?
- A copy of the quality manual and organizational charts are required in order to understand level of quality maturity and relative size of organization/reporting structure conflicts.

Quality and Laboratory Control:

- Which written information about laboratory instruments is/are available for review?
- What testing is performed on site? Were any external labs used for testing?

Sampling:

- Are samples stored, shipped and handled the same as the provided product?
- Are samples pulled in a statistically significant method to provide adequate representation of a product batch?
- Are there any environmentally controlled requirements for sample management?

Materials Management:

- Are returnable shipping containers used for the finished product?
- Do you have written procedures that describe finished goods storage?

The complete Rx-360 Supplier Assessment Questionnaire, which includes the Pre-Audit Survey can be requested directly at RX-360.org

REMOTE AUDITING DECISION TREE:

Factors to Consider on Whether or not to Conduct a Remote Audit versus an On-Site Audit

FACTOR OR CONSIDERATION	NOTE
IT Infrastructure	This could determine the ultimate feasibility of the audit being conducted as well as being successful. Without a proper IT platform being agreed upon, bandwidth, and security of portal, the risk assessment profile of the audit and its success is elevated and may lean towards waiting to conduct an onsite audit.
Confidentiality	It is important for all parties to fully understand and sign off appropriately on any confidentiality agreements, which should include documentation around the security and confidentiality of portal selected to share documents or conduct visual/audio interviews.
Travel Considerations	When considering a remote audit versus an onsite model, travel restrictions and cost need to be factored in. Are there barriers to entry in the country of origin, pandemic related quarantines, opportunity to access audit site? If these factors cannot be adhered to, the success and feasibility of the remote model being used may have to be adjusted to meet the needs of all parties involved in the audit.
Primary or Secondary Supplier	In many cases an organization will not meet an internal compliance metric or fulfill their audit need by conducting a remote audit on a primary supplier. That is an important factor in determining whether to proceed with a remote audit. From a best practice standpoint, being able to segregate suppliers and determine which would meet internal requirements from the results of a remote model.
Regulatory Acceptance	Will the results of the remote audit meet specified regulatory requirements as dictated by governing agency?
Remote Audit Experience	Do the auditor and point person at audit site have remote audit experience? Without appropriate experience, the timeline of the audit could be elongated. It is important for the auditor to note this experience on the CV or for Auditor Qualification Document to include.
Timeframe Requirements	Does the auditor or audit sponsor have the time to wait for an onsite to be scheduled?

SECTION FOUR
Frequently Asked Questions

This section offers examples of the most frequent questions and answers that have been queried as part of the Rx-360 Town Hall and Discussion Groups that focused on Remote Auditing.

What ultimately are some key best practices in remote auditing that need to paid attention to?

- The importance of confidentiality and security of the agreed upon ICT platform
- Do not take shortcuts just because it's a "remote" audit. Conduct the audit with the same focus as if you were onsite.
- Make sure that IT infrastructure (internet bandwidth etc.) is in place to support remote audit
- Audits should conform to the principles outlined in ISO 19001 whether performed in-person or remotely
- Make sure that auditor and auditee understand how to use the ICT platform correctly and determine whether training is necessary
- Does the remote model check the compliance requirements both internally and from a regulatory perspective?

Can I replace all of my onsite audits with a full remote or hybrid model?

- It is recommended that as a best practice each organization reviews its own decision tree to determine which type of supplier audits can be transitioned to a remote mode from an onsite model. Remote auditing is already occurring and growing in acceptance within the pharmaceutical and life sciences industries.

Are remote audits a short-term replacement option for onsite audits during the 2019-2020 pandemic, or is the model here to stay?

- From a best practice standpoint, each organization is encouraged to assess their own audit program and strategy. It is assumed that with the current trend in the importance of audits and patient safety that remote audits will continue to have a place in audit programs to mitigate bandwidth issues and costs.
- Given the time and cost savings benefits of remote auditing, the rapid expansion of enabling technology, and increased comfort with remote auditing experienced by both the industry and regulators, remote auditing appears to be a trend that will continue to gain acceptance and serve as an option even beyond the current pandemic crisis.

Does an auditor need to have previous experience in remote auditing in order to conduct a successful remote audit?

- It is recommended that an auditor have experience in conducting remote audits, however proper training before hand in processes as well as ICT platforms will suffice. Auditors with this experience should clearly note it within their CV or in an auditor qualification document.

SECTION FIVE
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3. Top Tips for Successful Virtual Auditing During COVID-19 (Matthew Hermon, Senior Compliance Consultant and Benjamin Frey, Senior Director Quality Systems at ProPharma Group: April 7, 2020)
4. Pharmaceutical Remote Audit Process by NSF (LPH-631-0320)
5. ISO 9001 Auditing Practices Group Guidance on: REMOTE AUDITS (Edition 1: April 16th 2020)

At Rx-360, our mission is to protect patient safety by sharing information and developing processes related to the integrity of the healthcare supply chain and quality of its materials. For information on becoming a member and membership benefits:

info@rx-360.org
www.rx-360.org
888-218-1164

"In light of the COVID-19 global pandemic, access to supplier sites has been limited in most cases. Thanks to programs such as Rx-360, which has facilitated best practice sharing and guidance from their members, many companies are able to consider Remote Audits as an alternative. This has been a great help to the pharmaceutical industry"

Tobias Parker
Director Global Quality Auditing and Compliance
Eli Lilly and Company