UL REGISTRAR PHARMACEUTICAL DRUG AUDIT TOOL RISK ASSESSMENT

UL GMP CERTIFICATION PROGRAM

BENEFITS	
Accreditation	Globally, UL Registrar LLC (UL) is ACLASS/ANAB Accredited by the ANSI-ASQ National Accreditation Board to provide the ACLASS/ANAB Symbol for a variety of technical schemes, which highlights UL Registrar's technical competence to perform inspections.
Marks	UL is permitted to use the UL Management System Certification Mark, the UL Management System Certification Badge, the ACLASS/ANAB Mark, and, when permitted, the ILAC MRA Mark. The purpose of these Marks is to highlight technical competence and increase customer confidence.
UL Expertise	UL has been a trusted advisor in consumer and product safety for 120 years. UL has produced talented auditors with years of industry experience and technical knowledge. The expertise of the UL Auditor is specialized by industry/the type of product produced.
Satisfy Multiple Customer Needs	Multiple retailers/brands accept UL Registrar's GMP Reports. Four separate audits for four separate customers may all be included in 1 audit report.
Reduce Annual Audit Fatigue and Cost	Since the GMP Audit Report can satisfy multiple annual customer requirements, the number of annual audits for a facility may be reduced, thus reducing annual audit cost.
Commitment to Integrity	UL carries out services with the highest level of integrity and has been doing so for 120 years. UL aims to boost confidence and foster trust in the marketplace.
Continuous Improvement	With each audit, a facility has the opportunity to improve, and every corrective action is a chance to show customers that an organization is moving towards higher quality.
Quality and Consistency	The improved UL Registrar Pharmaceutical Drug Audit Tool checklist mirrors the Food and Drug Administration's Code of Federal Regulations. The improved report has built in responses and sample sizes so that UL Auditors share a consistent approach.

AUDIT BASIS

The UL Pharmaceutical Drug Audit Tool is based strictly on the requirements of FDA's 21 CFR Parts 210/211. The audit tool was created around the following six elements: Quality System, Facilities & Equipment System, Materials System, Production System, Packaging System, and Laboratory System. This approach mirrors the *FDA's Guidance for Industry Quality Systems Approach to Pharmaceutical cGMP Regulations* (dtd. Sept. 2006).

The *FDA Guidance for Industry* is intended to help organizations implement modern quality systems and risk management approaches to meet the requirements of the FDA's current good manufacturing practice (cGMP) regulations (21 CFR parts 210 and 211).

Hence, the *FDA Guidance for Industry* forms the core structure under which UL's Audit Tool was based. This audit approach establishes the audit tool's consistency with the 21 CFR Part 210/211 regulatory requirements for manufacturing human and veterinary drugs, including biological drug products.

AUDIT SCOPE

UL Registrar LLC offers Good Manufacturing Practices audits for Finished Pharmaceuticals, Pharmaceutical Ingredients and Ophthalmics. UL certifies manufacturers, packagers, warehouses, distribution centers and contract facilities of pharmaceutical drugs.

The Report/Audit Findings will be created through visual observation, employee and management interviews, and documentation review conducted by the auditor on site.

AUDIT PROCESS

The audit process begins when the audit is confirmed and scheduled. The auditor arrives on site, conducts an opening meeting, performs the audit and ends with a closing meeting. Following the audit, any Corrective Actions (CAPA) that may have been issued must be answered before certification can be awarded. Finally, the process ends in a final report, Certification Mark and Certification Badge.

AUDIT REPORTING

DOCUMENT	PROVIDED TO FACILITY	PROVIDED TO CLIENT	PURPOSE
Audit Summary	■	■ (if requested)	This Document is used as a brief summary of the audit. The Audit Summary is received by the audited organization at the closing meeting and left on site.
Corrective Action Form	■	■	The Corrective Action (CAPA) Form is used to document audit findings, factory responses, approval of factory responses, and to track closure of nonconformity. The CAPA Form is left on site with the audited organization.
Final Report		■	The client/pay vendor receives the audit report. It is not UL's responsibility to pass reports on to customers or the contract facility.

UL REGISTRAR LLC PROCESS EVALUATION ASSESSMENT OF RISK (PEAR)

The Process Evaluation Assessment of Risk (PEAR)

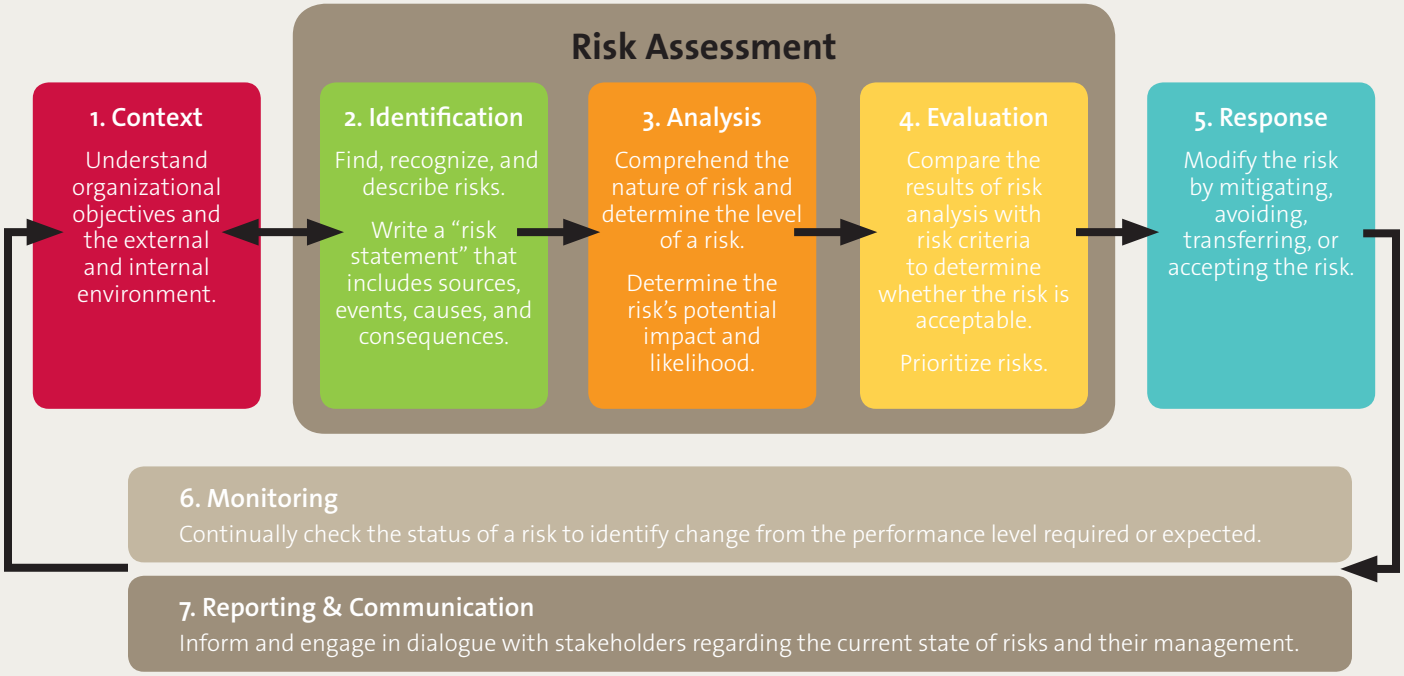
UL Registrar LLC is the first audit body to introduce risk assessment into the 21 CFR Part 210/211 family of GMP audit requirements. Risk can be defined as "the combination of the probability of an event and its consequences" (ISO/IEC Guide 73).

Over many months of careful study, evaluation, and analysis of the existing UL audit tools as well as the process for "scoring" audit results, UL has engaged industry experts, field auditors, retailers and other stakeholders in the development of an Audit Tool which is based solely on Risk.

The audit scoring criteria for this risk based audit tool is predicated on a risk assessment model known as the ***UL Process Evaluation Assessment of Risk or PEAR***.

This risk analysis concept revolves around two fundamental factors of risk: 1) the Probability of Nonconformance occurring and 2) the Severity of Risk to the consumer and/or end user of the UL Audit Report.

THE PEAR PROCESS



The Process Evaluation Assessment of Risk (PEAR) Description

The UL Risk Assessment is defined as a systematic process of organizing information to support a risk decision (Risk Priority Number (RPN) and Level of Risk Determination) to be made during the audit process.

"Risk assessment consists of the identification of hazards and the analysis and evaluation of risks associated with exposure to those hazards" (ICH Q9).

UL's proprietary PEAR model uses a combination of risk based criteria generated from a detailed analysis matrix. The risk matrix takes into account the probability of nonconformance occurring and the likelihood and severity of risk to consumers and other stakeholders.

These criteria were selected in order to establish a Risk Priority Number (RPN) for each specific CFR Clause or Paragraph specific to the Pharmaceutical audit and/or Standard under assessment. A mathematical equation is used to generate a Final Risk Priority Number (FRPN) at the conclusion of the assessment.

The PEAR and the Pharmaceutical Audit Tool take into account many factors, such as:

- FDA 483s
- FDA Warning Letters
- FDA Current "Hot Spots"
- Previous UL OTC CAPAs
- Recalls
- UL Technical Knowledge
- Personal Industry Experience
- Stakeholder Concerns

SCORING CRITERIA

Based on the enhanced Pharmaceutical Audit Tool and the resulting PEAR, the scoring criteria has changed from three colors: Green/Compliant (100-80), Yellow/Marginal (79-60) and Red/Noncompliant (59-0) to a new score model, noted below. The new approach now has five risk ranges.

The New UL Registrar Pharmaceutical GMP Risk Scoring Model

FINAL RISK PRIORITY NUMBER	RISK LEVEL
100 to 96	Reasonable Risk
95.99 to 89.99	Limited Risk
89.98 to 80.99	Average Risk
80.98 to 71.99	Medium Risk
71.98 and below	High Risk

Each audited facility will fall into one of the above risk levels and will receive an overall Risk Priority Number.

The risk levels can be defined as:

- **Reasonable Risk**: With all audit activities, there is assumed risk, but no current threats identified.
- **Limited Risk**: A minor departure from GMP/GCP Requirements.
- **Average Risk**: A minor departure from GMP/GCP/SOP Requirements, and objective evidence gathered during the audit that may conclude limited/no health risk to the consumer.
- **Medium Risk**: A Deviation from GMP/GCP (i.e. departure from Regulations and Requirements) or for which a 483 may be issued by FDA and would conclude some health risk to the consumer.
- **High Risk**: Potential risk of harm/death to the user/ warning letter may be issued by the FDA.

Additionally, the Final Risk Priority Number (FRPN) correlates to the level of risk deemed at the audited organization. Though this FRPN will look like a numerical score, it will simply express the level of risk based on a mathematical calculation associated with the level of risk noted on the PEAR. The audit tool and final report will not contain an overall numerical score like previous reports. This enhanced tool is strictly risk-based, so the outcome of the audit is also strictly risk-based.

Requirements will be weighted based on the risk severity and probability of occurrence. Corrective Actions will be defined as Critical, Major and Minor. Any Critical or Major CAPAs will require a follow-up assessment, as will falling within the Medium and High Risk Levels.

In terms of PEAR and our research on risk, we have updated our definitions of Minor and Major Nonconformances and, at the request of stakeholder feedback, added Critical Nonconformance. Nonconformance types can be defined as:

Minor Nonconformance – Objective evidence gathered during the audit would conclude an insignificant health risk to the consumer.

Major Nonconformance – Objective evidence gathered during the audit would conclude that a systemic failure of any system, procedure, process or failure to comply with required regulations was identified to have occurred.

Critical Nonconformance – Will or may result in a significant risk of producing an Pharmaceutical, API, ingredient, etc. that when used in a finished product, is harmful to the user.

The nonconformance types above were selected based on the severity of risk and the likelihood of occurrence.

UL has elected to remove "words of merit," such as "Pass," "Fail," "Compliant," "Marginal," etc. UL has also decided to remove the numerical, percentage score as the score can be interpreted differently by UL customers and end users of the report. Therefore, a Final Risk Priority Rating will be identified on the report.

UL is confident that by identifying and reporting the Risk Rating on the report, the end user has far greater understanding of the impact, and that risk has more weight and meaning to interested parties than a mere score or words of merit.

The UL risk evaluation of a factory and reporting on the level of risk observed at the factory during the audit allows stakeholders and report end users to make reasonable decisions about the factory based on the level of risk they are comfortable accepting, instead of basing such a decision on an arbitrary score.

References:

- ISO/IEC Guide 73 Risk Management Vocabulary – Guidelines for Use In Standards.
- ISO/IEC 31000:2009 Risk Management.
- The Institute of Risk Management's Standard.
- The World Health Organization.
- FDA ONDC's – Risk-Based Pharmaceutical Quality Assessment System.
- FDA Guidance for Industry – Q9 Quality Risk Management.
- ICH Q9 Guideline for Risk Management and Q10 Pharmaceutical Quality Systems International Conference On Harmonization Of Technical Requirements For Registration Of Pharmaceuticals For Human Use.

FAQs

Last year I had a score and this year I have a risk level. Where is my score this year?

The enhanced Pharmaceutical GMP Audit Tool is solely risk based. The outcome of the audit is a "risk level," not a numerical "percentage score." The Final Risk Priority Number (FPRN) is NOT a score or a percentage from 1% to 100%, but a mathematical calculation tied to the level of risk assigned to the associated RPN.

Have the UL GMP Requirements changed that were found in the Previous Final Report?

Yes. All UL-specific Requirements and Implementation Guidelines have been removed. The Audit Tool is strictly based on FDA 21 CFR Parts 210/211 along with corresponding risk levels.

I need a follow-up audit, but did not receive a new audit report and new FRPN/risk level. Why?

With the enhanced Pharmaceutical GMP Audit Tool, follow-up audits will be conducted to strictly close out the prior CAPAs. A follow-up report will not be generated, nor a new risk level/score issued. The closed/verified CAPA forms will be the output of the follow-up audit.

Have you added Critical Nonconformances to the audit report?

Yes, the nonconformance levels are now Minor, Major and Critical.

I have received corrective actions, how do I respond?

Please respond to corrective actions and send the form to **LST.ENF.CAPA@ul.com**. Please refer to the Procedure for Certification for further CAPA information.

What should I do with the UL Management System Certification Mark and UL Management System Certification Badge?

After successful completion of a GMP Certification audit, you will receive your final report, UL Certificate of Conformance and UL Certification Mark and Badge.* The UL Management System Certification Mark will be placed on your Certificate. The UL Management System Certification Badge may be used on your website, on your marketing materials, on your tradeshow booth, etc. The UL Certification Mark and Badge must be used properly and according to the Use of the UL Mark/Badge Document.

**Certification Badges are not available for Cosmetic and Non-Regulated Audits at this time.*

For more information on the UL Registrar Pharmaceutical Drug Audit Tool Risk Assessment, please contact industries.ul.com/Management-Systems