R & D INTERNAL AUDITING

A Key Consideration for Pharmaceutical Companies

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The Institute of Internal Auditors

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INTRODUCTION

Investments in research and development (R&D) by globally acting pharmaceutical corporations are substantial (see Table 1), reflecting the complexity and risks associated with identifying and developing novel and innovative medicines. The sheer amount of these investments are evidence that R&D is seen as a key contributor to long term and sustainable business performance. Besides great new business opportunities resulting from R&D, costly risks such as late-stage development failures, inefficient decision-making processes, and inappropriate protection of intellectual property are associated with R&D on top of noncompliance to various regulations (e.g., good clinical practice, pharmacovigilance legislation, clinical trial results disclosure requirements). To keep the R&D engine running productively and to find the right balance between risks and opportunities is ultimately a key responsibility of the board of directors (board) of a pharmaceutical company. The IIA's Three Lines Model[1] applies to all organizations, and when applied properly, supports achievement of objectives and facilitates strong governance and risk management. While the second line, which can include quality assurance, is tasked to provide assurance on compliance with laws and regulations, the third line, internal audit (IA), supports the board with "independent and objective assurance and advice on the adequacy and effectiveness of governance and risk management"[1] [see section below on "RDIA vs R&D, Second Line in a Pharma Company"]. In other words: internal audit can help the board make sure that the money spent on R&D is efficiently used and not wasted.

Table 1: Top 10 Pharma R&D Budgets in 2021[2]

Company budget	R&D budget*	R&D budget as percentage of revenue
Roche	$16.1	23%
Johnson & Johnson	$14.7	16%
Pfizer	$13.8	17%
Merck & Co.	$12.2	25%
Bristol Myers Squibb	$11.3	24%
AstraZeneca	$9.7	26%
Novartis	$9	17%
GlaxoSmithKline	$7.2	16%
AbbVie	$7.1	13%
Eli Lilly	$7	25%

* billions
Source: Adapted from Fierce Biotech, 2021, Special Reports

[1] The Institute of Internal Auditors, Inc., 2020, The IIA'S Three Lines Model: An update of the Three Lines of Defense
[2] Fierce Biotech, 2021, Special Reports: https://www.fiercebiotech.com/special-reports/top-10-pharma-rd-budgets-2021

Presumably driven by such considerations, various multinational pharmaceutical companies have established a specific team within their IA function, which is dedicated to providing assurance on R&D business processes. Often those R&D audit teams consist of both auditors with the classical education in business and internal auditing as well as auditors that have a scientific background. This helps identify R&D-specific risks and rapidly establish trust and confidence with the auditee.

This article examines considerations when establishing such an R&D Internal Audit team (RDIA), the uniqueness of such a team, the risks and processes such a team audits, and the resulting benefits for the corporation. Furthermore, trends and potential future opportunities and challenges are elaborated.

COMPARE AND CONTRAST

RDIA and Other Areas

While RDIA is similar to other audit teams, it also presents unique challenges in line with the nature of the R&D business. Internal audit's primary goals are to protect shareholder value and help the organization achieve its goals. As RDIA is a part of the audit function, it adopts the mission, vision, and purpose of the larger audit team. Within that context, every engagement contributes to the overall health of the business and should create meaningful, actionable outcomes. As in all audit teams, RDIA operates in compliance with The IIA's *International Standards for the Professional Practice of Internal Auditing* (*Standards*) and acts on behalf of the board. In providing assurance over these risks, RDIA should consider what inputs go into leadership's understanding of the R&D unit's control environment. The objective of R&D audits is to provide assurance on the management of key business risks and doing so is an integral part of corporate responsibility.

With all of these similarities, there are still some unique challenges. The risks reviewed vary greatly from one engagement to another. R&D risks can be centered on ethical conduct of research, patient safety, and the governance and delivery of pipeline and portfolio of medicines. In this context, R&D risks encompass a wide range of business activities such as the appropriate application of technology in a patient setting, scientific exchanges, the regulated (e.g., GxP), and non-regulated (non-GxP) areas of R&D, intellectual property (IP) risks, and data integrity, to name a few. RDIA can also assess project portfolio management and the governance and process of portfolio decision making and progression rather than just the decision being made. They aim at accelerating drug development by reviewing internal processes. They also have a goal to mitigate risks to quality, speed, dependency, and other areas when reviewing sponsor oversight of third parties. Finally, they assess risks and opportunities with novel therapeutic modalities, decentralized trials, or when a pharmaceutical company works with patient advocacy groups.

Unlike audits of commercial organizations in a country, R&D audits often involve global business processes that do not stop at the border of a country, or even at the borders of an organization. By auditing across organizational borders, R&D audits help to bring together different teams, break up organizational silos, and facilitate a mindset shift towards greater collaboration and more global perspectives. Therefore, the practicalities of RDIA can be unlike other areas of internal audit. Each audit engagement tends to be fashioned to the area of risk rather than executed from a prepared audit work plan, as R&D areas tend to be specialized areas of the business. The scope of the audits can also be a challenge; determining appropriate focus while providing the right level of assurance can be a balancing act.

The diversity and complexity of the R&D business requires auditors with the capability to learn fast, as the next audit engagement will be completely different from the current and the preceding one.The team composition in RDIA requires an atypical blend of skills. Ideally, RDIA has a mix of auditor and R&D subject matter experts (SMEs) not just to fully understand the control environment, but also to be able to effectively communicate to R&D stakeholders. Auditing global processes end-to-end also means that prior to COVID travel restrictions, R&D auditors were already accustomed to auditing in a hybrid mode, i.e., sometimes meeting auditees physically, sometimes connecting by video conference. As a consequence, while some auditors covering other risk areas sometimes struggled more to deliver meaningful assurance during the pandemic, R&D audit plan execution continued to be fulfilled almost to the same extent as before.

The R&D audit themes, exemplified above, have evolved over time. Indeed, consistent use of RDIA teams have expanded their roles from simple compliance reviewers to risk assessment, management, and governance, and ultimately

to the coveted role of trusted advisor. Collaborating as a partner while fulfilling the role of a critical, independent reviewer is not an easy balancing act. While in the past the audit focus was more about reviewing past activities, today's auditors are much more dedicated to mitigating future risk exposures, i.e., are forward looking and less interested in the past.

RDIA vs R&D

Second Line in a Pharma Company

The second line function is focused on compliance to regulation. In addition, the second line function may be monitoring business compliance on behalf of R&D leadership. In a heavily regulated pharma company, the second line group is named in specific regulation related to various aspects of R&D, including pharmacovigilance, labs, clinical investigator sites, investigations, and serious breaches. The second line group exists to fulfill health authority expectations for an audit function.

Whereas the third line group exists to protect shareholder value in the company and to serve the board of directors in fulfilling its duties, the third line group can highlight compliance gaps where noted, but the primary focus is on risk. In this respect, the governance and risk management decisions made by R&D senior leaders are in scope of third line audits. In large pharma companies, operating in full compliance with laws and regulations is expected and paramount to success. However, even when operating in full compliance with laws or regulations, residual risk exists in terms of emerging risk areas, medical governance, ethical conduct of laboratory operations and clinical studies, and effectiveness and efficiency of R&D governance and operations. The third line mandate includes, in principle, assurance over the efficacy of the second line function.

The difference in the groups has been captured by the sentiment that second line asks, “Did you do the thing right?” vs the third line question, “Did you do the right thing?” The coordination between second line and third line is especially important when the third line group is auditing in the GxP areas.

METHODOLOGY

Now that it is clear what the purpose and design of an RDIA group is, it is important to outline both the strategy and the underlying methodology or how a team with this remit functions. No discussion on methodology would be complete without walking through the audit cycle as it applies to the third line function.

Risk Assessment

Unlike more traditional audit groups, RDIA do not typically have a stable, discreet group of audit entities (e.g., processes, locations) that can be risk assessed year after year against a similarly stable, discreet group of risk criteria. Instead, third line inputs for risk assessment come from diverse sources such as:

- Changes in the external landscape and their impact on the company, e.g., new technology, proposed changes in regulations, new treatment modalities.
- Company strategy, i.e., the expected impact on processes and operations.
- Enterprise risk management (ERM). The ERM process often identifies specific actions and programs to mitigate the risks that are identified, and there is an opportunity to provide assurance on the status and operating effectiveness of those actions.

Consequently, the sources that inform RDIA risk assessments are diverse. The understanding begins with the objectives and business dependencies (including partners and customers). The overall business objectives, annual report, future strategy documents, and investor and other external presentations will capture the most important aspects of governance structure and deliverables for the company, the R&D unit, and the relevant sub-units. From there, a stakeholder engagement plan can be created with touchpoints with senior leaders across the business. These meetings can be described as the leadership stakeholder meetings. Typically, these would be scheduled periodically to discuss those business objectives and any changes or risks present or emerging on an ongoing basis. The objectives of leadership stakeholder meetings are to:

- Gather information to create and maintain a robust risk assessment and assurance plans, and
- Build relations that provide insights into areas that leaders would like more visibility of or assurance over.

Once risks are prioritized, there should be collaboration with the second line function to ensure optimal coverage and minimal overlap. RDIA should not regularly duplicate the scope of individual second line audits but can develop a higher-level theme that cuts across many second line reviews. The IA team can use the outputs of the second line groups to test how the business responds as well as to potentially descope well-covered areas. Governance, risk, and controls are central themes to third line audits.

Audit Scoping

RDIA audits are often one-of-a-kind, custom audits, which require more involved scoping than in traditional audits, and they are also less structured. Broadly, scoping a third line audit starts with broad risks and focuses on how those risks would cascade, i.e., be reflected into the management of existing or to-be operations, as well as what risk mitigation activities would be expected at multiple levels — governance, oversight, controls, and process design.

The first scoping iteration is at a high level, i.e., enough to know what organizations will be involved and to schedule the audit. The key risks that were identified and drove the need for assurance should determine the *breadth* and *altitude* of the audit. The breadth of the audit considers questions such as what processes/sub-processes, organizations, and types of risks to cover (e.g., lack of readiness to comply with a new regulation, financial risk, reputational risk). The altitude of the review depends largely on the maturity of the processes/organizations being audited and how well the risks around it are understood, and determines the level of detail that auditors will address. For example, a "high altitude" audit may cover only governance, whereas a low altitude audit may cover all key activities and controls within a process. It is key to align with the business/auditees again at this stage, as the decisions made here will shape the whole audit scope.

Audit planning and execution: third line audits typically require an advanced planning phase, as there are fewer pre-determined expectations around the governance, process, or controls in place. Approximately 12 weeks in advance, a formal notification is issued to the business. During advanced planning, the audit team familiarizes itself with the organization, processes/procedures (e.g., SOPs, work instructions) and associated risks. Throughout the planning phase, the team will define the high-level risks and hypothesis in the audit record. One method of articulating the key risks and controls is a risk and control matrix (RCM). The team should press into key risks around governance and objectives, both business and quality. Some questions consider:

- What changes have happened recently and how have risks been managed during the change?
- How are risk management and monitoring outcomes driving quality goals?
- What are the key hand-offs between processes and organizations and how could misalignment happen?
- How could completeness, accuracy, validity, or access to information be compromised?
- What are the key underlying IT systems and respective risks? What are the key regulatory compliance risks, and is the oversight adequate?

Execution

The audit execution would be very similar to a traditional audit, although, as noted above, the level of detail may be different. The audit may include review of records (meeting minutes, process documentation, procedures, findings/remediation plans from the prior audit), interviews, and walk-throughs. Selection of audit samples should be representative of the areas being audited to assess the design and operating effectiveness of the associated controls.

Unlike financial and/or IT audits, control reperformance may not be possible — e.g., the basis for completion of a test step could be based entirely on interviews with auditees. The emphasis for RDIA is on different types of controls. Management verification or monitoring might take on more importance, as well as verifying that the decision processes involved the right people, and they were presented with the right data.

Reporting of Audit Results

There is greater latitude on how to present audit results and findings at a third line audit — for example, they typically won't cite specific regulations or company policies as in a compliance audit. As a general rule, the same drivers that determine the level of granularity for audit scope will also determine the level of detail and rigidity of the findings. A process that's just been established around a new technology or new regulatory framework may be undertaken as a consultancy project or have an unrated report with high-level recommendations, whereas a more mature process with clear expectations and policies may have a rated audit report with findings pointing to very specific gaps in controls along the process. Equally flexible is the distribution and timing of the report, with considerable judgment being used to determine to whom the report should be addressed and distributed.

THE FUTURE OF RDIA

RDIA Must Embrace Change

Growing and emerging risks disrupting the current pharma portfolio delivery require RDIA to embrace new real-time evidence-based approaches to delivering assurance and to adjust the audit team's capabilities. Data savviness is becoming central to the IA knowledge base. Another aspect is increasing business acumen and domain knowledge across the business and within R&D of new treatment modalities and technologies. The teams must maintain a forward-thinking posture in order to stay ahead of the risk environment.

Both external factors (e.g., macroeconomic turmoil, heightened scrutiny from regulatory agencies and Department of Justice on data fraud risks) and internal factors (e.g., company transformations, business development and licensing deals, innovative therapeutic modalities, and more aggressive usage of technology by the business) are pushing RDIA teams to adjust their value proposition and provide on-time assurance in a fast-changing landscape.

Even more than before, close collaboration with the other lines and business partnering are crucial to keep abreast of the risks facing the business and make best use of the wealth of data available within the company to provide robust risk coverage. This requires a change in dynamics between first, second, and third lines, including more frequent and transparent exchanges, while maintaining the independence and objectivity inherent to the IA function.

Table 2: Evolving Practices in RDIA

What does good look like today?	What does it mean to be leading tomorrow?
Reactive risk assessment	**Proactive risk identification**
Retrospective trend analysis based on limited access to data and tools from other lines	**Predictive trend analysis using data-driven approaches**
Individual and distinct engagements	**More targeted and connected engagements, removing silos across the company**
Sharing of findings and remediation actions for specific engagements	**Sharing of actionable insights and simplification opportunities within and outside engagements**
Clear separation between first, second, and third lines	**Early involvement in process/governance redesign activities from the first line in an advisory capacity, ensuring preventive controls and effective key risk indicators (KRIs) are built in from the beginning, to inform monitoring solutions by the second line in real time and reduce future audit burden to the organization (assurance by design)**

About The IIA

The Institute of Internal Auditors (IIA) is a nonprofit international professional association that serves more than 230,000 global members and has awarded more than 185,000 Certified Internal Auditor (CIA) certifications worldwide. Established in 1941, The IIA is recognized throughout the world as the internal audit profession's leader in standards, certifications, education, research, and technical guidance. For more information, visit theiia.org.

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