Redefining QA/RA Management
to Gain Competitive Advantage of the Changing Regulatory Environment.
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Changes in standards have left many organizations struggling to update their design and documentations. This paper redefines Risk Management in light of the recent changes to the regulatory framework, including 21CFR 820.30, MDR, IVDR, ISO 13485:2016, and ISO 14971:2012, ICH Q8, Q9, Q10, Q11, ASTM E2500, etc…and prepares the organization to deal with additional upcoming changes. Equipped with this new definition, Management, with Executive Responsibilities, should be able to 1) reduce the most common problems related to receiving inspection, line shut downs, suppliers' inability to deliver to specifications, and the ineffectiveness of the CAPA system to resolve these, or external failures (complaints, MDR's Field Corrective Actions - FCO's); and 2) build the flexibility needed to deal with a continuously changing regulatory environment.

The main concept to understand to simplify compliance, and reduce its associated costs is the extended definition of risk (now covering the entire supply chain, and the whole product life cycle) and the portfolio of strategies management has at its disposal for an optimal mitigation of risks to patients. All the changes in the regulatory environment have for goal to better explain this concept in light of the most recent field experiences, and increased technological tools at our disposal.

The concept of risk management should not be limited to Design Failure Modes Effect Analysis (dFMEA). Inspection is a risk mitigation strategy, so is QMS, and vendor qualification. It is worth noting that reliance on any single method is likely to be less effective than a well-balanced portfolio of strategies that minimizes the risks to patient.

We define QA/RA management as a collaborative and iterative effort to mitigate risks across the product life cycle, and throughout the supply chain. The inputs to this process are the:

- *History of the product/process performance* - including its failure modes. This is key to remaining focused on the essentials
- *Management vision and commitment to quality* – ranging from "as good as the competition" through "defect free product and on time delivery", to "market dominance with quality by design".
- *Changes to Applicable Standards* – which increase the requirements for transparency, and extend to manufacturer's responsibility to manage risks to cover the supply chain, and life cycle from design to post-market.

The process output is an optimized portfolio of strategies designed to gain competitive advantage of the continuously changing regulatory environment by simplifying compliance so it becomes an inherent part of the business. See below for examples.

The process outputs are Risk Management Strategies – defined as control exercised via any of the following methods:

Risk Mitigation Strategy	Standard	New	Examples of opportunities for improvement
Quality Policy	Having a quality policy to show to FDA investigators, customers, and Notifying Bodies	Making sure the policy is inspiring, well shared, and provides good guidance. The aim of a policy is to encourage some activities, and discourage others. It is useless if it fails to do so.	"The competition is 60% good. We are good if we are 61% good". "We are here to save lives. Our outgoing defective rate will be better than 5/million. No lot received should have more than 0.5% defective". What is your policy?
Compliance	Neglecting to comply, and rushing to remediate when an audit is expected	Making compliance easy, so it becomes a state of doing business	The procedures are perfectly compliant, but difficult to understand. How do you expect a technician under the stress of daily work to apply these procedures? A procedure that does not provide guidance is failing its job of risk mitigation. Are your procedures easy to follow and implement? What are you doing to simplify them?

Submission	Making regulatory submissions that limits subsequent changes	Building a flexible design space that permits post-submission adjustments	A PMA submitted 5 years earlier has specified an oven temperature to be 75+/- 5 degrees F. Records indicate that for the past 5 years, at 70-degree F the system has produced perfectly functioning devices. The design in the submission was too rigid. Do your technicians have their own recipes (black book) to run the machines?
Design Control	Limiting the design gates to: 1) project initiation; and 2) project acceptance	1) Ensuring design input is complete with users' requirements, regulatory constraints, manufacturing, maintenance, and post-market risks; 2) Verifying design output meets design input requirements; 3) Validating the design; 4) Validating the critical processes when scaling up	The device is finished, ready to be produced. It looks like a cut and paste monster with expensive molded components, hard to package, easy to break, and allowing users to misassemble. A small number of design reviews by qualified engineers would have made the product right. Are you experiencing any conflict – beyond normal - between your design and manufacturing teams?

FMEA	Doing a design FMEA with limited knowledge of downstream concerns	Having a well-balanced portfolio of risk mitigation strategies which include a life-cycle FMEA. However not all eggs are placed in the FMEA.	Extensive dFMEA demonstrates that management is spending money to produce safe and effective products. Unfortunately, the design team did not have sufficient knowledge of the device interaction with hospitals electronic systems. As a result, multiple field failure occurred due to inadequate interface. How easily to you validate any correlation between a field failure and a design or process failure mode?
Critical to Quality (CTQ) factors identification	Limited, not well communicated	Quality requirements shared with the supply chain, and validated (many design reviews will involve the suppliers to help with the CTQ identifications). Associated validations are simplified so they can easily be performed after each maintenance activity, and on a scheduled basis.	The design team did not identify a cable connection as a critical to quality. As a result, the crimping was not validated, and loose cables resulted into multiple communication failures and field recalls. Is your design team collaborating with manufacturing engineering to identify CTQ factors? Do they validate the underlying processes? Are your validations easy to perform?
Talent acquisition, development, employee training	Limiting each employee to specific tasks assigned by their functional management. Employees are discouraged from stepping out of their functional boundaries.	Enabling employees to gain broader perspective of who their customers and suppliers, and how their products and services are used.	Employees are treated as replaceable commodities. Training are lengthy and boring. Goals are not shared. The system is sub-optimal, and everyone is used to it. Is your system promoting critical thinking? Do employees have a mean to express their disagreement with management?

Vendor qualification and development	Select vendors on the initial price. Squeeze them later for additional cost reduction.	Select suppliers based on their capabilities to deliver to CTQ factors to specifications, and treat them as partners.	At the time of the initial audit, weaknesses in engineering and management are identified, but classified as simple observations in order to allow the supplier selection to go through. A year later, weaknesses remain the same. How closely are your purchasing and quality functions cooperating to share risks?
Process and Test Method Validation. Independently of the language used (validation, qualification, PQ, PPQ…) what we are ensuring here is the control of process variability, so that the output is consistently on target.	Limited, excessive reliance on acceptance inspection. Dependence on suppliers to perform validations without guidance.	Suppliers are involved in the identification of CTQ factors, and validation of their underlying processes (critical processes).	An off the shelf purchased component fails on a PCBA, leading to a catastrophic failure of the device in the field. Investigation shows there are two sources of supplies – two manufacturers – for this component. Reducing the supply source to one single manufacturer is a risk mitigation strategy. Qualifying the purchased components through a test method is an alternative strategy that permits the maintenance of a second source, in case one of the sources has supply issues. For a problematic process, ask for an analysis of variance to see if the test method used is adequate.

Critical component qualification	Many critical components are purchased off the shelf without any validation	Critical components are purchased from qualified vendors, otherwise alternative measures are taken to mitigate associated risks.	After a catastrophic field failure, due to a commercial quality critical component, it was changed to medical grade, and a performance test was added at the end of the line to mitigate risks of handling damages. How many of your critical components are purchased without qualification?
Process Inspection	Mostly limited to first article inspection; some in process inspection	Critical processes are control charted. Frequency is adjusted based on process variation.	CTQ factors are monitored (by vendors if applicable) to ensure consistency and control. Periodic reports are generated for next level of management to take actions on opportunities that could not be addressed by line management. Are you asking to see process capability data?
Product Inspection (*)	Is performed at receiving, in process, also at suppliers. It is the main tool for risk mitigation in manufacturing. Most of the focus is in determination of sampling size, and inspection technique.	Limited to ensuring what is received is what was ordered. It is also used to determine process stability (see process inspection). It is not used to determine lot acceptance.	Received products are inspected against purchase orders and drawings to ensure what is received is what was ordered, in the right quantities. Check what part of your incoming inspection can more advantageously be perform by the vendor.

FCO's, MDR's Complaints, Holds, NCR, and other post-market failures	Typically, internal and external failures are treated as independent events, rarely used as a feedback mechanism for continuous improvement (CI). When they generate CAPA's the link to failure modes that generated the event is seldom established, and validated.	External and internal failure data basis are linked to the CAPA system. Associated failure modes are identified, validated, and provide feedback for design and process improvement (MDR Article 83).	Time is at essence. An informal line of communication is established between the Clinical and QA/RA VP's so that the filed information is analyzed before it becomes a complaint. When is the last time your VP of quality received a call from your VP of Sales/Clinical with a request to check a developing assumption?
CAPA System	Despite lots of resources spend in investigating "root causes", CAPA's remain open for long periods of time, and are ineffective in resolving recurring issues. Inadequately established CAPA and complaint procedures are the most frequently cited reasons for 483 observations	Fully established CAPA system takes input from inside and outside post-market failures and provides input to design and process improvement. CAPA's close in a timely manner, and are effective in solving existing system problems, and preventing similar problems.	Management plans a linkage between the complaint and CAPA systems, and a linkage between the CAPA system, and the Design improvement opportunity data base. It ensures timely, and accurate transfer of information between the data basis. How long are your CAPA's open? How effective are they in resolving field issues?

Internal and external audits	Are mostly performed to comply with requirements	Are performed to identify and eliminate potential sources of problems (the check in the plan, do, check, act cycle). Provide transparency.	An internal audit discloses a late MDR filing (more than 30 days). Actions are taken: 1) to see if there are other similar cases; 2) to determine the typical time between an event, and the initiation of the associated risk assessment; 3) to establish the time between the initiation and the conclusion of risk assessment; 4) to determine the time between the conclusion of risk assessment, and initiation of the next step (informing FDA, filing an MDR, starting a FCO). Do you have closure on your last audit actions?
Document Control and records	Performed as necessary paperwork with limited use	Essential for the purpose of simplifying guidance, and providing transparency, traceability and feedback.	How long does it take to trace a component failure backward (which subassembly lots used this component), and forward (which finished product SN's used the above lots, and who has received how many of each?).
Calibration	Is performed on a single point, most of the time independently of the usage	Calibration range is a function of the usage.	Is this measurement system calibrated for the range in which it is used?

Maintenance	Is performed only once a system fails. The system is inadequately validated after maintenance	Maintenance is preventive. It takes into account the history of the systems, and their critical factors.	If you examine the minutes of the last 30 daily operational meetings, how often do you see conversations about a specific machine being down?
Other Strategies, including purchasing control, inventory management, etc..	Functions treated as independent of quality with their own agenda	Coordinated agenda, mitigating safety and efficacy risks in all functions.	An approach advocated by Edwards Deming is that of a quality Tsar, reporting directly to the CEO, and coordinating cross functional activities for a well-balanced portfolio of risk mitigation strategies.

Conclusion: Regulatory changes are part of the landscape. Their direction is a better mitigation of risks to patients (reduction of probability of harm), as a function of technological development, and their resulting socio-economic changes. Viewing QA/RA as a CEO orchestrated effort to implement and optimize a portfolio of risk mitigation strategies rather than a function will turn regulatory changes into competitive advantage.

(*) Over-reliance on Inspection, or FMEA – this is a result of inadequate risk management. Historically, companies have been heavily relying on inspection to mitigate risks. The idea here is to imagine a company where product inspection (for the purpose lot acceptance or rejection) is not allowed (inspection for the purpose of process control is still OK).

(+) Mark offers an extensive, hands-on QA/RA experience, mitigating risks in product design, realization, and post-market surveillance with class II and III devices in the international market.