Retrospective Validation
by Mark Shal, Ph.D.

In the following we propose a process that takes advantage of the interdependencies, between various segments of the Quality System, and integrates various sources in Quality Records to build a more efficient process for improving process capability.

Product failures can be classified in two categories: 1) Those due to randomness; 2) those due to process failure. The size of the first category is a reflection of the design of the product and its realization processes (raw materials, storage and manufacturing conditions, tools, calibration, maintenance, and training). Based on their criticality, and the size of the market, medical devices typically accept random failures of the magnitude of parts per thousand or better (Sigma levels larger than 3). Any ratio of field failure larger than this is too costly in terms of recalls, customer loss, and FDA concerns to be acceptable by design and is due to process failure (inadequate or out of date Verification and Validation).

Based on this assumption, we promote the idea that a retrospective V&V's based on the quality records, and the correlation between analysis performed by various work groups provide an opportunity to speed up the improvement and/or compliance.

We start by making a Pareto analysis of the MDR's by product. From the MDR, we know the lot number. This leads us to the date, and location of the production. We examine, and correlate records of key processes where breakdowns might have occurred:

1) Housekeeping
2) Identification and traceability
3) Raw materials reception
4) Tooling maintenance and calibration
5) Training
6) In process inspection records and NCR's
7) Internal audits
8) ISO and customer audits
9) Supplier audits
10) Process changes and their required V&V, and training follow up
11) Storage and handling

Typically, complaints on file are following the standard cautionary language: "We performed a visual inspection. We examined the product lot number, and identified no other cases of related complaint. Review of the DHR disclosed no abnormality".

We work under an alternative assumption - conditional on the observation of a field failure rate above 63 per million, we assume a process failure has occurred, and commit to further the analysis until we identify where it has occurred, then we focus on revalidating the underlying processes (through a CAPA). We will examine the process

over time to check for the stability of its critical parameters (these are identified through the hazard analysis or process FMEA). We use a run chart or a control chart to detect shifts in the means or changes in the variations. When we identify an instance of instability, we will conduct an investigation to see if we can identify a pattern/property that is shared amongst the failing units. Doing so, we will work across several work groups whose cooperation will be essential to reduce the employee burn out. We investigate:

1) If the equipment and facility used to produce, measure, and test the product are calibrated, and adequately maintained. If there has been any change in the equipment (including spare parts), or operators. We examine the maintenance, and operators training records, and review the documentations for validation of changes made (software upgrades included).
2) We will examine operational consistencies, and check for the sources of variations in pressure, temperature, viscosity, cycle time. We will look into the risk management study and review the identification of critical process parameters. In case of a molding for example, we will look for consistencies between cavities, shot-size, ejection rate. …in case of extrusion, we will look for variations in air flow, OD, and if needed the flexibility of the tubing.
3) We will check if the parameters of production runs fit within the boundaries set during the operational qualifications.

To illustrate the process, consider the following example:

1) A diversified international organization with manufacturing facilities in multiple location is the subject of our study. They have received a warning letter after submitting a response to and FD483 observations for lack of compliance to CFR 820 and or 803.
A review of their MDR's provided multiple opportunities for improvement. We selected an easy case to illustrate the process.

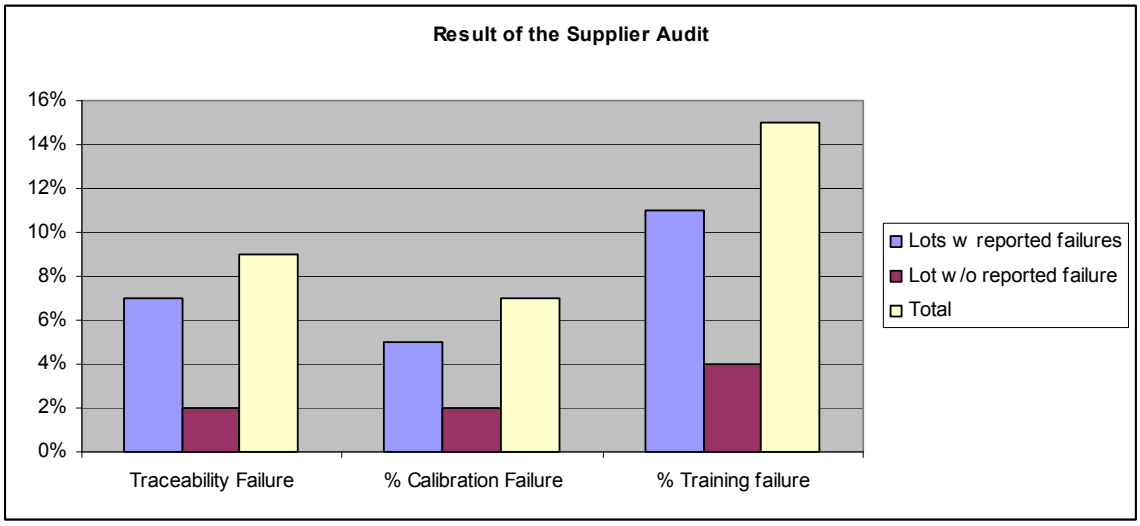
A total of 141 MDR's were filed in 2013 for broken drill bit on a surgical drill for a given location. Although none of these event resulted into death, they all are cause for concern in that they disrupted the surgeries, and at times required additional surgeries.
The investigation led to an audit of the supplier of raw material, and an inadequate control of

- Traceability
- Calibration; and
- Training

As seen in the chart, and graph below lots with reported failures correlate tightly with instances where the supplier's system lacked traceability, calibration, and training.

Result of Supplier Audit	Traceability Failure	% Calibration Failure	% Training failure
Lots w reported failures	7%	5%	11%
Lot w/o reported failure	2%	2%	4%

Total	9%	7%	15%



Of course, the CAPA initiated led to the vendor reviewing its procedures, and revalidating its processes.

About the author:
Mark Shal offers sixteen (16) years of result-focused experience assuring changes in manufacturing, quality, supply chain, and engineering of medical device are CFR820/ISO 13485/CMDCAS compliant. He has developed, brought to market, and/or CE marked several families of medical devices (Electronic infusion pumps, disposables administration sets, and pain management devices). He has managed the V&V's, changes and transfers of medical device manufacturing tooling and assemblies from US to Mexico, and Thailand. Transfers required validation of molding, extrusion, and sterilization.
His background, combining statistics with QA/RA enables him to extract relevant information from the Quality Records (DHF, DMR, DHR, CAPA, MDR, Complaints, Suppliers performance, NCR's..) to speed up design, validation, submissions, ECO's, mitigation efforts, and manage risk with present and future products.

Mark has a PhD in statistics, a MS in Stochastic Control, and a MS in Engineering Mathematics from the university of Paris VII, Paris France.
