RISK ASSESSMENT: A CLOSER LOOK

by Andy Barnett

We are all aware of the heightened emphasis the FDA is placing on risk assessment. ICH Q9, Quality Risk Management was adopted by the FDA in June 2006. You might expect, after 11 years, the industry would be fully on board with the practices recommended in this document, but we may not have come as far as one might think in the area of risk estimation.

The two primary principles of quality risk management, per ICH Q9, are:

> *The evaluation of the risk to quality should be based on scientific knowledge and ultimately link to the protection of the patient*

> *The level of effort, formality and documentation of the quality risk management process should be commensurate with the level of risk*

My first takeaway from these two expectations is that investigation reports should always include at least one or two sentences that explicitly describe the risk that the non-conformance may have on the patient, focused on the severity of the risk. If the non-conformance was not detected or escaped the containment system, would the patient be injured? Many non-conformances pose little risk. This does not absolve you of the obligation to discuss the risk. If the risk is low, say so! Just be sure to justify your decision.

My second takeaway based on the second bullet is that the level of effort should be commensurate with the level of risk. This is the focus of this article.

Risk assessment (or risk estimation) is the key.

> Do you have an objective, repeatable system to estimate risk?

> Do you prioritize these risks?

> Does your investigation SOP require a higher level of due diligence for non-conformances with higher risk?

ICH Q9 has a number of suggested tools for risk management. The most widely used tool is based on the scoring system used in failure mode and effects analysis (FMEA). Each non-conformance is evaluated for severity, occurrence and detection (The acronym SOD may help you remember these three categories). After assigning a risk score for each category, the numbers are multiplied to calculate an overall risk score, called a risk priority number (RPN). The higher the number, the greater the risk.

Many FDA-regulated companies have adopted a three-point rating scale for each category. For those of you who prefer words over numbers, the scores correspond to low, medium or high risk. The purpose of the risk prioritization is to discriminate between risk levels and ensure that higher risk events are subject to a higher standard of due diligence. But, as we will see below, your scoring practices may not deliver the expected results.

RPN COMBINATIONS																										
SEVERITY	1	1	1	1	1	1	1	1	1	2	2	2	2	2	2	2	2	2	3	3	3	3	3	3	3	3	3
OCCURRENCE	1	1	1	2	2	2	3	3	3	1	1	1	2	2	2	3	3	3	1	1	1	2	2	2	3	3	3
DETECTION	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3
RPN	1	2	3	2	4	6	3	6	9	2	4	6	4	8	12	6	12	18	3	6	9	6	12	18	9	18	27

figure 1.

First, let's consider the three-point scale used by most facilities. The table above (figure 1.) shows all possible combinations of risk scores and the resulting RPN numbers:

If you examine the RPN column, you will notice that the numbers 1 and 27 only appear one time. The number 2 appears three times. The number 6 appears most frequently – six times! The combinations of risk scores do not result in a nice, linear, continuous scale. Did you notice that there are no RPN scores between 18 and 27? The distribution is shown in figure 2.

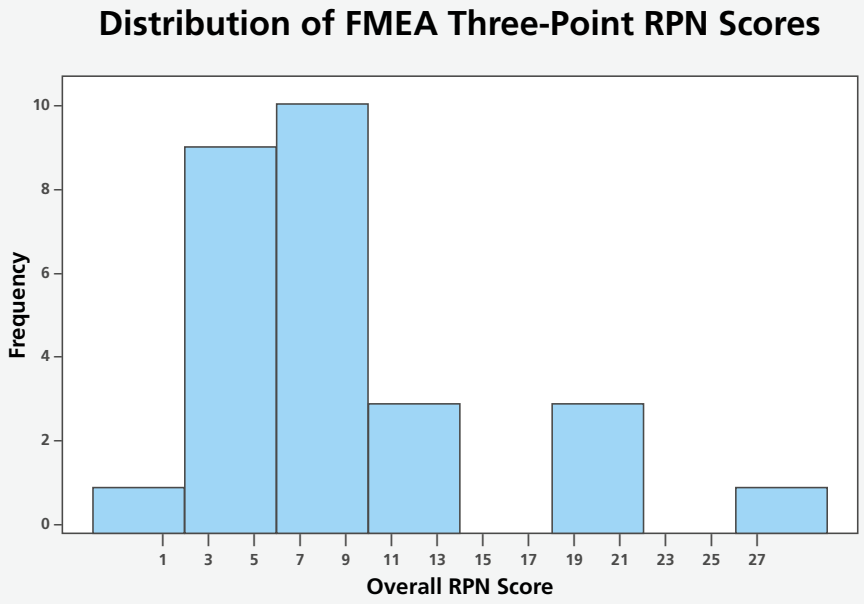

figure 2.

Why is this so important? Because if you do not understand how the RPN scoring system works, you may not discriminate properly.

Many companies assume that dividing the RPN scale into equal segments such as 1-9, 10-18 and 19-27 is sufficient. Think again! If you do this, 74 percent of the possible scores will fall into the low risk category, 22 percent will be medium risk, and less than 4 percent will be high risk. But that is not the end of the story. People have a natural tendency to minimize the scores to lower the overall risk. For example, they will discount severity based on their perception that the detection/containment system is robust. An example: "Although a patient could be injured, the risk is low because we have 100 percent automated inspection".

When I teach risk management courses, I always advise participants to evaluate each category *independently* of one another. This is the only way to ensure integrity when estimating risk.

We recommend that you evaluate your scoring system, including the scoring thresholds between risk categories. The review should also consider the scoring practices of your employees. Do they discount the risk when documenting the RPN numbers? Look at a large sample of investigations (at least 100) to see how many investigations fall into each category. The breakdown for one client was 95 percent low, 4.5 percent medium and 0.5 percent high risk. If everything is low risk,

then you are short-circuiting the intent of the risk assessment process.

Keep in mind that you cannot ignore non-conformances just because they are low risk. This is especially true for repetitive non-conformances. Eventually, management must override the RPN system and insist upon a thorough investigation for repetitive failures. This should be done during quarterly management reviews.

Some people believe they can improve the scoring system by using weighted scores for severity (3, 6 or 9) and regular scores (1, 2 or 3) for occurrence and detection. Such a scheme, while perhaps well intentioned, does not change the ability of the scoring system to improve discrimination. The revised scheme has exactly the same number and percentages of unique RPN numbers. The only way to improve discrimination is to change from a three-point scale to a five-point scale. Just be prepared to spend some time developing definitions and examples of each point on the scale. We think a three-point scale is sufficient, as long as you understand and avoid the pitfalls.

Have a question on this article? Contact us at **USpharma@nsf.org**.

ABOUT THE AUTHOR

For over 20 years, Andy Barnett has worked with clients in the pharmaceutical, medical device, biologic and biotechnology industries to develop quality assurance and regulatory strategies for compliance with U.S. FDA regulations. His particular expertise includes providing statistical support for process development, process characterization and optimization; assisting with remediation activities, especially corrective actions and process improvement; and providing training in root cause, corrective actions and statistical methods for process improvement.

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