

Risk Principles and Medical Devices: A Post-Market Perspective
A Draft White Paper for Public Review and Comment (February 6, 2015)
(Deadline for Comments: **MAY 20, 2015**)

Introduction

In collaboration with the U.S. Food and Drug Administration's Center for Devices and Radiological Health (CDRH), the Association for the Advancement of Medical Instrumentation (AAMI) convened an informal working group in the fall of 2014, whose purpose was to develop a shared understanding of *risk principles* that would guide both CDRH and the medical device industry in assessing and managing risk *in the post-market compliance setting*.

This white paper and the risk factors and risk principles it identifies are focused on post-market quality and safety issues and related activities by CDRH and industry. Representatives from the medical device industry and CDRH participated in the project, and this white paper is a synthesis of their work.

In the short run, the project was successful if for no other reason than to nurture open discussion between industry and CDRH staff. The open discussions served to build a more collaborative approach to tackling issues that both industry and CDRH have in common but see from very different perspectives. Longer term, this work will inform more discussion between industry and CDRH about additional post-market compliance issues where it would be helpful to have industry and CDRH alignment.

It is also anticipated that this work will inform future updates of AAMI/ANSI/ISO TC 210, the standards committee responsible for updating AAMI/ANSI/ISO 14971, which is an important resource for both the medical device industry and CDRH on risk assessment and risk management. During this work on developing risk principles and factors for the compliance setting, industry experts noted that AAMI/ANSI/ISO 14971 does not include much information about post-market risk assessment and risk management, and they noted that it would be helpful for the standards committee to address the work done here to help flesh out AAMI/ANSI/ISO 14971's consideration of post-market risk.

An additional goal of this joint CDRH-industry activity was to foster open discussion. The participants had deep academic and practical expertise on the subject of risk, and the discussions benefitted greatly from this collaborative atmosphere of mutual respect.

Why Work on Risk Principles

The public health in the United States is best served when industry, CDRH and other stakeholders understand, assess and approach risk consistently throughout the entire life cycle of medical devices.

If CDRH and industry have a shared view of risk based on a common set of risk principles, then less time will be lost resolving differences in understanding between regulators and industry, as well as all other stakeholders who are involved with or impacted by post-market safety and device quality issues. It is hoped that a shared view will minimize the differences in analyses of risk and resulting conclusions reached by industry and CDRH related to appropriate remedial actions. A common and consistent approach to risk will optimize and expedite patient care. This work will be considered successful in the long-term if it: 1) improves patient outcomes; 2) increases understanding of risk and factors influencing clinical risk in quality and device safety issues; 3) harmonizes the assessment process of risk and the evaluation of benefits and risk; 4) increases the consistency of post-market assessments; 5) speeds recognition and response to post-market safety issues; and 6) facilitates access to needed products.

Scope

The risk factors and principles described below are intended to be useful for clinical risk assessments of medical devices with *post-market quality and safety issues*. It includes assessment of risk above and beyond baseline recognized risk for devices (acknowledged in marketing clearance or approval). These risk issues arise in situations of device non-conformance, malfunctions or failures, or in limited availability situations. Post-market quality and safety includes but is not limited to recalls.

Out of Scope

The risk factors and principles are not intended to address: regulatory risk/benefit for premarket review, except for the basic understanding and definitions; quality system management in device design and manufacturing; detailed implementation of specific compliance activities by FDA or industry; academic theory about risk; or regulation changes.

There are a number of complex barriers to optimal risk management, such as:

- the legal/tort system in the United States, which may limit learning from adverse incidents because of concerns about openly sharing mistakes and lessons learned out of fear of the potential legal implications;
- the use of medical devices beyond their labeled indications for use or beyond their useful life because of cost pressures;
- the related practice of using multiple generations of the same medical device, which can add to risk in the environment of care;
- the complex societal and political views about how much risk we are willing to tolerate as a society and as individuals;
- the difficulty of learning about device issues in the field from service data on equipment that is serviced in hospitals, by third-party servicing organizations, or by other original equipment manufacturers (OEMs).

These barriers all directly or indirectly affect risk and device users but are difficult to specify and quantify in the limited scope of this paper. Manufacturers of medical devices also must address

many other complex issues in their assessment and management of risk across the full life cycle of medical devices (e.g., supply chain; quality and adequacy of sample size of the data for purposes of evaluating risk; other regulatory challenges). The existence of these complexities are acknowledged here because they impact how the risk factors and risk principles are applied for any given product or circumstance. In short, the application of risk factors and principles in real life is much more complex than it may appear from a simple reading of this white paper.

Definition of Risk

The standards and regulations include a number of useful definitions of terms. For purposes of this document, risk is defined as in ANSI/AAMI/ISO 14971: 2007/(R) 2010: *Risk is the combination of the probability of occurrence of harm and the severity of that harm.* Benefit is defined as *a helpful or good effect, or something intended to help.* ISO 16439: 2014 (en).

Decision Analysis

Consideration of risk principles and the factors that support them is only one part of the decision analysis in which risk is assessed and then managed. The ultimate goal for industry and CDRH is to make high-quality decisions about medical device risk. A good decision is not the same as a good outcome.

One of the industry experts provided the working group with a practical framework for decision analysis, called the Decision Quality (DQ) Chain. It is illustrated here:



Source: Decision Education Foundation. <http://www.decisioneducation.org/>.
For more information, the brief video on the DEF home page explains each link in the DQ chain.

Within each link of the DQ Chain we can identify the best practices and standards for medical device risk decisions. The DQ Chain thus serves as one organizing principle for thinking through risk. The DQ Chain is used here solely for purposes of illustrating the usefulness of some type of decision analysis tool. It certainly is not the only such tool.

The Significance of Risk Principles

Risk principles provide the foundational underpinning for risk assessment and risk management. Without alignment between CDRH and the medical device industry about risk principles, achieving harmonization on risk principles and risk management processes will not be possible.

Even so, an even deeper analysis and discussion between CDRH and industry will be needed for purposes of coming much closer to a shared understanding of how the principles are applied in real life when post-market examples of hazards and hazardous situations/harm occur. From an industry perspective, risk is characterized for a product as part of total product life cycle (TPLC) and is neither a premarket nor post-market specific concept. However, just as unexpected new infectious and contagious diseases come to North America and we don't have drugs or vaccines to deal with them, an issue or hazard can arise when a product is marketed that was not a hazard at the time of device creation or market clearance. A company may have even identified a hazard, but they anticipated the probability or severity was so low that it was not considered a reasonably foreseeable risk. Again, infectious and contagious diseases are useful illustrations of how this happens.

Identifying a baseline of the risk of harm prior to marketing is often difficult. When patients are harmed in a way or with a probability not anticipated, the original risk assessment may require revision. For example, there may be a grey area where FDA decides the benefit of having a device on the market outweighs the risk. When the device is marketed, however, patients experience the predicted harm at a rate or severity that is not readily comparable to the pre-market risk assessment. In such cases, an updated risk assessment is needed to determine if the benefits to patients still outweighs the risk, given the new understanding probability of harm and its severity.

Additionally, when considering responses to a revised risk assessment it may be necessary to consider the harm that may occur due to the consequences, such as a shortage caused by a recall. In such cases, Industry and CDRH need to evaluate the post-market risk assessment in the context of actions that may make the product unavailable in the marketplace.

Setting the Foundation for Risk Assessment and Risk Management

In preparation for thinking about risk principles, it is important to consider several philosophical points that are fundamental to any consideration and thus management of risk:

1. It is impossible to eliminate all risk. Consequently, one of the elements of a risk assessment is making a judgment of what overall risk is acceptable.

2. Risk assessments often are conducted without all of the information or data that would be helpful to the assessment. Delaying a decision to continue to gather more information may be a bad decision associated with greater risk than proceeding with (necessarily) incomplete information.
3. Compliance with applicable laws and regulations is a fundamental requirement. Risk principles do not govern all regulatory decision making, which must take into account the law and regulations. That said, it is important to note that regulatory reliability and quality issues may arise that are not associated with clinically significant safety issues and there may not always be reasonable actions that address these issues and that reduce risk.
4. AAMI/ANSI/ISO 14971 (2007)/(R)2010 (future references to the standard are specific to this version even when the shorthand “14971” or “AAMI/ANSI/ISO 14971” are used) lays out the risk management process that virtually all medical device companies doing business in the U.S. and Europe use for managing risk from a full life cycle perspective. That process starts with a risk analysis, and AAMI/ANSI/ISO 14971 states that identifying hazards and determining the severity and probability of harm is fundamental to assessing risk. Risk *evaluation* involves deciding what to do, which involves interpreting risks and benefits in the context of alternative actions. This will clarify whether accepting the risk is the best alternative.

Assessing a risk probability typically involves structuring the relationships between hazards (in both normal and fault condition), hazardous situations, and harms. This activity might be termed “qualitative.” At some point in the analysis numerical quantities (including but not limited to probabilities) may be useful. This activity might be termed “quantitative.” Both qualitative and quantitative thinking are important to risk assessment. Sometimes risk assessment requires nothing more than a verbal characterization (“qualitative”), but often the assessment will be characterized by both verbal formulations and increasingly detailed mathematical models (“quantitative”). Risk evaluation is reviewing the risk assessment and making a judgment of whether a risk is acceptable or unacceptable, applying company and/or community standards that attempt to capture patient and public preferences.

Ultimately, the analysis—whether quantitative or qualitative—is intended to support and *not* replace judgment. The goal of risk evaluation is to clarify a complex decision such that the judgment about what should be done is readily made, easily understood, and defensible. For example, a risk evaluation can help the decision makers understand how the probability of harm and thus risk varies with factors such as when the use occurs in a device life, whether it is used with multiple patients, and other clinical and nonclinical application characteristics. In the absence of high-quality analysis, people will naturally have more difficulty in the risk evaluation part of the overall risk process, because unassisted judgment is subject to widely recognized biases and thus is difficult to defend.

Risk management principles should also help address the issue of criticizing the decisions and actions made by others by providing standards for good risk management decision

making. While easier said than done, decisions should not be judged by the outcome. The standard should be: Was the risk management decision consistent with what a reasonable person would conclude, given what was known or what could be reasonably expected about the uncertain harms and benefits of various potential actions at the time the decision was made? Again, not all risks can be eliminated.

5. Judgments on acceptable or unacceptable risk made by industry need to be supported by analysis that explicitly assesses key uncertainties using experience, historical data, etc. The analysis will enable a defensible judgment that goes beyond just citing standards, data, or conventional practice/experience. A well done risk evaluation analysis will show that the alternative chosen best balances harm and benefits given what was known at the time the risk management decision was made.

Some experts would contend that it is important to distinguish “known” risks from “theoretical risks.” Both, however, can be characterized by probability of harm and severity of harm. So this seems to be a distinction without a difference. Identifying “immediate” risks, on the other hand, may be relevant. Given that people generally prefer present benefits over future benefits, and prefer future harms over present harms, so-called time-preference may need to be captured when risks and benefits occur at different times. Known and immediate risks may or may not require intervention; theoretical and delayed risk may or may not require intervention. With respect to the rationale to intervene to make changes to a product, the principle of balancing risks and benefits is the key, not distinctions about known versus theoretical or delayed risks.

6. Risk should be assessed from a systems perspective, looking at it in the entire context of the environment of use and considering evolving circumstances that could change the risk profile (e.g., would the risk change with the introduction of some new device into the environment of care; how would device integration impact risk; etc.).
7. Knowledge of state of the art in clinical understanding should be a part of the overall risk assessment: what are the current expectations of clinical use; are there any changes in medical practice that could increase risk. This knowledge has regulatory implications and is part of the risk management framework.

Risk Principles

While AAMI/ANSI/ISO 14971 provides the overall framework that the medical device industry uses for risk management of medical devices across the full life cycle of those devices, it does not specify what principles of risk should be used to guide risk assessment or the management of risk. In the context of post-market compliance, the industry and CDRH experts who worked together on this project agreed that the following risk principles should guide both CDRH and industry post-market assessment of risk. Again, it is hoped that if both CDRH and industry share the same view about the risk principles, then post-market assessments and decisions should be more closely aligned:

1. Evaluation and Judgment

All risk benefit analysis requires the use of informed judgment. Information to be considered in a post-market environment should include relevant information such as: experience with the device, similar devices and the general type of product, historical data, and company/community standards, other similar product information, experience with similar devices, and potential planned mitigations. Evaluation should be conducted by teams with expertise, including but not limited to qualified medical/clinical professionals and subject matter experts (e.g., engineers; scientists; etc.).

Note: Community standards may include: international, *local* diseases and frequencies, country norms, and technical standards.

Note: In some cases non-conforming products may not require regulatory action, but still need an assessment of whether the product can be shipped or recovered once distributed.

2. Loss of Benefit Assessment

A loss-of-benefit assessment needs to be considered as part of the overall structured risk assessment for issues that emerge post-market. In determining the appropriate action or inaction, the evaluator should consider multiple benefit/risk scenarios in order to arrive at the optimal outcome. Each scenario should consider the potential introduction of new risk and the consequent effect on benefit (e.g., same benefit/increased risk; decreased benefit/increased risk; loss of benefit/increased risk from product withdrawal), as well as the potential for field shortages, market share, cancellations of procedures, and other ripple effects of action that can impact loss of benefit.

Note: This is not a premarket risk/benefit analysis per AAMI/ANSI/ISO 14971.

3. Populations

In conducting the risk assessment intended to address a device failure, an unanticipated problem or a shortage post-market, the evaluator should determine if there are subpopulations included in the indication for use at greater risk or benefit than the overall population that should be considered separately.

Note: Subpopulations excluded in the indication for use are outside the scope of the assumed benefit. Post-market problems occurring during off-label use need to be addressed in a different Industry CDRH forum.

In conducting the risk assessment, the evaluator should focus on individual risk to the patient and/or user with balanced consideration to the impacted population. In some cases it may be that

post-market problems raise possible harm to the overall population (including clinicians) either directly or indirectly, e.g. spread of infectious disease, fire, and explosion. In such cases risk assessment and evaluation must consider harm beyond harm just to the patient, but also to the wider population.

4. Use Environment and Clinical Assessment

The risk assessment should be evaluated in the context of the environment in which the device will be used. Risk assessment (including benefit loss assessment outlined above) should be conducted considering the total clinical system within which the device will be used, including but not limited to, transport, hospital use, home use, backup systems, interaction with other devices and systems, impact of multiple device environments or multiple device use.

Consequently, a qualified clinical professional should participate in the post-market risk assessment. The clinical risk and benefits or reduction in benefits should be evaluated with a knowledge of current clinical practices, expectation of clinical use, and how changes in medical practice may change the assessment.

5. Communication

Important device risks and/or any reduced or loss of benefits to patients due to a failure, unanticipated problems, or shortages that occur once the device is marketed should be communicated effectively to relevant stakeholders.

Note: It is important that communication be effectively made to relevant stakeholders given that too much communication can cause audiences to stop listening, thereby increasing risk. It's also important to consider cultural diversity and health disparities in determining communication strategies.

Stakeholders input needs to include physicians and others such as:

- patients
- users
- regulators
- healthcare facilities
- healthcare providers
- hospital biomedical engineering, service providers, technicians
- SMEs (small and medium enterprises)
- Community partners

6. Recovering Loss of Benefit and Mitigation

After risks that develop post-market are identified and assessed, mitigations are used to return the benefit of the device to acceptable levels by recovering the full device benefit, if possible. Risk assessment and management tools will need to address potential actions when full benefit cannot be recovered. Effective risk management in a post-market environment requires understanding the potential impact of the loss of benefit from the device, risks to the patient caused by the defect or failure, and potential harm from other devices that may be used in place of the device. Various options available for minimizing or preventing re-occurring risks, and level of understanding of the business of healthcare and ownership of results of any risk management need to be considered in determining the options for mitigating a post-market event.

Note: Once a post-market event occurs that was not identified and accounted for in the risk management plan, the premarket mitigation has failed since the event was not prevented. Premarket mitigation may not have been provided if the event was not anticipated, but lack of mitigation is also a failure once a post-market event occurs.

Factors to Consider When Applying the Principles and Assessing Benefit/Risk to Post-Market Quality and Safety Issues

There are a number of factors that can be considered when applying these risk principles and assessing both benefit and risk in the context of post-market quality and safety issues. These factors should apply as they are relevant to the post-market event. Not every risk factor is applicable to every situation, and this list is intended to help stimulate a thorough analysis. From the perspective of CDRH, disagreements may require justification/documentation. It is noted that this is a long list and the items are categorized but not explained. There were too many possible factors to explain each one. It is still worth sharing the long list because it represents the best thinking of the industry and CDRH experts who did this work together.

1. Rating Harm and Hazard: Severity of Harm

- Duration of exposure
- Acute vs. chronic
- Reversibility of harm (e.g. death, injury)
- Body part impacted
- Pain intensity and duration of recovery
- Extent of event needed to create injury or disease
- Known and immediate injury vs. theoretical risk
- Patient vs. operator vs. others – who is harmed?
- Patient preferences (quality of life) context of benefit given known harm (consider alternatives)

2. Probability of Occurrence of Harm (Also Referred to as Frequency of Harm)

- Not all hazards result in harm

3. Complexity factors

- Complexity of use (human factors use error/usability of the device)
- Systemic vs. randomly occurring
- Unexpected or uncertain hazard vs known prior adverse events
- Chronic harm may take time to become evident
- Failure detectability / user awareness of an existing problem
- Single vs. multiple use device
- Intended use of the device
- Software dependency
- How many other devices are likely to be in use with this particular device – is there an additive nature of multiple devices used at the same time on the patient

4. Risk Management Factors

- Acceptable risk (rationale)
- Extent of change needed to recover lost benefit/reduce risk
- Impact on entire health system (e.g. replacing very expensive equipment means a hospital has less money for other capital improvements)
- Impact of defect or failure on other devices
- Does a mitigation option introduce another unacceptable risk?
- If a newer product has increased benefit, does previously acceptable risk ever become no longer acceptable?
- Balance between benefit vs. severity and frequency of harm
- Nature of the defect or failure relative to societal values and preferences
- Availability of products and suitable replacements or alternatives, percent of market share, delay in treatment. This is a consequence of device defect not a defect itself. (This is a post-market factor not considered in AAMI/ANSI/ISO14917).
- Cumulative history of repeated malfunctions/failure modes
- Whether reliability and quality issues will impact safety
- Level of risk may influence level of documentation by the manufacturer and level of FDA intervention.
- Consistency of quality system risk management framework (AAMI/ANSI/ISO 14971) across the entire device life cycle (unanticipated problem or shortages not addressed)

5. Affected Population Issues

- Clinical impact on users/patients
- Health status of users/patients (increased sensitivity to particular failure/fault)
- Age of population impacted
- Size of population involved
- Amount of benefit or harm in different populations (small benefit large population or large benefit in small population)
- Impact on other patients/populations
- Known vs. theoretical sensitive populations

6. Clinical Care Issues

- Mitigations taken or planned to recover lost benefit based on clinical practice
- Likely/known off-label uses and misuses
- Lifesaving / life sustaining uses for devices
- Where is the device being used and by whom (e.g., home care vs. ICU) – what is the skill level of the user?
- Other options available
- Effectiveness of communication to users (who is the user; what will they understand; who is translating the information to the patient; etc.)
- Unmet medical needs
- Risks with alternative choices
- Use in emergency/crisis situations
- Patient tolerance for risk
- Duration of device exposure:
 - a. implanted;
 - b. location;
 - c. patient age;
 - d. weight;
 - e. level of physical activity;
 - f. device aging
- Clinical understanding in evaluating risk
- Current expectations in clinical use
- Any changes in medical practice that could increase risk

7. Environment of Care Issues

- Causes of and interactions among various failures and faults and the potential impacts of multiple concurrent hazards or actual events resulting in harm
- Available medical device service information
- Labeling
- Training
- Experience with the device
- Mode of availability
- Overall use environment
- Age of the device and its estimated remaining shelf life or use life.
- How long on market without updates/change
- Do other products have similar issues
- When use occurs in a device life
- Multiple patient use or single patient use
- Multiple use or single use/disposable
- Consumables and incompatible consumables
- Evolution of the practice of medicine as it relates to the evolution of products e.g. a new drug or device enters the market that interferes with old product already marketed.
- Other impacts e.g. antibiotic coating and bacterial drug resistance

Risk Principles in Context

In this section of the white paper, several representative examples are provided from the set of examples that the working group used to help set the context for developing the above risk factors and risk principles.

The purpose of including these examples and the discussion points is to put the risk principles into real and meaningful context. They are illustrative only, with the caveat that every risk scenario is unique.

1. The following example was considered an excellent model of industry and CDRH working well together to solve a practical problem with a shared discussion of the risk and ways to solve that risk to minimize problems in the market. It is included here for that reason: A biological indicator was recalled and during the CAPA investigation, deterioration of the manufacturing machinery was found. The firm notified FDA that there would be a decrease in product available for some time. A few months later, the firm contacted FDA about reports that surgeries were being delayed due to lack of biological indicators. The firm did not expect to return to full production for some time.

The risk considerations included the risk of delayed surgeries/ prioritization of critical surgeries/ rationing of indicators versus the risk of using instruments without sterility confirmed. The firm proposed a temporary change in Instructions for Use that would allow monitoring of fewer loads. After review of data from the company, CDRH agreed that the risk of less frequent testing was acceptable until adequate supplies of the indicator were available. FDA also accelerated review of an in house 510(k) from the manufacturer of an alternate indicator.

One of the challenges faced was coordination of response to the shortage between offices. Another challenge was rapid review of additional scientific data to support the company's proposed strategy.

2. The following example illustrates the issue of potential “shortage” and the importance of including potential harm to patients from removing a product in the overall post-market risk assessment: A Class III implantable device has three (3) field complaints for a malfunction. MDRs are filed for malfunctions, blood loss occurs but no serious injuries occur, a complaint rate of 0.08%. The root cause was found to be design related. The investigation determines it is a low level, randomly occurring event that cannot be bounded. Removal of the product from the field will result in hundreds/thousands of cases being cancelled in critically ill patients with few options.
3. The following example illustrates the real life difficulty of post-compliance decisions when CDRH and industry do not have a shared view on how to prioritize the overall risk to patients when the severity is high and the frequency is very low. At extremely high blood glucose levels of 1024 mg/dL and above, the meter will display and store in its memory an incorrect test result that is 1024 mg/dL below the measured result. Device is a Class II device.

Company assessment of risks:

- Severity= High
- Frequency= Remote
- Probability of Harm= Rare – no change from initial assessment
- Overall Risk= Low
- Mitigation= The likelihood of experiencing extremely high blood glucose levels such as 1024 mg/dL and above is rare. For users of this meter, it is likely that a user would be testing on a regular basis. Hyperglycemia would likely be recognized prior to reaching levels above 1023 mg/dL. In addition, a user would be experiencing hyperglycemic symptoms which would prompt them to test more frequently and/or seek medical attention.

Factors that made assessment difficult: While the severity of this issue was High, the likelihood of the issue actually occurring was extremely Low due to known factors of use. The overall Risk to the user was determined to be Low and the rate of harm did not change, though a new hazard was identified. However the issue was deemed high risk (Class I recall) by FDA.

4. The following example illustrates why industry experts see “communication” as an important risk principle. It also illustrates the importance of evaluation and judgment in the risk assessment, as well as a deep understanding of the use environment and total clinical system in which the device will be used (in order to understand the implications of the options): A company initiated a global mailing to remind patients and healthcare providers about a feature in its drug delivery device that allows the user to scroll continuously from the maximum set amount to the minimum set amount, without having to scroll back in the other direction. This particular feature has been, by default, in every drug delivery device produced since the 1980’s.
5. The following example illustrates several issues, especially the importance of good documentation of the risk assessment. A sample of catheters failed an FDA import visual exam due to small clumps of debris on them. However, the inspection was performed using a microscope providing 20X magnification or more.

There was concern that the catheters did not comply with the following standards:

- ISO 10555-1, “Intravascular catheters — Sterile and single-use catheters — Part 1: General requirements”, Section 4.4, and
- ISO 11070-1998, “Sterile single-use intravascular catheter introducers”, Section 4.3, which both state:
- “When examined by normal or corrected to normal vision, with a minimum 2.5x magnification, the external surface of the effective length of the catheter shall appear free from extraneous matter”

The firm maintained that this was innocuous material with no risk to the patient, and it would meet the firm’s specification for cosmetic defects.

Without strong documentation, it was not clear whether the firm used ISO 10555-1 for their manufacturing specifications and, if so, had failed to meet it. Second, it was not clear whether debris seen at more than 2.5x magnification would pose a significant risk of adverse health events.

Challenges included (1) Documentation of how an external standard is used in order to assess manufacturing compliance to the standard. (2) The lack of clearly stated criteria such as level of magnification for examinations. (3) Assessment of risk with incomplete information about effects of intravascular introduction of small particles into the circulation, and impact of size

of particles on safety. If the assessment was done, it was not documented well, which raised the question of whether the risk had even been considered.

Next Steps

A number of issues surfaced in the working group discussions that will need to be addressed in more detail during the next phase of this risk project. Those issues are mentioned in the context of this white paper simply to provide context to the reader about the additional topics that the working group members acknowledged will need further work. As of the time of this writing, no determination has been made about when or how that work will be done, unless otherwise noted.

1. How will the risk principles be weighted? And how will the weighting criteria be evaluated to determine the “correct” results?
2. Issues that arise in determining Class 1 vs. Class 2 recalls.
3. Recalls of products with compliance issues that have no impact on safety (technical violations vs. substantive violations).
4. How to conduct a risk assessment.
5. How to interpret and use the risk assessment.
6. To what extent AAMI/ANSI/ISO 14971 would benefit from being augmented to address more *post-market* issues than it currently includes. For example, the standards committee might consider weaving in the use of the risk principles and factors in the section on evaluation of overall residual risk acceptability. The committee might also want to tie the risk factors into Annex C, which includes questions to help identify risk. It would also be useful for the committee to evaluate how else the risk factors and principles could interact with AAMI/ANSI/ISO 14971 in the future.
7. Issues around whether (if ever) to apply a worst case assessment vs. overall risk on a continuum. The industry experts in the working group found the notion of “worst case” to be problematic.
8. How to make precedents more transparent so industry can learn from them.
9. Several of the industry experts expressed that they would like to carry the risk principles further to provide standards for risk evaluation by codifying what are defensible judgments, in order to harmonize industry and regulatory perspectives on this important point. This was not discussed at any length and may or may not become part of further work. It is included here to memorialize the request from industry to address it.

10. Some industry experts would like to work on a definition of “baseline,” which is a term used by CDRH but not by industry. The industry experts think it must mean “the premarket risk file,” because this would clearly delineate the scope to only unexpected risks or new risk inputs, which either drive revisions to 1) The Risk File (to define and evaluate the risk), or 2) The Device (to further mitigate and bring the risk back in line with the pre-market risk profile). More work appears to be needed to gain a shared view of this.

Conclusion

FDA has stated publicly that it is dedicated to being more predictable, consistent, and transparent across the agency. Embedded in this goal is a dedication to seek input from stakeholders about its approach to risk and risk assessment and how they relate to continued benefit in post-market situation where new hazards develop that were not present or not known at the time of clearance or approval.

As applied to the compliance area, there is a strong shared desire by both FDA leadership and industry to harmonize expectations of FDA, industry, and other stakeholders. The first step has been achieved through this collaborative process that allowed for the development of mutually agreeable risk principles developed jointly by FDA staff and industry. The next steps will be even more important, as subgroups begin to tackle harder questions around the application of the risk principles in various compliance scenarios where industry and FDA in recent years have not been aligned with a shared view of risk.

Working Group

The three *national* industry trade associations (AdvaMed, Medical Imaging & Technology Alliance [MITA], and Medical Device Manufacturers Association [MDMA]) were invited to name three representatives each to the working group. As convener, AAMI also named three representatives to the working group. Additionally, FDA provided several representatives. The working group members are listed in Appendix A. Dr. Kimber Richter served as the FDA co-chair and project lead. Ginger Glaser served as the industry co-chair.

Instructions for Submission of Comments

Please submit all comments by e-mail to Mary Logan at mlogan@aami.org and Lauren Clauser at lclauser@aami.org.

Appendix A: Risk Principles Working Group

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