

Johnson & Johnson

410 GEORGE STREET
NEW BRUNSWICK, NJ 08901-2021

1063 10 SEP 22 AM '06

September 21, 2005

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. 2005D-0288; International Conference on Harmonization: Draft Guidance on Q9
Quality Risk Management

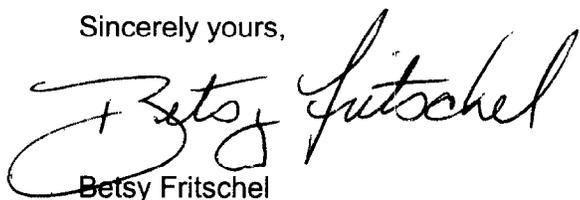
Dear Sir/Madam:

The attached comments on the above draft guidance are submitted on behalf of Johnson & Johnson and include a consensus summary from our family of companies. We feel that the document is overall well thought-out and well written. We especially appreciate the recognition that the level of effort and documentation should be commensurate with the level of risk.

We are however concerned that Figure 1 appears to be an endless loop of reassessing risk that has been determined to be unacceptable. We have a proposed revision that allows the consideration of additional information and the ability to stop the process. We have also proposed a number of revisions to the text to improve clarity.

Our detailed comments and rationale together with proposals for revision are provided in the attached Word table together with the Power Point file for the revision of Figure 1. Please feel free to contact me if you need further assistance or have any questions regarding these comments.

Sincerely yours,



Betsy Fritschel
Director, Quality and Compliance Worldwide

Attachments

2005D-0288

C1

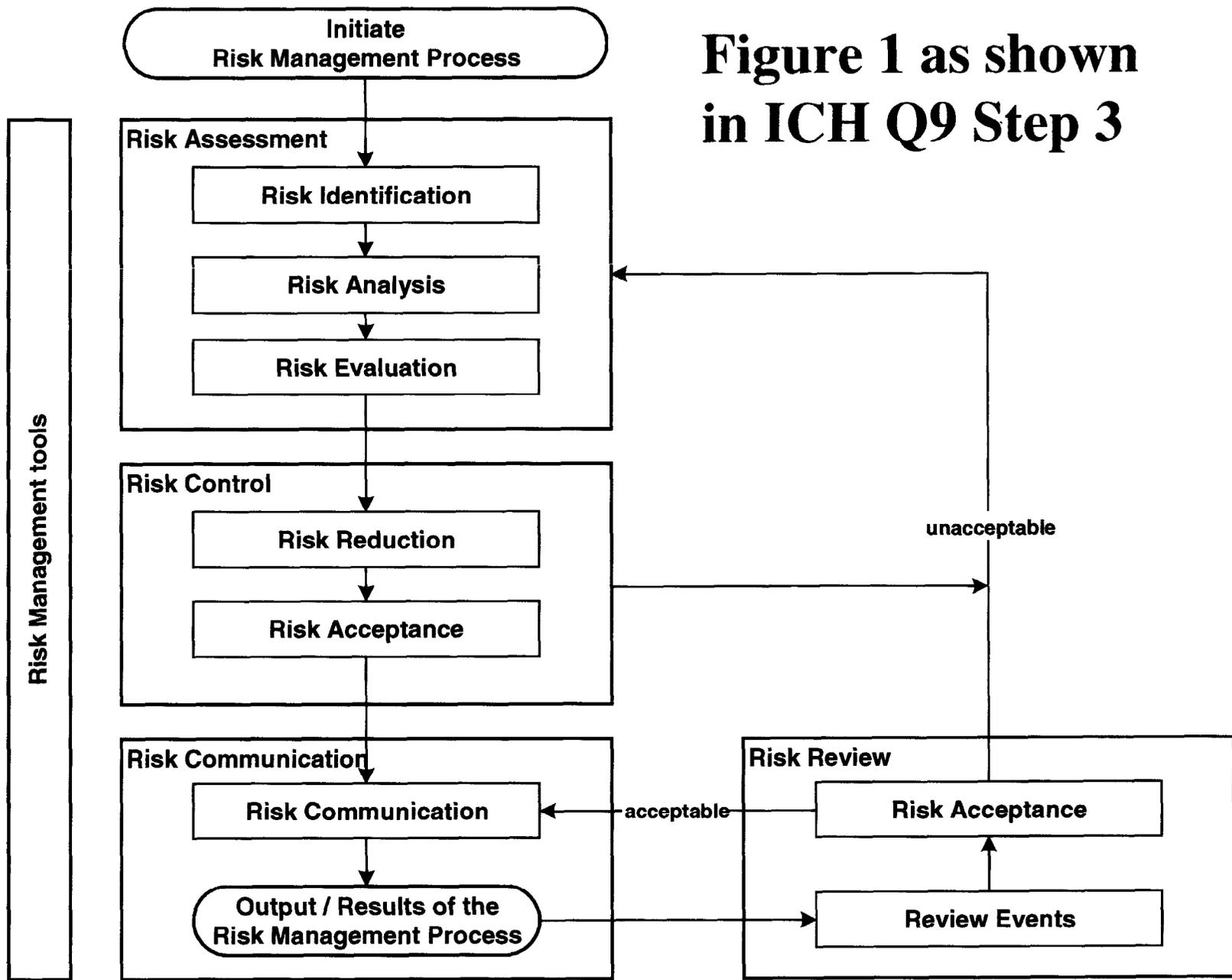
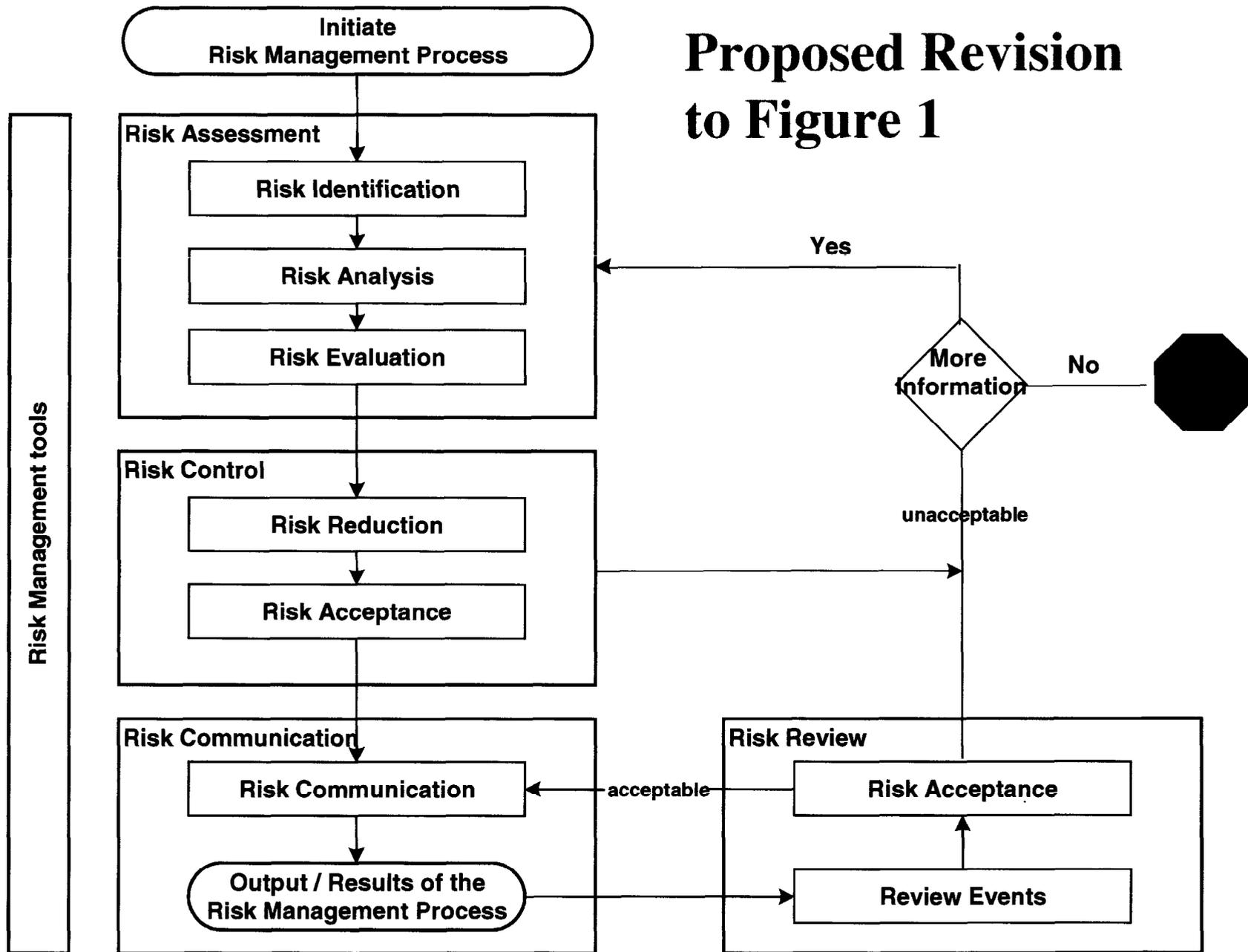


Figure 1 as shown in ICH Q9 Step 3

Proposed Revision to Figure 1



ICH Q9 - Quality Risk Management
 COMMENT SHEET for FDA at Step 3 (September, 2005)
 Comments Submitted by Johnson & Johnson

General comments:

Overall very well written and well thought-out.
Especially liked the statement in Section 3 : "The level of effort, formality and documentation of the quality risk management process should be commensurate with the level of risk and be based on scientific knowledge."
Clarify linkage between ICH Q8 and ICH Q9. Ensure that ICH Q10 also has clear linkage to ICH Q8 and ICH Q9. This clarification could be done in the upcoming training programs.

Please assign comments to a specific section and line number and indicate if the comment is:

- CRITICAL – Serious concerns that should be addressed
- Improvement – Needs to be considered and possibly corrected
- Editorial – Spelling, grammar, clarification

Section	Comment and Rationale	Proposed rewording or resolution (if applicable)	CRITICAL	Improvement	Editorial
2. Scope	Recommend including a clear statement of whether combination products are included or excluded from the Scope. Suggest including.	... throughout the lifecycle of drug substances and drug (medicinal) products, biological and biotechnological products, <u>drug device combination products</u> , including the use of raw materials, solvents, excipients, packaging and labeling materials.		x	
4 Figure 1	In the current figure, the arrow coming out of the Risk Control box makes a continuous loop back to Risk Assessment. There should be a decision point after unacceptable where either additional information is gained or the risk is determined to be too much and process is stopped.	See attached	x		
4.1	While risk management is everyone's responsibility. It should be "coordinated" at a very high level.	Decision makers <u>at appropriate levels</u> should take responsibility for coordinating quality risk management across various functions and departments of their organization. These decision makers should ensure that a quality risk management process is defined, <u>deployed and reviewed and adequate resources are available</u> , appropriate resources are involved and the quality risk management process is reviewed.	x		

ICH Q9 - Quality Risk Management
 COMMENT SHEET for FDA at Step 3 (September, 2005)
 Comments Submitted by Johnson & Johnson

Section	Comment and Rationale	Proposed rewording or resolution (if applicable)	CRITICAL	Improvement	Editorial
4.1	<ul style="list-style-type: none"> • Need to specify "Quality" Risk management • "dedicated to the task" implies that there are no other responsibilities other than risk management • it is helpful to provide examples of type of functions to include in the interdisciplinary teams 	<p>Quality Risk management activities are usually, but not always, undertaken by interdisciplinary teams dedicated to the task (e.g. QA, business development, engineering, regulatory affairs, operations, sales & marketing, legal).</p>	x		
4.2	Delete bullet 3. It is a restrictive statement. Decisions and conclusions should be a result of the analysis, not decided beforehand.	Define how decision makers will use the information, assessment and conclusions		x	
4.3	Add an additional fundamental question	4. What is the ability to detect?		x	
4.3	Risk analysis already refers to "an ability to detect". Clarify this by adding question 4 above and referring to it in this definition.	Risk analysis is the estimation of the risk associated with the identified hazards. It is the process that focuses on the second and third fourth questions, seeking the likelihood that risks identified in risk identification might occur and an ability to detect them.		x	
4.3	Clarify that the numerical probability scale is an example. Delete second half of the paragraph as it is confusing	The output of a risk assessment is either a quantitative estimate of risk or a qualitative description of a range of risk. When risk is expressed quantitatively, a numerical probability scale such as from 0 to 1 (0% to 100%) is used. Alternatively, risk can be expressed using qualitative descriptors, such as "high", "medium", or "low", and they should be defined in as much detail as possible. In quantitative risk assessments, a risk estimate provides the likelihood of a specific consequence, given a set of risk-generating circumstances. Thus, quantitative risk estimation is useful for one particular consequence at a time. Alternatively, some risk management tools use a relative risk measure to combine multiple levels of severity and probability into an overall estimate of relative risk. The intermediate steps within a scoring process can sometimes employ quantitative risk estimation.		x	
4.5	Clarify	The included information might relate to the existence, nature, form, probability, severity, acceptability, treatment risk mitigation , detectability or other aspects of risks to quality.		x	

ICH Q9 - Quality Risk Management
COMMENT SHEET for FDA at Step 3 (September, 2005)
Comments Submitted by Johnson & Johnson

Section	Comment and Rationale	Proposed rewording or resolution (if applicable)	CRITICAL	Improvement	Editorial
4.5	Specifying documentation only when a formal process is used, could drive behavior to informal processes in order to avoid documentation	The output of the quality risk management process should be appropriately communicated and documented when a formal process has been utilized.	x		
4.6	Periodic review of "events" is unclear. Recommend rewording as shown	Risk management should be an ongoing quality management process and a mechanism to perform periodic review of the decisions taken by the quality risk management process events should be implemented.		x	
5	Insert "Quality" into title for clarity	5 Quality Risk Management Tools			x
5	Add cross-reference to Section 8	The references are included as an aid to gain more knowledge and detail on the particular tool. This is not an exhaustive list. (See Section 8 for more detailed references.)		x	
5	Clarify last bullet	Supporting statistical and reliability tools		x	
5	Example does not help. Recommend deleting	Quality risk management tools and the supporting statistical tools can be used in combination (e.g. Probabilistic Risk Assessment).		x	
6	The whole subject of formal vs informal is confusing. Recommendation for clarifying.	The degree of rigor and formality of quality risk management can be commensurate with the complexity and/or criticality of the issue to be addressed. For simple, less critical situations, risk assessment is embedded in the existing systems (e.g. change control) . an informal approach is usually appropriate. For more complex or critical situations, a more formal approach, separate risk assessment using recognized tools (as described in section 5) to conduct and document the quality risk management might be beneficial.	x		
Annex 1.6	As written it implies that all process steps must be validated, but that non-critical may operate outside the validated range	To distinguish between critical process steps that must be operate within validated ranges and non-critical process steps that do not necessarily need to be have to operate within validated ranges.	x		