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October 3, 2005

**Division of Dockets Management (HFA-305)  
Food and Drug Administration (FDA)  
5630 Fishers Lane, rm. 1061  
Rockville, MD 20852  
U.S.A.**

**Re: Docket No. 2005D-0288**

**Dear Sir/Madam:**

**We, the Japan Society of Pharmaceutical Machinery and Engineering (JSPME) are pleased to submit you our offers and comments concerning "International Conference on Harmonisation; Draft Guidance on Q9 Quality Risk Management" (Docket No. 2005D-0288). We hope that you will consider our comments, and this guidance will be a very fruitful guidance for assuring product quality and ensuring risk management.**

**We would be much obliged if you give us FDA review of our comments by letter or e-mail.**

**Contacts;**

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**Sincerely,**



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2005D-0288

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**Comments on “International Conference on Harmonisation; Draft Guidance on Q9 Quality Risk Management” (Docket No.2005D-0288)**

**The Japan Society of Pharmaceutical Machinery and Engineering (JSPME)**

**Key Philosophical or Strategy Issues**

The guideline states first as “The purpose of this document is to serve as a foundational or resource document *that is independent yet supports other ICH Quality documents and complements existing quality practices, requirements, standards, and guidelines* within the pharmaceutical industry and regulatory environment.” in its “1. INTRODUCTION” section.

Actually, the guideline contains many descriptions relevant to other existing guidelines such as Q8. As explained in the next page of this comment, the guideline should clarify its position to other existing guidelines and include those guidelines in “8. References” section.

The guideline might be more useful when the basic understanding of “What is Quality Risk?” is shared by all the stakeholders. The guideline defines “*Quality*”, “*Risk*”, “*Risk Management*” and “*Quality Risk Management*”, respectively. However, it gives no definition for the term, “*Quality Risk*”. We can not find any definite example of “Quality Risk” even in “Annex I”. We propose that more descriptions that provide a common understanding of “What is Quality Risk” to stakeholders will be added.

**ICH Q9: Quality Risk Management Key Items for Consideration**

Japan Society of Pharmaceutical Machinery and Engineering

Item with Reference Line #	Key Concerns with Explanation of Position	Proposed change
<p><b>Section 1. Introduction</b> Line 33 of Page 5  <i>"The purpose of this document is to serve as a foundational or resource document <u>that is independent yet supports</u> other ICH Quality documents and complements existing quality practices, requirements, standards, and guidelines within the pharmaceutical industry and regulatory environment."</i>                      Line 40 of Page 5  <i>It is not intended to create any new expectations beyond the current regulatory requirements.</i></p>	<p>The guideline states that <i>"that is independent yet supports"</i> and <i>"complements existing quality practices, requirements, standards, and guidelines"</i>. In the other part, it states that <i>"It is not intended to create any new expectations beyond the current regulatory requirements"</i>.                      These statement may bring a certain confusion.</p>	<p>The guideline should clarify its position to other existing guidelines.</p>
<p><b>Section 1. Introduction</b> Line 42 of Page 5  <i>"Although a systematic approach to quality risk management is generally preferred, it is neither always appropriate nor necessary to use a <u>formal risk management process</u>. The use of <u>informal risk management processes</u> can also be acceptable."</i></p>	<p>Two terms, "formal risk management process" and "informal risk management process" are used. The difference between the two terms is to be clarified. We think it is not necessary to use the two terms separately.                      In Section "5.2 Informal Risk Management", "<i>informal risk management</i>" is explained. We think the use of "<i>informal risk management</i>" as a title of the contents is not adequate.</p>	<p>Suggest avoiding the term "informal"</p>
<p><b>Section 4. General Quality Risk Management Process</b> Line 19 of Page 6  <i>"The emphasis on each component of the framework might differ from case to case but a robust process will incorporate consideration of all the elements <u>at an appropriate level of detail</u>."</i></p>	<p>The expression, "<i>at an appropriate level of detail</i>" is hard to be interpreted.</p>	<p>Some specific criteria should be given or illustrated by examples.</p>
<p><b>Section 4. Responsibilities</b> Line 6 of Page 7  <i>"<u>Decision makers</u> should take responsibility for coordinating quality risk management across various functions and departments of their organization."</i></p>	<p>In development and manufacturing of pharmaceuticals, "Who is decision maker" should be given with a consideration under GMP regulation.</p>	
<p><b>Section 4.2 Initiating a Quality Risk Management Process</b> Line 20 of Page 7  <i>"• Define the problem and/or risk question, including pertinent assumptions identifying the potential for risk;"</i></p>	<p>The statement is hard to be interpreted.</p>	<p>Suggest expressing the content in multiple statements.</p>

**ICH Q9: Quality Risk Management Key Items for Consideration**

Japan Society of Pharmaceutical Machinery and Engineering

Item with Reference Line #	Key Concerns with Explanation of Position	Proposed change
<p><b>Section 4.3 Risk Assessment</b> Line 17 of Page 8 <i>"Typical sources of uncertainty include gaps in knowledge (e.g., gaps in pharmaceutical science and process understanding)"</i></p>	<p>We wonder why this example of pharmaceutical development was selected. This example may remind us Q8 guideline. We hope to provide a certain explanation on the background for the choice of the example.</p>	
<p><b>Section 4.5 Risk Communication</b> Line 19 of Page 9 <i>"Sometimes, a formal risk communication process is developed as a part of risk management."</i></p>	<p>Is it necessary to use the term "formal" in the context?</p>	<p>If it is, the guideline should clearly describe "formal" ones against "not formal" ones and the importance of "formal" ones in the scope of this guideline.</p>
<p><b>Section 5.2 Informal Risk Management</b> Line 31 of Page 10 <i>"The pharmaceutical industry and pharmaceutical regulators have assessed and managed risk in a variety of more empirical ways, based on, for example compilation of observations, trends and other information."</i></p>	<p>We understand that this content does not match the section title "Informal Risk Management".</p>	<p>Suggest avoid the term "informal".</p>
<p><b>Section 6 Integration of Quality Risk Management into Industry and Regulatory Operations</b> Line 25 of Page 14 <i>"Quality risk management should be integrated into existing operations and documented appropriately."</i></p>	<p>We understand that this actually means regulatory requirements in development and manufacturing of pharmaceutical products.</p>	
<p><b>Section I.2 Quality Risk Management as Part of Regulatory Operations</b> Line 29 of Page 19 <i>"To identify risks which should be shared between inspectors and assessors ..."</i></p>	<p>The time point when the risks should be identified is not clear. We may understand the risks should be identified at the point of submission. Please provide understanding of regulatory agencies.</p>	
<p><b>Section I.9 Quality Risk Management as Part of Continuous Improvement</b> Line 4 of Page 23 <i>"An illustrative model for continuous improvement:"</i></p>		<p>Suggest adding a certain explanation on the schematic diagram in the main body. We especially need meaning of each allows.</p>