附則 20 品質風險管理（QUALITY RISK MANAGEMENT）

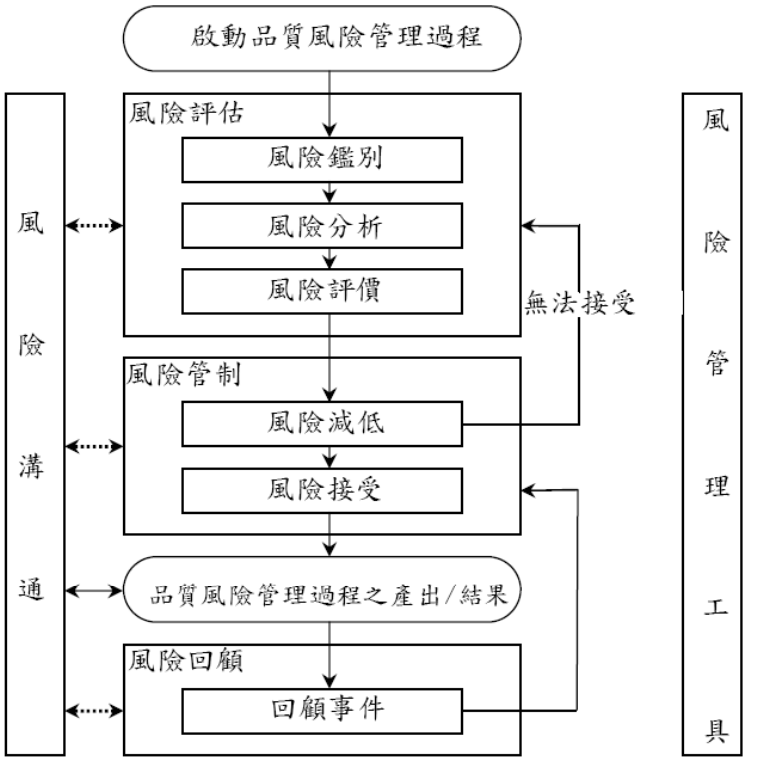
*本附則為自願性的/非強制性的。	* This Annex is voluntary.
序文和適用範圍 （FOREWORD AND SCOPE OF APPLICATION）	
1. 新的 GMP 附則 20 相當於 ICH Q9 關於品質風險管理的指引。它對於品質風險管理提供系統性方法之指引，以利遵守從 GMP 及其他品質之要求。當應用正式的品質風險管理方法時，它包括要使用之原理及可能使用之過程、方法和工具的選項。	1. The new GMP Annex 20 corresponds to ICH Q9 guideline on Quality Risk Management. It provides guidance on a systematic approach to quality risk management facilitating compliance with GMP and other quality requirements. It includes principles to be used and options for processes, methods and tools which may be used when applying a formal quality risk management approach.
2. 為確保其連貫性，已經修訂 GMP 第一部第一章關於品質管理之規定，以將品質風險管理的層面包含在品質系統架構內。計劃對本指引之第二部進行一個類似的修訂。GMP 指引之其他章節可能加以調整，以將品質風險管理的層面包含在將來那些章節之更為寬廣的修訂中。	2. To ensure coherence, GMP Part I, Chapter 1 on Quality Management, has been revised to include aspects of quality risk management within the quality system framework. A similar revision is planned for Part II of the Guide. Other sections of the GMP Guide may be adjusted to include aspects of quality risk management in future broader revisions of those sections.
3. 隨著在 GMP 第一部及第二部中之品質管理章節的修訂，品質風險管理變成製造廠品質系統之不可或缺的一部分。惟附則 20 本身並不意圖創造任何新的法規預期效果；它只是提供一份國際公認之風險管理方法及工具的清單，連同一份得由製造廠自由裁量其潛在應用的清單。	3. With the revision of the chapters on quality management in GMP Parts I and II quality risk management becomes an integral part of a manufacturer's quality system. Annex 20 itself is not intended, however, to create any new regulatory expectations; it provides an inventory of internationally acknowledged risk management methods and tools together with a list of potential applications at the discretion of manufacturers.
4. 據瞭解，ICH Q9 指引最初是為人用醫藥產品之品質風險管理而開發。隨著附則 20 的實施，指引之效益，諸如對品質風險管理之過程、方法及工具，亦可使用於動物用藥領域。	4. It is understood that the ICH Q9 guideline was primarily developed for quality risk management of medicinal products for human use. With the implementation in Annex 20 benefits of the guideline, such as processes, methods and tools for quality risk management are also made available to the veterinary sector.
5. GMP 指引主要係針對製造廠，而 ICH Q9 指引則與其他品質指引具有關聯，並包括對主管機關之特定部門。	5. While the GMP guide is primarily addressed to manufacturers, the ICH Q9 guideline, has relevance for other quality guidelines and

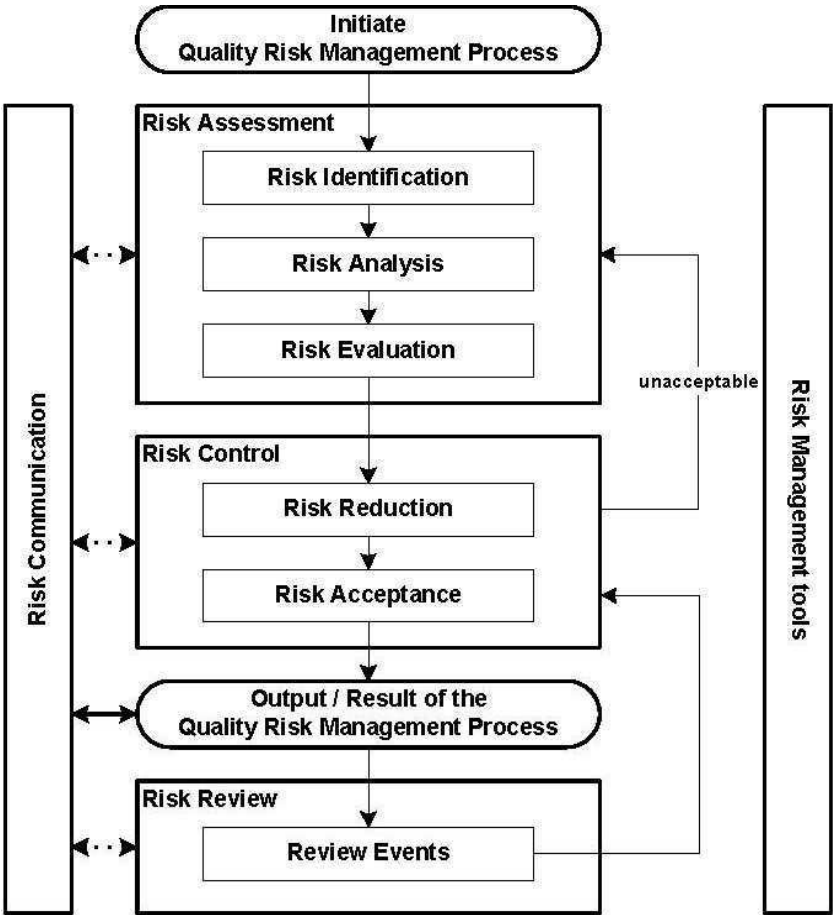
	includes specific sections for regulatory agencies.
6. 然而，為了連貫性及完整性，已將 ICH Q9 指引完全轉為 GMP 附則 20。	6. However, for reasons of coherence and completeness, the ICH Q9 guideline has been transferred completely into GMP Annex 20.
前言（Introduction）	
7. 風險管理原則，除有效地被利用在包括財政、保險、職業安全、公共衛生、藥物監視在內之許多商業及政府的領域外，亦被管理這些產業的主管機關有效地利用。雖然目前在製藥產業有一些*品質風險管理*之使用的實例，但他們是有限的，而且尚未代表風險管理應提供之全部的貢獻。此外，製藥產業中已經認知品質系統的重要性，而且變得越來越明顯的是，品質風險管理是一個有效品質系統之重要構成要素。	7. *Risk management* principles are effectively utilized in many areas of business and government including finance, insurance, occupational safety, public health, pharmacovigilance, and by agencies regulating these industries. Although there are some examples of the use of *quality risk management* in the pharmaceutical industry today, they are limited and do not represent the full contributions that risk management has to offer. In addition, the importance of *quality systems* has been recognized in the pharmaceutical industry and it is becoming evident that quality risk management is a valuable component of an effective quality system.
8. 普遍瞭解的是，風險經界定為損害之發生機率及該損害之嚴重度的結合。然而，因為每一位利害關係人可能感受不同的潛在損害，可能將不同的機率置於每一損害的發生上，並且將不同的嚴重度歸屬於每一種損害上，所以在不同利害關係人（stakeholders）間難以達成風險管理之應用的共識。關於醫藥產品，雖然有各種不同的利害關係人，包含病人和執業醫師以及政府與產業在內，但經由品質風險管理以保護病人應被視為最重要。	8. It is commonly understood that *risk* is defined as the combination of the probability of occurrence of *harm* and the *severity* of that harm. However, achieving a shared understanding of the application of risk management among diverse *stakeholders* is difficult because each stakeholder might perceive different potential harms, place a different probability on each harm occurring and attribute different severities to each harm. In relation to pharmaceuticals, although there are a variety of stakeholders, including patients and medical practitioners as well as government and industry, the protection of the patient by managing the risk to quality should be considered of prime importance.
9. 藥品(醫藥製品)之製造及使用，包含其組成物在內，必定伴隨著若干程度的風險。其品質之風險只是其整體風險的一個構成部分而已。重要的是，要瞭解在產品的整個	9. The manufacturing and use of a drug (medicinal) product, including its components, necessarily entail some degree of risk. The risk to its quality is just one

生命週期皆應維持產品品質，以將對於藥品(醫藥製品)之品質具有重要性的屬性，保持與臨床研究上所使用藥品的那些屬性一致。一個有效的品質風險管理方法，可以經由提供一個洞燭機先的方法，去確認和管制在開發及製造期間之潛在品質問題，以對病人進一步確保藥品的高度品質。此外，品質風險管理的使用，可以在品質問題發生時，改善其決策。有效的品質風險管理，可以幫助更好及具有更多情報的決策，可以就一個公司處理潛在風險的能力提供主管機關更大的保證，而且有利於影響主管機關監督的程度及等級。	component of the overall risk. It is important to understand that product *quality* should be maintained throughout the *product lifecycle* such that the attributes that are important to the quality of the drug (medicinal) product remain consistent with those used in the clinical studies. An effective quality risk management approach can further ensure the high quality of the drug (medicinal) product to the patient by providing a proactive means to identify and control potential quality issues during development and manufacturing. Additionally, use of quality risk management can improve the decision making if a quality problem arises. Effective quality risk management can facilitate better and more informed decisions, can provide regulators with greater assurance of a company's ability to deal with potential risks and can beneficially affect the extent and level of direct regulatory oversight.
10. 本文件之目的是要對品質風險管理提供一個系統性的方法。它當作一個基礎文件或資源文件，獨立但支持其他 ICH 品質文件，並補充製藥產業及管制環境內既存的品管慣例、要求、標準及指引。它具體地提供關於品質風險管理原則及一些工具的指引。該指引能使主管機關及產業二者基於風險，對於跨越產品生命週期之藥物和醫藥產品的品質所作的決策更為有效且一致。它無意創造超過當前法規要求之任何新的期望。	10. The purpose of this document is to offer a systematic approach to quality risk management. It serves as a foundation or resource document that is independent of, yet supports, other ICH Quality documents and complements existing quality practices, requirements, standards, and guidelines within the pharmaceutical industry and regulatory environment. It specifically provides guidance on the principles and some of the tools of quality risk management that can enable more effective and consistent risk based decisions, both by regulators and industry, regarding the quality of drug substances and drug (medicinal) products across the product lifecycle. It is not intended to create any new expectations beyond the current regulatory requirements.
11. 使用一個正式的風險管理程序（使用受承認的工具及/或內部程序，例如，標準作業程序）既非總是適合的，也非總是必需的。使用非正式的風險管理程序（使用經驗上的工具及/或內部程序）亦得認定為可接	11. It is neither always appropriate nor always necessary to use a formal risk management process (using recognized tools and/ or internal procedures e.g. standard operating procedures). The use of informal risk

受。	management processes (using empirical tools and/ or internal procedures) can also be considered acceptable.
12. 品質風險管理之適當的使用，可以是有幫助的，但不得排除產業需遵守法規要求的義務，也不取代產業與主管機關間之適當溝通。	12. Appropriate use of quality risk management can facilitate but does not obviate industry's obligation to comply with regulatory requirements and does not replace appropriate communications between industry and regulators.
範圍（Scope）	
13. 本指引提供可適用於製藥品質之不同層面的品質風險管理之原則及工具範例。這些層面涵蓋藥物、藥品、生物產品及生技產品（包含藥品、生物產品及生技產品之原料、溶媒、賦形劑、包裝及標示材料的使用在內）的開發、製造、運銷，以及檢查和申請/審查程序之整個生命週期。	13. This guideline provides principles and examples of tools for quality risk management that can be applied to different aspects of pharmaceutical quality. These aspects include development, manufacturing, distribution, and the inspection and submission/review processes throughout the lifecycle of drug substances, drug (medicinal) products, biological and biotechnological products (including the use of raw materials, solvents, excipients, packaging and labeling materials in drug (medicinal) products, biological and biotechnological products).
品質風險管理的原則（PRINCIPLES OF QUALITY RISK MANAGEMENT）	
14. 品質風險管理之二個主要原則是：	14. Two primary principles of quality risk management are:
• 品質風險之評估應以科學知識為基礎且最終連結到對病人的保護；以及	• The evaluation of the risk to quality should be based on scientific knowledge and ultimately link to the protection of the patient; and
• 品質風險管理過程之努力、正式性及文件制作的程度應與風險之層級相稱。	• The level of effort, formality and documentation of the quality risk management process should be commensurate with the level of risk.
一般品質風險管理過程 (GENERAL QUALITY RISK MANAGEMENT PROCESS)	
15. 品質風險管理是對藥物產品整個生命週期之品質風險的評價、管制、溝通及檢討之系統性的過程。品質風險管理的模式概述於圖 1。其他模式也可使用。該架構之每一構成部分的重點可能因個案而異，但健全的過程會將所有要素納入考慮，其詳細	15. Quality risk management is a systematic process for the assessment, control, communication and review of risks to the quality of the drug (medicinal) product across the product lifecycle. A model for quality risk management is outlined in the diagram

程度是與其特定風險相稱。	(Figure 1). Other models could be used. 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 at a level of detail that is commensurate with the specific risk.





16. 因為決策可能發生在過程中的任何一點，	16. Decision nodes are not shown in the diagram

所以決策結節(decision nodes)未顯示在上圖中。基於支持如此決策之資訊，這些決策可能會因而回到先前的步驟並尋求進一步的資訊，調整風險模式或甚至終止風險管理程序。**註：**流程圖中之「無法接受」並非只指法令、立法或行政管制的要求，而且亦指回顧風險評價過程的必要性。	above because decisions can occur at any point in the process. These decisions might be to return to the previous step and seek further information, to adjust the risk models or even to terminate the risk management process based upon information that supports such a decision. Note: "unacceptable" in the flowchart does not only refer to statutory, legislative or regulatory requirements, but also to the need to revisit the risk assessment process.
責任（Responsibilities）	
17. 品質風險管理活動，通常，但不是一直都由跨學科的團隊所從事。當組成團隊時，除了具有關於品質風險管理過程之知識的人員外，還應包含來自適當領域（例如，品質部門、業務開發、工程、法規事務、生產操作、銷售及行銷、法律、統計及臨床）的專家。	17. Quality risk management activities are usually, but not always, undertaken by interdisciplinary teams. When teams are formed, they should include experts from the appropriate areas (e.g. quality unit, business development, engineering, regulatory affairs, production operations, sales and marketing, legal, statistics and clinical) in addition to individuals who are knowledgeable about the quality risk management process.
18. *決策者*應該：	18. Decision *makers* should:
• 在其組織之不同職能與部門間負起協調品質風險管理的責任；而且	• take responsibility for coordinating quality risk management across various functions and departments of their organization; and
• 確保品質風險管理程序是經過界定、佈署及審查，並可獲得適當的資源。	• assure that a quality risk management process is defined, deployed and reviewed and that adequate resources are available.
引進品質風險管理程序（Initiating a Quality Risk Management Process）	
19. 品質風險管理過程應包含系統性決策程序，該過程經設計並可用於協調、幫助及改善基於科學所作風險之決策。使用於啟動及規劃一個品質風險管理過程之可能步驟包含如下：	19. Quality risk management should include systematic processes designed to coordinate, facilitate and improve science-based decision making with respect to risk. Possible steps used to initiate and plan a quality risk management process might include the following:
• 界定問題及/或風險疑問，包含確認風險之潛在性的相關假設在內；	• Define the problem and/or risk question, including pertinent assumptions identifying the potential for risk
• 組合有關風險評價之潛在危害、損害	• Assemble background information and/

或對人體健康之衝擊的背景資訊及/或數據；	or data on the potential hazard, harm or human health impact relevant to the risk assessment
• 確認一位領導者及必要的資源；	• Identify a leader and necessary resources
對風險管理過程規定其決策制定的時間表、可傳送的資訊及適當的層級。	Specify a timeline, deliverables and appropriate level of decision making for the risk management process
風險評價（Risk Assessment）	
20. 風險評價包含危害 之辨識及暴露於那些危害（如下面所界定）所相關之風險的分析與評估。品質風險評價始於完善界定問題的描述或風險問題。當完善界定風險問題時，則解決該風險問題所需要的適當風險管理工具(參見在第 5 節的範例)及資訊類型將更易辨識。為風險評價之目的，有三個基本問題，常有助於清楚界定風險：	20. Risk assessment consists of the identification of hazards and the analysis and evaluation of risks associated with exposure to those hazards (as defined below). Quality risk assessments begin with a well-defined problem description or risk question. When the risk in question is well defined, an appropriate risk management tool (see examples in section 5) and the types of information needed to address the risk question will be more readily identifiable. As an aid to clearly defining the risk(s) for risk assessment purposes, three fundamental questions are often helpful:
1. 什麼可能出錯？	1. What might go wrong?
2. 出錯的可能性(機率)為何？	2. What is the likelihood (probability) it will go wrong?
3. 後果(嚴重性)為何？	3. What are the consequences (severity)?
21. ***風險辨識***為系統性的使用資訊，以辨識有關風險問題的危害或問題描述。資訊可能包含歷史數據、理論分析、根據情報的意見，以及利害關係人的關切事項。風險辨識提示「什麼可能出錯？」的問題，包含辨識其可能的後果。這提供品質風險管理程序之後續步驟的基礎。	21. ***Risk identification*** is a systematic use of information to identify hazards referring to the risk question or problem description. Information can include historical data, theoretical analysis, informed opinions, and the concerns of stakeholders. Risk identification addresses the “What might go wrong?” question, including identifying the possible consequences. This provides the basis for further steps in the quality risk management process.
22. ***風險分析***是與經辨識之危害所關聯的風險進行估計。它是連結於事件發生之可能性及損害之嚴重度的定性與定量過程。在有些風險管理工具中，檢測損害的能力（可檢測性）亦是風險估計中的因素。	22. ***Risk analysis*** is the estimation of the risk associated with the identified hazards. It is the qualitative or quantitative process of linking the likelihood of occurrence and severity of harms. In some risk management

	tools, the ability to detect the harm (detectability) also factors in the estimation of risk.
23. ***風險評估***是將經辨識及分析的風險與已知的風險標準進行比對。風險評估是就所有三個基本問題考量其證據的強度。	23. ***Risk evaluation*** compares the identified and analyzed risk against given risk criteria. Risk evaluations consider the strength of evidence for all three of the fundamental questions.
24. 在執行有效之風險評價時，數據套組的健全性/耐用性是重要的，因為這決定產出（output）的品質。揭露不確定性（uncertainty）之假設及合理來源，將提高該產出之信心及/或幫助確認其限制。不確定性是由於過程的不完整知識及其預期或非預期之變異性的組合。不確定性之典型來源包括知識上的差距、製藥科學與製程瞭解上的差距、傷害的來源(例如過程的失敗模式、變異性的來源)，以及問題檢測的機率。	24. In doing an effective risk assessment, the robustness of the data set is important because it determines the quality of the output. Revealing assumptions and reasonable sources of uncertainty will enhance confidence in this output and/or help identify its limitations. Uncertainty is due to combination of incomplete knowledge about a process and its expected or unexpected variability. Typical sources of uncertainty include gaps in knowledge gaps in pharmaceutical science and process understanding, sources of harm (e.g., failure modes of a process, sources of variability), and probability of detection of problems.
25. 風險評價之產出是風險之定量估計或風險範圍之定性***描述***。當風險以定量表達時，使用數字表達其機率，或風險可以定性描述(例如「高」、「中」或「低」)表達。惟描述應盡可能界定其細節。有時可使用「風險分數」（risk score），以再進一步界定風險分級上的描述。在定量風險評價上，風險估計值指在假定之一套產生風險的情況下，提供一個特定後果的可能性。因此，逐一定量風險估計對於特別的結果是有用的。或者，有些風險管理工具使用一個相對風險計量（relative risk measure），以將不同層級嚴重度及機率組合成相對風險之一個整體估計值。在評分過程的中間步驟有時可以使用定量風險估計。	25. 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 is used. Alternatively, risk can be expressed using qualitative descriptors, such as “high”, “medium”, or “low”, which should be defined in as much detail as possible. Sometimes a "risk score" is used to further define descriptors in risk ranking. 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.
風險管制 （Risk Control）	
26. ***風險管制***包括為***降低***及/或接受風險之決策制定。風險管制之目的是要將風險減到一個可以接受的程度。使用於風險管制之努力程度應與風險的重要性成正比。為瞭解/確認風險管制之最適化等級，決策者可使用不同的過程，包含成本效益分析在內。	26. ***Risk control*** includes decision making to ***reduce*** and/or accept risks. The purpose of risk control is to reduce the risk to an acceptable level. The amount of effort used for risk control should be proportional to the significance of the risk. Decision makers might use different processes, including benefit-cost analysis, for understanding the optimal level of risk control.
27. 風險管制可以聚焦於下列問題：	27. Risk control might focus on the following questions:
• 風險是否高於可接受的程度？	• Is the risk above an acceptable level?
• 可做什麼以減低或消除風險？	• What can be done to reduce or eliminate risks?
• 效益、風險及資源三者之適當的平衡是什麼？	• What is the appropriate balance among benefits, risks and resources?
• 是否由於管制經辨識之風險的結果，而導入新的風險？	• Are new risks introduced as a result of the identified risks being controlled?
28. 當品質風險超過規定的（可接受的）水準時，***風險減低***將焦點放在減輕或避免品質風險的過程上（參見流程圖 1）。「風險減低」可能包括為減輕損害之嚴重度及機率所採取的行動。提高危害及品質風險之可檢測性的過程，亦可做為風險管制策略的一部分。風險減低措施之實施可能將新的風險導入系統中，或增加其他既有風險的嚴重性。因此，在實施風險減低過程後，應重新檢視風險評價，以確認及評估風險之任何可能的變更。	28. ***Risk reduction*** focuses on processes for mitigation or avoidance of quality risk when it exceeds a specified (acceptable) level (see Fig. 1). Risk reduction might include actions taken to mitigate the severity and probability of harm. Processes that improve the detectability of hazards and quality risks might also be used as part of a risk control strategy. The implementation of risk reduction measures can introduce new risks into the system or increase the significance of other existing risks. Hence, it might be appropriate to revisit the risk assessment to identify and evaluate any possible change in risk after implementing a risk reduction process.
29. ***風險接受***是對接受風險的一個決定。風險的接受可能是正式決定接受殘留風險，或可能是被動接受非特定殘留風險之決定。對於某些類型的損害，即使施行最好的品質風險管理，也不能完全消除風險。在這些情況中，可能同意其已經應用一個適當品質風險管理策略，且將品質風險降低至	29. ***Risk acceptance*** is a decision to accept risk. Risk acceptance can be a formal decision to accept the residual risk or it can be a passive decision in which residual risks are not specified. For some types of harms, even the best quality risk management practices might not entirely eliminate risk. In these

一個規定的（可接受的）水準。這個（規定的）可接受的水準受到多個參數影響，且應由不同個案之基礎決定之。	circumstances, it might be agreed that an appropriate quality risk management strategy has been applied and that quality risk is reduced to a specified (acceptable) level. This (specified) acceptable level will depend on many parameters and should be decided on a case-by-case basis.
風險溝通（Risk Communication）	
30. ***風險溝通***是在決策者與其他人員間關於風險及風險管理資訊的分享。各方都可以在風險管理過程的任何階段進行溝通（參見流程圖1：虛線箭頭）。品質風險管理過程之產出/結果應適當地溝通並且加以文件化（參見流程圖1：實線箭頭）。溝通可能包括那些有利害關係之各方間的溝通，例如主管機關與業者、業者與病人、在公司內、業界或主管機關內部等。所包含之資訊可能關於品質之風險的存在、性質、型式、機率、嚴重性、接受性、管制、處理、可檢測性或其它層面。不必就每一個風險的接受進行溝通。在業者與主管機關間，關於品質風險管理決策的溝通，可以透過法規及指引規範之既有管道進行。	30. ***Risk communication*** is the sharing of information about risk and risk management between the decision makers and others. Parties can communicate at any stage of the risk management process (see Fig. 1: dashed arrows). The output/result of the quality risk management process should be appropriately communicated and documented (see Fig. 1: solid arrows). Communications might include those among interested parties; e.g., regulators and industry, industry and the patient, within a company, industry or regulatory authority, etc. The included information might relate to the existence, nature, form, probability, severity, acceptability, control, treatment, detectability or other aspects of risks to quality. Communication need not be carried out for each and every risk acceptance. Between the industry and regulatory authorities, communication concerning quality risk management decisions might be effected through existing channels as specified in regulations and guidances.
風險檢討（Risk Review）	
31. 風險管理應是品質管理過程中持續進行的部分。檢討或監測事件的機制應予實施。	31. Risk management should be an ongoing part of the quality management process. A mechanism to review or monitor events should be implemented.
32. 風險管理過程的產出/結果應檢討並考慮採用新的知識及經驗。一旦啟動一個品質風險管理過程，則該過程應持續應用於可能衝擊原來品質風險管理決策之事件，不論是計畫性的(例如產品檢討、檢查、稽核、變更管制等之結果)或非計畫性的(例如調查失敗的根本原因、回收)，皆應繼續	32. The output/results of the risk management process should be reviewed to take into account new knowledge and experience. Once a quality risk management process has been initiated, that process should continue to be utilized for events that might impact the original quality risk management decision,

利用該過程。任何檢討的頻率應以風險之水準/程度為基礎。風險的檢討可能包含風險之接受決策的重新考慮(第 4.4 節)。	whether these events are planned (e.g. results of product review, inspections, audits, change control) or unplanned (e.g. root cause from failure investigations, recall). The frequency of any review should be based upon the level of risk. Risk review might include reconsideration of risk acceptance decisions (section 4.4).
風險管理方法 （RISK MANAGEMENT METHODOLOGY）	
33. 品質風險管理係支持以科學的及實用的方法制定決策。藉由現行關於評價風險之機率、嚴重性及有時是檢測性之知識，提供文件化、透明且可再現的方法，以完成品質風險管理過程的步驟。	33. Quality risk management supports a scientific and practical approach to decision-making. It provides documented, transparent and reproducible methods to accomplish steps of the quality risk management process based on current knowledge about assessing the probability, severity and sometimes detectability of the risk.
34. 傳統上，對品質之風險，會以各種非正式的方式（經驗的及/或內部的程序），譬如觀察、趨勢及其他資訊的彙集為基礎加以評價及管理。該等方法可持續提供有用的資訊，而這些資訊可支持諸如申訴、品質缺陷、偏離及資源配置之處理的主題。	34. Traditionally, risks to quality have been assessed and managed in a variety of informal ways (empirical and/ or internal procedures) based on, for example, compilation of observations, trends and other information. Such approaches continue to provide useful information that might support topics such as handling of complaints, quality defects, deviations and allocation of resources.
35. 此外，製藥產業及主管機關可使用經公認之風險管理工具及/或內部程序（例如，標準作業程序）評價及管理風險。下述內容為這些工具當中的一些非詳細周全的清單（附則 1 與第 8 章提供進一步的細節）。	35. Additionally, the pharmaceutical industry and regulators can assess and manage risk using recognized risk management tools and/ or internal procedures (e.g., standard operating procedures). Below is a non-exhaustive list of some of these tools (further details in Annex 1 and chapter 8):
• 基本風險管理簡易方法（流程表、檢查單等）；	• Basic risk management facilitation methods (flowcharts, check sheets etc.)
• 失敗模式效應分析(FMEA)；	• Failure Mode Effects Analysis (FMEA)
• 失敗模式效應及關鍵性分析(FMECA)；	• Failure Mode, Effects and Criticality Analysis (FMECA)
• 缺失之樹狀分析(FTA)；	• Fault Tree Analysis (FTA)
• 危害分析及關鍵管制點(HACCP)；	• Hazard Analysis and Critical Control Points (HACCP)
• 危害操作性分析(HAZOP)；	• Hazard Operability Analysis (HAZOP)

• 事先危害分析(PHA)；	• Preliminary Hazard Analysis (PHA)
• 風險分級及篩選；	• Risk ranking and filtering
• 輔助性統計工具。	• Supporting statistical tools
36. 在原料藥及醫藥品品質相關之特定領域運用這些工具可能是適當的。品質風險管理方法及輔助性統計工具可合併使用(例如機率性的風險評價)。合併使用提供可促進靈活的應用品質風險管理原則。	36. It might be appropriate to adapt these tools for use in specific areas pertaining to drug substance and drug (medicinal) product quality. Quality risk management methods and the supporting statistical tools can be used in combination (e.g. Probabilistic Risk Assessment). Combined use provides flexibility that can facilitate the application of quality risk management principles.
37. 品質風險管理之嚴格性及正式性的程度應反映可利用的知識，並應與所要論述之問題的複雜性，及/或關鍵性相當。	37. The degree of rigor and formality of quality risk management should reflect available knowledge and be commensurate with the complexity and/ or criticality of the issue to be addressed.
品質風險管理整合於產業及管制運作中 （INTEGRATION OF QUALITY RISK MANAGEMENT INTO INDUSTRY AND REGULATORY OPERATIONS）	
38. 當品質風險管理整合入品質系統中時，品質風險管理是一個支持基於科學及實用之決策的過程(參見附件 II)。如同在前言中所概述，品質風險管理的適當使用並不免除業者需遵從主管機關要求的義務。然而，有效的品質風險管理可以促成更好及更明智的決策，可以就一個公司處理潛在風險之能力對主管機關提供更大的保證，以及可能影響直接管制監督的範圍及程度。此外，品質風險管理還可促使各方更好的使用資源。	38. Quality risk management is a process that supports science-based and practical decisions when integrated into quality systems (see Annex II). As outlined in the introduction, appropriate use of quality risk management does not obviate industry's obligation to comply with regulatory requirements. However, effective quality risk management can facilitate better and more informed decisions, can provide regulators with greater assurance of a company's ability to deal with potential risks, and might affect the extent and level of direct regulatory oversight. In addition, quality risk management can facilitate better use of resources by all parties.
39. 業者及法規人員在品質風險管理過程上之訓練，提供對制定決策過程更多的瞭解，並建立對品質風險管理結果的信心。	39. Training of both industry and regulatory personnel in quality risk management processes provides for greater understanding of decision-making processes and builds confidence in quality risk management outcomes.
40. 品質風險管理應整合入既有操作中，並適當地文件化。附件 II 提供情況範例。在其	40. Quality risk management should be integrated into existing operations and

中，品質風險管理過程之使用可能提供以後在各種製藥操作，用得上的資訊。 這些範例只是為說明之目的而提供，不得將之視為一個最終的或詳細周全的清單。這些實例無意在現行法規明訂之要求外，創造任何新的期待。	documented appropriately. Annex II provides examples of situations in which the use of the quality risk management process might provide information that could then be used in a variety of pharmaceutical operations. These examples are provided for illustrative purposes only and should not be considered a definitive or exhaustive list. These examples are not intended to create any new expectations beyond the requirements laid out in the current regulations.
41. 業界及法規作業之範例（參見附件 II）：	41.Examples for industry and regulatory operations (see Annex II):
• 品質管理	• Quality management
42. 產業作業及活動範例（參見附件 II）：	42.Examples for industry operations and activities (see Annex II):
• 開發；	• Development
• 設施、設備及公用設施；	• Facility, equipment and utilities
• 物料管理；	• Materials management
• 生產；	• Production
• 實驗室管制及安定性試驗；	• Laboratory control and stability testing
• 包裝及標示。	• Packaging and labeling
43. 法規作業的範例（參見附件 II）：	43.Examples for regulatory operations (see Annex II):
• 檢查及評價活動	• Inspection and assessment activities
44. 雖然法規決策將持續在一個區域性的基礎上為之，但品質風險管理原則之普遍瞭解及應用可增進相互的信心，並在相同資訊的基礎上提升管制者間更為一致的決策。該協力合作，在整合及支持品質風險管理實務之政策及準則的發展上可能是重要的。	44. While regulatory decisions will continue to be taken on a regional basis, a common understanding and application of quality risk management principles could facilitate mutual confidence and promote more consistent decisions among regulators on the basis of the same information. This collaboration could be important in the development of policies and guidelines that integrate and support quality risk management practices.
定義（DEFINITIONS）	
決策者 具有資格及權能去做出適當且適時之品質風險管理決策的人。	Decision maker(s) – Person(s) with the competence and authority to make appropriate and timely quality risk management decisions

可檢測性 發現或確定一個危害之存在、出現或事實的能力。	Detectability -the ability to discover or determine the existence, presence, or fact of a hazard
傷害 對健康的損害，包含因產品品質或有效性之減失而導致的損害在內。	Harm –damage to health, including the damage that can occur from loss of product quality or availability
危害 傷害的潛在來源 (ISO/IEC Guide 51)。	Hazard - the potential source of harm (ISO/IEC Guide 51)
產品生命週期 產品從初始開發，經過上市直到產品終止之生命的全部階段。	Product Lifecycle –all phases in the life of the product from the initial development through marketing until the product's discontinuation
品質 一個產品、系統或製程之一組固有性質符合要求的程度（參見 ICH Q6A 針對藥物原料和藥物產品之 “品質” 的定義）。	Quality –the degree to which a set of inherent properties of a product, system or process fulfills requirements (see ICH Q6a definition specifically for "quality" of drug substance and drug (medicinal) products.)
品質風險管理 對藥品跨越產品生命週期之品質的風險為評價、管制、溝通及檢討之一個系統性的過程。	Quality risk management –a systematic process for the assessment, control, communication and review of risks to the quality of the drug (medicinal) product across the product lifecycle
品質系統 一個系統之全部層面的總和，用以實施品質政策並確保符合品質目標。	Quality system –the sum of all aspects of a system that implements quality policy and ensures that quality objectives are met
要求 病人或其代理人【例如，健康照護專業人員、主管機關及立法者】之明示或暗示的需求或期待。在本文件中，“要求” 不但指稱法律、立法或管制的要求，而且亦指稱該等需求及期望。	Requirements –the explicit or implicit needs or expectations of the patients or their surrogates (e.g. health care professionals, regulators and legislators). In this document, “requirements” refers not only to statutory, legislative, or regulatory requirements, but also to such needs and expectations.
風險 傷害之發生的機率及該傷害之嚴重度的組合(ISO/IEC Guide 51)。	Risk –the combination of the probability of occurrence of harm and the severity of that harm (ISO/IEC Guide 51)
風險接受 接受風險的決策(ISO Guide 73)。	Risk acceptance –the decision to accept risk (ISO Guide 73)
風險分析 與業經確認之危害所關聯的風險之估計。	Risk analysis –the estimation of the risk associated with the identified hazards

風險評價 一個組織資訊之系統性過程，用以支持在風險管理過程中做出的風險決策。這包含危害之確認及與暴露於該等危害有關之風險的分析及評估。	Risk assessment –a systematic process of organizing information to support a risk decision to be made within a risk management process. It consists of the identification of hazards and the analysis and evaluation of risks associated with exposure to those hazards.
風險溝通 在決策者與其他利害關係人間，關於風險及風險管理之資訊的分享。	Risk communication –the sharing of information about risk and risk management between the decision maker and other stakeholders
風險管制 執行風險管理決策的行動(ISO Guide 73)。	Risk control –actions implementing risk management decisions (ISO Guide 73)
風險評估 使用定量或定性尺度，比較估計之風險與已知之風險基準，以決定風險的重要性。	Risk evaluation –the comparison of the estimated risk to given risk criteria using a quantitative or qualitative scale to determine the significance of the risk
風險確認 資訊之系統性使用，以藉由風險疑問或問題描述能確認傷害(危害)之潛在來源。	Risk identification –the systematic use of information to identify potential sources of harm (hazards) referring to the risk question or problem description
風險管理 將品質管理政策、程序和實務系統性的應用於評價、管制、溝通及檢討風險的工作。	Risk management –the systematic application of quality management policies, procedures, and practices to the tasks of assessing, controlling, communicating and reviewing risk
風險減低 為減少傷害之發生機率及該傷害之嚴重度所採取的行動。	Risk reduction –actions taken to lessen the probability of occurrence of harm and the severity of that harm
風險檢討 考慮（如合適時）關於風險之新知識及經驗，以檢討或監測風險管理過程的產出/結果。	Risk review –review or monitoring of output/results of the risk management process considering (if appropriate) new knowledge and experience about the risk
嚴重度 衡量危害之可能後果。	Severity –a measure of the possible consequences of a hazard
利害關係人 可能影響或受風險影響，或感受其本身受風險影響之任何個人、團體或組織。決策者可能也是利害關係人。為本準則之目的，主要利害關係人是病人、健康照護專業人員、主管機關及業界。	Stakeholder –any individual, group or organization that can affect, be affected by, or perceive itself to be affected by a risk. Decision makers might also be stakeholders. For the purposes of this guideline, the primary stakeholders are the patient, healthcare professional, regulatory authority, and industry
趨勢	Trend –a statistical term referring to the

指出一個變數之改變方向或比率的統計學術語。	direction or rate of change of a variable(s)

8. 參考文獻 （References）

ICH Q8 Pharmaceutical Development. ISO/IEC Guide 73:2002 - Risk Management - Vocabulary - Guidelines for use in Standards.
ISO/IEC Guide 51:1999 - Safety Aspects - Guideline for their inclusion in standards.
Process Mapping by the American Productivity & Quality Center, 2002, ISBN 1928593739.
IEC 61025 - Fault Tree Analysis (FTA).
IEC 60812 Analysis Techniques for system reliability—Procedures for failure mode and effects analysis (FMEA).
Failure Mode and Effect Analysis, FMEA from Theory to Execution, 2nd Edition 2003, D. H. Stamatis, ISBN 0873895983.
Guidelines for Failure Modes and Effects Analysis (FMEA) for Medical Devices, 2003 Dyadem Press, ISBN 0849319102.
The Basics of FMEA, Robin McDermott, Raymond J. Mikulak, Michael R. Beauregard 1996, ISBN 0527763209.
WHO Technical Report Series No 908, 2003, Annex 7 Application of Hazard Analysis and Critical Control Point (HACCP) methodology to pharmaceuticals.
IEC 61882 - Hazard Operability Analysis (HAZOP).
ISO 14971:2000 - Application of Risk Management to Medical Devices.
ISO 7870:1993 - Control Charts.
ISO 7871:1997 - Cumulative Sum Charts.
ISO 7966:1993 - Acceptance Control Charts.
ISO 8258:1991 - Shewhart Control Charts.
What is Total Quality Control?; The Japanese Way, Kaoru Ishikawa (Translated by David J. Liu), 1985, ISBN 0139524339.

附件I：風險管理方法和工具 （Appendix I: Risk Management Methods and Tools）

本附件之目的在於就可能被業界及主管機關使用於品質風險管理之一些主要工具，提供其一般的概觀及參考資料。這些參考資料是為幫助取得關於特定工具之更多知識及細節而納入。這不是一個詳細周全的清單。重點是沒有任何一件或一套工具可適用於品質風險管理程序之每一種情況。	The purpose of this appendix is to provide a general overview of and references for some of the primary tools that might be used in quality risk management by industry and regulators. The references are included as an aid to gain more knowledge and detail about the particular tool. This is not an exhaustive list. It is important to note that no one tool or set of tools is applicable to every situation in which a quality risk management procedure is used.

I.1 基本風險管理之簡易方法 （Basic Risk Management Facilitation Methods）

一些藉由組織數據及促進決策之制定，以普遍用來建構風險管理之簡單技術是：	Some of the simple techniques that are commonly used to structure risk management by organizing data and facilitating