ICH Q9(R1)：
品質風險管理
(Quality Risk Management)

衛生福利部食品藥物管理署

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前言

國際醫藥法規協和會 (International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use, ICH) 於 2005 年發布 ICH Q9 (Quality Risk Management) 指引，而後因新增內容，於 2023 年 1 月發布 Q9 第一版 (R1)指引。

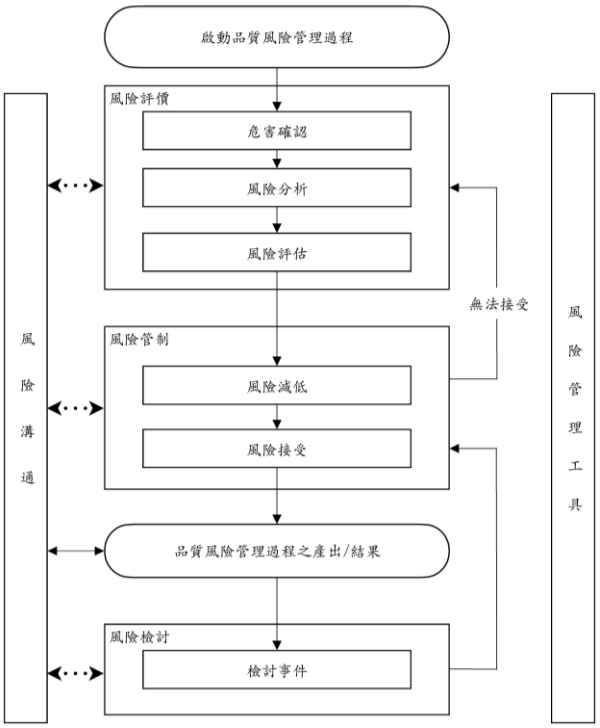
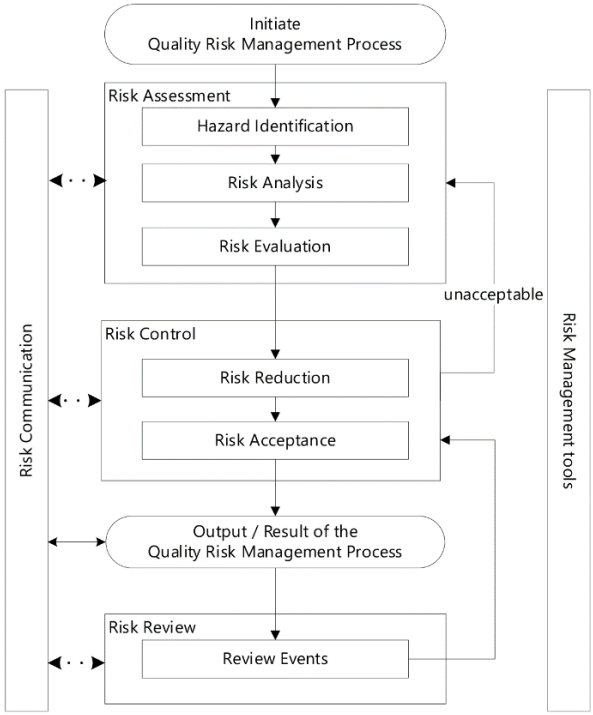
本指引針對製藥領域提供具體地品質風險管理原則及一些工具，以增進產業及主管機關對於有效品質風險管理的應用。

品質風險管理 Q9(R1)(Quality Risk Management Q9(R1))

1. 前言（INTRODUCTION）	
*風險管理*原則，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，亦被管理這些產業的主管機關有效地利用。在製藥領域，ICH Q9 之原則與架構，加上支持該指引的 ICH 正式訓練教材，有助於增進產業及主管機關對於有效品質風險管理的應用。製藥產業已經認知*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。	*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. In the pharmaceutical sector, the principles and framework of ICH Q9, coupled with the official ICH training material that supports this guideline, are instrumental in enhancing the application of effective quality risk management by industry and regulators. The importance of *quality systems* has been recognized in the pharmaceutical industry and it is evident that quality risk management is a valuable component of an effective quality system.
普遍瞭解的是，*風險*經界定為傷害之發生機率及該*傷害之嚴重度*的結合。然而，因為每一位利害關係人可能察覺不同的潛在傷害，可能將不同的機率置於每一傷害的發生上，並且將不同的嚴重度歸屬於每一種傷害上，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。此外，主觀性會直接影響風險管理活動與決策之有效性。因此，主觀性的管理與將其減至最低是重要的。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，但管理產品品質與可用性/可得性之風險時，當品質/製造問題引起可用性/可得性風險時，保護病人應被視為最重要。	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 addition, subjectivity can directly impact the effectiveness of risk management activities and the decisions made. Therefore, it is important that subjectivity is managed and minimized. 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 is of prime importance when managing the risk to product quality and availability, when availability risks arise from quality/manufacturing issues.
藥品之製造及使用，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*產品的整個生命週期*基於適當之以風險為基礎的決策確保產品品質，以維持對於藥品之品質具有重要性的屬性且產品保持安全與有效。	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 component of the overall risk. It is important to understand that product *quality* is assured based on appropriate risk-based decision-making throughout the *product lifecycle*, such that the attributes that are important to the quality of the drug (medicinal) product are maintained and the product remains safe and effective.
一個有效的品質風險管理方法，可以經由提供一個前瞻性的方法，去確認和管制在開發、製造及運銷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。其包括可識別與解決根本原因與此類問題之其他原因的因子（例如，與人有關之因子）之根本原因分析的適當	An effective quality risk management approach can further ensure the quality of the drug (medicinal) product to the patient by providing a proactive means to identify and control potential quality issues during development, manufacturing, and distribution. This includes an appropriate application of root cause analysis that can identify

應用。前瞻性的品質風險管理方法是有益的，因為其有助於穩健的產品設計與持續改善，且對於實現有效的製藥品質系統具有策略重要性。(參見 ICH Q10 與有效的製藥品質系統相關之指引。）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。	and address the root cause(s) and other causal factors (e.g., human-related) of such issues. A proactive approach to quality risk management is beneficial, as it facilitates robust product design and continual improvement, and it is of strategic importance in achieving an effective pharmaceutical quality system. (See ICH Q10 for guidance in relation to an effective pharmaceutical quality system.) Additionally, use of quality risk management can improve the decision-making if a quality problem arises.
於開發階段與作為確效的一部分，品質風險管理是建立知識與理解風險情境的一部分，使適當風險管制可被決定用於商業製造階段。在此情況下，知識被用來做出基於風險的明智決策、觸發重新評估與促進持續改進。有效且前瞻性的品質風險管理，可使決策於整個生命週期中能更好、更有依據而且及時。其可就一個公司處理潛在風險與避免問題的能力提供主管機關更大的保證，而且有利於影響法規監督的程度及等級。	In the development phase and as part of validation, quality risk management is part of building knowledge and understanding risk scenarios, so that appropriate risk control can be decided upon for use during the commercial manufacturing phase. In this context, knowledge is used to make informed risk-based decisions, trigger re-evaluations and stimulate continual improvements. Effective and proactive quality risk management can enable better, more informed and timely decisions throughout the lifecycle. This can provide regulators with greater assurance of a company's ability to deal with potential risks and avert problems, and can beneficially affect the extent and level of direct regulatory oversight.
當數位化與新興技術適合其預定用途時，於藥品之製造與管制中應用該等技術可導致風險降低。然而，該等技術亦能導入其他可能需要被管制之風險。品質風險管理之應用於先進製程與分析方法、先進數據分析方法與電腦化系統的設計、確效及技術移轉是重要的。	The application of digitalization and emerging technologies in the manufacture and control of drug (medicinal) products can lead to risk reduction, when such technologies are fit for their intended use. However, they can also introduce other risks that may need to be controlled. The application of quality risk management to the design, validation and technology transfer of advanced production processes and analytical methods, advanced data analysis methods and computerized systems is important.
本文件之目的是要對可導致更好、更有依據與及時決策的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，並補充製藥產業及法規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。	The purpose of this document is to offer a systematic approach to quality risk management that leads to better, more informed, and timely decisions. 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.
品質風險管理中對於正式性之瞭解可能導致資	An understanding of formality in quality risk

源使用更有效率：較低風險問題以較不正式之方式處理，釋放資源以管理可能需要提高嚴重性與努力程度之較高風險問題及更複雜問題。對於正式性之瞭解亦可支持基於風險的決策：所應用之正式性的程度可能反應決策的重要程度，以及可能呈現之不確定性與複雜性程度。	management may lead to resources being used more efficiently, where lower risk issues are dealt with via less formal means, freeing up resources for managing higher risk issues and more complex problems that may require increased levels of rigor and effort. An understanding of formality can also support risk-based decision-making, where the level of formality that is applied may reflect the degree of importance of the decision, as well as the level of uncertainty and complexity which may be present.
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。品質風險管理不應以做出證明作業符合法規及/或指引之決策的方式被使用，否則將被認為是不可接受的。	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. Quality risk management should not be used in a manner where decisions are made that justify a practice that would otherwise, in accordance with regulations and/or guidance, be deemed unacceptable.
2. 範圍（SCOPE）	
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。	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).
3. 品質風險管理的原則（PRINCIPLES OF QUALITY RISK MANAGEMENT）	
品質風險管理之二個主要原則是：	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。（備註：品質風險包括產品可用性/可得性可能被影響，導致潛在病人傷害之情況。）	• The evaluation of the risk to quality should be based on scientific knowledge and ultimately link to the protection of the patient. (Note: Risk to quality includes situations where product availability may be impacted, leading to potential patient harm.)
• 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.
4. 一般品質風險管理過程（GENERAL QUALITY RISK MANAGEMENT PROCESS）	
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，其詳細程度是與其特定風險相稱。	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 (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.
圖 1：典型之品質風險管理過程概觀	Figure 1: Overview of a typical quality risk management process
	
因為決策可能發生在過程中的任何一點，所以決策點（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。	Decision nodes are not shown in the diagram 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.
4.1. 責任	**4.1. Responsibilities**
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、產品開發、業務開發、工程、法規事務、生產操作、銷售及行銷、供應鏈、法律、統計及臨床）的專家。	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, product development, business development, engineering, regulatory affairs, production operations, sales and marketing, supply chain, legal, statistics and clinical) in addition to individuals who are knowledgeable about the quality risk management process.
*決策者*應該：	*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；	• take responsibility for coordinating quality risk management across various functions and departments of their organization;

• 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與知識；而且	• assure that a quality risk management process is defined, deployed and reviewed and that adequate resources and knowledge are available; and
• 確保品質風險管理活動中之主觀性被進行管理並使其減到最低，以利於科學上穩健之基於風險的決策。	• assure that subjectivity in quality risk management activities is managed and minimized, to facilitate scientifically robust risk-based decision-making.
4.2. 啟動品質風險管理過程	**4.2. Initiating a Quality Risk Management Process**
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：	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、傷害或對人體健康之衝擊的背景資訊及/或數據；	• Assemble background information and/ 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.
4.3. 風險評價	**4.3. Risk Assessment**
風險評價包含危害之確認及暴露於那些危害（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：	***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)?
危害確認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、有依據的意見，以及利害關係人的關切事項。危害確認提示「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。	***Hazard 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. Hazard 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.
風險分析是與經辨識之危害所關聯的風險進行	***Risk analysis*** is the estimation of the risk

估計。它是連結於事件發生之可能性及傷害之嚴重度的定性與定量過程。在有些風險管理工具中，檢測傷害的能力（可檢測性）亦是風險估計中的因子。	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.
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。	***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.
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。	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.
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。	Uncertainty is due to a 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.
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。	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.
4.4. 風險管制	**4.4. Risk Control**
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。	***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.
風險管制可以聚焦於下列問題：	Risk control might focus on the following questions:
1. 風險是否高於可接受的程度？	1. Is the risk above an acceptable level?

2. 可做什麼以減低或消除風險？	2. What can be done to reduce or eliminate risks?
3. 效益、風險及資源三者之適當的平衡是什麼？	3. What is the appropriate balance among benefits, risks and resources?
4. 是否由於管制經辨識之風險的結果，而導入新的風險？	4. Are new risks introduced as a result of the identified risks being controlled?
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」可能包括為減輕傷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。	***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.
風險接受是對接受風險的一個決定。對於某些類型的傷害，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。	***Risk acceptance*** is a decision to accept risk. For some types of harms, even the best quality risk management practices might not entirely eliminate risk. In these 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.
4.5. 風險溝通	**4.5. Risk Communication**
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、嚴重度、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。	***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 conducted through existing channels as specified in regulations and guidances.
4.6. 風險檢討	**4.6. Risk Review**
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。	Risk management should be an ongoing part of the quality management process. A mechanism to review or monitor events should be implemented.

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）。	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, 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).
5. 風險管理方法（RISK MANAGEMENT METHODOLOGY）	
品質風險管理係支持以科學的及實用的方法制定決策。藉由現行關於評價危害與其相關之風險的機率、嚴重度及有時是可檢測性之知識，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。雖然在某些品質風險管理方法中可檢測性可能不是相關因子，但檢測管制很重要，因為其可降低傷害發生的機率。	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 hazards, and their associated risks. While detectability may not be a discrete factor in some quality risk management methods, detection controls are important as they can reduce the probability of occurrence of harm.
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。	Traditionally, risks to quality have been assessed and managed in a variety of 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.
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（附件 I 與第 8 章提供進一步的細節）。	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 I and section 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.
在原料藥及醫藥品品質相關之特定領域運用這	It might be appropriate to adapt these tools for use

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。	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.
品質風險管理之嚴格性及正式性的程度應反映可得的知識，並應與所要論述之問題的不確定性程度、重要性與複雜性相稱。	The degree of rigor and formality of quality risk management should reflect available knowledge and be commensurate with the level of uncertainty, importance and complexity of the issue to be addressed.
5.1. 品質風險管理中之正式性	**5.1. Formality in Quality Risk Management**
正式性於品質風險管理並非一種二分法之概念（亦即，正式的/非正式的）；正式性的多樣程度可能於品質風險管理活動中被應用，包括做出基於風險的決策時。經由這種方式，正式性可被認為是一種範圍由低至高的連續體。	Formality in quality risk management is not a binary concept (i.e. formal/informal); varying degrees of formality may be applied during quality risk management activities, including when making risk-based decisions. In this way, formality can be considered a continuum (or spectrum), ranging from low to high.
當決定正式性的程度應用於品質風險管理活動時，可能被考慮的因子舉例如下：	When determining how much formality to apply to a given quality risk management activity, certain factors may be considered. These may include, for example, the following:
• ***不確定性***：「不確定性」一詞於品質風險管理中意指缺乏關於危害、傷害及與其相關風險之知識。與經風險評價範圍相關之不確定性程度，可得知管理潛在風險時可能需要正式性的程度。獲得、分析、儲存與傳播科學資訊的系統性方法對於形成知識是必需的，進而得知所有品質風險管理活動。不確定性可經由有效的知識管理予以降低，使累積的與新的資訊（內部及外部）能夠被用於支持整個產品生命週期中基於風險的決策。	• ***Uncertainty***: The term "uncertainty" in quality risk management means lack of knowledge about hazards, harms and, consequently, their associated risks. The level of uncertainty that is associated with the area being risk assessed informs how much formality may be required to manage potential risks. Systematic approaches for acquiring, analysing, storing and disseminating scientific information are essential for generating knowledge, which in turn informs all quality risk management activities. Uncertainty may be reduced via effective knowledge management, which enables accumulated and new information (both internal and external) to be used to support risk-based decisions throughout the product lifecycle.
• ***重要性***：可能與產品品質相關之基於風險的決策越重要，應被應用之正式性程度則越高，且降低與其相關之不確定性程度的需求越大。	• ***Importance***: The more important a risk-based decision may be in relation to product quality, the higher the level of formality that should be applied, and the greater the need to reduce the level of uncertainty associated with it.
• ***複雜性***：對於品質風險管理活動之程序或主題領域越複雜，應被應用之正式性程度則越高，以確保產品品質。	• ***Complexity***: The more complex a process or subject area is to a quality risk management activity, the higher the level of formality that should be applied to assure product quality.
不確定性、重要性或複雜性之程度越高，可能需要更正式的品質風險管理方法，以管理潛在風險與支持有效之基於風險的決策。	Higher levels of uncertainty, importance or complexity may require more formal quality risk management approaches to manage potential risks and to support effective risk-based decision-making.

在品質風險管理活動中，應用正式性程度之整體方法，應於品質系統內加以描述。品質風險管理過程中，資源有限不得被用於證明使用較低正式性程度之合理性。風險分數、風險等級與其評價應基於適當使用的證據、科學與知識。無論應用的正式性程度為何，健全的風險管理是該過程的目標。	The overall approach for determining how much formality to apply during quality risk management activities should be described within the quality system. Resource constraints should not be used to justify the use of lower levels of formality in the quality risk management process. Risk scores, ratings and assessments should be based on an appropriate use of evidence, science and knowledge. Regardless of how much formality is applied, the robust management of risk is the goal of the process.
下列項目可能為較高程度正式性的特性：	***The following may be characteristics of higher levels of formality:***
• 品質風險管理過程的所有部分（風險評價、風險管制、風險檢討與風險溝通）經明確執行，且可能製作並文件化該過程之獨立品質風險管理報告或處理所有層面的相關文件（例如，於品質系統中）。	• All parts of the quality risk management process (risk assessment, risk control, risk review and risk communication) are explicitly performed, and stand-alone quality risk management reports or related documents which address all aspects of the process may be generated and are documented (e.g., within the quality system).
• 品質風險管理工具（包含附件 I 中所示）被用於部分或整個過程中。	• Quality risk management tools, including those shown in Annex I, are used in some or all parts of the process.
• 為品質風險管理活動建立跨部門團隊。	• A cross-functional team is assembled for the quality risk management activity.
• 任用具有品質風險管理過程知識與經驗的引導者，可能使較高程度正式性的過程更完整。	• Use of a facilitator, with experience and knowledge of the quality risk management process, may be integral to a higher formality process.
下列項目可能為較低程度正式性的特性：	***The following may be characteristics of lower levels of formality:***
• 品質風險管理過程之一個或多個部分非以獨立活動執行，而是於其他品質系統要素中處理，其包含可能具有風險評價與風險管制活動。	• One or more parts of the quality risk management process are not performed as stand-alone activities but are addressed within other elements of the quality system which may have risk assessment and risk control activities embedded within them.
• 品質風險管理工具可能不被用於部分或整個過程中。	• Quality risk management tools might not be used in some or all parts of the process.
• 可能不需要跨部門團隊。	• A cross-functional team might not be necessary.
• 可能不會產生獨立之品質風險管理報告。品質風險管理過程的結果通常於品質系統相關部分中予以文件化。	• Stand-alone quality risk management reports might not be generated. The outcome of the quality risk management process is usually documented in the relevant parts of the quality system.
備註：如上所示，亦存在且可能使用介於上述較高與較低程度間之正式性程度。	**Note:** As indicated above, degrees of formality between the above higher and lower levels also exist and may be used.
5.2. 基於風險的決策	**5.2. Risk-Based Decision-Making**
基於風險的決策是所有品質風險管理活動中固有的，其提供組織中決策者必要之基礎。有效之基於風險的決策始於決定品質風險管理過程中應應用之努力、正式性與文件化的程度。來	Risk-based decision-making is inherent in all quality risk management activities; it provides an essential foundation for decision makers in an organization. Effective risk-based decision-making

自品質風險管理活動所做出之決策，包括與危害存在相關的決策、與該等危害有關的風險、所需要的風險管制、風險管制後殘留風險之可接受性，及品質風險管理活動之溝通與檢討以及其結果。	begins with determining the level of effort, formality and documentation that should be applied during the quality risk management process. The decisions made from quality risk management activities include those in relation to what hazards exist, the risks associated with those hazards, the risk controls required, the acceptability of the residual risk after risk controls, and also the communication and review of quality risk management activities and outputs.
由於所有決策倚賴知識之使用，參閱 ICH Q10 與知識管理相關之指引。確保基於風險的決策所用數據的完整性也是重要的。	As all decision-making relies on the use of knowledge, see ICH Q10 for guidance in relation to knowledge management. It is important also to ensure the integrity of the data that are used for risk-based decision-making.
基於風險的決策的方法：	***Approaches to risk-based decision-making:***
有不同過程可能被用於做出基於風險的決策，其與品質風險管理過程中所應用之正式性程度直接相關。（參見上述第 5.1 節對於品質風險管理中構成正式性之指引。）	There are different processes that may be used to make risk-based decisions; these are directly related to the level of formality that is applied during the quality risk management process. (See Section 5.1 above for guidance on what constitutes formality in quality risk management.)
品質風險管理中較高程度的正式性，可能需要與基於風險的決策相關之較高程度的結構。關於基於風險的決策的方法可以有不同程度的結構。該等程度可被認為是連續體。做出基於風險的決策時，高度結構化過程、較低結構化過程與基於規則的過程如下所述：	Higher levels of formality in quality risk management may require higher levels of structure in relation to risk-based decision-making. There can be varying degrees of structure with regard to approaches for risk-based decision-making. These degrees of structure can be considered to be on a continuum (or spectrum). Below are descriptions of highly structured vs. less structured processes, and for rule-based processes when making risk-based decisions:
• 某些基於風險的決策過程為高度結構化，且可能涉及決策前存在之可得選項的正式分析，其涉及與可得選項相關之因子的深度考量。該等過程於高度重要性與決策有關時，且當不確定性程度及/或複雜性程度高時可能被使用。	• Some risk-based decision-making processes are highly structured and can involve a formal analysis of the available options that exist before making a decision. They involve an in-depth consideration of relevant factors associated with the available options. Such processes might be used when there is a high degree of importance associated with the decision, and when the level of uncertainty and/or complexity is high.
• 其他基於風險的決策過程為較低結構化，使用較簡單的方法以做出決策，且其主要利用現有知識以支持危害評價、風險評價與其他所需之風險管制。該等過程於高度重要性與決策有關時，但不確定性程度及/或複雜性程度較低時可能仍被使用。	• Other risk-based decision-making processes are less structured; here, simpler approaches are used to arrive at decisions, and they primarily make use of existing knowledge to support an assessment of hazards, risks and any required risk controls. Such processes might still be used when there is a high degree of importance associated with the decision, but the degree of uncertainty and/or complexity is lower.
• 決策亦可能使用基於規則（或標準化）的方法做出，該方法不需要新的風險評價。此時要具備 SOPs、政策或清楚易懂的要求，以決定必須做出什麼決策。此處可能具備管理該	• Decisions might also be made using rule-based (or standardized) approaches, which do not require a new risk assessment to make such decisions. This is where there are SOPs, policies or well understood requirements in place which

等決策之規則（或限制）；該等規則可能基於先前獲得對於相關風險的了解，且通常導致預定的行動及/或預期的結果。	determine what decisions must be made. Here, rules (or limits) may be in place which govern such decisions; these may be based on a previously obtained understanding of the relevant risks and they usually lead to predetermined actions and/or expected outcomes.
上述方法對於基於風險的決策是有益的，因為其經由知識的使用解決了不確定性，並促進多個領域中主管機關與製藥產業有依據的決策。其亦幫助認知不確定性仍在之處，以利識別適當之風險管制（包括改善偵測）以加強對該等變數的瞭解並進一步減少不確定性的程度。	The above approaches to risk-based decision-making are beneficial because they address uncertainty through the use of knowledge, facilitating informed decisions by regulators and the pharmaceutical industry in a multitude of areas. They also help recognize where uncertainty remains, so that appropriate risk controls (including improved detection) may be identified to enhance understanding of those variables and further reduce the level of uncertainty.
5.3. 主觀性的管理與使其減到最低	**5.3. Managing and Minimizing Subjectivity**
主觀性可影響品質風險管理過程的每一階段，特別是危害之確認及估計發生機率與傷害嚴重性。其亦可影響品質風險管理活動中風險減低之估計與決策的有效性。	Subjectivity can impact every stage of a quality risk management process, especially the identification of hazards and the estimation of probability of occurrence and severity of harm. It can also impact the estimation of risk reduction and the effectiveness of decisions made from quality risk management activities.
主觀性可經由下列差異被導入於品質風險管理，包括風險如何被評價，及危害、傷害與風險如何被不同的利害關係人察覺（例如，偏見）。當風險問題不適當界定與工具具有不良設計的風險評分尺度時，主觀性亦可能被導入。	Subjectivity can be introduced in quality risk management through differences in how risks are assessed and in how hazards, harms and risks are perceived by different stakeholders, (e.g., bias). Subjectivity can also be introduced when risk questions are inadequately defined, and when tools have poorly designed risk scoring scales.
雖然主觀性不能完全自品質風險管理活動中消除，但可能可以經由處理偏見與假設、品質風險管理工具的適當使用，及最大化相關數據與知識來源的使用加以管制（參見 ICH Q10 第 1.6.1 節）。	While subjectivity cannot be completely eliminated from quality risk management activities, it may be controlled by addressing bias and assumptions, the proper use of quality risk management tools and maximizing the use of relevant data and sources of knowledge (see ICH Q10, Section 1.6.1).
所有涉及品質風險管理活動之參與者，應認知、預測與解決主觀性的潛在性。	All participants involved with quality risk management activities should acknowledge, anticipate, and address the potential for subjectivity.
6. 品質風險管理整合於產業及法規作業中（INTEGRATION OF QUALITY RISK MANAGEMENT INTO INDUSTRY AND REGULATORY OPERATIONS）	
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有依據的決策，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。	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.
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。	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.
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。	Quality risk management should be integrated into existing operations and 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.
產業及法規作業之範例（參見附件 II）：	Examples for industry and regulatory operations (see Annex II):
• 品質管理。	• Quality management.
產業作業及活動範例（參見附件 II）：	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;
• 原物料管理；	• 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;
• 供應鏈管制。	• Supply chain control.
法規作業的範例（參見附件 II）：	Examples for regulatory operations (see Annex II):
• 檢查及評價活動。	• Inspection and assessment activities.
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。	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.
6.1. 在處理源自於品質/製造議題之產品可得性風險中品質風險管理的角色	**6.1. The role of Quality Risk Management in Addressing Product Availability Risks Arising from Quality/Manufacturing Issues**
品質/製造議題，包含不符合 GMP 在內，是產品可得性議題（例如，產品短缺）的重要原因。病患的利益由基於風險之藥品短缺的預防與緩解活動所提供，該等活動有助於前瞻性地管理供應鏈的複雜性並確保所需藥品的可得性。	Quality/manufacturing issues, including non-compliance with Good Manufacturing Practice (GMP), are a significant cause of product availability issues (e.g., product shortages). The interests of patients are served by risk-based drug shortage prevention and mitigation activities that help to proactively manage supply chain

	complexities and ensure availability of needed drug (medicinal) products.
雖然製造與供應鏈多樣性可促進產品可得性，日益複雜的供應鏈導致互相依賴，可能帶來影響供應鏈穩健性之系統性的品質/製造風險。品質風險管理之應用可促使支持產品可得性之預防措施的前瞻性辨識與實施。	While manufacturing and supply chain diversity can be enablers of product availability, increasingly complex supply chains lead to interdependencies that can introduce systemic quality/manufacturing risks impacting supply chain robustness. The application of quality risk management enables the proactive identification and implementation of preventive measures that support product availability.
有效的製藥品質系統同時提供穩健的供應鏈與持續的 GMP 符合性。製藥品質系統包括管理人員職責在內，也使用品質風險管理與知識管理，以提供支持有效監督與回應來自藥廠或其外部合作夥伴之不斷變化的品質/製造風險的早期警報系統。當執行基於風險之藥品短缺預防與減低活動時，應用於該等活動之正式性的程度可能不同（參見第 5.1 節）並應與產品可得性損失相關的風險程度相稱。	An effective pharmaceutical quality system drives both supply chain robustness and sustainable GMP compliance. The pharmaceutical quality system, including management responsibilities, also uses quality risk management and knowledge management to provide an early warning system that supports effective oversight and response to evolving quality/manufacturing risks from the pharmaceutical company or its external partners. When risk-based drug shortage prevention and mitigation activities are performed, the level of formality that is applied to those activities may vary (see Section 5.1) and should be commensurate with the level of risk associated with a loss of availability of the product(s).
可影響供應可靠性並因此影響產品可得性之品質/製造因子包括但非侷限於下列各項：	Quality/manufacturing factors that can affect supply reliability, and hence product availability, include, but are not limited to, the following:
a) 製程變異性與管制狀態：	***a) Manufacturing Process Variability and State of Control:***
出現過度變異性（例如，製程偏離、非均一性）的製程，即有能力差距，可能導致不可預測之結果（例如，品質、及時性與產量），進而可能對產品可得性有不良影響。品質風險管理可幫助設計監測系統，該系統可偵測來自製程中管制狀態的偏離與缺陷，因此可對其進行調查以解決根本原因。	Processes that exhibit excessive variability (e.g., process drift, non-uniformity) have capability gaps that can result in unpredictable outputs (e.g., quality, timeliness and yield) and consequently can adversely impact product availability. Quality risk management can help design monitoring systems that are capable of detecting departures from a state of control and deficiencies in manufacturing processes, so they can be investigated to address root causes.
b) 製造設施與設備：	***b) Manufacturing Facilities and Equipment:***
穩健的基礎設施可促進可靠的供應，其包括適當的製造設備與完善設計的製造設施（包括包裝與測試）。穩健性可被多個因子影響，諸如設施老化、維護保養不足或易受人為錯誤影響的操作設計。經由解決該等因子及經由先進技術的使用（諸如數位化、自動化、隔離技術等）可減低對供應的風險。	A robust facility infrastructure can facilitate reliable supply; it includes suitable equipment and well-designed facilities for manufacturing (including packaging and testing). Robustness can be affected by multiple factors, such as an aging facility, insufficient maintenance or an operational design that is vulnerable to human error. Risks to supply can be reduced by addressing these factors, as well as through the use of modern technology, such as digitalization, automation, isolation technology, amongst others.
c) 委外活動與供應商監督：	***c) Oversight of Outsourced Activities and Suppliers:***

品質系統管理包括確保產品生命週期中供應鏈合作夥伴的可接受性。委外活動與原物料供應商的核准與監督是由對供應鏈合作夥伴績效之風險評價、有效的知識管理及有效的監控策略來進行。經由適當的溝通與協力合作機制（參見 ICH Q10 第 2.7 節）可強化成功的製造合作關係。當於所供應之原物料的品質與安全性中或所提供的服務中，識別出有重大變異時，加強檢討與監測活動是合理的。在有些情況，識別新的供應鏈實體（例如，事先認可的替代選項）以執行功能可能是必要的。	Quality system governance includes assuring the acceptability of supply chain partners over the product lifecycle. Approval and oversight of outsourced activities and material suppliers is informed by risk assessments, effective knowledge management, and an effective monitoring strategy for supply chain partner performance. A successful manufacturing partnership is strengthened by appropriate communication and collaboration mechanisms (See Section 2.7 of ICH Q10). When substantial variability is identified in the quality and safety of supplied materials or in the services provided, enhanced review and monitoring activities are justified. In some cases, it may be necessary to identify a new supply chain entity (e.g., a pre-qualified alternative option) to perform a function.
注意附件 II.2 中關於做為法規作業一部分之品質風險管理的應用指引，於考慮產品可得性風險可能是有用的。	Note that the guidance in Annex II.2, in relation to the application of quality risk management as part of Regulatory Operations, can be useful to consider in the context of product availability risks.
7. 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，包含因產品品質或可用性/可得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 51:2014)。	**Hazard:** The potential source of harm (ISO/IEC Guide 51:2014).
危害確認 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。	**Hazard Identification:** The systematic use of information to identify potential sources of harm (hazards) referring to the risk question or problem description.
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 51:2014）。	**Risk:** The combination of the probability of occurrence of harm and the severity of that harm (ISO/IEC Guide 51:2014).
風險接受 承擔特定風險之有依據的決策（ISO Guide 73:2009）。	**Risk Acceptance:** An informed decision to take a particular risk. (ISO Guide 73:2009).
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.
基於風險的決策 考慮與決策有關之風險的知識及風險是否在可接受程度的決策之方法或過程。	**Risk-Based Decision-Making:** An approach to, or a process of, making decisions that considers knowledge about risks relevant to the decision and whether risks are at an acceptable level.
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 73:2009）。	**Risk Control:** Actions implementing risk management decisions (ISO Guide 73:2009).
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	**Risk Review:** Review or monitoring of output/results of the risk

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。	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，或察覺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 指出一個變數之改變方向或比率的統計學術語。	**Trend:** A statistical term referring to the direction or rate of change of a variable(s).

8. 參考文獻（REFERENCES）

1. ICH Q8 Pharmaceutical Development.
2. ICH Q10 Pharmaceutical Quality System.
3. ICH Q11 Development and Manufacture of Drug Substances (Chemical Entities and Biotechnological/Biological Entities).
4. ICH Q12 Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management.
5. ISO/IEC Guide 73:2009 - Risk Management - Vocabulary - Guidelines for use in Standards.
6. ISO/IEC Guide 51:2014 - Safety Aspects - Guideline for their inclusion in standards.
7. IEC 61025 - Fault Tree Analysis (FTA).
8. IEC 60812:2018 Failure modes and effects analysis (FMEA and FMECA).
9. IEC 61882:2016 - Hazard and operability studies (HAZOP studies) °V Application guide.
10. ISO 14971:2019 °V Medical devices - Application of risk management to medical devices.
11. ISO 7870-1:2019 - Control Charts, General guidelines.
12. ISO 7870-4:2021- Cumulative Sum Charts.
13. ISO 7870-3:2020 - Acceptance Control Charts.
14. ISO 7870-2:2013 - Shewhart Control Charts.
15. WHO Technical Report Series No 908, 2003, Annex 7 Application of Hazard Analysis and Critical Control Point (HACCP) methodology to pharmaceuticals.
16. What is Total Quality Control?; The Japanese Way, Kaoru Ishikawa (Translated by David J. Liu), 1985, ISBN 0139524339.
17. Failure Mode and Effect Analysis, FMEA from Theory to Execution, 2nd Edition 2003, D. H. Stamatis, ISBN 0873895983.
18. Process Mapping by the American Productivity & Quality Center, 2002, ISBN 1928593739.
19. Parenteral Drug Association. Technical Report No. 54 Implementation of quality risk management for pharmaceutical and biotechnology manufacturing operations. 2012.
20. Parenteral Drug Association. Points to consider for aging facilities. 2017.
21. Parenteral Drug Association. Technical Report No. 68. Risk-based approach for prevention and management of drug shortages. 2014.
22. International Society for Pharmaceutical Engineering. Report on the ISPE Drug shortages survey. 2013.
23. International Society for Pharmaceutical Engineering. Drug shortages prevention plan. 2014.
24. Tabersky D, Woelfle M, Ruess J, Brem S, Brombacher S. Recent regulatory trends in pharmaceutical manufacturing and their impact on the industry. CHIMIA, 2018;72(3):146-150.

O'Donnell K, Tobin D, Butler S, Haddad G, Kelleher D. Understanding the concept of formality in quality risk management. J. Valid. Technol, 2020 Jun; 26(3).

附件 I：風險管理方法與工具
ANNEX I: QUALITY 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 annex 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.
使用高度正式的品質風險管理方法與工具既非總是適合的，也非總是必需的。使用較不正式的品質風險管理方法與工具亦得認定為可接受。參見第 5.1 節對於品質風險管理中構成正式性之指引。	It is neither always appropriate nor always necessary to use highly formal quality risk management methods and tools. The use of less formal quality risk management methods and tools can also be considered acceptable. See Section 5.1 for guidance on what constitutes formality in quality risk management.
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 decision-making are:
• 流程圖；	• Flowcharts;
• 檢查單；	• Check Sheets;
• 過程圖示；	• Process Mapping;
• 原因與效應圖表（亦稱為石川圖或魚骨圖）。	• Cause and Effect Diagrams (also called an Ishikawa diagram or fish bone diagram).
I.2 失敗模式效應分析（Failure Mode Effects Analysis (FMEA)）	
FMEA（參見 IEC 60812）係就程序及其對結果及/或產品性能之可能的效應，提供潛在失敗模式的評估。失敗模式一旦建立，風險減低便可用以排除、圍堵、減少或控制該潛在失敗。FMEA 倚賴對產品及製程的瞭解。FMEA 在方法上將複雜程序的分析分解成可管理的步驟。對於總結失敗之重要模式、引起這些失敗的因子及這些失敗之可能效應，這是一個強而有力的工具。	FMEA (see IEC 60812) provides for an evaluation of potential failure modes for processes and their likely effect on outcomes and/or product performance. Once failure modes are established, risk reduction can be used to eliminate, contain, reduce or control the potential failures. FMEA relies on product and process understanding. FMEA methodically breaks down the analysis of complex processes into manageable steps. It is a powerful tool for summarizing the important modes of failure, factors causing these failures and the likely effects of these failures.
潛在的使用領域	**Potential Areas of Use(s)**
FMEA 可用於安排風險優先順序及監測風險管制活動的效果。	FMEA can be used to prioritize risks and monitor the effectiveness of risk control activities.
FMEA 可應用於設備及設施，及可用於分析製造作業及其對產品或製程的影響。這可辨識使系統脆弱之因素/操作。FMEA 之產出/結果可用為設計或進一步分析或指引資源配置的基礎。	FMEA can be applied to equipment and facilities and might be used to analyze a manufacturing operation and its effect on product or process. It identifies elements/operations within the system that render it vulnerable. The output/ results of FMEA can be used as a basis for design or further analysis or to guide resource deployment.
I.3 失敗模式，效應及關鍵性分析（Failure Mode, Effects and Criticality Analysis	

(FMECA)）	
FMEA 可加以延伸，納入結果之嚴重程度的調查、其個別之發生機率，以及其檢測性，轉變為失敗模式，效應及關鍵性分析 FMECA；參見 IEC 60812。為執行這樣的分析，應建立產品或製程規格。FMECA 能確認在何處追加預防措施，可能將風險減至最低。	FMEA might be extended to incorporate an investigation of the degree of severity of the consequences, their respective probabilities of occurrence, and their detectability, thereby becoming a Failure Mode Effect and Criticality Analysis (FMECA; see IEC 60812). In order for such an analysis to be performed, the product or process specifications should be established. FMECA can identify places where additional preventive actions might be appropriate to minimize risks.
潛在的使用領域	**Potential Areas of Use(s)**
FMECA 在製藥產業之應用，應主要用於與製造過程有關之失敗及風險；然而，並不侷限於該應用。	FMECA application in the pharmaceutical industry should mostly be utilized for failures and risks associated with manufacturing processes; however, it is not limited to this application.
FMECA 之結果是每一失敗模式之相對風險「分數」。該分數在相對風險的基礎上，將這些模式分級。	The output of an FMECA is a relative risk "score" for each failure mode, which is used to rank the modes on a relative risk basis.
I.4 缺失之樹狀分析（Fault Tree Analysis (FTA)）	
FTA 工具（參見 IEC 61025）是假定一個產品或製程有功能性失效之方法。這個工具每次只評估造成系統（或子系統）失效的一個原因，但可將失效之數個原因以確認其為原因鏈的方式組合在一起。該結果以缺失模式樹的形式圖示之。在該模式樹中的每一層級，其缺失模式間的關連以邏輯運算符號（「及」、「或」等）描述之。FTA 有賴於專家對製程的瞭解，以確認原因的因子。	The FTA tool (see IEC 61025) is an approach that assumes failure of the functionality of a product or process. This tool evaluates system (or sub-system) failures one at a time but can combine multiple causes of failure by identifying causal chains. The results are represented pictorially in the form of a tree of fault modes. At each level in the tree, combinations of fault modes are described with logical operators (AND, OR, etc.). FTA relies on the experts' process understanding to identify causal factors.
潛在的使用領域	**Potential Areas of Use(s)**
FTA 得用於建立導致失敗之根本原因的路徑。FTA 得用來調查申訴或偏離，以完全瞭解其根本原因，並確保其預定的改善將會完全解決該問題，而不會引起其他問題（即，解決了一個問題卻又引起另一個不同的問題）。缺失之樹狀分析是評估多重因子對於一個已知問題影響的有效工具。FTA 之產出包含可見的失敗模式描述。這對於風險評價及監測計畫的開發都有助益。	FTA can be used to establish the pathway to the root cause of the failure. FTA can be used to investigate complaints or deviations in order to fully understand their root cause and to ensure that intended improvements will fully resolve the issue and not lead to other issues (i.e. solve one problem yet cause a different problem). Fault Tree Analysis is an effective tool for evaluating how multiple factors affect a given issue. The output of an FTA includes a visual representation of failure modes. It is useful both for risk assessment and in developing monitoring programs.
I.5 危害分析及關鍵管制點（Hazard Analysis and Critical Control Points (HACCP)）	
HACCP 是為確保產品品質、可靠性及安全性之系統性、前瞻性及預防性的工具（參見 WHO Technical Report Series No 908, 2003 Annex 7）。這是一個結構化的方法。該方法應用技術和科學的原理，分析、評估、預防及管制由產品之設計、開發、生產及使用的危害所	HACCP is a systematic, proactive, and preventive tool for assuring product quality, reliability, and safety (see WHO Technical Report Series No 908, 2003 Annex 7). It is a structured approach that applies technical and scientific principles to analyze, evaluate, prevent, and control the risk or adverse consequence(s) of hazard(s) due to the

產生之風險或不良後果。	design, development, production, and use of products.
HACCP 包含下列 7 個步驟：	HACCP consists of the following seven steps:
(1) 對製程的每一個步驟執行危害分析，並確認其預防措施；	(1) conduct a hazard analysis and identify preventive measures for each step of the process;
(2) 決定關鍵管制點；	(2) determine the critical control points;
(3) 建立關鍵限量；	(3) establish critical limits;
(4) 建立一個監測關鍵管制點的系統；	(4) establish a system to monitor the critical control points;
(5) 建立當監測出關鍵管制點不在管制狀態時，應採取的矯正措施；	(5) establish the corrective action to be taken when monitoring indicates that the critical control points are not in a state of control;
(6) 建立系統，證實 HACCP 系統在有效運作中；	(6) establish system to verify that the HACCP system is working effectively;
(7) 建立一個保存紀錄之系統。	(7) establish a record-keeping system.
潛在的使用領域	**Potential Areas of Use(s)**
HACCP 可能用於確認和管理與物理學、化學及生物學上之危害（包括微生物學上的污染）相關聯的風險。當對產品及製程之瞭解足夠廣泛，以支持關鍵管制點的確認時，則 HACCP 最為有用。HACCP 分析的產出是風險管理資訊。不僅在製造過程上，且亦在其他生命週期的階段中，該資訊皆有助於關鍵管制點的監測。	HACCP might be used to identify and manage risks associated with physical, chemical and biological hazards (including microbiological contamination). HACCP is most useful when product and process understanding is sufficiently comprehensive to support identification of critical control points. The output of a HACCP analysis is risk management information that facilitates monitoring of critical points not only in the manufacturing process but also in other life cycle phases.
I.6 危害操作性分析（Hazard Operability Analysis (HAZOP)）	
HAZOP（參見 IEC 61882）係以假定風險事件是由於偏離設計或作業目的而引起之理論為基礎。這是一個系統性腦力激盪技術。該技術利用所謂「指引字語」來確認危害。「指引字語」（例如，「無」、「更多」、「異於」、「部分」等）應用於相關的參數（例如，污染、溫度）上，以幫助確認離開正常使用或設計目的之潛在偏離。這常常使用一組人員組成之團隊。這些人員具有涵蓋該製程或產品之設計及其應用的專門知識。	HAZOP (see IEC 61882) is based on a theory that assumes that risk events are caused by deviations from the design or operating intentions. It is a systematic brainstorming technique for identifying hazards using so-called "guide-words". "Guide-words" (e.g., No, More, Other Than, Part of, etc.) are applied to relevant parameters (e.g., contamination, temperature) to help identify potential deviations from normal use or design intentions. It often uses a team of people with expertise covering the design of the process or product and its application.
潛在的使用領域	**Potential Areas of Use(s)**
HAZOP 可適用於原料及藥品之製造過程，包括委外生產與配方及上游供應商、設備和設施。這亦已使用於製藥工業，主要以評估製程安全性的危害。類似於 HACCP 之情況，HAZOP 分析之產出是一個對風險管理之關鍵作業的清單。這有助於製造過程中之關鍵點的定期監測。	HAZOP can be applied to manufacturing processes, including outsourced production and formulation as well as the upstream suppliers, equipment and facilities for drug substances and drug (medicinal) products. It has also been used primarily in the pharmaceutical industry for evaluating process safety hazards. As is the case with HACCP, the output of a HAZOP analysis is a list of critical operations for risk management. This facilitates regular monitoring of critical points in the manufacturing process.
I.7 事先危害分析（Preliminary Hazard Analysis (PHA)）	
HA 是一個分析工具，該工具應用先前關於一	PHA is a tool of analysis based on applying prior

個危害或失效之經驗或知識為基礎，以確認將來可能引起傷害之危害、危害狀況及事件，並預測其在一定的活動、設施、產品或系統之發生機率。其工具包含：1) 確認風險事件發生的可能性，2) 對健康可能造成之傷害或損害程度的定性評估，3) 利用綜合事件之嚴重度及可能性將危害相對分級，以及 4) 確認可能之改善措施。	experience or knowledge of a hazard or failure to identify future hazards, hazardous situations and events that might cause harm, as well as to estimate their probability of occurrence for a given activity, facility, product or system. The tool consists of: 1) the identification of the possibilities that the risk event happens, 2) the qualitative evaluation of the extent of possible injury or damage to health that could result, 3) a relative ranking of the hazard using a combination of severity and likelihood of occurrence, and 4) the identification of possible remedial measures.
潛在的使用領域	**Potential Areas of Use(s)**
當情況不允許使用一個更廣泛技術，則在分析既有系統或危害之優先順序時，PHA 可能是很有用的。這可用於產品、製程及設施之設計，亦可評估一般產品類型、次為產品分類及後為特殊產品之危害。PHA 是最普遍使用於一個計畫之開發的初期。那時候關於細部設計或作業程序都只有很少的資訊。因此，這常常會是進一步研究的一個前導。典型地，在 PHA 中確認之危害，將與像在本節中規定之其他風險管理工具一起，進一步加以評價。	PHA might be useful when analyzing existing systems or prioritizing hazards where circumstances prevent a more extensive technique from being used. It can be used for product, process and facility design as well as to evaluate the types of hazards for the general product type, then the product class, and finally the specific product. PHA is most commonly used early in the development of a project when there is little information on design details or operating procedures; thus, it will often be a precursor to further studies. Typically, hazards identified in the PHA are further assessed with other risk management tools such as those in this section.
I.8 風險分級及篩選（Risk Ranking and Filtering）	
風險分級及篩選是將風險比較與分級的工具。複雜系統之風險分級典型地需要對每一風險之多樣的定量和定性因子加以評估。這個工具包含視需要，將一個基本風險問題分解成許多構成要素，以捕捉在此風險中所涉及之因子。這些因子結合成一個單一的相對風險分數，而後可用以將風險分級。「篩選器」是以對風險分數進行加權或減去的形式存在，可用為將風險分級改變尺度或使風險分級合適於管理或政策目標。	Risk ranking and filtering is a tool for comparing and ranking risks. Risk ranking of complex systems typically requires evaluation of multiple diverse quantitative and qualitative factors for each risk. The tool involves breaking down a basic risk question into as many components as needed to capture factors involved in the risk. These factors are combined into a single relative risk score that can then be used for ranking risks. "Filters," in the form of weighting factors or cut-offs for risk scores, can be used to scale or fit the risk ranking to management or policy objectives.
潛在的使用領域	**Potential Areas of Use(s)**
風險分級及過濾可用於將製造場所排定優先順序，以供主管機關或工業界檢查/稽核。於風險組合與其需被管理的潛在後果之多樣化，且難以使用單一工具進行比較的情況時，風險分級方法尤其有效。當管理上需要在相同組織架構內，評估定量及定性評價之風險時，風險分級是有用的。	Risk ranking and filtering can be used to prioritize manufacturing sites for inspection/audit by regulators or industry. Risk ranking methods are particularly helpful in situations in which the portfolio of risks and the underlying consequences to be managed are diverse and difficult to compare using a single tool. Risk ranking is useful when management needs to evaluate both quantitatively-assessed and qualitatively-assessed risks within the same organizational framework.
I.9 輔助性統計工具（Supporting Statistical Tools）	
統計工具可支持及促進品質風險管理。其可進行有效的數據評價，幫助決定數據套組的重要性，並促成更可靠的決策。下面提供在製藥工	Statistical tools can support and facilitate quality risk management. They can enable effective data assessment, aid in determining the significance of

業普遍使用之一些主要的統計工具清單：	the data set(s), and facilitate more reliable decision-making. A listing of some of the principal statistical tools commonly used in the pharmaceutical industry is provided:
• 管制圖，例如：	• Control Charts, for example:
– 允收管制圖（參見 ISO 7870-3:2020）；	– Acceptance Control Charts (see ISO 7870-3:2020);
– 累積總和圖（ISO 7870-4:2021）；	– Cumulative Sum Charts (see ISO 7870-4:2021);
– Shewhart 管制圖（參見 ISO 7870-2:2013）；	– Shewhart Control Charts (see ISO 7870-2:2013);
– 加權移動平均。	– Weighted Moving Average.
• 實驗設計（DOE）；	• Design of Experiments (DOE);
• 直方圖；	• Histograms;
• Pareto 圖；	• Pareto Charts;
• 製程能力分析。	• Process Capability Analysis.

附件 II：品質風險管理的可能應用
ANNEX II: POTENTIAL APPLICATIONS FOR QUALITY RISK MANAGEMENT

本附件意在確認產業界及主管機構可能運用之品質風險管理的原則及工具。然而，特定風險管理工具之選擇完全取決於特定事實及情況。	This Annex is intended to identify potential uses of quality risk management principles and tools by industry and regulators. However, the selection of particular risk management tools is completely dependent upon specific facts and circumstances.
這些案例係為說明之目的而提供，並且只是建議可能運用之品質風險管理。本附件無意在超過現行法規之要求，創設任何新的期待。	These examples are provided for illustrative purposes and only suggest potential uses of quality risk management. This Annex is not intended to create any new expectations beyond the current regulatory requirements.
II.1 品質風險管理當作完整品質管理的一部分（Quality Risk Management as Part of Integrated Quality Management）	
文件	**Documentation**
檢討對現行法規所期望的解釋與應用。	To review current interpretations and application of regulatory expectations;
決定標準作業程序、準則等之需要性及/或開發其內容。	To determine the desirability of and/or develop the content for SOPs, guidelines, etc.
訓練與教育	**Training and education**
以人員之教育、經驗及工作習慣，以及以先前訓練之定期評價（例如，其成效）為基礎，決定職前及/或持續訓練的適當性。	To determine the appropriateness of initial and/or ongoing training sessions based on education, experience and working habits of staff, as well as on a periodic assessment of previous training (e.g., its effectiveness);
確認使人員可靠地執行作業且對產品品質無不良衝擊所需的訓練、經驗、資格檢定及體能。	To identify the training, experience, qualifications and physical abilities that allow personnel to perform an operation reliably and with no adverse impact on the quality of the product.
品質缺陷	**Quality defects**
提供基礎，以辨識、評估及溝通可疑的品質缺陷、申訴、趨勢、偏離、調查、偏離規格結果等之潛在的品質影響。	To provide the basis for identifying, evaluating, and communicating the potential quality impact of a suspected quality defect, complaint, trend, deviation, investigation, out of specification result, etc;
促進風險之溝通及決定適當的行動，並會同主管機關處理重大的產品缺陷（例如，回收）。	To facilitate risk communications and determine appropriate action to address significant product defects, in conjunction with regulatory authorities (e.g., recall).
稽核/檢查	**Auditing/Inspection**
界定內部與外部稽核的頻率及範圍，考慮諸如以下的因子：	To define the frequency and scope of audits, both internal and external, taking into account factors such as:
• 既有之法定要求；	• Existing legal requirements;
• 公司或設施之整體狀態與歷史；	• Overall compliance status and history of the company or facility;
• 公司之品質風險管理措施的健全性；	• Robustness of a company's quality risk management activities;
• 場所之複雜性；	• Complexity of the site;
• 製造過程之複雜性；	• Complexity of the manufacturing process;

• 產品之複雜性與其治療上的重要性；	• Complexity of the product and its therapeutic significance;
• 品質缺陷之次數與重要性（例如，回收）；	• Number and significance of quality defects (e.g., recall);
• 先前稽核/檢查之結果；	• Results of previous audits/inspections;
• 建築物、設備、製程、關鍵人員之重大變更；	• Major changes of building, equipment, processes, key personnel;
• 製造產品之經驗（例如，頻率、數量、批數）；	• Experience with manufacturing of a product (e.g., frequency, volume, number of batches);
• 官方管制實驗室之檢驗結果。	• Test results of official control laboratories.
定期檢討	**Periodic review**
在產品品質檢討之內，選擇、評估與解釋數據之趨勢結果；	To select, evaluate and interpret trend results of data within the product quality review;
解釋監測數據（例如支持再確效或變更抽樣之適當性的評價）。	To interpret monitoring data (e.g., to support an assessment of the appropriateness of revalidation or changes in sampling).
變更管理/變更管制	**Change management / change control**
變更之管理是基於在藥劑開發上及製造期間所累積之知識及資訊；	To manage changes based on knowledge and information accumulated in pharmaceutical development and during manufacturing;
評估變更對最終產品之可用性/可得性的影響；	To evaluate the impact of the changes on the availability of the final product;
評估設施、設備、原物料、製程之變更或技術移轉對產品品質之影響；	To evaluate the impact on product quality of changes to the facility, equipment, material, manufacturing process or technical transfers;
決定在變更實施前之適當行動，例如追加之測試、(再）驗證、(再）確效或與管理機構之溝通。	To determine appropriate actions preceding the implementation of a change, e.g., additional testing, (re)qualification, (re)validation or communication with regulators.
持續改善	**Continual improvement**
促進製程在產品生命週期全程之持續改善。	To facilitate continual improvement in processes throughout the product lifecycle.
II.2 品質風險管理作為法規作業的一部分（Quality Risk Management as Part of Regulatory Operations）	
檢查及評價措施	**Inspection and assessment activities**
協助資源配置，包含，例如檢查計畫及頻率，以及檢查和評價強度在內（參見附件 II.1 的「稽核」段）；	To assist with resource allocation including, for example, inspection planning and frequency, and inspection and assessment intensity (see "Auditing" section in Annex II.1);
評估例如，品質缺陷、潛在回收及檢查結果之重要性；	To evaluate the significance of, for example, quality defects, potential recalls and inspectional findings;
決定檢查後之後續措施的適當性及類型；	To determine the appropriateness and type of post-inspection regulatory follow-up;
評估由業界提出之資訊，包含藥劑開發的資訊在內；	To evaluate information submitted by industry including pharmaceutical development information;
評估所提出之變異或變更的影響；	To evaluate impact of proposed variations or changes;
確認應在檢查者與評估者間溝通之風險，以幫助更佳瞭解風險將如何管制或已受管制（例如，參數放行、製程分析技術（PAT））。	To identify risks which should be communicated between inspectors and assessors to facilitate better understanding of how risks can be or are controlled (e.g., parametric release, Process Analytical

	Technology (PAT)).
II.3 品質風險管理作為開發的一部分 （Quality Risk Management as Part of Development）	
設計一個高品質產品及其製造過程，以一致地交付預定性能的產品（參見 ICH Q8）；	To design a quality product and its manufacturing process to consistently deliver the intended performance of the product (see ICH Q8);
提高涵蓋寬廣範圍之原物料屬性（例如，粒子大小分佈、含水量、流動性質）之產品性能的知識、作業選項及製程參數；	To enhance knowledge of product performance over a wide range of material attributes (e.g., particle size distribution, moisture content, flow properties), processing options and process parameters;
評估原料、溶劑、原料藥（API）起始物、原料藥（APIs）、賦形劑或包裝材料的關鍵屬性；	To assess the critical attributes of raw materials, solvents, Active Pharmaceutical Ingredient (API) starting materials, APIs, excipients, or packaging materials;
建立適當的規格、確認關鍵製程參數，及建立製造管制（例如，使用得自藥劑開發研究的資料。該資料與品質屬性之臨床重要性及在操作期間管制其能力有關）；	To establish appropriate specifications, identify critical process parameters and establish manufacturing controls (e.g., using information from pharmaceutical development studies regarding the clinical significance of quality attributes and the ability to control them during processing);
減少品質屬性的變異性：	To decrease variability of quality attributes:
• 降低產品及原物料的缺陷；	• reduce product and material defects;
• 降低製造的缺陷。	• reduce manufacturing defects.
評估關於放大批量及技術移轉之進一步研究（例如，生體相等性、安定性）的需求；	To assess the need for additional studies (e.g., bioequivalence, stability) relating to scale up and technology transfer;
使用「設計空間」的概念（參見 ICH Q8）。	To make use of the "design space" concept (see ICH Q8).
II.4 設施、設備和公用設施的品質風險管理 （Quality Risk Management for Facilities, Equipment and Utilities）	
設施/設備的設計	**Design of facility / equipment**
當設計建築物及設施時，決定其適當的區域，例如：	To determine appropriate zones when designing buildings and facilities, e.g.,
• 物料及人員的動線；	• flow of material and personnel;
• 使污染減至最低；	• minimize contamination;
• 防蟲鼠措施；	• pest control measures;
• 混雜的防止；	• prevention of mix-ups;
• 開放設備相對於密閉設備；	• open versus closed equipment;
• 潔淨室相對於隔離裝置技術；	• clean rooms versus isolator technologies;
• 專用或隔離的設施/設備。	• dedicated or segregated facilities / equipment.
對設備及容器，決定其適當接觸產品之材料（例如不銹鋼等級、墊圈、潤滑劑的選擇）；	To determine appropriate product contact materials for equipment and containers (e.g., selection of stainless steel grade, gaskets, lubricants);
決定適當之公用設施（例如，蒸汽、氣體、電源、壓縮空氣、加熱、通風及空調（HVAC）、水）；	To determine appropriate utilities (e.g., steam, gases, power source, compressed air, heating, ventilation and air conditioning (HVAC), water);
相關之設備，決定適當之預防性維護保養（例如必要之備用零件的清單）。	To determine appropriate preventive maintenance for associated equipment (e.g., inventory of necessary spare parts).
設施的衛生狀況	**Hygiene aspects in facilities**

使產品免於受到環境之危害，包含化學、微生物學、物理學上的危害（例如，決定適當的服裝及更衣、衛生相關事項）；	To protect the product from environmental hazards, including chemical, microbiological, and physical hazards (e.g., determining appropriate clothing and gowning, hygiene concerns);
保護環境（例如人員及潛在的交叉污染）的免於受到與所製造之產品造成相關的危害。	To protect the environment (e.g., personnel, potential for cross-contamination) from hazards related to the product being manufactured.
設施/設備/公用設施的驗證	**Qualification of facility/equipment/utilities**
決定設施、建築物、生產設備及/或實驗室儀器之驗證範圍及程度（包含適當的校正方法）。	To determine the scope and extent of qualification of facilities, buildings, and production equipment and/or laboratory instruments (including proper calibration methods).
設備的清潔及環境管制	**Cleaning of equipment and environmental control**
以預定用途為基礎，區分影響及決策（例如多重目的相對於單一目的，批次生產相對於連續生產）；	To differentiate efforts and decisions based on the intended use (e.g., multi- versus single-purpose, batch versus continuous production);
決定可接受的（規定的）清潔確效限量。	To determine acceptable (specified) cleaning validation limits.
校正/預防性維護保養	**Calibration/preventive maintenance**
設定適當的校正及維護保養時程表。	To set appropriate calibration and maintenance schedules.
電腦系統及電腦管制設備	**Computer systems and computer controlled equipment**
選擇電腦硬體及軟體的設計（例如，模組的、故障耐受性）；	To select the design of computer hardware and software (e.g., modular, structured, fault tolerance);
決定確效的程度，例如，	To determine the extent of validation, e.g.,
• 關鍵性能參數的確認；	• identification of critical performance parameters;
• 需求與設計的選擇；	• selection of the requirements and design;
• 程式碼的回顧；	• code review;
• 測試的程度與測試方法；	• the extent of testing and test methods;
• 電子紀錄及簽章的可靠性。	• reliability of electronic records and signatures.
II.5 品質風險管理作為原/物料管理的一部分（Quality Risk Management as Part of Materials Management）	
供應商及合約製造商（受委託製造者）的評價及評估	**Assessment and evaluation of suppliers and contract manufacturers**
提供供應商及合約製造商（受委託製造者）一個廣泛的評估（例如稽核、供應商品質協議）。	To provide a comprehensive evaluation of suppliers and contract manufacturers (e.g., auditing, supplier quality agreements).
原料	**Starting material**
評估與原料上之變異有關聯的差異及可能的品質風險（例如年齡、合成路徑）。	To assess differences and possible quality risks associated with variability in starting materials (e.g., age, route of synthesis).
原物料的使用	**Use of materials**
決定使用待驗中的原物料是否適當（例如，為後續之廠內處理）；	To determine whether it is appropriate to use material under quarantine (e.g., for further internal processing);
決定退回物品之重製、再加工、使用的適當性。	To determine appropriateness of reprocessing, reworking, use of returned goods.
儲存、物流和運銷條件	**Storage, logistics and distribution conditions**

評估裝置之適當性，以確保適當儲存及輸送條件的維持（例如溫度、濕度、容器之設計）；	To assess the adequacy of arrangements to ensure maintenance of appropriate storage and transport conditions (e.g., temperature, humidity, container design);
結合其他 ICH 指引，決定在儲存或運輸條件上之差異對產品品質的影響（例如，冷鏈管理（cold chain management））；	To determine the effect on product quality of discrepancies in storage or transport conditions (e.g., cold chain management) in conjunction with other ICH guidelines;
維護基礎設施（例如，確保正確裝運條件、暫時儲存、危害性原物料及受管制原物料之處理、海關報關/海關結關的能力）；	To maintain infrastructure (e.g., capacity to ensure proper shipping conditions, interim storage, handling of hazardous materials and controlled substances, customs clearance);
提供確保藥品之可用性/可得性的資訊（例如，供應鏈之風險分級）。	To provide information for ensuring the availability of pharmaceuticals (e.g., ranking risks to the supply chain).
II.6 品質風險管理作為生產的一部分 （Quality Risk Management as Part of Production）	
確效	**Validation**
確認查證、驗證與確效措施之範圍及程度（例如分析方法、製程、設備及清潔方法）；	To identify the scope and extent of verification, qualification and validation activities (e.g., analytical methods, processes, equipment and cleaning methods);
決定後續管理措施的程度（例如抽樣、監測與再確效）；	To determine the extent for follow-up activities (e.g., sampling, monitoring and re-validation);
區分關鍵性與非關鍵性製程步驟，以便於確效研究之設計。	To distinguish between critical and non-critical process steps to facilitate design of a validation study.
製程中管制與測試	**In-process sampling & testing**
評估製程中之管制測試的頻率與程度（例如證明在核准之管制條件下縮減測試的正當性）；	To evaluate the frequency and extent of in-process control testing (e.g., to justify reduced testing under conditions of proven control);
評估結合參數放行與即時放行之製程分析技術（PAT）的使用並證明其合理性。	To evaluate and justify the use of process analytical technologies (PAT) in conjunction with parametric and real time release.
生產計畫	**Production planning**
決定適當之生產計畫（例如，專用的、時段切換的及併行性的生產順序）。	To determine appropriate production planning (e.g., dedicated, campaign and concurrent production process sequences).
II.7 品質風險管理作為實驗室管制與安定性研究的一部分 （Quality Risk Management as Part of Laboratory Control and Stability Studies）	
偏離規格結果	**Out of specification results**
在調查偏離規格結果期間中，用於確認可能的根本原因及矯正措施。	To identify potential root causes and corrective actions during the investigation of out of specification results.
再驗期間/末效日期	**Retest period / expiration date**
評估半製品/中間產物、賦形劑與原料之儲存及檢驗的適當性。	To evaluate adequacy of storage and testing of intermediates, excipients and starting materials.
II.8 品質風險管理做為包裝與標示的一部分 （Quality Risk Management as Part of Packaging and Labeling）	
包裝設計	**Design of packages**
設計外包裝以保護經直接包材包裝的產品（例	To design the secondary package for the protection

如確保產品之真實性、標示之易讀性）。	of primary packaged product (e.g., to ensure product authenticity, label legibility).
容器封蓋系統的選擇	**Selection of container closure system**
決定容器封蓋系統之關鍵性參數。	To determine the critical parameters of the container closure system.
標籤管制	**Label controls**
基於不同產品標籤可能產生混雜，包含相同標籤之不同版本在內，設計標籤之管制程序。	To design label control procedures based on the potential for mix-ups involving different product labels, including different versions of the same label.
II.9 品質風險管理作為供應鏈管制的一部分（Quality Risk Management as Part of Supply Chain Control）	
關於與品質/製造議題有關之產品可得性風險，供應鏈之產品生命週期監督包括維持現有品質/製造危害知識與優先致力於管理該等風險。瞭解品質/製造之危害對於維持供應鏈的可預測性是很重要的。當風險被完善地瞭解與管制時，可獲得對產品可得性更高的信心。	With regard to product availability risks related to quality/manufacturing issues, product lifecycle oversight of the supply chain includes maintaining current knowledge of quality/manufacturing hazards and prioritizing efforts to manage such risks. Understanding hazards to quality/manufacturing is critical to maintaining supply predictability. When risks are well understood and controlled, a higher confidence in product availability can be.
製程變異與管制狀態	**Manufacturing Process Variation and State of Control**
降低製程變異性（例如，製程偏離、非均一性）及相關之能力差距，該能力差距可能導致不可預測之結果，對品質及其所致之及時性、產量及產品可得性產生不良影響；	To decrease variability in the manufacturing process (e.g., process drift, non-uniformity) and associated capability gaps that can result in unpredictable outputs, adversely impact quality and consequently timeliness, yield and product availability;
設計能偵測來自製程中管制狀態之偏離與缺陷的監測系統，因此其可被適當的調查以確定根本原因及任何需要的風險減低措施。	To design monitoring systems that are capable of detecting departures from a state of control and deficiencies in manufacturing processes, so they can be appropriately investigated to determine root causes and any required risk mitigations.
製造設施與設備	**Manufacturing Facilities and Equipment**
確保基礎設施與設備是合適的，且為穩健製造（其包括包裝與測試）而設計（參見附件 II.4）；	To ensure that facility infrastructure and equipment are suitable and designed for robust manufacturing (this includes packaging and testing) (see Annex II.4);
建立維護保養計畫，以確保可靠的設施與設備性能；	To establish facility and equipment maintenance programmes that assure reliable facility and equipment performance;
確保設備之操作設計不易受人為錯誤所影響；	To ensure that the operational design of equipment is not vulnerable to human error;
經由對數位化、自動化、隔離技術與其他創新的利用，以獲得品質與效率提升。	To obtain quality and efficiency gains through the utilization of digitalization, automation, isolation technology, and other innovations.
供應商監督與關係	**Supplier Oversight and Relationships**
在所供應之原物料的品質與安全性或所提供服務被識別出重大變異時，加強對該等活動的檢討與監測（參見 ICH Q10 第 2.7 節）。	To enhance review and monitoring activities (see Section 2.7 of ICH Q10) when substantial variability is identified in the quality and safety of supplied materials or in the services provided.
管理與品質/製造有關之外部的產品可得性風險（例如，來自原料供應商、已簽訂合約機	To manage external product availability risks relating to quality/manufacturing, (e.g., from raw

構、服務提供者等）。	material suppliers, contracted organizations, service providers, etc.)