附件II：品質風險管理的可能應用 （Appendix 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。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。	This Appendix 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. 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，考慮諸如以下的因素：	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和歷史；	• 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
• 產品之複雜性及其治療上的重要性；	• Complexity of the product and its therapeutic significance
• 品質缺陷之次數及重要性(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、評估及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	To facilitate continual improvement in

善。	processes throughout the product lifecycle.
II.2品質風險管理作為受管理作業的一部分（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： • 降低產品及原物料的缺陷； • 降低製造的缺陷。	To decrease variability of quality attributes: • reduce product and material defects • 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
• 需求及設計的選擇；	• selection of the requirements and design
• 程式碼的回顧；	• code review
• 測試的程度及測試方法；	• 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 condition s）	
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、驗證及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、監測及再確效)；	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
製程中抽樣及測試 （In-process sampling & testing）	

評估製程中之管制測試的頻率及程度(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)
評估並證明結合參數放行及即時放行之製程分析技術（PAT）的使用之合理性。	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 品質風險管理當作實驗室管制及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、賦形劑及原料之儲存與檢驗的適當性。	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 Labelling）	
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(例如確保產品之真實性、標示之易讀性)。	To design the secondary package for the protection 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