西藥藥品優良製造規範
（第二部：原料藥）

PIC/S：Guide to Good Manufacturing Practice for Medicinal Products
（Part II）

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衛生福利部

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第二部（Part II）

目　錄

本規範係採 PIC/S GMP（Part II）（PE 009-17）制訂，考量本國國情及現況，將不適用之條文刪除，且本規範僅適用人用西藥原料藥。

1. 前言（INTRODUCTION）	
1.1 目的（Objective）	
本文件意在提供在適當品質管理系統下，原料藥製造之優良製造準則的指引，以確保其符合既定品質與純度的要求。	This document (Guide) is intended to provide guidance regarding good manufacturing practice (GMP) for the manufacturing of active pharmaceutical ingredients (APIs) under an appropriate system for managing quality. It is also intended to help ensure that APIs meet the requirements for quality and purity that they purport or are represented to possess.
在本規範中，所謂「製造」係指原料藥之原物料接收、生產、分包裝、重分包裝、標示、重標示、品質管制、放行、儲存與運銷以及相關的管制等全部作業。在本規範中，「應」係指期待其會受適用的建議，除非不適合、經 GMP 規範之任何相關附則修正或由經證明可提供至少同等品質保證水準之替代選項所取代。	In this Guide, “manufacturing” includes all operations of receipt of materials, production, packaging, repackaging, labeling, relabeling, quality control, release, storage and distribution of APIs and the related controls. In this Guide, the term” should” indicates recommendations that are expected to apply unless shown to be inapplicable, modified in any relevant annexes to the GMP Guide, or replaced by an alternative demonstrated to provide at least an equivalent level of quality assurance.
整體而言，本規範不涵蓋與從事製造人員的安全及與環境之保護相關的層面。此等管制是製藥廠固有的責任，按國家的法律管理之。	The GMP Guide as a whole does not cover safety aspects for the personnel engaged in the manufacture, nor aspects of protection of the environment. These controls are inherent responsibilities of the manufacturer and are governed by national laws.

本規範並非意在界定查驗登記/註冊的要求或修改藥典的要求，且不影響衛生主管機關在建立藥品之上市/製造許可申請中，對原料藥特定查驗登記/註冊之要求的職責。查驗登記/註冊文件中所做之全部承諾皆須符合。	This Guide is not intended to define registration requirements or modify pharmacopoeial requirements and does not affect the ability of the responsible competent authority to establish specific registration requirements regarding APIs within the context of marketing/manufacturing authorizations. All commitments in registration documents must be met.
1.2 範圍（Scope）	
本規範適用於人用藥品之原料藥的製造。本規範適用於無菌原料藥之製造，僅及於原料藥成為無菌之前，無菌原料藥的滅菌及無菌作業不包含在本規範中，但應遵循我國西藥藥品優良製造規範第一部及附則 1 之相關規定。	This Guide applies to the manufacture of APIs for medicial products for human use. It applies to the manufacture of sterile APIs only up to the point immediately prior to the APIs being rendered sterile. The sterilisation and aseptic processing of sterile APIs are not covered, but should be performed in accordance with the principles and guidelines of GMP as laid down in national legislations and interpreted in the GMP Guide including its Annex 1.
由於 PIC/S GMP 對血液機構訂有關於血液之收集及測試的詳細要求，本規範不含括全血及血漿。但包含以血液或血漿為原料所製造的原料藥。	This Guide excludes whole blood and plasma as the PIC/S GMP Guide for Blood Establishments lays down the detailed requirements for the collection and testing of blood. However, it does include APIs that are produced using blood or plasma as raw materials.
總之，本規範不適用於大包裝藥品，但適用於其他所有活性原料。該等活性原料適用於西藥藥品優良製造規範附則 2、3 及 6 所描述之任何關於變異規定。可於附則 2、3 及 6 找到某些原料藥類型之補充規範。	Finally, the Guide does not apply to bulk-packaged medicinal products. It applies to all other active starting materials subject to any derogations described in the annexes to the GMP Guide, in particular Annexes 2 to 7 where supplementary guidance for certain types of API may be found.

「原料藥之起始原料」 係指用於生產原料藥並且納入該原料藥結構中之一個重要結構部份的原料、中間產物或原料藥。原料藥之起始原料可以是依照契約或商業協議從一個或多個供應商購得的商品，或在廠內所生產的原料。原料藥之起始原料通常具有界定之化學性質與結構。	An “API Starting Material” is a raw material, intermediate, or an API that is used in the production of an API and that is incorporated as a significant structural fragment into the structure of the API. An API Starting Material can be an article of commerce, a material purchased from one or more suppliers under contract or commercial agreement, or produced in-house. API Starting Materials normally have defined chemical properties and structure.
製造者應依理論基礎指定原料藥之生產起始點並予以文件化。對合成製程而言，該起始點慣稱為「原料藥起始原料」進入製程之點。對於其他製程而言（例如醱酵、萃取、純化等），其理論基礎應依個案建立。表一提供原料藥之起始原料正常導入製程起始點的指引。	The manufacturer should designate and document the rationale for the point at which production of the API begins. For synthetic processes, this is known as the point at which "API Starting Materials" are entered into the process. For other processes (e.g. fermentation, extraction, purification, etc), this rationale should be established on a case-by-case basis. Table 1 gives guidance on the point at which the API Starting Material is normally introduced into the process.
從該起始點開始，本規範界定之適當的 GMP 應適用於這些中間產物及/或原料藥的製造步驟。這當包括經確定會影響原料藥品質之關鍵製程步驟的確效。不過，必須注意到的事實是：製造者選擇確效一個製程步驟，未必需要將該步驟界定為關鍵步驟。	From this point on, appropriate GMP as defined in this Guide should be applied to these intermediate and/or API manufacturing steps. This would include the validation of critical process steps determined to impact the quality of the API. However, it should be noted that the fact that a manufacturer chooses to validate a process step does not necessarily define that step as critical.

本規範通常適用於表一灰色區中顯示的步驟，這不意味以灰色顯示之所有步驟都應完成。在原料藥的製造中，GMP 的嚴謹性應隨製程從早期階段原料藥步驟進行到最終步驟，亦即至純化及包裝，而升高。原料藥的物理加工，例如製粒、加衣或粒子大小的物理操作（諸如粉碎、微細化），應至少按本規範的標準執行。	The guidance in this document would normally be applied to the steps shown in gray in Table 1. It does not imply that all steps shown should be completed. The stringency of GMP in API manufacturing should increase as the process proceeds from early API steps to final steps, purification, and packaging. Physical processing of APIs, such as granulation, coating or physical manipulation of particle size (e.g. milling, micronizing), should be conducted at least to the standards of this Guide.
本規範不適用於界定之「原料藥起始原料」導入製程之前的步驟。	This GMP Guide does not apply to steps prior to the introduction of the defined "API Starting Material".

Table 1: Application of this Guide to API Manufacturing

表一：本規範適用於原料藥之製造

Type of Manufacturing	Application of this Guide to steps (shown in grey) used in this type of manufacturing				
製造類型	本規範適用於本製造類型在著色欄位所示步驟				
Chemical Manufacturing	Production of the API Starting Material	Introduction of the API Starting Material into process	Production of Intermediate(s)	Isolation and purification	Physical processing, and packaging
化學製造	原料藥起始原料的生產	將原料藥起始原料導入製程	中間產物的生產	分離及純化	物理加工及包裝
API derived from animal sources	Collection of organ, fluid, or tissue	Cutting, mixing, and/or initial processing	Introduction of the API Starting Material into process	Isolation and purification	Physical processing, and packaging
自動物來源衍生的原料藥	器官、體液或組織的收集	切碎、混合及/或初步加工	將原料藥起始原料導入製程	分離及純化	物理加工及包裝
API extracted from plant sources	Collection of plant	Cutting and initial extraction(s)	Introduction of the API Starting Material into process	Isolation and purification	Physical processing, and packaging
自植物來源萃取的原料藥	植物的採集	切碎及初步萃取	將原料藥起始原料導入製程	分離及純化	物理加工及包裝
Herbal extracts used as API	Collection of plants	Cutting and initial extraction		Further extraction	Physical processing, and packaging
用為原料藥之草本植物的萃取物	植物的採集	切碎及初步萃取		再萃取	物理加工及包裝
API consisting of comminuted or powdered herbs	Collection of plants and/or cultivation and harvesting	Cutting/comminuting			Physical processing, and packaging

由磨碎或粉碎之草本植物所組成的原料藥	植物的採集及/或培育與採收	切碎/磨碎			物理加工及包裝
Biotechnology: fermentation/cell culture	Establishment of master cell bank and working cell bank	Maintenance of working cell bank	Cell culture and/or fermentation	Isolation and purification	Physical processing, and packaging
生物技術：醱酵/細胞培養	種細胞庫及工作細胞庫的建立	工作細胞庫的維護	細胞培養及/或醱酵	分離及純化	物理加工及包裝
“Classical” Fermentation to produce an API	Establishment of cell bank	Maintenance of the cell bank	Introduction of the cells into fermentation	Isolation and purification	Physical processing, and packaging
用傳統醱酵以生產原料藥	細胞庫的建立	細胞庫的維護	細胞導入醱酵	分離及純化	物理加工及包裝

2.	**品質管理（QUALITY MANAGEMENT）**		
2.1	**原則（Principles）**		
2.10	品質應為參與製造之所有人員的責任。	2.10	Quality should be the responsibility of all persons involved in manufacturing.
2.11	每一家藥廠皆應建立及實施有效的品質管理系統，並予以文件化。該系統包含管理階層及適當製造人員的主動參與。	2.11	Each manufacturer should establish, document, and implement an effective system for managing quality that involves the active participation of management and appropriate manufacturing personnel.
2.12	品質管理系統應包含組織架構、程序、流程及資源，以及必要的作業，以確保原料藥會符合其品質與純度之預定規格的信心。所有與品質有關之作業皆應加以界定並予以文件化。	2.12	The system for managing quality should encompass the organisational structure, procedures, processes and resources, as well as activities necessary to ensure confidence that the API will meet its intended specifications for quality and purity. All quality related activities should be defined and documented.
2.13	應有獨立於生產部門，並擔負品質保證與品質管制責任的品質單位。品質單位得為分離之品質保證（QA）部門及品質管制（QC）部門，或為單一個人或一組人員的形式，依組織之大小與架構而定。	2.13	There should be a quality unit(s) that is independent of production and that fulfills both quality assurance (QA) and quality control (QC) responsibilities. This can be in the form of separate QA and QC units or a single individual or group, depending upon the size and structure of the organization.
2.14	放行中間產物及原料藥的被授權人應予指定。	2.14	The persons authorised to release intermediates and APIs should be specified.
2.15	所有與品質有關的作業皆應在其執行時加以記錄。	2.15	All quality related activities should be recorded at the time they are performed.
2.16	與既定程序之任何偏差皆應加以文件化並予以說明。關鍵性的偏差應加以調查，且該調查及其結論應予以文件化。	2.16	Any deviation from established procedures should be documented and explained. Critical deviations should be investigated, and the investigation and its conclusions should be documented.

2.17	原物料在經品質單位滿意完成評估前不得放行或使用,除非備有適當的系統允許其使用（例如，在第 10.20 條所述的隔離/待驗下放行，或是在原料或中間產物等待完成評估前使用）。	2.17	No materials should be released or used before the satisfactory completion of evaluation by the quality unit(s) unless there are appropriate systems in place to allow for such use (e.g. release under quarantine as described in Section 10.20 or the use of raw materials or intermediates pending completion of evaluation).
2.18	就主管機關的檢查、嚴重 GMP 缺失、產品瑕疵及相關的行動（例如，與品質有關之申訴、回收及主管機關的管制行動等），應具備能及時通知負責管理者之程序。	2.18	Procedures should exist for notifying responsible management in a timely manner of regulatory inspections, serious GMP deficiencies, product defects and related actions (e.g. quality related complaints, recalls, regulatory actions, etc.).
2.19	為可靠達成該品質目標,應有全面設計並正確實施的品質系統。該系統涵蓋優良製造規範、品質管制及品質風險管理。	2.19	To achieve the quality objective reliably there must be a comprehensively designed and correctly implemented quality system incorporating Good Manufacturing Practice, Quality Control and Quality Risk Management.
2.2	**品質風險管理（Quality Risk Management）**		
2.20	品質風險管理是針對原料藥品質風險之評價、管制、溝通及檢討的系統過程。可用前瞻性及回溯性的方式來執行。	2.20	Quality risk management is a systematic process for the assessment, control, communication and review of risks to the quality of the active substance. It can be applied both proactively and retrospectively.
2.21	品質風險管理系統應確保下列項目：	2.21	The quality risk management system should ensure that:
	- 品質風險的評估是基於科學知識、製程的經驗，並且最終透過與原料藥的使用者之溝通連結至病患之保護。		- the evaluation of the risk to quality is based on scientific knowledge, experience with the process and ultimately links to the protection of the patient through communication with the user of the active substance.

- 品質風險管理過程的努力、正式化及文件化之程度應與風險程度相稱。	- the level of effort, formality and documentation of the quality risk management process is commensurate with the level of risk.
此外，品質風險管理之過程及應用的實例詳見附則 20。	Examples of the processes and applications of quality risk management can be found, inter alia, in Annex 20.
2.3 品質單位的職責【Responsibilities of the Quality Unit(s)】	
2.30 品質單位應參與所有與品質有關的事務。	2.30 The quality unit(s) should be involved in all quality-related matters.
2.31 品質單位應審查及核准所有與品質有關的適當文件。	2.31 The quality unit(s) should review and approve all appropriate quality-related documents.
2.32 獨立的品質單位之主要職責不得委由其他單位擔任。這些職責應以書面載明，並應包含，但未必限於下列各項：	2.32 The main responsibilities of the independent quality unit(s) should not be delegated. These responsibilities should be described in writing and should include, but not necessarily be limited to:
1. 放行或拒用/拒收所有原料藥。放行或拒用/拒收中間產物供在製造者管制之外的使用；	1. Releasing or rejecting all APIs. Releasing or rejecting intermediates for use outside the control of the manufacturing company;
2. 建立放行或拒用/拒收原料、中間產物、包裝與標示材料的系統；	2. Establishing a system to release or reject raw materials, intermediates, packaging, and labeling materials;
3. 在原料藥放行運銷之前，審查已完成的關鍵製程步驟之批次製造及實驗室管制紀錄；	3. Reviewing completed batch production and laboratory control records of critical process steps before release of the API for distribution;
4. 確保關鍵性偏差業經調查並解決；	4. Making sure that critical deviations are investigated and resolved;
5. 核准所有規格及製造管制標準書；	5. Approving all specifications and master production instruction;
6. 核准會影響中間產物或原料藥品質的所有程序；	6. Approving all procedures impacting the quality of intermediates or APIs;

7. 確保已執行內部稽查(自我查核)；	7. Making sure that internal audits (self-inspections) are performed;
8. 核准中間產物及原料藥之受託製造者；	8. Approving intermediate and API contract manufacturers;
9. 核准可能衝擊中間產物或原料藥品質的變更；	9. Approving changes that potentially impact intermediate or API quality;
10. 審查與核准確效計畫書及報告；	10. Reviewing and approving validation protocols and reports;
11. 確保與品質相關之申訴經過調查並解決；	11. Making sure that quality related complaints are investigated and resolved;
12. 確保使用有效系統以維護與校正關鍵性設備；	12. Making sure that effective systems are used for maintaining and calibrating critical equipment;
13. 確保原物料經過適當測試並提報其結果；	13. Making sure that materials are appropriately tested and the results are reported;
14. 確保對原料藥及/或合適時對中間產物有安定性資料支持其再驗日期或末效日期及儲存條件；	14. Making sure that there is stability data to support retest or expiry dates and storage conditions on APIs and/or intermediates where appropriate; and
15. 執行產品品質檢討（如第 2.6 節所界定）。	15. Performing product quality reviews (as defined in Section 2.6).
2.4 生產作業的責任（Responsibility for Production Activities）	
對生產作業的責任應以書面說明，並應包括，但未必限於下列各項：	The responsibility for production activities should be described in writing and should include, but not necessarily be limited to
1. 依照書面程序擬訂、審查、核准及發佈中間產物或原料藥的生產指令；	1. Preparing, reviewing, approving, and distributing the instructions for the production of intermediates or APIs according to written procedure;
2. 依照預先核准之指令，生產原料藥及合適時生產中間產物；	2. Producing APIs and, when appropriate, intermediates according to pre-approved instructions;

3. 審查所有批次製造紀錄，並確保這些紀錄已經完成與簽章；	3. Reviewing all production batch records and ensuring that these are completed and signed;
4. 確保所有生產偏差已經提報與評估，且關鍵性偏差經過調查並記錄其結論；	4. Making sure that all production deviations are reported and evaluated and that critical deviations are investigated and the conclusions are recorded;
5. 確保生產設施/設備是潔淨的，並經消毒（合適時）；	5. Making sure that production facilities are clean and, when appropriate, disinfected;
6. 確保必要之校正已經執行並保存其紀錄；	6. Making sure that the necessary calibrations are performed and records kept;
7. 確保廠房設施與設備經維護保養並保存其紀錄；	7. Making sure that the premises and equipment are maintained and records kept;
8. 確保確效計畫書與報告經審查及核准；	8. Making sure that validation protocols and reports are reviewed and approved;
9. 評估產品、製程或設備上所提議的變更；以及	9. Evaluating proposed changes in product, process or equipment; and
10. 確保新增，及合適時經修改之設施及設備經過驗證。	10. Making sure that new and, when appropriate, modified facilities and equipment are qualified.
2.5 內部稽查（自我查核）【Internal Audits (Self Inspection)】	
2.50 為證實遵從原料藥 GMP 之原則，應依照核定的時程表執行定期的內部稽查。	2.50 In order to verify compliance with the principles of GMP for APIs, regular internal audits should be performed in accordance with an approved schedule.
2.51 稽查所見與改正措施應予以文件化，並呈報公司的負責管理人。同意之改正措施應以適時且有效的方式完成。	2.51 Audit findings and corrective actions should be documented and brought to the attention of responsible management of the firm. Agreed corrective actions should be completed in a timely and effective manner.
2.6 產品品質檢討（Product Quality Review）	

2.60 應以證實製程的一致性為目標，執行原料藥之定期的品質檢討。該等檢討通常應每年執行一次，並予以文件化，且至少應包含下列各項：	2.60 Regular quality-reviews of APIs should be conducted with the objective of verifying the consistency of the process. Such reviews should normally be conducted and documented annually and should include at least:
➢ 關鍵製程中管制及關鍵原料藥試驗結果之檢討；	➢ A review of critical in-process control and critical API test results;
➢ 不符合既定規格之所有批次的檢討；	➢ A review of all batches that failed to meet established specification(s);
➢ 所有關鍵偏差或不符合及相關調查的檢討；	➢ A review of all critical deviations or non-conformances and related investigations;
➢ 對製程或分析方法所執行之任何變更的檢討；	➢ A review of any changes carried out to the processes or analytical methods;
➢ 安定性監測計畫之結果的檢討；	➢ A review of results of the stability monitoring program;
➢ 所有與品質有關之退回、申訴及回收的檢討；以及	➢ A review of all quality-related returns, complaints and recalls; and
➢ 改正措施之適當性的檢討。	➢ A review of adequacy of corrective actions.
2.61 本檢討之結果應進行評估，並評估是否應採取改正措施或任何再確效。對該改正措施的理由應予以文件化。同意之改正措施應以適時且有效的方式完成。	2.61 The results of this review should be evaluated and an assessment made of whether corrective action or any revalidation should be undertaken. Reasons for such corrective action should be documented. Agreed corrective actions should be completed in a timely and effective manner.
3. 人事（PERSONNEL）	
3.1 人員資格檢核（Personnel Qualifications）	
3.10 應有適當教育、訓練及/或經驗並經檢核符合資格的足夠人員，以執行與監督中間產物及原料藥的製造。	3.10 There should be an adequate number of personnel qualified by appropriate education, training, and/or experience to perform and supervise the manufacture of intermediates and APIs.

3.11	參與中間產物及原料藥之製造的所有人員之責任，應以書面規定之。	3.11	The responsibilities of all personnel engaged in the manufacture of intermediates and APIs should be specified in writing.
3.12	訓練應由符合資格的人員定期執行，且至少應涵蓋作業人員執行之特定作業及與該作業人員的職能有關之 GMP。訓練紀錄應予保存。訓練應定期評估。	3.12	Training should be regularly conducted by qualified individuals and should cover, at a minimum, the particular operations that the employee performs and GMP as it relates to the employee's functions. Records of training should be maintained. Training should be periodically assessed.
3.2	**個人衛生（Personnel Hygiene）**		
3.20	作業人員應力行優良的衛生及健康習慣。	3.20	Personnel should practice good sanitation and health habits.
3.21	作業人員應穿戴適合其參與之製造作業的潔淨衣服，且合適時，該衣服應予更換。必要時，應穿戴附加的保護性裝備，例如頭、臉、手及臂膀的覆罩，以防止中間產物及原料藥受到污染。	3.21	Personnel should wear clean clothing suitable for the manufacturing activity with which they are involved and this clothing should be changed, when appropriate. Additional protective apparel, such as head, face, hand, and arm coverings, should be worn, when necessary, to protect intermediates and APIs from contamination.
3.22	作業人員應避免直接接觸中間產物或原料藥。	3.22	Personnel should avoid direct contact with intermediates or APIs.
3.23	吸菸、飲食、咀嚼及食物的存放，應限制在與製造區分離之某特定場所。	3.23	Smoking, eating, drinking, chewing and the storage of food should be restricted to certain designated areas separate from the manufacturing areas.

3.24	罹患傳染性疾病或身體之暴露表面有開放性傷口的人員，不得參與可能導致損及原料藥之品質結果的作業。任何人員在任何時刻（經由體檢或監督者的觀察）顯現有明顯疾病或開放性傷口，且該健康狀態對原料藥之品質可能會有不良影響時，應排除在生產作業外，直到該病況已治癒或合格的醫療人員認定該員之加入不會損害該原料藥的安全性或品質為止。	3.24	Personnel suffering from an infectious disease or having open lesions on the exposed surface of the body should not engage in activities that could result in compromising the quality of APIs. Any person shown at any time (either by medical examination or supervisory observation) to have an apparent illness or open lesions should be excluded from activities where the health condition could adversely affect the quality of the APIs until the condition is corrected or qualified medical personnel determine that the person's inclusion would not jeopardize the safety or quality of the APIs.
3.3	**顧問（Consultants）**		
3.30	指導中間產物或原料藥之製造及管制的顧問，應有充分的教育、訓練及經驗，或其中之任何組合，以指導其受聘指導的主題。	3.30	Consultants advising on the manufacture and control of intermediates or APIs should have sufficient education, training, and experience, or any combination thereof, to advise on the subject for which they are retained.
3.31	載明姓名、地址、資格以及這些顧問提供之服務類型的紀錄應予保存。	3.31	Records should be maintained stating the name, address, qualifications, and type of service provided by these consultants.
4.	**建築物與設施（BUILDINGS AND FACILITIES）**		
4.1	**設計與建造（Design and Construction）**		

4.10	使用於製造中間產物及原料藥之建築物及設施應予配置、設計及建造，以適合該製造類型及階段並便於清潔、維護保養及操作。設施也應予設計，以將潛在的污染減到最低。對中間產物或原料藥已建立其微生物學上的規格者，合適時，其設施也應予設計，以限制其暴露於不合宜之微生物學上的污染物。	4.10	Buildings and facilities used in the manufacture of intermediates and APIs should be located, designed, and constructed to facilitate cleaning, maintenance, and operations as appropriate to the type and stage of manufacture. Facilities should also be designed to minimize potential contamination. Where microbiological specifications have been established for the intermediate or API, facilities should also be designed to limit exposure to objectionable microbiological contaminants, as appropriate.
4.11	建築物及設施應有為整齊放置設備及原物料之適當空間，以防止混雜及污染。	4.11	Buildings and facilities should have adequate space for the orderly placement of equipment and materials to prevent mix-ups and contamination.
4.12	設備本身（例如，密閉性或圍堵性系統）對原物料提供適合之保護者，該設備得座落於室外。	4.12	Where the equipment itself (e.g., closed or contained systems) provides adequate protection of the material, such equipment can be located outdoors.
4.13	通過建築物或設施之物流及人流應予設計，以防止混雜或污染。	4.13	The flow of materials and personnel through the building or facilities should be designed to prevent mix-ups or contamination.
4.14	對於下列作業，應有經界定之區域或其他管制系統：	4.14	There should be defined areas or other control systems for the following activities:
	➢ 等候放行或拒用之進廠原物料的接收、識別、抽樣及隔離/待驗；		➢ Receipt, identification, sampling, and quarantine of incoming materials, pending release or rejection;
	➢ 中間產物及原料藥在放行或拒用前之隔離/待驗；		➢ Quarantine before release or rejection of intermediates and APIs;
	➢ 中間產物及原料藥的抽樣；		➢ Sampling of intermediates and APIs

➢ 拒用的原物料在進一步處置（例如，退回、重處理或銷毀）前之保存；	➢ Holding rejected materials before further disposition (e.g., return, reprocessing or destruction);
➢ 已放行之原物料的儲存；	➢ Storage of released materials;
➢ 生產作業；	➢ Production operations;
➢ 分裝或包裝及標示作業；以及	➢ Packaging and labeling operations; and
➢ 實驗室作業。	➢ Laboratory operations.
4.15 應對於人員提供足夠且潔淨之盥洗設施。該設施應提供冷水與熱水，合適時並提供肥皂或清潔劑、烘乾機，或單次使用的紙巾。盥洗設施應與製造區分離，但便於使用。合適時，並應提供足夠之淋浴及/或更衣的設施。	4.15 Adequate and clean washing and toilet facilities should be provided for personnel. These facilities should be equipped with hot and cold water, as appropriate, soap or detergent, air dryers, or single service towels. The washing and toilet facilities should be separate from, but easily accessible to, manufacturing areas. Adequate facilities for showering and/or changing clothes should be provided, when appropriate.
4.16 實驗室（區）通常應與生產區隔離。若生產作業對實驗室量測之準確性無不良影響，且實驗室及其作業對生產作業或中間產物或原料藥無不良影響者，則有些實驗室（區）得座落在生產區中，特別是使用於製程中管制的實驗室（區）。	4.16 Laboratory areas/operations should normally be separated from production areas. Some laboratory areas, in particular those used for in-process controls, can be located in production areas, provided the operations of the production process do not adversely affect the accuracy of the laboratory measurements, and the laboratory and its operations do not adversely affect the production process or intermediate or API.
4.2 公用設施（Utilities）	

4.20	會影響產品品質之所有公用設施（例如，蒸汽、氣體、壓縮空氣及空調系統）應予驗證並適當地監測，且當超過限值時，應採取行動。應有這些公用設施系統之建構圖。	4.20	All utilities that could impact on product quality (e.g. steam, gases, compressed air, and heating, ventilation and air conditioning) should be qualified and appropriately monitored and action should be taken when limits are exceeded. Drawings for these utility systems should be available.
4.21	合適時，應提供適當的通風、空氣過濾及排氣系統。這些系統應經設計及建造，以將污染及交叉污染的風險降到最低，並應包含適合該製造階段之空氣壓力、微生物（合適時）、粉塵、濕度以及溫度的控制設備。對於原料藥暴露於環境的區域，應給予特別注意。	4.21	Adequate ventilation, air filtration and exhaust systems should be provided, where appropriate. These systems should be designed and constructed to minimise risks of contamination and cross-contamination and should include equipment for control of air pressure, microorganisms (if appropriate), dust, humidity, and temperature, as appropriate to the stage of manufacture. Particular attention should be given to areas where APIs are exposed to the environment.
4.22	空氣再循環至生產區者，應採取適當措施，以管制污染及交叉污染的風險。	4.22	If air is recirculated to production areas, appropriate measures should be taken to control risks of contamination and cross-contamination.
4.23	永久性安裝的管線應適當地識別。這可利用辨識個別管線、文件製作、電腦管制系統，或其他替代方法達成之。管線應裝設於適當位置，以避免中間產物或原料藥之污染的風險。	4.23	Permanently installed pipework should be appropriately identified. This can be accomplished by identifying individual lines, documentation, computer control systems, or alternative means. Pipework should be located to avoid risks of contamination of the intermediate or API.
4.24	排水管應有足夠的尺寸，且配置空氣阻斷裝置，或在合適時配置適當裝置，以防止虹吸回流。	4.24	Drains should be of adequate size and should be provided with an air break or a suitable device to prevent back-siphonage, when appropriate.
4.3 水（Water）			

4.30	原料藥之製造用水應證明適合其預定之用途。	4.30	Water used in the manufacture of APIs should be demonstrated to be suitable for its intended use.
4.31	除另有正當理由外，製程用水應至少符合世界衛生組織對飲用水品質之指引。	4.31	Unless otherwise justified, process water should, at a minimum, meet World Health Organization (WHO) guidelines for drinking (potable) water quality.
4.32	飲用水不足以確保原料藥之品質，且要求更嚴格之化學及/或微生物學上的水質規格者，應另訂其物理/化學屬性、總生菌數、不合宜的微生物及/或內毒素的適當規格。	4.32	If drinking (potable) water is insufficient to ensure API quality and tighter chemical and/or microbiological water quality specifications are called for, appropriate specifications for physical/chemical attributes, total microbial counts, objectionable organisms, and/or endotoxins should be established.
4.33	製程用水係由藥廠自行處理，以達界定之品質者，該處理程序應予確效，並按適當的行動限值監測之。	4.33	Where water used in the process is treated by the manufacturer to achieve a defined quality, the treatment process should be validated and monitored with appropriate action limits.
4.34	非無菌原料藥之製造廠意欲或宣稱其非無菌原料藥適合進一步加工，以生產無菌藥品者，其最終分離與純化步驟之用水的總生菌數、不合宜微生物以及內毒素應加以監測與管制。	4.34	Where the manufacturer of a nonsterile API either intends or claims that it is suitable for use in further processing to produce a sterile drug (medicinal) product, water used in the final isolation and purification steps should be monitored and controlled for total microbial counts, objectionable organisms, and endotoxins.
4.4	**圍堵（Containment）**		
4.40	在高致敏性物質，例如，青黴素或頭孢子菌素的生產上，應使用專用生產區，該區可包括設施、空氣處理設備及/或製程設備。	4.40	Dedicated production areas, which can include facilities, air handling equipment and/or process equipment, should be employed in the production of highly sensitizing materials, such as penicillins or cephalosporins.

4.41	除建立並維持經確效之去活化及/或清潔程序者外，當涉及具感染本質或高藥理活性或高毒性的物質時（例如，某些類固醇或細胞毒性的抗癌劑），也應考慮專用生產區。	4.41	Dedicated production areas should also be considered when material of an infectious nature or high pharmacological activity or toxicity is involved (e.g., certain steroids or cytotoxic anti-cancer agents) unless validated inactivation and/or cleaning procedures are established and maintained.
4.42	應制訂並執行適當的措施，以防止源自人員及原物料等從一個專用區移動到另外一個專用區的交叉污染。	4.42	Appropriate measures should be established and implemented to prevent cross-contamination from personnel, materials, etc. moving from one dedicated area to another.
4.43	高毒性非藥用原料，例如，除草劑與殺蟲劑之任何生產作業（包含秤重、粉碎或分裝或包裝），不得使用原料藥之生產的建築物及/或設備。高毒性非藥用原料的處理與儲存，應與原料藥隔離。	4.43	Any production activities (including weighing, milling, or packaging) of highly toxic non-pharmaceutical materials such as herbicides and pesticides should not be conducted using the buildings and/or equipment being used for the production of APIs. Handling and storage of these highly toxic non-pharmaceutical materials should be separate from APIs.
4.5	**照明（Lighting）**		
4.50	在所有區域皆應提供足夠的照明，使便於清潔、維護保養，以及正確作業。	4.50	Adequate lighting should be provided in all areas to facilitate cleaning, maintenance, and proper operations.
4.6	**污水與廢料（Sewage and Refuse）**		
4.60	源自廠房內及其緊鄰之周圍區域的污水、廢料及其他廢棄物（例如，源自製造之固體、液體或氣體的副產物）應以安全、適時且衛生的方式處置。廢棄物的容器及/或管線應清楚地識別。	4.60	Sewage, refuse, and other waste (e.g., solids, liquids, or gaseous by-products from manufacturing) in and from buildings and the immediate surrounding area should be disposed of in a safe, timely, and sanitary manner. Containers and/or pipes for waste material should be clearly identified.
4.7	**衛生措施與維護保養（Sanitation and Maintenance）**		

4.70	中間產物及原料藥之製造使用的建築物，應適當地維護保養及維修，並保持在潔淨狀態中。	4.70	Buildings used in the manufacture of intermediates and APIs should be properly maintained and repaired and kept in a clean condition.
4.71	應制訂書面程序，指定衛生處理之職責及規定在建築物及設施之清潔上使用的清潔時程表、方法、設備，以及材料。	4.71	Written procedures should be established assigning responsibility for sanitation and describing the cleaning schedules, methods, equipment, and materials to be used in cleaning buildings and facilities.
4.72	必要時，對適當的滅鼠劑、殺蟲劑、殺黴菌劑、燻蒸劑，以及清潔與滅菌劑的使用，也應制訂書面程序，以防止設備、原料、包裝/標示材料、中間產物，以及原料藥受污染。	4.72	When necessary, written procedures should also be established for the use of suitable rodenticides, insecticides, fungicides, fumigating agents, and cleaning and sanitizing agents to prevent the contamination of equipment, raw materials, packaging/labeling materials, intermediates, and APIs.
5.	**製程設備（PROCESS EQUIPMENT）**		
5.1	**設計與建造（Design and Construction）**		
5.10	中間產物及原料藥之製造設備，應有適當的設計及足夠的大小，並安裝在適當的位置，以適合預定用途、清潔、合適時之滅菌處理及維護保養。	5.10	Equipment used in the manufacture of intermediates and APIs should be of appropriate design and adequate size, and suitably located for its intended use, cleaning, sanitization (where appropriate), and maintenance.
5.11	設備應適當建造，以使其接觸原料、中間產物或原料藥的表面，不會改變中間產物及原料藥的品質超出法定或其他既定規格。	5.11	Equipment should be constructed so that surfaces that contact raw materials, intermediates, or APIs do not alter the quality of the intermediates and APIs beyond the official or other established specifications.
5.12	生產設備應只在其驗證過的作業範圍內使用。	5.12	Production equipment should only be used within its qualified operating range.
5.13	在中間產物或原料藥之生產中使用的主要設備（例如，反應器、儲存容器）及永久性安裝的作業線，應適當地識別。	5.13	Major equipment (e.g., reactors, storage containers) and permanently installed processing lines used during the production of an intermediate or API should be appropriately identified.

5.14	與設備之操作關聯的任何物質，例如，潤滑劑、熱媒或冷媒，不得接觸中間產物或原料藥，以免導致其品質改變而超出法定或其他既定規格。有異於此之任何偏差，應加以評估，以確保其對該中間產物或原料藥之預定用途的適用性無有害的影響。可能時，應使用食品級的潤滑劑及油品。	5.14	Any substances associated with the operation of equipment, such as lubricants, heating fluids or coolants, should not contact intermediates or APIs so as to alter their quality beyond the official or other established specifications. Any deviations from this should be evaluated to ensure that there are no detrimental effects upon the fitness for purpose of the material. Wherever possible, food grade lubricants and oils should be used.
5.15	合適時，應使用密閉性或圍堵性的設備。當使用開放性的設備，或設備打開時，應採取適當的防範措施，以使污染的風險降到最低。	5.15	Closed or contained equipment should be used whenever appropriate. Where open equipment is used, or equipment is opened, appropriate precautions should be taken to minimize the risk of contamination.
5.16	設備及關鍵的裝置（例如，儀表裝置及公用設施系統），應保存一套其最新的建構圖。	5.16	A set of current drawings should be maintained for equipment and critical installations (e.g., instrumentation and utility systems).
5.2	**設備維護保養及清潔（Equipment Maintenance and Cleaning）**		
5.20	應建立設備之預防性維護保養的時程表及程序（包含責任的指派）。	5.20	Schedules and procedures (including assignment of responsibility) should be established for the preventative maintenance of equipment.
5.21	設備之清潔及其隨後放行供中間產物及原料藥之製造使用，應建立書面程序。清潔程序應包含充分的細節，以使操作者能以可再現且有效的方式清潔每一型式的設備。這些程序應包括：	5.21	Written procedures should be established for cleaning of equipment and its subsequent release for use in the manufacture of intermediates and APIs. Cleaning procedures should contain sufficient details to enable operators to clean each type of equipment in a reproducible and effective manner. These procedures should include:
	➢ 設備之清潔責任的指派；		➢ Assignment of responsibility for cleaning of equipment;

➢ 清潔時程，合適時，包含滅菌處理時程表；	➢ Cleaning schedules, including, where appropriate, sanitizing schedules;
➢ 清潔方法及材料之完整說明，包含清潔設備使用之清潔劑的稀釋方法；	➢ A complete description of the methods and materials, including dilution of cleaning agents used to clean equipment;
➢ 合適時，拆解及組裝設備之每一物件的指令，以確保正確之清潔；	➢ When appropriate, instructions for disassembling and reassembling each article of equipment to ensure proper cleaning;
➢ 先前批次標識之移除或塗消的指令；	➢ Instructions for the removal or obliteration of previous batch identification;
➢ 保護潔淨設備在使用前免於污染的指令；	➢ Instructions for the protection of clean equipment from contamination prior to use;
➢ 可行時，使用前檢查設備之潔淨度；以及	➢ Inspection of equipment for cleanliness immediately before use, if practical; and
➢ 合適時，建立在作業完成後與設備清潔前最長的時間間隔。	➢ Establishing the maximum time that may elapse between the completion of processing and equipment cleaning, when appropriate.
5.22 設備及器具應予清潔、儲存，以及可行時，滅菌處理或滅菌，以防止污染或殘留物的移轉，導致改變中間產物或原料藥的品質超出法定或既定之規格。	5.22 Equipment and utensils should be cleaned, stored, and, where appropriate, sanitized or sterilized to prevent contamination or carry-over of a material that would alter the quality of the intermediate or API beyond the official or other established specifications.

5.23	當設備用於連續或時段切換生產同一中間產物或原料藥時，設備應在適當間隔時間予以清潔，以防止污染物的積集及移轉（例如，分解產物或過量的微生物）。	5.23	Where equipment is assigned to continuous production or campaign production of successive batches of the same intermediate or API, equipment should be cleaned at appropriate intervals to prevent build-up and carry-over of contaminants (e.g., degradants or objectionable levels of microorganisms).
5.24	非專用設備在不同物質的生產間應加以清潔，以防止交叉污染。	5.24	Non-dedicated equipment should be cleaned between productions of different materials to prevent cross-contamination.
5.25	殘留物之允收標準及清潔程序與清潔劑的選擇，應予界定並證明其合理。	5.25	Acceptance criteria for residues and the choice of cleaning procedures and cleaning agents should be defined and justified.
5.26	設備之內容物及其潔淨度狀態應以適當方法予以識別。	5.26	Equipment should be identified as to its contents and its cleanliness status by appropriate means.
5.3	**校正（Calibration）**		
5.30	為確保中間產物或原料藥品質，其關鍵性之管制、秤重、量測、監測，以及測試的設備，應依書面程序及既定時程表予以校正。	5.30	Control, weighing, measuring, monitoring and test equipment that is critical for assuring the quality of intermediates or APIs should be calibrated according to written procedures and an established schedule.
5.31	如有可追溯到公認標準的標準件，則應使用該標準件執行設備校正。	5.31	Equipment calibrations should be performed using standards traceable to certified standards, if existing.
5.32	校正紀錄應予保存。	5.32	Records of these calibrations should be maintained.
5.33	應知悉關鍵設備之最近校正狀態並可證實。	5.33	The current calibration status of critical equipment should be known and verifiable.
5.34	不得使用未符合校正標準的儀器。	5.34	Instruments that do not meet calibration criteria should not be used.

5.35	關鍵儀器之校正結果與核可標準有偏差時，應予調查，以認定自最後一次成功校正後是否對中間產物或原料藥的品質造成影響。	5.35	Deviations from approved standards of calibration on critical instruments should be investigated to determine if these could have had an impact on the quality of the intermediate(s) or API(s) manufactured using this equipment since the last successful calibration.
5.4	**電腦化系統（Computerized Systems）**		
5.40	與 GMP 有關的電腦化系統應予確效。確效的深度與範圍依該電腦化應用之多樣性、複雜性以及關鍵性而定。	5.40	GMP-related computerized systems should be validated. The depth and scope of validation depends on the diversity, complexity, and criticality of the computerized application.
5.41	適當的安裝驗證及操作驗證應證明電腦硬體及軟體的適當性，以執行指定的工作。	5.41	Appropriate installation qualification and operational qualification should demonstrate the suitability of computer hardware and software to perform assigned tasks.
5.42	經驗證之市售套裝軟體不要求相同程度的測試。現有系統在安裝時未經確效者，如有適當文件憑證，則可執行回溯性確效。	5.42	Commercially available software that has been qualified does not require the same level of testing. If an existing system was not validated at time of installation, a retrospective validation could be conducted if appropriate documentation is available.
5.43	電腦化系統應有充分之管制，以防止未經授權的侵入或對資料的變更。應有防止資料遺漏（例如，系統中斷及資料漏載）的管制。進行任何資料的變更、先前的輸入、誰進行變更，以及何時進行變更應有紀錄。	5.43	Computerized systems should have sufficient controls to prevent unauthorized access or changes to data. There should be controls to prevent omissions in data (e.g., system turned off and data not captured). There should be a record of any data change made, the previous entry, who made the change, and when the change was made.
5.44	電腦化系統之操作及維護保養應有書面程序。	5.44	Written procedures should be available for the operation and maintenance of computerized systems.

5.45	在以手工輸入關鍵資料時，對該輸入之準確性應有額外的核對。這可由第二位操作者或由系統本身達成。	5.45	Where critical data are being entered manually, there should be an additional check on the accuracy of the entry. This can be done by a second operator or by the system itself.
5.46	與可能影響中間產物或原料藥之品質、紀錄或試驗結果之可靠性的電腦化系統有關之意外事件，應予記錄與調查。	5.46	Incidents related to computerized systems that could affect the quality of intermediates or APIs or the reliability of records or test results should be recorded and investigated.
5.47	電腦化系統之變更，應依變更程序為之，且應經正式授權、文件化及測試。含對硬體、軟體以及該系統之其他關鍵組件，有修改及升級之所有變更者，其記錄均應予保存。這些紀錄應證明該系統是維持在確效狀態中。	5.47	Changes to computerized systems should be made according to a change procedure and should be formally authorized, documented, and tested. Records should be kept of all changes, including modifications and enhancements made to the hardware, software, and any other critical component of the system. These records should demonstrate that the system is maintained in a validated state.
5.48	系統當機或失效會導致紀錄之永久喪失者，應有備用系統。對於所有電腦化系統皆應建立確保資料的方法。	5.48	If system breakdowns or failures would result in the permanent loss of records, a back-up system should be provided. A means of ensuring data protection should be established for all computerized systems.
5.49	除電腦系統外，資料得以第二種方法記錄之。	5.49	Data can be recorded by a second means in addition to the computer system.
6.	**文件製作及紀錄（DOCUMENTATION AND RECORDS）**		
6.1	**文件製作系統及規格（Documentation System and Specifications）**		
6.10	與中間產物或原料藥之製造有關的所有文件均應依書面程序，訂定、審查、核定及分發。該文件得為紙本或電子的方式。	6.10	All documents related to the manufacture of intermediates or APIs should be prepared, reviewed, approved, and distributed according to written procedures. Such documents can be in paper or electronic form.

6.11	所有文件之發行、修訂、取代及撤回，皆應保存其修訂沿革。	6.11	The issuance, revision, superseding, and withdrawal of all documents should be controlled with maintenance of revision histories.
6.12	應建立保存所有適當文件（例如，開發沿革之報告、放大規模之報告、技術移轉之報告、製程確效之報告、訓練紀錄、生產紀錄、管制紀錄，以及運銷紀錄）的程序。這些文件之保存期限應予規定。	6.12	A procedure should be established for retaining all appropriate documents (e.g., development history reports, scale-up reports, technical transfer reports, process validation reports, training records, production records, control records, and distribution records). The retention periods for these documents should be specified.
6.13	所有生產、管制，以及運銷的紀錄應保存至該批次末效日期後至少一年。對於有再驗日期之原料藥，其紀錄應保存至該批次完全運銷後至少三年。	6.13	All production, control, and distribution records should be retained for at least 1 year after the expiry date of the batch. For APIs with retest dates, records should be retained for at least 3 years after the batch is completely distributed.
6.14	應緊接在作業完成後於紀錄中予以記載，該記載應以無法擦除的方式於所提供的空格中為之，並識別記載之人員。記載資料之更正，應註明日期並簽章，且應讓原始記載之資料依然可讀。	6.14	When entries are made in records, these should be made indelibly in spaces provided for such entries, directly after performing the activities, and should identify the person making the entry. Corrections to entries should be dated and signed and leave the original entry still legible.
6.15	在保存期間，紀錄之正本或複本應易於在該紀錄所述作業發生處所取得。紀錄得以電子或其他方法從另一地點立即擷取者，亦可接受。	6.15	During the retention period, originals or copies of records should be readily available at the establishment where the activities described in such records occurred. Records that can be promptly retrieved from another location by electronic or other means are acceptable.

6.16	規格、指令、程序，以及紀錄得以正本或真實複本保存之，例如，原始紀錄之影印本、微縮影片、單片縮影膠片，或其他準確的複製本。使用如微縮影片或電子紀錄之微縮技術者，應備有合適的擷取設備及紙本複本的工具。	6.16	Specifications, instructions, procedures, and records can be retained either as originals or as true copies such as photocopies, microfilm, microfiche, or other accurate reproductions of the original records. Where reduction techniques such as microfilming or electronic records are used, suitable retrieval equipment and a means to produce a hard copy should be readily available.
6.17	對原料、中間產物（必要時）、原料藥，以及標示與包裝材料應訂定規格並予以文件化。此外，對某些其他物料，諸如使用在中間產物或原料藥的生產中，可能嚴重影響品質的製程助劑、襯墊或其他材料，訂定規格可能是適當的。製程中管制之允收標準應予建立並文件化。	6.17	Specifications should be established and documented for raw materials, intermediates where necessary, APIs, and labelling and packaging materials. In addition, specifications may be appropriate for certain other materials, such as process aids, gaskets, or other materials used during the production of intermediates or APIs that could critically impact on quality. Acceptance criteria should be established and documented for in-process controls.
6.18	在文件上使用電子簽章者，該簽章應經認證並確保其安全。	6.18	If electronic signatures are used on documents, they should be authenticated and secure.
6.2	**設備清潔及使用紀錄（Equipment Cleaning and Use Record）**		
6.20	主要設備之使用、清潔、滅菌處理及/或滅菌，以及維護保養的紀錄，應顯示在此設備經加工之每一批次的日期、時間（合適時）、產品、批號，以及執行該清潔與維護保養的人員。	6.20	Records of major equipment use, cleaning, sanitization and/or sterilization and maintenance should show the date, time (if appropriate), product, and batch number of each batch processed in the equipment, and the person who performed the cleaning and maintenance.

6.21 設備專用於製造一種中間產物或原料藥者，若中間產物或原料藥的各批次依循可追溯之順序時，則個別設備紀錄是不必要的。在使用專用設備的情形，清潔、維護保養及使用的紀錄，得為批次紀錄的一部分，或分開保存。	6.21 If equipment is dedicated to manufacturing one intermediate or API, then individual equipment records are not necessary if batches of the intermediate or API follow in traceable sequence. In cases where dedicated equipment is employed, the records of cleaning, maintenance, and use can be part of the batch record or maintained separately.
6.3 原料、中間產物、原料藥之標示材料與包裝材料的紀錄（Records of Raw Materials, Intermediates, API Labeling and Packaging Materials）	
6.30 應予保存之紀錄包括：	6.30 Records should be maintained including:
➢ 對於原料藥，每一批次之原料、中間產物，或標示材料及包裝材料的每一裝運，其製造廠名稱、識別及數量；供應商名稱；供應商的管制號碼（若知悉），或其他識別號碼；收據上配置的號碼；以及收據的日期；	➢ The name of the manufacturer, identity, and quantity of each shipment of each batch of raw materials, intermediates, or labeling and packaging materials for API's; the name of the supplier; the supplier's control number(s), if known, or other identification number; the number allocated on receipt; and the date of receipt;
➢ 執行之任何測試或檢查的結果，以及自此衍生的結論；	➢ The results of any test or examination performed and the conclusions derived from this;
➢ 追蹤原物料之使用的紀錄；	➢ Records tracing the use of materials;
➢ 原料藥標示材料及包裝材料符合既定規格之檢查與審核的文件憑證；	➢ Documentation of the examination and review of API labeling and packaging materials for conformity with established specifications;
➢ 關於原料、中間產物，或原料藥之標示材料及包裝材料的拒用之最後決定。	➢ The final decision regarding rejected raw materials, intermediates, or API labeling and packaging materials.

6.31 核定的主標籤應予保存，以供與發出的標籤比對。	6.31 Master (approved) labels should be maintained for comparison to issued labels.
6.4 製造管制標準書（生產及管制紀錄）【Master Production Instructions (Master Production and Control Records)】	
6.40 為確保從批次到批次之均一性，對每一中間產物及原料藥的製造管制標準書應由一人訂定、註明日期並簽章，並由品質單位中的一人獨立核對、註明日期及簽章。	6.40 To ensure uniformity from batch to batch, master production instructions for each intermediate and API should be prepared, dated, and signed by one person and independently checked, dated, and signed by a person in the quality unit(s).
6.41 製造管制標準書應包括：	6.41 Master production instructions should include:
➢ 製造之中間產物或原料藥的名稱及識別文件之參考碼(如適用時)；	➢ The name of the intermediate or API being manufactured and an identifying document reference code, if applicable;
➢ 用特定的名稱或代碼，以識別所指定的原料或中間產物其品質特性的完整清單；	➢ A complete list of raw materials and intermediates designated by names or codes sufficiently specific to identify any special quality characteristics;
➢ 要使用之每一原料或中間產物的數量或比率之準確的陳述，包含其量度單位。在其數量不固定時，應包含每一批次之批量或生產比率的計算。經證明為合理者，應包含數量之異動；	➢ An accurate statement of the quantity or ratio of each raw material or intermediate to be used, including the unit of measure. Where the quantity is not fixed, the calculation for each batch size or rate of production should be included. Variations to quantities should be provided they are justified;
➢ 要使用之生產場所及主要生產設備；	➢ The production location and major production equipment to be used;
➢ 詳細的生產指令，包括：	➢ Detailed production instructions, including the:
– 要遵循的順序，	– sequences to be followed,

– 要使用之製程參數的範圍，	– ranges of process parameters to be used,
– 抽樣指令及具有允收標準（合適時）之製程中管制，	– sampling instructions and in-process controls with their acceptance criteria, where appropriate,
– 個別加工步驟及/或總製程（合適時）之完成時間的限制；及	– time limits for completion of individual processing steps and/or the total process, where appropriate; and
– 在適當加工階段或時間預期之產量/產率範圍；	– expected yield ranges at appropriate phases of processing or time;
➢ 合適時，要遵循之特別註釋及預防措施，或對這些註釋及預防措施的交互參照；及	➢ Where appropriate, special notations and precautions to be followed, or cross-references to these; and
➢ 中間產物或原料藥之儲存指令，以確保其適用性，包括標示材料和包裝材料，以及具有時間限制（合適時）之特別儲存條件。	➢ The instructions for storage of the intermediate or API to assure its suitability for use, including the labelling and packaging materials and special storage conditions with time limits, where appropriate.
6.5 批次製造紀錄（批次製造及管制紀錄）【Batch Production Records (Batch Production and Control Records)】	

6.50	每一中間產物及原料藥應製作批次製造紀錄，且應包含關於每一批次之製造及管制的完整資訊。批次製造紀錄在發放前應予核對，以確保其為正確版本及為適當製造管制標準書之清楚易讀的準確複製本。若批次製造紀錄來自製造管制標準書的一部分，則該紀錄應包含所參照之現行製造管制標準書。	6.50	Batch production records should be prepared for each intermediate and API and should include complete information relating to the production and control of each batch. The batch production record should be checked before issuance to ensure that it is the correct version and a legible accurate reproduction of the appropriate master production instruction. If the batch production record is produced from a separate part of the master document, that document should include a reference to the current master production instruction being used.
6.51	發放時，這些紀錄應附以獨特的批號或識別號編碼、註明日期並簽章。在連續生產，於指配最終號碼前，產品代碼連同其日期與時間，能充當獨特的識別碼使用。	6.51	These records should be numbered with a unique batch or identification number, dated and signed when issued. In continuous production, the product code together with the date and time can serve as the unique identifier until the final number is allocated.
6.52	批次製造紀錄（批次製造及管制紀錄）中，記錄其完成每一重要步驟的文件憑證應包括：	6.52	Documentation of completion of each significant step in the batch production records (batch production and control records) should include:
	➢ 日期與時間（合適時）；		➢ Dates and, when appropriate, times;
	➢ 使用之主要設備（例如，反應器、乾燥機、粉碎機等）的識別；		➢ Identity of major equipment (e.g., reactors, driers, mills, etc.) used;
	➢ 每一批次之特定識別，包括在製造中使用之原料、中間產物，或任何重處理之中間產物的重量、量度及批號；		➢ Specific identification of each batch, including weights, measures, and batch numbers of raw materials, intermediates, or any reprocessed materials used during manufacturing;
	➢ 關鍵製程參數之實際結果的紀錄；		➢ Actual results recorded for critical process parameters;
	➢ 從事之任何抽樣；		➢ Any sampling performed;

➢ 執行及直接監督或核對作業中之每一關鍵步驟的人員之簽章；	➢ Signatures of the persons performing and directly supervising or checking each critical step in the operation;
➢ 製程中及實驗室之測試結果；	➢ In-process and laboratory test results;
➢ 在適當階段或時間的實際產量/產率；	➢ Actual yield at appropriate phases or times;
➢ 中間產物或原料藥之包裝及標籤的說明；	➢ Description of packaging and label for intermediate or API;
➢ 如商品化，原料藥或中間產物之代表性標籤；	➢ Representative label of API or intermediate if made commercially available;
➢ 經記錄之任何偏差，其執行之評估、調查（合適時），或參照該調查（如分開儲存時）；以及	➢ Any deviation noted, its evaluation, investigation conducted (if appropriate) or reference to that investigation if stored separately; and
➢ 放行檢驗的結果。	➢ Results of release testing.
6.53 為調查一批中間產物或原料藥之關鍵偏差或未能符合規格，應建立書面程序並予遵循。該調查應延伸至可能與該特定偏差或未能符合規格有關聯之其他批次。	6.53 Written procedures should be established and followed for investigating critical deviations or the failure of a batch of intermediate or API to meet specifications. The investigation should extend to other batches that may have been associated with the specific failure or deviation.
6.6 實驗室管制紀錄（Laboratory Control Records）	
6.60 實驗室管制紀錄應包含衍生自所有執行之試驗的完整數據/資料以確保符合既定規格及標準，包括檢查及含量測定在內，如下所示：	6.60 Laboratory control records should include complete data derived from all tests conducted to ensure compliance with established specifications and standards, including examinations and assays, as follows:

➢ 收到供測試之樣品的描述，包括原物料名稱或來源，批號或其他獨特代碼，抽樣日期，以及合適時，收到供測試之樣品的量及日期；	➢ A description of samples received for testing, including the material name or source, batch number or other distinctive code, date sample was taken, and, where appropriate, the quantity and date the sample was received for testing;
➢ 每一使用之試驗方法的陳述或參考資料；	➢ A statement of or reference to each test method used;
➢ 如同方法所述，使用於每一試驗之樣品的重量或量度的陳述；關於對照標準品、試劑及標準溶液之製備及測試的數據/資料或交互參照；	➢ A statement of the weight or measure of sample used for each test as described by the method; data on or cross-reference to the preparation and testing of reference standards, reagents and standard solutions;
➢ 在每一試驗中產生之所有原始數據/資料的完整紀錄。該記錄除應包含源自實驗室儀器裝置的圖、表及光譜外，也應含對該等原始紀錄之適當辨識，以顯示測試之特定原物料及批次；	➢ A complete record of all raw data generated during each test, in addition to graphs, charts and spectra from laboratory instrumentation, properly identified to show the specific material and batch tested;
➢ 所從事與該試驗有關之所有計算的紀錄，包含例如，量測單位、轉換係數/因數及當量係數/因數；	➢ A record of all calculations performed in connection with the test, including, for example, units of measure, conversion factors, and equivalency factors;
➢ 試驗結果的陳述及其如何與既定之允收標準比較；	➢ A statement of the test results and how they compare with established acceptance criteria;
➢ 執行每一試驗之人員的簽章及執行該試驗的日期；以及	➢ The signature of the person who performed each test and the date(s) the tests were performed; and

➢ 第二人之簽章及其日期，以顯示對原始紀錄之準確性、完整性及其與既定標準之符合性已經審查。	➢ The date and signature of a second person showing that the original records have been reviewed for accuracy, completeness, and compliance with established standards.
6.61 完整紀錄也應保存下列資料：	6.61 Complete records should also be maintained for:
➢ 對既定分析方法的任何修改；	➢ Any modifications to an established analytical method;
➢ 實驗室儀器、裝置、儀錶，以及記錄裝置之定期校正；	➢ Periodic calibration of laboratory instruments, apparatus, gauges, and recording devices;
➢ 對原料藥執行之所有安定性試驗；以及	➢ All stability testing performed on APIs; and
➢ 偏離規格（OOS）之調查。	➢ Out-of-specification (OOS) investigations.
6.7 批次製造紀錄審查（Batch Production Record Review）	
6.70 批次製造及實驗室管制紀錄，包括分裝或包裝及標示的審查與核定，應建立書面程序並遵循之，以確定中間產物或原料藥在批次放行或運銷前與既定規格相符。	6.70 Written procedures should be established and followed for the review and approval of batch production and laboratory control records, including packaging and labeling, to determine compliance of the intermediate or API with established specifications before a batch is released or distributed.
6.71 關鍵製程步驟之批次製造及實驗室管制紀錄，應在原料藥批次放行或運銷前，由品質單位審查與核准。非關鍵製程步驟之製造及實驗室管制紀錄，得由符合資格之生產人員或其他單位依循品質單位核定之程序審查之。	6.71 Batch production and laboratory control records of critical process steps should be reviewed and approved by the quality unit(s) before an API batch is released or distributed. Production and laboratory control records of noncritical process steps can be reviewed by qualified production personnel or other units following procedures approved by the quality unit(s).

6.72	所有偏差、調查及偏離規格的報告，應在該批次放行前，當成該批次之紀錄的一部分審查之。	6.72	All deviation, investigation, and OOS reports should be reviewed as part of the batch record review before the batch is released.
6.73	除運送至製造者管制外之中間產物，品質單位得將中間產物之放行責任及權能委由生產單位執行之。	6.73	The quality unit(s) can delegate to the production unit the responsibility and authority for release of intermediates, except for those shipped outside the control of the manufacturing company.
7.	**原物料管理（MATERIALS MANAGEMENT）**		
7.1	**一般管制（General Controls）**		
7.10	應有描述原物料之接收、識別、隔離/待驗、儲存、處理、抽樣、測試及核定或拒用的書面程序。	7.10	There should be written procedures describing the receipt, identification, quarantine, storage, handling, sampling, testing, and approval or rejection of materials.
7.11	中間產物及/或原料藥的製造廠，應有評估其關鍵原物料供應商的系統。	7.11	Manufacturers of intermediates and/or APIs should have a system for evaluating the suppliers of critical materials.
7.12	原物料應依照協議的規格，向經品質單位核准之一家或多家供應商採購。	7.12	Materials should be purchased against an agreed specification, from a supplier, or suppliers, approved by the quality unit(s).
7.13	關鍵原物料之供應商非該原物料的製造廠時，中間產物及/或原料藥的製造廠應知悉該關鍵原物料之製造廠的名稱與地址。	7.13	If the supplier of a critical material is not the manufacturer of that material, the name and address of that manufacturer should be known by the intermediate and/or API manufacturer.
7.14	關鍵原料之供應源的變更，應依第 13 章變更管制的規定辦理。	7.14	Changing the source of supply of critical raw materials should be treated according to Section 13, Change Control.
7.2	**接收及隔離/待驗（Receipt and Quarantine）**		

7.20	在接收並於驗收前，每一個或每一組原物料容器皆應經目視檢查其標示之正確性（包括供應商使用之名稱與廠內名稱不同時，其間的關聯性）、容器之損壞、封緘之破損、竄改或污染的證據。原物料完成抽樣、檢查或測試（合適時），以及放行使用前，應在隔離/待驗下保存。	7.20	Upon receipt and before acceptance, each container or grouping of containers of materials should be examined visually for correct labeling (including correlation between the name used by the supplier and the in-house name, if these are different), container damage, broken seals and evidence of tampering or contamination. Materials should be held under quarantine until they have been sampled, examined, or tested, as appropriate, and released for use.
7.21	進廠之原料與現有庫存品（例如，儲存槽中的溶劑或存貨）混合前，應鑑別為正確，並經測試（合適時）與放行。應有書面程序，以防止將進廠原料誤卸到現有庫存品中。	7.21	Before incoming materials are mixed with existing stocks (e.g., solvents or stocks in silos), they should be identified as correct, tested, if appropriate, and released. Procedures should be available to prevent discharging incoming materials wrongly into the existing stock.
7.22	以非專用槽車運送大宗原料者，應確保無來自槽車的任何交叉污染。提供該確保的方法得包含一種以上之下列方法：	7.22	If bulk deliveries are made in non-dedicated tankers, there should be assurance of no cross-contamination from the tanker. Means of providing this assurance could include one or more of the following:
	➢ 清潔證明書		➢ certificate of cleaning
	➢ 微量不純物的測試		➢ testing for trace impurities
	➢ 供應商的稽查。		➢ audit of the supplier.
7.23	大型儲存容器及其附屬的歧管、充填及卸料管線，應予適當標示。	7.23	Large storage containers and their attendant manifolds, filling, and discharge lines should be appropriately identified.

7.24	原料之每一個或一組容器（多批次）應以一獨特的代碼、批號或收貨號碼指定及識別。在記錄每一批次之處置上應使用該號碼。應備有識別每一批次之狀態的系統。	7.24	Each container or grouping of containers (batches) of materials should be assigned and identified with a distinctive code, batch, or receipt number. This number should be used in recording the disposition of each batch. A system should be in place to identify the status of each batch.
7.3	**進廠供生產之原料的抽樣及測試（Sampling and Testing of Incoming Production Materials）**		
7.30	除 7.32 條所述之原料外，至少應執行一項試驗，以確認每一批原料的同一性。製造廠有一套適當的系統評估供應商者，供應商之分析證明書得用以取代執行其他試驗。	7.30	At least one test to verify the identity of each batch of material should be conducted, with the exception of the materials described below in 7.32. A supplier's certificate of analysis can be used in place of performing other tests, provided that the manufacturer has a system in place to evaluate suppliers.
7.31	供應商之核准應包含提供製造廠能一致地供應符合規格之原料的適當證據（例如，過去的品質史實）之評估。在減免廠內測試項目前，至少應執行三個批次之完整分析。惟在適當時間間隔，至少應執行一次完整的分析，並與分析證明書比較。分析證明書的可靠性應定期進行核對。	7.31	Supplier approval should include an evaluation that provides adequate evidence (e.g., past quality history) that the manufacturer can consistently provide material meeting specifications. Full analyses should be conducted on at least three batches before reducing in-house testing. However, as a minimum, a full analysis should be performed at appropriate intervals and compared with the certificates of analysis. Reliability of certificates of analysis should be checked at regular intervals.

7.32	取得製造廠之分析證明書，顯示製程助劑、有危害性的或高毒性原料、其他特別的原料、或移轉至公司管制內之另一單位的原料符合既定規格者，該等原料無需進行測試。容器、標籤及批號紀錄之目視檢查，應有助於建立該等原料的識別。該等原料未執行現場測試者，應證明其合理性並予以文件化。	7.32	Processing aids, hazardous or highly toxic raw materials, other special materials, or materials transferred to another unit within the company's control do not need to be tested if the manufacturer's certificate of analysis is obtained, showing that these raw materials conform to established specifications. Visual examination of containers, labels, and recording of batch numbers should help in establishing the identity of these materials. The lack of on-site testing for these materials should be justified and documented.
7.33	樣品應具被抽樣之原料批次的代表性。抽樣方法應規定所要抽取樣品之容器的數目、抽樣之容器的部位，以及從每一容器所要抽取之原料量。抽取樣品的容器數目及樣品量應根據抽樣計畫。該抽樣計畫應將原料之關鍵性、原料之變異性、供應商之過去品質史實，以及分析需要之數量列入考慮。	7.33	Samples should be representative of the batch of material from which they are taken. Sampling methods should specify the number of containers to be sampled, which part of the container to sample, and the amount of material to be taken from each container. The number of containers to sample and the sample size should be based upon a sampling plan that takes into consideration the criticality of the material, material variability, past quality history of the supplier, and the quantity needed for analysis.
7.34	抽樣應在界定的位置並依設計的程序執行，以防止已抽樣之原料被污染以及污染其他原料。	7.34	Sampling should be conducted at defined locations and by procedures designed to prevent contamination of the material sampled and contamination of other materials.
7.35	被抽取樣品的容器應小心開啟，並在取樣後重新密封。已被抽取樣品之容器應予標記。	7.35	Containers from which samples are withdrawn should be opened carefully and subsequently reclosed. They should be marked to indicate that a sample has been taken.

7.4	**儲存（Storage）**		
7.40	原料應以可防止分解、污染，以及交叉污染的方式處理及儲存。	7.40	Materials should be handled and stored in a manner to prevent degradation, contamination, and cross-contamination.
7.41	貯於纖維桶、袋或盒中的原料應離地儲存，且合適時，應適當分隔，以容許清潔及檢查。	7.41	Materials stored in fiber drums, bags, or boxes should be stored off the floor and, when appropriate, suitably spaced to permit cleaning and inspection.
7.42	原料應在對其品質無不良影響的條件下及期間內儲存，並應予正常管制，以使最久的庫存品，最先取用。	7.42	Materials should be stored under conditions and for a period that have no adverse effect on their quality, and should normally be controlled so that the oldest stock is used first.
7.43	某些原料儲存於適當容器者，若其識別標籤能保持清晰易讀，且容器在開啟與使用前予以適當清潔，得在室外儲存。	7.43	Certain materials in suitable containers can be stored outdoors, provided identifying labels remain legible and containers are appropriately cleaned before opening and use.
7.44	拒用之原料應在經設計之系統下進行識別與管制，以防止其未經授權而使用於製造。	7.44	Rejected materials should be identified and controlled under a system designed to prevent their unauthorised use in manufacturing.
7.5	**再評估（Re-evaluation）**		
7.50	合適時，原料應進行再評估，以確定其使用之適合性（例如，在延長儲存或暴露於熱或潮濕之後）。	7.50	Materials should be re-evaluated, as appropriate, to determine their suitability for use (e.g., after prolonged storage or exposure to heat or humidity).
8.	**生產及製程中管制（PRODUCTION AND IN-PROCESS CONTROLS）**		
8.1	**生產作業（Production Operations）**		
8.10	製造中間產物及原料藥的原料，應在不影響其使用適合性之適當條件下秤重或量度。秤重及量度裝置對於預定用途應具適合之準確度。	8.10	Raw materials for intermediate and API manufacturing should be weighed or measured under appropriate conditions that do not affect their suitability for use. Weighing and measuring devices should be of suitable accuracy for the intended use.

8.11 原料為後來生產作業之使用而分裝者，盛裝該原料之容器應合適，且其識別應具有下列資訊：	8.11 If a material is subdivided for later use in production operations, the container receiving the material should be suitable and should be so identified that the following information is available:
➢ 原料名稱及/或品項代碼；	➢ Material name and/or item code;
➢ 接收或管制號碼；	➢ Receiving or control number;
➢ 新容器中原料的重量或量度值；及	➢ Weight or measure of material in the new container; and
➢ 再評估或再驗日期（如合適時）。	➢ Re-evaluation or retest date if appropriate.
8.12 關鍵性的秤重、量度或分裝作業，應經見證或接受同等的管制。使用前，生產人員應確認該等原料即為批次紀錄中所規定，預定生產之中間產物或原料藥的原料。	8.12 Critical weighing, measuring, or subdividing operations should be witnessed or subjected to an equivalent control. Prior to use, production personnel should verify that the materials are those specified in the batch record for the intended intermediate or API.
8.13 其他關鍵性作業應經見證或接受同等的管制。	8.13 Other critical activities should be witnessed or subjected to an equivalent control.
8.14 在生產過程中之每一指定步驟的實際產量/產率應與其預期產量/產率進行比較。具有適當範圍之預期產量/產率，應根據先前實驗室、先導規模或製造資料建立之。與關鍵性製程步驟關聯之產量/產率的偏差，應進行調查，以確定其對受影響批次品質所造成的衝擊或潛在衝擊。	8.14 Actual yields should be compared with expected yields at designated steps in the production process. Expected yields with appropriate ranges should be established based on previous laboratory, pilot scale, or manufacturing data. Deviations in yield associated with critical process steps should be investigated to determine their impact or potential impact on the resulting quality of affected batches.
8.15 任何偏差均應予以文件化並解釋之。任何關鍵性偏差均應進行調查。	8.15 Any deviation should be documented and explained. Any critical deviation should be investigated.

8.16	主要設備單元的作業狀態，應標示在個別設備單元上，或以適當的文件憑證、電腦管制系統，或其他替代方法標示之。	8.16	The processing status of major units of equipment should be indicated either on the individual units of equipment or by appropriate documentation, computer control systems, or alternative means.
8.17	要進行重處理或再加工之原料應予以適當管制，以防止未經授權的使用。	8.17	Materials to be reprocessed or reworked should be appropriately controlled to prevent unauthorized use.
8.2	**時間限制（Time Limits）**		
8.20	製造管制標準書中有時間限制之規定者（參見 6.41 條），應符合該等限制，以確保中間產物及原料藥的品質。偏差均應予以文件化並評估之。當操作模式為達一目標值（例如，pH 調整、氫化、乾燥至預設的規格）時，就沒有時間限制的必要，因為反應或作業步驟之完成取決於製程中之抽樣與測試。	8.20	If time limits are specified in the master production instruction (see 6.41), these time limits should be met to ensure the quality of intermediates and APIs. Deviations should be documented and evaluated. Time limits may be inappropriate when processing to a target value (e.g., pH adjustment, hydrogenation, drying to predetermined specification) because completion of reactions or processing steps are determined by in-process sampling and testing.
8.21	為進一步加工而保存的中間產物，應儲存在適當的條件下，以確保其使用之適合性。	8.21	Intermediates held for further processing should be stored under appropriate conditions to ensure their suitability for use.
8.3	**製程中之抽樣及管制（In-process Sampling and Controls）**		
8.30	應建立書面程序以監測製程，並管制可能引起中間產物或原料藥品質特性變異之製程步驟的效能。製程中管制及其允收標準，應根據開發階段中取得之資訊或歷史資料予以界定。	8.30	Written procedures should be established to monitor the progress and control the performance of processing steps that cause variability in the quality characteristics of intermediates and APIs. In-process controls and their acceptance criteria should be defined based on the information gained during the developmental stage or historical data.

8.31	測試之允收標準及類型與程度，取決於製造的中間產物或原料藥之本質、執行之反應或製程步驟，以及該製程導入產品品質之變異性的程度。較不嚴格的製程中管制在前段的製程步驟可能適合，然而在後段的製程步驟（例如，分離及純化步驟），宜進行較嚴格的管制。	8.31	The acceptance criteria and type and extent of testing can depend on the nature of the intermediate or API being manufactured, the reaction or process step being conducted, and the degree to which the process introduces variability in the product's quality. Less stringent in-process controls may be appropriate in early processing steps, whereas tighter controls may be appropriate for later processing steps (e.g., isolation and purification steps).
8.32	關鍵製程中管制（及關鍵製程監測），包括管制點及方法在內，應以書面陳述並由品質單位核定。	8.32	Critical in-process controls (and critical process monitoring), including the control points and methods, should be stated in writing and approved by the quality unit(s).
8.33	製程中管制得由符合資格之生產部門人員執行之，且製程的調整係在品質單位核定之預設限值內時，該製程得不經品質單位事先核准逕行調整。所有測試及結果應當成批次紀錄的一部分完全文件化。	8.33	In-process controls can be performed by qualified production department personnel and the process adjusted without prior quality unit(s) approval if the adjustments are made within pre-established limits approved by the quality unit(s). All tests and results should be fully documented as part of the batch record.
8.34	書面程序應描述製程中原料、中間產物及原料藥的抽樣方法。抽樣計畫及程序應根據科學上完整的抽樣實務。	8.34	Written procedures should describe the sampling methods for in-process materials, intermediates, and APIs. Sampling plans and procedures should be based on scientifically sound sampling practices.

8.35	製程中抽樣應使用經設計的程序執行，以防止被抽樣之原料及其他中間產物或原料藥受污染。應制訂程序以確保收集後之樣品的完整性。	8.35	In-process sampling should be conducted using procedures designed to prevent contamination of the sampled material and other intermediates or APIs. Procedures should be established to ensure the integrity of samples after collection.
8.36	對於監視及/或調整製程之目的所執行的製程中測試，所產生之偏離規格（OOS）的調查通常是不需要。	8.36	Out-of-specification (OOS) investigations are not normally needed for in-process tests that are performed for the purpose of monitoring and/or adjusting the process.
8.4 中間產物或原料藥批次的混合（Blending Batches of Intermediates or APIs）			
8.40	為本文件之目的，混合是界定為將符合相同規格之中間產物或原料藥合併，以產生一均質之中間產物或原料藥的製程。在製程中，從單一批次的一部分混合（例如，從一個單一結晶批次中收集幾次離心機荷載/裝載）或從數個批次之一部分合併，以供進一步加工，係認定為生產過程的一部分，而非混合。	8.40	For the purpose of this document, blending is defined as the process of combining materials within the same specification to produce a homogeneous intermediate or API. In-process mixing of fractions from single batches (e.g., collecting several centrifuge loads from a single crystallization batch) or combining fractions from several batches for further processing is considered to be part of the production process and is not considered to be blending.
8.41	不得為符合規格之目的，而將偏離規格之批次與其他批次混合。在混合前，每一納入混合物中之批次均應經使用既定的製程製造，且個別測試，並認定其符合適當的規格。	8.41	Out-of-specification batches should not be blended with other batches for the purpose of meeting specifications. Each batch incorporated into the blend should have been manufactured using an established process and should have been individually tested and found to meet appropriate specifications prior to blending.
8.42	可接受之混合作業包含，但並不侷限於下列各項：	8.42	Acceptable blending operations include, but are not limited to:

➢ 將小批量混合，以增大批量；	➢ Blending of small batches to increase batch size;
➢ 從相同中間產物或原料藥之不同批次的尾料（亦即，相當小量之分離的中間產物或原料藥）混合，以形成單一批次。	➢ Blending of tailings (i.e., relatively small quantities of isolated material) from batches of the same intermediate or API to form a single batch.
8.43 混合製程應適當管制並文件化。為確認經混合之批次符合既定規格，應進行測試（合適時）。	8.43 Blending processes should be adequately controlled and documented, and the blended batch should be tested for conformance to established specifications, where appropriate.
8.44 該混合製程之批次紀錄，應有允許溯及至構成該混合物之各個批次的可追溯性。	8.44 The batch record of the blending process should allow traceability back to the individual batches that make up the blend.
8.45 原料藥之物理屬性係關鍵屬性者（例如，原料藥預定供固體口服劑型或懸浮劑使用），混合作業應予以確效，以顯示混合批次之均質性。確效應包括可能會受混合過程影響之關鍵屬性的測試（例如，粒子大小分佈、粉體密度，以及敲擊密度）。	8.45 Where physical attributes of the API are critical (e.g., APIs intended for use in solid oral dosage forms or suspensions), blending operations should be validated to show homogeneity of the combined batch. Validation should include testing of critical attributes (e.g., particle size distribution, bulk density, and tap density) that may be affected by the blending process.
8.46 混合對安定性可能有不良影響者，應執行最終混合批次之安定性試驗。	8.46 If the blending could adversely affect stability, stability testing of the final blended batches should be performed.
8.47 混合批次之末效日期或再驗日期，應根據混合物中最早的尾料或批次之製造日期訂定之。	8.47 The expiry or retest date of the blended batch should be based on the manufacturing date of the oldest tailings or batch in the blend.
8.5 污染管制（Contamination Control）	

8.50	如有適當的管制，殘留的中間產物或原料藥可以移轉到相同中間產物或原料藥的後續批次中。其實例，包括附著在微細化粉碎機內壁上的殘留物，卸料後留在離心機轉筒內壁之潮濕結晶殘留層，以及將物料移送到製程中的下一個步驟時，製程容器不完全卸放之液體或結晶。此移轉不得造成分解產物的移轉或微生物污染，該移轉或污染可能不利地改變既定原料藥不純物描述。	8.50	Residual materials can be carried over into successive batches of the same intermediate or API if there is adequate control. Examples include residue adhering to the wall of a micronizer, residual layer of damp crystals remaining in a centrifuge bowl after discharge, and incomplete discharge of fluids or crystals from a processing vessel upon transfer of the material to the next step in the process. Such carryover should not result in the carryover of degradants or microbial contamination that may adversely alter the established API impurity profile.
8.51	生產作業應以能夠防止中間產物或原料藥被其他物質污染的方式執行。	8.51	Production operations should be conducted in a manner that will prevent contamination of intermediates or APIs by other materials.
8.52	在純化後處理原料藥時，應採取預防措施，以避免污染。	8.52	Precautions to avoid contamination should be taken when APIs are handled after purification.
9.	**原料藥及中間產物的包裝與識別標示（PACKAGING AND IDENTIFICATION LABELING OF APIs AND INTERMEDIATES）**		
9.1	**一般規定（General）**		
9.10	應有書面的程序，敘述包裝及標示材料的接收、識別、隔離/待驗、抽樣、檢查及/或測試、放行，以及處理。	9.10	There should be written procedures describing the receipt, identification, quarantine, sampling, examination, and/or testing, release, and handling of packaging and labeling materials.
9.11	包裝及標示材料應符合既定規格。不符合該等規格的材料應予拒用，以防止該等不適合之材料使用於生產作業。	9.11	Packaging and labeling materials should conform to established specifications. Those that do not comply with such specifications should be rejected to prevent their use in operations for which they are unsuitable.

9.12	標籤及包裝材料之每一次裝運，皆應保存紀錄，以顯示其接收、檢查或測試，以及接受或拒用。	9.12	Record should be maintained for each shipment of labels and packaging materials showing receipt, examination, or testing, and whether accepted or rejected.
9.2	**包裝材料（Packaging Materials）**		
9.20	容器應提供適當的保護，避免中間產物或原料藥在運送及建議的儲存期間，可能發生變質或污染。	9.20	Containers should provide adequate protection against deterioration or contamination of the intermediate or API that may occur during transportation and recommended storage.
9.21	容器應為潔淨，且在依中間產物或原料藥的性質而有指示時，並應經滅菌處理，以確保其適合預定用途。該等容器不得具有反應性、加成性或吸收性，以致改變中間產物或原料藥的品質，至超出所規定的限值。	9.21	Containers should be clean and, where indicated by the nature of the intermediate or API, sanitized to ensure that they are suitable for their intended use. These containers should not be reactive, additive, or absorptive so as to alter the quality of the intermediate or API beyond the specified limits.
9.22	容器再度使用者，應按文件所載程序加以清潔，且先前的所有標示應予移除或抹滅。	9.22	If containers are reused, they should be cleaned in accordance with documented procedures, and all previous labels should be removed or defaced.
9.3	**標籤發放與管制（Label Issuance and Control）**		
9.30	標籤儲存區應限於被授權人員始得進入。	9.30	Access to the label storage areas should be limited to authorised personnel.
9.31	應運用一定的程序，以調和標籤之發放、使用及退回的數量，並評估所發現貼上標籤之容器的數量與發放之標籤數量間的差異。該等差異應予調查，且該調查應經品質單位核可。	9.31	Procedures should be uesd to reconcile the quantities of labels issued, used, and returned and to evaluate discrepancies found between the number of containers labeled and the number of labels issued. Such discrepancies should be investigated, and the investigation should be approved by the quality unit(s).

9.32	帶有批號或有其他與批次相關之印刷的所有過剩標籤，應予銷毀。退回之標籤應予保存，且以能防止混雜，並提供正確識別的方式予以儲存。	9.32	All excess labels bearing batch numbers or other batch-related printing should be destroyed. Returned labels should be maintained and stored in a manner that prevents mix-ups and provides proper identification.
9.33	廢棄的及過期的標籤應予銷毀。	9.33	Obsolete and out-dated labels should be destroyed.
9.34	使用於印刷分裝或包裝作業之標籤的印刷裝置應予管制，以確保所印者皆符合該批次製造紀錄中的規定。	9.34	Printing devices used to print labels for packaging operations should be controlled to ensure that all imprinting conforms to the print specified in the batch production record.
9.35	對一個批次發放之已印標籤，應小心檢查其與製造管制標準書中規格的同一性及符合性。該檢查結果應予以文件化。	9.35	Printed labels issued for a batch should be carefully examined for proper identity and conformity to specifications in the master production record. The results of this examination should be documented.
9.36	應從所使用之已印標籤中，取一份代表品納入批次製造紀錄。	9.36	A printed label representative of those used should be included in the batch production record.
9.4	**分裝或包裝及標示作業（Packaging and Labeling Operations）**		
9.40	應有經設計之文件化的程序，以確保使用正確之分裝或包裝材料及標籤。	9.40	There should be documented procedures designed to ensure that correct packaging materials and labels are used.
9.41	標示作業應予設計，以防止混雜。該標示作業與涉及其他中間產物或原料藥之標示作業，應有實體或空間的隔離。	9.41	Labeling operations should be designed to prevent mix-ups. There should be physical or spatial separation from operations involving other intermediates or APIs.
9.42	在中間產物或原料藥容器上所使用之標籤，應有顯示名稱或識別代碼、批號，以及對於確保中間產物或原料藥之品質具關鍵性儲存條件的資訊。	9.42	Labels used on containers of intermediates or APIs should indicate the name or identifying code, batch number, and storage conditions when such information is critical to assure the quality of intermediate or API.

9.43	中間產物或原料藥預定運送到製造廠原物料管理系統的管制之外者，其製造廠的名稱與地址、內容量、特別的運送條件，以及任何特別的法定要求，也皆應納入標籤中。對於具有末效日期的中間產物或原料藥，其末效日期應標示在標籤及分析證明書上。對於具有再驗日期的中間產物或原料藥，其再驗日期應標示在標籤及/或分析證明書上。	9.43	If the intermediate or API is intended to be transferred outside the control of the manufacturer's material management system, the name and address of the manufacturer, quantity of contents, special transport conditions, and any special legal requirements should also be included on the label. For intermediates or APIs with an expiry date, the expiry date should be indicated on the label and certificate of analysis. For intermediates or APIs with a retest date, the retest date should be indicated on the label and/or certificate of analysis.
9.44	在臨用前，應檢查分裝或包裝及標示設施，以確保在下一個分裝或包裝作業不需要之所有原物料皆已移除。該檢查應記錄在該批次之製造紀錄、設施使用日誌、或其他文件憑證系統中。	9.44	Packaging and labeling facilities should be inspected immediately before use to ensure that all materials not needed for the next packaging operation have been removed. This examination should be documented in the batch production records, the facility log, or other documentation system.
9.45	經分裝或包裝及標示之中間產物或原料藥應予檢查，以確保該批次中之容器及分裝或包裝皆有正確的標籤。該檢查應為分裝或包裝作業的一部分。檢查結果應記錄在該批次製造紀錄或管制紀錄中。	9.45	Packaged and labeled intermediates or APIs should be examined to ensure that containers and packages in the batch have the correct label. This examination should be part of the packaging operation. Results of these examinations should be recorded in the batch production or control records.
9.46	運送到製造廠管制之外的中間產物或原料藥的容器，應以其封籤如有破損或遺失時，接收人將會警覺到其內容物或許已被改變之可能性的方式進行封籤。	9.46	Intermediate or API containers that are transported outside of the manufacturer's control should be sealed in a manner such that, if the seal is breached or missing, the recipient will be alerted to the possibility that the contents may have been altered.
10.	**儲存與運銷（STORAGE AND DISTRIBUTION）**		

10.1 倉儲程序（Warehousing Procedures）	
10.10 應具備在適當條件（例如，必要時，控制的溫度及濕度）下儲存所有原物料的設施。儲存條件對保持原物料特性具關鍵性者，應將這些條件的紀錄加以保存。	10.10 Facilities should be available for the storage of all materials under appropriate conditions (e.g., controlled temperature and humidity when necessary). Records should be maintained of these conditions if they are critical for the maintenance of material characteristics.
10.11 除非有替代系統防止隔離/待驗、拒用、退回或回收之原物料的非故意或未經授權之使用，在決定其未來使用前，應該為其暫時儲存指定隔離的儲存區。	10.11 Unless there is an alternative system to prevent the unintentional or unauthorised use of quarantined, rejected, returned, or recalled materials, separate storage areas should be assigned for their temporary storage until the decision as to their future use has been taken.
10.2 運銷程序（Distribution Procedures）	
10.20 原料藥及中間產物，應僅在品質單位放行後，始得放行運銷到第三方。經品質單位授權，且備有適當的管制與文件憑證者，原料藥與中間產物在公司的管制下，得在隔離/待驗狀態下轉交另一單位。	10.20 APIs and intermediates should only be released for distribution to third parties after they have been released by the quality unit(s). APIs and intermediates can be transferred under quarantine to another unit under the company's control when authorized by the quality unit(s) and if appropriate controls and documentation are in place.
10.21 原料藥及中間產物應以不會有不利影響其品質的方式運送之。	10.21 APIs and intermediates should be transported in a manner that does not adversely affect their quality.
10.22 原料藥或中間產物之特殊的運送或儲存條件，應載明於標籤上。	10.22 Special transport or storage conditions for an API or intermediate should be stated on the label.
10.23 為原料藥或中間產物的運送，製造廠應確保承包運送者（合約人）瞭解並遵守適當之運送條件及儲存條件。	10.23 The manufacturer should ensure that the contract acceptor (contractor) for transportation of the API or intermediate knows and follows the appropriate transport and storage conditions.

10.24 應備有可易於確定每批中間產物及/或原料藥之運銷的系統，以使其得以回收。	10.24 A system should be in place by which the distribution of each batch of intermediate and/or API can be readily determined to permit its recall.
11. 實驗室管制（LABORATORY CONTROLS）	
11.1 一般管制（General Controls）	
11.10 獨立的品質單位應有由其支配的適當實驗室設施。	11.10 The independent quality unit(s) should have at its disposal adequate laboratory facilities.
11.11 應有描述原物料之抽樣、測試、核准或拒用及實驗室數據/資料的紀錄與保存之文件化的程序。實驗室紀錄應依 6.6 節之規範保存之。	11.11 There should be documented procedures describing sampling, testing, approval, or rejection of materials and recording and storage of laboratory data. Laboratory records should be maintained in accordance with Section 6.6.
11.12 所有規格、抽樣計畫，以及試驗程序在科學上應健全與適當，以確保原料、中間產物、原料藥、標籤與分裝或包裝材料符合品質及/或純度的既定標準。規格及試驗程序應與查驗登記/註冊/申請所包含者一致。除在查驗登記/申請所包含之規格外，可另追加其他規格。規格、抽樣計畫以及試驗程序，包含其變更，應由適當的組織單位草擬，並經由品質單位審查與核准。	11.12 All specifications, sampling plans, and test procedures should be scientifically sound and appropriate to ensure that raw materials, intermediates, APIs, and labels and packaging materials conform to established standards of quality and/or purity. Specifications and test procedures should be consistent with those included in the registration/filing. There can be specifications in addition to those in the registration/filing. Specifications, sampling plans, and test procedures, including changes to them, should be drafted by the appropriate organizational unit and reviewed and approved by the quality unit(s).

11.13 原料藥應依允收標準建立與製程一致的適當規格。該規格應包含不純物（例如，有機不純物、無機不純物及殘留溶劑）的管制。原料藥如有微生物學上之純度規格者，應建立其總生菌數及不合宜微生物的適當行動限值並符合之。原料藥如有內毒素規格者，應建立其適當行動限值並符合之。	11.13 Appropriate specifications should be established for APIs in accordance with accepted standards and consistent with the manufacturing process. The specifications should include a control of the impurities (e.g. organic impurities, inorganic impurities, and residual solvents). If the API has a specification for microbiological purity, appropriate action limits for total microbial counts and objectionable organisms should be established and met. If the API has a specification for endotoxins, appropriate action limits should be established and met.
11.14 實驗室管制應予遵行，並在執行時予以文件化。與上述程序的任何偏離皆應予以文件化並解釋之。	11.14 Laboratory controls should be followed and documented at the time of performance. Any departures from the above-described procedures should be documented and explained.
11.15 有任何偏離規格（OOS）結果皆應進行調查並依程序進行文件化。該程序應要求數據/資料分析、是否有重大問題存在的評估、改正措施之工作配置以及結論。有偏離規格結果後的任何重新抽樣及/或重新測試，皆應依文件化的程序執行之。	11.15 Any out-of-specification result obtained should be investigated and documented according to a procedure. This procedure should require analysis of the data, assessment of whether a significant problem exists, allocation of the tasks for corrective actions, and conclusions. Any resampling and/or retesting after OOS results should be performed according to a documented procedure.
11.16 試劑與標準溶液應依照書面程序配製及標示。合適時，分析試劑或標準溶液應註明最終可用日期。	11.16 Reagents and standard solutions should be prepared and labelled following written procedures. “Use by” dates should be applied as appropriate for analytical reagents or standard solutions.

11.17 對於原料藥的製造，應取得一級對照標準品（合適時）。各一級對照標準品的來源皆應予以文件化。各一級對照標準品之儲存與使用紀錄，皆應依供應商的建議保存之。得自主管機關認可之來源的一級對照標準品，其在與供應商之建議一致的條件下儲存者，通常不需測試即可使用。	11.17 Primary reference standards should be obtained as appropriate for the manufacture of APIs. The source of each primary reference standard should be documented. Records should be maintained of each primary reference standard's storage and use in accordance with the supplier's recommendations. Primary reference standards obtained from an officially recognised source are normally used without testing if stored under conditions consistent with the supplier's recommendations.
11.18 一級對照標準品未能自主管機關認可之來源取得者，應建立廠內一級標準品。此一級對照標準品應執行適當的測試，以充分建立其同一性及純度。該測試的適當文件應予以保存。	11.18 Where a primary reference standard is not available from an officially recognized source, an in-house primary standard should be established. Appropriate testing should be performed to establish fully the identity and purity of the primary reference standard. Appropriate documentation of this testing should be maintained.
11.19 二級對照標準品應適當地製備、識別、測試、核准與儲存。每一批二級對照標準品的適用性，應在初次使用前，經由與一級對照標準品比對以決定之。每一批二級對照標準品應依書面計畫書進行定期再標定。	11.19 Secondary reference standards should be appropriately prepared, identified, tested, approved, and stored. The suitability of each batch of secondary reference standard should be determined prior to first use by comparing against a primary reference standard. Each batch of secondary reference standard should be periodically requalified in accordance with a written protocol.
11.2 中間產物及原料藥的測試（Testing of Intermediates and APIs）	
11.20 對於每一批次的中間產物與原料藥，均應執行適當的實驗室測試，以確定其符合規格。	11.20 For each batch of intermediate and API, appropriate laboratory tests should be conducted to determine conformance to specifications.

11.21 通常對各原料藥，應建立其經由特定管制之生產過程產生的典型批次中，敘述其所存在之已鑑定不純物及未鑑定不純物的不純物描述。不純物描述應包含鑑別或某些定性分析指標（例如，滯留時間）、觀測到之每一不純物量的範圍，以及每一已鑑定不純物的類別（例如，無機的、有機的、溶劑）。不純物描述通常取決於原料藥的生產過程與來源。不純物描述對於來自草本植物或動物組織之原料藥通常是不需要的。生物技術的考量事項涵蓋於 ICH 指引 Q6B 中。	11.21 An impurity profile describing the identified and unidentified impurities present in a typical batch produced by a specific controlled production process should normally be established for each API. The impurity profile should include the identity or some qualitative analytical designation (e.g. retention time), the range of each impurity observed, and classification of each identified impurity (e.g. inorganic, organic, solvent). The impurity profile is normally dependent upon the production process and origin of the API. Impurity profiles are normally not necessary for APIs from herbal or animal tissue origin. Biotechnology considerations are covered in ICH Guideline Q6B.
11.22 為檢測由於原料、設備操作參數或生產過程之修改對原料藥造成的改變，其不純物描述應在適當間隔時間與法規提交之不純物描述比較，或與歷史數據/資料比較。	11.22 The impurity profile should be compared at appropriate intervals against the impurity profile in the regulatory submission or compared against historical data in order to detect changes to the API resulting from modifications in raw materials, equipment operating parameters, or the production process.
11.23 對有規定微生物品質者，則每批次的中間產物及原料藥應執行適當的微生物學上的測試。	11.23 Appropriate microbiological tests should be conducted on each batch of intermediate and API where microbial quality is specified.
11.3 分析程序的確效-請參見第 12 章（Validation of Analytical Procedures- see Section 12）	
11.4 分析證明書（Certificates of Analysis）	
11.40 原料藥廠對每一批次之中間產物或原料藥應該可應要求發給可靠的分析證明書。	11.40 Authentic certificates of analysis should be issued for each batch of intermediate or API on request.

11.41 中間產物或原料藥之分析證明書的資訊，應包含名稱、等級、批號以及放行日期（合適時）。中間產物或原料藥無論使用末效日期或再驗日期，都應將末效日期或再驗日期標示於標籤及/或分析證明書上。	11.41 Information on the name of the intermediate or API including where appropriate its grade, the batch number, and the date of release should be provided on the Certificate of Analysis. For intermediates or APIs with an expiry date, the expiry date should be provided on the label and Certificate of Analysis. For intermediates or APIs with a retest date, the retest date should be indicated on the label and/or Certificate of Analysis.
11.42 分析證明書應列出每個依據藥典或客戶要求之試驗項目，包含其允收限量，以及得到之數字結果(如果試驗結果為數字時）。	11.42 The certificate should list each test performed in accordance with compendial or customer requirements, including the acceptance limits, and the numerical results obtained (if test results are numerical).
11.43 分析證明書應由品質單位之經授權的人員簽名並註明日期，且應顯示原製造廠的名稱、地址與電話號碼。該分析係由重分包裝廠或重處理廠為之者，分析證明書應顯示重分包裝廠/重處理廠的名稱、地址及電話號碼，並註明原製造廠的名稱。	11.43 Certificates should be dated and signed by authorised personnel of the quality unit(s) and should show the name, address and telephone number of the original manufacturer. Where the analysis has been carried out by a repacker or reprocessor, the Certificate of Analysis should show the name, address and telephone number of the repacker/reprocessor and a reference to the name of the original manufacturer.

11.44 若新的分析證明書係由重分包裝廠/重處理廠或代理商所發出，則該證明書應顯示執行分析之實驗室的名稱、地址及電話號碼，並應註明原製造廠之名稱及地址，且檢附原始批次分析證明書之複本。	11.44 If new Certificates are issued by or on behalf of repackers/reprocessors or agents, these Certificates should show the name, address and telephone number of the laboratory that performed the analysis. They should also contain a reference to the name and address of the original manufacturer and to the original batch Certificate, a copy of which should be attached.
11.5 原料藥的安定性監測（Stability Monitoring of APIs）	
11.50 持續進行測試之書面計畫應予設計，以監測原料藥的安定性特性，且該等結果應使用於確認適當的儲存條件及再驗日期或末效日期。	11.50 A documented, on-going testing program should be designed to monitor the stability characteristics of APIs, and the results should be used to confirm appropriate storage conditions and retest or expiry dates.
11.51 使用於安定性試驗的試驗程序應經確效，並應具安定指標性。	11.51 The test procedures used in stability testing should be validated and be stability indicating.
11.52 安定性試驗之樣品應儲存於模擬上市產品的容器中。例如，原料藥盛裝在纖維桶內之袋子銷售者，安定性試驗之樣品得包裝在相同材質之袋子及與市售桶相似或相同材質組成之尺寸較小的儲存桶中。	11.52 Stability samples should be stored in containers that simulate the market container. For example, if the API is marketed in bags within fiber drums, stability samples can be packaged in bags of the same material and in smaller-scale drums of similar or identical material composition to the market drums.
11.53 通常應以最初三個量產批次納入安定性監測計畫中，以確認再驗日期或末效日期。但是，先前研究之數據/資料顯示原料藥預期可維持至少兩年安定者，得使用少於三個批次。	11.53 Normally the first three commercial production batches should be placed on the stability monitoring program to confirm the retest or expiry date. However, where data from previous studies show that the API is expected to remain stable for at least two years, fewer than three batches can be used.

11.54 此後,每年至少有一批次製造的原料藥（除非該年沒有生產)應加入安定性監測計畫中，並每年至少測試一次，以確認其安定性。	11.54 Thereafter, at least one batch per year of API manufactured (unless none is produced that year) should be added to the stability monitoring program and tested at least annually to confirm the stability.
11.55 對架儲期較短的原料藥應增加測試頻率。例如，具有架儲期一年或少於一年的生技/生物原料藥及其他原料藥，應取得其安定性試驗的樣品,並在起始三個月，逐月測試；其後應每三個月測試一次。有數據/資料證實對原料藥安定性不造成損害時,得考慮取消特定的試驗間隔（例如，第九個月的測試）。	11.55 For APIs with short shelf-lives, testing should be done more frequently. For example, for those biotechnological/biologic and other APIs with shelf-lives of one year or less, stability samples should be obtained and should be tested monthly for the first three months, and at three month intervals after that. When data exist that confirm that the stability of the API is not compromised, elimination of specific test intervals (e.g. 9 month testing) can be considered.
11.56 合適時，該安定性儲存條件應與 ICH 的安定性指引一致。	11.56 Where appropriate, the stability storage conditions should be consistent with the ICH guidelines on stability.
11.6 末效日期及再驗日期（Expiry and Retest Dating）	
11.60 中間產物預定要運送到製造廠原物料管理系統的管制外,且有指定末效日期或再驗日期者,應備有支持安定性的數據（例如，發表的數據、試驗結果）。	11.60 When an intermediate is intended to be transferred outside the control of the manufacturer's material management system and an expiry or retest date is assigned, supporting stability information should be available (e.g., published data, test results).
11.61 原料藥之末效日期或再驗日期,應以自安定性研究所得數據/資料之評估為基礎。一般實務應使用再驗日期，而非末效日期。	11.61 An API expiry or retest date should be based on an evaluation of data derived from stability studies. Common practice is to use a retest date, not an expiration date.

11.62 如果（1）原料藥先導批次採用模擬所要使用於商業製造規模之最後製程的製造方法與程序，且（2）其品質能代表將於商業規模製造之物質者，則該原料藥之初步末效日期或再驗日期得以先導規模批次為基礎。	11.62 Preliminary API expiry or retest dates can be based on pilot scale batches if (1) the pilot batches employ a method of manufacture and procedure that simulates the final process to be used on a commercial manufacturing scale and (2) the quality of the API represents the material to be made on a commercial scale.
11.63 為執行再驗之目的，應抽取有代表性的樣品。	11.63 A representative sample should be taken for the purpose of performing a retest.
11.7 留樣品/留存樣品（Reserve/Retention Samples）	
11.70 留樣品之包裝與保存的目的是為原料藥批次品質之未來可能進行的評估，而非為未來的安定性測試。	11.70 The packaging and holding of reserve samples is for the purpose of potential future evaluation of the quality of batches of API and not for future stability testing purposes.
11.71 每一批次原料藥經適當辨識的留樣品，應保留至製造廠指定該批次之末效日期後一年，或至該批次運銷後三年，兩者中取其較長者。對於具有再驗日期的原料藥，其類似的留樣品應保留至製造廠完全運銷該批次後三年。	11.71 Appropriately identified reserve samples of each API batch should be retained for one year after the expiry date of the batch assigned by the manufacturer, or for three years after distribution of the batch, whichever is the longer. For APIs with retest dates, similar reserve samples should be retained for three years after the batch is completely distributed by the manufacturer.
11.72 留樣品應貯存在與原料藥之貯存相同的分裝或包裝系統中，或貯存在與市售分裝或包裝系統相同或更具保護性的系統中。應保存足夠的數量，以供執行至少兩次完全的藥典分析，或在無藥典各論時，執行至少兩次完全規格分析。	11.72 The reserve sample should be stored in the same packaging system in which the API is stored or in one that is equivalent to or more protective than the marketed packaging system. Sufficient quantities should be retained to conduct at least two full compendial analyses or, when there is no pharmacopoeial monograph, two full specification analyses.
12. 確效（VALIDATION）	
12.1 確效政策（Validation Policy）	

12.10 公司對於確效之整體政策、目的/意向及做法應予文件化，包含製程、清潔程序、分析方法、製程中管制試驗程序、電腦化系統等的確效，以及負責每一個確效階段之設計、審查、核准及文件製作的人員。	12.10 The company's overall policy, intentions, and approach to validation, including the validation of production processes, cleaning procedures, analytical methods, in-process control test procedures, computerized systems, and persons responsible for design, review, approval and documentation of each validation phase, should be documented.
12.11 通常，關鍵參數/屬性應在開發階段的期間或從歷史的數據/資料加以確認，並且應對於能再現之操作的必要範圍加以界定。其內容包括：	12.11 The critical parameters/attributes should normally be identified during the development stage or from historical data, and the ranges necessary for the reproducible operation should be defined. This should include:
➢ 以其關鍵的產品屬性界定原料藥；	➢ Defining the API in terms of its critical product attributes;
➢ 辨識會影響原料藥之關鍵品質屬性的製程參數；	➢ Identifying process parameters that could affect the critical quality attributes of the API;
➢ 決定在例行製造與製程管制時預期使用之每一個關鍵製程的參數範圍。	➢ Determining the range for each critical process parameter expected to be used during routine manufacturing and process control.
12.12 確效應延伸到經確定對原料藥的品質與純度具有關鍵性的操作。	12.12 Validation should extend to those operations determined to be critical to the quality and purity of the API.
12.2 確效文件（Validation Documentation）	
12.20 應制訂書面確效計畫書規定應如何執行特定製程的確效。該計畫書應由品質單位及其他經指定的單位審查及核准。	12.20 A written validation protocol should be established that specifies how validation of a particular process will be conducted. The protocol should be reviewed and approved by the quality unit(s) and other designated units.

12.21 確效計畫書應規定關鍵製程步驟及允收標準，以及待執行之確效類型（例如，回溯性、先期性、併行性確效）及製程執行的次數。	12.21 The validation protocol should specify critical process steps and acceptance criteria as well as the type of validation to be conducted (e.g., retrospective, prospective, concurrent) and the number of process runs.
12.22 應製作交互參照確效計畫書之確效報告，摘要敘述取得的結果，評論觀察到之任何偏差，以及歸納適當的結論，包含對改正缺點之變更的建議。	12.22 A validation report that cross-references the validation protocol should be prepared, summarizing the results obtained, commenting on any deviations observed, and drawing the appropriate conclusions, including recommending changes to correct deficiencies.
12.23 確效計畫書之任何變異，應予文件化並備有正當理由。	12.23 Any variations from the validation protocol should be documented with appropriate justification.
12.3 驗證（Qualification）	
12.30 啟動製程確效作業之前，關鍵設備及輔助系統的適當驗證應先完成。通常，驗證應經由個別或合併執行下列作業實施之：	12.30 Before starting process validation activities, appropriate qualification of critical equipment and ancillary systems should be completed. Qualification is usually carried out by conducting the following activities, individually or combined:
➢ 設計驗證（DQ）：廠房設施、系統及設備之建議設計適合於預定目的之文件化的確認作業。	➢ Design Qualification (DQ): documented verification that the proposed design of the facilities, equipment, or systems is suitable for the intended purpose.
➢ 安裝驗證（IQ）：設備及系統經安裝或修改時，其符合核准的設計及製造廠的建議之文件化的確認作業。	➢ Installation Qualification (IQ): documented verification that the equipment or systems, as installed or modified, comply with the approved design, the manufacturer's recommendations and/or user requirements.

➢ 操作驗證（OQ）：設備及系統經安裝或修改時，在期望的操作範圍中執行預期操作之文件化的確認作業。	➢ Operational Qualification (OQ): documented verification that the equipment or systems, as installed or modified, perform as intended throughout the anticipated operating ranges.
➢ 性能驗證（PQ）：在核准的製程方法及產品規格的基礎上，與設備及系統連結，能有效執行並具再現性之文件化的確認作業。	➢ Performance Qualification (PQ): documented verification that the equipment and ancillary systems, as connected together, can perform effectively and reproducibly based on the approved process method and specifications.
12.4 製程確效的方法（Approaches to Process Validation）	
12.40 製程確效（Process Validation，PV）為製程在已建立之參數內操作時，能有效且再現性地生產符合其預定規格及品質屬性的中間產物或原料藥之文件化的證據。	12.40 Process Validation (PV) is the documented evidence that the process, operated within established parameters, can perform effectively and reproducibly to produce an intermediate or API meeting its predetermined specifications and quality attributes.
12.41 有三種確效方法。先期性確效雖是較為優先的方法，但在有些例外的情形，得採用其他方法。這些方法及其適用性列舉如下。	12.41 There are three approaches to validation. Prospective validation is the preferred approach, but there are exceptions where the other approaches can be used. These approaches and their applicability are listed below.
12.42 通常，所有原料藥製程應按 12.12 條所界定者，執行先期性確效。由該原料藥製成之最終產品商業運銷前，應先完成該原料藥製程之先期性確效。	12.42 Prospective validation should normally be performed for all API processes as defined in 12.12. Prospective validation performed on an API process should be completed before the commercial distribution of the final drug product manufactured from that API.

12.43 當因僅生產有限之原料藥批次數、原料藥批次生產頻率偏低或原料藥批次以經過修改之已確效的製程生產，而無法取得來自重複生產作業之數據/資料時，得執行併行性確效。在併行性確效完成前，得以該原料藥批次之充分監視及測試為基礎放行該批次，並使用於生產供商業運銷之最終產品。	12.43 Concurrent validation can be conducted when data from replicate production runs are unavailable because only a limited number of API batches have been produced, API batches are produced infrequently, or API batches are produced by a validated process that has been modified. Prior to the completion of concurrent validation, batches can be released and used in final drug product for commercial distribution based on thorough monitoring and testing of the API batches.
12.44 使用已完善建立的製程，對原料藥品質不因原料、設備、系統、設施或製程的變更，而致顯著改變者，得例外就該製程從事回溯性確效。符合下列情形時始得使用回溯性確效方法：	12.44 An exception can be made for retrospective validation for well established processes that have been used without significant changes to API quality due to changes in raw materials, equipment, systems, facilities, or the production process. This validation approach may be used where:
(1) 關鍵品質屬性及關鍵製程參數已確認者；	(1) Critical quality attributes and critical process parameters have been identified;
(2) 適當之製程中允收標準及管制已建立者；	(2) Appropriate in-process acceptance criteria and controls have been established;
(3) 未曾由於「操作人員失誤或與設備適用性無關之設備失敗」以外的原因，而有重大製程/產品失敗者；以及	(3) There have not been significant process/product failures attributable to causes other than operator error or equipment failures unrelated to equipment suitability; and
(4) 既有原料藥已建立不純物描述者。	(4) Impurity profiles have been established for the existing API.

12.45 回溯性確效選用之批次，應為回顧期間所生產的所有批次之代表，包括在此期間不符規格的任何批次，並應有足夠的批次數以證明製程之一致性。留樣品得進行測試，以取得數據/資料供回溯確效該製程。	12.45 Batches selected for retrospective validation should be representative of all batches made during the review period, including any batches that failed to meet specifications, and should be sufficient in number to demonstrate process consistency. Retained samples can be tested to obtain data to retrospectively validate the process.
12.5 製程確效計畫（Process Validation Program）	
12.50 為確效所執行之製程操作的次數，應取決於製程複雜性或考慮製程改變的幅度。對先期及併行確效，應使用三個連續成功的量產批次為原則。但有可能需追加製程操作以確實證明製程一致性的情況（例如，複雜之原料藥製程或延長完成時間之製程）。回溯性確效，通常應檢查來自十到三十個連續批次的數據/資料，以評估製程之一致性。但有正當理由時，得檢查較少的批次。	12.50 The number of process runs for validation should depend on the complexity of the process or the magnitude of the process change being considered. For prospective and concurrent validation, three consecutive successful production batches should be used as a guide, but there may be situations where additional process runs are warranted to prove consistency of the process (e.g., complex API processes or API processes with prolonged completion times). For retrospective validation, generally data from ten to thirty consecutive batches should be examined to assess process consistency, but fewer batches can be examined if justified.
12.51 在製程確效試驗期間，關鍵製程參數應予管制及監測。與品質無關之製程參數，例如，使能源消耗或設備使用減到最低之控制的變數，不需包含在製程確效中。	12.51 Critical process parameters should be controlled and monitored during process validation studies. Process parameters unrelated to quality, such as variables controlled to minimize energy consumption or equipment use, need not be included in the process validation.

12.52 製程確效應確認每一原料藥的不純物描述都在規定的限度內。不純物描述應相當於或優於歷史數據/資料，而且適用時，應相當於或優於在製程開發期間或為使用於樞紐性臨床試驗與毒理學試驗批次而確定之不純物描述。	12.52 Process validation should confirm that the impurity profile for each API is within the limits specified. The impurity profile should be comparable to or better than historical data and, where applicable, the profile determined during process development or for batches used for pivotal clinical and toxicological studies.
12.6 經確效之系統的定期檢討（Periodic Review of Validated Systems）	
12.60 系統及製程應定期評估，以確認其仍然以有效的方式運作。系統或製程上未經顯著變更，且品質檢討確認該系統或製程持續生產符合其規格之中間產物/原料藥者，通常不需再確效。	12.60 Systems and processes should be periodically evaluated to verify that they are still operating in a valid manner. Where no significant changes have been made to the system or process, and a quality review confirms that the system or process is consistently producing material meeting its specifications, there is normally no need for revalidation.
12.7 清潔確效（Cleaning Validation）	
12.70 通常，清潔程序應加以確效。一般而言，清潔確效應針對污染或移轉之物質對原料藥品質有最大風險的情況或製程步驟。例如，殘留物在後續的純化步驟中會被移除者，在生產初期可能未必需要確效設備的清潔程序。	12.70 Cleaning procedures should normally be validated. In general, cleaning validation should be directed to situations or process steps where contamination or carryover of materials poses the greatest risk to API quality. For example, in early production it may be unnecessary to validate equipment cleaning procedures where residues are removed by subsequent purification steps.

12.71 清潔程序之確效應反映設備之實際的使用方式。如果不同的原料藥或中間產物在相同的設備上製造，且該設備經以相同程序清潔，則可選擇一代表性的中間產物或原料藥供清潔確效之用。該選擇應根據溶解度及清潔的困難度，而且殘留限量的計算應以力價、毒性及安定性為基礎。	12.71 Validation of cleaning procedures should reflect actual equipment usage patterns. If various APIs or intermediates are manufactured in the same equipment and the equipment is cleaned by the same process, a representative intermediate or API can be selected for cleaning validation. This selection should be based on the solubility and difficulty of cleaning and the calculation of residue limits based on potency, toxicity, and stability.
12.72 清潔確效計畫書應敘述所要清潔的設備、程序、物質、可接受的清潔程度、待監測及管制的參數，以及分析方法。該計畫書也應指出要取得之樣品類型及其如何收集與標示。	12.72 The cleaning validation protocol should describe the equipment to be cleaned, procedures, materials, acceptable cleaning levels, parameters to be monitored and controlled, and analytical methods. The protocol should also indicate the type of samples to be obtained and how they are collected and labelled.
12.73 取樣應包含擦拭、沖洗或合適時其他替代方法（例如，直接萃取），以檢測不溶性及可溶性殘留物兩者。使用之取樣方法，應能定量量測在清潔後留於設備表面的殘留物量。由於設備設計及/或製程限制（例如，軟質管線、輸送管線、小開口反應槽等之內壁或處理毒性物質，以及小型複雜設備，例如，微細化機與微細流體化機），產品接觸面不易進入取樣時，擦拭取樣法可能是不切實際的。	12.73 Sampling should include swabbing, rinsing, or alternative methods (e.g., direct extraction), as appropriate, to detect both insoluble and soluble residues. The sampling methods used should be capable of quantitatively measuring levels of residues remaining on the equipment surfaces after cleaning. Swab sampling may be impractical when product contact surfaces are not easily accessible due to equipment design and/or process limitations (e.g., inner surfaces of hoses, transfer pipes, reactor tanks with small ports or handling toxic materials, and small intricate equipment such as micronizers and microfluidizers).

12.74 應使用對殘留物或污染物具檢測靈敏度之經確效的分析方法。每一種分析方法的檢測限度，應足夠靈敏以檢測殘留物或污染物的既定允收標準。應建立該方法可以達到的回收率。殘留物限量應為實用的、可達成的、可確認的，而且應以最有害的殘留物為基礎。允收限量得以該原料藥之已知最低的藥理、毒理、生理活性或其最有害成分為基礎建立之。	12.74 Validated analytical methods having sensitivity to detect residues or contaminants should be used. The detection limit for each analytical method should be sufficiently sensitive to detect the established acceptable level of the residue or contaminant. The method's attainable recovery level should be established. Residue limits should be practical, achievable, verifiable, and based on the most deleterious residue. Limits can be established based on the minimum known pharmacological, toxicological, or physiological activity of the API or its most deleterious component.
12.75 設備清潔與衛生處理試驗，應對減少原料藥中的總生菌數或內毒素污染具有要求之製程，或對亟需關切該污染之其他製程（例如，使用於製造無菌產品的非無菌原料藥），提示微生物學上及內毒素的污染。	12.75 Equipment cleaning/sanitation studies should address microbiological and endotoxin contamination for those processes where there is a need to reduce total microbiological count or endotoxins in the API, or other processes where such contamination could be of concern (e.g., non-sterile APIs used to manufacture sterile products).
12.76 確效後，清潔程序應在適當間隔期間加以監測，以確保這些清潔程序在例行生產期間使用時是有效的。可行時，設備潔淨度可經由分析測試及目視檢查加以監測。目視檢查可以允許檢測集中在小區域的顯著污染。否則，以取樣及/或分析方式可能無法檢出該污染。	12.76 Cleaning procedures should be monitored at appropriate intervals after validation to ensure that these procedures are effective when used during routine production. Equipment cleanliness can be monitored by analytical testing and visual examination, where feasible. Visual inspection can allow detection of gross contamination concentrated in small areas that could otherwise go undetected by sampling and/or analysis.
12.8 分析方法確效（Validation of Analytical Methods）	

12.80 除非採用的分析方法是包含在相關藥典或其他經認可的標準參考文獻中，否則，該方法應予確效。使用之所有測試方法的適用性，仍應在實際使用的條件下予以確認，並進行文件化。	12.80 Analytical methods should be validated unless the method employed is included in the relevant pharmacopoeia or other recognised standard reference. The suitability of all testing methods used should nonetheless be verified under actual conditions of use and documented.
12.81 分析方法應經確效，以包含 ICH 分析方法確效指引中之特徵的考量。分析確效執行的程度，應反映分析之目的及原料藥製程的階段。	12.81 Methods should be validated to include consideration of characteristics included within the ICH guidelines on validation of analytical methods. The degree of analytical validation performed should reflect the purpose of the analysis and the stage of the API production process.
12.82 開始分析方法之確效前，應考慮分析設備的適當驗證。	12.82 Appropriate qualification of analytical equipment should be considered before starting validation of analytical methods.
12.83 經確效之分析方法的任何修正皆應保持完整的紀錄。這些紀錄應包含該修正的理由及適當的數據/資料，以確認該修正產生與既定方法具等同之準確及可靠的結果。	12.83 Complete records should be maintained of any modification of a validated analytical method. Such records should include the reason for the modification and appropriate data to verify that the modification produces results that are as accurate and reliable as the established method.
13. 變更管制（CHANGE CONTROL）	
13.10 正式的變更管制系統應予建立，以評估可能影響中間產物或原料藥之生產及管制的所有變更。	13.10 A formal change control system should be established to evaluate all changes that may affect the production and control of the intermediate or API.

13.11 對於原料、規格、分析方法、設施、支援系統、設備（包含電腦硬體）、製程步驟、標示與包裝材料，以及電腦軟體之變更的識別、文件製作、適當審查及核准，應提供書面的程序。	13.11 Written procedures should provide for the identification, documentation, appropriate review, and approval of changes in raw materials, specifications, analytical methods, facilities, support systems, equipment (including computer hardware), processing steps, labelling and packaging materials, and computer software.
13.12 對與 GMP 有關之變更的任何提議，皆應由組織內之適當單位草擬、審查及核准，並且應經品質單位審查及核准。	13.12 Any proposals for GMP relevant changes should be drafted, reviewed, and approved by the appropriate organisational units, and reviewed and approved by the quality unit(s).
13.13 經提議之變更對中間產物或原料藥之品質的可能影響應予評估。該等變更之分類程序可能有助於決定所需之測試、確效及文件製作的程度，以證明對經過確效之製程的變更之合理性。變更可依變更的性質及程度，以及依這些變更對該製程可能的影響加以分類（例如，分類為次要或主要）。科學的判斷應確定何種附加測試及確效試驗適合用來證明經確效之製程的變更之合理性。	13.13 The potential impact of the proposed change on the quality of the intermediate or API should be evaluated. A classification procedure may help in determining the level of testing, validation, and documentation needed to justify changes to a validated process. Changes can be classified (e.g., as minor or major) depending on the nature and extent of the changes, and the effects these changes may impart on the process. Scientific judgment should determine what additional testing and validation studies are appropriate to justify a change in a validated process.
13.14 實施經核准之變更時，應採取措施，以確保受變更影響之所有文件皆已修訂。	13.14 When implementing approved changes, measures should be taken to ensure that all documents affected by the changes are revised.
13.15 經變更後，應有在該變更下，首次生產或測試之批次的評估。	13.15 After the change has been implemented, there should be an evaluation of the first batches produced or tested under the change.

13.16 關鍵變更對既定再驗日期與末效日期之影響的可能性應予評估。必要時，經由修改過之製程所生產的中間產物或原料藥的樣品，可納入加速安定性計畫及/或可加入安定性監測計畫中。	13.16 The potential for critical changes to affect established retest or expiry dates should be evaluated. If necessary, samples of the intermediate or API produced by the modified process can be placed on an accelerated stability program and/or can be added to the stability monitoring program.
13.17 既定生產與製程之管制程序的變更可能影響原料藥之品質者，應告知現行使用該原料藥之劑型製造廠。	13.17 Current dosage form manufacturers should be notified of changes from established production and process control procedures that can impact the quality of the API.
14. 中間產物及原料藥的拒用與再用（REJECTION AND RE-USE OF MATERIALS）	
14.1 拒用（Rejection）	
14.10 不符合既定規格之中間產物及原料藥應予以識別並隔離。這些中間產物或原料藥，得依照以下所述予以重處理或再加工。拒用中間產物及原料藥的最終處置應予紀錄。	14.10 Intermediates and APIs failing to meet established specifications should be identified as such and quarantined. These intermediates or APIs can be reprocessed or reworked as described below. The final disposition of rejected materials should be recorded.
14.2 重處理（Reprocessing）	
14.20 將中間產物或原料藥，包含不符合標準或規格者在內，導回原製程，並經由重複既定製造過程之一部分的結晶步驟，或其他適當之化學或物理操作步驟（例如，蒸餾、過濾、層析、粉碎）重處理，通常認為是可以接受的。然而，如該重處理被使用於大多數之批次，則應納為標準製程的一部分。	14.20 Introducing an intermediate or API, including one that does not conform to standards or specifications, back into the process and reprocessing by repeating a crystallization step or other appropriate chemical or physical manipulation steps (e.g., distillation, filtration, chromatography, milling) that are part of the established manufacturing process is generally considered acceptable. However, if such reprocessing is used for a majority of batches, such reprocessing should be included as part of the standard manufacturing process.

14.21 在一個製程中管制試驗後，已經顯示該製程步驟不完全者，該步驟之延續認定為正常製程的一部分，而非屬重處理。	14.21 Continuation of a process step after an in-process control test has shown that the step is incomplete is considered to be part of the normal process. This is not considered to be reprocessing.
14.22 將未反應完全的原料導回原製程並重複化學反應時，應認定為重處理，除非其為既定製程的一部分。該重處理的進行應小心評估，以確保中間產物或原料藥的品質不會由於副產物及過度反應物質的可能生成而受到不良的影響。	14.22 Introducing unreacted material back into a process and repeating a chemical reaction is considered to be reprocessing unless it is part of the established process. Such reprocessing should be preceded by careful evaluation to ensure that the quality of the intermediate or API is not adversely affected due to the potential formation of by-products and over-reacted materials.
14.3 再加工（Reworking）	
14.30 在決定將不符合既定標準或規格的批次再加工前，應執行其不符合之理由的調查。	14.30 Before a decision is taken to rework batches that do not conform to established standards or specifications, an investigation into the reason for nonconformance should be performed.
14.31 有必要時，對經再加工的批次應進行適當的評估、測試、安定性試驗，並予以文件化，以顯示該再加工的產品具有與經由原製程生產之產品等同的品質。併行性確效對再加工程序常為適當的確效方法。該方法允許以計畫書界定再加工程序、如何執行再加工及其預期的結果。如只有一個批次需要再加工，則一經確定該批次可被接受，即可撰寫報告，並予放行。	14.31 Batches that have been reworked should be subjected to appropriate evaluation, testing, stability testing if warranted, and documentation to show that the reworked product is of equivalent quality to that produced by the original process. Concurrent validation is often the appropriate validation approach for rework procedures. This allows a protocol to define the rework procedure, how it will be carried out, and the expected results. If there is only one batch to be reworked, then a report can be written and the batch released once it is found to be acceptable.

14.32 對於每一再加工的批次與經由既定製程製造之批次的不純物描述之比較，應提供程序。例行分析方法不足以確定再加工批次之特徵時，應使用追加的方法。	14.32 Procedures should provide for comparing the impurity profile of each reworked batch against batches manufactured by the established process. Where routine analytical methods are inadequate to characterize the reworked batch, additional methods should be used.
14.4 原料（含反應物、中間產物、原料藥）及溶劑的回收（Recovery of Materials and Solvents）	
14.40 若反應物、中間產物或原料藥有核准的回收程序，且回收之物質適合其預定用途之規格時，則回收（例如，從母液或濾液）認定為可以接受。	14.40 Recovery (e.g., from mother liquor or filtrates) of reactants, intermediates, or the API is considered acceptable, provided that approved procedures exist for the recovery and the recovered materials meet specifications suitable for their intended use.
14.41 若溶劑回收的程序經管制及監測，以確保該溶劑在重用或與其他經核准之物質混合前符合適當標準時，則該溶劑得在相同或不同之製程中回收及重用。	14.41 Solvents can be recovered and reused in the same processes or in different processes, provided that the recovery procedures are controlled and monitored to ensure that solvents meet appropriate standards before reuse or co-mingling with other approved materials.
14.42 新的及回收的溶劑，以及新的及回收的試劑，若經充分測試已顯示對可能被使用之所有製造過程的適用性時，則新的及回收的溶劑/試劑得以合併。	14.42 Fresh and recovered solvents and reagents can be combined if adequate testing has shown their suitability for all manufacturing processes in which they may be used.
14.43 回收的溶劑、母液，以及其他回收物質的使用，應予適當地文件化。	14.43 The use of recovered solvents, mother liquors, and other recovered materials should be adequately documented.
14.5 退回品（Returns）	
14.50 退回的中間產物或原料藥應予以識別並加隔離。	14.50 Returned intermediates or APIs should be identified as such and quarantined.

14.51 若退回的中間產物或原料藥在其退回以前之儲存或運送的條件，或其容器的狀況，使其品質有所疑慮時，則退回的中間產物或原料藥得視情況予以重處理、再加工或銷毀。	14.51 If the conditions under which returned intermediates or APIs have been stored or shipped before or during their return or the condition of their containers casts doubt on their quality, the returned intermediates or APIs should be reprocessed, reworked, or destroyed, as appropriate.
14.52 退回的中間產物或原料藥之紀錄應予保存。就每一退回物件之文件應包括：	14.52 Records of returned intermediates or APIs should be maintained. For each return, documentation should include:
➢ 收貨人之姓名及地址	➢ Name and address of the consignee
➢ 退回之中間產物或原料藥的批號及數量	➢ Intermediate or API, batch number, and quantity returned
➢ 退回的理由	➢ Reason for return
➢ 退回之中間產物或原料藥的使用或處置	➢ Use or disposal of the returned intermediate or API
15. 申訴與回收（COMPLAINTS AND RECALLS）	
15.10 無論是以口頭或書面收到之所有與品質有關的申訴，均應依照書面程序加以記錄及調查。	15.10 All quality related complaints, whether received orally or in writing, should be recorded and investigated according to a written procedure.
15.11 申訴紀錄應包括：	15.11 Complaint records should include:
➢ 申訴者之姓名及地址；	➢ Name and address of complainant;
➢ 提出該申訴的人之姓名（及合適時，其頭銜）及電話號碼；	➢ Name (and, where appropriate, title) and phone number of person submitting the complaint;
➢ 申訴之本質（包含原料藥的名稱及批號）；	➢ Complaint nature (including name and batch number of the API);
➢ 收到申訴的日期；	➢ Date complaint is received;
➢ 初始採取的行動（包含採取該行動之日期及人員的身分）；	➢ Action initially taken (including dates and identity of person taking the action);
➢ 任何所採取之追蹤行動；	➢ Any follow-up action taken;
➢ 提供給原申訴人的回應（包含送出回應的日期）；	➢ Response provided to the originator of complaint (including date response sent); and

➢ 對中間產物或原料藥批次的最終決定。	➢ Final decision on intermediate or API batch or lot.
15.12 為評估趨勢、產品相關的申訴頻度及嚴重性，以便採取追加的與立即的（合適時）改正措施，申訴紀錄應予保存。	15.12 Records of complaints should be retained in order to evaluate trends, product-related frequencies, and severity with a view to taking additional, and if appropriate, immediate corrective action.
15.13 應有書面程序，界定中間產物或原料藥應考慮回收的情況。	15.13 There should be a written procedure that defines the circumstances under which a recall of an intermediate or API should be considered.
15.14 回收程序應指定參與評估該資訊的人員、應如何啟動回收、該回收應被通知的對象，以及應如何處理回收品。	15.14 The recall procedure should designate who should be involved in evaluating the information, how a recall should be initiated, who should be informed about the recall, and how the recalled material should be treated.
15.15 有嚴重或可能危及生命之情況時，應通知當地、國家及/或國際主管機關並徵詢其意見。	15.15 In the event of a serious or potentially life-threatening situation, local, national, and/or international authorities should be informed and their advice sought.
16. 委受託製造廠（含實驗室）【CONTRACT MANUFACTURERS (INCLUDING LABORATORIES)】	
16.10 所有受託製造廠（含實驗室）應遵守本規範中所界定的 GMP。對於防止交叉污染及保持可追溯性應予特別考慮。	16.10 All contract manufacturers (including laboratories) should comply with the GMP defined in this Guide. Special consideration should be given to the prevention of cross-contamination and to maintaining traceability.
16.11 委託者應評估受託製造廠（含實驗室），以確保在受託場所執行之特定作業符合 GMP。	16.11 Contract manufacturers (including laboratories) should be evaluated by the contract giver to ensure GMP compliance of the specific operations occurring at the contract sites.

16.12 委託者與其受託者間應有經核准的書面合約或正式的協議書，詳細界定 GMP 責任，包含每一方的品質措施在內。	16.12 There should be a written and approved contract or formal agreement between the contract giver and the contract acceptor that defines in detail the GMP responsibilities, including the quality measures, of each party.
16.13 該合約書應允許委託者稽查其受託者之廠房/設施的 GMP 符合性。	16.13 The contract should permit the contract giver to audit the contract acceptor's facilities for compliance with GMP.
16.14 在容許轉委託時，非經委託者就該轉委託之安排的事先評估及核准，受託者不得將任何依照合約書所受託的工作轉委託給第三方。	16.14 Where subcontracting is allowed, the contract acceptor should not pass to a third party any of the work entrusted to him under the contract without the contract giver's prior evaluation and approval of the arrangements.
16.15 製造及實驗紀錄應保存在執行該作業活動之場所且易於取得。	16.15 Manufacturing and laboratory records should be kept at the site where the activity occurs and be readily available.
16.16 除非通知委託者並經其核准，不得就製程、設備、試驗方法、規格或其他合約之要求事項作出變更。	16.16 Changes in the process, equipment, test methods, specifications, or other contractual requirements should not be made unless the contract giver is informed and approves the changes.
17. 代理商、貿易商、經銷商、重分包裝廠及重標示廠（AGENTS, TRADERS, DISTRIBUTORS, REPACKERS, AND RELABELLERS）	
17.1 適用性（Applicability）	
17.10 本章適用於原製造廠以外，從事原料藥或中間產物之貿易及/或持有、重分包裝、重標示、處理、運銷或儲存的任何一方。	17.10 This section applies to any party other than the original manufacturer who may trade and/or take possession, repack, relabel, manipulate, distribute, or store an API or intermediate.
17.11 所有代理商、貿易商、經銷商、重分包裝廠及重標示廠皆應符合本規範所界定之 GMP。	17.11 All agents, traders, distributors, repackers, and relabellers should comply with GMP as defined in this Guide.
17.2 運銷之原料藥及中間產物的可追溯性（Traceability of Distributed APIs and Intermediates）	

17.20 代理商、貿易商、經銷商、重分包裝廠或重標示廠應保存其運銷之原料藥與中間產物的完整可追溯性。應保存並可取得的文件包括：	17.20 Agents, traders, distributors, repackers, or relabellers should maintain complete traceability of APIs and intermediates that they distribute. Documents that should be retained and available include:
➢ 原製造廠的識別	➢ Identity of original manufacturer
➢ 原製造廠的地址	➢ Address of original manufacturer
➢ 採購訂單	➢ Purchase orders
➢ 裝貨憑單/提貨單（運輸憑證）	➢ Bills of lading (transportation documentation)
➢ 接收文件	➢ Receipt documents
➢ 原料藥或中間產物的名稱或指定名稱	➢ Name or designation of API or intermediate
➢ 製造廠的批號	➢ Manufacturer's batch number
➢ 運送與運銷紀錄	➢ Transportation and distribution records
➢ 所有真實的分析證明書，包含原製造廠的證明書	➢ All authentic Certificates of Analysis, including those of the original manufacturer
➢ 再驗日期或末效日期	➢ Retest or expiry date
17.3 品質管理（Quality Management）	
17.30 代理商、貿易商、經銷商、重分包裝廠或重標示廠應依第 2 章規定建立有效之品質管理系統，並進行文件化及履行之。	17.30 Agents, traders, distributors, repackers, or relabelers should establish, document and implement an effective system of managing quality, as specified in Section 2.
17.4 原料藥及中間產物的重分包裝、重標示以及保存（Repackaging, Relabeling, and Holding of APIs and Intermediates）	
17.40 原料藥及中間產物之重分包裝、重標示及保存應如同本規範中所規定之適當的 GMP 管制執行，以避免原料藥或中間產物混雜及其識別或純度的喪失。	17.40 Repackaging, relabelling and holding of APIs and intermediates should be performed under appropriate GMP controls, as stipulated in this Guide, to avoid mix-ups and loss of API or intermediate identity or purity.
17.41 重分包裝應在適當環境條件下執行，以避免污染及交叉污染。	17.41 Repackaging should be conducted under appropriate environmental conditions to avoid contamination and cross-contamination.

17.5 安定性（Stability）	
17.50 若將原料藥或中間產物重分包裝於與原料藥或中間產物製造廠所使用之容器類型不同時，則應執行證明指定之未效日期或再驗日期之合理性的安定性試驗。	17.50 Stability studies to justify assigned expiration or retest dates should be conducted if the API or intermediate is repackaged in a different type of container than that used by the API or intermediate manufacturer.
17.6 資訊的移轉（Transfer of Information）	
17.60 代理商、經銷商、重分包裝廠或重標示廠應將從原料藥或中間產物製造廠所收到的所有品質或法規資訊移轉給客戶，並將從客戶所收到的資訊移轉給原料藥或中間產物製造廠。	17.60 Agents, distributors, repackers, or relabellers should transfer all quality or regulatory information received from an API or intermediate manufacturer to the customer, and from the customer to the API or intermediate manufacturer.
17.61 供應原料藥或中間產物給客戶之代理商、貿易商、經銷商、重分包裝廠或重標示廠，應提供原料藥或中間產物之原製造廠的名稱及其所供應的批號。	17.61 The agent, trader, distributor, repacker, or relabeller who supplies the API or intermediate to the customer should provide the name of the original API or intermediate manufacturer and the batch number(s) supplied.
17.62 代理商應該應主管機關之要求，提供原料藥或中間產物之原製造廠的身分識別。視被授權之代理商與原料藥或中間產物原製造廠間的法律關係，原製造廠可直接或透過被授權之代理商回應主管機關。（在此，「被授權」意指經由製造廠授權）。	17.62 The agent should also provide the identity of the original API or intermediate manufacturer to regulatory authorities upon request. The original manufacturer can respond to the regulatory authority directly or through its authorized agents, depending on the legal relationship between the authorized agents and the original API or intermediate manufacturer. (In this context "authorized" refers to authorized by the manufacturer.)
17.63 應符合包含於第 11.4 節之「分析證明書」的特定規範。	17.63 The specific guidance for Certificates of Analysis included in Section 11.4 should be met.
17.7 申訴與回收的處理（Handling of Complaints and Recalls）	

17.70 所有申訴與回收引起代理商、貿易商、經銷商、重分包裝廠或重標示廠注意者，應依第 15 章中的規定，保存申訴與回收的紀錄。	17.70 Agents, traders, distributors, repackers, or relabellers should maintain records of complaints and recalls, as specified in Section 15, for all complaints and recalls that come to their attention.
17.71 如果情況許可，代理商、貿易商、經銷商、重分包裝廠或重標示廠應與原料藥或中間產物原製造廠檢討該申訴，以決定是否與可能已收到該原料藥或中間產物之其他客戶，及/或與主管機關啟動任何進一步的行動。申訴與回收原因的調查應由適當之當事人執行並予以文件化。	17.71 If the situation warrants, the agents, traders, distributors, repackers, or relabellers should review the complaint with the original API or intermediate manufacturer in order to determine whether any further action, either with other customers who may have received this API or intermediate or with the regulatory authority, or both, should be initiated. The investigation into the cause for the complaint or recall should be conducted and documented by the appropriate party.
17.72 在申訴經提交給原料藥或中間產物之原製造廠時，代理商、貿易商、經銷商、重分包裝廠或重標示廠所保存之紀錄，應包括從原料藥或中間產物之原製造廠所收到的任何回應（包括日期及提供的資訊）。	17.72 Where a complaint is referred to the original API or intermediate manufacturer, the record maintained by the agents, traders, distributors, repackers, or relabellers should include any response received from the original API or intermediate manufacturer (including date and information provided).
17.8 退回品之處理（Handling of Returns）	
17.80 退回品應按第 14.52 條之規定處理之。代理商、貿易商、經銷商、重分包裝廠或重標示廠應保存該退回之原料藥及中間產物的文件。	17.80 Returns should be handled as specified in Section 14.52. The agents, traders, distributors, repackers, or relabellers should maintain documentation of returned APIs and intermediates.
18. 以細胞培養/醱酵製造之原料藥的特定規範（SPECIFIC GUIDANCE FOR APIs MANUFACTURED BY CELL CULTURE/FERMENTATION）	
18.1 一般規定（General）	

18.10 本章主要說明在前述章節中未能適當加以涵蓋的部份，針對使用天然或經由基因改造的微生物，進行細胞培養或醱酵來製造原料藥或中間產物特定的管制。本章與其他部分章節並非獨立而不相關的。一般而言，在其他章節所描述之原則是適用的。以傳統製程製造小分子量物質之醱酵原理與利用基因改造或非基因改造微生物來製造蛋白質及/或多肽之醱酵原理是相同的，主要的不同是在管制的程度。本章節主要在強調其不同點。一般而言，用在生產蛋白質及/或多肽之生物技術製程的管制等級，較傳統醱酵的管制為高。	18.10 Section 18 is intended to address specific controls for APIs or intermediates manufactured by cell culture or fermentation using natural or recombinant organisms and that have not been covered adequately in the previous sections. It is not intended to be a stand-alone Section. In general, the GMP principles in the other sections of this document apply. Note that the principles of fermentation for “classical” processes for production of small molecules and for processes using recombinant and non-recombinant organisms for production of proteins and/or polypeptides are the same, although the degree of control will differ. Where practical, this section will address these differences. In general, the degree of control for biotechnological processes used to produce proteins and polypeptides is greater than that for classical fermentation processes.

18.11 「生物技術製程」（生技）係指以細胞或微生物經由重組 DNA、融合瘤或其他生物技術來生產原料藥。「生物技術製程」生產的原料藥，通常是大分子量物質，如蛋白質與多肽，應依本章特定的規範來執行。一些小分子量的原料藥如抗生素、胺基酸、維生素以及碳水化合物，也能經由重組 DNA 的技術來生產。這些小分子原料藥管制的程度和傳統的醱酵相似。	18.11 The term “biotechnological process” (biotech) refers to the use of cells or organisms that have been generated or modified by recombinant DNA, hybridoma or other technology to produce APIs. The APIs produced by biotechnological processes normally consist of high molecular weight substances, such as proteins and polypeptides, for which specific guidance is given in this Section. Certain APIs of low molecular weight, such as antibiotics, amino acids, vitamins, and carbohydrates, can also be produced by recombinant DNA technology. The level of control for these types of APIs is similar to that employed for classical fermentation.
18.12 「傳統醱酵」係指用自然界的微生物及/或利用傳統方法（例如，照射/輻射或化學突變）改造的微生物，來生產原料藥。以傳統醱酵生產的原料藥通常是小分子量的產品，如抗生素、胺基酸、維生素及碳水化合物。	18.12 The term “classical fermentation” refers to processes that use microorganisms existing in nature and/or modified by conventional methods (e.g. irradiation or chemical mutagenesis) to produce APIs. APIs produced by “classical fermentation” are normally low molecular weight products such as antibiotics, amino acids, vitamins, and carbohydrates.

18.13 由細胞培養或醱酵方法生產原料藥或中間產物之生物學的製程包括有：細胞培養，或由微生物來進行萃取及純化。要注意的是，在製程中可能會有追加的步驟，如物理化學性質的修飾。由於所使用的原料來源（培養基、緩衝劑組成物）也可能提供潛在微生物污染源的生長環境。依據所使用的細胞或微生物來源、製備方法、原料藥或中間產物之預定用途在製程中適當製造的階段，必須監測及管制負荷菌、病毒污染及/或內毒素。	18.13 Production of APIs or intermediates from cell culture or fermentation involves biological processes such as cultivation of cells or extraction and purification of material from living organisms. Note that there may be additional process steps, such as physicochemical modification, that are part of the manufacturing process. The raw materials used (media, buffer components) may provide the potential for growth of microbiological contaminants. Depending on the source, method of preparation, and the intended use of the API or intermediate, control of bioburden, viral contamination, and/or endotoxins during manufacturing and monitoring of the process at appropriate stages may be necessary.
18.14 在製造過程中的所有階段，應建立適當的管制，以確保中間產物及/或原料藥之品質。由於本規範是由細胞培養/醱酵之步驟開始，在此之前的步驟（例如，建置細胞庫）應於適當的管制下執行。本規範適用於由細胞庫取出後，開始細胞培養/醱酵階段的製程。	18.14 Appropriate controls should be established at all stages of manufacturing to assure intermediate and/or API quality. While this Guide starts at the cell culture/fermentation step, prior steps (e.g. cell banking) should be performed under appropriate process controls. This Guide covers cell culture/fermentation from the point at which a vial of the cell bank is retrieved for use in manufacturing.
18.15 應使用適當的設備及環境管制，以使污染的風險降到最低。訂定環境品質的允收標準及監測的頻率應取決於生產步驟及生產條件（開放性、密閉性或圍堵性的系統）。	18.15 Appropriate equipment and environmental controls should be used to minimize the risk of contamination. The acceptance criteria for quality of the environment and the frequency of monitoring should depend on the step in production and the production conditions (open, closed, or contained systems).

18.16 通常，製程管制應考慮：	18.16 In general, process controls should take into account:
➢ 工作細胞庫的維護（合適時）；	➢ Maintenance of the working cell bank (where appropriate);
➢ 正確的細胞接種及細胞製程放大；	➢ Proper inoculation and expansion of the culture;
➢ 在醱酵/細胞培養期間之關鍵操作參數的管制；	➢ Control of the critical operating parameters during fermentation/cell culture;
➢ 合適時，監測製程之細胞生長、存活率（對大多數細胞的培養過程）及生產率；	➢ Monitoring of the process for cell growth, viability (for most cell culture processes) and productivity, where appropriate;
➢ 收集與移除細胞、細胞碎片及培養基組成物之純化程序的同時，保護中間產物或原料藥免於受污染（特別是微生物學上本質方面的污染）及品質的減損；	➢ Harvest and purification procedures that remove cells, cellular debris and media components while protecting the intermediate or API from contamination (particularly of a microbiological nature) and from loss of quality;
➢ 當需要時，在生產之適當階段監測負荷菌及內毒素的含量；以及	➢ Monitoring of bioburden and, where needed, endotoxin levels at appropriate stages of production; and
➢ 病毒安全性的考量應參閱 ICH 指引 Q5A 所述*「生物技術產品的品質」：源自人類或動物細胞株之生物技術產品的病毒安全性評估。*	➢ Viral safety concerns as described in ICH Guideline Q5A *Quality of Biotechnological Products: Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin.*
18.17 合適時，應證明如何由產品去除培養基組成物、宿主細胞之蛋白質、其他與製程及產品相關的不純物與污染物。	18.17 Where appropriate, the removal of media components, host cell proteins, other process-related impurities, product-related impurities and contaminants should be demonstrated.
18.2 細胞庫之維護及紀錄之保存（Cell Bank Maintenance and Record Keeping）	

18.20 細胞庫之進入/取用應限於經過授權的人員。	18.20 Access to cell banks should be limited to authorized personnel.
18.21 細胞庫應維持在經設計之儲存條件下，以維持細胞存活率並防止污染。	18.21 Cell banks should be maintained under storage conditions designed to maintain viability and prevent contamination.
18.22 取自細胞庫的細胞小瓶之使用及儲存條件的紀錄應加以保存。	18.22 Records of the use of the vials from the cell banks and storage conditions should be maintained.
18.23 合適時，細胞庫應定期監測，以確定其適用性。	18.23 Where appropriate, cell banks should be periodically monitored to determine suitability for use.
18.24 關於細胞庫建置之較完整的討論，參見 ICH 指引 Q5D *生物技術產品之品質：用於生物技術/生物產品之生產的細胞基質之衍生及特徵訂定*。	18.24 See ICH Guideline Q5D *Quality of Biotechnological Products: Derivation and Characterization of Cell Substrates Used for Production of Biotechnological/Biological Products* for a more complete discussion of cell banking.
18.3 細胞培養/醱酵（Cell Culture/Fermentation）	
18.30 細胞基質、培養基、緩衝劑及氣體等需在無菌條件下添加時，可能時應使用密閉性或圍堵性的系統。若在開放性的容器中執行接種或後續的移轉或添加（培養基、緩衝劑）時，應備有管制及程序，以使污染的風險降到最低。	18.30 Where aseptic addition of cell substrates, media, buffers, and gases is needed, closed or contained systems should be used where possible. If the inoculation of the initial vessel or subsequent transfers or additions (media, buffers) are performed in open vessels, there should be controls and procedures in place to minimize the risk of contamination.
18.31 由於原料藥之品質可能受微生物之污染的影響，使用開放性容器之操作應在生物安全櫃中或受類似管制之環境中執行。	18.31 Where the quality of the API can be affected by microbial contamination, manipulations using open vessels should be performed in a biosafety cabinet or similarly controlled environment.
18.32 處理細胞培養的人員應穿戴適當的防護，並應採取特別的預防措施。	18.32 Personnel should be appropriately gowned and take special precautions handling the cultures.

18.33 應監測關鍵的操作參數（例如，溫度、pH 值、振盪/攪拌速率、氣體的添加、壓力）應予監測，以確保與既定製程之一致性。細胞生長、存活率（對大多數之細胞的培養過程），合適時，生產率也應予監測。關鍵參數可能隨製程而改變。對於傳統的醱酵，某些參數（例如，細胞存活率）可能不需要監測。	18.33 Critical operating parameters (for example temperature, pH, agitation rates, addition of gases, pressure) should be monitored to ensure consistency with the established process. Cell growth, viability (for most cell culture processes), and, where appropriate, productivity should also be monitored. Critical parameters will vary from one process to another, and for classical fermentation, certain parameters (cell viability, for example) may not need to be monitored.
18.34 細胞培養設備在使用後應予清潔並滅菌。合適時，醱酵設備應予清潔、滅菌處理或滅菌。	18.34 Cell culture equipment should be cleaned and sterilized after use. As appropriate, fermentation equipment should be cleaned, sanitized, or sterilized.
18.35 合適時，培養基應於使用前加以滅菌，以保護原料藥的品質。	18.35 Culture media should be sterilized before use when appropriate to protect the quality of the API.
18.36 應有適當的管制程序，以檢測污染及決定要採行的措施。該管制程序應包括評估產品污染所造成的影響、去除設備污染以及確保下一批次產品繼續生產不會受到污染的條件。如果在醱酵製程中，發現有外來微生物，應予以適當的鑑別，必要時，該污染源對產品品質的影響應予以評估。評估的結果應做為該產品處置的考量。	18.36 There should be appropriate procedures in place to detect contamination and determine the course of action to be taken. This should include procedures to determine the impact of the contamination on the product and those to decontaminate the equipment and return it to a condition to be used in subsequent batches. Foreign organisms observed during fermentation processes should be identified as appropriate and the effect of their presence on product quality should be assessed, if necessary. The results of such assessments should be taken into consideration in the disposition of the material produced.

18.37 污染事件的紀錄應予保存。	18.37 Records of contamination events should be maintained.
18.38 在多種產品的生產過程中，若有使用共用的設備時，在產品切換時，應採取適當的清潔措施，必要時，需採取適當的測試，以使交叉污染的風險降至最低。	18.38 Shared (multi-product) equipment may warrant additional testing after cleaning between product campaigns, as appropriate, to minimize the risk of cross-contamination.
18.4 收集、分離與純化（Harvesting, Isolation and Purification）	
18.40 收集的步驟，不論是移除細胞或細胞組成物，或是在細胞破碎後收集細胞組成物，均應在適當的設備及特別設計的環境下操作，使污染的風險降至最低。	18.40 Harvesting steps, either to remove cells or cellular components or to collect cellular components after disruption should be performed in equipment and areas designed to minimize the risk of contamination.
18.41 收集及純化應有適當的管制程序，包括移除或去活化生產用之微生物、細胞碎片及培養基組成物（同時使分解、污染及品質減損降至最低），以確保回收之中間產物或原料藥具一致品質。	18.41 Harvest and purification procedures that remove or inactivate the producing organism, cellular debris and media components (while minimizing degradation, contamination, and loss of quality) should be adequate to ensure that the intermediate or API is recovered with consistent quality.
18.42 所有設備使用後均應適當清潔，合適時並進行滅菌處理。若不損及中間產物或原料藥之品質情況時，得使用在連續批次間不予清潔之方式生產。	18.42 All equipment should be properly cleaned and, as appropriate, sanitized after use. Multiple successive batching without cleaning can be used if intermediate or API quality is not compromised.
18.43 若使用開放性系統時，純化應在適合保持產品品質的環境條件下執行。	18.43 If open systems are used, purification should be performed under environmental conditions appropriate for the preservation of product quality.
18.44 若多種產品使用同一設備，追加一些適當的管制可能是合適的，例如使用專用的層析樹脂，或是增加必要的測試。	18.44 Additional controls, such as the use of dedicated chromatography resins or additional testing, may be appropriate if equipment is to be used for multiple products.
18.5 病毒移除/去活化步驟（Viral Removal/Inactivation steps）	

18.50 關於更多特定資訊，參閱ICH指引Q5A *生物技術產品的品質：源自人類或動物細胞株之生物技術產品的病毒安全性評估*。	18.50 See the ICH Guideline Q5A *Quality of Biotechnological Products: Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin* for more specific information.
18.51 對於某些製程，病毒之移除及去活化步驟為關鍵的製程步驟。該步驟應在經過確效之參數範圍內執行。	18.51 Viral removal and viral inactivation steps are critical processing steps for some processes and should be performed within their validated parameters.
18.52 應採取適當的預防措施，以防止自病毒之移除/去活化步驟前及步驟後之間的潛在病毒污染。因此，開放性的製程作業應在與其他製程作業隔離之區域中執行。該區域並應有分開的空調系統。	18.52 Appropriate precautions should be taken to prevent potential viral contamination from pre-viral to post-viral removal/inactivation steps. Therefore, open processing should be performed in areas that are separate from other processing activities and have separate air handling units.
18.53 不同純化的步驟，通常不使用相同的設備。若要使用相同的設備，則於再使用之前，設備應予以正確的清潔及滅菌處理。應採取適當的預防措施，以避免潛在的病毒，經由設備或環境，由先前步驟傳遞下來。	18.53 The same equipment is not normally used for different purification steps. However, if the same equipment is to be used, the equipment should be appropriately cleaned and sanitized before reuse. Appropriate precautions should be taken to prevent potential virus carry-over (e.g., through equipment or environment) from previous steps.
19. 臨床試驗用原料藥（APIs FOR USE IN CLINICAL TRIALS）	
19.1 一般規定（General）	
19.10 並非所有本規範先前章節中之管制皆適合研究用新原料藥在其開發期間的製造。本章特別針對此等情況提供特定規範。	19.10 Not all the controls in the previous sections of this Guide are appropriate for the manufacture of a new API for investigational use during its development. Section 19 provides specific guidance unique to these circumstances.

19.11 臨床試驗用原料藥之製造所採用的管制，應與將該原料藥納入藥物產品之開發階段的管制一致。製程及試驗程序應具彈性，以隨製程知識之增進及隨藥物產品之臨床測試從臨床前階段到臨床階段之進展而提供改變。一旦達到原料藥預定供臨床試驗用藥物產品而生產之藥品開發的階段時，則製造廠應確保該原料藥是在使用適當生產及管制程序的適當設施中所製造，以確保該原料藥的品質。	19.11 The controls used in the manufacture of APIs for use in clinical trials should be consistent with the stage of development of the drug product incorporating the API. Process and test procedures should be flexible to provide for changes as knowledge of the process increases and clinical testing of a drug product progresses from pre-clinical stages through clinical stages. Once drug development reaches the stage where the API is produced for use in drug products intended for clinical trials, manufacturers should ensure that APIs are manufactured in suitable facilities using appropriate production and control procedures to ensure the quality of the API.
19.2 品質（Quality）	
19.20 適當的 GMP 概念應該應用於臨床試驗用原料藥的生產，並有適宜之批次放行機制。	19.20 Appropriate GMP concepts should be applied in the production of APIs for use in clinical trials with a suitable mechanism of approval of each batch.
19.21 為臨床試驗用原料藥之每一批次的核准或拒用，應設置獨立於生產部門之品質單位。	19.21 A quality unit(s) independent from production should be established for the approval or rejection of each batch of API for use in clinical trials.
19.22 有些測試功能通常由品質單位執行者，得在其他組織單位內執行之。	19.22 Some of the testing functions commonly performed by the quality unit(s) can be performed within other organizational units.
19.23 品質措施應包括原料、包裝材料、中間產物，以及原料藥的測試系統。	19.23 Quality measures should include a system for testing of raw materials, packaging materials, intermediates, and APIs.
19.24 製程及品質問題，應進行評估。	19.24 Process and quality problems should be evaluated.

19.25 預定為臨床試驗使用之原料藥的標示應經適當管制，並應將該物質識別為研究用。	19.25 Labeling for APIs intended for use in clinical trials should be appropriately controlled and should identify the material as being for investigational use.
19.3 設備與設施（Equipment and Facilities）	
19.30 在臨床開發之所有階段中，包含小規模設施/設備或實驗室的使用，以製造臨床試驗用原料藥之批次在內，應備有程序，以確保該設備業經校正、潔淨而且適合其預定用途。	19.30 During all phases of clinical development, including the use of small-scale facilities or laboratories to manufacture batches of APIs for use in clinical trials, procedures should be in place to ensure that equipment is calibrated, clean, and suitable for its intended use.
19.31 設施之使用的程序應確保該等材料係以使污染及交叉污染之風險降到最低的方式處理。	19.31 Procedures for the use of facilities should ensure that materials are handled in a manner that minimizes the risk of contamination and cross-contamination.
19.4 原料管制（Control of Raw Materials）	
19.40 臨床試驗用原料藥之生產所使用的原料，應經由測試加以評估，或應附有供應商的分析而接受並且進行鑑別測試。當原料經認定為具危害性時，憑供應商之分析應足以取代測試。	19.40 Raw materials used in production of APIs for use in clinical trials should be evaluated by testing, or received with a supplier's analysis and subjected to identity testing. When a material is considered hazardous, a supplier's analysis should suffice.
19.41 有些情況中，原料的適用性得在使用前根據小規模反應（亦即，試用測試）的可接受性予以決定之，而非單以分析測試為基礎。	19.41 In some instances, the suitability of a raw material can be determined before use based on acceptability in small-scale reactions (i.e., use testing) rather than on analytical testing alone.
19.5 生產（Production）	

19.50 臨床試驗用原料藥之生產，應以實驗筆記本、批次紀錄，或經由其他適當方式予以文件化。該等文件應包含關於生產原料、設備、操作以及科學觀察所見之使用等的資訊。	19.50 The production of APIs for use in clinical trials should be documented in laboratory notebooks, batch records, or by other appropriate means. These documents should include information on the use of production materials, equipment, processing, and scientific observations.
19.51 預期的產量/產率比使用於商業製程中之預期的產量/產率可能變異較多及較不確定。對產量/產率之變動不期望進行調查。	19.51 Expected yields can be more variable and less defined than the expected yields used in commercial processes. Investigations into yield variations are not expected.
19.6 確效（Validation）	
19.60 在生產單一原料藥批次時，或在原料藥開發中有製程變更，而使批次複製困難或不準確時，臨床試驗用原料藥之生產的製程確效通常是不適當的。管制、校正及合適時設備驗證的組合，可在該發展階段確保原料藥的品質。	19.60 Process validation for the production of APIs for use in clinical trials is normally inappropriate, where a single API batch is produced or where process changes during API development make batch replication difficult or inexact. The combination of controls, calibration, and, where appropriate, equipment qualification assures API quality during this development phase.
19.61 當批次是為商業用途而生產時，即使該等批次係屬先導規模或小規模生產，仍應依第 12 章規定執行製程確效。	19.61 Process validation should be conducted in accordance with Section 12 when batches are produced for commercial use, even when such batches are produced on a pilot or small scale.
19.7 變更（Changes）	
19.70 在開發期間中，當獲得知識並放大生產規模時，變更是可預期的。生產、規格或試驗程序上之每一變更，均應予以適當記錄。	19.70 Changes are expected during development, as knowledge is gained and the production is scaled up. Every change in the production, specifications, or test procedures should be adequately recorded.
19.8 實驗室管制（Laboratory Controls）	

19.80 對於評估臨床試驗用原料藥之批次所執行的分析方法雖然可能未經確效，但該等方法在科學上應該是健全的。	19.80 While analytical methods performed to evaluate a batch of API for clinical trials may not yet be validated, they should be scientifically sound.
19.81 應備有保存所有批次之留樣品的系統。該系統應確保每一留樣品之足夠數量，在臨床試驗申請的核准、終止或中止之後，皆應保存一段適當時間。	19.81 A system for retaining reserve samples of all batches should be in place. This system should ensure that a sufficient quantity of each reserve sample is retained for an appropriate length of time after approval, termination, or discontinuation of an application.
19.82 末效日期及再驗日期，如同第 11.6 節中所界定者，適用於既有臨床試驗用之原料藥。對於新原料藥，通常第 11.6 節不適用於臨床試驗的早期階段。	19.82 Expiry and retest dating as defined in Section 11.6 applies to existing APIs used in clinical trials. For new APIs, Section 11.6 does not normally apply in early stages of clinical trials.
19.9 文件/文件製作（Documentation）	
19.90 應備有一個系統，確保臨床試驗用原料藥在開發及製造期間得到的資訊，均經文件化且可隨時取得。	19.90 A system should be in place to ensure that information gained during the development and the manufacture of APIs for use in clinical trials is documented and available.
19.91 用於支持臨床試驗用原料藥之批次放行的分析方法之開發與履行，應予適當地文件化。	19.91 The development and implementation of the analytical methods used to support the release of a batch of API for use in clinical trials should be appropriately documented.
19.92 應使用保存生產與管制紀錄及文件的系統。該系統應確保紀錄及文件在臨床試驗申請之核准、終止或中止之後，保存一段適當時間。	19.92 A system for retaining production and control records and documents should be used. This system should ensure that records and documents are retained for an appropriate length of time after the approval, termination, or discontinuation of an application.
20. 術語彙編（GLOSSARY）	
允收標準 對於試驗結果之接受性的數值限量、範圍或其他適當的量度。	**Acceptance Criteria** Numerical limits, ranges, or other suitable measures for acceptance of test results.

原料藥/藥物 預定用於藥物產品/藥品之製造的任何物質或物質的混合物，當其使用於藥品的生產時，成為該藥品之有效成分。該等物質意在對疾病之診斷、治療、緩解、處理或預防提供藥理活性或其他直接效應，或意在影響身體之結構與機能。	**Active Pharmaceutical Ingredient (API) (*or Drug Substance*)** Any substance or mixture of substances intended to be used in the manufacture of a drug (medicinal) product and that, when used in the production of a drug, becomes an active ingredient of the drug product. Such substances are intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease or to affect the structure and function of the body.
原料藥之起始物 使用於原料藥之生產，經化學反應併入該原料藥結構中，成為其重要化學結構片段之原料、中間產物或另一原料藥。原料藥之起始物可以是市售商品，或自一家以上之供應商依據契約/商業協議採購或在廠內所生產的物質。通常，原料藥之起始物具有經界定之化學性質及結構。	**API Starting Material** A raw material, intermediate, or an API that is used in the production of an API and that is incorporated as a significant structural fragment into the structure of the API. An API starting material can be an article of commerce, a material purchased from one or more suppliers under contract or commercial agreement, or produced in-house. API starting materials are normally of defined chemical properties and structure.
批 在一個製程中或一系列製程中所生產之特定量的物質，因此預期在規定的限量內是均質的。在連續的生產中，一個批次可能是相當於該生產過程所界定的段落。批量得以一固定量或以在固定時間間隔內所生產之量來界定。	**Batch (or Lot)** A specific quantity of material produced in a process or series of processes so that it is expected to be homogeneous within specified limits. In the case of continuous production, a batch may correspond to a defined fraction of the production. The batch size can be defined either by a fixed quantity or by the amount produced in a fixed time interval.
批號 識別一個批次之數字、文字及/或符號的獨特組合。藉此，可以確定其生產及運銷的歷史。	**Batch Number (or Lot Number)** A unique combination of numbers, letters, and/or symbols that identifies a batch (or lot) and from which the production and distribution history can be determined.

負荷菌 可能存在於原料、原料藥之起始物、中間產物或原料藥中之微生物的量及類型（例如，不論其是否為不合宜微生物）。除非其數量已超過限量，或經界定之不合宜微生物已被檢出，否則，負荷菌不得認定為污染。	**Bioburden** The level and type (e.g. objectionable or not) of micro-organisms that can be present in raw materials, API starting materials, intermediates or APIs. Bioburden should not be considered contamination unless the levels have been exceeded or defined objectionable organisms have been detected.
校正 一特定儀器或裝置，與對照標準品或可追溯標準品在適當量測範圍內所產生的結果進行比較，證明其產生之結果在規定限值內。	**Calibration** The demonstration that a particular instrument or device produces results within specified limits by comparison with results produced by a reference or traceable standard over an appropriate range of measurements.
電腦系統 經設計與組裝的一組硬體組件及相關軟體，以執行一特定功能或一組功能。	**Computer System** A group of hardware components and associated software designed and assembled to perform a specific function or group of functions.
污染 原料、中間產物或原料藥在生產、抽樣、分包裝或重分包裝、儲存或運送中，遭受到化學或微生物學特性之不純物或異物混入。	**Contamination** The undesired introduction of impurities of a chemical or microbiological nature, or of foreign matter, into or onto a raw material, intermediate, or API during production, sampling, packaging, or repackaging, storage or transport.
受託製造廠 代表原始製造廠執行一些製造方面的製造廠。	**Contract Manufacturer** A manufacturer performing some aspect of manufacturing on behalf of the original manufacturer.
關鍵性的 敘述必須管制在預定之標準內的製程步驟、製程條件、試驗要求，或其他相關參數或項目，以確保原料藥符合其規格。	**Critical** Describes a process step, process condition, test requirement, or other relevant parameter or item that must be controlled within predetermined criteria to ensure that the API meets its specification.

偏差 偏離經核准之指令或既定之標準。	**Deviation** Departure from an approved instruction or established standard.
藥物產品/藥品 在最終直接包裝中預定上市之劑型。（參考 ICH Q1A）。	**Drug (Medicinal) Product** The dosage form in the final immediate packaging intended for marketing. (Reference Q1A)
藥物/原料藥 參見「原料藥/藥物」。	**Drug Substance** See Active Pharmaceutical Ingredient.
末效日期 在原料藥之容器/標籤上所載之日期，指定該原料藥於所指定期間內，如儲存在所界定的條件下，可期待維持在既定架儲期規格內，並且在該日期之後不得使用。	**Expiry Date (or Expiration Date)** The date placed on the container/labels of an API designating the time during which the API is expected to remain within established shelf life specifications if stored under defined conditions and after which it should not be used.
不純物 出現於中間產物或原料藥中之任何非所預期的物質。	**Impurity** Any component present in the intermediate or API that is not the desired entity.
不純物描述 對出現於原料藥中之經辨識或未經辨識的不純物之敘述。	**Impurity Profile** A description of the identified and unidentified impurities present in an API.
製程中管制或製程管制 爲監測，或合適時為調整製程及/或確保中間產物或原料藥符合其規格，而在生產中執行的檢測。	**In-Process Control (or Process Control)** Checks performed during production in order to monitor and, if appropriate, to adjust the process and/or to ensure that the intermediate or API conforms to its specifications.
中間產物 在原料藥之製程步驟中產生的物質。該物質在變成原料藥前，需要進行進一步之分子改變或純化。中間產物可以是經分離的或是不經分離的。（註：本規範只規範在公司界定為原料藥之開始生產點後所生產的中間產物。）	**Intermediate** A material produced during steps of the processing of an API that undergoes further molecular change or purification before it becomes an API. Intermediates may or may not be isolated. (Note: this Guide only addresses those intermediates produced after the point that the company has defined as the point at which the production of the API begins.)

製造 原料藥之原物料接收、生產、分裝或包裝、重分包裝、標示、重標示、品質管制、放行、儲存，以及運銷等之所有作業及其相關的管制。	**Manufacture** All operations of receipt of materials, production, packaging, repackaging, labelling, relabelling, quality control, release, storage, and distribution of APIs and related controls.
原物料 用以指稱原料（起始原料、試劑、溶劑）、製程助劑、中間產物、原料藥，以及分裝或包裝與標示材料的一般術語。	**Material** A general term used to denote raw materials (starting materials, reagents, solvents), process aids, intermediates, APIs, and packaging and labeling materials.
母液 在結晶或分離過程後所留下之殘留液體。母液可能含有未反應的原料、中間產物、不同量/濃度的原料藥及/或不純物。這可能用於進一步處理。	**Mother Liquor** The residual liquid which remains after the crystallization or isolation processes. A mother liquor may contain unreacted materials, intermediates, levels of the API and/or impurities. It may be used for further processing.
包裝材料 預定用在儲存及運送期間保護中間產物或原料藥之任何物料。	**Packaging Material** Any material intended to protect an intermediate or API during storage and transport.
程序 直接或間接與中間產物或原料藥之製造有關之待執行的作業、待採取之預防及待運用之措施的文件化說明。	**Procedure** A documented description of the operations to be performed, the precautions to be taken, and measures to be applied directly or indirectly related to the manufacture of an intermediate or API.
製程助劑 除溶劑外，其本身不參與化學或生物學反應，用為中間產物或原料藥之製造的輔助物質（例如，過濾助劑、活性碳等）。	**Process Aids** Materials, excluding solvents, used as an aid in the manufacture of an intermediate or API that do not themselves participate in a chemical or biological reaction (e.g. filter aid, activated carbon, etc).
生產 原料藥之製備所涉及的所有操作，自原物料接收直到該原料藥之加工及分裝或包裝。	**Production** All operations involved in the preparation of an API from receipt of materials through processing and packaging of the API.

品質保證 為確保所有原料藥具有其預定用途所需之品質及其品質系統之維持的目標，所做之整體有組織的安排。	**Quality Assurance (QA)** The sum total of the organised arrangements made with the object of ensuring that all APIs are of the quality required for their intended use and that quality systems are maintained.
品質部門 獨立於生產並履行品質保證與品質管制責任之組織單元。該單元的型式得為分開之品質保證部門及品質管制部門或單一個人或一組人，依組織之大小與結構而定。	**Quality Unit(s)** An organizational unit independent of production which fulfills both Quality Assurance and Quality Control responsibilities. This can be in the form of separate QA and QC units or a single individual or group, depending upon the size and structure of the organization.
原料 用於指示供中間產物或原料藥生產用之起始物、試劑及溶劑的一般術語。	**Raw Material** A general term used to denote starting materials, reagents, and solvents intended for use in the production of intermediates or APIs.
一級對照標準品 經由一套廣泛的分析測試已經顯示應為高純度之真正品質的物質。該標準品可以是：（1）得自法定認可的來源，或（2）經由獨立合成所製備，或(3)得自高純度的既有生產物質，或（4）經由既有生產物質的進一步純化所製備。	**Reference Standard, Primary** A substance that has been shown by an extensive set of analytical tests to be authentic material that should be of high purity. This standard can be: (1) obtained from an officially recognised source, or (2) prepared by independent synthesis, or (3) obtained from existing production material of high purity, or (4) prepared by further purification of existing production material.
二級對照標準品 作為例行實驗室分析之對照標準品使用的既定品質與純度之物質，該品質與純度係與一級對照標準品的比較所顯示。	**Reference Standard, Secondary** A substance of established quality and purity, as shown by comparison to a primary reference standard, used as a reference standard for routine laboratory analysis.

重處理 將一中間產物或原料藥，包含不符合標準或規格者在內，導回製程中，並重複結晶步驟或其他適當的化學或物理操作步驟（例如，蒸餾、過濾、層析、粉碎），該等步驟為既定製造過程的一部分。製程中管制試驗已經顯示該步驟為不完全/尚未完成後，繼續該製程步驟是被認定為正常製程的一部分而非重處理。	**Reprocessing** Introducing an intermediate or API, including one that does not conform to standards or specifications, back into the process and repeating a crystallization step or other appropriate chemical or physical manipulation steps (e.g., distillation, filtration, chromatography, milling) that are part of the established manufacturing process. Continuation of a process step after an in-process control test has shown that the step is incomplete is considered to be part of the normal process, and not reprocessing.
再驗日期 當一原料、中間產物或原料藥應當再度檢驗，以確保其仍然適合使用的日期。	**Retest Date** The date when a material should be re-examined to ensure that it is still suitable for use.
再加工 對不符合標準或規格之中間產物或原料藥，使其接受已建立之製程的一個或一個以上不同之步驟製造（例如，使用不同溶劑進行再結晶），以獲得可接受之品質的中間產物或原料藥。	**Reworking** Subjecting an intermediate or API that does not conform to standards or specifications to one or more processing steps that are different from the established manufacturing process to obtain acceptable quality intermediate or API (e.g., recrystallizing with a different solvent).
簽名（經簽署的） 參見經簽署的定義。	**Signature (signed)** See definition for signed.
經…簽署（簽名） 執行一特定行動或審查之個人紀錄。該紀錄得為姓名之首字母、完整手寫簽名、私章或經認證且可靠的電子簽章。	**Signed (signature)** The record of the individual who performed a particular action or review. This record can be initials, full handwritten signature, personal seal, or authenticated and secure electronic signature.
溶劑 在中間產物或原料藥的製造中，作為溶液或懸浮液之製備的載劑/載體所使用的無機或有機的液體。	**Solvent** An inorganic or organic liquid used as a vehicle for the preparation of solutions or suspensions in the manufacture of an intermediate or API.

規格 試驗、參照之分析程序與適當允收標準的清單。該允收標準係對所描述之試驗的數字限值、範圍或其他標準。規格為對一原物料為其預定用途所建立之成套應符合的標準。符合規格意指，當原物料依照所列舉之分析程序進行測試時，將符合所列舉的允收標準。	**Specification** A list of tests, references to analytical procedures, and appropriate acceptance criteria that are numerical limits, ranges, or other criteria for the test described. It establishes the set of criteria to which a material should conform to be considered acceptable for its intended use. Conformance to specification means that the material, when tested according to the listed analytical procedures, will meet the listed acceptance criteria.
確效 係一個經文件化之計畫，對一特定製程、方法或系統，提供高度保證其會持續一致地產生符合預定允收標準的結果。	**Validation** A documented program that provides a high degree of assurance that a specific process, method, or system will consistently produce a result meeting pre-determined acceptance criteria.
確效計畫書 陳述確效將如何執行並界定允收標準的書面計畫。譬如，一個製造過程的計畫書。該計畫書是確認其製程/操作設備、關鍵製程參數/操作範圍、產品特徵、抽樣、所要收集的測試數據/資料、執行確效的次數，以及可接受的試驗結果。	**Validation Protocol** A written plan stating how validation will be conducted and defining acceptance criteria. For example, the protocol for a manufacturing process identifies processing equipment, critical process parameters/operating ranges, product characteristics, sampling, test data to be collected, number of validation runs, and acceptable test results.
預期產率 根據先前實驗室、先導規模或製造數據/資料，預期在任何適當的生產階段中，中間產物或原料藥的產量或理論產量的百分比（產率）。	**Yield, Expected** The quantity of material or the percentage of theoretical yield anticipated at any appropriate phase of production based on previous laboratory, pilot scale, or manufacturing data.
理論產量/產率 根據所要使用的原料量，在實際生產上無任何損失或錯誤時，將在任何適當的生產階段產出的量。	**Yield, Theoretical** The quantity that would be produced at any appropriate phase of production based upon the quantity of material to be used, in the absence of any loss or error in actual production.