國際醫藥品稽查協約組織之
藥品優良製造指引
（第一部、附則）

PIC/S：Guide to Good Manufacturing Practice for Medicinal Products
（Part I、Annexes）

PE009-9 (1 September 2009)

行政院衛生署

中華民國 100 年 1 月

檔　　號：
保存年限：

行政院衛生署　公告

發文日期　中華民國100年1月13日
發文字號　署授食字第0991104248號
附件：

主旨：公告「國際醫藥品稽查協約組織之藥品優良製造指引（PIC/S：Guide to Good Manufacturing Practice for Medicinal Products）」。

依據：藥物製造工廠設廠標準第三十四條。

公告事項：

一、本署已於99年2月26日會銜經濟部以署授食字第0991100269號、經工字第09904601110號令公布「藥物製造工廠設廠標準」部分條文。其中第三十四條條文明定：「西藥藥品之製造、加工、分裝或包裝，依國際醫藥品稽查協約組織有關藥品優良製造指引（PIC/S：Guide to Good Manufacturing Practice for Medicinal Products）之規定。」

二、配合該標準之施行，本署公告「國際醫藥品稽查協約組織之藥品優良製造指引（Guide to Good Manufacturing

Practice for Medicinal Products）」第一部及附則之中英文對照條文，供業者執行GMP之參考標準。

三、本條文另載於本署食品藥物管理局（網址：http://www.fda.gov.tw/）之「公告資訊」下之「本局公告」網頁及本署網站（網址：http://www.doh.gov.tw/）。

副本：

署長楊志良

本案依分層負責規定授權局長決行

序

藥品品質攸關國民健康，為維護國民用藥安全及建構西藥製造業持續的競爭優勢，並配合行政院「加強生物技術產業推動方案」，衛生署將提升我國GMP管理層次及國產製藥品質列為施政首要目標之一。

我國自民國71 年5 月公布實施「優良藥品製造標準(GMP) 」以來，國內藥廠製藥水準已有大幅度的提升。隨後，於民國84 年推動無菌製劑確效作業，更於民國88 年10 月21 日公告「藥品確效作業實施表」，全面推動藥品實施確效作業。衛生署近年來積極參與國際事務，尋求國際合作，面對國際間cGMP管理新趨勢，本署積極推動國內藥廠GMP管理制度國際化。國際醫藥品稽查協約組織（ The Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme, PIC/S ）對於促進GMP 之國際協合及標準一致化扮演重要角色，其所公布之「Guide to GMP for Medicinal Products」勢必成為未來GMP 之國際標準，透過採用GMP 國際標準（PIC/S GMP Guide），將提升製藥品質及促進產業成長，進而提升國際競爭力。

配合推動藥品GMP標準國際化，本署於96 年8 月30 日公布「國際醫藥品稽查協約組織(PIC/S) 藥品優良製造規範指導手冊（總則與附則），並於99年2月26日正式修正藥物製造工廠設廠標準第三編藥品優良製造規範第三十四條之規定，明確規範西藥藥品之製造、加工、分裝或包裝，應依國際醫藥品稽查協約組織有關藥品優良製造指引（PIC/S：Guide to Good Manufacturing Practice for Medicinal Products）之規定。

PIC/S組織所公布之藥品GMP指引分為二部（Part I及Part II）及附則（Annexes），第一部（Part I）涵蓋藥品製造之GMP原則，第二部（Part II）則涵蓋原料藥之GMP作業，而附則提供特殊領域之詳細作業規範，不同之附則可同時運用於產品之製造；另，部分使用於指引中之專有名詞，則併於附則內供參。本公告之GMP指引涵蓋PIC/S於2009 年9 月1日（PE009-9）公布之PIC/S GMP Guide 第一部（Part I）與附則（Annex 1,2,3,6,8,9,10,11,12,13,14,15,19&20），內容以中英文對照方式呈現。其中第一部第一章新增品質風險管理之要求，業者可參酌附則20之內容進行藥品品質風險之評估、管制、溝通及檢討。未來，PIC/S 組織若更新其GMP條文時，本署將配合隨時更新並公告週知。

行政院衛生署食品藥物管理局

中華民國 100 年 1 月

第一部（Part I）

目　錄

附 則（Annexes）

目　錄

第一章　品質管理（QUALITY MANAGEMENT）

原則（PRINCIPLE）	
製造許可的持有者製造藥品時，應確保該藥品適合其預定用途，符合上市許可的要求，且不會由於安全性、品質或有效性的不足而使病人陷於危險。該品質目標之達成是高層管理者的責任，且需要公司內各部門及所有階層之人員，以及公司之供應商與經銷商的參與和許諾。	The holder of a manufacturing authorisation must manufacture medicinal products so as to ensure that they are fit for their intended use, comply with the requirements of the Marketing Authorisation and do not place patients at risk due to inadequate safety, quality or efficacy. The attainment of this quality objective is the responsibility of senior management and requires the participation and commitment by staff in many different departments and at all levels within the company, by the company's suppliers and by the distributors.
為可靠達成該品質目標，應有全面設計並正確實施的品質保證系統。該系統涵蓋優良製造規範、品質管制及品質風險管理，應充分文件化，並監測其效果。品質保證系統的所有部門應適當配置能勝任的人員，以及合適且足夠的廠房、設備與設施。製造許可的持有者及被授權人員另有其他法律責任。	To achieve the quality objective reliably there must be a comprehensively designed and correctly implemented system of Quality Assurance incorporating Good Manufacturing Practice, and thus Quality Control and Quality Risk Management. It should be fully documented and its effectiveness monitored. All parts of the Quality Assurance systems should be adequately resourced with competent personnel, and suitable and sufficient premises, equipment and facilities. There are additional legal responsibilities for the holder of the manufacturing authorisation and for the authorised person(s).
品質保證、優良製造規範、品質管制及品質風險管理的基本概念是相互關聯的。在本章中將予以描述，以強調其間之關係及其對於藥品生產及管制之基本的重要性。	The basic concepts of Quality Assurance, Good Manufacturing Practice, Quality Control and Quality Risk Management are inter-related. They are described here in order to emphasise their relationships and their fundamental importance to the production and control of medicinal products.
品質保證（QUALITY ASSURANCE）	

1.1. 品質保證是一個廣泛的概念。該概念涵蓋單獨或共同影響產品品質的所有事項。品質保證是經組織之安排的總和，以確保藥品具有預定用途所需之品質。因此，品質保證係結合優良製造規範加上本指引範圍外之其他因素。該適合於藥品製造的品質保證系統應確保下列事項：	1.1 . Quality Assurance is a wide-ranging concept, which covers all matters, which individually or collectively influence the quality of a product. It is the sum total of the organised arrangements made with the objective of ensuring that medicinal products are of the quality required for their intended use. Quality Assurance therefore incorporates Good Manufacturing Practice plus other factors outside the scope of this Guide. The system of Quality Assurance appropriate for the manufacture of medicinal products should ensure that:
i. 藥品之設計與開發方式應考慮優良製造規範的要求；	i. medicinal products are designed and developed in a way that takes account of the requirements of Good Manufacturing Practice ;
ii. 生產和管制作業應予清楚界定，並採用優良製造規範；	ii. production and control operations are clearly specified and Good Manufacturing Practice adopted;
iii. 管理責任應予清楚界定；	iii. managerial responsibilities are clearly specified;
iv. 為正確之原料及包裝材料的製造、供應與使用做出安排；	iv. arrangements are made for the manufacture, supply and use of the correct starting and packaging materials;
v. 半製品/中間產品的所有必要管制，以及任何其他製程中管制與確效均已執行；	v. all necessary controls on intermediate products, and any other in-process controls and validations are carried out;
vi. 最終產品依界定的程序，正確地操作及核對；	vi. the finished product is correctly processed and checked, according to the defined procedures;

vii. 未經被授權人員認可每一生產批次皆已依上市許可及任何有關藥品之生產、管制及放行的法規之要求生產與管制前，該藥品不得銷售或供應；	vii. medicinal products are not sold or supplied before an authorised person has certified that each production batch has been produced and controlled in accordance with the requirements of the marketing authorisation and any other regulations relevant to the production, control and release of medicinal products;
viii. 藥品之儲存、運銷及後續的處理應有妥善的安排，以確保在架儲期間能維持其品質；	viii. satisfactory arrangements exist to ensure, as far as possible, that the medicinal products are stored, distributed and subsequently handled so that quality is maintained throughout their shelf life;
ix. 有自我查核及/或品質稽查的程序，以定期評估品質保證系統之有效性及適用性。	ix. there is a procedure for self-inspection and/or quality audit which regularly appraises the effectiveness and applicability of the quality assurance system.
藥品優良製造規範（GMP） **GOOD MANUFACTURING PRACTICE FOR MEDICINAL PRODUCTS (GMP)**	
1.2. 優良製造規範係品質保證的一部分，用以確保藥品一致地生產及管制，以達到適合其預定用途及如同上市許可或產品規格所要求之品質標準。GMP 的基本要求為：	1.2. Good Manufacturing Practice is that part of Quality Assurance which ensures that Medicinal products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing authorisation or product specification. The basic requirements of GMP are that:
i. 所有製造過程均已清楚地界定，按照經驗有系統地檢討，顯示其能一致地製造所要求之品質並符合其規格的藥品。	i. all manufacturing processes are clearly defined, systematically reviewed in the light of experience and shown to be capable of consistently manufacturing medicinal products of the required quality and complying with their specifications:
ii. 製程的關鍵步驟及對製程的重大變更業經確效；	ii. critical steps of manufacturing processes and significant changes to the process are validated;

iii. 提供優良製造規範所需之資源包括：	iii. all necessary facilities for GMP are provided including:
a. 經適當資格檢定與訓練的人員；	a. appropriately qualified and trained personnel;
b. 足夠的廠房與作業空間；	b. adequate premises and space;
c. 適當的設備及支援服務；	c. suitable equipment and services;
d. 正確的原物料、容器及標籤；	d. correct materials, containers and labels;
e. 經核定之程序及指令；	e. approved procedures and instructions;
f. 適當之儲存及運送；	f. suitable storage and transport;
iv. 以清楚且不含糊的表達方式，將指令及程序書寫成指導性的型式。這特別適用於提供的資源；	iv. instructions and procedures are written in an instructional form in clear and unambiguous language, specifically applicable to the facilities provided;
v. 訓練操作者正確地執行程序；	v. operators are trained to carry out procedures correctly;
vi. 製造過程中，以手寫及/或記錄儀器所作紀錄，證明界定的程序與指令所要求之所有步驟皆已實際執行，且產品的數量與品質皆如所預期。任何重大的偏差均已完整記錄並經調查；	vi. records are made, manually an(and)/or by recording instruments, during manufacture which demonstrate that all the steps required by the defined procedures and instructions were in fact taken and that the quantity and quality of the product was as expected. Any significant deviations are fully recorded and investigated;
vii. 包含運銷在內之製造紀錄，應以可理解及可取得的形式保存，以利追溯批次之完整歷程；	vii. records of manufacture including distribution which enable the complete history of a batch to be traced, are retained in a comprehensible and accessible form;
viii. 產品的運銷(批發)應使其對於產品品質的任何風險降到最低；	viii. the distribution (wholesaling) of the products minimises any risk to their quality;
ix. 應有一套自銷售或供應點回收任何批次產品之系統；	ix. a system is available to recall any batch of product, from sale or supply;
x. 審查關於上市產品的申訴，調查品質瑕疵的原因，且對於該瑕疵產品採取適當的措施，以防止其再度發生。	x. complaints about marketed products are examined, the causes of quality defects investigated and appropriate measures taken in respect of the defective products and to prevent re-occurrence.

品質管制（QUALITY CONTROL）	
1.3. 品質管制是優良製造規範的一部分，涉及抽樣、規格及檢驗，且與組織、文件與放行程序有關，用以確保必要且相關的試驗已確實執行，並確保品質判定合格前，原物料不會放行使用，產品不會放行銷售或供應。品質管制的基本要求是：	1.3. Quality Control is that part of Good Manufacturing Practice which is concerned with sampling, specifications and testing, and with the organisation, documentation and release procedures which ensure that the necessary and relevant tests are actually carried out and that materials are not released for use, nor products released for sale or supply, until their quality has been judged to be satisfactory. The basic requirements of Quality Control are that:
i. 具有適當的設施、受過訓練的人員及經認可的程序，以供抽樣、檢查和檢驗原料、包裝材料、半製品/中間產品、待分/包裝產品及最終產品，並於適當時為優良製造規範之目的監測環境條件；	i. adequate facilities, trained personnel and approved procedures are available for sampling, inspecting and testing starting materials, packaging materials, intermediate, bulk, and finished products, and where appropriate for monitoring environmental conditions for GMP purposes;
ii. 原料、包裝材料、半製品/中間產品、待分/包裝產品及最終產品的樣品應經品質管制部門核准的人員及方法抽取之；	ii. samples of starting materials, packaging materials, intermediate products, bulk products and finished products are taken by personnel and by methods approved by Quality Control;
iii. 檢驗方法業經確效；	iii. test methods are validated;
iv. 應以手寫及/或記錄儀器製作紀錄，證明所有要求的抽樣、檢查及檢驗程序皆已實際執行。任何偏差均完整記錄並經調查；	iv. records are made, manually and/or by recording instruments which demonstrate that all the required sampling, inspecting and testing procedures were actually carried out. Any deviations are fully recorded and investigated;
v. 含符合上市許可的定性與定量組成之有效成分的最終產品，應符合所要求之純度，且密封在適當容器內，並正確地標示；	v. the finished products contain active ingredients complying with the qualitative and quantitative composition of the marketing authorisation, are of the purity required, and are enclosed within their proper containers and correctly labelled;

vi. 原物料、半製品/中間產品、待分/包裝產品及最終產品的檢查與檢驗結果均應予記錄，並對照其規格正式評估之。產品評價包含相關生產文件的審核與評估，以及與規定程序偏差的評價；	vi. records are made of the results of inspection and that testing of materials, intermediate, bulk, and finished products is formally assessed against specification. Product assessment includes a review and evaluation of relevant production documentation and an assessment of deviations from specified procedures;
vii. 每批產品，非經被授權人員認可符合相關許可之要求，不得放行銷售或供應；	vii. no batch of product is released for sale or supply prior to certification by an authorised person that it is in accordance with the requirements of the relevant authorisations;
viii. 應保留足夠的原料與產品的對照樣品，以容許未來必要時對該產品的檢查與檢驗。除非該產品以特別的大包裝生產，否則應保留在其最終包裝中。	viii. sufficient reference samples of starting materials and products are r etained to permit future examination of the product if necessary and that the product is retained in its final pack unless exceptionally large packs are produced.
產品品質檢討（PRODUCT QUALITY REVIEW）	
1.4. 所有經許可的藥品，含外銷專用產品，其常規定期性或輪動式的品質檢討應以證實既有製程的一致性、現行規格對原料與最終產品的適當性為目標執行之，以凸顯任何趨勢並確認產品與製程之改善事項。	1.4. Regular periodic or rolling quality reviews of all licensed medicinal products, including export only products, should be conducted with the objective of verifying the consistency of the existing process, the appropriateness of current specifications for both starting materials and finished product to highlight any trends and to identify product and process improvements.
考量先前之檢討，通常應每年執行一次並加以文件化，且至少包含下列項目：	Such reviews should normally be conducted and documented annually, taking into account previous reviews, and should include at least:
i. 用於產品之起始原料及包裝材料，特別是那些來自新來源者之檢討。	i. A review of starting materials including packaging materials used in the product, especially those from new sources.
ii. 關鍵之製程中管制及最終產品結果的檢討。	ii. A review of critical in-process controls and finished product results.

iii. 不符合既定規格的所有批次及其調查之檢討。	iii. A review of all batches that failed to meet established specification(s) and their investigation.
iv. 所有顯著的偏差或不符合、其相關的調查及採取的矯正預防措施效果之檢討。	iv. A review of all significant deviations or non- conformances, their related investigations, and the effectiveness of resultant corrective and preventative actions taken.
v. 製程或分析方法所有變更之檢討。	v. A review of all changes carried out to the processes or analytical methods.
vi. 上市許可變更所提交/核准/否准文件之檢討，包含外銷專用文件在內。	vi. A review of Marketing Authorisation variations submitted/granted/ refused, including those for third country (export only) dossiers.
vii. 安定性監測計畫的結果及任何不良趨勢之檢討。	vii. A review of the results of the stability monitoring programme and any adverse trends.
viii. 所有與品質相關之退回、申訴、回收及當時所執行調查之檢討。	viii. A review of all quality-related returns, complaints and recalls and the investigations performed at the time.
ix. 任何其他先前產品製程或設備矯正措施適當性之檢討。	ix. A review of adequacy of any other previous product process or equipment corrective actions.
x. 為新上市許可及變更上市許可所做之上市後許諾之檢討。	x. For new marketing authorisations and variations to marketing authorisations, a review of post-marketing commitments.
xi. 相關設備與公用設施，例如，空調系統（HVAC）、水系統、壓縮氣體等的驗證狀態。	xi. The qualification status of relevant equipment and utilities, e.g. HVAC, water, compressed gases, etc.
xii. 如同在第七章所界定之任何合約安排的檢討，確保其為最新。	xii. A review of any contractual arrangements as defined in Chapter 7 to ensure that they are up to date.

製造者與上市許可持有者不同時，雙方應評估本檢討的結果，而且應評估是否採取矯正預防措施或任何再確效。該矯正措施之理由應予文件化。雙方同意之矯正預防措施應以適時且有效的方式完成。對於持續進行之管理及這些行動的檢討應有管理程序，且在自我查核期間應證明這些程序之有效性。當符合科學正當性時，品質檢討得按其產品類型，例如固體劑型、液體劑型、無菌製劑等予以分組。	The manufacturer and marketing authorisation holder should evaluate the results of this review, where different, and an assessment made of whether corrective and preventative action or any revalidation should be undertaken. Reasons for such corrective actions should be documented. Agreed corrective and preventative actions should be completed in a timely and effective manner. There should be management procedures for the ongoing management and review of these actions and the effectiveness of these procedures verified during self inspection. Quality reviews may be grouped by product type, e.g. solid dosage forms, liquid dosage forms, sterile products, etc. where scientifically justified.
若上市許可持有者不是製造者時，雙方應有一份界定其各自在產品品質檢討上所負職責之技術協議書。負責批次之最終核定的被授權人員與上市許可持有者應確保品質檢討係適時執行且為準確的。	Where the marketing authorisation holder is not the manufacturer, there should be a technical agreement in place between the various parties that defines their respective responsibilities in producing the quality review. The authorised person responsible for final batch certification together with the marketing authorisation holder should ensure that the quality review is performed in a timely manner and is accurate.
品質風險管理（QUALITY RISK MANAGEMENT）	
1.5. 品質風險管理是針對藥品品質風險之評價、管制、溝通及檢討的系統過程。可用先期性及回溯性的方式來執行。	1.5. Quality risk management is a systematic process for the assessment, control, communication and review of risks to the quality of the medicinal product. It can be applied both proactively and retrospectively.
1.6 品質風險管理系統應確保下列項目：	1.6 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，最終並連結至病患之保護；	- 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;

-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.

第二章　人事（PERSONNEL）

原則（PRINCIPLE）	
一套令人滿意之品質保證系統的建立和維持，以及藥品的正確製造，均仰賴人員。因此，藥廠有責任配置足夠的合格人員。個別工作人員應清楚瞭解其負責之工作並作成紀錄。所有人員均應認知優良製造規範的原則與其息息相關，並接受職前及持續的訓練，包括與工作有關的衛生指導。	The establishment and maintenance of a satisfactory system of quality assurance and the correct manufacture of medicinal products relies upon people. For this reason there must be sufficient qualified personnel to carry out all the tasks which are the responsibility of the manufacturer. Individual responsibilities should be clearly understood by the individuals and recorded. All personnel should be aware of the principles of Good Manufacturing Practice that affect them and receive initial and continuing training, including hygiene instructions, relevant to their needs.
一般規定（GENERAL）	
2.1. 藥廠應配置足夠人員，且具必要資格及實務經驗。賦予每一個人的責任不應過廣，以致呈現對於品質的風險。	2.1 The manufacturer should have an adequate number of personnel with the necessary qualifications and practical experience. The responsibilities placed on any one individual should not be so extensive as to present any risk to quality.
2.2. 藥廠應有組織圖。各職位的負責人應有書面工作說明記載的特定職責，並經適當授權，以執行其職責。其職責得委由足以勝任的指定代理人行之。適用優良製造規範之有關人員，其職責不應有漏洞或未經說明的重疊。	2.2 The manufacturer must have an organisation chart. People in responsible positions should have specific duties recorded in written job descriptions and adequate authority to carry out their responsibilities. Their duties may be delegated to designated deputies of a satisfactory qualification level. There should be no gaps or unexplained overlaps in the responsibilities of those personnel concerned with the application of Good Manufacturing Practice.
關鍵人員（KEY PERSONNEL）	

2.3 關鍵人員包括生產主管、品質管制主管，以及如果這兩個人中至少有一位不負責產品之放行時，為放行之目的所指定的被授權人員。重要的職位通常應由專職人員擔任。生產和品質管制部門的主管應相互獨立。大藥廠可能有必要委派人員，擔任 2.5、2.6 及 2.7 中所列之部分職務。	2.3 Key Personnel includes the head of Production, the head of Quality Control, and if at least one of these persons is not responsible for the release of products the authorised person(s) designated for the purpose. Normally key posts should be occupied by full-time personnel. The heads of Production and Quality Control must be independent from each other. In large organisations, it may be necessary to delegate some of the functions listed in 2.5., 2.6. and 2.7.
2.4 …	2.4 …
2.5 生產部門的主管通常有下列職責：	2.5 The head of the Production Department generally has the following responsibilities:
i. 為獲得要求的品質，應確保該等產品依適當的文件生產與儲存；	i. to ensure that products are produced and stored according to the appropriate documentation in order to obtain the required quality;
ii. 核准與生產作業有關的指令，並確保其嚴格的實施；	ii. to approve the instructions relating to production operations and to ensure their strict implementation;
iii. 確保生產紀錄送到品質管制部門前，已由被授權人員評估與簽章；	iii. to ensure that the production records are evaluated and signed by an authorised person before they are sent to the Quality Control Department;
iv. 檢查/核對其部門、廠房設施及設備的維護保養；	iv. to check the maintenance of his department, premises and equipment;
v. 確保已完成適當的確效；	v. to ensure that the appropriate validations are done;
vi. 確保其部門的人員已執行所要求的職前與持續訓練，並依需求進行調適。	vi. to ensure that the required initial and continuing training of his department personnel is carried out and adapted according to need.
2.6 品質管制部門的主管通常有下列職責：	2.6 The head of the Quality Control Department generally has the following responsibilities:

i. 合適時，核准或拒用原料、包裝材料、半製品/中間產品、待分/包裝產品及最終產品；	i. to approve or reject, as he sees fit, starting materials, packaging materials, and intermediate, bulk and finished products;
ii. 評估批次紀錄；	ii. to evaluate batch records;
iii. 確保已執行所有必要的試驗；	iii. to ensure that all necessary testing is carried out;
iv. 核准規格、抽樣指令、檢驗方法及其他品質管制程序；	iv. to approve specifications, sampling instructions, test methods and other Quality Control procedures;
v. 受託檢驗者之核准及監督；	v. to approve and monitor any contract analysts;
vi. 檢查/核對其部門、廠房設施與設備的維護保養；	vi. to check the maintenance of his department, premises and equipment;
vii. 確保已完成適當的確效；	vii. to ensure that the appropriate validations are done;
viii. 確保其部門的人員已執行所要求的職前與持續訓練，並依需求進行調適。品質管制部門的其他職責概述於第六章。	viii. to ensure that the required initial and continuing training of his department personnel is carried out and adapted according to need. Other duties of the Quality Control Department are summarised in Chapter 6.
2.7 生產和品質管制的主管通常有一些分擔或共同負擔之關於品質的職責。這些職責應受國家法規的規範，包括：	2.7 The heads of Production and Quality Control generally have some shared, or jointly exercised, responsibilities relating to quality. These may include, subject to any national regulations:
➢ 書面的程序和其他文件的認可，包括修訂在內；	➢ the authorisation of written procedures and other documents, including amendments;
➢ 製造環境的監測與管制；	➢ the monitoring and control of the manufacturing environment;
➢ 工廠衛生；	➢ plant hygiene;
➢ 製程確效；	➢ process validation;
➢ 訓練；	➢ training;
➢ 原物料供應商的認可及監督；	➢ the approval and monitoring of suppliers of materials;
➢ 受託製造廠的認可及監督；	➢ the approval and monitoring of contract manufacturers;

➢ 原物料及產品之儲存條件的指示與監測；	➢ the designation and monitoring of storage conditions for materials and products;
➢ 紀錄的保存；	➢ the retention of records;
➢ 符合 GMP 要求之監督；	➢ the monitoring of compliance with the requirements of GMP;
➢ 樣品的檢查、調查與抽取，以便監測可能會影響產品品質的因素。	➢ the inspection, investigation, and taking of samples, in order to monitor factors which may affect product quality.
訓練（TRAINING）	
2.8 藥廠對於因其職責會進入生產區或管制實驗室的所有人員(包括技術、維修保養及清潔人員)，以及對於其活動可能影響產品品質的其他人員，應提供訓練。	2.8 The manufacturer should provide training for all the personnel whose duties take them into production areas or into control laboratories (including the technical, maintenance and cleaning personnel), and for other personnel whose activities could affect the quality of the product.
2.9 除了有關優良製造規範的理論與實務的基本訓練之外，新招募的人員應接受適合於其指定職責之適當訓練。同時也應提供持續的訓練，並應對訓練的實際效果定期予以評估。應有視情況經生產部門或品質管制部門的主管核准的訓練計畫。訓練紀錄應予保存。	2.9 Beside the basic training on the theory and practice of Good Manufacturing Practice, newly recruited personnel should receive training appropriate to the duties assigned to them. Continuing training should also be given, and its practical effectiveness should be periodically assessed. Training programmes should be available, approved by either the head of Production or the head of Quality Control, as appropriate. Training records should be kept.
2.10 對於在一有污染即產生危害之區域，例如在潔淨區域或在處理高活性、毒性、傳染性或致敏性物質之區域中工作的人員，應給予特別的訓練。	2.10 Personnel working in areas where contamination is a hazard, e.g. clean areas or areas where highly active, toxic, infectious or sensitising materials are handled, should be given specific training.

2.11 對於參訪人員及未受過訓練的人員，盡量不要帶入生產區及品質管制區中。無法避免時，應予事先提供資訊並密切監督，特別是關於個人衛生及規定的防護裝。	2.11 Visitors or untrained personnel should, preferably, not be taken into the production and Quality Control areas. If this is unavoidable, they should be given information in advance, particularly about personal hygiene and the prescribed protective clothing. They should be closely supervised.
2.12 訓練期間，應充分討論品質保證的概念及所有能增進其理解與執行的措施。	2.12 The concept of Quality Assurance and all the measures capable of improving its understanding and implementation should be fully discussed during the training sessions.
個人衛生（PERSONAL HYGIENE）	
2.13 詳細的衛生計畫應予建立，並針對工廠內的不同需求調適。該計畫應包括人員健康、衛生習慣及服裝等相關程序。因其職責而進入生產區及管制區的每個人員，皆應了解這些程序並嚴格遵守。管理階層應推動衛生計畫並在訓練期間予以廣泛討論。	2.13 Detailed hygiene programmes should be established and adapted to the different needs within the factory. They should include procedures relating to the health, hygiene practices and clothing of personnel. These procedures should be understood and followed in a very strict way by every person whose duties take him into the production and control areas. Hygiene programmes should be promoted by management and widely discussed during training sessions.
2.14 所有人員於雇用時皆應接受體檢。藥廠應有職責建立指令，以確保人員與產品品質可能有關之健康狀況會為藥廠所悉。第一次體檢後，視工作與人員健康之需要，應再執行體檢。	2.14 All personnel should receive medical examination upon recruitment. It must be the manufacturer's responsibility that there are instructions ensuring that health conditions that can be of relevance to the quality of products come to the manufacturer's knowledge. After the first medical examination, examinations should be carried out when necessary for the work and personal health.

2.15 應盡可能採取步驟，確保不會有受到傳染性疾病感染的人或在暴露的身體表面上有開放性傷口的人從事於藥品的製造。	2.15 Steps should be taken to ensure as far as is practicable that no person affected by an infectious disease or having open lesions on the exposed surface of the body is engaged in the manufacture of medicinal products.
2.16 進入製造區的每個人員皆應穿戴適合其所要執行操作之防護裝。	2.16 Every person entering the manufacturing areas should wear protective garments appropriate to the operations to be carried out.
2.17 生產區及儲存區應禁止飲食、嚼食或吸煙，或是儲存食物、飲料、菸類或個人的醫療用品。通常在製造區或產品可能會受到不良影響的任何其他區域中，應禁止任何不合衛生的行為。	2.17 Eating, drinking, chewing or smoking, or the storage of food, drink, smoking materials or personal medication in the production and storage areas should be prohibited. In general, any unhygienic practice within the manufacturing areas or in any other area where the product might be adversely affected, should be forbidden.
2.18 工作人員應避免雙手直接接觸暴露的產品及與產品接觸之設備的任何部分。	2.18 Direct contact should be avoided between the operator's hands and the exposed product as well as with any part of the equipment that comes into contact with the products.
2.19 應指導工作人員使用洗手設施。	2.19 Personnel should be instructed to use the hand-washing facilities.
2.20 其他任何特定的要求，例如製造無菌製劑等特殊類別的產品，收載於相關補充指引中。	2.20 Any specific requirements for the manufacture of special groups of products, for example sterile preparations, are covered in the Supplementary Guidelines.

第三章　廠房設施與設備（PREMISES AND EQUIPMENT）

原則（PRINCIPLE）	
廠房設施及設備的定位、設計、建造、調適及維護皆應適合於其所要執行的作業。其配置與設計應將產生錯誤的風險降到最低並容許有效的清潔及維護保養，以避免交叉污染、聚積粉塵或污垢，總之應以避免對產品品質有任何不利影響為目標。	Premises and equipment must be located, designed, constructed, adapted and maintained to suit the operations to be carried out. Their layout and design must aim to minimise the risk of errors and permit effective cleaning and maintenance in order to avoid cross-contamination, build up of dust or dirt and, in general, any adverse effect on the quality of products.
廠房設施（PREMISES）	
一般規定（General）	
3.1. 當與保護產品製造的措施一併考量時，廠房設施應坐落於引起原物料或產品之最低污染風險環境中。	3.1. Premises should be situated in an environment which, when considered together with measures to protect the manufacture, presents minimal risk of causing contamination of materials or products.
3.2. 廠房設施應謹慎維護，以確保其修理及維護作業不會危害於產品品質。廠房應予清潔，適當時並依詳細的書面程序消毒之。	3.2. Premises should be carefully maintained, ensuring that repair and maintenance operations do not present any hazard to the quality of products. They should be cleaned and, where applicable, disinfected according to detailed written procedures.
3.3. 照明、溫度、濕度及通風均應適當，且不會對製造及儲存中的藥品或設備的正確功能有直接或間接之不利影響。	3.3. Lighting, temperature, humidity and ventilation should be appropriate and such that they do not adversely affect, directly or indirectly, either the medicinal products during their manufacture and storage, or the accurate functioning of equipment.
3.4. 廠房設施的設計與配置應提供最大的保護，以防止昆蟲或其他動物的入侵。	3.4. Premises should be designed and equipped so as to afford maximum protection against the entry of insects or other animals.

3.5. 為防止未被授權的人員進入廠房，應採取步驟。生產區、儲存區及品質管制區應不得作為非該區工作人員的通路。	3.5. Steps should be taken in order to prevent the entry of unauthorised people. Production, storage and quality control areas should not be used as a right of way by personnel who do not work in them.
生產區（Production Area）	
3.6. 為使因交叉污染所引起之嚴重醫療傷害的風險降到最低，對於一些特殊藥品的生產，例如高致敏性物質（例如：青黴素類）或生物性製劑（例如：來自活的微生物），應有專用且自足圍堵的設施；尚有一些產品，例如某些抗生素、某些荷爾蒙、某些細胞毒類、某些高活性藥物及非藥品的生產不得在同一設施中為之。如採取特別的預防措施，並執行必要的確效時，在例外的情形下，可以接受在同一設施中的時段切換生產原則。工業毒物諸如殺蟲劑及除草劑，不得於藥品之廠房設施中製造。	3.6. In order to minimise the risk of a serious medical hazard due to cross contamination, dedicated and self-contained facilities must be available for the production of particular medicinal products, such as highly sensitising materials (e.g. penicillins) or biological preparations (e.g. from live micro-organisms). The production of certain additional products, such as certain antibiotics, certain hormones, certain cytotoxics, certain highly active drugs and non-medicinal products should not be conducted in the same facilities. For those products, in exceptional cases, the principle of campaign working in the same facilities can be accepted provided that specific precautions are taken and the necessary validations are made. The manufacture of technical poisons, such as pesticides and herbicides, should not be allowed in premises used for the manufacture of medicinal products.
3.7. 廠房設施應配合作業順序及所要求的潔淨度等級予以配置，以容許在合乎邏輯順序的相連區域中生產。	3.7. Premises should preferably be laid out in such a way as to allow the production to take place in areas connected in a logical order corresponding to the sequence of the operations and to the requisite cleanliness levels.

3.8. 作業空間與製程中儲存空間的適當性，應允許設備與原物料有條理且合乎邏輯的放置，使不同藥品或其組成物/組件間之混淆風險降到最低、避免交叉污染，並使任何製造或管制步驟的遺漏或是誤用的風險降到最低。	3.8. The adequacy of the working and in-process storage space should permit the orderly and logical positioning of equipment and materials so as to minimise the risk of confusion between different medicinal products or their components, to avoid cross-contamination and to minimise the risk of omission or wrong application of any of the manufacturing or control steps.
3.9. 原料與直接包裝材料、半製品/中間產品或待分/包裝產品暴露的環境，其內部表面(牆壁、地板及天花板)應平滑、無裂縫及無開口接縫，且不得脫落微粒物質，並應容易且有效地清潔，如有必要，還可消毒。	3.9. Where starting and primary packaging materials, intermediate or bulk products are exposed to the environment, interior surfaces (walls, floors and ceilings) should be smooth, free from cracks and open joints, and should not shed particulate matter and should permit easy and effective cleaning and, if necessary, disinfection.
3.10. 管路工程、照明裝置、通氣口以及其他設施之設計與定位應避免產生難以清潔的凹處。為維護保養之目的，應盡量從製造區外進行。	3.10. Pipe work, light fittings, ventilation points and other services should be designed and sited to avoid the creation of recesses which are difficult to clean. As far as possible, for maintenance purposes, they should be accessible from outside the manufacturing areas.
3.11. 排水孔的大小應合適，並備有隔氣彎管的集水溝。應盡量避免開放式溝渠，必要時，應為淺溝，以利清潔與消毒。	3.11. Drains should be of adequate size, and have trapped gullies. Open channels should be avoided where possible, but if necessary, they should be shallow to facilitate cleaning and disinfection.
3.12. 生產區應有效通風，並備有適合於所處理的產品、在該區域內從事的作業及外在環境等之空調設備（包含溫度，必要時包含濕度與過濾）。	3.12. Production areas should be effectively ventilated, with air control facilities (including temperature and, where necessary, humidity and filtration) appropriate both to the products handled, to the operations undertaken within them and to the external environment.
3.13. 原料的秤重，通常應在專為該用途所設	3.13. Weighing of starting materials usually

計之一間隔離的秤量室內為之。	should be carried out in a separate weighing room designed for that use.
3.14. 會產生粉塵的情況 (例如：抽樣、秤重、混合、製程操作及乾燥產品的分/包裝等期間中)，應採取特別的措施，以避免交叉污染並利於清潔。	3.14. In cases where dust is generated (e.g. during sampling, weighing, mixing and processing operations, packaging of dry products), specific provisions should be taken to avoid cross-contamination and facilitate cleaning.
3.15. 藥品分/包裝的廠房設施，應特別設計與配置，以避免混雜或交叉污染。	3.15. Premises for the packaging of medicinal products should be specifically designed and laid out so as to avoid mix-ups or cross-contamination.
3.16. 生產區應有良好的照明，特別是在執行線上目視管制的場所。	3.16. Productions areas should be well lit, particularly where visual on-line controls are carried out.
3.17. 製程中管制不會對生產帶來任何風險者，可在生產區內執行。	3.17. In-process controls may be carried out within the production area provided they do not carry any risk for the production.
儲存區（Storage Areas）	
3.18. 儲存區應有足夠的容量，以容許各種類別的原物料及產品有條理的儲存，包括：原料、包裝材料、半製品/中間產品、待分/包裝產品及最終產品、待驗產品、放行產品、拒用產品、退回產品或回收產品等。	3.18. Storage areas should be of sufficient capacity to allow orderly storage of the various categories of materials and products: starting and packaging materials, intermediate, bulk and finished products, products in quarantine, released, rejected, returned or recalled.
3.19. 儲存區應經設計或調適，以確保良好的儲存條件。特別是儲存區應保持潔淨與乾燥，並維持在可接受的溫度範圍內。有特別儲存條件要求時(例如溫度及濕度)，應提供這些儲存場所，並加以檢查/核對與監測。	3.19. Storage areas should be designed or adapted to ensure good storage conditions. In particular, they should be clean and dry and maintained within acceptable temperature limits. Where special storage conditions are required (e.g. temperature, humidity) these should be provided, checked and monitored.

3.20. 收貨區及出貨區應保護原物料及產品免於受天氣的影響。收貨區應加以設計並配置，以容許必要時能在儲存前清潔進廠原物料之容器。	3.20. Receiving and dispatch bays should protect materials and products from the weather. Receptions areas should be designed and equipped to allow containers of incoming materials to be cleaned where necessary before storage.
3.21. 藉由儲存於分開的區域來確保隔離/待驗狀態者，該區域應標識清楚，其進入應限於經授權之人員。任何取代該實體隔離的系統，應提供同等的安全性。	3.21. Where quarantine status is ensured by storage in separate areas, these areas must be clearly marked and their access restricted to authorised personnel. Any system replacing the physical quarantine should give equivalent security.
3.22. 原料通常應有隔離的抽樣區域。在儲存區內執行抽樣者，應以可防止污染或交叉污染的方式執行之。	3.22. There should normally be a separate sampling area for starting materials. If sampling is performed in the storage area, it should be conducted in such a way as to prevent contamination or cross-contamination.
3.23. 對於拒用、回收或退回的原物料或產品應提供隔離的儲存區域。	3.23. Segregated areas should be provided for the storage of rejected, recalled or returned materials or products.
3.24. 高活性物質或產品應儲存於安全且牢靠的區域中。	3.24. Highly active materials or products should be stored in safe and secure areas.
3.25. 印刷的包裝材料對於藥品的符合性是很重要的，應特別注意這些包裝材料之安全及牢靠的儲存。	3.25. Printed packaging materials are considered critical to the conformity of the medicinal products and special attention should be paid to the safe and secure storage of these materials.
品質管制區（Quality Control Areas）	
3.26. 通常，品質管制實驗室應與生產區隔離。這對生物學、微生物學及放射性同位素的管制實驗室特別重要。這些實驗室亦應互相隔離。	3.26. Normally, Quality Control laboratories should be separated from production areas. This is particularly important for laboratories for the control of biological, microbiological and radioisotopes, which should also be separated from each other.

3.27. 管制實驗室應設計成適合於在這些實驗室內執行的作業，並應給予足夠空間，以防止混雜及交叉污染。對於樣品與紀錄亦應有足夠且適當的儲存空間。	3.27. Control laboratories should be designed to suit the operations to be carried out in them. Sufficient space should be given to avoid mix-ups and cross contamination. There should be adequate suitable storage space for samples and records.
3.28. 為保護靈敏的儀器設備免於受振動、電子干擾及濕氣等之影響，分開的儀器室可能是必需的。	3.28. Separate rooms may be necessary to protect sensitive instruments from vibration, electrical interference, humidity, etc.
3.29. 處理特別物質，例如生物樣品或放射性樣品的實驗室，需要有特別的要求。	3.29. Special requirements are needed in laboratories handling particular substances, such as biological or radioactive samples.
附屬區域（Ancillary Areas）	
3.30. 休息室與餐廳應與其他區域隔離。	3.30. Rest and refreshment rooms should be separate from other areas.
3.31. 以更衣、盥洗及如廁為目的之設施應易於使用並適合使用之人數。廁所與生產區或儲存區不得直接相通。	3.31. Facilities for changing clothes, and for washing and toilet purposes should be easily accessible and appropriate for the number of users. Toilets should not directly communicate with production or storage areas.
3.32. 維修保養之工場應與生產區隔離並盡可能遠離。在生產區儲存零件及工具者，應儲存在其專用室或專用櫃中。	3.32. Maintenance workshops should as far as possible be separated from production areas. Whenever parts and tools are stored in the production area, they should be kept in rooms or lockers reserved for that use.
3.33. 動物室應與其他區域妥善隔離，並有分別的入口（動物的出入口）及空調處理設施。	3.33. Animal houses should be well isolated from other areas, with separate entrance (animal access) and air handling facilities.
設備（EQUIPMENT）	
3.34. 製造設備應經設計、配置及維修保養，以符合其預定目的。	3.34. Manufacturing equipment should be designed, located and maintained to suit its intended purpose.
3.35. 修理及維修保養作業不得對產品的品質呈現任何危害。	3.35. Repair and maintenance operations should not present any hazard to the quality of the products.

3.36. 製造設備之設計，應使其能容易且徹底地清洗。該設備應依詳細的書面程序清洗，並僅以潔淨且乾燥的狀態儲存。	3.36. Manufacturing equipment should be designed so that it can be easily and thoroughly cleaned. It should be cleaned according to detailed and written procedures and stored only in a clean and dry condition.
3.37. 洗滌及清潔設備應加以選擇與使用，使其不會成為污染的來源。	3.37. Washing and cleaning equipment should be chosen and used in order not to be a source of contamination.
3.38. 設備應以適當的方式安裝，以防止任何錯誤或污染的風險。	3.38. Equipment should be installed in such a way as to prevent any risk of error or of contamination.
3.39. 生產設備不得呈現對產品有任何危害。生產設備與產品接觸的部分，其反應性、加成性或吸附性不得高到足以影響產品的品質，而呈現任何危害。	3.39. Production equipment should not present any hazard to the products. The parts of the production equipment that come into contact with the product must not be reactive, additive or absorptive to such an extent that it will affect the quality of the product and thus present any hazard.
3.40. 應備有適當測量範圍與精密度的天平與量測設備，以供生產與管制作業使用。	3.40. Balances and measuring equipment of an appropriate range and precision should be available for production and control operations.
3.41. 量測、秤重、記錄及管制之設備應在界定的時間間隔內，使用適當的方法校正並核對之。這些檢測的適當紀錄應予保存。	3.41. Measuring, weighing, recording and control equipment should be calibrated and checked at defined intervals by appropriate methods. Adequate records of such tests should be maintained.
3.42. 固定的管線應清楚標示其內容物，可行時，流向亦應標示。	3.42. Fixed pipework should be clearly labelled to indicate the contents and, where applicable, the direction of flow.
3.43. 蒸餾水、去離子水及合適時其他用水之配管應依書面程序執行滅菌處理。該文件應詳載微生物污染的行動限量及應採取的措施。	3.43. Distilled, deionized and, where appropriate, other water pipes should be sanitised according to written procedures that detail the action limits for microbiological contamination and the measures to be taken.

3.44. 有缺陷的設備，如果可能，應從生產區及品質管制區移出，或至少清楚標示其為有缺陷的設備。	3.44. Defective equipment should, if possible, be removed from production and quality control areas, or at least be clearly labeled as defective.

第四章　文件（DOCUMENTATION）

原則（PRINCIPLE）	
優良的文件構成品質保證系統必要的部分。清楚的書面文件避免來自於口頭溝通的誤解，並且容許批次歷史的追蹤。規格、製造配方與指令、程序及紀錄必須免於錯誤，且可取得其書面資料。這些文件的易讀性極為重要。	Good documentation constitutes an essential part of the quality assurance system. Clearly written documentation prevents errors from spoken communication and permits tracing of batch history. Specifications, Manufacturing Formulae and instructions, procedures, and records must be free from errors and available in writing. The legibility of documents is of paramount importance.
一般規定（GENERAL）	
4.1. 規格應詳細描述於製造期間所使用或所得之產品或原物料必須符合的要求。規格為品質評估的基礎。製造配方、操作程序及分/包裝指令載明使用的全部原料，並明訂所有操作及分/包裝之作業程序。程序提供執行某些作業的指引，例如清潔、著裝、環境管制、抽樣、檢驗及設備的操作等。紀錄提供每批產品的歷史，包括其運銷及其他所有與最終產品品質有關的細節。	4.1. Specifications describe in detail the requirements with which the products or materials used or obtained during manufacture have to conform. They serve as a basis for quality evaluation. Manufacturing Formulae, Processing and Packaging Instructions state all the starting materials used and lay down all processing and packaging operations. Procedures give directions for performing certain operations e.g. cleaning, clothing, environmental control, sampling, testing, equipment operations. Records provide a history of each batch of product, including its distribution, and also of all other relevant circumstances pertinent for the quality of the final product.
4.2. 文件應謹慎設計、制訂、審核與分發，並應符合製造許可及上市許可文件中之相關部分。	4.2. Documents should be designed, prepared, reviewed and distributed with care. They should comply with the relevant parts of the manufacturing and marketing authorisation dossiers.
4.3. 文件應由適當之被授權人員核定、簽章並註明日期。	4.3. Documents should be approved, signed and dated by appropriate and authorised persons.

4.4. 文件應有明確的內容；其標題、性質及目的應清楚說明，並以整齊的方式編排，且易於核對。複製的文件應清楚易讀。由正本複製的工作文件不得因複製過程而導入任何錯誤。	4.4. Documents should have unambiguous contents; title, nature and purpose should be clearly stated. They should be laid out in an orderly fashion and be easy to check. Reproduced documents should be clear and legible. The reproduction of working documents from master documents must not allow any error to be introduced through the reproduction process.
4.5. 文件應定期再予檢查並不斷更新。當一份文件經修訂後，應有一系統運作，以防止作廢文件被誤用。	4.5. Documents should be regularly reviewed and kept up-to-date. When a document has been revised, systems should be operated to prevent inadvertent use of superseded documents.
4.6. 文件本身不得用手寫，但需手寫填入數據時，應清晰、可讀且擦不掉，並應有足夠的空間供此類數據的填入。	4.6. Documents should not be hand-written; although, where documents require the entry of data, these entries may be made in clear, legible, indelible handwriting. Sufficient space should be provided for such entries.
4.7. 文件上對於填入項目所做的任何更改應予簽章並註明日期；該更改應允許讀取原來的資訊。合適時，更改理由應記錄之。	4.7. Any alteration made to the entry on a document should be signed and dated; the alteration should permit the reading of the original information. Where appropriate, the reason for the alteration should be recorded.
4.8. 採取每項行動時，即應記錄。因此，與藥品製造有關的所有重要活動皆可追溯。這些紀錄應保存至最終產品的末效日期後至少一年。	4.8. The records should be made or completed at the time each action is taken and in such a way that all significant activities concerning the manufacture of medicinal products are traceable. They should be retained for at least one year after the expiry date of the finished product.

4.9. 數據可用電子數據處理系統、照相或其他可靠的方法記錄之，但應可取得關於使用中系統的詳細程序，且這些紀錄的精確性應予核對。文件化係由電子數據處理系統處理者，只有被授權人員才可進入或更改電腦中的數據，並應有修改和刪除的紀錄。進入系統應以密碼或其他方法限制之；重要數據輸入的結果應有獨立的核對。使用電子方法儲存的批次紀錄應以備份轉錄在磁帶、微縮軟片、紙張上或以其他方法保護之。保存期間可隨時取得數據是特別重要的。	4.9. Data may be recorded by electronic data processing systems, photographic or other reliable means, but detailed procedures relating to the system in use should be available and the accuracy of the records should be checked. If documentation is handled by electronic data processing methods, only authorised persons should be able to enter or modify data in the computer and there should be a record of changes and deletions; access should be restricted by passwords or other means and the result of entry of critical data should be independently checked. Batch records electronically stored should be protected by back-up transfer on magnetic tape, microfilm, paper or other means. It is particularly important that the data are readily available throughout the period of retention.
要求的文件（DOCUMENTS REQUIRED）	
規格（Specifications）	
4.10. 原料、包裝材料及最終產品，應有適當經核准且註明日期的規格；合適時，對於半製品/中間產品或待分/包裝產品，亦應有其規格。	4.10. There should be appropriately authorised and dated specifications for starting and packaging materials, and finished products; where appropriate, they should be also available for intermediate or bulk products.
原料及包裝材料的規格（Specifications for starting and packaging materials）	
4.11. 原料及直接包裝或印刷包裝材料之規格，如果可行，應包括下列項目:	4.11. Specifications for starting and primary or printed packaging materials should include, if applicable:
a) 原物料的描述，包括：	a) description of the materials, including:
➢ 指定的名稱及內部的參考代碼；	➢ the designated name and the internal code reference;
➢ 藥典個論的參考資料(如有時)；	➢ the reference, if any, to a pharmacopoeial monograph;

➢ 認可的供應商，及其原始的生產者(如可能時)；	➢ the approved suppliers and, if possible, the original producer of the products;
➢ 印刷材料的樣本；	➢ a specimen of printed materials;
b) 抽樣、檢驗的指示或相關的程序；	b) directions for sampling and testing or reference to procedures;
c) 具有合格標準範圍之定性及定量的要求；	c) qualitative and quantitative requirements with acceptance limits;
d) 儲存的條件及注意事項；	d) storage conditions and precautions;
e) 再驗前的最長儲存期間。	e) the maximum period of storage before re-examination.
半製品/中間產品及待分/包裝產品的規格（Specifications for intermediate and bulk products）	
4.12. 採購或發送半製品/中間產品和待分/包裝產品時，或從半製品/中間產品取得的數據使用於最終產品的評估時，應有半製品/中間產品與待分/包裝產品的規格。合適時，這些規格應類似於原料或最終產品的規格。	4.12. Specifications for intermediate and bulk products should be available if these are purchased or dispatched, or if data obtained from intermediate products are used for the evaluation of the finished product. The specifications should be similar to specifications for starting materials or for finished products, as appropriate.
最終產品的規格（Specifications for finished products）	
4.13. 最終產品的規格應包括下列項目:	4.13. Specifications for finished products should include:
a) 產品之指定名稱及其參考代碼(可行時)；	a) the designated name of the product and the code reference where applicable;
b) 配方或參考資料；	b) the formula or a reference to;
c) 產品劑型及包裝細節的描述；	c) a description of the pharmaceutical form and package details;
d) 抽樣及檢驗的指示或相關的程序；	d) directions for sampling and testing or a reference to procedures;
e) 具有合格標準範圍之定性及定量的要求；	e) the qualitative and quantitative requirements, with the acceptance limits;
f) 儲存條件及任何特別處理的注意事項(可行時)；	f) the storage conditions and any special handling precautions, where applicable;
g) 架儲期。	g) the shelf-life.

製造配方及操作指令 （MANUFACTURING FORMULA AND PROCESSING INSTRUCTIONS）	
每一產品及其批量應有經正式批准的製造配方及操作指令。這些常合併在一份文件中。	Formally authorised Manufacturing Formula and Processing Instructions should exist for each product and batch size to be manufactured. They are often combined in one document.
4.14. 製造配方應包括下列項目:	4.14. The Manufacturing Formula should include:
a) 產品名稱及其規格有關的產品參考代碼；	a) the name of the product, with a product reference code relating to its specification;
b) 產品劑型、含量及批量的描述；	b) description of the pharmaceutical form, strength of the product and batch size;
c) 所有使用之原料及其用量的清單，並描述其指定的名稱及專有的代碼；敘明在操作過程中可能喪失之任何物質；	c) a list of all starting materials to be used, with the amount of each, described using the designated name and a reference which is unique to that material; mention should be made of any substance that may disappear in the course of processing;
d) 說明預期最終產率及其允收範圍，以及相關半製品/中間產品產率 (可行時)。	d) a statement of the expected final yield with the acceptable limits, and of relevant intermediate yields, where applicable.
4.15. 操作指令應包括下列項目：	4.15. The Processing Instructions should include：
a) 作業場所及主要設備的說明；	a) statement of the processing location and the principal equipment to be used;
b) 準備關鍵設備所要使用的方法(例如清潔、組裝、校正、滅菌)或該等方法的參考資料；	b) the methods, or reference to the methods, to be used for preparing the critical equipment (e.g. cleaning, assembling, calibrating, sterilising);
c) 詳細之逐步操作的指令(例如原物料的檢查/核對、前處理、添加原料的順序、混合時間、溫度)；	c) detailed stepwise processing instructions (e.g. checks on materials, pretreatments, sequence for adding materials, mixing times, temperatures);
d) 任何製程中管制的指令及其範圍；	d) the instructions for any in-process controls with their limits;

e) 必要時，待分/包裝產品之儲存要求；可行時，包括其容器、標示及特別的儲存條件；	e) where necessary, the requirements for bulk storage of the products; including the container, labelling and special storage conditions where applicable;
f) 應遵守的任何特別注意事項。	f) any special precautions to be observed.
分/包裝指令（PACKAGING INSTRUCTIONS）	
4.16. 每項產品的包裝量與形式應有經正式核准的分/包裝指令。這些指令通常應包括下列項目或其參考資料：	4.16. There should be formally authorised Packaging Instructions for each product for pack size and type. These should normally include, or have a reference to, the following：
a) 產品名稱；	a) name of the product;
b) 劑型，及其含量(可行時)的描述；	b) description of its pharmaceutical form, and strength where applicable;
c) 包裝量，以產品在最終容器的數量、重量或容量表示；	c) the pack size expressed in terms of the number, weight or volume of the product in the final container;
d) 一個標準批量所需之全部包裝材料的清單，包括其數量、尺寸與型式及每種包裝材料之規格有關的代碼或參考號碼；	d) a complete list of all the packaging materials required for a standard batch size, including quantities, sizes and types, with the code or reference number relating to the specifications of each packaging material;
e) 合適時，相關已印刷之包裝材料的實例或複製品，以及產品批號及架儲期打印位置之樣本；	e) where appropriate, an example or reproduction of the relevant printed packaging materials, and specimens indicating where to apply batch number references, and shelf-life of the product;
f) 應遵行的特別注意事項，包括謹慎檢查作業區與設備，以確認作業開始前已完成分/包裝線的清線工作；	f) special precautions to be observed, including a careful examination of the area and equipment in order to ascertain the line clearance before operations begin;
g) 分/包裝作業之描述，包括任何重要的輔助作業及所需使用的設備；	g) a description of the packaging operation, including any significant subsidiary operations, and equipment to be used;
h) 製程中管制的細節，並有抽樣指令及允收範圍。	h) details of in-process controls with instructions for sampling and acceptance limits.

批次製造紀錄（BATCH PROCESSING RECORDS）	
4.17. 每一製造的批次應保存其批次製造紀錄，且依據現行認可的製造配方及操作指令。這些紀錄的製作方法應加以設計，避免抄錄錯誤。該紀錄應有該批次之批號。	4.17. A Batch Processing Record should be kept for each batch processed. It should be based on the relevant parts of the currently approved Manufacturing Formula and Processing Instructions. The method of preparation of such records should be designed to avoid transcription errors. The record should carry the number of the batch being manufactured.
任何操作開始前，應有檢查/核對紀錄，包括設備及工作場所無先前的產品、亦無非本製程所需的文件或原物料，且該設備是潔淨並適合使用。	Before any processing begins, there should be recorded checks that the equipment and work station are clear of previous products, documents or materials not required for the planned process, and that equipment is clean and suitable for use.
操作期間，操作者應在採取每一行動時記錄下列資訊，且在完成後，此紀錄應由該製程負責人員同意簽章並註明日期：	During processing, the following information should be recorded at the time each action is taken and, after completion, the record should be dated and signed in agreement by the person responsible for the processing operations :
a) 產品的名稱；	a) the name of the product;
b) 生產之開始、重要中間階段及完成的日期與時間；	b) dates and times of commencement, of significant intermediate stages and of completion of production;
c) 負責每一生產階段人員的姓名；	c) name of the person responsible for each stage of production;
d) 不同重要生產步驟之作業人員的簽名，以及合適時，這些作業(例如稱重)之每一步驟的核對人員簽名；	d) initials of the operator of different significant steps of production and, where appropriate, of the person who checked each of these operations (e.g. weighing);

e) 每一原料的批號及/或分析管制的號碼以及實際秤取之重量(包括所添加之任何收回或重處理的半製品之批號及重量)；	e) the batch number and/or analytical control number as well as the quantities of each starting material actually weighed (including the batch number and amount of any recovered or reprocessed material added);
f) 任何相關之操作作業或事件及使用之主要設備；	f) any relevant processing operation or event and major equipment used;
g) 製程中管制的紀錄、執行該管制人員的簽名及結果；	g) a record of the in-process controls and the initials of the person(s) carrying them out, and the results obtained;
h) 製造的不同階段及相關階段所獲得產品之產率；	h) the amount of product yield obtained at different and pertinent stages of manufacture;
i) 特別問題之備註，包含來自製造配方及操作指令之任何偏差的詳細記錄，並有經簽章認可。	i) notes on special problems including details, with signed authorisation for any deviation from the Manufacturing Formula and Processing Instructions.
批次分/包裝紀錄（BATCH PACKAGING RECORDS）	
4.18. 每一操作批次或部分批次應保存其批次分/包裝紀錄，該記錄應依據分/包裝指令的相關部分。該等紀錄的製作方法應加以設計，以避免抄錄錯誤，且應有批號及待分/包裝產品數量，以及將獲得最終產品的批號與預計的數量。	4.18. A Batch Packaging Record should be kept for each batch or part batch processed. It should be based on the relevant parts of the Packaging Instructions and the method of preparation of such records should be designed to avoid transcription errors. The record should carry the batch number and the quantity of bulk product to be packed, as well as the batch number and the planned quantity of finished product that will be obtained.
任何分/包裝作業開始前，應檢查/核對紀錄，包括設備和工作場所無先前的產品，亦無非本分/包裝作業所需的文件或原物料，且該設備是潔淨並適合使用。	Before any packaging operation begins, there should be recorded checks that the equipment and work station are clear of previous products, documents or materials not required for the planned packaging operations, and that equipment is clean and suitable for use.

下列資訊應由操作者在採取每一行動時記錄之，且在完成後，此紀錄應由該分/包裝作業負責人員同意簽章並註明日期：	The following information should be entered at the time each action is taken and, after completion, the record should be dated and signed in agreement by the person(s) responsible for the packaging operations:
a) 產品名稱；	a) the name of the product;
b) 分/包裝作業的日期及時間；	b) the date(s) and times of the packaging operations;
c) 負責執行分/包裝作業人員的姓名；	c) the name of the responsible person carrying out the packaging operation;
d) 不同重要步驟之作業人員的簽名；	d) the initials of the operators of the different significant steps;
e) 分/包裝指令之識別與符合性的核對紀錄，至少包含製程中管制的結果；	e) records of checks for identity and conformity with the Packaging Instructions including the results of in-process controls;
f) 執行分/包裝作業的細節，包含使用的設備與分/包裝線的參考資料；	f) details of the packaging operations carried out, including references to equipment and the packaging lines used;
g) 每當可能時，使用之印刷包裝材料的樣品，包括批次代碼、末效日期及任何附加套印的樣本；	g) whenever possible, samples of printed packaging materials used, including specimens of the batch coding, expiry dating and any additional overprinting;
h) 特別問題或異常事件之備註，包含來自製造配方及操作指令之任何偏差的詳細記錄，並有經簽章認可；	h) notes on any special problems or unusual events including details with signed authorisation for any deviation from the Manufacturing Formula and Processing Instructions;
i) 所有發出、使用、銷毀或退回庫存之印刷的包裝材料與待分/包裝產品的數量、參考號碼或其識別，及所得之產品數量，以提供適當的數量調和。	i) the quantities and reference number or identification of all printed packaging materials and bulk product issued, used, destroyed or returned to stock and the quantities of obtained product, in order to provide for an adequate reconciliation.
程序與紀錄（PROCEDURES AND RECORDS）	
接收（Receipt）	

4.19. 每一原料、直接包裝材料及印刷包裝材料於每次交貨時的接收，皆應有書面程序與紀錄。	4.19. There should be written procedures and records for the receipt of each delivery of each starting and primary and printed packaging material.
4.20. 接收紀錄應包括:	4.20. The records of the receipts should include:
a) 送貨單及容器上原物料之名稱；	a) the name of the material on the delivery note and the containers;
b) 原物料之"廠內"的名稱及/或代碼(如異於 a 時)；	b) the "in-house" name and/or code of material (if different from a);
c) 接收日期；	c) date of receipt;
d) 供應商的名稱及製造廠的名稱(如有可能)；	d) supplier's name and, if possible, manufacturer's name;
e) 製造廠的批號或參考號碼；	e) manufacturer's batch or reference number;
f) 接收的總量及容器的數目；	f) total quantity, and number of containers received;
g) 接收後指定的批號；	g) the batch number assigned after receipt;
h) 任何相關的加註 (例如：容器的狀態)。	h) any relevant comment (e.g. state of the containers).
4.21. 應有原料、包裝材料及合適時其他材料的廠內標示、隔離/待驗及儲存的書面程序。	4.21. There should be written procedures for the internal labelling, quarantine and storage of starting materials, packaging materials and other materials, as appropriate.
抽樣（Sampling）	
4.22. 抽樣應有書面程序。該程序應包括被授權抽樣之人員、所要使用的方法與設備、抽樣量及應遵守的預防措施，以避免原物料的污染或其品質的降低(請參見第六章，第十三條)	4.22. There should be written procedures for sampling, which include the person(s) authorised to take samples, the methods and equipment to be used, the amounts to be taken and any precautions to be observed to avoid contamination of the material or any deterioration in its quality (see Chapter 6, Item 13).
檢驗（Testing）	
4.23. 在不同製造階段檢驗原物料及產品，應有書面的程序。該程序描述使用的方法及設備。執行的檢驗應加以記錄 (請參見第六章，第十七條)。	4.23. There should be written procedures for testing materials and products at different stages of manufacture, describing the methods and equipment to be used. The tests performed should be recorded (see Chapter 6, Item 17).
其他（Other）	

4.24. 原物料及產品之放行與拒用，特別是由指派之被授權人員對最終產品放行供銷售，應有書面程序。	4.24. Written release and rejection procedures should be available for materials and products, and in particular for the release for sale of the finished product by the authorised person(s) designated for the purpose.
4.25. 應保存每一產品之運銷紀錄，以利必要時該批次的回收 (參見第八章)。	4.25. Records should be maintained of the distribution of each batch of a product in order to facilitate the recall of the batch if necessary (see Chapter 8).
4.26. 對下列事項應有書面程序及採取之行動，或合適時，其已達成結論的相關紀錄：	4.26. There should be written procedures and the associated records of actions taken or conclusions reached, where appropriate, for:
➢ 確效；	➢ validation;
➢ 設備之組裝及校正；	➢ equipment assembly and calibration;
➢ 維護保養、清潔與滅菌處理；	➢ maintenance, cleaning and sanitization;
➢ 人事，包括教育訓練、衣著及衛生；	➢ personnel matters including training, clothing, hygiene;
➢ 環境監測；	➢ environmental monitoring;
➢ 防蟲鼠；	➢ pest control;
➢ 申訴；	➢ complaints;
➢ 回收；	➢ recalls;
➢ 退回。	➢ returns.
4.27. 主要的製造與檢驗設備應有清楚的操作程序。	4.27. Clear operating procedures should be available for major items of manufacturing and test equipment.
4.28. 適當時，應保存主要或關鍵設備之任何確效、校正、維護保養及清潔或維修作業等紀錄之日誌，包括日期及作業人員身分。	4.28. Log books should be kept for major or critical equipment recording, as appropriate, any validations, calibrations, maintenance, cleaning or repair operations, including the dates and identity of people who carried these operations out.
4.29. 日誌亦應依時序記錄主要或關鍵設備的使用，並包括操作這些產品的區域。	4.29. Log books should also record in chronological order the use of major or critical equipment and the areas where the products have been processed.

第五章　生產（PRODUCTION）

原則（PRINCIPLE）	
生產作業應遵循清楚界定的程序，且符合優良製造規範的原則，以獲得要求之品質的產品，並應符合相關的製造及上市許可。	Production operations must follow clearly defined procedures; they must comply with the principles of Good Manufacturing Practice in order to obtain products of the requisite quality and be in accordance with the relevant manufacturing and marketing authorisations.
一般規定（GENERAL）	
5.1. 生產應由能勝任者執行與監督。	5.1. Production should be performed and supervised by competent people.
5.2 原物料與產品的所有處理，例如接收、待驗、抽樣、儲存、標示、調配、製造、分/包裝及運銷，應依書面程序或指令執行，必要時應予記錄。	5.2. All handling of materials and products, such as receipt and quarantine, sampling, storage, labelling, dispensing, processing, packaging and distribution should be done in accordance with written procedures or instructions and, where necessary, recorded.
5.3 所有進廠的原物料應予核對，以確保託運物與訂單相符。必要時，容器應予清潔，並以規定的資料標示。	5.3. All incoming materials should be checked to ensure that the consignment corresponds to the order. Containers should be cleaned where necessary and labelled with the prescribed data.
5.4 容器之破損及對原物料品質可能產生其不利影響的任何其他問題，應予調查、記錄並提報給品質管制部門。	5.4. Damage to containers and any other problem which might adversely affect the quality of a material should be investigated, recorded and reported to the Quality Control Department.
5.5 進廠原物料及最終產品在接收或加工後，應即為實體或行政管理上的隔離，直到其經放行供使用或運銷為止。	5.5. Incoming materials and finished products should be physically or administratively quarantined immediately after receipt or processing, until they have been released for use or distribution.
5.6 採購的半製品/中間產品或待分/包裝產品，在接收時應視同原料處理。	5.6. Intermediate and bulk products purchased as such should be handled on receipt as though they were starting materials.

5.7 所有原物料及產品皆應在藥廠建立的適當條件下，並以有條理的方式儲存，以容許批次的區隔及庫存品的輪換。	5.7. All materials and products should be stored under the appropriate conditions established by the manufacturer and in an orderly fashion to permit batch segregation and stock rotation.
5.8 視需要，應核對產率及進行重量/數量調和，以確保無超出允收範圍的差異。	5.8. Checks on yields, and reconciliation of quantities, should be carried out as necessary to ensure that there are no discrepancies outside acceptable limits.
5.9 不同產品的生產作業，不得在同一作業室內同時或接續地執行，除非無混雜或交叉污染的風險。	5.9. Operations on different products should not be carried out simultaneously or consecutively in the same room unless there is no risk of mix-up or cross-contamination.
5.10 製程的每一階段，皆應防止產品及原物料受微生物及其他污染。	5.10. At every stage of processing, products and materials should be protected from microbial and other contamination.
5.11 處理乾燥的原物料及產品時，應採取特別的防範措施，以防止粉塵的產生及散佈。特別適用於高活性或高致敏性物質的處理。	5.11. When working with dry materials and products, special precautions should be taken to prevent the generation and dissemination of dust. This applies particularly to the handling of highly active or sensitising materials.
5.12 操作全程中，所有原物料、半製品容器、設備的主要項目及合適時使用的操作室皆應標示，否則，應以操作中產品或原物料、其含量（如果可行）及批號等標示予以識別。可行時，該標示亦應提及生產階段。	5.12. At all times during processing, all materials, bulk containers, major items of equipment and where appropriate rooms used should be labelled or otherwise identified with an indication of the product or material being processed, its strength (where applicable) and batch number. Where applicable, this indication should also mention the stage of production.
5.13 用於容器、設備或作業場所的標示卡應清楚、明確，且使用公司一致的格式。標籤上除文字外，使用顏色標示其狀態(例如：待驗、合格、拒用、清潔…等)，通常是有幫助的。	5.13. Labels applied to containers, equipment or premises should be clear, unambiguous and in the company's agreed format. It is often helpful in addition to the wording on the labels to use colours to indicate status (for example, quarantined, accepted, rejected, clean, ...).

5.14 為確保用於將產品從一個區域輸送到另外一個區域的管線及其他設備係以正確的方式連接，應執行檢查。	5.14. Checks should be carried out to ensure that pipelines and other pieces of equipment used for the transportation of products from one area to another are connected in a correct manner.
5.15 應盡可能避免來自指令或作業程序的任何偏差。發生偏差時，應由權責人員以書面認可，適當時需有品質管制部門的參與。	5.15. Any deviation from instructions or procedures should be avoided as far as possible. If a deviation occur, it should be approved in writing by a competent person, with the involvement of the Quality Control Department when appropriate.
5.16 進入生產廠房應限於被授權人員。	5.16. Access to production premises should be restricted to authorised personnel.
5.17 通常，非藥品之生產應避免在預定生產藥品的區域與設備中為之。	5.17. Normally, the production of non-medicinal products should be avoided in areas and with the equipment destined for the production of medicinal products.
生產中交叉污染的防止 （PREVENTION OF CROSS-CONTAMINATION IN PRODUCTION）	
5.18 應防止原料或產品被另一原物料或產品污染。該意外交叉污染的風險，源於製程中未管制之原物料及產品所產生的粉塵、氣體、蒸氣、噴霧或微生物、設備上的殘留物及因作業人員的服裝等。該風險的嚴重性隨污染物的種類及被污染的產品而異，其中最具危害的污染物是高致敏性物質、含有活體的生物製劑、某些荷爾蒙類、細胞毒類及其他高活性的物質。污染尤對以注射、大劑量及/或長期投用的產品之使用最具風險。	5.18. Contamination of a starting material or of a product by another material or product must be avoided. This risk of accidental cross-contamination arises from the uncontrolled release of dust, gases, vapours, sprays or organisms from materials and products in process, from residues on equipment, and from operators' clothing. The significance of this risk varies with the type of contaminant and of product being contaminated. Amongst the most hazardous contaminants are highly sensitising materials, biological preparations containing living organisms, certain hormones, cytotoxics, and other highly active materials. Products in which contamination is likely to be most significant are those administered by injection, those given in large doses and/or

	over a long time.
5.19 交叉污染應以適當的技術或有組織的措施避免之，例如：	5.19. Cross-contamination should be avoided by appropriate technical or organisational measures, for example:
a) 在隔離的區域(對諸如青黴素類、活疫苗、活細菌製劑及一些其他生物性製劑的產品所要求)，或採分隔時段切換生產，其後應緊接著適當的清潔處理；	a) production in segregated areas (required for products such as penicillins, live vaccines, live bacterial preparations and some other biologicals), or by campaign (separation in time) followed by appropriate cleaning;
b) 備有適當的氣鎖室及空氣抽除設備；	b) providing appropriate air-locks and air extraction;
c) 將未經處理或未經充分處理的空氣之再循環或再進入所引起的污染風險降到最低；	c) minimising the risk of contamination caused by recirculation or re-entry of untreated or insufficiently treated air;
d) 製造具交叉污染特別風險之產品的區域內應保持穿著防護裝；	d) keeping protective clothing inside areas where products with special risk of cross-contamination are processed;
e) 設備的無效清潔是交叉污染的普遍來源，故應使用已知有效的清潔及去污染程序；	e) using cleaning and decontamination procedures of known effectiveness, as ineffective cleaning of equipment is a common source of cross contamination;
f) 使用密閉的生產系統；	f) using "closed systems" of production;
g) 檢驗設備上的殘留物並使用清潔狀態標籤。	g) testing for residues and use of cleaning status labels on equipment.
5.20 應依規定程序定期檢查防止交叉污染的措施及其有效性。	5.20. Measures to prevent cross-contamination and their effectiveness should be checked periodically according to set procedures.
確效（Validation ）	
5.21 確效試驗應強化優良製造規範，並依所界定的程序實施。其結果及結論應予記錄。	5.21. Validation studies should reinforce Good Manufacturing Practice and be conducted in accordance with defined procedures. Results and conclusions should be recorded.

5.22 當採用任何新的製造配方或製備方法時，應採取步驟以證明其對例行操作的適用性。使用規定的原物料及設備時，該界定的製程應表現其能生產出與所要求品質一致之產品。	5.22. When any new manufacturing formula or method of preparation is adopted, steps should be taken to demonstrate its suitability for routine processing. The defined process, using the materials and equipment specified, should be shown to yield a product consistently of the required quality.
5.23 對製造過程可能會影響產品品質及/或製程之再現性的重大修正，包括設備或原物料的任何變更，應加以確效。	5.23. Significant amendments to the manufacturing process, including any change in equipment or materials, which may affect product quality and/or the reproducibility of the process should be validated.
5.24 製程及程序應執行定期關鍵性再確效，以確保其維持達成預定結果的能力。	5.24. Processes and procedures should undergo periodic critical revalidation to ensure that they remain capable of achieving the intended results.
原料（STARTING MATERIALS）	
5.25 原料的採購是一項重要的作業，應有對供應商具特別且充分瞭解的人員參與。	5.25. The purchase of starting materials is an important operation which should involve staff who have a particular and thorough knowledge of the suppliers.
5.26 原料僅可向在相關規格上列名之經認可的供應商購買；可能時，應直接向生產者購買。建議藥廠建立原料規格時應與供應商討論。涉及原料之生產與管制的所有層面，包括其處理、標示、分/包裝的要求，以及申訴和拒用的程序等，與製造廠及供應商討論是有助益的。	5.26. Starting materials should only be purchased from approved suppliers named in the relevant specification and, where possible, directly from the producer. It is recommended that the specifications established by the manufacturer for the starting materials be discussed with the suppliers. It is of benefit that all aspects of the production and control of the starting material in question, including handling, labelling and packaging requirements, as well as complaints and rejection procedures are discussed with the manufacturer and the supplier.

5.27 每一次交貨，應檢查/核對容器的包裝、封條的完整性及送貨單與供應商標示之一致性。	5.27. For each delivery, the containers should be checked for integrity of package and seal and for correspondence between the delivery note and the supplier's labels.
5.28 原物料之一次交貨是由不同批次所組成者，每一批次應各自考慮其抽樣、檢驗與放行。	5.28. If one material delivery is made up of different batches, each batch must be considered as separate for sampling, testing and release.
5.29 儲存區的原料應適當地標示 (請參見第五章，第十三條)。標籤上應至少記載下列資料：	5.29. Starting materials in the storage area should be appropriately labelled (see Chapter 5, Item 13). Labels should bear at least the following information:
➢ 產品的指定名稱及其內部參考代碼(可行時)；	➢ the designated name of the product and the internal code reference where applicable;
➢ 接收時所給予的批號；	➢ a batch number given at receipt;
➢ 合適時，內容物的狀態(例如：待驗中、檢驗中、放行、拒用)；	➢ where appropriate, the status of the contents (e.g. in quarantine, on test, released, rejected);
➢ 合適時，末效日期或再檢驗的日期。	➢ where appropriate, an expiry date or a date beyond which retesting is necessary.
採用完全電腦化之儲存系統者，上述所有資料不必以易讀的方式印在標籤上。	When fully computerised storage systems are used, all the above information should not necessarily be in a legible form on the label.
5.30 應有適當的程序或措施來確保每一個原料容器之內容物的同一性。已抽樣之原包裝容器應予識別與標示 (請參見第六章，第十三條)。	5.30. There should be appropriate procedures or measures to assure the identity of the contents of each container of starting material. Bulk containers from which samples have been drawn should be identified (see Chapter 6, Item 13).
5.31 僅有經品質管制部門放行，且還在架儲期間內的原料始可使用。	5.31. Only starting materials which have been released by the Quality Control Department and which are within their shelf-life should be used.

5.32 原料只得由指定的人員依書面程序調配，以確保將正確的原料準確地稱入或量入潔淨且適切標示的容器中。	5.32. Starting materials should only be dispensed by designated persons, following a written procedure, to ensure that the correct materials are accurately weighed or measured into clean and properly labelled containers.
5.33 每一經調配之原料及其重量或容量，皆應個別檢查/核對並予以記錄。	5.33. Each dispensed material and its weight or volume should be independently checked and the check recorded.
5.34 每一批次調配的原料應保存在一起，並明顯地標示。	5.34. Materials dispensed for each batch should be kept together and conspicuously labelled as such.
半製品/中間產品及待分/包裝產品的操作作業（PROCESSING OPERATIONS INTERMEDIATE AND BULK PRODUCTS）	
5.35 任何操作作業開始前，應採取步驟，以確保作業區及設備是潔淨且無任何現行作業所不需要的原料、產品、產品殘留物或文件。	5.35. Before any processing operation is started, steps should be taken to ensure that the work area and equipment are clean and free from any starting materials, products, product residues or documents not required for the current operation.
5.36 半製品/中間產品或待分/包裝產品應保存在適當的條件下。	5.36. Intermediate and bulk products should be kept under appropriate conditions.
5.37 關鍵製程應經確效(參見本章之「確效」)。	5.37. Critical processes should be validated (see "VALIDATION" in this Chapter).
5.38 任何必要的製程中管制及環境管制均應執行並予記錄。	5.38. Any necessary in-process controls and environmental controls should be carried out and recorded.
5.39 與預期產率的任何顯著偏差均應予記錄並加以調查。	5.39. Any significant deviation from the expected yield should be recorded and investigated.
包裝材料（PACKAGING MATERIALS）	
5.40 直接包裝材料及經印刷的包裝材料之採購、處理及管制應比照原料給予同等注意。	5.40. The purchase, handling and control of primary and printed packaging materials should be accorded attention similar to that given to starting materials.

5.41 經印刷的包裝材料應予特別注意。該材料應儲存在足夠安全的條件中，使其足以排除未經授權的取用。切式標籤及其他散裝之印好的包裝材料應在分別的密閉容器中儲存與搬運，以免混雜。包裝材料應只得由被授權人員，依認可且文件化的程序發放使用。	5.41. Particular attention should be paid to printed materials. They should be stored in adequately secure conditions such as to exclude unauthorised access. Cut labels and other loose printed materials should be stored and transported in separate closed containers so as to avoid mix-ups. Packaging materials should be issued for use only by authorised personnel following an approved and documented procedure.
5.42 每一次交貨或每一批次之經印刷的包裝材料或直接包裝材料，均應給予專有的參考號碼或辨識標記。	5.42. Each delivery or batch of printed or primary packaging material should be given a specific reference number or identification mark.
5.43 過期或作廢的直接包裝材料或經印刷的包裝材料應予銷毀，並將該處置加以記錄。	5.43. Outdated or obsolete primary packaging material or printed packaging material should be destroyed and this disposal recorded.
分/包裝作業（PACKAGING OPERATIONS）	
5.44 建立分/包裝作業計畫時應特別注意，將交叉污染、混雜或替代的風險降到最低。除有實體隔離外，不同的產品不得在緊密相鄰處分/包裝。	5.44. When setting up a programme for the packaging operations, particular attention should be given to minimising the risk of cross-contamination, mix-ups or substitutions. Different products should not be packaged in close proximity unless there is physical segregation.
5.45 分/包裝作業開始前應採取步驟，以確保作業區、分/包裝線、印刷機及其他設備是潔淨的，且無現行作業所不要求之先前使用的任何產品、原物料或文件。分/包裝線的清線應依適當的查檢表執行。	5.45. Before packaging operations are begun, steps should be taken to ensure that the work area, packaging lines, printing machines and other equipment are clean and free from any products, materials or documents previously used, if these are not required for the current operation. The line-clearance should be performed according to an appropriate check-list.
5.46 作業中的產品名稱及批號，應標明在每一個分/包裝站或線上。	5.46. The name and batch number of the product being handled should be displayed at each packaging station or line.

5.47 所有產品及待用的包裝材料，交給分/包裝部門時皆應與分/包裝指令檢查/核對其數量、同一性及一致性。	5.47. All products and packaging materials to be used should be checked on delivery to the packaging department for quantity, identity and conformity with the Packaging Instructions.
5.48 充填用的容器在充填前應為潔淨的。應注意避免任何污染物並予以移除，例如玻璃碎片及金屬粒子。	5.48. Containers for filling should be clean before filling. Attention should be given to avoiding and removing any contaminants such as glass fragments and metal particles.
5.49 通常，充填與密封後應盡快加以標示。若非如此，則應採取適當的程序，以確保不會發生混雜或貼錯標籤。	5.49. Normally, filling and sealing should be followed as quickly as possible by labelling. If it is not the case, appropriate procedures should be applied to ensure that no mix-ups or mislabelling can occur.
5.50 任何印刷作業（例如代碼、末效日期）的正確性，不管是個別進行或是在分/包裝作業的過程中進行，應予以檢查/核對並加以記錄。手工印刷應予注意，並定時再檢查/核對。	5.50. The correct performance of any printing operation (for example code numbers, expiry dates) to be done separately or in the course of the packaging should be checked and recorded. Attention should be paid to printing by hand which should be re-checked at regular intervals.
5.51 當使用切式標籤和執行離線套印時，應予特別注意。在幫助避免混雜方面，捲筒式標籤通常優於切式標籤。	5.51. Special care should be taken when using cut-labels and when over-printing is carried out off-line. Roll-feed labels are normally preferable to cut-labels, in helping to avoid mix-ups.
5.52 為確保電子讀碼機、標籤計數器或其他類似的裝置係正確操作，應執行檢查/核對。	5.52. Checks should be made to ensure that any electronic code readers, label counters or similar devices are operating correctly.
5.53 經印刷或凸印在包裝材料上的資訊，應明顯且能阻抗褪色或擦除。	5.53. Printed and embossed information on packaging materials should be distinct and resistant to fading or erasing.
5.54 於分/包裝期間，產品的線上管制應進行檢查/核對，至少包括下列項目：	5.54. On-line control of the product during packaging should include at least checking the following:
a) 包裝的一般外觀；	a) general appearance of the packages;
b) 包裝是否完整；	b) whether the packages are complete;

c) 是否使用正確的產品與包裝材料;	c) whether the correct products and packaging materials are used;
d) 任何套印是否正確；	d) whether any over-printing is correct;
e) 分/包裝線上監視器的正確運轉。	e) correct functioning of line monitors.
從分/包裝線上取出的樣品不得置回。	Samples taken away from the packaging line should not be returned.
5.55 已涉及異常事件的產品，須經被授權人員的特別查核、調查及認可後，始得再導入分/包裝過程中。應保存該作業之詳細紀錄。	5.55. Products which have been involved in an unusual event should only be reintroduced into the process after special inspection, investigation and approval by authorised personnel. Detailed record should be kept of this operation.
5.56 在待分/包裝產品與印刷之包裝材料的數量及產出單元數目間的數量調和中，觀察到之任何顯著或異常的差異應於放行前進行調查並予以滿意地說明。	5.56. Any significant or unusual discrepancy observed during reconciliation of the amount of bulk product and printed packaging materials and the number of units produced should be investigated and satisfactorily accounted for before release.
5.57 分/包裝作業一經完成後，任何未使用而印有批號之印刷包裝材料應予銷毀，並將該銷毀加以記錄。未印批號之印刷包裝材料要退回庫存者,應遵循書面程序。	5.57. Upon completion of a packaging operation, any unused batch-coded packaging materials should be destroyed and the destruction recorded. A documented procedure should be followed if uncoded printed materials are returned to stock.
最終產品（FINISHED PRODUCTS）	
5.58 最終產品應依藥廠既訂條件下保存於隔離待驗區，直到最終放行為止。	5.58. Finished products should be held in quarantine until their final release under conditions established by the manufacturer.
5.59 產品為供販售放行前，最終產品與文件所需之評估規定於第六章(品質管制)。	5.59. The evaluation of finished products and documentation which is necessary before release of product for sale are described in Chapter 6 (Quality Control).
5.60 放行後，最終產品應依藥廠既訂條件作為可用庫存品儲存。	5.60. After release, finished products should be stored as usable stock under conditions established by the manufacturer.

拒用的、收回的以及退回的原物料 （REJECTED, RECOVERED AND RETURNED MATERIALS）	
5.61 拒用的原物料及產品應清楚標示其係拒用物品，並分別儲存於限制區中。該物品應退回供應商，或於合適時，予以重處理或銷毀。不論採取任何行動皆應經被授權人員的認可並予記錄。	5.61. Rejected materials and products should be clearly marked as such and stored separately in restricted areas. They should either be returned to the suppliers or, where appropriate, reprocessed or destroyed. Whatever action is taken should be approved and recorded by authorised personnel.
5.62 拒用產品的重處理應屬例外。該重處理僅在最終產品的品質不受影響、符合規格，且經評估所涉風險後，依界定且經核准的程序執行時方始允許，且其紀錄應予保存。	5.62. The reprocessing of rejected products should be exceptional. It is only permitted if the quality of the final product is not affected, if the specifications are met and if it is done in accordance with a defined and authorised procedure after evaluation of the risks involved. Record should be kept of the reprocessing.
5.63 符合所需品質之先前批次的全部或一部分，在界定的製造階段，併入相同產品之一個批次的收回，應經事先許可。這種收回應在其所涉風險，包含其對架儲期間之任何可能影響之評估後，依界定的程序執行之。該收回應予記錄。	5.63. The recovery of all or part of earlier batches, which conform to the required quality by incorporation into a batch of the same product at a defined stage of manufacture should be authorised beforehand. This recovery should be carried out in accordance with a defined procedure after evaluation of the risks involved, including any possible effect on shelf life. The recovery should be recorded.
5.64 經過重處理或併入收回之產品的任何最終產品，應由品質管制部門考慮其追加試驗的必要性。	5.64. The need for additional testing of any finished product which has been reprocessed, or into which a recovered product has been incorporated, should be considered by the Quality Control Department.

5.65 從市場退回及已經離開藥廠之管制的產品，應予銷毀，除非其品質毫無疑問是令人滿意的；只有在其已經為品質管制部門依書面程序嚴格評估後，始得考慮重新銷售、重新標示或是併入下一批收回。這種評估中，產品的性質、所要求的任何特別儲存條件、其狀況及歷史，以及自銷出後已經過的時間等皆應列入考慮。縱使基本的化學重處理能使有效成分收回，只要對此產品的品質產生任何疑問，就不得認為其還適合重新出貨或重新使用。採取的任何行動皆應予適當地記錄。	5.65. Products returned from the market and which have left the control of the manufacturer should be destroyed unless without doubt their quality is satisfactory; they may be considered for re-sale, re-labelling or recovery with a subsequent batch only after they have been critically assessed by the Quality Control Department in accordance with a written procedure. The nature of the product, any special storage conditions it requires, its condition and history, and the time elapsed since it was issued should all be taken into account in this assessment. Where any doubt arises over the quality of the product, it should not be considered suitable for re-issue or re-use, although basic chemical reprocessing to recover active ingredients may be possible. Any action taken should be appropriately recorded.

第六章 品質管制（QUALITY CONTROL）

原則（PRINCIPLE）	
品質管制與抽樣、規格與試驗以及組織、文件與放行程序有關，確保必要與相關的檢驗皆已執行，並確保在品質經判斷滿意前，無原物料會被放行供使用，無產品會被放行供銷售或供應。品質管制不侷限於實驗室的作業，而應涉及可能與該產品品質有關的所有決定。將品質管制部門從生產部門獨立出來被認為是品質管制之滿意運作的基礎(詳見第一章)。	Quality Control is concerned with sampling, specifications and testing as well as the organisation, documentation and release procedures which ensure that the necessary and relevant tests are carried out, and that materials are not released for use, nor products released for sale or supply, until their quality has been judged satisfactory. Quality Control is not confined to laboratory operations, but must be involved in all decisions which may concern the quality of the product. The independence of Quality Control from Production is considered fundamental to the satisfactory operation of Quality Control (see also Chapter 1).
一般規定（GENERAL）	
6.1. 每一個製造許可的持有者均應有品質管制部門。此部門應從其他部門獨立出來，並由具有適當資格及經驗的人員負責。該人員擁有可由其支配之一個或多個品管實驗室。此部門應有適當的資源，以確保有效且可靠地執行所有品質管制的安排。	6.1. Each holder of a manufacturing authorisation should have a Quality Control Department. This department should be independent from other departments, and under the authority of a person with appropriate qualifications and experience, who has one or several control laboratories at his disposal. Adequate resources must be available to ensure that all the Quality Control arrangements are effectively and reliably carried out.

6.2. 品質管制主管的主要職責概述於第二章。整體而言，品質管制部門亦有其他的職責，例如：制訂、確效並執行所有品質管制程序，保存原物料與產品的對照樣品，確保原物料與產品容器的正確標示，確保產品安定性的監測，參與和產品品質有關之申訴的調查等。這些作業皆應依書面程序執行，且在必要時，應予記錄。	6.2. The principal duties of the head of Quality Control are summarised in Chapter 2. The Quality Control Department as a whole will also have other duties, such as to establish, validate and implement all quality control procedures, keep the reference samples of materials and products, ensure the correct labelling of containers of materials and products, ensure the monitoring of the stability of the products, participate in the investigation of complaints related to the quality of the product, etc. All these operations should be carried out in accordance with written procedures and, where necessary, recorded.
6.3. 最終產品的評價應包含所有相關的因素，包括生產條件、製程中檢驗的結果、製造(包括分/包裝)文件的檢討、符合最終產品規格及最終包裝產品的檢查。	6.3. Finished product assessment should embrace all relevant factors, including production conditions, results of in-process testing, a review of manufacturing (including packaging) documentation, compliance with Finished Product Specification and examination of the final finished pack.
6.4. 為抽樣與調查，合適時，品質管制人員應進入生產區。	6.4. Quality Control personnel should have access to production areas for sampling and investigation as appropriate.
優良品質管制實驗室規範 （GOOD QUALITY CONTROL LABORATORY PRACTICE）	
6.5. 管制實驗室的廠房及設備應符合第三章所定品質管制區之一般及特別的要求。	6.5. Control Laboratory premises and equipment should meet the general and specific requirements for Quality Control areas given in Chapter 3.

6.6. 實驗室中的人員、廠房設施及設備應與該製造作業的性質與規模所須執行的工作相稱。在符合第七章委/受託檢驗所詳述的原則下，有特別的理由者，得接受使用外部實驗室。這應在品質管制紀錄中加以陳述。	6.6. The personnel, premises, and equipment in the laboratories should be appropriate to the tasks imposed by the nature and the scale of the manufacturing operations. The use of outside laboratories, in conformity with the principles detailed in Chapter 7, Contract Analysis, can be accepted for particular reasons, but this should be stated in the Quality Control records.
文件（DOCUMENTATION）	
6.7. 實驗室文件的製作應遵照第四章所定的原則。與品質管制有關的重要文件以及下列細節資料應供品質管制部門易於取用：	6.7. Laboratory documentation should follow the principles given in Chapter 4. An important part of this documentation deals with Quality Control and the following details should be readily available to the Quality Control Department:
➢ 規格；	➢ specifications;
➢ 抽樣程序；	➢ sampling procedures;
➢ 檢驗程序和紀錄(包括分析工作單及/或實驗室筆記本)；	➢ testing procedures and records (including analytical worksheets and/or laboratory notebooks);
➢ 分析報告及/或檢驗證明書；	➢ analytical reports and/or certificates;
➢ 環境監測數據/資料（要求時）；	➢ data from environmental monitoring, where required;
➢ 檢驗方法的確效紀錄（可行時）；	➢ validation records of test methods, where applicable;
➢ 儀器校正與設備維護保養的程序及紀錄。	➢ procedures for and records of the calibration of instruments and maintenance of equipment.
6.8. 與批次紀錄有關的任何品質管制文件，應保存至該批次產品的末效日期後一年。	6.8. Any Quality Control documentation relating to a batch record should be retained for one year after the expiry date of the batch.
6.9. 某些類型的數據 (如：分析檢驗結果、產率、環境的管制…等)建議應以允許趨勢評估的方式保存其紀錄。	6.9. For some kinds of data (e.g. analytical tests results, yields, environmental controls, ...) it is recommended that records in a manner permitting trend evaluation be kept.

6.10. 除批次紀錄之部分資訊外，其他原始資料，例如實驗室筆記本及/或紀錄，皆應予保存且易於取用。	6.10. In addition to the information which is part of the batch record, other original data such as laboratory notebooks and/or records should be retained and readily available.
抽樣（SAMPLING）	
6.11. 抽樣應依經認可之書面程序執行。該程序描述下列項目：	6.11. The sample taking should be done in accordance with approved written procedures that describe:
➢ 抽樣的方法；	➢ the method of sampling;
➢ 使用的設備；	➢ the equipment to be used;
➢ 抽取的樣品量；	➢ the amount of the sample to be taken;
➢ 任何要求將樣品再細分的指令；	➢ instructions for any required sub-division of the sample;
➢ 使用之樣品容器的類型及條件；	➢ the type and condition of the sample container to be used;
➢ 經抽取樣品之容器的識別；	➢ the identification of containers sampled;
➢ 應遵行的任何特殊注意事項，特別是關於無菌的或有毒物質的抽樣；	➢ any special precautions to be observed, especially with regard to the sampling of sterile or noxious materials;
➢ 儲存條件；	➢ the storage conditions;
➢ 抽樣設備之清潔與儲存的指令。	➢ instructions for the cleaning and storage of sampling equipment.
6.12. 對照樣品對於其取自之原物料或產品批次應有代表性。用以監測製程之最困難的部分，亦可另取其他樣品（例如：製程的開始或結束）為之。	6.12. Reference samples should be representative of the batch of materials or products from which they are taken. Other samples may also be taken to monitor the most stressed part of a process (e.g. beginning or end of a process).
6.13. 樣品容器的標籤應標示其內容物、批號、抽樣日期及樣品所取自之容器。	6.13. Sample containers should bear a label indicating the contents, with the batch number, the date of sampling and the containers from which samples have been drawn.
6.14. 來自每批最終產品的對照樣品應儲存至該批產品之末效日期後一年。最終產品通常應保存在其最終包裝中，並儲存在建議的條件下。在原料的安定性容許	6.14. Reference samples from each batch of finished products should be retained till one year after the expiry date. Finished products should usually be kept in their

下，其樣品(不包括溶劑、氣體及水)應保存至該產品放行後至少兩年。相關規格中提到其安定性較短者，該兩年的保存期限得縮短之。原物料及產品之對照樣品的數量應至少足以允許執行一次完整的再驗。	final packaging and stored under the recommended conditions. Samples of starting materials (other than solvents, gases and water) should be retained for at least two years after the release of the product if their stability allows. This period may be shortened if their stability, as mentioned in the relevant specification, is shorter. Reference samples of materials and products should be of a size sufficient to permit at least a full re-examination.
檢驗（TESTING）	
6.15. 分析方法應予確效。上市許可中所描述的所有檢驗作業皆應依認可的方法執行之。	6.15. Analytical methods should be validated. All testing operations described in the marketing authorisation should be carried out according to the approved methods.
6.16. 獲得的結果應予記錄並檢查/核對，以確保彼此間是一致的。任何計算均應予嚴格驗算。	6.16. The results obtained should be recorded and checked to make sure that they are consistent with each other. Any calculations should be critically examined.
6.17. 執行的試驗應予記錄且至少應包括下列數據/資料：	6.17. The tests performed should be recorded and the records should include at least the following data:
a) 原物料或產品名稱，及其劑型(可行時)；	a) name of the material or product and, where applicable, dosage form;
b) 批號，及其製造廠及/或供應商(合適時)；	b) batch number and, where appropriate, the manufacturer and/or supplier;
c) 相關規格與檢驗程序的參考資料；	c) references to the relevant specifications and testing procedures;
d) 檢驗的結果，包括觀察、計算及任何檢驗證明書的參考資料；	d) test results, including observations and calculations, and reference to any certificates of analysis;
e) 檢驗日期；	e) dates of testing;
f) 執行該檢驗之人員的簽名；	f) initials of the persons who performed the testing;
g) 合適時，確認檢驗及計算結果之人員的簽名；	g) initials of the persons who verified the testing and the calculations, where appropriate;
h) 放行或拒用(或其他狀態的決定)之清楚	h) a clear statement of release or rejection (or

說明及指定之負責人員註明日期的簽章。	other status decision) and the dated signature of the designated responsible person.
6.18. 所有製程中管制，包括由生產人員在生產區中所執行的管制，應依品質管制部門認可的方法執行，並記錄其結果。	6.18. All the in-process controls, including those made in the production area by production personnel, should be performed according to methods approved by Quality Control and the results recorded.
6.19. 應特別注意實驗室試劑、容量玻璃器皿、溶液、對照標準品及培養基等之品質，並應依書面的程序製備。	6.19. Special attention should be given to the quality of laboratory reagents, volumetric glassware and solutions, reference standards and culture media. They should be prepared in accordance with written procedures.
6.20. 預定供長期使用的實驗室試劑，應標記其配製日期及配製人員的簽章。不穩定的試劑及培養基的末效日期，應與其特別的儲存條件一同標示在標籤上。此外，對於容量分析溶液，應標示其最近一次標定日期及最近的換算係數。	6.20. Laboratory reagents intended for prolonged use should be marked with the preparation date and the signature of the person who prepared them. The expiry date of unstable reagents and culture media should be indicated on the label, together with specific storage conditions. In addition, for volumetric solutions, the last date of standardisation and the last current factor should be indicated.
6.21. 必要時，應將用於檢驗作業之任何物質(例如：試劑及對照標準品)的接收日期標示在容器上。使用及儲存的指令應予遵循。某些情形，於接收時或使用前，可能有必要執行試劑材料的鑑別試驗及/或其他試驗。	6.21. Where necessary, the date of receipt of any substance used for testing operations (e.g. reagents and reference standards) should be indicated on the container. Instructions for use and storage should be followed. In certain cases it may be necessary to carry out an identification test and/or other testing of reagent materials upon receipt or before use.

6.22. 用於檢驗組成物、原物料或產品的動物，合適時，使用前應予隔離。它們應以能確保其合於預定用途之適用性的方式飼養及管制，且應予識別與標示，並應保存顯示其使用歷程之適當紀錄。	6.22. Animals used for testing components, materials or products, should, where appropriate, be quarantined before use. They should be maintained and controlled in a manner that assures their suitability for the intended use. They should be identified, and adequate records should be maintained, showing the history of their use.
持續進行之安定性計畫（ON-GOING STABILITY PROGRAMME）	
6.23. 藥品上市後，其安定性應依持續的適當計畫進行監測。該計畫將容許檢出與上市包裝中的配方組成關聯之任何安定性的問題（例如，在雜質含量，或溶離圖像描述的變化）。	6.23. After marketing, the stability of the medicinal product should be monitored according to a continuous appropriate programme that will permit the detection of any stability issue (e.g. changes in levels of impurities, or dissolution profile) associated with the formulation in the marketed package.
6.24. 持續進行的安定性計畫之目的係在產品架儲期全期中監測該產品，並確定在所標示的儲存條件下，該產品的品質仍可預期保持在其規格內。	6.24. The purpose of the on-going stability programme is to monitor the product over its shelf life and to determine that the product remains, and can be expected to remain, within specifications under the labelled storage conditions.

6.25. 這主要應用於包裝藥品之販售，但亦應考慮將待分/包裝產品包括到計畫中。例如，當待分/包裝產品在包裝前及/或從製造場所裝運到包裝場所前，儲存一段長的期間時，其對於包裝產品之安定性的衝擊應加以評估，並在週遭的自然條件下研究之。此外，對於歷經長期間之儲存與使用的中間產品也應給予考慮。臨用調配之產品的安定性之研究已在產品開發期間執行者，不需要在一個持續進行的基礎上監測之。然而，臨用調配之產品的安定性於合適時亦可以加以監測。	6.25. This mainly applies to the medicinal product in the package in which it is sold, but consideration should also be given to the inclusion in the programme of bulk product. For example, when the bulk product is stored for a long period before being packaged and/or shipped from a manufacturing site to a packaging site, the impact on the stability of the packaged product should be evaluated and studied under ambient conditions. In addition, consideration should be given to intermediates that are stored and used over prolonged periods. Stability studies on reconstituted product are performed during product development and need not be monitored on an on-going basis. However, when relevant, the stability of reconstituted product can also be monitored.
6.26. 持續進行之安定性計畫，應遵循第四章的一般規則，以書面計畫書描述之，並將其結果正式作成一份報告。使用於持續進行之安定性計畫的設備（尤其是安定性試驗箱/艙室）應依循第三章與附則 15 加以驗證並予維護。	6.26. The on-going stability programme should be described in a written protocol following the general rules of Chapter 4 and results formalised as a report. The equipment used for the on-going stability programme (stability chambers among others) should be qualified and maintained following the general rules of Chapter 3 and annex 15.
6.27. 對於持續進行之安定性計畫的計畫書，應涵蓋至架儲期間的終點，且應包括但不限於下列的參數：	6.27. The protocol for an on-going stability programme should extend to the end of the shelf life period and should include, but not be limited to, the following parameters:
•每種含量與不同批量之批次數目（合適時）	• number of batch(es) per strength and different batch sizes, if applicable
•相關的物理、化學、微生物學及生物學的檢驗方法	• relevant physical, chemical, microbiological and biological test methods
•允收標準	• acceptance criteria
•檢驗方法的參考資料	• reference to test methods
•容器封蓋系統的描述	• description of the container closure

	system(s)
•測試間隔（時間點）	• testing intervals (time points)
•儲存條件的描述(應使用與產品標示一致之標準化的 ICH 長期試驗條件)	• description of the conditions of storage (standardised ICH conditions for long term testing, consistent with the product labelling, should be used)
•其他特別適用於該藥品的參數。	• other applicable parameters specific to the medicinal product.
6.28. 若持續安定性計畫之計畫書中已證明其正當性並予以文件化者，得與當初在上市許可檔案中所提交之長期安定性試驗的計畫書不同（例如：測試頻率，或配合 ICH 之建議事項更新時）。	6.28. The protocol for the on-going stability programme can be different from that of the initial long-term stability study as submitted in the marketing authorisation dossier provided that this is justified and documented in the protocol (for example the frequency of testing, or when updating to ICH recommendations).
6.29. 批次數目與測試頻率應能提供足夠的數據量，以容許趨勢分析。除非另有正當理由，否則，所製造之每一含量及每一直接包裝類型的產品，相關時，每年至少應有一個批次包含在安定性計畫中(除非該年中沒有生產)。產品之持續進行的安定性監測通常需要使用動物來測試而無適當經確效的替代技術時，其測試頻率可以考慮風險效益方法。經在計畫書中科學地證明其正當者，得採用籃狀設計與矩陣設計的原理。	6.29. The number of batches and frequency of testing should provide a sufficient amount of data to allow for trend analysis. Unless otherwise justified, at least one batch per year of product manufactured in every strength and every primary packaging type, if relevant, should be included in the stability programme (unless none are produced during that year). For products where on-going stability monitoring would normally require testing using animals and no appropriate alternative, validated techniques are available, the frequency of testing may take account of a risk-benefit approach. The principle of bracketing and matrixing designs may be applied if scientifically justified in the protocol.

6.30. 某些情況，應在持續進行的安定性計畫中納入追加的批次。例如，製程或包裝有任何重大變更或重大偏差後，應執行持續進行的安定性研究。任何再加工、重處理或收回作業亦應考慮納入。	6.30. In certain situations, additional batches should be included in the on-going stability programme. For example, an on-going stability study should be conducted after any significant change or significant deviation to the process or package. Any reworking, reprocessing or recovery operation should also be considered for inclusion.
6.31. 持續進行之安定性試驗的結果，應使關鍵人員，特別是被授權人員能夠取得。持續進行的安定性試驗係在待分/包裝或最終產品的製造場所外之另一個場所執行者，相關各方之間應有書面協議。在製造廠應可取得持續安定性試驗的結果，以備供主管機關檢查。	6.31. Results of on-going stability studies should be made available to key personnel and, in particular, to the Authorised Person(s). Where on-going stability studies are carried out at a site other than the site of manufacture of the bulk or finished product, there should be a written agreement between the parties concerned. Results of on-going stability studies should be available at the site of manufacture for review by the competent authority.
6.32. 有偏離規格或有顯著非典型趨勢時，應予調查。有任何經證實之偏離規格的結果或顯著的負面趨勢，應向主管機關報告，並應依優良製造規範指引第八章及與相關主管機關之研商結果，考慮對於已上市產品之批次可能造成的衝擊。	6.32. Out of specification or significant atypical trends should be investigated. Any confirmed out of specification result, or significant negative trend, should be reported to the relevant competent authorities. The possible impact on batches on the market should be considered in accordance with chapter 8 of the GMP Guide and in consultation with the relevant competent authorities.
6.33. 產生之所有數據/資料的摘要，包含計畫中之任何暫時的結論在內，均應作成書面並予以保存。該摘要應定期檢討。	6.33. A summary of all the data generated, including any interim conclusions on the programme, should be written and maintained. This summary should be subjected to periodic review.

第七章 委/受託製造與委/受託檢驗（CONTRACT MANUFACTURE AND ANALYSIS）

委/受託製造與委/受託檢驗原則（PRINCIPLE）	
委/受託製造與委/受託檢驗應正確地予以界定、協議及管制，以避免因誤解而可能導致不滿意品質的產品或作業。委託者與受託者間應有清楚訂定雙方職責的書面契約。該契約應清楚約定，負責放行每批供銷售之產品的被授權人員執行其完整職責的方式。	Contract manufacture and analysis must be correctly defined, agreed and controlled in order to avoid misunderstandings which could result in a product or work of unsatisfactory quality. There must be a written contract between the Contract Giver and the Contract Acceptor which clearly establishes the duties of each party. The contract must clearly state the way in which the authorised person releasing each batch of product for sale exercises his full responsibility.
註：本章規定藥廠對於授予銷售與製造許可之主管機關應負的責任。本章無意以任何方式影響委託者與受託者對於消費者之個別義務。	Note: This Chapter deals with the responsibilities of manufacturers towards the Component Authorities of the Participating authorities with respect to the granting of marketing and manufacturing authorisations. It is not intended in any way to affect the respective liability of contract acceptors and contract givers to consumers.
一般規定（GENERAL）	
7.1. 該委託契約，應有涵蓋製造及/或委/受託檢驗之書面契約及其有關的技術安排。	7.1. There should be a written contract covering the manufacture and/or analysis arranged under contract and any technical arrangements made in connection with it.
7.2. 為委/受託製造與委/受託檢驗之所有安排，包括技術或其他安排中所建議之任何改變，均應符合相關產品之上市許可。	7.2. All arrangements for contract manufacture and analysis including any proposed changes in technical or other arrangements should be in accordance with the marketing authorisation for the product concerned.
委託者（THE CONTRACT GIVER）	
7.3. 委託者應負責評估受託者成功履行要求之工作的能力，並負責藉由該契約，	7.3. The Contract Giver is responsible for assessing the competence of the Contract

確保本指引所闡釋之優良製造規範的原則與指引受到遵循。	Acceptor to carry out successfully the work required and for ensuring by means of the contract that the principles and Guidelines of GMP as interpreted in this Guide are followed.
7.4. 委託者應提供受託者所有必需的資訊，以使其依上市許可及任何其他法律要求，正確地履行約定的作業。委託者應確保受託者完全認知與本產品或工作有關之任何可能會對其廠房設施、設備、人員、其他原物料或其他產品造成危害的問題。	7.4. The Contract Giver should provide the Contract Acceptor with all the information necessary to carry out the contracted operations correctly in accordance with the marketing authorisation and any other legal requirements. The Contract Giver should ensure that the Contract Acceptor is fully aware of any problems associated with the product or the work which might pose a hazard to his premises, equipment, personnel, other materials or other products.
7.5. 委託者應確保受託者所交付之所有處理過的產品及原物料均符合其規格，或這些產品係經由被授權人員放行。	7.5. The Contract Giver should ensure that all processed products and materials delivered to him by the Contract Acceptor comply with their specifications or that the products have been released by an authorised person.
受託者（THE CONTRACT ACCEPTOR）	
7.6. 受託者應有適當的廠房設施與設備、知識與經驗及能勝任的人員，滿意地執行委託者所託付的工作。接受委託製造僅得由取得製造許可者為之。	7.6. The Contract Acceptor must have adequate premises and equipment, knowledge and experience, and competent personnel to carry out satisfactorily the work ordered by the Contract Giver. Contract manufacture may be undertaken only by a manufacturer who is the holder of a manufacturing authorisation.
7.7. 受託者應確認所交付的所有產品或原物料皆符合其預定之目的。	7.7. The Contract Acceptor should ensure that all products or materials delivered to him are suitable for their intended purpose.
7.8. 受託者未經委託者之事先評估及同意，不得將契約所委託的任何工作轉託給第三方。受託者與任何第三方間所做的任何安排，應確保其製造及檢驗資訊以原委託者與受託者間約定的相同方	7.8. 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.

式提供之。	Arrangements made between the Contract Acceptor and any third party should ensure that the manufacturing and analytical information is made available in the same way as between the original Contract Giver and Contract Acceptor.
7.9. 受託者應避免對委託者委託製造及/或檢驗之產品品質可能會造成不良影響的任何活動。	7.9. The Contract Acceptor should refrain from any activity which may adversely affect the quality of the product manufactured and/or analysed for the Contract Giver.
合約（THE CONTRACT）	
7.10. 委託者與受託者間應簽訂契約。該契約明定雙方關於產品製造與管制的個別責任。契約中的技術層面應由具有製藥技術、檢驗及優良製造規範之適當知識的勝任人員擬定。製造及檢驗的所有安排均應依上市許可的規定，並為雙方所同意。	7.10. A contract should be drawn up between the Contract Giver and the Contract Acceptor which specifies their respective responsibilities relating to the manufacture and control of the product. Technical aspects of the contract should be drawn up by competent persons suitably knowledgeable in pharmaceutical technology, analysis and Good Manufacturing Practice. All arrangements for manufacture and analysis must be in accordance with the marketing authorisation and agreed by both parties
7.11. 契約應明定被授權人員放行供銷售之批次的方式，以確保每一批次皆已符合上市許可的要求而製造與檢查/核對。	7.11. The contract should specify the way in which the authorised person releasing the batch for sale ensures that each batch has been manufactured and checked for compliance with the requirements of Marketing Authorisation.
7.12. 契約中應清楚載明何方負責採購、測試及放行原物料、承擔生產及品質管制，含製程中管制，以及何方負責抽樣及檢驗。委託檢驗契約中應載明受託者是否應於製造者之廠房中抽樣。	7.12. The contract should describe clearly who is responsible for purchasing materials, testing and releasing materials, undertaking production and quality controls, including in-process controls, and who has responsibility for sampling and analysis. In the case of contract analysis, the contract should state whether or not the Contract Acceptor should take samples at the premises of the manufacturer.

7.13. 製造、檢驗及運銷之紀錄及對照樣品應由委託者保存，或可為委託者取得。當有申訴或懷疑有瑕疵時，應能取得與產品品質評估有關的任何紀錄。這應明定於委託者之不良品/回收程序中。	7.13. Manufacturing, analytical and distribution records, and reference samples should be kept by, or be available to, the Contract Giver. Any records relevant to assessing the quality of a product in the event of complaints or a suspected defect must be accessible and specified in the defect/recall procedures of the Contract Giver.
7.14. 契約應明定容許委託者訪視受託者的廠房設施及設備。	7.14. The contract should permit the Contract Giver to visit the facilities of the Contract Acceptor.
7.15. 委/受託檢驗時，受託者應了解其應受主管機關的查核。	7.15. In case of contract analysis, the Contract Acceptor should understand that he is subject to inspection by the competent Authorities.

第八章 申訴和產品回收（COMPLAINTS AND PRODUCT RECALL）

原則（PRINCIPLE）	
所有申訴及其他可能之瑕疵產品有關的資訊，均應遵循書面的程序詳實審核。為對所有意外事件作準備，應設計一套系統，以便必要時，能立即且有效地自市場回收已知或懷疑其有瑕疵的產品。	All complaints and other information concerning potentially defective products must be carefully reviewed according to written procedures. In order to provide for all contingencies, a system should be designed to recall, if necessary, promptly and effectively products known or suspected to be defective from the market.
申訴（COMPLAINTS）	
8.1. 應指定人員，並配以足夠的支援人員給予協助，以負責處理申訴及決定要採取的措施。該指定人員若非被授權人員，應使被授權人員知悉任何申訴、調查或回收事宜。	8.1. A person should be designated responsible for handling the complaints and deciding the measures to be taken together with sufficient supporting staff to assist him. If this person is not the authorised person, the latter should be made aware of any complaint, investigation or recall.
8.2. 若涉及可能之產品瑕疵的申訴，應有書面的程序描述要採取的行動，包括考慮回收的需要。	8.2. There should be written procedures describing the action to be taken, including the need to consider a recall, in the case of a complaint concerning a possible product defect.
8.3. 關於產品瑕疵的任何申訴，應記錄其全部原始細節並徹底調查。負責品質管制的人員通常應參與這些問題的研究。	8.3. Any complaint concerning a product defect should be recorded with all the original details and thoroughly investigated. The person responsible for Quality Control should normally be involved in the study of such problems.
8.4 任一批次中發現或懷疑有產品瑕疵時，應考慮檢查/核對其他批次的產品，以確定其是否也受到影響。特別是可能含有該瑕疵批次之再加工的其他批次應予調查。	8.4. If a product defect is discovered or suspected in a batch, consideration should be given to checking other batches should be checked in order to determine whether they are also affected. In particular, other batches

	which may contain reworks of the defective batch should be investigated.
8.5 因申訴而做之所有決定與採取之措施應予記錄，並對照其對應的批次紀錄。	8.5. All the decisions and measures taken as a result of a complaint should be recorded and referenced to the corresponding batch records.
8.6 申訴紀錄應定期檢討，以發現需注意及可能造成已上市產品回收之特定或重發性問題的任何跡象。	8.6. Complaints records should be reviewed regularly for any indication of specific or recurring problems requiring attention and possibly the recall of marketed products.
8.7 應特別注意確立申訴是否因仿冒所引起。	8.7. Special attention should be given to establishing whether a complaint was caused because of counterfeiting.
8.8 藥廠若由於可能有製造瑕疵、產品變質、發現仿冒品或任何其他嚴重的產品品質問題，而考慮採取行動時，應通知主管機關。	8.8. The Competent Authorities should be informed if a manufacturer is considering action following possibly faulty manufacture, product deterioration, detection of counterfeiting or any other serious quality problems with a product.
回收（RECALLS）	
8.9 應指定人員負責回收之執行與協調，並應給予足夠的支援人力，以適切迅速的程度處理所有回收事宜。該負責人員通常應與銷售部門相互獨立且該人員並非被授權人員者，應使被授權人員知悉任何回收作業。	8.9. A person should be designated as responsible for execution and co-ordination of recalls and should be supported by sufficient staff to handle all the aspects of the recalls with the appropriate degree of urgency. This responsible person should normally be independent of the sales and marketing organisation. If this person is not the authorised person, the latter should be made aware of any recall operation.
8.10 為有效的組織任何回收作業，應建立書面的程序、定期檢查/核對，且於必要時予以更新。	8.10. There should be established written procedures, regularly checked and updated when necessary, in order to organise any recall activity.
8.11 回收作業應能立即且在任何時候啟動。	8.11. Recall operations should be capable of

	being initiated promptly and at any time.
8.12 因產品有瑕疵或懷疑其有瑕疵，而要將其回收時，應立即通知可能已經對其運銷該產品之所有國家的主管機關。	8.12. All Competent Authorities of all countries to which products may have been distributed should be informed promptly if products are intended to be recalled because they are, or are suspected of, being defective.
8.13 運銷紀錄應易為負責回收的人員取得，且應包含關於批發商和直銷客戶的充分資訊(連同地址、上、下班時間的電話/傳真號碼、送交的批次和數量)，包含輸出的產品和醫療用樣品在內。	8.13. The distribution records should be readily available to the person(s) responsible for recalls, and should contain sufficient information on wholesalers and directly supplied customers (with addresses, phone and/or fax numbers inside and outside working hours, batches and amounts delivered), including those for exported products and medical samples.
8.14 回收的產品在等候決定其最終處置方式的期間中，應予識別與標示並隔離儲存於安全區域。	8.14. Recalled products should be identified and stored separately in a secure area while awaiting a decision on their fate.
8.15 回收過程之進度應予記錄並提出最終報告。該報告應包含送交產品與收回產品的數量調和。	8.15. The progress of the recall process should be recorded and a final report issued, including a reconciliation between the delivered and recovered quantities of the products.
8.16 回收作業之安排的有效性應予定期評估。	8.16. The effectiveness of the arrangements for recalls should be evaluated regularly.

第九章 自我查核（SELF INSPECTION）

原則（PRINCIPLE）	
為監測優良製造規範原則之實施與遵守，應執行自我查核，並就必要的矯正措施提出建議。	Self inspections should be conducted in order to monitor the implementation and compliance wit（with） Good Manufacturing Practice principles and to propose necessary corrective measures.
9.1. 人事、廠房、設施、設備、文件、生產、品質管制、藥品的運銷、有關申訴與回收的安排，以及自我查核，皆應依預先安排之計畫的間隔時間進行檢查，以便證實其符合品質保證的原則。	9.1. Personnel matters, premises, equipment, documentation, production, quality control, distribution of the medicinal products, arrangements for dealing with complaints and recalls, and self inspection, should be examined at intervals following a pre-arranged programme in order to verify their conformity with the principles of Quality Assurance.
9.2. 自我查核應由公司指定能勝任的人員，以獨立且詳細的方式執行。外部專家的獨立稽核可能也是有用的。	9.2. Self inspections should be conducted in an independent and detailed way by designated competent person(s) from the company. Independent audits by external experts may also be useful.
9.3. 所有自我查核應予記錄。報告應包含在檢查期間所執行之所有觀察，合適時，並含矯正措施的建議。後續採取之行動的說明亦應予記錄。	9.3. All self inspections should be recorded. Reports should contain all the observations made during the inspections and, where applicable, proposals for corrective measures. Statements on the actions subsequently taken should also be recorded.

附則 1　無菌藥品的製造(MANUFACTURE OF STERILE MEDICINAL PRODUCTS)

*** 本附則中關於小瓶之上蓋規定條款於 2010 年 3 月 1 日生效。**	***Provisions on capping of vials in this Annex will enter into force on 1 March 2010 only.**
原則	**PRINCIPLE**
為使微生物學上之污染，與微粒及熱原污染之風險降到最低，無菌產品之製造應受制於特別之要求。大部分的要求取決於參與人員之技巧、訓練及態度。品質保證特別重要，且這種類型之製造應嚴格遵循，謹慎建立經確效的製備方法及程序。無菌性或其他品質層面之信賴度不得僅仰賴於最終製程或最終產品的檢驗。	The manufacture of sterile products is subject to special requirements in order to minimise risks of microbiological contamination, and of particulate and pyrogen contamination. Much depends on the skill, training and attitudes of the personnel involved. Quality Assurance is particularly important, and this type of manufacture must strictly follow carefully established and validated methods of preparation and procedure. Sole reliance for sterility or other quality aspects must not be placed on any terminal process or finished product test.
註：本附則並未規定關於測定空氣、表面等之微生物及微粒的潔淨度之詳細方法。請參考其他的規範，例如 EN/ISO 標準。	Note: This guidance does not lay down detailed methods for determining the microbiological and particulate cleanliness of air, surfaces, etc. Reference should be made to other documents such as the EN/ISO Standards.
概述	**GENERAL**
1. 無菌產品的製造應在潔淨區中執行，人員及/或設備與原物料進入該潔淨區，應分別經由各氣鎖室。潔淨區應維持在適當的潔淨度標準，並提供已通過具適當效率之濾器的空氣。	1. The manufacture of sterile products should be carried out in clean areas, entry to which should be through airlocks for personnel and/or for equipment and materials. Clean areas should be maintained to an appropriate cleanliness standard and supplied with air which has passed through filters of an appropriate efficiency.
2. 組件的準備、產品的製備及充填之不同作業應在潔淨區內之個別的區域中為之。製造作業劃分成兩類；第一類，其產品係經最終滅菌，及第二類，其產品在製程中的某些階段或全部階段係以無菌技術執行。	2. The various operations of component preparation, product preparation and filling should be carried out in separate areas within the clean area. Manufacturing operations are divided into two categories; firstly those where the product is terminally sterilised, and secondly those which are conducted aseptically at some or all stages.

3. 無菌產品之製造，其潔淨區是依要求的環境特徵分級。為使處理中之產品或原物料的微粒或微生物污染之風險降到最低，每一製造作業在操作狀態中，均須有適當的環境潔淨度等級。	3. Clean areas for the manufacture of sterile products are classified according to the required characteristics of the environment. Each manufacturing operation requires an appropriate environmental cleanliness level in the operational state in order to minimise the risks of particulate or microbial contamination of the product or materials being handled.
為符合「動態」的條件，這些區域應經設計，使其在靜態時達到特定之空氣潔淨度標準。「靜態」，指該生產設施已完成生產設備之安裝並在運轉中，但無操作人員在場的狀態。「動態」，指設備已於操作狀態中運轉，且有特定人數執行操作。	In order to meet “in operation” conditions these areas should be designed to reach certain specified air-cleanliness levels in the “at rest” occupancy state. The “at rest” state is the condition where the installation is installed and operating, complete with production equipment but with no operating personnel present. The “in operation” state is the condition where the installation is functioning in the defined operating mode with the specified number of personnel working.
對於每間潔淨室或每套潔淨室，皆應界定其「動態」及「靜態」 的狀態。	The “in operation” and “at rest” states should be defined for each clean room or suite of clean rooms.
無菌藥品的製造區分成四個等級。	For the manufacture of sterile medicinal products 4 grades can be distinguished.
A 級： 高風險作業的局部區域，例如，充填區、橡皮塞貯盆、開口安瓿、小瓶及執行無菌連接等區域。通常，此種環境由層流工作站提供。在開放潔淨室應用（open clean room application）的作業位置，層流空氣系統應提供每秒 0.36 至 0.54 公尺（指引值）的均勻空氣流速。 層流性（laminarity）的維持應予以證明並確效。單向氣流（uni-directional air flow）及較低速率可使用於密閉的隔離裝置及手套箱（glove boxes）。	Grade A: The local zone for high risk operations, e.g. filling zone, stopper bowls, open ampoules and vials, making aseptic connections. Normally such conditions are provided by a laminar air flow work station. Laminar air flow systems should provide a homogeneous air speed in a range of 0.36 – 0.54 m/s(guidance value) at the working position in open clean room applications. The maintenance of laminarity should be demonstrated and validated. A uni-directional air flow and lower velocities may be used in closed isolators and glove boxes.
B 級： 對於無菌操作之製備及充填，B 級區為 A 級區的背景環境。	Grade B: For aseptic preparation and filling, this is the background environment for the grade A zone.

C 級與 D 級： 無菌產品的製造中，C 級與 D 級區係執行較非關鍵性階段的潔淨區。	Grade C and D: Clean areas for carrying out less critical stages in the manufacture of sterile products.
潔淨室及潔淨空氣裝置分級	**CLEAN ROOM AND CLEAN AIR DEVICE CLASSIFICATION**
4. 潔淨室及潔淨空氣裝置應依EN ISO 14644-1予以分級。分級應與操作過程之環境監測清楚區分。下表提供每一個等級所容許的最大浮游微粒濃度：	4. Clean rooms and clean air devices should be classified in accordance with ENISO 14644-1. Classification should be clearly differentiated from operational process environmental monitoring. The maximum permitted airborne particle concentration for each grade is given in the following table:

等 級	每立方公尺等於或大於下述粒徑之微粒的最大容許量			
	靜態		動態	
	0.5 μm	5.0 μm	0.5 μm	5.0 μm
A	3,520	20	3,520	20
B	3,520	29	352,000	2,900
C	352,000	2,900	3,520 000	29,000
D	3,520,000	29,000	未界定	未界定

Grade	Maximum permitted number of particles/m^3 equal to or greater than the tabulated size			
	At rest		In operation	
	0.5 μm	5.0 μm	0.5 μm	5.0 μm
A	3,520	20	3,520	20
B	3,520	29	352,000	2,900
C	352,000	2,900	3,520 000	29,000
D	3,520,000	29,000	Not defined	Not defined

5. 針對 A 級區分級之驗證，每一個取樣位置應採取最少樣品容量 1m^3。A 級之浮游微粒分級為 ISO 4.8，依≥ 5.0 μm 微粒限量決定。B 級 (靜態)之浮游微粒分級為 ISO 5，係考慮兩種微粒大小。對於 C 級 (靜態及動態)，浮游微粒分級分別為 ISO 7 及 ISO 8。對於 D 級 (靜態)，浮游微粒分級為 ISO 8。針對分級，EN/ISO 14644-1 界定最低取樣點數及樣品量，考量最大的微粒大小及所收集的數據之估算方式，作為各分級限量之基礎。	5. For classification purposes in Grade A zones, a minimum sample volume of 1m3 should be taken per sample location. For Grade A the airborne particle classification is ISO 4.8 dictated by the limit for particles ≥5.0 μm. For Grade B (at rest) the airborne particle classification is ISO 5 for both considered particle sizes. For Grade C (at rest & in operation) the airborne particle classification is ISO 7 and ISO 8 respectively. For Grade D (at rest) the airborne particle classification is ISO 8. For classification purposes EN/ISO 14644-1 methodology defines both the minimum number of sample locations and the sample

	size based on the class limit of the largest considered particle size and the method of evaluation of the data collected.
6. 為分級之目的，應使用具短取樣管的手提式微粒計數器，因具長管線的遙控取樣系統 ≧5μm 之微粒的沉降速率相對較高。單向氣流系統中，應使用等速採樣頭（isokinetic sample heads）。	6. Portable particle counters with a short length of sample tubing should be used for classification purposes because of the relatively higher rate of precipitation of particles ≥5.0μm in remote sampling systems with long lengths of tubing. Isokinetic sample heads should be used in unidirectional airflow systems.
7. 「動態」之等級可在正常操作或模擬操作中確認。當需要模擬最差狀況時，則於培養基充填期間予以確認。對於確認持續遵循指定的潔淨度分級，EN ISO 14644-2 提供關於其測試的資訊。	7. "In operation" classification may be demonstrated during normal operations, simulated operations or during media fills as worst-case simulation is required for this. EN ISO 14644-2 provides information on testing to demonstrate continued compliance with the assigned cleanliness classifications.
潔淨室及潔淨空氣裝置的監測	**CLEAN ROOM AND CLEAN AIR DEVICE MONITORING**
8. 潔淨室及潔淨空氣裝置應在動態中例行監測，且監測位置應依正式的風險分析研究，及在潔淨室及/或潔淨空氣裝置之分級期間所得結果為基礎。	8. Clean rooms and clean air devices should be routinely monitored in operation and the monitoring locations based on a formal risk analysis study and the results obtained during the classification of rooms and/or clean air devices.

9. 對於A級區，應在關鍵操作的全程中監測微粒，包括設備組裝在內，除非證明製程中之污染物會損壞微粒計數器或呈現危害，例如活微生物及放射性的危害；在此種情況下，設備之例行安裝操作期間的監測，應在暴露於該風險之前為之。模擬操作期間之監測亦應執行。A級區應以適當的頻率及採樣量加以監測，使所有介入、短暫突發事件及任何系統劣化皆會被偵測到，且如果超出警戒限量將會啟動警報器。當進行充填時，在充填點，因產品本身產生之微粒或小液滴，充填點可能無法一直維持≥5.0 μm之微粒的限量是可接受的。	9. For Grade A zones, particle monitoring should be undertaken for the full duration of critical processing, including equipment assembly, except where justified by contaminants in the process that would damage the particle counter or present a hazard, e.g. live organisms and radiological hazards. In such cases monitoring during routine equipment set up operations should be undertaken prior to exposure to the risk. Monitoring during simulated operations should also be performed. The Grade A zone should be monitored at such a frequency and with suitable sample size that all interventions, transient events and any system deterioration would be captured and alarms triggered if alert limits are exceeded. It is accepted that it may not always be possible to demonstrate low levels of ≥5.0 μm particles at the point of fill when filling is in progress, due to the generation of particles or droplets from the product itself.
10. 針對B級區，雖取樣頻率可能會減少，但仍建議使用類似的系統。微粒監測系統之重要性應由相鄰之A級區及B級區間的隔離效果確定。B級區應依此頻率及適當的採樣量加以監測，使得污染程度之變化，及系統之任何劣化將會被偵測到，且若超出警戒限量將啟動警報器。	10. It is recommended that a similar system be used for Grade B zones although the sample frequency may be decreased. The importance of the particle monitoring system should be determined by the effectiveness of the segregation between the adjacent Grade A and B zones. The Grade B zone should be monitored at such a frequency and with suitable sample size that changes in levels of contamination and any system deterioration would be captured and alarms triggered if alert limits are exceeded.

11. 浮游微粒監測系統可能包括獨立的微粒計數器，以歧管相繼連接取樣點到個別微粒計數器之網狀系統，或該二者之組合。所選擇之系統必須適合所考量的微粒大小。使用遙控取樣系統時，必須考慮在管線中微粒之減失（例如：沈降附著），以決定取樣管線之長度及管線中之任何彎曲的半徑。監測系統之選擇應考量使用於製造作業之原料所呈現之任何風險，例如涉及活微生物或放射性藥品者。	11. Airborne particle monitoring systems may consist of independent particle counters; a network of sequentially accessed sampling points connected by manifold to a single particle counter; or a combination of the two. The system selected must be appropriate for the particle size considered. Where remote sampling systems are used, the length of tubing and the radii of any bends in the tubing must be considered in the context of particle losses in the tubing. The selection of the monitoring system should take account of any risk presented by the materials used in the manufacturing operation, for example those involving live organisms or radiopharmaceuticals.
12. 為監測目的，使用自動化系統之採樣量，通常與該系統之採樣速率有關(具函數關係)。其樣品容量與使用於潔淨室及潔淨空氣裝置之正式分級的採樣量不需要相同。	12. The sample sizes taken for monitoring purposes using automated systems will usually be a function of the sampling rate of the system used. It is not necessary for the sample volume to be the same as that used for formal classification of clean rooms and clean air devices.
13. 在 A 級區及 B 級區中，≥ 5.0 μm 微粒濃度計數的監測具有特別的重要性，因為它對於失敗之早期檢測是一重要診斷工具。≥ 5.0 μm 微粒計數之偶爾顯示，可能係由於電子雜訊、迷光（stray light）、偶合等所致之非真實計數（false counts）。然而，連貫性或規則性的低計數，可能是一污染事件的指標，且應加以調查。該等事件可能指出 HVAC 系統之早期異常、充填設備異常，或者，亦可能係在機器安裝及例行操作期間不良操作實務的徵兆。	13. In Grade A and B zones, the monitoring of the ≥5.0 μm particle concentration count takes on a particular significance as it is an important diagnostic tool for early detection of failure. The occasional indication of ≥5.0 μm particle counts may be false counts due to electronic noise, stray light, coincidence, etc. However consecutive or regular counting of low levels is an indicator of a possible contamination event and should be investigated. Such events may indicate early failure of the HVAC system, filling equipment failure or may also be diagnostic of poor practices during machine set-up and routine operation.

14. 在「靜態」表中所示之微粒限量應在作業完成後的無人狀態中，於 15-20 分鐘(指引值)之短暫「清除」期間（“clean up” period）中達成。	14. The particle limits given in the table for the “at rest” state should be achieved after a short “clean up” period of 15-20 minutes (guidance value) in an unmanned state after completion of operations.
15. C 級與 D 級區之動態監測應依品質風險管理的原則執行。其要求及警戒/行動值將取決於所執行操作作業之本質，但應於「清除期間」內達到建議之靜態潔淨區要求。	15. The monitoring of Grade C and D areas in operation should be performed in accordance with the principles of quality risk management. The requirements and alert/action limits will depend on the nature of the operations carried out, but the recommended “clean up period” should be attained.
16. 其他特徵，例如溫度及相對濕度，取決於產品及執行之作業的性質。這些參數不應影響已定義之潔淨度標準。	16. Other characteristics such as temperature and relative humidity depend on the product and nature of the operations carried out. These parameters should not interfere with the defined cleanliness standard.

17. 在各種不同等級從事之作業的實例，如下表所示（亦請參見第 28 及 35 節段）：

等級	最終滅菌產品的作業實例（請參見第 28-30 節）
A	當產品的充填處於異常風險時。
C	當溶液的調製處於異常風險時、產品的充填。
D	供後續充填溶液的製備及組件之準備。

等級	無菌製備作業的實例（請參見第 31-35 節）
A	無菌製備與充填。
C	要過濾之溶液的調製。
	待過濾溶液之製備。
D	洗滌後之組件的處理。

17. Examples of operations to be carried out in the various grades are given in the table below (see also paragraphs 28 to 35):

Grade	Examples of operations for terminally sterilised products (see para. 28-30)
A	**Filling of products, when unusually at risk**
C	**Preparation of solutions, when unusually at risk. Filling of products**
D	**Preparation of solutions and components for subsequent filling**

Grade	Examples of operations for aseptic preparations (see para. 31-35)
A	**Aseptic preparation and filling**
C	**Preparation of solutions to be filtered**
D	**Handling of components after washing**

18. 從事無菌作業時，作業區應時常使用諸如落菌培養皿、容量測定空氣取樣及表面取樣(例如擦拭法與培養皿接觸法)等方法監測。使用於動態中的取樣方法不得影響區域的保護措施。當審查最終產品放行的批次文件時，監測結果應列入考慮。關鍵操作後應監測表面及人員。	18. Where aseptic operations are performed monitoring should be frequent using methods such as settle plates, volumetric air and surface sampling (e.g. swabs and contact plates). Sampling methods used in operation should not interfere with zone protection. Results from monitoring should be considered when reviewing batch documentation for finished product release. Surfaces and personnel should be monitored after critical operations.
生產作業外之作業，例如在系統確效、清潔及滅菌處理後，亦需執行微生物學監測。	Additional microbiological monitoring is also required outside production operations, e.g. after validation of systems, cleaning and sanitation.

19. 動態潔淨區之微生物監測的建議限量

	微生物污染的建議限量[(a)]			
等級	空氣樣品 cfu/m^3	落菌培養皿 (直徑 90 mm)，cfu/4 時[(b)]	接觸培養皿 (直徑 55 mm)，cfu/培養皿	手套指印 印 5 根手指/手套 cfu/手套
A	<1	<1	<1	<1
B	10	5	5	5
C	100	50	25	-
D	200	100	50	-

註： (a) 這些都是平均值.
(b) 個別的落菌培養皿暴露時間得少於 4 小時.

19. Recommended limits for microbiological monitoring of clean areas in operation:

	Recommended limits for microbial contamination[(a)]			
Grade	Air sample cfu/m^3	Settle plates (diam. 90 mm) cfu/4hours[(b)]	Contact plates (diam. 55 mm), cfu/plate	Glove print 5 fingers cfu/glove
A	< 1	< 1	< 1	< 1
B	10	5	5	5
C	100	50	25	-
D	200	100	50	-

Notes: (a) These are average values.
(b) Individual settle plates may be exposed for less than 4 hours.

20. 微粒及微生物監測的結果，應設定適當的警戒與行動限量。作業程序應規定超出這些限量時之矯正措施。	20. Appropriate alert and action limits should be set for the results of particulate and microbiological monitoring. If these limits are exceeded, operating procedures should prescribe corrective action.
隔離裝置技術	**ISOLATOR TECHNOLOGY**
21. 隔離裝置技術之使用，將製造區域之人為的介入降到最低，可顯著降低無菌製造產品受來自環境之微生物污染的風險。隔離及轉送裝置有多種設計。隔離裝置及其背景環境應經設計以使其達到個別區域要求之空氣品質。隔離裝置由不同材料所建造，該等材料多少會有穿孔及漏裂之傾向。轉送裝置會有單門、雙門，到與滅菌機制結合之完全密閉系統等不同設計。	21. The utilisation of isolator technology to minimise human interventions in processing areas may result in a significant decrease in the risk of microbiological contamination of aseptically manufactured products from the environment. There are many possible designs of isolators and transfer devices. The isolator and the background environment should be designed so that the required air quality for the respective zones can be realised. Isolators are constructed of various materials more or less prone to puncture and leakage. Transfer devices may vary from a single door to double door designs to fully sealed systems incorporating sterilisation mechanisms.
22. 原物料轉入及轉出隔離裝置是污染的最大潛在來源之一。即使層流空氣可能不會存在於所有此種裝置的作業區中是被認可的，但一般而言，隔離裝置的內部區域通常是高風險作業的局部區域。	22. The transfer of materials into and out of the unit is one of the greatest potential sources of contamination. In general the area inside the isolator is the local zone for high risk manipulations, although it is recognised that laminar air flow may not exist in the working zone of all such devices.
23. 背景環境所需之空氣等級取決於隔離裝置的設計及其應用。該背景環境應加以管制，且應至少在 D 級背景環境下執行該無菌操作。	23. The air classification required for the background environment depends on the design of the isolator and its application. It should be controlled and for aseptic processing be at least grade D.
24. 隔離裝置應僅在適當確效後始得採用。確效應考慮隔離裝置技術之全部關鍵性因素，例如，隔離裝置內部與外部（背景環境）的空氣品質、隔離裝置的滅菌處理、轉送過程及隔離裝置的完整性等。	24. Isolators should be introduced only after appropriate validation. Validation should take into account all critical factors of isolator technology, for example the quality of the air inside and outside (background) the isolator, sanitation of the isolator, the transfer process and isolator integrity.

25. 監測應例行執行，且應包含隔離裝置及手套/袖套系統頻繁之洩漏試驗。	25. Monitoring should be carried out routinely and include frequent leak testing of the isolator and glove/sleeve system.
成型/充填/密封技術	**BLOW/FILL/SEAL TECHNOLOGY**
26. 成型/充填/密封設備係為一定目的建造之機器。容器從熱塑性塑膠粒成型、充填並密封之連續作業，完全由此自動化機器完成。若作業人員使用 A/B 級衣著時，則配備有效 A 級氣浴裝置而使用於無菌操作生產的成型/充填/密封設備，得安裝在至少 C 級的環境中。該背景環境在靜態時，應符合微生物及浮游微粒的限量；在動態時，只要符合微生物的限量。 使用於生產最終滅菌產品之成型/充填/密封設備，應安裝在至少為 D 級的環境中。	26. Blow/fill/seal units are purpose built machines in which, in one continuous operation, containers are formed from a thermoplastic granulate, filled and then sealed, all by the one automatic machine. Blow/fill/seal equipment used for aseptic production which is fitted with an effective grade A air shower may be installed in at least a grade C environment, provided that grade A/B clothing is used. The environment should comply with the viable and non viable limits at rest and the viable limit only when in operation. Blow/fill/seal equipment used for the production of products which are terminally sterilised should be installed in at least a grade D environment.
27. 因這是特殊的技術，故至少要特別注意下列事項： - 設備之設計及驗證 - 原位清潔(cleaning-in-place)及原位滅菌(sterilisation-in-place)的確效及再現性 - 設備座落之背景潔淨室環境 - 操作者之訓練及著衣 - 設備之關鍵區域的介入，包括在充填開始前之任何無菌組裝在內。	27. Because of this special technology particular attention should be paid to, at least the following: - equipment design and qualification - validation and reproducibility of cleaning-in-place and sterilisation-inplace - background clean room environment in which the equipment is located - operator training and clothing - interventions in the critical zone of the equipment including any aseptic assembly prior to the commencement of filling.
最終滅菌的產品	**TERMINALLY STERILISED PRODUCTS**
28. 為提供微生物與微粒污染的低風險環境，以適合於過濾與滅菌，組件之準備及大多數產品之製備應至少在 D 級中為之。當該產品有微生物污染之高風險或異常風險時（例如，因該產品滋養微生物生長，或滅菌前必需長期間保存，或主要需在密閉設備中加工但無法達成者），則其準備/製備應在 C 級環境中執行。	28. Preparation of components and most products should be done in at least a grade D environment in order to give low risk of microbial and particulate contamination, suitable for filtration and sterilisation. Where the product is at a high or unusual risk of microbial contamination, (for example, because the product actively

	supports microbial growth or must be held for a long period before sterilisation or is necessarily processed not mainly in closed vessels), then preparation should be carried out in a grade C environment.
29. 最終滅菌產品的充填，應至少在 C 級環境中為之。	29. Filling of products for terminal sterilisation should be done in at least a grade C environment.
30. 產品處於來自環境的污染之異常風險者，例如，因充填作業緩慢，或容器為廣口，或在密封前必需暴露數秒鐘以上的時間，其充填應在具有至少 C 級背景環境之 A 級區中為之。軟膏劑、乳膏劑、懸液劑及乳劑於最終滅菌前，其製備與充填，通常應在 C 級環境中為之。	30. Where the product is at unusual risk of contamination from the environment, for example because the filling operation is slow or the containers are wide-necked or are necessarily exposed for more than a few seconds before sealing, the filling should be done in a grade A zone with at least a grade C background. Preparation and filling of ointments, creams, suspensions and emulsions should generally be carried out in a grade C environment before terminal sterilisation.
無菌製備	**ASEPTIC PREPARATION**
31. 洗滌後的組件，應在至少 D 級環境中處理。無菌原料與組件的處理應在具有 B 級背景的 A 級環境中執行，除非須經滅菌，或在製程中的後段經由微生物滯留濾器過濾。	31. Components after washing should be handled in at least a grade D environment. Handling of sterile starting materials and components, unless subjected to sterilisation or filtration through a micro-organism-retaining filter later in the process, should be done in a grade A environment with grade B background.
32. 製程中待無菌過濾之溶液的製備，應在 C 級環境中為之；不經無菌過濾者，其原物料的準備與產品的製備，應在具有 B 級背景的 A 級環境中為之。	32. Preparation of solutions which are to be sterile filtered during the process should be done in a grade C environment; if not filtered, the preparation of materials and products should be done in a grade A environment with a grade B background.
33. 無菌製備之產品的處理及充填應在具有 B 級背景的 A 級環境中為之。	33. Handling and filling of aseptically prepared products should be done in a grade A environment with a grade B background.
34. 完成封塞前，部分封閉之容器的轉送，如使用在冷凍乾燥中，應在具有 B 級背景的 A 級環境中，或應在 B 級環境中以密閉的轉送盤為之。	34. Prior to the completion of stoppering, transfer of partially closed containers, as used in freeze drying, should be done either in a grade A environment with grade B background or in sealed transfer trays in a grade B environment.

35. 製程中暴露之無菌軟膏劑、乳膏劑、懸液劑及乳劑不經後續過濾者，其製備與充填應在具有 B 級背景的 A 級環境中執行。	35. Preparation and filling of sterile ointments, creams, suspensions and emulsions should be done in a grade A environment, with a grade B background, when the product is exposed and is not subsequently filtered.
人員	**PERSONNEL**
36. 應僅有所需之最少人員可在潔淨區的現場，在無菌作業期間這是特別重要。檢查與管制應盡可能在潔淨區外執行。	36. Only the minimum number of personnel required should be present in clean areas; this is particularly important during aseptic processing. Inspections and controls should be conducted outside the clean areas as far as possible.
37. 潔淨區中工作的所有人員（包含從事清潔及維修保養之人員），應接受有關正確製造無菌產品之規範的定期訓練。該訓練應包含衛生及微生物學的基本原理。有必要將未接受過此種訓練的外部人員（例如，建築或維修保養的承包商）帶進無菌區時，應特別注意對其指導及監督。	37. All personnel (including those concerned with cleaning and maintenance) employed in such areas should receive regular training in disciplines relevant to the correct manufacture of sterile products. This training should include reference to hygiene and to the basic elements of microbiology. When outside staff who have not received such training (e.g. building or maintenance contractors) need to be brought in, particular care should be taken over their instruction and supervision.
38. 已從事於非目前製造過程使用的動物組織材料或微生物培養物之工作人員，不得進入無菌產品區，除非已遵守嚴格且清楚界定的進入程序。	38. Staff who have been engaged in the processing of animal tissue materials or of cultures of micro-organisms other than those used in the current manufacturing process should not enter sterile-product areas unless rigorous and clearly defined entry procedures have been followed.
39. 高標準的個人衛生及潔淨度是必要的。對參與無菌製劑製造的人員，應指導其提報任何可能引起異常數目或類型之污染物脫落的狀況；對該等狀況，定期健康檢查是有其必要的。對可能引起不適當之微生物危險的人員採取之行動，應由指派之權責人員決定。	39. High standards of personal hygiene and cleanliness are essential. Personnel involved in the manufacture of sterile preparations should be instructed to report any condition which may cause the shedding of abnormal numbers or types of contaminants; periodic health checks for such conditions are desirable. Actions to be taken about personnel who could be introducing undue microbiological hazard should be decided by a designated competent person.
40. 潔淨區中不得配戴手錶、珠寶及使用化妝	40. Wristwatches, make-up and jewellery

品。	should not be worn in clean areas.
41. 衣服之更換與洗滌應遵循指定之書面程序，以將潔淨區衣著的污染或帶入潔淨區之污染物降至最低。	41. Changing and washing should follow a written procedure designed to minimise contamination of clean area clothing or carry-through of contaminants to the clean areas.
42. 衣著及其品質應適合於製程與作業區的等級。應以保護產品免於受到污染的方式穿戴。	42. The clothing and its quality should be appropriate for the process and the grade of the working area. It should be worn in such a way as to protect the product from contamination.
43. 每一等級的區域要求之衣著，其說明如下：	43. The description of clothing required for each grade is given below:
D級： 人員的頭髮及蓄留之鬍鬚，應予覆蓋。應穿著一般的保護套裝及適當的鞋子或鞋套。為避免任何來自潔淨區外的污染，應採取適當的措施。	Grade D: Hair and, where relevant, beard should be covered. A general protective suit and appropriate shoes or overshoes should be worn. appropriate measures should be taken to avoid any contamination coming from outside the clean area.
C 級： 人員的頭髮、蓄留之鬍鬚及八字鬍，應予覆蓋。應穿著在腕部收緊及高領的單件式或兩件式褲套裝，及適當的鞋子或鞋套。此衣著應無纖維或微粒異物釋出。	Grade C: Hair and where relevant beard and moustache should be covered. A single or two-piece trouser suit, gathered at the wrists and with high neck and appropriate shoes or overshoes should be worn. They should shed virtually no fibres or particulate matter.
A/B 級： 頭罩應完全包覆頭髮，及如有蓄留鬍鬚及八字鬍；頭罩末端應塞入套裝的領子內；應戴面罩，以防止液滴之散逸。應穿戴經適當滅菌、未沾粉末的橡皮或塑膠手套及滅菌過或消毒過的鞋子；褲管底端應塞入鞋內，衣袖應塞入手套內。防護衣實際上應幾無纖維或微粒物釋出，並阻擋由身體脫落的微粒。	Grade A/B: Headgear should totally enclose hair and, where relevant, beard and moustache; it should be tucked into the neck of the suit; a face mask should be worn to prevent the shedding of droplets. Appropriate sterilised, non-powdered rubber or plastic gloves and sterilised or disinfected footwear should be worn. Trouser-legs should be tucked inside the footwear and garment sleeves into the gloves. The protective clothing should shed virtually no fibres or particulate matter and retain particles shed by the body.

44. 廠外衣服不得帶入通往B級及C級區之更衣室中。應對每位在 A/B 級區之工作人員，在每一工作時段提供潔淨無菌(經滅菌或經適當滅菌)的防護裝。作業期間，應定期消毒手套。面罩及手套至少應在每一工作時段更換之。	44. Outdoor clothing should not be brought into changing rooms leading to grade B and C rooms. For every worker in a grade A/B area, clean sterile (sterilised or adequately sanitised) protective garments should be provided at each work session. Gloves should be regularly disinfected during operations. Masks and gloves should be changed at least for every working session.
45. 潔淨區的衣服應以不致積聚可能會在後來脫落之額外污染物的方式清潔及處理。這些作業應遵循書面程序。對於此類衣服，最好有其單獨的洗衣設備。衣服之不適當的處理會損傷其纖維，從而可能增加微粒脫落的風險。	45. Clean area clothing should be cleaned and handled in such a way that it does not gather additional contaminants which can later be shed. These operations should follow written procedures. Separate laundry facilities for such clothing are desirable. Inappropriate treatment of clothing will damage fibres and may increase the risk of shedding of particles.
廠房	**PREMISES**
46. 潔淨區內，所有暴露的表面均應平滑、不滲透且無破裂，使微粒或微生物的釋出或積聚降到最低，且所有暴露的表面可容許重覆使用清洗劑，及消毒劑(如有使用時)。	46. In clean areas, all exposed surfaces should be smooth, impervious and unbroken in order to minimise the shedding or accumulation of particles or micro-organisms and to permit the repeated application of cleaning agents, and disinfectants where used.
47. 為減少灰塵的積聚及利於清潔，不應有無法清潔的凹處，且應盡量避免突出的壁架、儲架、杯架/櫃及設備。門之設計應避免無法清潔的凹處；因此，滑動門可能不合適。	47. To reduce accumulation of dust and to facilitate cleaning there should be no uncleanable recesses and a minimum of projecting ledges, shelves, cupboards and equipment. Doors should be designed to avoid those uncleanable recesses; sliding doors may be undesirable for this reason.
48. 夾層天花板應予密封，以防止來自其上方空間的污染。	48. False ceilings should be sealed to prevent contamination from the space above them.
49. 管線、管道及其他公用設施之安裝，應使其不產生凹處、未密封的開口及難以清潔的表面。	49. Pipes and ducts and other utilities should be installed so that they do not create recesses, unsealed openings and surfaces which are difficult to clean.
50. A/B級區之無菌製造場所，應禁用水槽與排水設施。其他區域，應在機器、水槽及排水設施間裝配空氣阻斷裝置。潔淨度等級較低的潔淨室內，其地板的排水設施應裝配捕集器或水封，以防止逆流。	50. Sinks and drains should be prohibited in grade A/B areas used for aseptic manufacture. In other areas air breaks should be fitted between the machine or sink and the drains. Floor drains in lower grade clean rooms should be fitted with

	traps or water seals to prevent backflow.
51. 更衣室應設計成氣鎖室，用來提供不同更衣階段之實體的隔離，以將防護裝之微生物及微粒污染減到最低。更衣室應以過濾的空氣有效地沖洗。在靜態時，更衣室最後階段之潔淨度應與將進入之潔淨區的潔淨度等級相同。進入與離開潔淨區，使用各自的更衣室有時是必要的。通常，洗手設備應只在更衣室的第一個階段提供。	51. Changing rooms should be designed as airlocks and used to provide physical separation of the different stages of changing and so minimise microbial and particulate contamination of protective clothing. They should be flushed effectively with filtered air. The final stage of the changing room should, in the at-rest state, be the same grade as the area into which it leads. The use of separate changing rooms for entering and leaving clean areas is sometimes desirable. In general hand washing facilities should be provided only in the first stage of the changing rooms.
52. 氣鎖室兩邊的門不得同時開啟，應啟動互鎖系統或視覺及/或聽覺的警報系統，以防止在同一時間有一個以上的門同時開啟。	52. Both airlock doors should not be opened simultaneously. An interlocking system or a visual and/or audible warning system should be operated to prevent the opening of more than one door at a time.
53. 全部的作業條件下，相對於較低潔淨度等級的周圍區域，過濾過的空氣應維持其正壓及空氣的流動，且應有效地沖洗該潔淨區。不同等級之毗鄰潔淨室應有10-15 pa (1.0-1.5 mm水柱)的壓差（指引值）。最大風險區域的保護措施應予特別注意。該區域為產品及接觸產品之潔淨組件所暴露之直接環境。需要圍堵某些物質，例如，致病性、高毒性、放射性或活病毒或活細菌的原料或產品的情況時，其空氣供應及壓差的各種建議可能需要修改。對於某些作業，設施的去污染與離開潔淨室之空氣的處理可能是必須的。	53. A filtered air supply should maintain a positive pressure and an air flow relative to surrounding areas of a lower grade under all operational conditions and should flush the area effectively. Adjacent rooms of different grades should have a pressure differential of 10-15 pascals (guidance values). Particular attention should be paid to the protection of the zone of greatest risk, that is, the immediate environment to which a product and cleaned components which contact the product are exposed. The various recommendations regarding air supplies and pressure differentials may need to be modified where it becomes necessary to contain some materials, e.g. pathogenic, highly toxic, radioactive or live viral or bacterial materials or products. Decontamination of facilities and treatment of air leaving a clean area may be necessary for some operations.

54. 應證明空氣流動的型態不會造成污染風險，例如，應小心確保空氣流動不會將人員、作業或機器產生之微粒散佈到較高產品風險的區域。	54. It should be demonstrated that air-flow patterns do not present a contamination risk, e.g. care should be taken to ensure that air flows do not distribute particles from a particlegenerating person, operation or machine to a zone of higher product risk.
55. 應提供警報系統，以顯示空氣供應上的失靈。在壓差重要的區域間，應安裝壓差計。這些壓差應定期記錄，或用其他的方法予以文件化。	55. A warning system should be provided to indicate failure in the air supply. Indicators of pressure differences should be fitted between areas where these differences are important. These pressure differences should be recorded regularly or otherwise documented.
設備	**EQUIPMENT**
56. 輸送帶不得通過介於 A 級或 B 級區與較低空氣潔淨度之作業區間的隔板/隔牆，除非該輸送帶本身是持續地滅菌的（例如：在一個滅菌的隧道中）。	56. A conveyor belt should not pass through a partition between a grade A or B area and a processing area of lower air cleanliness, unless the belt itself is continually sterilised (e.g. in a sterilising tunnel).
57. 設備、配件及支援服務之設計與安裝，應盡可能使其作業(註：非生產作業)、維護保養及修理能在潔淨區外執行。需要滅菌者，應盡可能在完成組裝後為之。	57. As far as practicable equipment, fittings and services should be designed and installed so that operations, maintenance and repairs can be carried out outside the clean area. If sterilisation is required, it should be carried out, wherever possible, after complete reassembly.
58. 倘若設備之維護保養已在潔淨區內執行，且在該維修工作期間未維持所要求之潔淨度及/或無菌性的標準者，於製造作業再開始前，該區域應予清潔、消毒及/或滅菌(合適時)。	58. When equipment maintenance has been carried out within the clean area, the area should be cleaned, disinfected and/or sterilised where appropriate, before processing recommences if the required standards of cleanliness and/or asepsis have not been maintained during the work.
59. 水處理設施及輸送系統，應經設計、建造及維護保養，以確保適當品質之可靠水源。該系統之運轉不得超出其設計能量（capacity）。注射用水應以阻止微生物生長的方式生產、儲存及輸送，例如在70 ℃以上恆定循環。	59. Water treatment plants and distribution systems should be designed, constructed and maintained so as to ensure a reliable source of water of an appropriate quality. They should not be operated beyond their designed capacity. Water for injections should be produced, stored and distributed in a manner which prevents microbial growth, for example by constant circulation at a temperature above 70 °C.

60. 所有設備，例如：滅菌器、空氣處理及過濾系統、空氣通氣口及氣體過濾器、水處理、水製造、儲存與輸送系統，均應確效及有計畫的維護保養；其再使用應經核可。	60. All equipment such as sterilisers, air handling and filtration systems, air vent and gas filters, water treatment, generation, storage and distribution systems should be subject to validation and planned maintenance; their return to use should be approved.
衛生處理	**SANITATION**
61. 潔淨區的衛生處理特別重要，應依書面程序徹底清潔。使用消毒劑者，應採用一種以上的消毒劑。為了檢測抗藥性菌株的產生，應進行定期監測。	61. The sanitation of clean areas is particularly important. They should be cleaned thoroughly in accordance with a written programme. Where disinfectants are used, more than one type should be employed. Monitoring should be undertaken regularly in order to detect the development of resistant strains.
62. 消毒劑與清潔劑應監測其微生物的污染；稀釋液應保存在預先洗淨的容器中，且除非經過滅菌，應只在界定的期間內儲存。使用於A級及B級區的消毒劑與清潔劑，使用前應是無菌的。	62. Disinfectants and detergents should be monitored for microbial contamination; dilutions should be kept in previously cleaned containers and should only be stored for defined periods unless sterilised. Disinfectants and detergents used in Grades A and B areas should be sterile prior to use.
63. 潔淨區的燻蒸對於降低不易接近/進入之處所的微生物污染，可能是有用的。	63. Fumigation of clean areas may be useful for reducing microbiological contamination in inaccessible places.
製程作業	**PROCESSING**
64. 所有製程階段中，包含滅菌前的階段，應採取預防措施，以將污染降到最低。	64. Precautions to minimise contamination should be taken during all processing stages including the stages before sterilisation.
65. 源自於微生物的製劑，不得於其他藥品之製造區域中製備或充填；然而，在去活化後之死微生物體的疫苗或細菌萃取物疫苗，可在其他無菌藥品之相同的廠房設施中充填。	65. Preparations of microbiological origin should not be made or filled in areas used for the processing of other medicinal products; however, vaccines of dead organisms or of bacterial extracts may be filled, after inactivation, in the same premises as other sterile medicinal products.
66. 無菌作業的確效，應包含使用營養培養基之製程模擬試驗（培養基充填）。營養培養基的選擇應基於產品的劑型及營養培	66. Validation of aseptic processing should include a process simulation test using a nutrient medium (media fill). Selection of

養基之選擇性、澄明度、濃度及滅菌的適合性。	the nutrient medium should be made based on dosage form of the product and selectivity, clarity, concentration and suitability for sterilisation of the nutrient medium.
67. 製程模擬試驗應盡可能模擬例行的無菌製造過程，並包含所有關鍵的後續製造步驟，並應考量已知在正常生產中，及在最差狀況發生的各種介入。	67. The process simulation test should imitate as closely as possible the routine aseptic manufacturing process and include all the critical subsequent manufacturing steps. It should also take into account various interventions known to occur during normal production as well as worst-case situations.
68. 製程模擬試驗應對每個作業輪班，執行三次連續滿意的模擬試驗作為初始確效，並在界定的時間間隔及對 HVAC 系統、設備、製程與輪班次數有任何重大變更後，重複執行。通常，製程模擬試驗應對每一輪班與製程每年重複兩次。	68. Process simulation tests should be performed as initial validation with three consecutive satisfactory simulation tests per shift and repeated at defined intervals and after any significant modification to the HVAC system, equipment, process and number of shifts. Normally process simulation tests should be repeated twice a year per shift and process.
69. 使用於培養基充填的容器數目應足使其能夠有效評估。對於小批量的生產，其培養基充填的容器數目應至少等於該產品批次的批量。目標值應為無生長並適用下列規定：	69. The number of containers used for media fills should be sufficient to enable a valid evaluation. For small batches, the number of containers for media fills should at least equal the size of the product batch. The target should be zero growth and the following should apply:
● 充填少於 5000 單元者，不得有任何污染單元。	● When filling fewer than 5000 units, no contaminated units should be detected.
● 充填 5000 至 10,000 單元者： a) 有一個受污染單元時，應予以調查，包含重複執行培養基充填的考量在內； b) 有二個受污染單元時，應於調查後，就其原因進行再確效。	● When filling 5,000 to 10,000 units: a) One (1) contaminated unit should result in an investigation, including consideration of a repeat media fill; b) Two (2) contaminated units are considered cause for revalidation, following investigation.
● 充填多於 10,000 單元者， a) 有一個受污染單元時，應予以調查； b) 有二個受污染單元時，應於調查後，就其原因進行再確效[1]。	● When filling more than 10,000 units: a) One (1) contaminated unit should result in an investigation; b) Two (2) contaminated units are considered cause for revalidation, following investigation[1].
[1] *關於無菌操作之確效的進一步細節，請參考 PIC/S 關於無菌操作之確效的建議*	[1] *For further details on the validation of aseptic processing, please refer to the*

(PI 007) 。	*PIC/S Recommendation on the Validation of Aseptic Processing (PI 007)*
70. 對於任何測試之單元數，其微生物污染之間歇性事件，可能是低度污染的徵象應予調查。對於重大失敗之調查，應包括對前次成功的培養基充填後，所製造批次之無菌性保證的可能影響。	70. For any run size, intermittent incidents of microbial contamination may be indicative of low-level contamination that should be investigated. Investigation of gross failures should include the potential impact on the sterility assurance of batches manufactured since the last successful media fill.
71. 應注意任何確效不得損及製程。	71. Care should be taken that any validation does not compromise the processes.
72. 水源、水處理設備及經過處理的水均應定期監測其化學及生物學的污染，及內毒素(當合適時)，該監測的結果及採取的任何行動之紀錄均應予以保存。	72. Water sources, water treatment equipment and treated water should be monitored regularly for chemical and biological contamination and, as appropriate, for endotoxins. Records should be maintained of the results of the monitoring and of any action taken.
73. 潔淨區中，尤其是當無菌作業正進行時，應保持最小的作業活動，且人員的移動應加以管制並使其井然有序，以避免由於過度激烈的活動引起微粒及微生物的過度散落。由於作業人員穿戴衣著的特質，周遭的溫度與濕度不應高到令其不舒適。	73. Activities in clean areas and especially when aseptic operations are in progress should be kept to a minimum and movement of personnel should be controlled and methodical, to avoid excessive shedding of particles and organisms due to over-vigorous activity. The ambient temperature and humidity should not be uncomfortably high because of the nature of the garments worn.
74. 原料之微生物學上的污染應為最低。經由監測顯示需要微生物學上之品質要求者，其規格應包含該要求。	74. Microbiological contamination of starting materials should be minimal. Specifications should include requirements for microbiological quality when the need for this has been indicated by monitoring.
75. 潔淨區中，容易產生纖維的容器與原物料，應降至最低。	75. Containers and materials liable to generate fibres should be minimised in clean areas.
76. 合適時，應採取措施，將最終產品的微粒污染降至最低。	76. Where appropriate, measures should be taken to minimise the particulate contamination of the end product.

77. 組件、容器及設備在最終清潔過程後，應以使其不再被污染的方式處理。	77. Components, containers and equipment should be handled after the final cleaning process in such a way that they are not recontaminated.
78. 組件、容器及設備之洗滌及乾燥與滅菌的間隔期間，以及其滅菌與使用之間隔期間，應縮至最短，且應受適合其儲存條件的時間限制。	78. The interval between the washing and drying and the sterilisation of components, containers and equipment as well as between their sterilization and use should be minimised and subject to a time-limit appropriate to the storage conditions.
79. 從溶液製備開始至其滅菌之時間，或從溶液製備開始至其經微生物滯留濾器過濾之時間，應縮至最短。每一產品考量其組成及規定之儲存方法，應有設定之最長容許時間。	79. The time between the start of the preparation of a solution and its sterilisation or filtration through a micro-organism-retaining filter should be minimised. There should be a set maximum permissible time for each product that takes into account its composition and the prescribed method of storage.
80. 滅菌前應監測其負荷菌。緊接滅菌前之污染應有作業限量，該限量與要採用之滅菌方法的效能有關。對於無菌充填的產品及最終滅菌的產品之每一批次皆應執行負荷菌分析。對於最終滅菌產品設定為過度滅菌參數者，負荷菌得僅在適當排定之時間間隔監測。對參數放行系統，負荷菌分析應對每一批次執行，並作為製程中測試。合適時，應監測內毒素含量。所有溶液，尤其是大型輸注液，應通過微生物滯留濾器過濾。如果可能，該過濾器位置應緊接於充填之前。	80. The bioburden should be monitored before sterilisation. There should be working limits on contamination immediately before sterilisation, which are related to the efficiency of the method to be used. Bioburden assay should be performed on each batch for both aseptically filled product and terminally sterilised products. Where overkill sterilisation parameters are set for terminally sterilised products, bioburden might be monitored only at suitable scheduled intervals. For parametric release systems, bioburden assay should be performed on each batch and considered as an in-process test. Where appropriate the level of endotoxins should be monitored. All solutions, in particular large volume infusion fluids, should be passed through a microorganism-retaining filter, if possible sited immediately before filling.
81. 潔淨區進行無菌作業所需要之組件、容器、設備及任何其他物品，應予滅菌，並通過密封在牆壁中的雙門滅菌器進入該潔淨區，或經由可達到不會導入污染的相同目的之程序進入。非可燃性氣體應通過微生物滯留濾器。	81. Components, containers, equipment and any other article required in a clean area where aseptic work takes place should be sterilised and passed into the area through double-ended sterilisers sealed into the wall, or by a procedure which achieves the

	same objective of not introducing contamination. Noncombustible gases should be passed through micro-organism retentive filters.
82. 任何新程序的效能都應予以確效，且該確效應依其性能表現歷史為基礎，在排定時間間隔進行確認，或在製程或設備做出任何重大變更時，亦應進行確認。	82. The efficacy of any new procedure should be validated, and the validation verified at scheduled intervals based on performance history or when any significant change is made in the process or equipment.
滅菌	**STERILISATION**
83. 所有滅菌過程應予以確效。當採用的滅菌方法為非現行版本之相關藥典所述的方法，或當該藥典方法使用於非單純水性或油性溶液的產品時，應予特別注意。可行時，加熱滅菌是首選的方法。在任何情況中，滅菌過程應符合上市與製造許可。	83. All sterilisation processes should be validated. Particular attention should be given when the adopted sterilisation method is not described in the current edition of the European Pharmacopoeia, or when it is used for a product which is not a simple aqueous or oily solution. Where possible, heat sterilisation is the method of choice. In any case, the sterilisation process must be in accordance with the marketing and manufacturing authorisations.
84. 任何滅菌過程在被採用前，對產品及其在每一種要滅菌處理之裝載型式的所有部位，達成所期望滅菌條件效能的適當性，應以物理量測及生物指示劑(合適時)加以證明。該滅菌過程的有效性應在排定的時間間隔，至少每年一次，及每當對設備做出重大修改時，加以確認。這些結果的紀錄應予以保存。	84. Before any sterilisation process is adopted its suitability for the product and its efficacy in achieving the desired sterilising conditions in all parts of each type of load to be processed should be demonstrated by physical measurements and by biological indicators where appropriate. The validity of the process should be verified at scheduled intervals, at least annually, and whenever significant modifications have been made to the equipment. Records should be kept of the results.
85. 為有效滅菌，物料的全部皆應接受所需之處理，且該過程應經設計以確保其已達成有效滅菌。	85. For effective sterilisation the whole of the material must be subjected to the required treatment and the process should be designed to ensure that this is achieved.
86. 所有滅菌過程，應建立經確效的裝載型式。	86. Validated loading patterns should be established for all sterilisation processes.

87. 生物指示劑應視為監測滅菌之附加方法。生物指示劑應依製造者的指示儲存及使用，並應以陽性對照品核對其品質。如果使用生物指示劑，應採取嚴格的防範措施，以避免由其移轉微生物污染。	87. Biological indicators should be considered as an additional method for monitoring the sterilisation. They should be stored and used according to the manufacturer's instructions, and their quality checked by positive controls. If biological indicators are used, strict precautions should be taken to avoid transferring microbial contamination from them.
88. 應有清楚區分未滅菌及已滅菌產品的方法。每一個盛裝產品或組件的籃子、盤子或其他搬運架，皆應清楚標示其名稱、批號及是否經滅菌。合適時，可使用指示劑，例如高壓蒸氣滅菌指示帶，標示一個批次（或次批次）是否已完成滅菌過程，惟其結果無法實際作為該批次為無菌的可靠指標。	88. There should be a clear means of differentiating products which have not been sterilised from those which have. Each basket, tray or other carrier of products or components should be clearly labelled with the material name, its batch number and an indication of whether or not it has been sterilised. Indicators such as autoclave tape may be used, where appropriate, to indicate whether or not a batch (or sub-batch) has passed through a sterilisation process, but they do not give a reliable indication that the lot is, in fact, sterile.
89. 每一個滅菌操作應有其滅菌紀錄，且應當作批次放行程序的一部份予以核准。	89. Sterilisation records should be available for each sterilisation run. They should be approved as part of the batch release procedure.
加熱滅菌法	**STERILISATION BY HEAT**
90. 每一個加熱滅菌週期應記錄在具足夠大刻度的時間/溫度圖表上，或以具有適當準確度與精密度之其他適當設備記錄。使用於控制及/或記錄之溫度探針的位置，應在確效時即已決定；可行時，亦應以置放在相同位置之第二個獨立溫度探針核對。	90. Each heat sterilisation cycle should be recorded on a time/temperature chart with a sufficiently large scale or by other appropriate equipment with suitable accuracy and precision. The position of the temperature probes used for controlling and/or recording should have been determined during the validation, and where applicable also checked against a second independent temperature probe located at the same position.
91. 化學或生物指示劑雖亦可使用，但不得取代物理量測。	91. Chemical or biological indicators may also be used, but should not take the place of physical measurements.

92. 滅菌時間之期間的量測於開始前，應有足夠的時間容許裝載物的全部達到所要求的溫度。該時間應針對要處理之每一種裝載型式訂定。	92. Sufficient time must be allowed for the whole of the load to reach the required temperature before measurement of the sterilising time-period is commenced. This time must be determined for each type of load to be processed.
93. 在加熱滅菌週期的高溫階段後，應採取防範措施，防止經滅菌的裝載物在冷卻中受到污染。與產品接觸之任何冷卻流體或氣體應已滅菌，除非能顯示任何洩漏的容器不會被核准使用。	93. After the high temperature phase of a heat sterilisation cycle, precautions should be taken against contamination of a sterilised load during cooling. Any cooling fluid or gas in contact with the product should be sterilised, unless it can be shown that any leaking container would not be approved for use.
濕熱滅菌法	**MOIST HEAT**
94. 溫度與壓力均應用來監測濕熱滅菌過程。通常，控制儀器裝置與監測儀器裝置及其記錄圖表應各自獨立。對這些使用之自動控制與監測系統應加以確效，以確保其符合關鍵過程的要求。系統及滅菌週期之錯誤，應由系統所記錄並為操作者觀察到。滅菌期間，獨立溫度指示器的讀數，應與圖表記錄器例行核對。滅菌艙底部裝有排水口的滅菌器，可能亦須在滅菌期間全程記錄該位置的溫度。真空階段為該滅菌週期之一部分者，對該艙應執行頻繁的洩漏試驗。	94. Both temperature and pressure should be used to monitor the process. Control instrumentation should normally be independent of monitoring instrumentation and recording charts. Where automated control and monitoring systems are used for these applications they should be validated to ensure that critical process requirements are met. System and cycle faults should be registered by the system and observed by the operator. The reading of the independent temperature indicator should be routinely checked against the chart recorder during the sterilisation period. For sterilisers fitted with a drain at the bottom of the chamber, it may also be necessary to record the temperature at this position, throughout the sterilisation period. There should be frequent leak tests on the chamber when a vacuum phase is part of the cycle.

95. 非置於密封容器中而要滅菌之產品，應以容許空氣之移除及蒸氣之穿透，而在滅菌後能防止再污染的材料包覆之。裝載物的所有部位在要求的溫度及期間應與滅菌劑保持接觸。	95. The items to be sterilised, other than products in sealed containers, should be wrapped in a material which allows removal of air and penetration of steam but which prevents recontamination after sterilisation. All parts of the load should be in contact with the sterilising agent at the required temperature for the required time.
96. 應注意確保用於滅菌的蒸氣具有適當的品質，且其所含之添加物濃度不致引起產品或設備污染。	96. Care should be taken to ensure that steam used for sterilisation is of suitable quality and does not contain additives at a level which could cause contamination of product or equipment.
乾熱滅菌法	**DRY HEAT**
97. 乾熱滅菌採用的製程，應包含艙內空氣的循環及正壓的維持，以防止非無菌空氣的進入。任何容許進入的空氣，應通過 HEPA 過濾器。製程亦需移除熱原時，使用內毒素的挑戰試驗應列為確效的一部分。	97. The process used should include air circulation within the chamber and the maintenance of a positive pressure to prevent the entry of non-sterile air. Any air admitted should be passed through a HEPA filter. Where this process is also intended to remove pyrogens, challenge tests using endotoxins should be used as part of the validation.
輻射滅菌法	**STERILISATION BY RADIATION**
98. 輻射滅菌主要用於對熱敏感的原物料與產品的滅菌。許多藥品及一些包裝材料是對輻射線敏感的，因此，本方法僅在經由實驗確認其對於產品不具有害效應時，始可使用。紫外線照射通常不是一個可接受的滅菌方法。	98. Radiation sterilisation is used mainly for the sterilisation of heat sensitive materials and products. Many medicinal products and some packaging materials are radiation-sensitive, so this method is permissible only when the absence of deleterious effects on the product has been confirmed experimentally. Ultraviolet irradiation is not normally an acceptable method of sterilisation.

99. 輻射滅菌程序中，輻射劑量應予以量測。為達此目的，應使用與劑量率無關的劑量指示劑，以提供產品本身接受之劑量的定量性量測。在裝載物中應插入足夠數目與分布的劑量計，以確保在輻射照射器中一直都有一個劑量計。使用塑膠劑量計者，應在其校正的時間限度內使用。劑量計的吸光度應在暴露於輻射後的短時間內讀取。	99. During the sterilisation procedure the radiation dose should be measured. For this purpose, dosimetry indicators which are independent of dose rate should be used, giving a quantitative measurement of the dose received by the product itself. Dosimeters should be inserted in the load in sufficient number and close enough together to ensure that there is always a dosimeter in the irradiator. Where plastic dosimeters are used they should be used within the time-limit of their calibration. Dosimeter absorbances should be read within a short period after exposure to radiation.
100. 生物指示劑可作為附加的管制使用。	100. Biological indicators may be used as an additional control.
101. 確效程序應確保考量到包裝密度上之差異所造成的效應。	101. Validation procedures should ensure that the effects of variations in density of the packages are considered.
102. 原物料之處理程序，應防止已輻射滅菌與未經輻射滅菌之原物料間的混雜。輻射敏感性的變色圓片，亦應使用在每件包裝上，以區分已輻射滅菌及未經輻射滅菌的包裝。	102. Materials handling procedures should prevent mix-up between irradiated and nonirradiated materials. Radiation sensitive colour disks should also be used on each package to differentiate between packages which have been subjected to irradiation and those which have not.
103. 總輻射劑量應在預定的照射時間內達到。	103. The total radiation dose should be administered within a predetermined time span.
環氧乙烯滅菌	**STERILISATION WITH ETHYLENE OXIDE**
104. 本方法應只用在沒有其他方法可用的情形。在滅菌製程確效期間，應顯示對產品無損害的效應，及其除氣所容許的條件與時間，可將任何殘留氣體及反應產物減低至該類型產品或原物料界定之允許限量。	104. This method should only be used when no other method is practicable. During process validation it should be shown that there is no damaging effect on the product and that the conditions and time allowed for degassing are such as to reduce any residual gas and reaction products to defined acceptable limits for the type of product or material.

105. 氣體與微生物細胞間的直接接觸是必需的。為避免可能會包在像結晶或乾燥蛋白質這類物質之微生物的存在，應採取預防措施。包裝材料的特質與數量會顯著影響該滅菌過程。	105. Direct contact between gas and microbial cells is essential; precautions should be taken to avoid the presence of organisms likely to be enclosed in material such as crystals or dried protein. The nature and quantity of packaging materials can significantly affect the process.
106. 暴露於氣體之前，應使原物料達到該過程所要求之濕度與溫度的平衡狀態。達到該狀態所需的時間，應針對在滅菌前應縮減至最短的相對需求加以均衡。	106. Before exposure to the gas, materials should be brought into equilibrium with the humidity and temperature required by the process. The time required for this should be balanced against the opposing need to minimise the time before sterilisation.
107. 每一個滅菌週期皆應以適當的生物指示劑試驗片監測，並將適當數量之試驗片分佈在整個裝載。取得的資訊應涵蓋於批次紀錄中。	107. Each sterilisation cycle should be monitored with suitable biological indicators, using the appropriate number of test pieces distributed throughout the load. The information so obtained should form part of the batch record.
108. 每一滅菌週期，應將完成該週期所用的時間、滅菌期間艙內的壓力、溫度、濕度、所使用之氣體濃度及氣體總量做成紀錄。滅菌週期的全程，應將壓力與溫度記錄在一張圖表上。該等紀錄應納入該批次紀錄中。	108. For each sterilisation cycle, records should be made of the time taken to complete the cycle, of the pressure, temperature and humidity within the chamber during the process and of the gas concentration and of the total amount of gas used. The pressure and temperature should be recorded throughout the cycle on a chart. The record(s) should form part of the batch record.
109. 滅菌後，裝載物應以管制的方式，在通風的條件下儲存，以容許將殘留氣體及反應產物降低到界定的水準，此製程應予以確效。	109. After sterilisation, the load should be stored in a controlled manner under ventilated conditions to allow residual gas and reaction products to reduce to the defined level. This process should be validated.
不能在其最終容器中滅菌之藥品的過濾	**FILTRATION OF MEDICINAL PRODUCTS WHICH CANNOT BE STERILISED IN THEIR FINAL CONTAINER**

110. 可在最終容器中滅菌者，只使用過濾除菌不被認為是足夠的。目前可用的方法中，蒸氣滅菌是較好的。產品不能在最終容器中滅菌者，溶液或液體可通過 0.22 μm（或更小）之孔徑，或至少具有同等微生物滯留性質之濾器，濾入預先已滅菌的容器中。此種濾器能移除大多數的細菌及黴菌，但不能移除全部的病毒或黴漿菌，應考慮以某種程度的熱處理補充該過濾過程。	110. Filtration alone is not considered sufficient when sterilisation in the final container is possible. With regard to methods currently available, steam sterilisation is to be preferred. If the product cannot be sterilised in the final container, solutions or liquids can be filtered through a sterile filter of nominal pore size of 0.22 micron (or less), or with at least equivalent micro-organism retaining properties, into a previously sterilised container. Such filters can remove most bacteria and moulds, but not all viruses or mycoplasmas. Consideration should be given to complementing the filtration process with some degree of heat treatment.
111. 與其他滅菌製程相較，由於過濾方法有潛在之附加風險，所以，在緊接於充填前，進一步透過一個滅菌過之微生物滯留濾器作為第二道過濾是可取的。最終的無菌過濾應盡可能接近於充填點為之。	111. Due to the potential additional risks of the filtration method as compared with other sterilisation processes, a second filtration via a further sterilised microorganism retaining filter, immediately prior to filling, may be advisable. The final sterile filtration should be carried out as close as possible to the filling point.
112. 濾器之纖維脫落應為最少。	112. Fibre-shedding characteristics of filters should be minimal.
113. 使用前應證明滅菌過之濾器的完整性，且應在使用後，立即以適當的方法，例如起泡點、擴散流或持壓試驗確認。過濾已知容量的大量溶液所需之時間及通過濾器要使用之壓差，應在確效期間予以決定。例行製造中，與之任何顯著之差異，應予以註記及調查。這些檢查的結果應包含在該批次的紀錄中。關鍵之氣體及空氣通氣過濾器應在使用後確認其完整性。其他濾器亦應在適當的時間間隔確認其完整性。	113. The integrity of the sterilised filter should be verified before use and should be confirmed immediately after use by an appropriate method such as a bubble point, diffusive flow or pressure hold test. The time taken to filter a known volume of bulk solution and the pressure difference to be used across the filter should be determined during validation and any significant differences from this during routine manufacturing should be noted and investigated. Results of these checks should be included in the batch record. The integrity of critical gas and air vent filters should be confirmed after use. The integrity of other filters should be confirmed at appropriate intervals.

114. 同一濾器不得使用超過一個工作天，除非已經過確效。	114. The same filter should not be used for more than one working day unless such use has been validated.
115. 濾器不得因移除產品之成分或將其組成物釋入產品，而影響到產品。	115. The filter should not affect the product by removal of ingredients from it or by release of substances into it.
無菌產品的完成	**FINISHING OF STERILE PRODUCTS**
以下為 PE009-8 GMP Guide 新增：	
116. 經部分封塞之冷凍乾燥小瓶應一直維持在 A 級條件下，直到橡皮塞完全塞入為止。	116. Partially stoppered freeze drying vials should be maintained under Grade A conditions at all times until the stopper is fully inserted.
117. 容器應以經過適當確效的方法封閉。以熔封法封閉的容器，例如玻璃或塑膠的安瓿應接受百分之百之完整性試驗。其他容器樣品，應依適當的程序檢查其完整性。	117. Containers should be closed by appropriately validated methods. Containers closed by fusion, e.g. glass or plastic ampoules should be subject to 100% integrity testing. Samples of other containers should be checked for integrity according to appropriate procedures.
118. 鋁蓋捲縮定位在經封塞之小瓶前，該無菌充填小瓶之容器封塞系統並不完整。因此，鋁蓋捲縮應在膠塞塞入後盡快執行。	118. The container closure system for aseptically filled vials is not fully integral until the aluminium cap has been crimped into place on the stoppered vial. Crimping of the cap should therefore be performed as soon as possible after stopper insertion.
119. 因鋁蓋捲縮設備會產生大量非微生物性微粒，該設備應裝設於配有適當抽氣裝置之隔離站中。	119. As the equipment used to crimp vial caps can generate large quantities of nonviable particulates, the equipment should be located at a separate station equipped with adequate air extraction.
120. 小瓶之捲縮封蓋，可作為無菌操作過程執行，或在無菌核心外，作為潔淨過程執行，惟前者應使用經滅菌的蓋子。採用後者時，小瓶應以 A 級條件保護，直到離開無菌操作區的作業點。之後，經封塞的小瓶應以 A 級空氣保護，直到鋁蓋已經捲縮為止。	120. Vial capping can be undertaken as an aseptic process using sterilised caps or as a clean process outside the aseptic core. Where this latter approach is adopted, vials should be protected by Grade A conditions up to the point of leaving the aseptic processing area, and thereafter stoppered vials should be protected with a Grade A air supply until the cap has been crimped.

121. 小瓶之膠塞有漏塞或位置偏移者，應在捲縮封蓋前移除。封蓋作業站需要人員介入時，應使用適當的技術，防止直接接觸小瓶，並使微生物污染減到最低。	121. Vials with missing or displaced stoppers should be rejected prior to capping. Where human intervention is required at the capping station, appropriate technology should be used to prevent direct contact with the vials and to minimise microbial contamination.
122. 限制性進入屏障(RABS)及隔離裝置可能有助於確保所需之條件，並將人員直接介入捲縮封蓋作業中之情形減到最低。	122. Restricted access barriers and isolators may be beneficial in assuring the required conditions and minimising direct human interventions into the capping operation.
123. 真空下密封的容器，應在適當及預先設定的期間後，測試該真空度的維持。	123. Containers sealed under vacuum should be tested for maintenance of that vacuum after an appropriate, pre-determined period.
124. 已充填的容器應個別檢查其外來污染或其他瑕疵。以目視檢查者，應在適當且經控制的照明與背景條件下執行。執行該檢查的作業人員，應通過定期的視力健檢，戴眼鏡者，應戴上眼鏡接受健檢，並在產品檢查中給予定時的休息。使用其他檢查方法者，其過程應予以確效，並在一定時間間隔檢查該設備的性能。其結果應予以記錄。	124. Filled containers of parenteral products should be inspected individually for extraneous contamination or other defects. When inspection is done visually, it should be done under suitable and controlled conditions of illumination and background. Operators doing the inspection should pass regular eye-sight checks, with spectacles if worn, and be allowed frequent breaks from inspection. Where other methods of inspection are used, the process should be validated and the performance of the equipment checked at intervals. Results should be recorded.
品質管制	**QUALITY CONTROL**
125. 最終產品的無菌試驗，應僅被認為是一系列確保無菌性之控制下的最後措施。該測試應就所涉產品加以確效。	125. The sterility test applied to the finished product should only be regarded as the last in a series of control measures by which sterility is assured. The test should be validated for the product(s) concerned.
126. 在允許以參數放行的情形下，應特別注意全部製造過程的確效與監測。	126. In those cases where parametric release has been authorised, special attention should be paid to the validation and the monitoring of the entire manufacturing process.
127. 無菌試驗所抽取之樣品，須為整個批次中的代表性樣品，尤其應包含取自該批次中被認為最具污染風險之部分的樣品，例如：	127. Samples taken for sterility testing should be representative of the whole of the batch, but should in particular include samples taken from parts of the batch considered to be most at risk of contamination, e.g.:

a) 對於經無菌充填的產品，其樣品應包含在該批次之開始與結束時，及在任何重大介入後充填的容器；	a) for products which have been filled aseptically, samples should include containers filled at the beginning and end of the batch and after any significant intervention;
b) 對於以最終容器形式加熱滅菌的產品，應考慮取自該滅菌裝載中可能最冷位置的樣品。	b) for products which have been heat sterilised in their final containers, consideration should be given to taking samples from the potentially coolest part of the load.

附則 2　人用生物藥品的製造 （MANUFACTURE OF BIOLOGICAL MEDICINAL PRODUCTS FOR HUMAN USE）

範圍（SCOPE）	
生物藥品之製造所使用的方法，在擬定適當的法規管制上是一個關鍵的因素。因此，生物藥品大致可參照其製造方法予以界定。以下列製造方法製備的生物藥品將歸屬於本附則的範圍[1]：	The methods employed in the manufacture of biological medicinal products are a critical factor in shaping the appropriate regulatory control. Biological medicinal products can be defined therefore largely by reference to their method of manufacture. Biological medicinal products prepared by the following methods of manufacture will fall under the scope of this annex[1]:
[1] 以這些方法所製造的生物藥品包含： 疫苗（vaccines）、免疫血清 （immunosera）、抗原（antigens）、荷爾蒙（hormones）、細胞因子(cytokines)、酶/酵素（enzymes）與其他醱酵產品〔包含單株抗體（monoclonal antibodies） 及自重組 DNA(r-DNA)衍生的產品〕。	[1] Biological medicinal products manufactured by these methods include: vaccines, immunosera, antigens, hormones, cytokines, enzymes and other products of fermentation (including monoclonal antibodies and products derived from r-DNA).
a) 微生物之培養物，但利用重組 DNA 技術者除外。	a) Microbial cultures, excluding those resulting from r-DNA techniques.
b) 微生物及細胞培養物，包含來自重組 DNA 或融合瘤(hybridoma)技術所產生者。	b) Microbial and cell cultures, including those resulting from recombinant DNA or hybridoma techniques.
c) 自生物組織的萃取。	c) Extraction from biological tissues.
d) 活體物質在胚胎或動物內的增殖。	d) Propagation of live agents in embryos or animals.
（本附則中的原則未必全都適用於類別 a 的產品）	(Not all of the principles of this guideline may necessarily apply to products in category a.)
註:擬定本附則時已將世界衛生組織（WHO）對製造廠與管制實驗室所提議之一般要求列入考慮。 *對生物產品的特定類別並未規定其詳細的要求。*	*Note: In drawing up this guidance, due consideration has been given to the general requirements for manufacturing establishments and control laboratories proposed by the WHO. The present guidance does not lay down detailed requirements for specific classes of biological products.*

原則（PRINCIPLE）	
生物藥品的製造源於產品及製程之特質而有特殊考量。生產、管制及投予的方法，使某些特別的預防措施成為必需。不同於使用化學及物理技術製造之傳統藥品，其品質可能具有高度的一致性，生物藥品的生產涉及生物製程及材料，例如細胞之培養或從活體生物體的物質萃取。因這些生物製程可能展現固有的變異性，故其副產物的範圍及性質是可變的。且這些培養過程中使用的材料亦會提供微生物污染物之生長的良好基質。	The manufacture of biological medicinal products involves certain specific considerations arising from the nature of the products and the processes. The way in which biological medicinal products are produced, controlled and administered make some particular precautions necessary. Unlike conventional medicinal products, which are reproduced using chemical and physical techniques capable of a high degree of consistency, the production of biological medicinal products involves biological processes and materials, such as cultivation of cells or extraction of material from living organisms. These biological processes may display inherent variability, so that the range and nature of by-products are variable. Moreover, the materials used in these cultivation processes provide good substrates for growth of microbial contaminants.
生物藥品的管制，常涉及比物理/化學測定法有更大變異性的生物分析技術。因此，在生物藥品的製造上，製程中管制是非常重要。	Control of biological medicinal products usually involves biological analytical techniques which have a greater variability than physico-chemical determinations. In-process controls therefore take on a great importance in the manufacture of biological medicinal products.
任何優良製造規範的法規中皆要求仔細考量生物藥品的特別性質，本附則的研訂亦將這些要點列入考慮。	The special properties of biological medicinal products require careful consideration in any code of Good Manufacturing Practice and the development of this annex takes these points into account.
人員（PERSONNEL）	

1. 在製造生物藥品區域中的所有工作人員（包含與清潔、維護保養或品質管制有關的人員），應接受與製造產品及其工作相關之額外訓練；並應給予人員在衛生與微生物學上的相關資訊及訓練。	1. All personnel (including those concerned with cleaning, maintenance or quality control) employed in areas where biological medicinal products are manufactured should receive additional training specific to the products manufactured and to their work. Personnel should be given relevant information and training in hygiene and microbiology.
2. 負責生產與品質管制的人員，應具有適當的相關科學背景，例如細菌學、生物學、生物統計學、化學、醫學、藥學、藥理學、病毒學、免疫學及獸醫學，以及足夠的實務經驗，使其能管理所涉及之製程。	2. Persons responsible for production and quality control should have an adequate background in relevant scientific disciplines, such as bacteriology, biology, biometry, chemistry, medicine, pharmacy, pharmacology, virology, immunology and veterinary medicine, together with sufficient practical experience to enable them to exercise their management function for the process concerned.
3. 為產品的安全性，人員身體之免疫狀態必須予以考慮。所有從事於製造、維護保養、檢驗及動物照顧的人員（及稽查人員）應於必要時接種適當的特定疫苗，並應有定期的健康檢查。除因人員暴露於感染性微生物、劇毒性毒素或過敏原所造成的明顯問題外，還必需避免生產批次受到感染性微生物污染的風險。通常，應禁止訪客進入生產區域。	3. The immunological status of personnel may have to be taken into consideration for product safety. All personnel engaged in production, maintenance, testing and animal care (and inspectors) should be vaccinated where necessary with appropriate specific vaccines and have regular health checks. Apart from the obvious problem of exposure of staff to infectious agents, potent toxins or allergens, it is necessary to avoid the risk of contamination of a production batch with infectious agents. Visitors should generally be excluded from production areas.
4. 若人員的免疫狀態發生任何變化可能影響產品品質時，應排除其在生產區中工作。卡介苗及結核菌素產品的生產應限由經定期檢查其免疫狀態或胸部 X-光檢查之受監控人員執行。	4. Any changes in the immunological status of personnel which could adversely affect the quality of the product should preclude work in the production area. Production of BCG vaccine and tuberculin products should be restricted to staff who are carefully monitored by regular checks of immunological status or chest X-ray.

5. 同一工作天的操作中，作業人員不得從可能暴露於活生物體或動物的區域，穿越至處理其他產品或不同生物體的區域。當此種穿越無可避免時，所涉及之任何生產人員，均應遵循清楚界定的去污染措施，包含更衣及更鞋，以及必要時需淋浴。	5. In the course of a working day, personnel should not pass from areas where exposure to live organisms or animals is possible to areas where other products or different organisms are handled. If such passage is unavoidable, clearly defined decontamination measures, including change of clothing and shoes and, where necessary, showering should be followed by staff involved in any such production.
廠房設施與設備（PREMISES AND EQUIPMENT）	
6. 切記原料污染程度及對最終產品的風險，應將生產之廠房設施的微粒與微生物污染等環境管制，調整到適合該產品及其生產步驟之程度。	6. The degree of environmental control of particulate and microbial contamination of the production premises should be adapted to the product and the production step, bearing in mind the level of contamination of the starting materials and the risk to the finished product.
7. 考量生物藥品間交叉污染的風險，特別是在使用活生物體製程階段的期間中，其設施及設備，可能須採取額外之防範措施。例如，使用專用的設施與設備、採用時段切換生產及使用密閉系統。避免交叉污染所需之隔離層級，取決於其產品特質及所使用之設備。	7. The risk of cross-contamination between biological medicinal products, especially during those stages of the manufacturing process in which live organisms are used, may require additional precautions with respect to facilities and equipment, such as the use of dedicated facilities and equipment, production on a campaign basis and the use of closed systems. The nature of the product as well as the equipment used will determine the level of segregation needed to avoid cross-contamination.
8. 原則上，卡介苗之生產及用來生產結核菌素產品的活生物體之處理，應使用專用的廠房設施及設備。	8. In principle, dedicated facilities should be used for the production of BCG vaccine and for the handling of live organisms used in production of tuberculin products.
9. 炭疽桿菌(*Bacillus anthracis*)、肉毒桿菌(*Clostridium botulinum*)及破傷風桿菌(*Clostridium tetani*)的處理直到去活化過程完成為止，均應使用專用的廠房設施及設備。	9. Dedicated facilities should be used for the handling of Bacillus anthracis, of Clostridium botulinum and of Clostridium tetani until the inactivation process is accomplished.

10. 如該廠房設施及設備是專用於其他產芽孢菌類的產品，且在任何同一時間無超過一個以上產品之操作，則可接受以時段切換為基礎之生產方式。	10. Production on a campaign basis may be acceptable for other spore forming organisms provided that the facilities are dedicated to this group of products and not more than one product is processed at any one time.
11. 可接受同時有多個密閉系統式的醱酵槽在相同區域內生產不同產品，例如： 單株抗體產品及由重組 DNA 技術製備之產品。	11. Simultaneous production in the same area using closed systems of biofermenters may be acceptable for products such as monoclonal antibodies and products prepared by r-DNA techniques.
12. 如採取適當的預防措施以防止交叉污染，則在收集（harvesting）後的操作步驟，得在相同生產區域中同時執行。對於經殺滅之疫苗與類毒素，該類平行操作應僅在培養物去活化後或在減毒（detoxification）後，始得執行。	12. Processing steps after harvesting may be carried out simultaneously in the same production area provided that adequate precautions are taken to prevent cross-contamination. For killed vaccines and toxoids, such parallel processing should only be performed after inactivation of the culture or after detoxification.
13. 無菌產品之製程應於正壓區操作，但為圍堵的理由，可接受在病原菌暴露點的特定區域使用負壓。在使用負壓區或安全櫃進行病原菌之無菌操作時，應以正壓無菌區予以圍繞。	13. Positive pressure areas should be used to process sterile products but negative pressure in specific areas at point of exposure of pathogens is acceptable for containment reasons. Where negative pressure areas or safety cabinets are used for aseptic processing of pathogens, they should be surrounded by a positive pressure sterile zone.
14. 空氣處理裝置應隨所涉操作區特別規定，且來自處理活病原性生物體區域的空氣不得再循環使用。	14. Air handling units should be specific to the processing area concerned and recirculation of air should not occur from areas handling live pathogenic organisms.
15. 生產區及設備的配置與設計應允許有效的清潔及去污染（例如，使用燻蒸法）。清潔及去污染作業程序的適當性應予以確效。	15. The layout and design of production areas and equipment should permit effective cleaning and decontamination (e.g. by fumigation). The adequacy of cleaning and decontamination procedures should be validated.

16. 使用於活生物體處理的設備應經適當設計，以維持培養物之純淨狀態，並確保在操作期間不受外源污染。	16. Equipment used during handling of live organisms should be designed to maintain cultures in a pure state and uncontaminated by external sources during processing.
17. 管道系統、閥件及通氣口濾器應正確設計，以利清潔與滅菌。應鼓勵使用原位清潔與原位滅菌系統。醱酵槽上的閥件應全部予以蒸氣滅菌。空氣通氣口濾器應為疏水性，對其預定使用壽命應予以確效。	17. Pipework systems, valves and vent filters should be properly designed to facilitate cleaning and sterilisation. The use of "clean in place" and "sterilise in place" systems should be encouraged. Valves on fermentation vessels should be completely steam sterilisable. Air vent filters should be hydrophobic and validated for their scheduled life span.
18. 一級圍堵應經設計並測試證明其無洩漏的風險。	18. Primary containment should be designed and tested to demonstrate freedom from leakage risk.
19. 可能含有致病微生物之排放物，應有效地去污染。	19. Effluents which may contain pathogenic microorganisms should be effectively decontaminated.
20. 由於生物性產品或製程的變異性，有些添加物或成分需在生產過程中再予以量測或秤重（例如：緩衝劑）。因此，這些物質得於製造區域中保存少量的庫存。	20. Due to the variability of biological products or processes, some additives or ingredients have to be measured or weighed during the production process (e.g. buffers). In these cases, small stocks of these substances may be kept in the production area.
動物房及動物照顧（ANIMAL QUARTERS AND CARE）	
21. 有些生物藥品之製造使用動物，例如：小兒麻痺疫苗(猴子)、抗蛇毒血清(馬及山羊)、狂犬病疫苗[兔、小鼠(mice)與倉鼠]及血清促性腺激素（馬）。此外，動物也可能使用在多數血清和疫苗的品質管制上，例如百日咳疫苗[小鼠(mice)]、熱原(兔)、卡介苗(天竺鼠)。	21. Animals are used for the manufacture of a number of biological products, for example polio vaccine (monkeys), snake antivenoms (horses and goats), rabies vaccine (rabbits, mice and hamsters) and serum gonadotropin (horses). In addition, animals may also be used in the quality control of most sera and vaccines, e.g. pertussis vaccine (mice), pyrogenicity (rabbits), BCG vaccine (guinea-pigs).

22. 使用於生物藥品之生產與品管的動物房，應與生產區及品管區隔離。用於生產原料與品質管制及安全試驗之動物的健康狀態應予以監控並記錄。該區域工作之人員應配備適當的服裝及更衣設備。當生物藥品之生產或品質管制使用猴子時，應特別考量現行世界衛生組織對生物物質之第七號（current WHO Requirements for Biological Substances No. 7.）要求中的規定。	22. Quarters for animals used in production and control of biological products should be separated from production and control areas. The health status of animals from which some starting materials are derived and of those used for quality control and safety testing should be monitored and recorded. Staff employed in such areas must be provided with special clothing and changing facilities. Where monkeys are used for the production or quality control of biological medicinal products, special consideration is required as laid down in the current WHO Requirements for Biological Substances No. 7.
文件（DOCUMENTATION）	
23. 生物原料的規格需附加有關其來源、起源、製造及管制方法等文件，特別是對微生物的管制。	23. Specifications for biological starting materials may need additional documentation on the source, origin, method of manufacture and controls applied, particularly microbiological controls.
24. 生物藥品之半製品/中間產品及待分/包裝產品應有例行要求的規格。	24. Specifications are routinely required for intermediate and bulk biological medicinal products.
生產（PRODUCTION）	
原料（Starting materials）	
25. 原料的來源、起源及適合性應予以清楚界定。若原料檢驗中之必要的檢驗需花一段長時間者，可容許在獲得檢驗結果前加工該原料。惟最終產品應依其合格的檢驗結果放行。	25. The source, origin and suitability of starting materials should be clearly defined. Where the necessary tests take a long time, it may be permissible to process starting materials before the results of the tests are available. In such cases, release of a finished product is conditional on satisfactory results of these tests.
26. 原料之滅菌應盡可能以加熱方式執行。必要時，其他適當的方法(例如：輻射照射)，亦可使用於生物原料的去活化。	26. Where sterilisation of starting materials is required, it should be carried out where possible by heat. Where necessary, other appropriate methods may also be used for inactivation of biological materials (e.g. irradiation).

種批與細胞庫系統（Seed lot and cell bank system）	
27. 為避免因重複的繼代培養或多世代培養可能造成非預期性的特性漂移（drift），以微生物培養、胚胎及動物體內增殖之細胞培養取得之生物藥品的生產，應以主種批及工作種批及/或種細胞庫及工作細胞庫的系統為基礎。	27. In order to prevent the unwanted drift of properties which might ensue from repeated subcultures or multiple generations, the production of biological medicinal products obtained by microbial culture, cell culture of propagation in embryos and animals should be based on a system of master and working seed lots and/or cell banks.
28. 種批或細胞庫與最終產品間的世代數(細胞倍增數、繼代數)應與上市許可文件檔案一致。放大製程規模不得改變該基本關係。	28. The number of generations (doublings, passages) between the seed lot or cell bank and the finished product should be consistent with the marketing authorisation dossier. Scaling up of the process should not change this fundamental relationship.
29. 種批及細胞庫應適當地描述其特徵並檢測其污染物。其適用性應以產品連續批次之特徵與品質的一致性進一步予以證明。種批及細胞庫之建立、儲存及使用應使其污染或變質之風險降到最低。	29. Seed lots and cell banks should be adequately characterised and tested for contaminants. Their suitability for use should be further demonstrated by the consistency of the characteristics and quality of the successive batches of product. Seed lots and cell banks should be established, stored and used in such a way as to minimise the risks of contamination or alteration.
30. 種批及細胞庫的建立應在適當管制的環境內執行，以保護該種批及細胞庫，並視情況保護其處理人員。在種批及細胞庫之建立期間，不得同時在同一區域內或由相同人員處理其他活的或具感染性的物質(例如病毒、動物細胞株或微生物細胞株)。	30. Establishment of the seed lot and cell bank should be performed in a suitably controlled environment to protect the seed lot and the cell bank and, if applicable, the personnel handling it. During the establishment of the seed lot and cell bank, no other living or infectious material (e.g. virus, cell lines or cell strains) should be handled simultaneously in the same area or by the same persons.

31. 種批及細胞庫之安定性及活化（recovery）的證據，應予以文件化。儲存容器應緊密密封、清楚標示，且保存在適當溫度。庫存清單應仔細保存。冷凍庫的儲存溫度應予以連續記錄，並對所使用之液態氮採取適當的監測。超出設定範圍的任何偏差及採取的任何矯正措施應予以記錄。	31. Evidence of the stability and recovery of the seeds and banks should be documented. Storage containers should be hermetically sealed, clearly labeled and kept at an appropriate temperature. An inventory should be meticulously kept. Storage temperature should be recorded continuously for freezers and properly monitored for liquid nitrogen. Any deviation from set limits and any corrective action taken should be recorded.
32. 只有被授權的人員始得處理該原物料，且需在負責人員的監督下執行。庫存原物料之存取應予以管制。不同的種批或細胞庫應以避免混淆或交叉污染的方式儲存。種批及細胞庫最好分成幾個部分，並將各部分儲存在不同的處所，使全部損失的風險降到最低。	32. Only authorised personnel should be allowed to handle the material and this handling should be done under the supervision of a responsible person. Access to stored material should be controlled. Different seed lots or cell banks should be stored in such a way to avoid confusion or cross-contamination. It is desirable to split the seed lots and cell banks and to store the parts at different locations so as to minimise the risks of total loss.
33. 所有種細胞庫或工作細胞庫及種批的容器，在儲存期間應以一致的方式處理。一旦容器從儲存處移出，即不得再放回庫存。	33. All containers of master or working cell banks and seed lots should be treated identically during storage. Once removed from storage, the containers should not be returned to the stock.
作業原則（Operating principles）	
34. 培養基之促進生長性質應予以證明。	34. The growth promoting properties of culture media should be demonstrated.
35. 將原料或接種液加到醱酵槽及其他容器，以及取樣皆應在謹慎管制下執行，以確保維持無污染。加料或取樣時，應注意確保各容器已正確連接。	35. Addition of materials or cultures to fermenters and other vessels and the taking of samples should be carried out under carefully controlled conditions to ensure that absence of contamination is maintained. Care should be taken to ensure that vessels are correctly connected when addition or sampling take place.
36. 產品的離心及混合可能導致氣霧形成，因此必需圍堵這些作業，以防止活微生物的散布。	36. Centrifugation and blending of products can lead to aerosol formation and containment of such activities to prevent transfer of live microorganisms is

	necessary.
37. 如果可能，培養基應以原位滅菌。且氣體、培養基、酸或鹼溶液及消泡劑等例行添加到醱酵槽時，應儘可能使用線上除菌過濾器。	37. If possible, media should be sterilised in situ. In-line sterilising filters for routine addition of gases, media, acids or alkalis, defoaming agents etc. to fermenters should be used where possible.
38. 執行任何必要之病毒的移除或去活化之確效，應謹慎考量。	38. Careful consideration should be given to the validation of any necessary virus removal or inactivation undertaken.
39. 製造過程中，執行病毒之去活化或移除時，應採取措施以避免經處理之產品，被未經處理之產品再污染的風險。	39. In cases where a virus inactivation or removal process is performed during manufacture, measures should be taken to avoid the risk of recontamination of treated products by non-treated products.
40. 對於層析法所使用之各種不同設備，通常應專用於一種產品的純化，且在批次間以滅菌或滅菌處理。不同製程階段，應避免使用相同的設備。層析管柱的允收標準、使用期限及滅菌或滅菌方法應予以界定。	40. A wide variety of equipment is used for chromatography, and in general such equipment should be dedicated to the purification of one product and should be sterilised or sanitised between batches. The use of the same equipment at different stages of processing should be discouraged. Acceptance criteria, life span and sanitization or sterilisation method of columns should be defined.
品質管制（QUALITY CONTROL）	
41. 生物藥品品質的一致性，製程中管制扮演特別重要的角色。一些與產品品質相關的管制(例如：病毒的移除)，但在最終產品無法執行時，則應於生產過程的適當階段中執行。	41. In-process controls play a specially important role in ensuring the consistency of the quality of biological medicinal products. Those controls which are crucial for quality (e.g. virus removal) but which cannot be carried out on the finished product, should be performed at an appropriate stage of production.
42. 保留足夠數量之半製品/中間產品的樣品，並於適當條件下儲存，可能是必需的，以供批次管制的重複試驗或確認用。	42. It may be necessary to retain samples of intermediate products in sufficient quantities and under appropriate storage conditions to allow the repetition or confirmation of a batch control.

43. 某些生產過程必須連續監測，例如醱酵。此等數據應涵蓋於批次紀錄中。	43. Continuous monitoring of certain production processes is necessary, for example fermentation. Such data should form part of the batch record.
44. 採用連續培養方式進行生產時，應予以特別考慮源於該類型之生產方法所需的品質管制要求。	44. Where continuous culture is used, special consideration should be given to the quality control requirements arising from this type of production method.

附則 3　放射性藥品的製造(MANUFACTURE OF RADIOPHARMACEUTICALS)

原則（PRINCIPLE）	
放射性藥品之製造應依照藥品 GMP 第一部及第二部所定原則執行。本附則特別針對放射性藥品特定的實務進行論述。	The manufacture of radiopharmaceuticals should be undertaken in accordance with the principles of Good Manufacturing Practice for Medicinal Products Part I and II. This annex specifically addresses some of the practices, which may be specific for radiopharmaceuticals.
註 i. 本指引未涵蓋在放射性藥品藥局（醫院或特定藥局）使用具有上市許可或國家執照之發生器及套組（Generators and Kits）製備放射性藥品。但國家有要求者，應予納入。	Note i. Preparation of radiopharmaceuticals in radiopharmacies (hospitals or certain pharmacies), using Generators and Kits with a marketing authorisation or a national licence, is not covered by this guideline, unless covered by national requirement.
註 ii. 依輻射防護法規，應確保任何醫療暴露皆在專門執業人員之臨床責任下執行。在執行診斷及治療之核子醫學業務時，應聘有一位醫學物理學專家。	Note ii. According to radiation protection regulations it should be ensured that any medical exposure is under the clinical responsibility of a practitioner. In diagnostic and therapeutic nuclear medicine practices a medical physics expert should be available.
註 iii. 本附則亦適用於臨床試驗使用之放射性藥品。	Note iii. This annex is also applicable to radiopharmaceuticals used in clinical trials.
註 iv. 放射性藥品的運送受國際原子能協會(International Atomic Energy Association ，IAEA)及輻射防護要求之管制。	Note iv. Transport of radiopharmaceuticals is regulated by the International Atomic Energy Association (IAEA) and radiation protection requirements.
註 v. 除本附則中所描述之方法外，尚有其他能達到品質保證之可接受的方法，該等方法應經確效，並提供至少等同於本附則所訂之品質保證水準。	Note v. It is recognised that there are acceptable methods, other than those described in this annex, which are capable of achieving the principles of Quality Assurance. Other methods should be validated and provide a level of Quality Assurance at least equivalent to those set out in this annex.
前言（INTRODUCTION）	

1. 放射性藥品之製造與處理具有潛在的危害性。危險的程度特別取決於輻射的類型、輻射能及放射性同位素之半衰期。對於交叉污染的防止、放射性核種污染物的滯留，以及廢棄物的處置應特別注意。	1. The manufacturing and handling of radiopharmaceuticals is potentially hazardous. The level of risk depends in particular upon the types of radiation, the energy of radiation and the half-lives of radioactive isotopes. Particular attention must be paid to the prevention of cross-contamination, to the retention of radionuclide contaminants, and to waste disposal.
2.由於放射性核種之架儲期短，故有些放射性藥品可能在其所有品管試驗完成前先予放行。於此情形下，整體放行程序之準確及詳細的描述是必要的，包含參與人員的責任及與品質保證系統之有效性的持續評估在內。	2. Due to short shelf-life of their radionuclides, some radiopharmaceuticals may be released before completion of all quality control tests. In this case, the exact and detailed description of the whole release procedure including the responsibilities of the involved personnel and the continuous assessment of the effectiveness of the quality assurance system is essential.
3. 本指引可適用於由工業製造廠、核醫中心/機構（Nuclear Centres/ Institutes）與正子斷層造影中心(positron emission tomography，PET Centres）使用於下列產品類型之生產及品質管制的製造程序：	3. This guideline is applicable to manufacturing procedures employed by industrial manufacturers, Nuclear Centres/Institutes and PET Centres for the production and quality control of the following types of products:
• 放射性藥品	• Radiopharmaceuticals
• 正子放射性藥品	• Positron Emitting (PET) Radiopharmaceuticals
• 生產放射性藥品之放射性前驅物	• Radioactive Precursors for radiopharmaceutical production
• 放射性核種發生器	• Radionuclide Generators

製造類型	非 GMP*	GMP第2部及第1部（漸增）包含相關附則在內			
1. 放射性藥品 2. 正子放射性藥品 3.放射性藥品前驅物	反應器/迴旋加速器生產	化學合成	純化步驟	操作，配方設計及調配	無菌製備或最終滅菌
放射性核種發生器	反應器/迴旋加速器生產	操作過程			

Type of manufacture	Non - GMP *	GMP part II & I (Increasing) including relevant annexes			
Radiopharmaceuticals PET Radiopharmaceuticals Radioactive Precursors	Reactor/Cyclotron Production	Chemical synthesis	Purification steps	Processing, formulation and dispensing	Aseptic or final sterilization

Radionuclide Generators	Reactor/Cyclotron Production	Processing

* 從迴旋加速器到合成裝置之標的物及傳送系統可認定為原料藥製造的第一步。	* Target and transfer system from cyclotron to synthesis rig may be considered as the first step of active substance manufacture.
4. 最終放射性藥品之製造廠應描述原料藥及最終藥品之製造步驟,並判斷該特定的製程/製造步驟所適用之 GMP 要求 (第 1 部或第 2 部)。	4. The manufacturer of the final radiopharmaceutical should describe and justify the steps for manufacture of the active substance and the final medicinal product and which GMP (part I or II) applies for the specific process/manufacturing steps.
5. 放射性藥品之製備包含遵守輻射防護法規。	5. Preparation of radiopharmaceuticals involves adherence to regulations on radiation protection.
6.以注射投用的放射性藥品應符合注射劑之無菌性要求，而且相關時，應該遵守 PIC/S GMP 指引附則 1 所訂無菌藥品製造之無菌操作條件。	6. Radiopharmaceuticals to be administered parenterally should comply with sterility requirements for parenterals and, where relevant, aseptic working conditions for the manufacture of sterile medicinal products, which are covered in PIC/S GMP Guide, Annex 1.
7. 常用之放射性藥品的規格及品質管制測試程序規定在相關藥典或上市許可中。	7. Specifications and quality control testing procedures for the most commonly used radiopharmaceuticals are specified in the European (or other relevant) Pharmacopoeia or in the marketing authorisation.
臨床試驗	***Clinical Trials***
8.預定在臨床試驗上用為研究用藥品之放射性藥品另應依照 PIC/S GMP 指引附則 13（研究用藥品的製造）所訂原則生產。	8. Radiopharmaceuticals intended for use in clinical trials as investigational medicinal products should in addition be produced in accordance with the principles in PIC/S GMP Guide, Annex 13.
品質保證（QUALITY ASSURANCE）	
9. 因為放射性藥品之特定特性、低容量而且在有些情形需要在完成測試前就投用該產品，所以，在放射性藥品的製造上，品質保證更加重要。	9. Quality assurance is of even greater importance in the manufacture of radiopharmaceuticals because of their particular characteristics, low volumes and in some circumstances the need to administer the product before testing is

	complete.
10. 如同所有藥品，本產品必須妥善保護以避免污染及交叉污染。然而，環境與操作者亦須防護輻射照射。這意指有效之品質保證系統的角色極具重要性。	10. As with all pharmaceuticals, the products must be well protected against contamination and cross-contamination. However, the environment and the operators must also be protected against radiation. This means that the role of an effective quality assurance system is of the utmost importance.
11. 精確地記錄監測廠房設施及製程所產生之數據，並作為放行過程的一部分予以評估，是重要的。	11. It is important that the data generated by the monitoring of premises and processes are rigorously recorded and evaluated as part of the release process.
12.驗證及確效之原則應適用於放射性藥品的製造，驗證/確效之程度應使用風險管理方法決定，該方法之重點集中於結合優良製造規範與輻射防護。	12. The principles of qualification and validation should be applied to the manufacturing of radiopharmaceuticals and a risk management approach should be used to determine the extent of qualification/validation, focusing on a combination of Good Manufacturing Practice and Radiation Protection.
人員（PERSONNEL）	
13. 所有製造作業皆應在額外配備具輻射防護能力之人員的負責下執行。參與放射性藥品之生產、分析管制及放行的人員，應經放射性藥品之品質管理體系的特定方面之適當訓練。被授權人員應具有產品放行的全部責任。	13. All manufacturing operations should be carried out under the responsibility of personnel with additional competence in radiation protection. Personnel involved in production, analytical control and release of radiopharmaceuticals should be appropriately trained in radiopharmaceutical specific aspects of the quality management system. The Authorised Person should have the overall responsibility for release of the products.
14. 放射性產品製造區域內的所有人員(包括與清潔及維護保養有關的人員)應接受配合此類產品之額外訓練。	14. All personnel (including those concerned with cleaning and maintenance) employed in areas where radioactive products are manufactured should receive additional training adapted to this class of products.

15. 生產設施/設備與研究機構共用者，研究人員應受過 GMP 法規的適當訓練，且 QA 的職責必須包括研究活動之檢討及核准，以確保該活動不對放射性藥品之製造引起任何危害。	15. Where production facilities are shared with research institutions, the research personnel must be adequately trained in GMP regulations and the QA function must review and approve the research activities to ensure that they do not pose any hazard to the manufacturing of radiopharmaceuticals.
廠房設施及設備（PREMISES AND EQUIPMENT）	
概述（General）	
16. 放射性產品應在受管制 (環境的及放射性) 的區域中製造。所有製造步驟應在專用於放射性藥品之自足圍堵的設施/設備中執行。	16. Radioactive products should be manufactured in controlled (environmental and radioactive) areas. All manufacturing steps should take place in self-contained facilities dedicated to radiopharmaceuticals.
17. 應建立並採取措施，以防止來自人員、原物料及放射性核種等之交叉污染。每當合適時，應使用密閉或圍堵的設備。使用開放設備，或開啟設備時，應採取防範措施，以將污染風險減到最低。風險評價應證明建議之環境潔淨度水準適合於擬製造的產品類型。	17. Measures should be established and implemented to prevent cross-contamination from personnel, materials, radionuclides etc. Closed or contained equipment should be used whenever appropriate. Where open equipment is used, or equipment is opened, precautions should be taken to minimize the risk of contamination. The risk assessment should demonstrate that the environmental cleanliness level proposed is suitable for the type of product being manufactured.
18. 進入製造區應經由更衣區，且應限於被授權的人員。	18. Access to the manufacturing areas should be via a gowning area and should be restricted to authorised personnel.
19. 關於在性能驗證期間中所建立之放射活性、微粒及微生物學上之品質，工作站及其環境應予監測。	19. Workstations and their environment should be monitored with respect to radioactivity, particulate and microbiological quality as established during performance qualification (PQ).

20. 預防性維護保養、校正及驗證計畫應予運作，以確保使用於放射性藥品之製造的所有設施與設備皆合適且經過驗證。這些活動應由有勝任能力之人員執行，且其記錄與日誌應予保存。	20. Preventive maintenance, calibration and qualification programmes should be operated to ensure that all facilities and equipment used in the manufacture of radiopharmaceutical are suitable and qualified. These activities should be carried out by competent personnel and records and logs should be maintained.
21. 應採取防範措施，以避免設施內之放射性污染。應備有適當的管制，以檢測任何放射性污染。這可直接透過輻射偵測儀的使用或間接透過例行的擦拭作業。	21. Precautions should be taken to avoid radioactive contamination within the facility. Appropriate controls should be in place to detect any radioactive contamination, either directly through the use of radiation detectors or indirectly through a swabbing routine.
22. 設備應經設計建造，使其與產品接觸之表面不具反應性、加成性或吸附性以避免改變放射性藥品之品質。	22. Equipment should be constructed so that surfaces that come into contact with the product are not reactive, additive or absorptive so as to alter the quality of the radiopharmaceutical.
23. 如無正當理由，應避免將從處理放射性產品之區域排出的空氣再循環。排風口應經設計，以將放射性微粒及氣體所致之環境污染減到最低；且應採取適當的措施，以防護管制區域受到微粒及微生物的污染。	23. Re-circulation of air extracted from area where radioactive products are handled should be avoided unless justified. Air outlets should be designed to minimize environmental contamination by radioactive particles and gases and appropriate measures should be taken to protect the controlled areas from particulate and microbial contamination.
24. 為圍堵放射性微粒，產品暴露之區域的空氣壓力可能有必要比其周圍區域的壓力為低。不過，仍然需要防護產品受到環境污染，例如可利用屏障技術或氣鎖室當成壓力沈槽（pressure sinks）來達成。	24. In order to contain radioactive particles, it may be necessary for the air pressure to be lower where products are exposed, compared with the surrounding areas. However, it is still necessary to protect the product from environmental contamination. This may be achieved by, for example, using barrier technology or airlocks, acting as pressure sinks.
無菌生產（Sterile production）	

25. 無菌放射性藥品可區分為以無菌製備的產品及以最終滅菌製造的產品。廠房/設施/設備應保持於執行中之作業類型的適當環境潔淨度水準。為無菌產品的製造，在產品或容器可能暴露於環境之作業區，其潔淨度應符合 PIC/S GMP 指引附則 1 所描述的要求。	25. Sterile radiopharmaceuticals may be divided into those, which are manufactured aseptically, and those, which are terminally sterilised. The facility should maintain the appropriate level of environmental cleanliness for the type of operation being performed. For manufacture of sterile products the working zone where products or containers may be exposed to the environment, the cleanliness requirements should comply with the requirements described in the PIC/S GMP Guide, Annex 1.
26. 對放射性藥品的製造，可應用風險評價，以決定其適當之壓差、氣流方向及空氣品質。	26. For manufacture of radiopharmaceuticals a risk assessment may be applied to determine the appropriate pressure differences, air flow direction and air quality.
27. 如使用密閉及自動化系統(化學合成、純化、線上無菌過濾)，C 級環境【通常是「鉛室/鉛櫃」(Hot-cell)】將是適當的。「鉛室/鉛櫃」應符合高度的空氣潔淨度，且當密閉時，應供應經過濾之空氣。無菌作業必須在 A 級區中執行。	27. In case of use of closed and automated systems (chemical synthesis, purification, on-line sterile filtration) a grade C environment (usually “Hot-cell”) will be suitable. Hot-cells should meet a high degree of air cleanliness, with filtered feed air, when closed. Aseptic activities must be carried out in a grade A area.
28. 製造開始前，經滅菌之設備及消耗品 (連接至密封之流體路徑的管線、經滅菌之過濾器、無菌密閉及密封的小瓶)的組裝必須在無菌條件下執行。	28. Prior to the start of manufacturing, assembly of sterilised equipment and consumables (tubing, sterilised filters and sterile closed and sealed vials to a sealed fluid path) must be performed under aseptic conditions
文件製作（DOCUMENTATION）	
29 與放射性藥品製造有關之所有文件，皆應依書面程序製作、審查、核准及分發。	29. All documents related to the manufacture of radiopharmaceuticals should be prepared, reviewed, approved and distributed according to written procedures.

30. 原料、標示及包裝材料、關鍵中間體/中間產品及最終放射性藥品，皆應建立其規格並文件化。使用於製程中之任何其他關鍵品項，諸如，對品質可能會有關鍵性影響之製程助劑、墊圈、無菌過濾套組等，亦應備有規格。	30. Specifications should be established and documented for raw materials, labelling and packaging materials, critical intermediates and the finished radiopharmaceutical. Specifications should also be in place for any other critical items used in the manufacturing process, such as process aids, gaskets, sterile filtering kits, that could critically impact on quality.
31 放射性藥品應建立其允收標準，包括放行標準及架儲期規格在內【例如，同位素之化學同一性（chemical identity）、放射性濃度、純度以及特定活性】。	31. Acceptance criteria should be established for the radiopharmaceutical including criteria for release and shelf life specifications (examples: chemical identity of the isotope, radioactive concentration, purity, and specific activity).
32. 主要設備之使用、清潔、滅菌處理/滅菌及維護保養的紀錄，除應顯示人員參與這類活動之日期、時間及簽名外，合適時，並應顯示該產品名稱及批號。	32. Records of major equipment use, cleaning, sanitisation or sterilisation and maintenance should show the product name and batch number, where appropriate, in addition to the date and time and signature for the persons involved in these activities.
33. 除了國家要求另有規定外，紀錄應保存至少三年。	33. Records should be retained for at least 3 years unless another timeframe is specified in national requirements.
生產（PRODUCTION）	
34. 為了將交叉污染或混雜的風險減到最低，應避免在相同作業區中【亦即，鉛室/鉛櫃、層流空氣單元】於相同時間生產不同的放射性產品。	34. Production of different radioactive products in the same working area (i.e. hotcell, LAF unit), at the same time should be avoided in order to minimise the risk of cross-contamination or mix-up.
35. 確效應予以特別注意，包含電腦化系統在內，該系統之確效應依照 PIC/S GMP 指引附則 11 執行。新製程應進行先期性確效。	35. Special attention should be paid to validation including validation of computerised systems which should be carried out in accordance in compliance PIC/S GMP Guide, Annex 11. New manufacturing processes should be validated prospectively.
36. 關鍵參數通常應在確效前或在確效期間予以確認，並應界定再現性操作所需的範圍。	36. The critical parameters should normally be identified before or during validation and the ranges necessary for reproducible operation should be defined.

37 考慮輻射防護的需要及過濾器無菌性的維護，無菌充填的產品應執行濾膜過濾器的完整性測試。	37. Integrity testing of the membrane filter should be performed for aseptically filled products, taking into account the need for radiation protection and maintenance of filter sterility.
38. 由於輻射暴露，所以大部分直接容器的標示在製造前即已完成是可接受的。若該標示程序不損及無菌性或妨礙經充填小瓶的目視管制，則空的無菌密閉小瓶得在充填前標示部分資訊。	38. Due to radiation exposure it is accepted that most of the labelling of the direct container, is done prior to manufacturing. Sterile empty closed vials may be labelled with partial information prior to filling providing that this procedure does not compromise sterility or prevent visual control of the filled vial.
品質管制（QUALITY CONTROL）	
39. 有些放射性藥品可能必須在完成所有化學的與微生物學上的檢驗前，即依據批次文件之評估予以運銷及使用。	39. Some radiopharmaceuticals may have to be distributed and used on the basis of an assessment of batch documentation and before all chemical and microbiology tests have been completed.
放射性藥品之放行，得在完整分析檢驗前，以二或二個以上的階段執行：	Radiopharmaceutical product release may be carried out in two or more stages, before and after full analytical testing:
a) 在允許放射性藥品於隔離待驗狀態下運送至臨床部門前，經由指定人員對其批次操作紀錄之評估，應涵蓋至當時已執行之生產條件及分析檢驗。	a) Assessment by a designated person of batch processing records, which should cover production conditions and analytical testing performed thus far, before allowing transportation of the radiopharmaceutical under quarantine status to the clinical department.
b) 被授權人員出具書面證明前，應評估最終分析數據，以確保與正常程序之所有偏離業經文件化並證明其適當性，且適當地放行。在產品使用前無法獲得某些檢驗結果時，被授權人員應在其使用前有條件地證明該產品，並應在取得所有檢驗結果後，予以最終證明。	b) Assessment of the final analytical data, ensuring all deviations from normal procedures are documented, justified and appropriately released prior to documented certification by the Authorised Person. Where certain test results are not available before use of the product, the Authorised Person should conditionally certify the product before it is used and should finally certify the product after all the test results are obtained.

40. 大多數放射性藥品均預定在短時間內使用，關於放射性架儲有效期間必需清楚地陳述。	40. Most radiopharmaceuticals are intended for use within a short time and the period of validity with regard to the radioactive shelf-life, must be clearly stated.
41. 具有長半衰期之放射性核種的放射性藥品應經測試，以顯示其在由被授權人員放行及給予證明前，符合所有相關的允收標準。	41. Radiopharmaceuticals having radionuclides with long half-lives should be tested to show, that they meet all relevant acceptance criteria before release and certification by the Authorised Person.
42. 在執行檢驗前，得將樣品儲存，以允許足夠之放射活性衰變。所有檢驗，包括無菌試驗在內，應盡速執行。	42. Before testing is performed samples can be stored to allow sufficient radioactivity decay. All tests including the sterility test should be performed as soon as possible.
43. 應建立詳述生產與分析數據評估的書面程序。該評估在批次發送前即應考慮。	43. A written procedure detailing the assessment of production and analytical data, which should be considered before the batch is dispatched, should be established.
44. 不符合允收標準之產品應予拒用。若該物質經重處理應依循預先建立之程序，且最終產品在放行前應符合允收標準。退回之產品不能重處理，且必須視為放射性廢棄物予以儲存。	44. Products that fail to meet acceptance criteria should be rejected. If the material is reprocessed, pre-established procedures should be followed and the finished product should meet acceptance criteria before release. Returned products may not be reprocessed and must be stored as radioactive waste.
45. 產品若在發送後且末效日期屆滿前得到不滿意的試驗結果 (偏離規格) 時，程序亦應描述被授權人員所要採取之措施。該等事件應予調查，以包括防止未來類似事件所應採取之相關的矯正及預防措施。	45. A procedure should also describe the measures to be taken by Authorised Person if unsatisfactory test results (Out-of-Specification) are obtained after dispatch and before expiry. Such events should be investigated to include the relevant corrective and preventative actions taken to prevent future events.
這個過程應予以文件化。	This process must be documented.
46. 必要時，應將資訊提供臨床負責人員。為便利這種做法，應對放射性藥品實施一可追溯性系統。	46. Information should be given to the clinical responsible persons, if necessary. To facilitate this, a traceability system should be implemented for radiopharmaceuticals.

47. 應備有確認原料品質的系統。供應商之核准應包含提供該原料一致地符合規格之適當保證的評估。原料、包裝材料及關鍵製程助劑應購自經核准的供應商。	47. A system to verify the quality of starting materials should be in place. Supplier approval should include an evaluation that provides adequate assurance that the material consistently meets specifications. The starting materials, packaging materials and critical process aids should be purchased from approved suppliers.
對照樣品及留存樣品（REFERENCE AND RETENTION SAMPLES）	
48. 放射性藥品每批待分/包裝產品應留存足夠的樣品。除透過風險管理證明其適當性者外，該等樣品應保存到最終產品的末效日期後至少六個月。	48. For radiopharmaceuticals sufficient samples of each batch of bulk formulated product should be retained for at least six months after expiry of the finished medicinal product unless otherwise justified through risk management.
49. 使用於製造過程之原料的樣品，不屬於溶劑、氣體或水者，應留存至該產品放行後至少兩年。相關規格中所示之原料的安定性期間較短者，該期間得縮短之。	49. Samples of starting materials, other than solvents gases or water used in the manufacturing process should be retained for at least two years after the release of the product. That period may be shortened if the period of stability of the material as indicated in the relevant specification is shorter.
50. 原料及個別製造或小量製造、或其儲存可能引起特別問題之產品，其抽樣及留存得與主管機關以協議界定其他條件。	50. Other conditions may be defined by agreement with the competent authority, for the sampling and retaining of starting materials and products manufactured individually or in small quantities or when their storage could raise special problems.
運銷（DISTRIBUTION）	
51. 這些放射性藥品，直到獲得滿意的檢驗結果，並經指定的人員進行評估前不會被接收機構所投用，則在獲得所有適當檢驗結果前，最終產品在管制條件下的運銷是可以接受的。	51. Distribution of the finished product under controlled conditions, before all appropriate test results are available, is acceptable for radiopharmaceuticals, providing the product is not administered by the receiving institute until satisfactory test results has been received and assessed by a designated person.

術語彙編（GLOSSARY）	
製備： *自醫院內之發生器或放射性前驅物溶洗出具有放射性核種之套組的處理及輻射標示。套組、發生器及前驅物應有上市許可或國家執照。*	***Preparation:*** *handling and radiolabelling of kits with radionuclide eluted from generators or radioactive precursors within a hospital. Kits, generators and precursors should have a marketing authorisation or a national licence.*
製造： *放射性藥品從活性物質與原料之生產、品質管制、放行及送交。*	***Manufacturing:*** *roduction, quality control and release and delivery of radiopharmaceuticals from the active substance and starting materials.*
鉛室/鉛櫃： *為放射性物質之製造及處理的具有遮蔽之作業站。鉛室/鉛櫃未必需要設計成隔離裝置。*	***Hot–cells:*** *shielded workstations for manufacture and handling of radioactive materials. Hot-cells are not necessarily designed as an isolator.*
被授權人員： *經權責機關認定為具備必要之基礎科學與技術背景及經驗的人員。*	***Authorised person:*** *Person recognised by the authority as having the necessary basic scientific and technical background and experience.*

附則 6　醫用氣體的製造（MANUFACTURE OF MEDICINAL GASES）

1. 原則（PRINCIPLE）	
本附則涉及醫用氣體的工業製造，該製造為特別的工業製程，通常不是由製藥公司來執行。醫院中受制於國家法律管制之醫用氣體的製造與處理不在本附則範圍。不過，本附則之相關部分可以當做該等作業活動之基礎使用。	This annex deals with industrial manufacturing of medicinal gases, which is a specialised industrial process not normally undertaken by pharmaceutical companies. It does not cover manufacturing and handling of medicinal gases in hospitals, which will be subject to national legislation. However relevant parts of this annex may be used as a basis for such activities.
通常，製造醫用氣體時係在密閉系統中進行，因此產品之環境污染最少，惟不同的氣體間仍有交叉污染的風險。	The manufacture of medicinal gases is generally carried out in closed equipment. Consequently, environmental contamination of the product is minimal. However, there is a risk of cross-contamination with other gases.
醫用氣體之製造應符合 GMP 的基本要求、可適用之附則、藥典標準及下列的詳細指引。	Manufacture of medicinal gases should comply with the basic requirements of GMP, with applicable annexes, Pharmacopoeial standards and the following detailed guidelines.
2. 人員（PERSONNEL）	
2.1　負責醫用氣體放行之被授權人員，應具備醫用氣體之生產與管制的充分知識。	2.1　The authorised person responsible for release of medicinal gases should have a thorough knowledge of the production and control of medicinal gases.
2.2　涉及醫用氣體製造之所有人員，應瞭解與醫用氣體製造相關之 GMP 要求，且應意識到特別重要的層面，及該氣體對於病人之潛在的危害。	2.2　All personnel involved engaged in the manufacture of medicinal gases should understand the GMP requirements relevant to medicinal gases and should be aware of the critically important aspects and potential hazards for patients from products in the form of medicinal gases.
3. 廠房設施及設備（PREMISES AND EQUIPMENT）	
3.1　廠房設施（Premises）	
3.1.1　醫用氣體應在與非醫用氣體隔離的區域灌充/充填。這些區域間之容器不得互換。在例外的情況下，如採取特別防範措施並完成必要之確效，可接受在同一作業區域內的時段切換灌充/充填。	3.1.1　Medicinal gases should be filled in a separate area from non-medicinal gases and there should be no exchange of containers between these areas. In exceptional cases, the principal of campaign filling in the same area can be

	accepted provided that specific precautions are taken and necessary validation is done.
3.1.2 應具備足夠的空間供製造、測試及儲存作業，以避免混雜的風險。廠房設施應保持整齊清潔，以利有條理的作業及適當的儲存。	3.1.2 Premises should provide sufficient space for manufacturing, testing and storage operations to avoid the risk of mix-up. Premises should be clean and tidy to encourage orderly working and adequate storage.
3.1.3 灌充/充填區域應具備足夠的大小及有條理的配置，以提供：	3.1.3 Filling areas should be of sufficient size and have an orderly layout to provide:
a. 不同氣體之各自標記區域；	a. separate marked areas for different gases
b. 空鋼瓶與製程中不同階段的鋼瓶（例如待灌充、已灌充、待驗、合格或拒用等）能明確辨識及隔離。	b. clear identification and segregation of empty cylinders and cylinders at various stages of processing (e.g. "awaiting filling", "filled", "quarantine", "approved", "rejected").
達到這些不同層次所使用之隔離方法，取決於整體作業之本質、程度及複雜性，但可使用經標記之地板區域、隔板、柵欄、符號或其他適當方法等。	The method used to achieve these various levels of segregation will depend on the nature, extent and complexity of the overall operation, but marked-out floor areas, partitions, barriers and signs could be used or other appropriate means.
3.2 設備（Equipment）	
3.2.1 所有用於製造及分析醫用氣體的設備應經驗證與適當的定期校正。	3.2.1 All equipment for manufacture and analyses should be qualified and calibrated regularly as appropriate.
3.2.2 必須確保正確的氣體裝入正確的容器中。除經確效的自動灌充/充填作業外，輸送不同氣體的管路間不應相連。歧管上應配置專屬灌充/充填的接頭，該接頭僅對應於標的氣體或標的混合氣體之閥，以便僅有正確的容器可與歧管相連。（歧管與容器閥之接頭的使用，可能受國際或國家標準之管制。）	3.2.2 It is necessary to ensure that the correct gas is put into the correct container. Except for validated automated filling processes there should be no interconnections between pipelines carrying different gases. The manifolds should be equipped with fill connections that correspond only to the valve for that particular gas or particular mixture of gases so that only the correct containers can be attached to the manifold. (The use of manifold and container valve connections may be subject to international or national standards.)
3.2.3 修理及維護保養作業，不得影響醫用氣體的品質。	3.2.3 Repair and maintenance operations should not affect the quality of the medicinal

	gases.
3.2.4 灌充/充填非醫用氣體時，應避免使用醫用氣體生產之專用區域及設備，除非該等非醫用氣體之品質至少等於醫用氣體之品質，且能維持 GMP 標準。供應非醫用氣體灌充/充填區域之管路，應有經確效防止回流的方法，以避免污染醫用氣體。	3.2.4 Filling of non-medicinal gases should be avoided in areas and with equipment destined for the production of medicinal gases. Exceptions can be acceptable if the quality of the gas used for non-medicinal purposes is at least equal to the quality of the medicinal gas and GMP-standards are maintained. There should be a validated method of backflow prevention in the line supplying the filling area for non-medicinal gases to prevent contamination of the medicinal gas.
3.2.5 儲槽及移動式槽車應專用於一種氣體且該氣體之品質業經明確界定。但非醫用氣體品質至少等於醫用氣體的品質時，則液化醫用氣體可在相同的儲槽儲存或運送。	3.2.5 Storage tanks and mobile delivery tanks should be dedicated to one gas and a well-defined quality of this gas. However liquefied medicinal gases may be stored or transported in the same tanks as the same non-medicinal gas provided that the quality of the latter is at least equal to the quality of the medicinal gas.
4 文件（DOCUMENTATION）	
4.1 每批經灌充之鋼瓶的紀錄所含資料，必需確保所灌充的每一鋼瓶能追溯到相關灌充作業之重要層面。合適時，下列內容應予登錄：	4.1 Data included in the records for each batch of cylinders filled must ensure that each filled cylinder is traceable to significant aspects of the relevant filling operations. As appropriate, the following should be entered:
➢ 產品名稱；	➢ the name of the product;
➢ 灌充日期與時間；	➢ the date and the time of the filling operations;
➢ 所涉及使用之灌充站；	➢ a reference to the filling station used;
➢ 所使用之設備；	➢ equipment used;
➢ 該氣體或混合氣體中各組成氣體之名稱及相關規格；	➢ name and reference to the specification of the gas or each gas in a mixture;
➢ 灌充前所執行的作業；(參閱 5.3.5)	➢ pre filling operations performed (see point 5.3.5);
➢ 灌充前、後之鋼瓶數量與大小；	➢ the quantity and size of cylinders before and after filling;
➢ 執行灌充作業之人員姓名；	➢ the name of the person carrying out the filling operation;
➢ 各重要灌充步驟之操作人員簽章（如清線、鋼瓶接收、鋼瓶排空等）；	➢ the initials of the operators for each significant step (line clearance, receipt of

	cylinders, emptying of cylinders etc);
➢ 需要確保在標準條件下正確灌充之關鍵參數；	➢ key parameters that are needed to ensure correct fill at standard conditions;
➢ 品管檢驗之結果，以及在每一檢驗前設備進行校正時，其對照氣體規格與校正核對結果；	➢ the results of quality control tests and where test equipment is calibrated before each test, the reference gas specification and calibration check results;
➢ 確保容器已完成灌充之檢查結果；	➢ results of appropriate checks to ensure the containers have been filled;
➢ 批次代碼標籤之樣品；	➢ a sample of the batch code label;
➢ 任何問題或異常事件之詳細資料，與灌充指令之任何偏差的簽章認可；	➢ details of any problems or unusual events, and signed authorisation for any deviation from filling instructions;
➢ 顯示負責灌充作業主管之認可、簽章及日期。	➢ to indicate agreement, the date and signature of the supervisor responsible for the filling operation.
5 生產（PRODUCTION）	
5.1 不同製造過程中，所有的關鍵性步驟均應予以確效。	5.1 All critical steps in the different manufacturing processes should be subject to validation.
5.2 大宗氣體生產（Bulk production）	
5.2.1 醫用之大宗氣體，可利用化學合成法製得，或由天然來源經必要的精製（例如空氣分離工廠）所取得。此等氣體得依主管機關規定，視為原料藥或大宗藥品。	5.2.1 Bulk gases intended for medicinal use could be prepared by chemical synthesis or obtained from natural resources followed by purification steps if necessary (as for example in an air separation plant). These gases could be regarded as Active Pharmaceutical Ingredients (API) or as bulk pharmaceutical products as decided by the national competent authority.
5.2.2 應備有文件規定其純度、其他組成物以及合適時可能出現於來源氣體及純化步驟的雜質。另應備有各不同製程之流程圖。	5.2.2 Documentation should be available specifying the purity, other components and possible impurities that may be present in the source gas and at purification steps, as applicable. Flow charts of each different process should be available.
5.2.3 所有分離與純化步驟應經設計以在最佳效率下操作。例如雜質對於純化步驟可能會有不良的影響，故應於純化步驟前將其移除。	5.2.3 All separation and purification steps should be designed to operate at optimal effectiveness. For example, impurities that may adversely affect a purification step should be removed before this step is reached.
5.2.4 分離及純化步驟，應針對其有效性予以	5.2.4 Separation and purification steps should

確效，並以確效結果進行監測。必要時，製程中管制應包含連續分析以監測製程。消耗性設備組件（例如純化用濾器），應依據監測與確效之結果進行維護與替換。	be validated for effectiveness and monitored according to the results of the validation. Where necessary, in-process controls should include continuous analysis to monitor the process. Maintenance and replacement of expendable equipment components, e.g. purification filters, should be based on the results of monitoring and validation.
5.2.5 可行時，製程溫度之限值應予以文件化，製程中監測應包含溫度量測。	5.2.5 If applicable, limits for process temperatures should be documented and in-process monitoring should include temperature measurement.
5.2.6 用於控制或監測製程的電腦系統應予以確效。	5.2.6 Computer systems used in controlling or monitoring processes should be validated.
5.2.7 連續製程批次的定義應予以文件化，並與大宗氣體之分析互為關連。	5.2.7 For continuous processes, a definition of a batch should be documented and related to the analysis of the bulk gas.
5.2.8 氣體生產應對其品質與雜質進行持續監測。	5.2.8 Gas production should be continuously monitored for quality and impurities.
5.2.9 空氣壓縮期間所使用的冷卻用水，如與醫用氣體接觸時，應對其微生物學上的品質進行監測。	5.2.9 Water used for cooling during compression of air should be monitored for microbiological quality when in contact with the medicinal gas.
5.2.10 液化氣體從主儲存槽之所有運送作業，包括運送前的管制，應依照經設計之書面程序，以避免任何污染。運送用的管路應配備逆止閥或其他適當的替代品。對於橈性/伸縮性連接裝置、配置之軟管及連接器/耦合軟管及接頭，應特別注意加以沖吹。	5.2.10 All the transfer operations, including controls before transfers, of liquefied gases from primary storage should be in accordance with written procedures designed to avoid any contamination. The transfer line should be equipped with a non-return valve or any other suitable alternative. Particular attention should be paid to purge the flexible connections and to coupling hoses and connectors.
5.2.11 氣體之交貨可將其加入含有先前交貨之相同氣體的大宗儲槽內。其樣品之檢驗結果必須顯示交貨氣體之品質是可接受的。該樣品可取自：	5.2.11 Deliveries of gas may be added to bulk storage tanks containing the same gas from previous deliveries. The results of a sample must show that the quality of the delivered gas is acceptable. Such a sample could be taken from
➢ 加入儲槽前之交貨氣體；或	➢ the delivered gas before the delivery is added; or
➢ 加入並混和後之大宗儲槽。	➢ from the bulk tank after adding and mixing.

5.2.12 供醫用之大宗氣體應界定為一個批次，並依相關藥典個論予以管控並放行供灌充。	5.2.12 Bulk gases intended for medicinal use should be defined as a batch, controlled in accordance with relevant Pharmacopoeial monographs and released for filling.
5.3 灌充/充填與標示（Filling and labeling）	
5.3.1 灌充醫用氣體時，應界定其批次。	5.3.1 For filling of medicinal gases the batch should be defined.
5.3.2 醫用氣體之容器應符合適當的技術規格。灌充後，閥出口處應配置竄改易顯封緘。為得到適當的防止污染，鋼瓶最好具有維持瓶內最低壓力之殘壓閥。	5.3.2 Containers for medicinal gases should conform to appropriate technical specifications. Valve outlets should be equipped with tamper-evident seals after filling. Cylinders should preferably have minimum pressure retention valves in order to get adequate protection against contamination.
5.3.3 醫用氣體之灌充歧管與鋼瓶應專用於單一種醫用氣體或已知的醫用混合氣體(參閱 3.2.2)。應備有確保鋼瓶與閥之可追溯的系統。	5.3.3 The medicinal gases filling manifold as well as the cylinders should be dedicated to a single medicinal gas or to a given mixture of medicinal gases (see also 3.2.2). There should be a system in place ensuring traceability of cylinders and valves.
5.3.4 灌充設備與管路之清潔及沖吹，應依書面程序執行。這在維護保養或系統完整性之破壞後特別重要。在灌充線放行使用前，應檢查其無污染，並保存紀錄。	5.3.4 Cleaning and purging of filling equipment and pipelines should be carried out according to written procedures. This is especially important after maintenance or breaches of system integrity. Checks for the absence of contaminants should be carried out before the line is released for use. Records should be maintained.
5.3.5 於下列狀況，應對鋼瓶內部進行目視檢查：	5.3.5 Cylinders should be subject to an internal visual inspection when
➢ 新的鋼瓶；	➢ they are new;
➢ 進行水壓試驗或與其相當的試驗時；	➢ in connection with any hydrostatic pressure test or equivalent test.
閥門安裝好後，應維持於關閉位置，以防止污染物進入鋼瓶內。	After fitting of the valve, the valve should be maintained in a closed position to prevent any contamination from entering the cylinder.
5.3.6 灌充作業前的檢查應包括下列各項：	5.3.6 Checks to be performed before filling should include:
➢ 檢查鋼瓶內之殘壓〈> 3~5 bars〉，以確保鋼瓶未排空。	➢ a check to determine the residual pressure (>3 to 5 bar) to ensure that the cylinder is

	not emptied;
➢ 無殘壓之鋼瓶應另外存放供追加的測試，以確保未被水或其他污染物污染。該測試可包含經確效之方法予以清潔或證明可行時的目視檢查。	➢ Cylinders with no residual pressure should be put aside for additional measures to make sure they are not contaminated with water or other contaminants. These could include cleaning with validated methods or visual inspection as justified;
➢ 確保所有批次標籤以及損壞之其他標籤均已移除。	➢ Assuring that all batch labels and other labels if damaged have been removed;
➢ 目視檢查每一閥及鋼瓶之外部是否有凹陷、電弧燒傷、破片、其他損傷及油污污染等。鋼瓶應以適當方式予以清潔、測試與維護。	➢ visual external inspection of each valve and container for dents, arc burns, debris, other damage and contamination with oil or grease; Cylinders should be cleaned, tested and maintained in an appropriate manner;
➢ 檢查每一個鋼瓶或低溫容器閥的連接，以確定其為特定醫用氣體用之正確類型。	➢ a check of each cylinder or cryogenic vessel valve connection to determine that it is the proper type for the particular medicinal gas involved;
➢ 檢查鋼瓶之「測試代碼日期」，以確定已執行水壓測試或其相當的測試，且依國家或國際規範的要求仍然有效。	➢ a check of the cylinder “test code date” to determine that the hydrostatic pressure test or equivalent test has been conducted and still is valid as required by national or international guidelines;
➢ 檢查並確定每一鋼瓶符合相關標準之色碼規定。	➢ a check to determine that each container is colour-coded according to the relevant standard.
5.3.7 為使污染之風險降至最低，應小心處理回收供再灌充的鋼瓶。以壓縮氣體而言，在 200 bar 之灌充壓力下，其雜質理論上限為 500 ppm v/v〈其他灌充壓力也相當〉。	5.3.7 Cylinders which have been returned for refilling should be prepared with great care in order to minimise risks for contamination. For compressed gases a maximum theoretical impurity of 500 ppm v/v should be obtained for a filling pressure of 200 bar (and equivalent for other filling pressures).
回收之鋼瓶應如下處理：	Cylinders could be prepared as follows:
➢ 任何殘留於鋼瓶的氣體，應抽氣移除〈至少達到殘留 150 mbar 之絕對壓力〉；或	➢ any gas remaining in the cylinders should be removed by evacuating the container (at least to a remaining absolute pressure of 150 millibar), or
➢ 將每一鋼瓶洩壓後，以確效過的方法沖吹〈部分加壓至少達 7 bar，然後洩壓。〉	➢ by blowing down each container, followed by purging using validated methods (partial pressurisation at least to 7 bar and then

	blowing down).
配置有殘壓〈正壓〉閥的鋼瓶，如為正壓時，在 150 mbar 真空下，一次排空即已足夠。如以其他替代方法時，則對每一個鋼瓶的殘留氣體，應執行全項分析。	For cylinders equipped with residual (positive) pressure valves, one evacuation under vacuum at 150 millibar is sufficient if the pressure is positive. As an alternative, full analysis of the remaining gas should be carried out for each individual container.
5.3.8 應有適當的檢查方法來確認鋼瓶是否已完成灌充。在灌充時輕觸鋼瓶之外壁確保其具暖和感，可能是適當灌充的指標。	5.3.8 There should be appropriate checks to ensure that containers have been filled. An indication that it is filling properly could be to ensure that the exterior of the cylinder is warm by touching it lightly during filling.
5.3.9 每一個鋼瓶都應加標示並標色碼。批號及/或灌充日期與末效日期得用另一標籤加以註明。	5.3.9 Each cylinder should be labeled and colour-coded. The batch number and/or filling date and expiry date may be on a separate label.
6 品質管制（QUALITY CONTROL）	
6.1 用於水壓測試的水，至少應符合飲用水品質，並應例行監測微生物學上的污染。	6.1 Water used for hydrostatic pressure testing should be at least of drinking water quality and monitored routinely for microbiological contamination.
6.2 每一種醫用氣體均應依其既定規格檢驗及放行。此外，應以充分的頻率執行相關藥典要求的全項檢驗，以確保持續符合要求。	6.2 Each medicinal gas should be tested and released according to its specifications. In addition, each medicinal gas should be tested to full relevant pharmacopoeial requirements at sufficient frequency to assure ongoing compliance.
6.3 大宗氣體應經放行後始供灌充(參閱 5.2.12)。	6.3 The bulk gas supply should be released for filling. (see 5.2.12)
6.4 單一種醫用氣體經由多鋼瓶歧管進行灌充時，從每一歧管灌充之產品至少一個鋼瓶應測試其同一性、含量分析，且在歧管上每次更換鋼瓶時，視需要測定其水分含量。	6.4 In the case of a single medicinal gas filled via a multi-cylinder manifold, at least one cylinder of product from each manifold filling should be tested for identity, assay and if necessary water content each time the cylinders are changed on the manifold.
6.5 單一種醫用氣體經由個別的灌充操作，每次灌充一個鋼瓶時，每一未中斷灌充之週期，至少一個鋼瓶應測試其同一性與含量分析。未中斷灌充週期之實例，是同一工作班次之生產以相同人員、相同設備與同批大宗氣體。	6.5 In the case of a single medicinal gas filled into cylinders one at a time by individual filling operations, at least one cylinder of each uninterrupted filling cycle should be tested for identity and assay. An example of an uninterrupted filling operation cycle is

	one shift's production using the same personnel, equipment, and batch of bulk gas.
6.6 經由同一歧管灌充兩種或兩種以上氣體於同一鋼瓶中混合時，在每一歧管灌充作業週期中，應至少取一鋼瓶測試其同一性與含量分析；必要時對所有的組成氣體之水分含量與混合氣體中之平衡氣體〈balancegas〉之同一性進行測試。當鋼瓶個別灌充時，每一鋼瓶應測試其所有組成氣體之同一性與含量分析，以及在每一不中斷的灌充週期中，至少一個鋼瓶應測試其混合氣體中之平衡氣體的同一性。	6.6 In the case of a medicinal gas produced by mixing two or more different gases in a cylinder from the same manifold, at least one cylinder from each manifold filling operation cycle should be tested for identity, assay and if necessary water content of all of the component gases and for identity of the balancegas in the mixture. When cylinders are filled individually, every cylinder should be tested for identity and assay of all of the component gases and at least one cylinder of each uninterrupted filling cycle should be tested for identity of the balancegas in the mixture.
6.7 當氣體灌充前，在管路中進行混合時(例如一氧化二氮/氧混合物)，則需對該灌充之混合氣體進行連續分析。	6.7 When gases are mixed in-line before filling (e.g. nitrous oxide/oxygen mixture) continuous analysis of the mixture being filled is required.
6.8 當鋼瓶以一種以上的氣體灌充時，灌充過程必須確保氣體在每一個鋼瓶中正確混合，而且是完全均質的。	6.8 When a cylinder is filled with more than one gas, the filling process must ensure that the gases are correctly mixed in every cylinder and are fully homogeneous.
6.9 每一經灌充之鋼瓶，應在裝上竄改易顯封緘前，使用適當方法測試其洩漏。執行取樣與分析時，洩漏試驗應在分析後完成。	6.9 Each filled cylinder should be tested for leaks using an appropriate method, prior to fitting the tamper evident seal. Where sampling and testing is carried out the leak test should be completed after testing.
6.10 為交付給使用者，將低溫氣體充填至低溫家用容器時，每一容器應測試其同一性及含量分析。	6.10 In the case of cryogenic gas filled into cryogenic home vessels for delivery to users, each vessel should be tested for identity and assay.
6.11 由客戶保管之低溫容器，且醫用氣體係由專用移動式槽車就地充填，若充填公司提交取自移動式槽車之樣品的分析證明書(COA)時，則充填後不需抽樣。由客戶保管之低溫容器應定期進行測試，以確認其內容物符合藥典規定。	6.11 Cryogenic vessels which are retained by customers and where the medicinal gas is refilled in place from dedicated mobile delivery tanks need not be sampled after filling provided the filling company delivers a certificate of analysis for a sample taken from the mobile delivery tank. Cryogenic vessels retained by customers should be

	periodically tested to confirm that the contents comply with pharmacopoeial requirements.
6.12 除另有規定者外，不須保留樣品。	6.12 Retained samples are not required, unless otherwise specified.
7 儲存與放行（STORAGE AND RELEASE）	
7.1 經灌充之鋼瓶應保存於隔離區，直至被授權人員放行為止。	7.1 Filled cylinders should be held in quarantine until released by the authorised person.
7.2 氣體之鋼瓶應在遮蔽下儲存且不受極端溫度的影響。儲存的區域應為潔淨、乾燥且通風良好並無可燃物，以確保鋼瓶保持潔淨直至使用時。	7.2 Gas cylinders should be stored under cover and not be subjected to extremes of temperature. Storage areas should be clean, dry, well ventilated and free of combustible materials to ensure that cylinders remain clean up to the time of use.
7.3 儲存安排應允許不同氣體及充滿/空的鋼瓶之隔離，並且允許依先進先出(FIFO)進行庫存輪換。	7.3 Storage arrangements should permit segregation of different gases and of full/empty cylinders and permit rotation of stock on a first in – first out basis.
7.4 氣體鋼瓶在運送期間應避免不良氣候條件，對於在冰凍時會發生相分離之混合氣體，其儲存與運輸應有特定的條件。	7.4 Gas cylinders should be protected from adverse weather conditions during transportation. Specific conditions for storage and transportation should be employed for gas mixtures for which phase separation occurs on freezing.
術語彙編（GLOSSARY）	
空氣分離工廠 *取用大氣中的空氣，透過純化、淨化、壓縮、冷卻、液化、與蒸餾等程序，將空氣中的氧、氮與氬等成分加以分離的工廠。*	***Air separation plant*** *Air separation plants take atmospheric air and through processes of purification, cleaning, compression, cooling, liquefaction and distillation which separates the air into the gases oxygen, nitrogen and argon.*
作業場所 *專供製造醫用氣體之部分廠房設施。*	***Area*** *Part of premises that is specific to the manufacture of medicinal gases.*
洩壓 *放氣將壓力下降到大氣壓力。*	***Blowing down*** *Blow the pressure down to atmospheric pressure.*
大宗氣體 *已完成各種製程並擬供醫用的任何氣體，但不包含最終包裝。*	***Bulk gas*** *Any gas intended for medicinal use, which has completed all processing up to but not including final packaging.*
壓縮氣體 *加壓下包裝的氣體，於 -50℃時完全氣態 (ISO*	***Compressed gas*** *A gas which when packaged under pressure is*

10286)。	*entirely gaseous at -50℃. (ISO10286).*
容器 *指與醫用氣體直接接觸的低溫容器、儲槽、槽車、鋼瓶、集束鋼瓶或其他包裝型式。*	***Container*** *A container is a cryogenic vessel, a tank, a tanker, a cylinder, a cylinder bundle or any other package that is in direct contact with the medicinal gas.*
低溫氣體 *在 1.013bar 與溫度低於 -150℃之條件下會液化的氣體。*	***Cryogenic gas*** *Gas which liquefies at 1.013 bar at temperature below –150℃.*
低溫容器 *經設計以容納液化或低溫氣體之固定或可移動式熱絕緣容器。該等氣體可以氣態或液態移出。*	***Cryogenic vessel*** *A static or mobile thermally insulated container designed to contain liquefied or cryogenic gases. The gas is removed in gaseous or liquid form.*
鋼瓶 *指不超過 150 公升水容積之可搬運的壓力容器。本文件所稱之鋼瓶，合適時包括集束鋼瓶。*	***Cylinder*** *A transportable, pressure container with a water capacity not exceeding 150 liters. In this document when using the word cylinder it includes cylinder bundle (or cylinder pack) when appropriate.*
集束鋼瓶 *指鋼瓶之組合，通常將若干鋼瓶一起固定於一框架中，以歧管連接、一起運送並整組作為一個單元供使用。*	***Cylinder bundle*** *An assembly of cylinders, which are fastened together in a frame and interconnected by a manifold, transported and used as a unit.*
抽氣排空 *將容器內的殘留氣體以抽真空的方式排出。*	***Evacuate*** *To remove the residual gas in a container by pulling a vacuum on it.*
氣體 *為一種物質或物質之混合物，在 1.013 bar (101.325 kPa)與＋15℃時完全氣化，或在＋50℃時蒸汽壓超過 3 bar (300 kPa) (ISO 10286)。*	***Gas*** *A substance or a mixture of substances that is completely gaseous at 1,013 bar (101,325 kPa) and +15℃ or has a vapour pressure exceeding 3 bar (300 kPa) at +50℃. (ISO 10286).*
水壓試驗 *為確保鋼瓶或儲槽能承受高壓，由國家或國際之相關規定為安全理由所執行的試驗。*	***Hydrostatic pressure test*** *Test performed for safety reasons as required by national or international guideline in order to make sure that cylinders or tanks can withhold high pressures.*
液化氣體 *於壓力下包裝的氣體，在-50℃下部分氣體液化〈氣態與液態共存〉。*	***Liquefied gas*** *A gas which when packaged under pressure, is partially liquid (gas over a liquid) at –50℃.*
歧管 *經設計能用於同時將一個或多個鋼瓶排空與灌充的設備或器具。*	***Manifold*** *Equipment or apparatus designed to enable one or more gas containers to be emptied and filled at a time.*

最高理論殘留雜質 *來自於可能之迴流污染與灌充前對鋼瓶作預處理時的殘留污染所造成的氣態雜質。最高理論殘留雜質的計算只與壓縮氣體有關，且假設此氣體為理想氣體。*	***Maximum theoretical residual impurity*** *Gaseous impurity coming from a possible retropollution and remaining after the cylinders pre-treatment before filling. The calculation of the maximum theoretical impurity is only relevant for compressed gases and supposes that these gases act as perfect gases.*
醫用氣體 *使用藥理作用，預定為治療、診斷或預防之目的投用於病人並歸類為藥品的任何氣體或混合氣體。*	***Medicinal gas*** *Any gas or mixture of gases intended to be administered to patients for therapeutic, diagnostic or prophylactic purposes using pharmacological action and classified as a medicinal product.*
最低壓力殘壓閥 *為防止使用中發生污染，配備有不可逆流裝置的系統之閥門，可維持明確的壓力〈約高於大氣壓力 3-5 bars〉。*	***Minimum pressure retention valve*** *Valve equipped with a non-return system which maintains a definite pressure (about 3 to 5 bars over atmospheric pressure) in order to prevent contamination during use.*
逆止閥 *只允許單向流動的閥門。*	***Non-return valve*** *Valve which permits flow in one direction only.*
沖吹 *為了排空與清潔鋼瓶所作的動作，通常如下處理：* *〈1〉進行洩壓及再抽真空；或* *〈2〉進行洩壓，再適量充填入目標氣體，然後再次進行洩壓。*	***Purge*** *To empty and clean a cylinder* *(1) by blowing down and evacuating or* *(2) by blowing down, partial pressurisation with the gas in question and then blowing down.*
儲槽 *為固定的容器，供儲存液化或低溫氣體之用。*	***Tank*** *Static container for the storage of liquefied or cryogenic gas.*
槽車 *固定於車輛上，供液化或低溫氣體運送的容器。*	***Tanker*** *Container fixed on a vehicle for the transport of liquefied or cryogenic gas.*
閥 *供開關容器用的裝置。*	***Valve*** *Device for opening and closing containers.*

附則 8　原料及包裝材料的抽樣（SAMPLING OF STARTING AND PACKAGING MATERIALS）

原則（PRINCIPLE）	
抽樣是一個重要的作業。抽樣係只抽取一個批次中的一小部分。整體而言，有效結論不能以不具代表性之樣品所執行的試驗為依據。因此，正確的抽樣是品質保證系統的必要部分。	Sampling is an important operation in which only a small fraction of a batch is taken. Valid conclusions on the whole cannot be based on tests which have been carried out on non-representative samples. Correct sampling is thus an essential part of a system of Quality Assurance.
註：抽樣規定於 GMP 總則中的第 6 章 6.11 到 6.14 條。本附則係就原料及包裝材料之抽樣提供附加的規定。	*Note: Sampling is dealt with in Chapter 6 of the Guide to GMP, items 6.11 to 6.14. These supplementary guidelines give additional guidance on the sampling of starting and packaging materials.*
人員（PERSONNEL）	
1. 抽樣人員應接受與正確抽樣相關之職前及持續定期訓練。本訓練應包括：	1. Personnel who take samples should receive initial and on-going regular training in the disciplines relevant to correct sampling. This training should include:
➢ 抽樣計畫；	➢ sampling plans,
➢ 書面抽樣程序；	➢ written sampling procedures,
➢ 抽樣技術及設備；	➢ the techniques and equipment for sampling,
➢ 交叉污染的風險；	➢ the risks of cross-contamination,
➢ 關於不安定的及/或無菌的物質要採取的預防措施；	➢ the precautions to be taken with regard to unstable and/or sterile substances,
➢ 考慮原物料、容器及標籤之目視外觀的重要性；	➢ the importance of considering the visual appearance of materials, containers and labels,
➢ 記錄任何非預期或異常狀況的重要性。	➢ the importance of recording any unexpected or unusual circumstances.
原料（STARTING MATERIALS）	
2. 原料之完整批次的鑑識，通常只有在自全部容器中抽取個別樣品，並對每一樣品執行鑑別試驗時始能確保。已建立確效程序確保無任何原料容器會被不正確的標示者，可容許只對一定比例之容器抽樣。	2. The identity of a complete batch of starting materials can normally only be ensured if individual samples are taken from all the containers and an identity test performed on each sample. It is permissible to sample only a proportion of the containers where a validated procedure has been established to

	ensure that no single container of starting material will be incorrectly identified on its label.
3. 本確效應至少考慮下列項目：	3. This validation should take account of at least the following aspects:
➢ 製造商與供應商的本質與狀況及其對製藥工業 GMP 要求的瞭解；	➢ nature and status of the manufacturer and of the supplier and their understanding of the GMP requirements of the Pharmaceutical Industry;
➢ 原料製造商的品質保證系統；	➢ the Quality Assurance system of the manufacturer of the starting material;
➢ 原料之生產及管制所依循的製造條件；	➢ the manufacturing conditions under which the starting material is produced and controlled;
➢ 原料的特質及將使用該原料之藥品。	➢ the nature of the starting material and the medicinal products in which it will be used.
在上述安排下，一個經確效的程序，對於下列情形，可接受免除每一進廠容器中原料的鑑別試驗：	Under such arrangements, it is possible that a validated procedure exempting identity testing of each incoming container of starting material could be accepted for:
➢ 來自單一產品製造商或工廠的原料；	➢ starting materials coming from a single product manufacturer or plant;
➢ 直接來自於製造商的原料或源自製造商已封緘之容器中的原料，其製造商應具有可信賴的歷史紀錄及由買方(藥品的製造商或經由官方認證的團體)定期稽查製造商之品質保證系統。	➢ starting materials coming directly from a manufacturer or in the manufacturer's sealed container where there is a history of reliability and regular audits of the manufacturer's Quality Assurance system are conducted by the purchaser (the manufacturer of the medicinal products or by an officially accredited body.)
對於下列情形，上述程序欲達成滿意的確效是不可能的：	It is improbable that a procedure could be satisfactorily validated for:
➢ 由中間商，例如由仲介者所供應之原料，其製造來源不明或未經稽查者；	➢ starting materials supplied by intermediaries such as brokers where the source of manufacture is unknown or not audited;
➢ 供注射產品使用的原料。	➢ starting materials for use in parenteral products.

4. 原料批次的品質，可藉由抽取並測試具代表性的樣品予以評價。供鑑別試驗抽取之樣品，可供此目的使用。為製備代表性樣品所抽取的樣品數，應依統計學的方法決定，並規定於抽樣計畫書中。個別樣品可能可以混合以構成一個組合樣品，混合之樣品數應考量原料的特質、供應商的瞭解及組合樣品的均質性予以界定。	4. The quality of a batch of starting materials may be assessed by taking and testing a representative sample. The samples taken for identity testing could be used for this purpose. The number of samples taken for the preparation of a representative sample should be determined statistically and specified in a sampling plan. The number of individual samples which may be blended to form a composite sample should also be defined, taking into account the nature of the material, knowledge of the supplier and the homogeneity of the composite sample.
包裝材料（PACKAGING MATERIAL）	
5. 包裝材料的抽樣計畫應至少考量下列事項：接收的數量、要求的品質、物料的特質(例如，直接包裝材料及/或印刷的包裝材料)、生產方法及藉由稽查瞭解包裝材料製造商之品質保證系統。抽取之樣品數應依統計學的方法決定並規定在抽樣計畫書中。	5. The sampling plan for packaging materials should take account of at least the following： the quantity received, the quality required, the nature of the material (e.g. primary packaging materials and/or printed packaging materials), the production methods, and the knowledge of Quality Assurance system of the packaging materials manufacturer based on audits. The number of samples taken should be determined statistically and specified in a sampling plan.

附則 9　液劑、乳膏及軟膏的製造（MANUFACTURE OF LIQUIDS, CREAMS AND OINTMENTS）

原則（PRINCIPLE）	
製造過程中，液劑、乳膏及軟膏可能特別容易受到微生物及其他污染。因此，應採取特別措施，以防止任何污染。	Liquids, creams and ointments may be particularly susceptible to microbial and other contamination during manufacture. Therefore special measures must be taken to prevent any contamination.
註：液劑、乳膏劑和軟膏劑的製造，應依 GMP 之總則及其他適用的附則，本附則僅強調該類產品製造之重點。	*Note: The manufacture of liquids, creams and ointments must be done in accordance with the GMP described in the PIC Guide to GMP and with the other supplementary guidelines, where applicable. The present guidelines only stress points which are specific to this manufacture.*
廠房設施及設備（PREMISES AND EQUIPMENT）	
1. 為防止產品受到污染，建議使用密閉的作業及轉送系統。產品或未封口之潔淨容器所暴露的生產區，通常應以過濾空氣予以有效通風。	1. The use of closed systems of processing and transfer is recommended in order to protect the product from contamination. Production areas where the products or open clean containers are exposed should normally be effectively ventilated with filtered air.
2. 儲槽、容器、管路及幫浦應予設計及安裝，使其易於清潔，且必要時應予以滅菌處理。特別是設備的設計，應使可能積聚殘留物及可能促進微生物增殖的盲管或部位減至最小。	2. Tanks, containers, pipework and pumps should be designed and installed so that they may be readily cleaned and if necessary sanitised. In particular, equipment design should include a minimum of dead-legs or sites where residues can accumulate and promote microbial proliferation.
3. 應盡可能避免玻璃器具的使用。高品質的不銹鋼常是與產品接觸的首選材質。	3. The use of glass apparatus should be avoided wherever possible. High quality stainless steel is often the material of choice for product contact parts.
生產（PRODUCTION）	

4. 生產用水之化學與微生物學上的品質應予規定並監測。水系統的維護保養應予以注意，以避免微生物增殖的風險。水系統之任何化學滅菌處理後，接著應有經過確效的沖洗程序，以確保滅菌處理劑已有效移除。	4. The chemical and microbiological quality of water used in production should be specified and monitored. Care should be taken in the maintenance of water systems in order to avoid the risk of microbial proliferation. After any chemical sanitization of the water systems, a validated flushing procedure should be followed to ensure that the sanitising agent has been effectively removed.
5. 以大容量槽車接收之原料的品質，在被輸送到大容量儲槽前，應予以檢查。	5. The quality of materials received in bulk tankers should be checked before they are transferred to bulk storage tanks.
6. 經由管路輸送原料時應小心，以確保其送至正確的目的地。	6. Care should be taken when transferring materials via pipelines to ensure that they are delivered to their correct destination.
7. 易於釋出纖維或其他污染物的材料，例如厚紙板或木質棧板，不得進入產品或潔淨容器暴露所在的區域。	7. Materials likely to shed fibres or other contaminants, like cardboard or wooden pallets, should not enter the areas where products or clean containers are exposed.
8. 充填時應小心維持混合物或懸液劑等之均質性。混合及充填製程應予確效。充填製程開始時、暫停後及製程終了時，應予特別注意，以確保維持其均質性。	8. Care should be taken to maintain the homogeneity of mixtures, suspensions, etc. during filling. Mixing and filling processes should be validated. Special care should be taken at the beginning of a filling process, after stoppages and at the end of the process to ensure that homogeneity is maintained.
9. 最終產品不立即分/包裝者，應規定其最長的儲存期間及儲存條件並遵循之。	9. When the finished product is not immediately packaged, the maximum period of storage and the storage conditions should be specified and respected.

附則 10 加壓計量劑量之吸入用氣化噴霧劑的製造（MANUFACTURE OF PRESSURISED METERED DOSE AEROSOL PREPARATIONS FOR INHALATION）

原則（PRINCIPLE）	
附有計量閥之吸入用加壓氣化噴霧劑產品的製造，需要源自該藥劑劑型之特質的特別規定。其製造應在使微生物及微粒污染能減到最低的條件下進行。計量閥組件之品質的確保，以及，若為懸液劑，其均一性的確保均特別重要。	Manufacture of pressurised aerosol products for inhalation with metering valves requires some special provisions arising from the particular nature of this pharmaceutical form. It should occur under conditions which minimise microbial and particulate contamination. Assurance of the quality of the valve components and, in the case of suspensions, of uniformity is also of particular importance.
註：計量劑量氣化噴霧劑的製造必須依 PIC/S 指引所述之 GMP，及可行時，依其他補充指引執行。本附則僅強調針對本製造的重點。	Note: The manufacture of metered dose aerosols must be done in accordance with the GMP described in the PIC Guide to GMP and with the other supplementary guidelines, where applicable. The present guidelines only stress points which are specific to this manufacture.
概述（GENERAL）	
1. 目前，氣化噴霧劑有如下兩種通用的製造及灌充方法：	1. There are presently two common manufacturing and filling methods as follows:
a) 二次灌充系統（壓力灌充法）(Two-shot system)：先將有效成分懸浮於高沸點的推進劑中，再將該劑量充填到氣化噴霧劑的容器，後將計量閥捲縮於容器上，並透過計量閥桿將較低沸點的推進劑灌入，以製得最終產品。推進劑中之有效成分的懸浮液應保持低溫，以減少揮發損失。	a) Two-shot system (pressure filling). The active ingredient is suspended in a high boiling point propellant, the dose is filled into the container, the valve is crimped on and the lower boiling point propellant is injected through the valve stem to make up the finished product. The suspension of active ingredient in propellant is kept cool to reduce evaporation loss.
b) 一次灌充製程(One-shot process)（冷充填法）：將有效成分懸浮於推進劑的混合物中，並在高壓及/或在低溫下保存。後在一次灌充/充填中，將懸浮液直接注入容器中。	b) One-shot process (cold filling). The active ingredient is suspended in a mixture of propellants and held either under high pressure and/or at a low temperature. The suspension is then filled directly into the container in one shot.

廠房設施與設備（PREMISES AND EQUIPMENT）	
2. 製造與充填作業應盡可能在密閉系統中執行。	2. Manufacture and filling should be carried out as far as possible in a closed system.
3. 產品或潔淨的組件暴露之區域，應供應經過濾的空氣、至少符合 D 級環境的要求，且應通過氣鎖室進入。	3. Where products or clean components are exposed, the area should be fed with filtered air, should comply with the requirements of at least a Grade D environment and should be entered through airlocks.
生產與品質管制（PRODUCTION AND QUALITY CONTROL）	
4. 氣化噴霧劑之計量閥的設計是比大多數藥用組件更複雜，故規格、抽樣與測試應合適於此情況。稽查計量閥製造廠的品質保證系統特別重要。	4. Metering valves for aerosols are a more complex engineering article than most pharmaceutical components. Specifications, sampling and testing should be appropriate for this situation. Auditing the Quality Assurance system of the valve manufacturer is of particular importance.
5. 所有流體（例如液態或氣態推進劑）應經過濾，以除去大於 0.2 μm 的粒子。如有可能，緊臨充填前最好再次過濾。	5. All fluids (e.g. liquid or gaseous propellants) should be filtered to remove particles greater than 0.2 micron. An additional filtration where possible immediately before filling is desirable.
6. 容器與計量閥之清潔應使用適合於該產品且經確效的方法，以確保無任何污染物例如設備裝配助劑（例如潤滑油）或微生物學上的污染。在清潔之後，計量閥應保存在潔淨且密閉的容器中，並於後續處理，例如取樣，採取預防污染的措施。容器應以潔淨的狀態提供至充填線，或在緊臨充填前於線上清潔。	6. Containers and valves should be cleaned using a validated procedure appropriate to the use of the product to ensure the absence of any contaminants such as fabrication aids (e.g. lubricants) or undue microbiological contaminants. After cleaning, valves should be kept in clean, closed containers and precautions taken not to introduce contamination during subsequent handling, e.g. taking samples. Containers should be provided to the filling line in a clean condition or cleaned on line immediately before filling.
7. 在整個充填過程中應採取預防措施，以確保懸浮液在充填點的均一性。	7. Precautions should be taken to ensure uniformity of suspensions at the point of fill throughout the filling process.
8. 採用二次灌充製程者，為達到正確的組成，需要確保兩次充填皆有正確的重量。為此目的，最好在每一階段執行 100%的重量檢查。	8. When a two-shot filling process is used, it is necessary to ensure that both shots are of the correct weight in order to achieve the correct composition. For this purpose, 100% weight checking at each stage is often desirable.
9. 充填後的管制應確保無洩漏。任何洩漏試	9. Controls after filling should ensure the

驗應以避免微生物污染或殘留水分的方式執行。	absence of undue leakage. Any leakage test should be performed in a way which avoids microbial contamination or residual moisture.

附則 11 電腦化系統（COMPUTERISED SYSTEMS）

原則（PRINCIPLE）	
電腦化系統導入製造系統中，包括儲存、運銷及品質管制仍應遵守本指引中於他處規定之相關原則的要求。電腦化系統取代手工作業時，不得有降低產品品質或品質保證之結果。應考慮因減少操作人員的參與而漏失先前手工系統具有之作業層面的風險。	The introduction of computerised systems into systems of manufacturing, including storage, distribution and quality control does not alter the need to observe the relevant principles given elsewhere in the Guide. Where a computerised system replaces a manual operation, there should be no resultant decrease in product quality or quality assurance. Consideration should be given to the risk of losing aspects of the previous system by reducing the involvement of operators.
人員（PERSONNEL）	
1. 關鍵人員與涉及電腦系統的人員間密切的合作是必要的。承擔責任的人員，在其使用電腦的責任領域內，對於系統之管理及使用應有適當的訓練。這應包括確保其具有適當的專門技術，及就電腦化系統的設計、確效、安裝及操作方面提供建議。	1. It is essential that there is the closest co-operation between key personnel and those involved with computer systems. Persons in responsible positions should have the appropriate training for the management and use of systems within their field of responsibility which utilises computers. This should include ensuring that appropriate expertise is available and used to provide advice on aspects of design, validation, installation and operation of computerised system.
確效（VALIDATION）	
2. 確效的程度將取決於許多因素，包含該系統之使用，不論是先期性或回溯性，亦不論其是否結合新的元件。確效應認定係電腦系統完整生命週期的一部分。該週期包括規劃、制訂規格、程式設計、測試、試運轉、建立文件、操作、監測及變更等階段。	2. The extent of validation necessary will depend on a number of factors including the use to which the system is to be put, whether it is prospective or retrospective and whether or not novel elements are incorporated. Validation should be considered as part of the complete life cycle of a computer system. This cycle includes the stages of planning, specification, programming, testing, commissioning, documentation, operation, monitoring and changing.
系統（SYSTEM）	

3. 設備應注意設置在外在因素不會干擾該系統的適當地點。	3. Attention should be paid to the siting of equipment in suitable conditions where extraneous factors cannot interfere with the system.
4. 應有該系統之書面的詳細說明，(合適時包含圖解)，並保持其最新。應說明該系統的原理、目的、安全措施及範圍，以及該電腦使用上的主要特性及如何與其他系統及程序互動。	4. A written detailed description of the system should be produced (including diagrams as appropriate) and kept up to date. It should describe the principles, objectives, security measures and scope of the system and the main features of the way in which the computer is used and how it interacts with other systems and procedures.
5. 軟體為電腦化系統的關鍵組件。該軟體的使用者應採取所有合理的步驟，以確保該軟體已依品質保證系統所製作。	5. The software is a critical component of a computerised system. The user of such software should take all reasonable steps to ensure that it has been produced in accordance with a system of Quality Assurance.
6. 合適時，本系統應包括數據輸入與數據處理之正確性的內建核對功能。	6. The system should include, where appropriate, built-in checks of the correct entry and processing of data.
7. 電腦系統納入使用前，應予徹底測試並確認其能達成預期的結果。手工系統要被取代時，該二系統應併行運作一段時間，作為其測試與確效的一部分。	7. Before a system using a computer is brought into use, it should be thoroughly tested and confirmed as being capable of achieving the desired results. If a manual system is being replaced, the two should be run in parallel for a time, as part of this testing and validation.
8. 僅有經授權的人員始得輸入或修改資料/數據。阻止未經授權的輸入其適當方法包含鑰匙、通行卡、個人密碼及限制電腦終端機之使用。輸入及修正資料/數據之授權的發給、撤銷及變更，包括個人密碼的變更，應有一界定的程序。應考慮該系統可記錄未經授權人員之進入。	8. Data should only be entered or amended by persons authorised to do so. Suitable methods of deterring unauthorised entry of data include the use of keys, pass cards, personal codes and restricted access to computer terminals. There should be a defined procedure for the issue, cancellation, and alteration of authorisation to enter and amend data, including the changing of personal passwords. Consideration should be given to systems allowing for recording of attempts to access by unauthorised persons.

9. 關鍵資料以手工輸入者(例如，在調配時，成分的重量與批號)，應就所做紀錄的準確性再次核對。該核對得由第二位操作者，或由已確效的電子方法執行。	9. When critical data are being entered manually (for example the weight and batch number of an ingredient during dispensing), there should be an additional check on the accuracy of the record which is made. This check may be done by a second operator or by validated electronic means.
10. 該系統應記錄輸入或確認關鍵資料之操作者的身分。修正輸入之資料的授權應限於經指定的人員。關鍵資料之輸入的任何變更應經授權並記錄其變更的理由。應考慮使該系統能建立全部輸入與修改的完整紀錄(一種“追蹤稽核“)。	10. The system should record the identity of operators entering or confirming critical data. Authority to amend entered data should be restricted to nominated persons. Any alteration to an entry of critical data should be authorised and recorded with the reason for the change. Consideration should be given to the system creating a complete record of all entries and amendments (an "audit trail ").
11. 系統或電腦程式之修改，皆應依界定之程序執行。該程序應包括確效、核對、核准及施行該變更的規定。對該系統之一部分作修改時，須經該部分的負責人員同意，且該修改應予記錄。每個重大的修改應予以確效。	11. Alterations to a system or to a computer program should only be made in accordance with a defined procedure which should include provision for validating, checking, approving and implementing the change. Such an alteration should only be implemented with the agreement of the person responsible for the part of the system concerned, and the alteration should be recorded. Every significant modification should be validated.
12. 為了品質稽核目的，應可取得電子儲存資料/數據之列印副本。	12. For quality auditing purposes, it shall be possible to obtain meaningful printed copies of electronically stored data.
13. 資料應以物理或電子方法確保其不受故意或意外的毀損；這與總則第 4.9 條相符。儲存之資料應檢查其可存取性、耐久性及準確性。對電腦設備或其程式提出變更時，上述核對應以適合之頻率執行。	13. Data should be secured by physical or electronic means against wilful or accidental damage, and this in accordance with item 4.9 of the Guide. Stored data should be checked for accessibility, durability and accuracy. If changes are proposed to the computer equipment or its programs, the above mentioned checks should be performed at a frequency appropriate to the storage medium being used.

14. 資料應定期備份。備份資料應依需要的期間儲存於隔離且安全的地方。	14. Data should be protected by backing-up at regular intervals. Back-up data should be stored as long as necessary at a separate and secure location.
15. 當機時亦需運轉之系統，應備有適當的替代措施。替代措施啟用的時間，應與需求之急迫性相關連。例如，為達成回復所需資訊應在接到通知時即可取得。	15. There should be available adequate alternative arrangements for systems which need to be operated in the event of a breakdown. The time required to bring the alternative arrangements into use should be related to the possible urgency of the need to use them. For example, information required to effect a recall must be available at short notice.
16. 電腦系統失效或當機時應遵守的程序應予以界定並確效。任何失效及採取的補救行動均應予以記錄。	16. The procedures to be followed if the system fails or breaks down should be defined and validated. Any failures and remedial action taken should be recorded.
17. 應建立程序以記錄及分析錯誤，並能採取矯正措施。	17. A procedure should be established to record and analyse errors and to enable corrective action to be taken.
18. 使用外包廠商提供電腦服務者，應有正式協議，包括該外包廠商之責任說明 (參閱第七章)。	18. When outside agencies are used to provide a computer service, there should be a formal agreement including a clear statement of the responsibilities of that outside agency (see Chapter 7).
19. 使用電腦化系統為批次之放行以供銷售或供應者，該系統應識別只有被授權之人員才能放行該批次，並應清楚辨識及記錄放行該批次的人員。	19. When the release of batches for sale or supply is carried out using a computerised system, the system should recognise that only an Authorised Person can release the batches and it should clearly identify and record the person releasing the batches.

附則 12 游離輻射在藥品製造上的應用（USE OF IONISING RADIATION IN THE MANUFACTURE OF MEDICINAL PRODUCTS）

前言（INTRODUCTION）	
游離輻射可因應不同目的，使用在製造過程中，包括負荷菌的減少與原料、包材或產品的滅菌及血液產品之處理等。	Ionising radiation may be used during the manufacturing process for various purposes including the reduction of bioburden and the sterilisation of starting materials, packaging components or products and the treatment of blood products.
有兩種類型的輻射照射程序：一為來自放射源的加馬輻射照射，二為來自加速器的高能電子輻射照射（貝他輻射）。	There are two types of irradiation process: Gamma irradiation from a radioactive source and high energy Electron irradiation (Beta radiation) from an accelerator.
加馬輻射照射：有兩種不同的操作模式可供使用：	Gamma irradiation: two different processing modes may be employed:
(i) 批次模式：指將產品放置在環繞於放射源的固定位置上，且在放射源暴露時，不能進行裝載或卸載。	(i) Batch mode: the products is arranged at fixed locations around the radiation source and cannot be loaded or unloaded while the radiation source is exposed.
(ii) 連續模式：指自動化系統將產品輸送到照射室中，沿著經界定的路徑並以適當的速度通過暴露的放射源後，離開照射室。	(ii) Continuous mode: an automatic system conveys the products into the radiation cell, past the exposed radiation source along a defined path and at an appropriate speed, and out of the cell.
電子輻射照射：指將產品輸送通過一連續式或脈衝式高能電子束(貝他輻射)，並將該電子束來回掃描該產品的穿越路徑。	Electron irradiation: the product is conveyed past a continuous or pulsed beam of high energy electrons (Beta radiation) which is scanned back and forth across the product pathway.
責任（RESPONSIBILITIES）	
1. 輻射照射處理得由藥廠或根據合約由輻射照射廠(受託製造者)的操作者執行。兩者皆應持有製造許可。	1. Treatment by irradiation may be carried out by the pharmaceutical manufacturer or by an operator of a radiation facility under contract (a "contract manufacturer"), both of whom must hold an appropriate manufacturing authorization.

2. 藥廠承擔產品品質的責任，包含達成輻射照射的目標。輻射照射廠的受託操作者所負擔的責任是確保將藥廠要求的輻射劑量傳送到照射容器(亦即，產品受照射時最外側的容器)。	2. The pharmaceutical manufacturer bears responsibility for the quality of the product including the attainment of the objective of irradiation. The contract operator of the radiation facility bears responsibility for ensuring that the dose of radiation required by the manufacturer is delivered to the irradiation container (i.e. the outermost container in which the products are irradiated).
3. 載明所要求的輻射劑量於該產品的上市許可申請中，包括經證明為合理的限量。	3. The required dose including justified limits will be stated in the marketing authorization for the product.
劑量測定法（DOSIMETRY）	
4. 劑量測定法，係界定為使用劑量計量測所吸收的劑量。對此技術之瞭解及正確使用，對該過程的確效、試運轉及管制是必需的。	4. Dosimetry is defined as the measurement of the absorbed dose by the use of dosimeters. Both understanding and correct use of the technique is essential for the validation, commissioning and control of the process.
5. 每批例行劑量計之校正，應可追溯至國家標準或國際標準。校正的有效期間應予載明、經證明為合理並應遵守。	5. The calibration of each batch of routine dosimeters should be traceable to a national or international standard. The period of validity of the calibration should be stated, justified and adhered to.
6. 通常，應使用同一儀器來建立例行劑量計之校正曲線，並用來量測輻射照射後，劑量計之吸收度的變異。使用不同儀器者，應建立各儀器之絕對吸收度。	6. The same instrument should normally be used to establish the calibration curve of the routine dosimeters and to measure the change in their absorbance after irradiation. If a different instrument is used, the absolute absorbance of each instrument should be established.
7. 隨使用之劑量計的類型，應注意其不精確的可能原因，包括水分含量的改變、溫度的改變、照射與量測間所經歷的時間及劑量率等。	7. Depending on the type of dosimeter used, due account should be taken of possible causes of inaccuracy including the change in moisture content, change in temperature, time elapsed between irradiation and measurement, and the dose rate.

8. 用來量測劑量計吸收度變化之儀器的波長及用來量測劑量計厚度之儀器，應根據其穩定性、目的與用途所建立之時間間隔，進行定期檢查其校正狀態。	8. The wavelength of the instrument used to measure the change in absorbance of dosimeters and the instrument used to measure their thickness should be subject to regular checks of calibration at intervals established on the basis of stability, purpose and usage.
過程確效（VALIDATION OF THE PROCESS）	
9. 確效是證實把預定被吸收之劑量傳送到產品的過程，將會達到預期之結果的行動。關於確效之要求，在「游離輻射在藥品製造上之應用」的指引中有更充分說明。	9. Validation is the action of proving that the process, i.e. the delivery of the intended absorbed dose to the product, will achieve the expected results. The requirements for validation are given more fully in the note for guidance on "the use of ionising radiation in the manufacture of medicinal products"
10. 確效應包含劑量分佈圖之繪製，以建立照射容器內經界定之產品裝載型式時，其吸收劑量的分佈。	10. Validation should include dose mapping to establish the distribution of absorbed dose within the irradiation container when packed with product in a defined configuration.
11. 輻射照射過程的規格至少應包括下列各項：	11. An irradiation process specification should include at least the following:
a) 產品分/包裝的細節；	a) details of the packaging of the product;
b) 產品在照射容器內之裝載型式。照射容器中允許不同產品之混合裝載時，應特別注意，不使其發生高密度產品之劑量不足，或其他產品被高密度產品遮蔽的情形。每一混裝產品的安排皆應予以規定與確效；	b) the loading pattern(s) of product within the irradiation container. Particular care needs to be taken, when a mixture of products is allowed in the irradiation container, that there is no underdosing of dense product or shadowing of other products by dense product. Each mixed product arrangement must be specified and validated;
c) 環繞放射源(批次模式)或通過照射室的路徑(連續模式)之照射容器的裝載型式；	c) the loading pattern of irradiation containers around the source (batch mode) or the pathway through the cell (continuous mode);
d) 產品之最大及最小的吸收劑量限量【以及相關的例行劑量量測法】；	d) maximum and minimum limits of absorbed dose to the product [and associated routine dosimetry];
e) 照射容器之最大及最小的吸收劑量限量及監測該吸收劑量之相關的例行劑量量測法；	e) maximum and minimum limits of absorbed dose to the irradiation container and associated routine dosimetry to monitor this absorbed dose;

f) 其他過程參數，包括劑量率、最長暴露時間、暴露次數等。	f) other process parameters, including dose rate, maximum time of exposure, number of exposures, etc.
依契約提供輻射照射時，至少照射過程規格中之(d)及(e)兩個項目應明列於契約中。	When irradiation is supplied under contract at least parts (d) and (e) of the irradiation process specification should form part of that contract.
輻射照射廠的試運轉（COMMISSIONING OF THE PLANT）	
概述（General）	
12. 試運轉是取得並作成文件證據的作業，以證明輻射照射廠在依過程規格操作時，將會持續一致地在預定限量內運轉。本附則中，預定限量指設計將為被照射容器吸收之最大及最小劑量。工廠的運轉不應在操作者不知悉的情形下，發生供應照射容器之劑量超出限量的變異。	12. Commissioning is the exercise of obtaining and documenting evidence that the irradiation plant will perform consistently within predetermined limits when operated according to the process specification. In the context of this annex, predetermined limits are the maximum and minimum doses designed to be absorbed by the irradiation container. It must not be possible for variations to occur in the operation of the plant which give a dose to the container outside these limits without the knowledge of the operator.
13. 試運轉應包括下列的基本要件：	13. Commissioning should include the following elements:
a. 設計	a. Design;
b. 繪製劑量分佈圖	b. Dose mapping;
c. 文件製作	c. Documentation;
d. 重新試運轉之要求	d. Requirement for re-commissioning.
加馬照射器（Gamma irradiators）	
設計 （Design）	
14. 在加馬照射器內之任一特定點上，由照射容器的特定位置接受之吸收劑量，主要取決於下列因素：	14. The absorbed dose received by a particular part of an irradiation container at any specific point in the irradiator depends primarily on the following factors:
a) 放射源的活性與幾何形狀；	a) the activity and geometry of the source;
b) 放射源到容器的距離；	b) the distance from source to container;
c) 由計時器設定或輸送帶速度所控制之輻射照射的期間；	c) the duration of irradiation controlled by the timer setting or conveyor speed;
d) 放射源與照射容器之特定位置間，材料(包含其他產品在內) 的組成與密度。	d) the composition and density of material, including other products, between the source and the particular part of the container.

15. 總吸收劑量還將取決於照射容器通過連續照射器之路徑或在批次照射器中的裝載型式及暴露週期的次數。	15. The total absorbed dose will in addition depend on the path of containers through a continuous irradiator or the loading pattern in a batch irradiator, and on the number of exposure cycles.
16. 具有固定路徑的連續性照射器，或具有固定裝載型式的批次照射器，如具有一定之放射源強度與產品類型，則由操作者控制之關鍵參數即為輸送帶的速度或計時器的設定。	16. For a continuous irradiator with a fixed path or a batch irradiator with a fixed loading pattern, and with a given source strength and type of product, the key plant parameter controlled by the operator is conveyor speed or timer setting.
繪製劑量分佈圖 （Dose Mapping）	
17. 為劑量分佈圖之繪製程序，該照射器應滿載裝有模擬產品或裝有均勻密度之代表性產品。通過照射器之裝載的輻射照射容器，至少三個容器應遍及放置劑量計，且為相似容器或模擬產品所圍繞。產品非均一包裝者，應將劑量計置於更多的照射容器中。	17. For the dose mapping procedure, the irradiator should be filled with irradiation containers packed with dummy products or a representative product of uniform density. Dosimeters should be placed throughout a minimum of three loaded irradiation containers which are passed through the irradiator, surrounded by similar containers or dummy products. If the product is not uniformly packed, dosimeters should be placed in a larger number of containers.
18. 劑量計放置的位置取決於照射容器的大小。例如照射容器大小在 1× 1 × 0.5 公尺以下者，一個遍及該容器及該容器外部表面之每邊 20 公分三度空間的格子可能是適當的。從先前照射器表現之特性已知悉其最小及最大劑量之預期的位置者，有些劑量計可以從平均劑量區移出，並將之放置在極端劑量區，以形成一個每邊 10 公分格子的佈置。	18. The positioning of dosimeters will depend on the size of the irradiation container. For example, for containers up to 1 x 1 x 0.5 m, a three-dimensional 20 cm grid throughout the container including the outside surfaces might be suitable. If the expected positions of the minimum and maximum dose are known from a previous irradiator performance characterisation, some dosimeters could be removed from regions of average dose and replaced to form a 10 cm grid in the regions of extreme dose.
19. 對於已知的工廠參數、產品密度及裝載型式，該劑量分佈圖繪製的結果將可提供在產品中及在容器表面之最大及最小吸收劑量。	19. The results of this procedure will give minimum and maximum absorbed doses in the product and on the container surface for a given set of plant parameters, product density and loading pattern.

20. 對照劑量計由於其較佳的精密度，理想上應使用在劑量分佈圖繪製作業上。雖可使用例行劑量計，但建議在預計會有最大及最小劑量的位置邊及在每一受重複照射容器的例行監測位置放置對照劑量計。該測得的劑量值將會有相關的隨機不確定值。該不確定值可從重複量測中之變異進行估算。	20. Ideally, reference dosimeters should be used for the dose mapping exercise because of their greater precision. Routine dosimeters are permissible but it is advisable to place reference dosimeters beside them at the expected positions of minimum and maximum dose and at the routine monitoring position in each of the replicate irradiation containers. The observed values of dose will have an associated random uncertainty which can be estimated from the variations in replicate measurements.
21. 為確保所有照射容器接收之最低要求劑量，例行劑量計所測得之最小劑量，將依該使用之例行劑量計隨機變異性的了解予以設定。	21. The minimum observed dose, as measured by the routine dosimeters, necessary to ensure that all irradiation containers receive the minimum required dose will be set in the knowledge of the random variability of the routine dosimeters used.
22. 繪製劑量分佈圖時，照射器參數應維持恆定，並予以監測及記錄。該紀錄應連同劑量測定的結果及其他產生的紀錄一併保存。	22. Irradiator parameters should be kept constant, monitored and recorded during dose mapping. The records, together with the dosimetry results and all other records generated, should be retained.
電子束照射器（Electron Beam Irradiators）	
設計 （Design）	
23. 受照射產品之特定位置所接收到的吸收劑量，主要取決於下列因素：	23. The absorbed dose received by a particular portion of an irradiated product depends primarily on the following factors:
a) 電子束的特性，亦即：電子能量、平均電子束電流、掃描寬度及掃描均勻性；	a) the characteristics of the beam, which are: electron energy, average beam current, scan width and scan uniformity;
b) 輸送帶速度；	b) the conveyor speed;
c) 產品組成與密度；	c) the product composition and density;
d) 介於輸出窗口與產品之特定位置間的材料之組成、密度與厚度；	d) the composition, density and thickness of material between the output window and the particular portion of product;
e) 輸出窗口到照射容器的距離。	e) the output window to container distance.
24. 由操作者控制之關鍵參數為電子束的特性及輸送帶的速度。	24. Key parameters controlled by the operator are the characteristics of the beam and the conveyor speed.
繪製劑量分佈圖 （Dose Mapping）	

25. 為繪製劑量分佈圖，劑量計應放置在具均質吸收之模擬產品的層與層之間，或放置在具均質密度之代表性產品的層與層之間，以便在電子束的最大照射範圍內，至少可作出十個量測。並參考本附則第 18 至第 21 條。	25. For the dose mapping procedure, dosimeters should be placed between layers of homogeneous absorber sheets making up a dummy product, or between layers of representative products of uniform density, such that at least ten measurements can be made within the maximum range of the electrons. Reference should also be made to sections 18 to 21.
26. 繪製劑量分佈圖時，照射器參數應保持恆定，並予以監測及記錄。該紀錄應連同劑量計的量測結果及其他產生的紀錄一併保存。	26. Irradiator parameters should be kept constant, monitored and recorded during dose mapping. The records, together with the dosimetry results and all other records generated, should be retained.
重新試運轉（Re-commissioning）	
27. 過程或照射器的變更(例如，放射源的改變)如會影響照射器之劑量分佈時，應重新執行試運轉。重新執行試運轉的程度，取決於照射器或裝載經改變的程度。如有任何懷疑，則應重新執行試運轉。	27. Commissioning should be repeated if there is a change to the process or the irradiator which could affect the dose distribution to the irradiation container (e.g. change of source pencils). The extent to re-commissioning depends on the extent of the change in the irradiator or the load that has taken place. If in doubt, re-commission.
廠房設施（PREMISES）	
28. 廠房設施應經設計與運作，以將已照射與未經照射的容器隔離，避免其交叉污染/混雜。原物料在密閉的照射容器內處理時，若藥用原物料無被非藥用原物料污染的風險，則兩者不須隔離。	28. Premises should be designed and operated to segregate irradiated from non-irradiated containers to avoid their cross-contamination. Where materials are handled within closed irradiation containers, it may not be necessary to segregate pharmaceutical from non-pharmaceutical materials, provided there is no risk of the former being contaminated by the latter.
任何來自放射源之放射核種對產品污染的可能性皆應予以排除。	Any possibility of contamination of the products by radionuclide from the source must be excluded.
照射處理/加工處理（PROCESSING）	
29. 照射容器應依確效時所建立之特定型式予以裝載。	29. Irradiation containers should be packed in accordance with the specified loading pattern(s) established during validation.

30.照射過程中，應使用經確效的劑量偵測程序，監測照射容器所受輻射劑量。製程確效及工廠試運轉期間該劑量與照射容器內之產品所吸收劑量間的關係應已建立完成。	30. During the process, the radiation dose to the irradiation containers should be monitored using validated dosimetry procedures. The relationship between this dose and the dose absorbed by the product inside the container must have been established during process validation and plant commissioning.
31. 已照射與未照射的容器應使用輻射指示劑做為輔助的區分方法。輻射指示劑不得用作區分的唯一方法，或作為完成照射處理的指標。	31. Radiation indicators should be used as an aid to differentiating irradiated from non-irradiated containers. They should not be used as the sole means of differentiation or as an indication of satisfactory processing.
32. 從試運轉試驗或其他證據，已知個別容器接收之照射劑量維持在特定的限量之內者，始得在照射室內照射處理混合裝載的容器。	32. Processing of mixed loads of containers within the irradiation cell should only be done when it is known from commissioning trials or other evidence that the radiation dose received by individual containers remains within the limits specified.
33. 所需之輻射劑量係由照射工廠設計利用多次暴露或多次通過照射源所達成者，應有上市許可持有者的同意，並在預定的期間內完成。因照射期間非計畫性之中斷導致延長照射過程超過先前同意的期間者，應通知上市許可持有者。	33. When the required radiation dose is by design given during more than one exposure or passage through the plant, this should be with the agreement of the holder of the marketing authorization and occur within a predetermined time period. Unplanned interruptions during irradiation should be notified to the holder of the marketing authorization if this extends the irradiation process beyond a previously agreed period.
34. 任何時候，未經照射的產品應與已照射的產品隔離，其作法包括輻射指示劑的使用(31 條)及廠房設施的適當設計(28 條)。	34. Non-irradiated products must be segregated from irradiated products at all times. Methods or doing this include the use of radiation indicators (31.) and appropriate design of premises (28.).
加馬照射器（Gamma irradiators）	
35. 連續式照射處理模式，其劑量計之放置至少應使兩個劑量計全程暴露於照射中。	35. For continuous processing modes, dosimeters should be placed so that at least two are exposed in the irradiation at all times.
36. 批次式模式，至少有兩個劑量計應暴露於與最低照射劑量相關的位置。	36. For batch modes, at least two dosimeters should be exposed in positions related to the minimum dose position.

37. 連續式照射處理模式，應有放射源之正確位置的明確指標，且在放射源位置與輸送帶移動間應有互鎖裝置。輸送帶的速度應予以連續監測並記錄。	37. For continuous process modes, there should be a positive indication of the correct position of the source and an interlock between source position and conveyor movement. Conveyor speed should be monitored continuously and recorded.
38. 批次式照射處理模式，放射源的移動及每批次的暴露時間應予以監測並記錄。	38. For batch process modes source movement and exposure times for each batch should be monitored and recorded.
39. 對某一期望劑量，其計時器的設定或輸送帶的速度需依放射源的衰變及放射源的添加予以調整。該設定或速度的有效期間應予以記錄並且遵循。	39. For a given desired dose, the timer setting or conveyor speed requires adjustment for source decay and source additions. The period of validity of the setting or speed should be recorded and adhered to.
電子束照射器（Electron Beam Irradiators）	
40. 每一容器上應放置一個劑量計。	40. A dosimeter should be placed on every container.
41. 平均電子束電流、電子能量、掃描寬度及輸送帶速度應予以連續記錄。輸送帶速度以外的上述變數，因易發生瞬間性變化，必須將其控制於試運轉期間所界定之限量內。	41. There should be continuous recording of average beam current, electron energy, scan-width and conveyor speed. These variables, other than conveyor speed, need to be controlled within the defined limits established during commissioning since they are liable to instantaneous change.
文件製作（DOCUMENTATION）	
42. 接收、照射及送出的容器數目應調和一致並符合相關文件。任何差異均應提出報告並解決。	42. The numbers of containers received, irradiated and dispatched should be reconciled with each other and with the associated documentation. Any discrepancy should be reported and resolved.
43. 照射廠的操作者，應以書面方式證明於批次或交貨中的每一照射容器所接受的劑量範圍。	43. The irradiation plant operator should certify in writing the range of doses received by each irradiated container within a batch or delivery.
44. 每一照射批次之照射處理與管制紀錄應由指定的負責人員核對、簽章並予以保存。其保存的方法與場所應由照射廠操作者與上市許可持有者進行協議。	44. Process and control records for each irradiation batch should be checked and signed by a nominated responsible person and retained. The method and place of retention should be agreed between the plant operator and the holder of the marketing authorization.

45. 與照射廠的確效及試運轉有關的文件應保存至產品的末效日後一年，或自照射廠照射處理之最後產品放行後至少五年。兩者中取其較長者。	45. The documentation associated with the validation and commissioning of the plant should be retained for one year after the expiry date or at least five years after the release of the last product processed by the plant, whichever is the longer.
微生物的監測（MICROBIOLOGICAL MONITORING）	
46. 微生物的監測係藥廠的責任。可能包括產品製造場所之環境及上市許可中所規定該產品之輻射照射前的監測。	46. Microbiological monitoring is the responsibility of the pharmaceutical manufacturer. It may include environmental monitoring where product is manufactured and pre-irradiation monitoring of the product as specified in the marketing authorisation.

附則 13 研究用藥品的製造（MANUFACTURE OF INVESTIGATIONAL MEDICINAL PRODUCTS）

原則（PRINCIPLE）	
研究用藥品應依藥品優良製造規範的原則與詳細的指引生產。其他相關指引並適合於產品之開發階段者，亦應列入考慮。製造程序需要有彈性，以供製程知識增加時之變更，並適合於產品開發階段。	Investigational medicinal products should be produced in accordance with the principles and the detailed guidelines of Good Manufacturing Practice for Medicinal Products. Other guidelines should be taken into account where relevant and as appropriate to the stage of development of the product. Procedures need to be flexible to provide for changes as knowledge of the process increases, and appropriate to the stage of development of the product.
臨床試驗上，相較於使用已上市藥品治療的病人，受試者可能會有較多的風險。將GMP應用於研究用藥品的製造上，係要確保受試者不會處於風險中，及臨床試驗結果不會受到源自不滿意之製造的不適當安全性、品質或療效所影響。同樣地，亦要確保用於相同或不同臨床試驗之相同研究用藥品的批次間具有一致性，以及確保將研究用藥品在開發期間的變更充分文件化，並證明其正當性。	In clinical trials there may be added risk to participating subjects compared to patients treated with marketed products. The application of GMP to the manufacture of investigational medicinal products is intended to ensure that trial subjects are not placed at risk, and that the results of clinical trials are unaffected by inadequate safety, quality or efficacy arising from unsatisfactory manufacture. Equally, it is intended to ensure that there is consistency between batches of the same investigational medicinal product used in the same or different clinical trials, and that changes during the development of an investigational medicinal product are adequately documented and justified.
與上市的藥品相較，研究用藥品之生產由於固定例行程序的欠缺、臨床試驗設計的多樣性、後續的包裝設計、常有隨機與盲性化試驗的需要及藥品交互污染與混雜之風險的增加，而且還可能對該研究用藥品之效價與毒性的知識不足及欠缺完整的製程確效，或可能將上市產品已經重新包裝或經以某種方式修改過，因此會涉及附加的複雜性。	The production of investigational medicinal products involves added complexity in comparison to marketed products by virtue of the lack of fixed routines, variety of clinical trial designs, consequent packaging designs, the need, often, for randomisation and blinding and increased risk of product cross-contamination and mix up. Furthermore, there may be incomplete knowledge of the potency and toxicity of the product and a lack of full process validation, or, marketed products may be used which have been re-packaged or modified in

	some way.
這些挑戰需要對GMP應用於研究用藥品有充分瞭解並受過訓練的人員。與試驗委託者的合作是必需的。試驗委託者對包含研究用藥品的品質在內之臨床試驗的一切層面，需負最終責任。	These challenges require personnel with a thorough understanding of, and training in, the application of GMP to investigational medicinal products. Co-operation is required with trial sponsors who undertake the ultimate responsibility for all aspects of the clinical trial including the quality of investigational medicinal products.
因製造作業複雜性的增加，需有高度有效的品質系統。	The increased complexity in manufacturing operations requires a highly effective quality system.
本附則另包含關於下訂單、裝運及退回研究用藥品的指引。這些指引是連結並補充藥品優良臨床試驗準則。	The annex also includes guidance on ordering, shipping, and returning clinical supplies, which are at the interface with, and complementary to, guidelines on Good Clinical Practice.
註： 除研究用藥品外，安慰劑或比對產品可能提供給參與試驗的受試者。這些藥品可能為預防、診斷或治療的理由，而當做支持或免除給藥使用，及（或）可能為確保對受試者提供適當的醫療照護之所需。該等藥品亦可能依計畫書使用於誘發生理學上的反應。這些藥品不在研究用藥品的定義內，而且可能由試驗委託者或試驗主持人所提供。試驗委託者應確保該等藥品與執行該試驗許可申請書一致，且不論其是否為已上市藥品或已重新分/包裝，皆應考慮到其來源，確保該等藥品具有為本試驗目的之適當品質。本項工作宜有一位被授權人員的意見及參與。	Note: Products other than the test product, placebo or comparator may be supplied to subjects participating in a trial. Such products may be used as support or escape medication for preventative, diagnostic or therapeutic reasons and/or needed to ensure that adequate medical care is provided for the subject.They may also be used in accordance with the protocol to induce a physiological response. These products do not fall within the definition of investigational medicinal products and may be supplied by the sponsor, or the investigator. The sponsor should ensure that they are in accordance with the notification/ request for authorisation to conduct the trial and that they are of appropriate quality for the purposes of the trial taking into account the source of the materials, whether or not they are the subject of a marketing authorisation and whether they have been repackaged. The advice and involvement of an Authorised Person is recommended in this task.

術語彙編（GLOSSARY）	
盲性化 *使參與試驗之一方或多方不知試驗治療分配之方式。單盲係指受試者不知治療分配之方式，雙盲是指受試者、試驗主持人、監測者，及在某些情況下，數據分析者亦不清楚治療分配之方式。關於一件研究用藥品，盲性化意指依試驗委託者的指示刻意偽裝藥品的識別性。解盲意指揭露盲性化藥品的識別性。*	***Blinding*** *A procedure in which one or more parties to the trial are kept unaware of the treatment assignment(s). Single-blinding usually refers to the subject(s) being unaware, and double-blinding usually refers to the subject(s), investigators(s), monitor, and, in some cases, data analyst(s) being unaware of the treatment assignment(s). In relation to an investigational medicinal product, blinding means the deliberate disguising of the identity of the product in accordance with the instructions of the sponsor. Unblinding means the disclosure of the identity of blinded products.*
臨床試驗 *指在受試者人體上執行的任何試驗。該試驗意在發現或確認研究用藥品之臨床、藥理及/或其他藥效學效應，及/或意在辨識研究用藥品的任何不良反應，及/或意在研究一種或一種以上研究用藥品的吸收、分佈、代謝及排泄，以確認研究用藥品之安全性及/或療效為目的。*	***Clinical trial*** *Any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of an investigational product(s) and/or to identify any adverse reactions to an investigational product(s), and/or to study absorption, distribution, metabolism, and excretion of one or more investigational medicinal product(s) with the object of ascertaining its/their safety and/or efficacy.*
比對用產品 *在臨床試驗上作為比對使用的研究用藥品或已上市藥品(亦即，活性對照品)，或安慰劑。*	***Comparator product*** *An investigational or marketed product (i.e. active control), or placebo, used as a reference in clinical trial.*
研究用藥品 *指在臨床試驗中，被用來試驗或當做對照之活性成分藥品或安慰劑，包括已上市藥品使用於與其核准內容不同的用途、配方、分/包裝、適應症，或用於獲得有關核准用途之進一步資料。*	***Investigational medicinal product*** *A pharmaceutical form of an active substance or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorisation when used or assembled (formulated or packaged) in a way different from the authorised form, or when used for an unauthorised indication, or when used to gain further information about the authorised form.*
直接包裝 *指直接接觸藥品或研究用藥品的容器或其他包裝型式。*	***Immediate packaging*** *The container or other form of packaging immediately in contact with the medicinal or investigational medicinal product.*

試驗主持人 *指在試驗場所負責從事臨床試驗的人。若試驗是在試驗場所由一個團隊執行者，試驗主持人是該團隊的主導負責人，亦可稱為總主持人。*	***Investigator*** *A person responsible for the conduct of the clinical trial at a trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the principal investigator.*
研究用藥品的製造廠/進口商 *指製造/輸入研究用藥品之許可的持有者。*	***Manufacturer/importer of Investigational Medicinal Products*** *Any holder of the authorisation to manufacture/import.*
訂單 *製造、分/包裝及/或裝運一定單位數之研究用藥品的指令。*	***Order*** *Instruction to process, package and/or ship a certain number of units of investigational product(s).*
外包裝 *指放置直接容器的包裝。*	***Outer packaging*** *The packaging into which the immediate container is placed.*
產品規格檔案 *指參考檔案或所引述的檔案，包含所有必需資料，用以草擬關於研究用藥品之製造、分/包裝、品質管制測試、批次放行及裝運的詳細書面指令。*	***Product specification file*** *A reference file containing, or referring to files containing, all the information necessary to draft the detailed written instructions on processing, packaging, quality control testing, batch release and shipping of an investigational medicinal product.*
隨機化 *指為了減少偏差，使用機會因素以決定受試者指派至試驗組或對照組的指派過程。*	***Randomisation*** *The process of assigning trial subjects to treatment or control groups using an element of chance to determine the assignments in order to reduce bias.*
隨機化編碼 *指用來辨識每一受試者按隨機化過程的試驗/治療指派清單。*	***Randomisation Code*** *A listing in which the treatment assigned to each subject from the randomisation process is identified.*
裝運 *指依訂單分/包裝及寄送臨床試驗研究用藥品的作業。*	***Shipping*** *The operation of packaging for shipment, and sending of ordered medicinal products for clinical trials.*
試驗委託者 *指負責臨床試驗之發起、管理及/或財務的個人、公司、機構或組織。*	***Sponsor*** *An individual, company, institution or organization which takes responsibility for the initiation, management and/or financing of a clinical trial.*

品質管理（QUALITY MANAGEMENT）	
1. 製造廠或進口商應考量應用GMP原則與指引於研究用藥品，其設計、建立及確認的品質系統，應以書面程序描述，並可為試驗委託者取得。	1. The Quality System, designed, set up and verified by the manufacturer or importer, should be described in written procedures available to the sponsor, taking into account the GMP principles and guidelines applicable to investigational medicinal products.
2. 開發期間，研究用藥品之規格及製造指令得以變更。該變更的完整管制及可追溯性應予以保存。	2. The product specifications and manufacturing instructions may be changed during development but full control and traceability of the changes should be maintained.
人事（PERSONNEL）	
3. 所有涉及研究用藥品的人員，應經這類藥品其特定要求之適當訓練。	3. All personnel involved with investigational medicinal products should be appropriately trained in the requirements specific to these types of product.
4. 被授權人員尤其應負責確保備有符合本附則之要求的系統，且應具有藥品開發及臨床試驗過程的廣博知識。認證研究用藥品之被授權人員之相關指引，規定於本附則的38至41條。	4. The Authorised Person should in particular be responsible for ensuring that there are systems in place that meet the requirements of this Annex and should therefore have a broad knowledge of pharmaceutical development and clinical trial processes. Guidance for the Authorised Person in connection with the certification of investigational medicinal products is given in paragraphs 38 to 41.
廠房設施與設備（PREMISES AND EQUIPMENT）	
5. 由於可能無法充分瞭解研究用藥品之毒性、效價與潛在致敏性，更須強調將所有交叉污染之風險減至最低。設備與廠房之設計、在清潔後使用之檢查/檢驗方法以及允收標準，應該反映這些風險的本質。合適時，應考慮時段切換作業。在清潔溶劑的選定上，應考量藥品的溶解度。	5. The toxicity, potency and sensitising potential may not be fully understood for investigational medicinal products and this reinforces the need to minimise all risks of cross-contamination. The design of equipment and premises, inspection / test methods and acceptance limits to be used after cleaning should reflect the nature of these risks. Consideration should be given to campaign working where appropriate. Account should be taken of the solubility of the product in decisions about the choice of cleaning solvent.

文件（DOCUMENTATION）	
規格與指令（Specifications and instructions）	
6. 規格（起始原料、直接包裝材料、中間產品/半製品、待分/包裝產品與最終產品）、製造配方及製造與分/包裝指令，應盡可能廣泛提供知識現況。且在開發期間，應定期再予以評估，並視需要更新。每一新版本應考量最新之數據、所使用之現行技術、法規與藥典的要求，且應容許可追溯到先前的文件。任何變更應依書面程序執行。該變更程序應提及例如安定性及生體相等性等任何對產品品質的連帶影響。	6. Specifications (for starting materials, primary packaging materials, intermediate, bulk products and finished products), manufacturing formulae and processing and packaging instructions should be as comprehensive as possible given the current state of knowledge. They should be periodically re-assessed during development and updated as necessary.Each new version should take into account the latest data, current technology used, regulatory and pharmacopoeial requirements, and should allow traceability to the previous document. Any changes should be carried out according to a written procedure, which should address any implications for product quality such as stability and bio equivalence.
7. 變更的理論基礎應予以記錄。一有變更，對於藥品品質及任何持續之臨床試驗的結果，應予以調查並文件化。	7. Rationales for changes should be recorded and the consequences of a change on product quality and on any on-going clinical trials should be investigated and documented.
研究用藥品訂單（Order）	
8. 研究用藥品訂單應要求一定單位數之製造、及/或分/包裝、及/或其裝運，並由試驗委託者或其代表交予研究用藥品的製造廠。該訂單應為書面(亦可經由電子方法傳送)且足夠精確，以避免任何模糊不清。這應經過正式的授權，並應引述產品規格檔案，及合適時，引述相關的臨床試驗計畫書。	8. The order should request the processing and/or packaging of a certain number of units and/or their shipping and be given by or on behalf of the sponsor to the manufacturer. It should be in writing (though it may be transmitted by electronic means), and precise enough to avoid any ambiguity. It should be formally authorised and refer to the Product Specification File and the relevant clinical trial protocol as appropriate.
產品規格檔案（Product specification file）	

9. 產品規格檔案（參見術語彙編）應隨產品開發持續更新，並確保可適當追溯至先前版本。該檔案應包含或引述下列文件：	9. The Product Specification File (see glossary) should be continually updated as development of the product proceeds, ensuring appropriate traceability to the previous versions. It should include, or refer to, the following documents:
• 起始原料、包裝材料、中間產品、待分/包裝產品及最終產品的規格與分析方法	• Specifications and analytical methods for starting materials, packaging materials, intermediate, bulk and finished product.
• 製造方法。	• Manufacturing methods.
• 製程中檢驗及方法。	• In-process testing and methods.
• 核准的標籤複印本。	• Approved label copy.
• 相關臨床試驗計畫書及隨機化編碼（合適時）。	• Relevant clinical trial protocols and randomisation codes, as appropriate.
• 與合約提供者（委託者）之相關技術協議書（合適時）。	• Relevant technical agreements with contract givers, as appropriate.
• 安定性數據。	• Stability data.
• 儲存及裝運條件。	• Storage and shipment conditions.
上述項目並不意謂其為完全的或無遺漏的，其內容會依產品及開發階段而改變。該資訊應構成被授權人員認證與放行一特定批次之適當性的評估基礎，且應可被其取得。不同的製造步驟在不同場所進行時，於不同被授權人員的權責下，以各別檔案保存限於各該場所之相關活動的資訊，是可以接受的。	The above listing is not intended to be exclusive or exhaustive. The contents will vary depending on the product and stage of development. The information should form the basis for assessment of the suitability for certification and release of a particular batch by the Authorised Person and should therefore be accessible to him/her. Where different manufacturing steps are carried out at different locations under the responsibility of different Authorised Persons, it is acceptable to maintain separate files limited to information of relevance to the activities at the respective locations.
製造配方及操作指令（Manufacturing formulae and Processing instructions）	

10. 每一製造作業或供應，應有清楚且適當之書面指令及紀錄。當作業不具反覆性時，可能不必制定主配方與操作指令。一旦獲得上市許可時，該紀錄對將用於例行製造文件最終版本的制作是特別重要。	10. For every manufacturing operation or supply there should be clear and adequate written instructions and written records. Where an operation is not repetitive it may not be necessary to produce Master Formulae and Processing Instructions. Records are particularly important for the preparation of the final version of the documents to be used in routine manufacture once the marketing authorisation is granted.
11. 產品規格檔案的資訊應使用於制訂有關製造、分/包裝、品質管制檢驗、儲存條件及裝運的詳細書面指令。	11. The information in the Product Specification File should be used to produce the detailed written instructions on processing, packaging, quality control testing, storage conditions and shipping.
分/包裝指令（Packaging instructions）	
12. 研究用藥品通常是爲包含在臨床試驗中的每一位受試者以個別方式包裝。要包裝之單位數目，包含爲執行品質管制及要保存的任何留存樣品在內，應在包裝操作開始前加以規定。爲確保在每一製造階段，所需每一藥品之正確數量皆已計算過，應執行充分的數量調和。	12. Investigational medicinal products are normally packed in an individual way for each subject included in the clinical trial. The number of units to be packaged should be specified prior to the start of the packaging operations, including units necessary for carrying out quality control and any retention samples to be kept. Sufficient reconciliations should take place to ensure the correct quantity of each product required has been accounted for at each stage of processing.
製造、測試及分/包裝批次紀錄（Processing, testing and packaging batch records）	
13. 為準確訂定操作順序，批次紀錄應保持足夠的細節。這些紀錄應包含任何相關的註記，用以證明所使用之程序及所做任何變更的正當性，並增進對該產品的瞭解，以及製程開發。	13. Batch records should be kept in sufficient detail for the sequence of operations to be accurately determined. These records should contain any relevant remarks which justify the procedures used and any changes made, enhance knowledge of the product and develop the manufacturing operations.
14. 批次製造紀錄應至少保存至相關法規明定的期間。	14. Batch manufacturing records should be retained at least for the periods specified in relevant regulations.
生產（PRODUCTION）	
分/包裝材料（Packaging materials）	

15. 規格與品質管制檢查應包括防範措施，以防止由於不同批次分/包裝材料間之外觀上變更所引起的無意解盲。	15. Specifications and quality control checks should include measures to guard against unintentional unblinding due to changes in appearance between different batches of packaging materials.
製造操作（Manufacturing operations）	
16. 開發期間，關鍵參數應予以確定，且製程中管制應主要用來管控其製程。暫定的操作參數與製程中管制，可從先前的經驗推論，包含由早期開發工作中所獲得者。隨著所獲得之製程經驗，必要之指令需持續調適，並要求關鍵人員規劃其指令時應謹慎考量。已確定及管制的參數，應以當時可獲得的知識為基礎證明其正當性。	16. During development critical parameters should be identified and in-process controls primarily used to control the process. Provisional production parameters and in-process controls may be deduced from prior experience, including that gained from earlier development work. Careful consideration by key personnel is called for in order to formulate the necessary instructions and to adapt them continually to the experience gained in production. Parameters identified and controlled should be justifiable based on knowledge available at the time.
17. 研究用藥品的生產過程雖不被期望確效到例行生產所需要的程度。但廠房設施與設備的確效是被期望的。對於無菌產品，滅菌過程的確效應與許可上市之產品達到相同的標準。同樣地，必要時，應證明已依循在本領域中既有之指引所界定的科學原理與技術將病毒去活化/移除，以及除去其他起源於生物的雜質，以確保利用生物技術衍生之產品的安全性。	17. Production processes for investigational medicinal products are not expected to be validated to the extent necessary for routine production but premises and equipment are expected to be validated. For sterile products, the validation of sterilising processes should be of the same standard as for products authorised for marketing. Likewise, when required, virus inactivation/removal and that of other impurities of biological origin should be demonstrated, to assure the safety of biotechnologically derived products, by following the scientific principles and techniques defined in the available guidance in this area.
18. 當批量小時，無菌操作的確效會出現特別的問題。在這些狀況中，充填之單元數目可能是在生產中充填之最大的數目。如果可行，除與該過程之模擬一致外，應以充填較多單元數目的培養基，以對結果取得較大的信心。充填與密封常常是以人工或半自動操作，這對無菌性呈現很大的挑	18. Validation of aseptic processes presents special problems when the batch size is small; in these cases the number of units filled may be the maximum number filled in production. If practicable, and otherwise consistent with simulating the process, a larger number of units should be filled with

戰，因此，對操作人員的訓練，以及個別操作者無菌技術的確效應特別注意。	media to provide greater confidence in the results obtained. Filling and sealing is often a manual or semi-automated operation presenting great challenges to sterility so enhanced attention should be given to operator training, and validating the aseptic technique of individual operators.
可適用於比對用產品的原則（Principles applicable to comparator product	
19. 如果產品經過修改，應可取得其資料（例如：安定性、溶離度比對、生體可用率），以證明這些變更無顯著地改變該產品的原始品質特性。	19. If a product is modified, data should be available (e.g. stability, comparative dissolution, bioavailability) to demonstrate that these changes do not significantly alter the original quality characteristics of the product.
20. 比對用產品經重新包裝在不同容器中，可能不再提供相等的保護，或其容器可能與該產品不相容，而使該比對用產品原始包裝上所載之末效日期可能不再適用。考慮該產品的本質、容器的特徵及該產品可能受制的儲存條件，試驗委託者或其代表應決定適當的用畢日期。該日期必須證明其正當性，且不得晚於原始包裝的末效日期。末效日期與臨床試驗期間應具相容性。	20. The expiry date stated for the comparator product in its original packaging might not be applicable to the product where it has been repackaged in a different container that may not offer equivalent protection, or be compatible with the product. A suitable use-by date, taking into account the nature of the product, the characteristics of the container and the storage conditions to which the article may be subjected, should be determined by or on behalf of the sponsor. Such a date should be justified and must not be later than the expiry date of the original package. There should be compatibility of expiry dating and clinical trial duration.
盲性化作業（Blinding operations）	
21. 產品經盲性化，雖然容許「盲性」產品於必要時之識別，包含在盲性化作業前該產品的批號在內，但應有系統確保該盲性化之達成與維持，且緊急時亦能快速識別該產品。	21. Where products are blinded, systems should be in place to ensure that the blind is achieved and maintained while allowing for identification of “blinded” products when necessary, including the batch numbers of the products before the blinding operation. Rapid identification of product should also be possible in an emergency.
隨機化編碼（Randomization code）	
22. 應說明使用於分/包裝研究用藥品之任何隨機化編碼的產生、保全、分配、處理和保存之作業程序，以及其解碼機制。適當	22. Procedures should describe the generation, security, distribution, handling and retention of any randomisation code used

的紀錄應予以保存。	for packaging investigational products, and code-break mechanisms. Appropriate records should be maintained.
分/包裝（Packaging）	
23. 研究用藥品的分/包裝期間，可能必須於相同時間在相同分/包裝線上，處理不同的藥品。應利用適當的程序及/或特別的設備（合適時）及相關人員的訓練，將產品混雜的風險減到最低。	23. During packaging of investigational medicinal products, it may be necessary to handle different products on the same packaging line at the same time. The risk of product mix up must be minimised by using appropriate procedures and/or, specialised equipment as appropriate and relevant staff training.
24. 研究用藥品的包裝與標示比已上市藥品可能更為複雜及更易出差錯(該差錯也較難以檢測），尤其是當使用有相似外觀之「盲性」產品時。為防範錯標，諸如強調由經適當訓練之人員從事標籤數量的調和、清線、製程中管制檢查。	24. Packaging and labelling of investigational medicinal products are likely to be more complex and more liable to errors (which are also harder to detect) than for marketed products, particularly when "blinded" products with similar appearance are used. Precautions against mis-labelling such as label reconciliation, line clearance, in-process control checks by appropriately trained staff should accordingly be intensified.
25. 包裝必須確保研究用藥品在運輸及在中間目的地之儲存期間維持於良好的狀態中。運輸期間，其外包裝的開啟或竄改應易於識別。	25. The packaging must ensure that the investigational medicinal product remains in good condition during transport and storage at intermediate destinations. Any opening or tampering of the outer packaging during transport should be readily discernible.
標示作業（Labelling）	
26. 表1摘述下列26至30條的內容。下列的資訊應包含在標籤上，除非可證明其不包含之正當理由，例如，中央電子隨機系統的使用：	26. Table 1 summarises the contents of articles 26-30 that follow. The following information should be included on labels, unless its absence can be justified, e.g. use of a centralised electronic randomisation system:
a) 試驗委託者、受託研究機構或試驗主持人的姓名/名稱、地址及電話號碼（關於藥品、臨床試驗及緊急解盲之資訊的主要接洽對象）；	a) name, address and telephone number of the sponsor, contract research organisation or investigator (the main contact for information on the product, clinical trial and emergency unblinding);

b) 藥品劑型、給藥途徑、劑型單元數，以及如為開放性試驗，其名稱/識別符號及強度/效價；	b) pharmaceutical dosage form, route of administration, quantity of dosage units, and in the case of open trials, the name/identifier and strength/potency;
c) 用以識別內容物與分/包裝作業之批號及/或代碼；	c) the batch and/or code number to identify the contents and packaging operation;
d) 他處未提供者，應有能夠識別該試驗、場所、試驗主持人及試驗委託者之試驗對照代碼；	d) a trial reference code allowing identification of the trial, site, investigator and sponsor if not given elsewhere;
e) 試驗受試者之識別號碼、試驗/治療號碼及訪視號碼（合適時）；	e) the trial subject identification number/treatment number and where relevant, the visit number;
f) 試驗主持人之姓名（如果未包含在(a)或(d)中）；	f) the name of the investigator (if not included in (a) or (d));
g) 使用說明(可參考供受試者或投用該產品者所製作之說明書或其他解釋文件）；	g) directions for use (reference may be made to a leaflet or other explanatory document intended for the trial subject or person administering the product);
h) 「僅供臨床試驗使用」或相似措辭；	h) “For clinical trial use only” or similar wording;
i) 儲存條件；	i) the storage conditions;
j) 使用期間(用畢日期、末效日期或再驗日期（合適時）），以年/月之格式及避免任何不明確的方式；	j) period of use (use-by date, expiry date or re-test date as applicable), in month/year format and in a manner that avoids any ambiguity.
k) 「避免孩童觸及」，除非該產品是使用於非由受試者帶回家裡投用的試驗。	k) “keep out of reach of children” except when the product is for use in trials where the product is not taken home by subjects.
27. 已給予受試者載有藥品、臨床試驗及緊急解盲所需資料之主要接洽對象的地址與電話號碼之說明書或卡片，且已指示其隨身攜帶時，則該地址與電話號碼不需出現於標籤上。	27. The address and telephone number of the main contact for information on the product, clinical trial and for emergency unblinding need not appear on the label where the subject has been given a leaflet or card which provides these details and has been instructed to keep this in their possession at all times.

28. 細節應以研究用藥品要使用之所在國家的官方語言標示。除在29至30條中所述情況之直接容器外，第26條所列之細節應標示於直接容器及外包裝上。關於在直接容器與外包裝上之標籤內容的要求摘述於表1，可包括其他語言。	28. Particulars should appear in the official language(s) of the country in which the investigational medicinal product is to be used. The particulars listed in Article 26 should appear on the immediate container and on the outer packaging (except for immediate containers in the cases described in Articles 29 and 30). The requirements with respect to the contents of the label on the immediate container and outer packaging are summarised in table 1. Other languages may be included.
29. 提供受試者或投用該藥品者之產品係置於連同外包裝之直接容器內，且該外包裝帶有第26條所列舉的特定項目時，直接容器（或包含直接容器之任何密封的給藥裝置）之標籤上應包含下列資訊：	29. When the product is to be provided to the trial subject or the person administering the medication within an immediate container together with outer packaging that is intended to remain together, and the outer packaging carries the particulars listed in paragraph 26, the following information should be included on the label of the immediate container (or any sealed dosing device that contains the immediate container):
a) 試驗委託者、受託研究機構或試驗主持人的名稱/姓名；	a) name of sponsor, contract research organisation or investigator;
b) 藥品劑型、給藥途徑（可排除口服固體劑型）、劑型單元數及在如為開放性試驗時，名稱或姓名/識別符號以及強度/效價；	b) pharmaceutical dosage form, route of administration (may be excluded for oral solid dose forms), quantity of dosage units and in the case of open label trials, the name/identifier and strength/potency;
c) 批號及/或代碼，以識別內容物及分/包裝作業；	c) batch and/or code number to identify the contents and packaging operation;
d) 他處未提供者，應有能夠識別該試驗、場所、試驗主持人及試驗委託者之試驗對照代碼；	d) a trial reference code allowing identification of the trial, site, investigator and sponsor if not given elsewhere;
e) 試驗受試者之識別號碼/治療（或處理）號碼及訪視號碼（合適時）。	e) the trial subject identification number/treatment number and where relevant, the visit number.

30. 直接容器採泡殼包裝或其上之小單元，諸如安瓿不能標示第26條要求之特定項目時，該項目應標示於外包裝。其直接容器仍應包含下列項目：	30. If the immediate container takes the form of blister packs or small units such as ampoules on which the particulars required in paragraph 26 cannot be displayed, outer packaging should be provided bearing a label with those particulars. The immediate container should nevertheless contain the following:
a) 試驗委託者、受託研究機構或試驗主持人之名稱/姓名；	a) name of sponsor, contract research organisation or investigator;
b) 給藥途徑（可排除口服固體劑型）及在如為開放性試驗時，名稱或姓名/識別符號以及強度/效價；	b) route of administration (may be excluded for oral solid dose forms) and in the case of open label trials, the name/identifier and strength/potency;
c) 批號及/或代碼，以識別內容物及分/包裝作業；	c) batch and/or code number to identify the contents and packaging operation;
d) 他處未提供者，應有能夠識別該試驗、場所、試驗主持人及試驗委託者之試驗對照代碼；	d) a trial reference code allowing identification of the trial, site, investigator and sponsor if not given elsewhere;
e) 試驗受試者之識別號碼/治療（或處理）號碼及訪視號碼（合適時）。	e) the trial subject identification number/treatment number and where relevant, the visit number;
31. 標示作業可包含符號或統計圖表，以釐清上述某些資料。可標示附加的資料、警告及/或處理指示。	31. Symbols or pictograms may be included to clarify certain information mentioned above. Additional information, warnings and/or handling instructions may be displayed.
32. 具有某些特徵的臨床試驗，下列的特定項目應加到原始容器上，但不得遮蔽原始的標示資料：	32. For clinical trials with certain characteristics the following particulars should be added to the original container but should not obscure the original labelling:
試驗委託者、受託研究機構或試驗主持人的名稱或姓名；	name of sponsor, contract research organisation or investigator;
能夠辨識該試驗之場所、試驗主持人及受試者之試驗對照代碼。	trial reference code allowing identification of the trial site, investigator and trial subject.

33. 有變更用畢日期之必要者，應對研究用藥品貼上附加的標籤。該附加標籤應載明新的用畢日期，並重複該批號。這可覆蓋貼在原用畢日期上。為品管的理由，不可貼在原批號上。該作業應在適當的製造場所為之，但有正當理由時，得於試驗場所由該臨床試驗場所之藥師或符合國家法規之其他健康照護專業人員執行，或在其監督下為之。該做法不可能時，得由受過適當訓練之臨床試驗監督人員為之。其作業應依GMP原則、特定及標準之作業程序以及視情形依契約為之，並應由第二者核對。該附加的標示，應在試驗文件及在批次紀錄上適當記載。	33. If it becomes necessary to change the use-by date, an additional label should be affixed to the investigational medicinal product. This additional label should state the new use-by date and repeat the batch number. It may be superimposed on the old use-by date, but for quality control reasons, not on the original batch number. This operation should be performed at an appropriately authorised manufacturing site.However, when justified, it may be performed at the investigational site by or under the supervision of the clinical trial site pharmacist, or other health care professional in accordance with national regulations.Where this is not possible, it may be performed by the clinical trial monitor(s) who should be appropriately trained. The operation should be performed in accordance with GMP principles, specific and standard operating procedures and under contract, if applicable, and should be checked by a second person. This additional labelling should be properly documented in both the trial documentation and in the batch records.
品質管制（QUALITY CONTROL）	
34. 由於製程可能無法標準化或完全確效，於確保每批產品皆符合其規格上，檢驗作業擔負重責。	34. As processes may not be standardised or fully validated, testing takes on more importance in ensuring that each batch meets its specification.
35. 品質管制之執行應依該產品規格檔案及要求之資訊。盲性化之確認應執行並記錄。	35. Quality control should be performed in accordance with the Product Specification File and in accordance with the required information. Verification of the effectiveness of blinding should be performed and recorded.
36. 研究用藥品之每批次的樣品，包含盲性化產品在內，應保存至所要求的期間。	36. Samples of each batch of investigational medicinal product, including blinded product should be retained for the required periods.

37. 直到臨床報告完成前，應對每一分/包裝操作/試驗期間所得之留存樣品列入考量，以便在調查不一致試驗結果時，使產品同一性能確認，並成為調查之一部分。	37. Consideration should be given to retaining samples from each packaging run/trial period until the clinical report has been prepared to enable confirmation of product identity in the event of, and as part of an investigation into inconsistent trial results.
批次放行（RELEASE OF BATCHES）	
38. 於被授權人員確認相關的要求已符合前（詳見第39條），不得放行研究用藥品（詳見第43條）。適合時，被授權人員應考量第40條所列之要項。	38. Release of investigational medicinal products (see paragraph 43) should not occur until after the Authorised Person has certified that the relevant requirements have been met (see paragraph 39). The Authorised Person should take into account the elements listed in paragraph 40 as appropriate.
39. [...]PIC/S不採用	39. [...]*
40. 於放行前，每一批次證明之評估，合適時，可包括：	40. Assessment of each batch for certification prior to release may include as appropriate:
➢ 批次紀錄，包含品管報告、製程中檢驗報告及放行報告，以證明符合產品規格檔案、訂單、計畫書及隨機編碼。這些紀錄應包括所有偏差或經計畫的變更，以及任何隨後附加的核對或檢驗，且應由依品質系統授權之人員完成與背書；	batch records, including control reports, in-process test reports and release reports demonstrating compliance with the product specification file, the order, protocol and randomisation code. These records should include all deviations or planned changes, and any consequent additional checks or tests, and should be completed and endorsed by the staff authorised to do so according to the quality system;
➢ 生產條件；	➢ production conditions;
➢ 廠房設施、製程及方法的確效狀態；	➢ the validation status of facilities, processes and methods;
➢ 最終包裝品的檢查；	➢ examination of finished packs;
➢ 合適時，在輸入後所執行之所有分析或檢驗的結果；	➢ where relevant, the results of any analyses or tests performed after importation;
➢ 安定性報告；	➢ stability reports;
➢ 來源及儲存與裝運條件之確認；	➢ the source and verification of conditions of storage and shipment;

➢ 關於製造廠品質系統之稽查報告；	➢ audit reports concerning the quality system of the manufacturer;
➢ 輸出國家的主管機關證明該製藥廠係經授權，以製造供輸出之研究用藥品或比對用產品的文件；	➢ Documents certifying that the manufacturer is authorised to manufacture investigational medicinal products or comparators for export by the appropriate authorities in the country of export;
➢ 合適時，上市許可的法規要求、適用的GMP標準及任何遵循GMP之官方證明；	➢ where relevant, regulatory requirements for marketing authorisation, GMP standards applicable and any official verification of GMP compliance;
➢ 負責產品放行者所知悉與該批次品質有關的所有其他因素。	➢ all other factors of which the QP is aware that are relevant to the quality of the batch.
上述因素的關聯性受該產品的原產地、製造廠、該製品之上市狀態（在美、日、歐盟或在第三國具有或不具有上市許可）及其開發階段的影響。	The relevance of the above elements is affected by the country of origin of the product, the manufacturer, and the marketed status of the product (with or without a marketing authorisation, in the EU or in a third country) and its phase of development.
試驗委託者應確保被授權人員，在證明該批次時，所考慮的要項與要求的資料一致。詳見第44條。	The sponsor should ensure that the elements taken into account by the Authorised Person when certifying the batch are consistent with the required information. See also 44.
41. 如研究用藥品於不同的場所製造與分/包裝時，在不同的被授權人員監督下，合適時，應遵循相關建議。	41. Where investigational medicinal products are manufactured and packaged at different sites under the supervision of different Authorised Persons, recommendations should be followed as applicable.

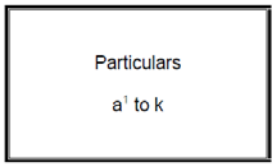
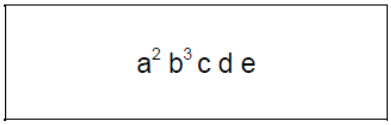
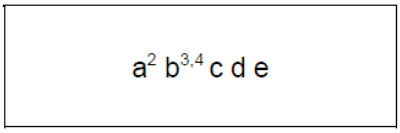
42. 當地法規容許時，分/包裝或標示得在試驗主持人的場所，由臨床試驗藥師或該等法規允許的其他健康照護專業人員執行，或在其監督下為之。該情形，被授權人員不需認證該作業。然試驗委託者仍應負責確保該作業經適當的文件化並依GMP原則執行，及應尋求被授權人員在這方面的意見。	42. Where, permitted in accordance with local regulations, packaging or labelling is carried out at the investigator site by, or under the supervision of a clinical trials pharmacist, or other health care professional as allowed in those regulations, the Authorised Person is not required to certify the activity in question. The sponsor is nevertheless responsible for ensuring that the activity is adequately documented and carried out in accordance with the principles of GMP and should seek the advice of the Authorised Person in this regard.
裝運（Shipping）	
43. 研究用藥品的裝運，應依試驗委託者或其代表在裝運單中之指示為之。	43. Shipping of investigational products should be conducted according to instructions given by or on behalf of the sponsor in the shipping order.
44. 直到二階段放行程序經被授權人員的認證及滿足相關要求之放行完成前，研究用藥品應維持於試驗委託者的管制下。試驗委託者應確保這些皆與被授權人員實際上考慮的細節一致。該二階段放行程序均應予以記錄，並保存於試驗委託者或其代表保管之相關檔案中。	44. Investigational medicinal products should remain under the control of the Sponsor until after completion of a two-step release procedure: certification by the Authorised Person; and release following fulfilment of the relevant requirements. The sponsor should ensure that these are consistent with the details actually considered by the Authorised Person. Both releases should be recorded and retained in the relevant trial files held by or on behalf of the sponsor.
45. 研究用藥品裝運至試驗主持人之場所前，適當的負責人員應可取得解碼方法。	45. De-coding arrangements should be available to the appropriate responsible personnel before investigational medicinal products are shipped to the investigator site.
46. 製造或輸入者所製作之裝運藥品的詳細清單應予以保存。該清單應特別提示收件者的身分識別。	46. A detailed inventory of the shipments made by the manufacturer or importer should be maintained. It should particularly mention the addressees' identification.

47. 從一試驗場所到另一試驗場所轉送研究用藥品，應屬例外。該轉送應為標準作業程序所涵蓋。離開製造廠的管制外之產品歷史，涵蓋例如在原始試驗場所的試驗監測報告及儲存條件紀錄應予以審查，並當作該產品轉送適當性評估的一部分，另應尋求被授權人員的意見。如有必要，該產品應退回製造廠或其他被授權之製造廠重貼標籤，並由被授權人員認證/證明。紀錄應予以保存並確保可完全追溯。	47. Transfers of investigational medicinal products from one trial site to another should remain the exception. Such transfers should be covered by standard operating procedures. The product history while outside of the control of the manufacturer, through for example, trial monitoring reports and records of storage conditions at the original trial site should be reviewed as part of the assessment of the product's suitability for transfer and the advice of the Authorised Person should be sought. The product should be returned to the manufacturer, or another authorised manufacturer for re-labelling, if necessary, and certification by a Authorised Person. Records should be retained and full traceability ensured.
申訴（COMPLAINTS）	
48. 由產品品質所引起的相關申訴，其完成調查後之結論，應在製造或輸入者與試驗委託者間(若兩者不同時)討論。這應有被授權人員及為相關臨床試驗負責的人員參與，以評估其對該臨床試驗、藥品開發及受試者之任何潛在影響。	48. The conclusions of any investigation carried out in relation to a complaint which could arise from the quality of the product should be discussed between the manufacturer or importer and the sponsor (if different). This should involve the Authorised Person and those responsible for the relevant clinical trial in order to assess any potential impact on the trial, product development and on subjects.
回收品和退回品（RECALLS AND RETURNS）	
回收品（Recalls）	
49. 取回研究用藥品之程序及其文件化應經試驗委託者與製造或輸入者(若兩者不同時)同意。試驗主持人及監測人員需瞭解於該取回程序中之義務。	49. Procedures for retrieving investigational medicinal products and documenting this retrieval should be agreed by the sponsor, in collaboration with the manufacturer or importer where different. The investigator and monitor need to understand their obligations under the retrieval procedure.

50. 試驗委託者應確保將使用於臨床試驗之任何比對用藥品或其它藥品的供應者有一套系統，以聯繫試驗委託者回收其供應之任何產品的需要。	50. The Sponsor should ensure that the supplier of any comparator or other medication to be used in a clinical trial has a system for communicating to the Sponsor the need to recall any product supplied.
退回品（Returns）	
51. 研究用藥品應依同意的條件退回。該條件由試驗委託者界定，並在核可之書面程序中明定。	51. Investigational medicinal products should be returned on agreed conditions defined by the sponsor, specified in approved written procedures.
52. 退回的研究用藥品應予以清楚識別並儲存於適當管控之專屬區域中。退回之研究用藥品的庫存紀錄應予以保存。	52. Returned investigational medicinal products should be clearly identified and stored in an appropriately controlled, dedicated area. Inventory records of the returned medicinal products should be kept.
銷毀（Destruction）	
53. 試驗委託者應負責，將未使用的及/或退回之研究用藥品銷毀。因此，研究用藥品非有試驗委託者之事先書面授權，不得銷毀。	53. The Sponsor is responsible for the destruction of unused and/or returned investigational medicinal products. Investigational medicinal products should therefore not be destroyed without prior written authorization by the Sponsor.
54. 送交、使用及收回的藥品數量應由試驗委託者或其代表就每一試驗場所及每一試驗期間予以記錄、數量調和及確認。每一試驗場所及每一試驗期間未使用之研究用藥品的銷毀，應僅於任何差異皆已調查並滿意地解釋，且其數量調和已被接受後，才可執行。銷毀作業的紀錄應以所有作業皆可獲得說明的方式執行。這些紀錄應由試驗委託者保存。	54. The delivered, used and recovered quantities of product should be recorded, reconciled and verified by or on behalf of the sponsor for each trial site and each trial period. Destruction of unused investigational medicinal products should be carried out for a given trial site or a given trial period only after any discrepancies have been investigated and satisfactorily explained and the reconciliation has been accepted. Recording of destruction operations should be carried out in such a manner that all operations may be accounted for. The records should be kept by the Sponsor.

55. 當研究用藥品的銷毀時，應將載明日期之銷毀證明書或收據提供給試驗委託者。這些文件應清楚地識別或可追溯到所涉批次及/或病人代碼及銷毀之實際數量。	55. When destruction of investigational medicinal products takes place a dated certificate of, or receipt for destruction, should be provided to the sponsor. These documents should clearly identify, or allow traceability to, the batches and/or patient numbers involved and the actual quantities destroyed.

表1. 標示細節摘要 **TABLE 1. SUMMARY OF LABELLING DETAILS (§26 to 30)**	
a）試驗委託者、受託研究機構或試驗主持人的姓名/名稱、地址及電話號碼（關於藥品、臨床試驗及緊急解盲之資訊的主要接洽對象）；	a) name, address and telephone number of the sponsor, contract research organisation or investigator (the main contact for information on the product, clinical trial and emergency unblinding);
b)，藥品劑型、給藥途徑、劑型單元數，以及如為開放性試驗，其名稱/識別符號及強度/效價；	b) pharmaceutical dosage form, route of administration, quantity of dosage units, and in the case of open trials, the name/identifier and strength/potency;
c）用以識別內容物與分/包裝作業之批號及/或代碼；	c) the batch and/or code number to identify the contents and packaging operation;
d）他處未提供者，應有能夠識別該試驗、場所、試驗主持人及試驗委託者之試驗對照代碼；	d) a trial reference code allowing identification of the trial, site, investigator and sponsor if not given elsewhere;
e）試驗受試者之識別號碼、試驗/治療號碼及訪視號碼（合適時）；	e) the trial subject identification number / treatment number and where relevant, the visit number;
f）試驗主持人之姓名（如果未包含在(a)或(d)中）；	f) the name of the investigator (if not included in (a) or (d);
g）使用說明（可參考供受試者或投用該產品者所製作之說明書或其他解釋文件）；	g) directions for use (reference may be made to a leaflet or other explanatory document intended for the trial subject or person administering the product
h）「僅供臨床試驗使用」或相似措辭；	h) “for clinical trial use only” or similar wording;
i）儲存條件；	i) the storage conditions;
j）使用期間（用畢日期、末效日期或再驗日期（合適時）），以年/月之格式及避免任何不明確的方式；	j) period of use (use-by date, expiry date or retest date as applicable), in month/year format and in a manner that avoids any ambiguity.
k)「避免孩童觸及」，除非該產品是使用於非由受試者帶回家裡投用的試驗。	k) “keep out of reach of children” except when the product is for use in trials where the product is not taken home by subjects.
一般情況 對間接包裝/外包裝與直接容器 (第26條)	GENERAL CASE For both the outer packaging and immediate container(§26)

特別事項 A[1]至k	
直接容器 在整個期間中在直接容器與間接包裝保持在一時（第29條） A[2] b[3] c d e	IMMEDIATE CONTAINER Where immediate container and outer packaging remain together throughout (§29)[5] 
直接容器 泡型包裝或小包裝單元（第30條） A[2] b[3,4] c d e	IMMEDIATE CONTAINER Blisters or small packaging units (§30)[5] 
1 已給予受試者載有藥品、臨床試驗及緊急解盲所需資料之主要接洽對象的地址與電話號碼之說明書或卡片，且已指示其隨身攜帶時，則該地址與電話號碼不需出現於標籤上（第 27 條）。	1 The address and telephone number of the main contact for information on the product, clinical trial and for emergency unblinding need not appear on the label where the subject has been given a leaflet or card which provides these details and has been instructed to keep this in their possession at all times (§ 27).
2 不需要包括藥品、臨床試驗及緊急解盲所需資料之主要接洽對象的地址與電話號碼。	2 The address and telephone number of the main contact for information on the product, clinical trial and for emergency unblinding need not be included.
3 口服固體劑型投用途徑可以排除。	3 Route of administration may be excluded for oral solid dose forms.
4 藥物劑型與劑量單元數量可以省略。	4 The pharmaceutical dosage form and quantity of dosage units may be omitted.
5 當間接包裝/外包裝帶有第 26 條中所列舉的特別事項時。	5 When the outer packaging carries the particulars listed in Article 26.

附則 14 人類血液或血漿衍生之產品的製造（MANUFACTURE OF PRODUCTS DERIVED FROM HUMAN BLOOD OR HUMAN PLASMA）

原則（PRINCIPLE）	
對於自人類血液或血漿衍生的生物藥品，其原料包含像細胞或含有血液或血漿之液體的來源原料。自人類血液或血漿衍生的藥品具有起因於來源原料之生物性質的特色。例如，傳染疾病之病原體，特別是病毒，可能污染該來源原料。因此，該產品的安全性仰賴於來源原料及其源頭之管制，以及其後續之製造程序，包括病毒去除及去活化。	For biological medicinal products derived from human blood or plasma, starting materials include the source materials such as cells or fluids including blood or plasma. Medicinal products derived from human blood or plasma have certain special features arising from the biological nature of the source material. For example, disease-transmitting agents, especially viruses, may contaminate the source material. The safety of these products relies therefore on the control of source materials and their origin as well as on the subsequent manufacturing procedures, including virus removal and inactivation.
除另有規定外，GMP 總則的一般章節適用於自人類血液或血漿衍生的藥品。一些附則亦適用，例如無菌藥品的製造、游離輻射在藥品製造的使用、生物藥品的製造及電腦化系統。	The general chapters of the guide to GMP apply to medicinal products derived from human blood or plasma, unless otherwise stated. Some of the Annexes may also apply, e.g. manufacture of sterile medicinal products, use of ionising radiation in the manufacture of medicinal products, manufacture of biological medicinal products and computerised systems.
由於所有製造步驟皆會對最終產品品質造成影響，包括血液或血漿的收集。因此所有相關作業之執行均應符合適當之品質保證系統及現行藥品優良製造規範。	Since the quality of the final products is affected by all the steps in their manufacture, including the collection of blood or plasma, all operations should therefore be done in accordance with an appropriate system of Quality Assurance and current Good Manufacturing Practice.

為防止傳染性疾病的散佈，應採取必要措施；關於分離用血漿及自人類血液或血漿衍生的藥品，應適用相關藥典之個論的要求和標準。這些措施亦應包含其他相關的指導方針，例如「關於在歐洲共同體血液及血漿之捐贈者與捐贈之血液篩選的適當性」("On the suitability of blood and plasma donors and the screening of donated blood in the European Community[1] (98/463/EC)")之 1998 年 6 月 29 日歐盟議會建議（Council Recommendation）、歐洲議會組織（Council of Europe）的建議 (參見「血液成分之準備、使用與品質保證指引」，歐洲議會組織公報)（"Guide to the preparation, use and quality assurance of blood components"，Council of Europe Press)及世界衛生組織的建議(參見 WHO 專家委員會關於生物學上的標準化，WHO 技術報告集 840, 1994)（WHO Expert Committee on Biological Standardization, WHO Technical Report Series 840, 1994)。（[1] O.J.L 203201.7.1998 p. 14）	Necessary measures should be taken to prevent the transmission of infectious diseases and the requirements and standards of the European Pharmacopoeia (or other relevant pharmacopoeias) monographs regarding plasma for fractionation and medicinal products derived from human blood or plasma should be applicable. These measures should also comprise other relevant guidelines such as the Council Recommendation of 29 June 1998 "On the suitability of blood and plasma donors and the screening of donated blood in the European Community[1] (98/463/EC), the recommendations of the Council of Europe (see "Guide to the preparation, use and quality assurance of blood components", Council of Europe Press) and the World Health Organisation (see report by the WHO Expert Committee on Biological Standardisation, WHO Technical Report Series 840, 1994).
另 CPMP (Committee for Proprietary Medicinal Products)所採用的指導方針，特別是「自血漿衍生之藥品指引的注意事項」（"Note for guidance on plasma-derived medicinal products）(CPMP/BWP/269/95rev.2)"，發表在 Volume 3A of 1 O.J. L 20321.7.1998 p.14 之「歐洲共同體藥品的管理規則」（"The rules governing medicinal products in the European Community"）系列中的「病毒確效研究:確效病毒之去活化及去除的研究之設計、推廣與解釋」（"Virus validation studies: the design, contribution and interpretation of studies validating the inactivation and removal of viruses"）可能有幫助。因為這些文件定期修訂，所以，應參考現行指引的最新版本。本附則的規定適用於自人類血液及血漿衍生的藥品，而不涵蓋輸注醫療用之血液成分。惟，這些規定中有許多可以適用於此種血液組成物，主管機關並得要求與這些規定相符。	Furthermore, the guidelines adopted by the CPMP, in particular "Note for guidance on plasma-derived medicinal products (CPMP/BWP/269/95rev.2)", "Virus validation studies: the design, contribution and interpretation of studies validating the inactivation and removal of viruses" published in Volume 3A of 1 O.J. L 20321.7.1998 p.14 the series "The rules governing medicinal products in the European Community" may be helpful. These documents are regularly revised and reference should be made to the latest revisions for current guidance. The provisions of this annex apply to medicinal products derived from human blood and plasma. They do not cover blood components used in transfusion medicine. However many of these provisions may be applicable to such components and competent authorities may require compliance with them.

術語彙編（GLOSSARY）	
血液 *是指收集自單一捐血者，並經處理以供輸血或進一步製造之全血。*	***Blood*** *Whole blood collected from a single donor and processed either for transfusion or further manufacturing*
成分血 *使用傳統血庫的方法，經由離心、過濾及冷凍等步驟製備而得，供治療用之血液成分(紅血球、白血球、血漿、血小板)。*	***Blood components*** *Therapeutic components of blood (red cells, white cells, plasma, platelets), that can be prepared by centrifugation, filtration and freezing using conventional blood bank methodology*
自血液或血漿衍生的藥品 *以血液組成物為基礎之藥品，該等藥品係經由公營或民營機構經工業生產製備之藥品。*	***Medicinal product derived from blood or plasma*** *Medicinal products based on blood constituents which are prepared industrially by public or private establishments*
品質管理（QUALITY MANAGEMENT）	
1. 品質保證系統應涵蓋至最終產品的全部製造階段，從收集（包括捐血者的篩選、血袋、抗凝劑及試驗套組）到儲存、運送、加工、品質管制及最終產品的配送，並全部符合本附則在前述原則項下引述的正文。	1. Quality Assurance should cover all stages leading to the finished product, from collection (including donor selection, blood bags, anticoagulant solutions and test kits) to storage, transport, processing, quality control and delivery of the finished product, all in accordance with the texts referred to under Principle at the beginning of this Annex.
2. 作為製造藥品之來源材料的血液或血漿，應由業經主管機關稽查與核准之機構及實驗室進行收集與檢驗。	2. Blood or plasma used as a source material for the manufacture of medicinal products should be collected by establishments and be tested in laboratories which are subject to inspection and approved by a competent authority.
3. 作為藥品來源材料之個人捐贈血液及血漿，其決定捐贈者的合適性之程序及其捐贈之血液及血漿的測試結果，應由收集機構予以文件化，且可被藥品的製造廠所取得。	3. Procedures to determine the suitability of individuals to donate blood and plasma, used as a source material for the manufacture of medicinal products, and the results of the testing of their donations should be documented by the collection establishment and should be available to the manufacturer of the medicinal product.

4. 應採用可檢測出與品質規格之任何偏差的方法，以執行自人類血液或血漿衍生藥品之品質監測。	4. Monitoring of the quality of medicinal products derived from human blood or plasma should be carried out in such a way that any deviations from the quality specifications can be detected.
5. 未經使用而退回之自人類血液或血漿衍生的藥品，通常不得重新出貨（參閱 GMP 之總則第 5.65 條）。	5. Medicinal products derived from human blood or plasma which have been returned unused should normally not be re-issued; (see also point 5.65 of the main GMP guide).
廠房設施及設備（PREMISES AND EQUIPMENT）	
6. 用於血液或血漿之收集的場所與設施應有適當的大小、建造和位置，以利執行正確之操作、清潔及維護保養。血液及血漿的收集、製程加工及檢驗不得在同一場所內進行。應有適合捐血者面談之設施，使該面談在隱密下進行。	6. The premises used for the collection of blood or plasma should be of suitable size, construction and location to facilitate their proper operation, cleaning and maintenance. Collection, processing and testing of blood and plasma should not be performed in the same area. There should be suitable donor interview facilities so that these interviews are carried out in private.
7. 製造、收集及檢驗的設備應加以設計、驗證及維護保養，以符合其預定之目的，且不會造成任何危害。另應依既定的程序實施定期的維護保養及校正，並將相關程序予以文件化。	7. Manufacturing, collection and testing equipment should be designed, qualified and maintained to suit its intended purpose and should not present any hazard. Regular maintenance and calibration should be carried out and documented according to established procedures.
8. 製備自血漿衍生的藥品時，應使用病毒去活化或去除的程序，並採取防止已處理產品與未處理產品之交叉污染措施；已處理的產品應使用專用且區隔的廠房設施及設備。	8. In the preparation of plasma-derived medicinal products, viral inactivation or removal procedures are used and steps should be taken to prevent cross contamination of treated with untreated products; dedicated and distinct premises and equipment should be used for treated products.
血液及血漿之收集（BLOOD AND PLASMA COLLECTION）	

9. 自人類血液或血漿衍生之藥品的製造廠與負責血液/血漿之收集的機構或組織間應建立一份標準合約書。	9. A standard contract is required between the manufacturer of the medicinal product derived from human blood or plasma and the blood/plasma collection establishment or organisation responsible for collection.
10. 報到時,必須確認每一位捐血者之正確身分，且需於靜脈穿刺前再確認。	10. Each donor must be positively identified at reception and again before venepuncture.
11. 使用於消毒捐血者皮膚的方法應明確界定，並證實該方法之有效性，之後應持續遵循。	11. The method used to disinfect the skin of the donor should be clearly defined and shown to be effective. Adherence to that method should then be maintained.
12. 捐血的號碼標籤，應再獨立核對之，以確保與血袋、檢體試管及捐血紀錄上之號碼標籤完全相同。	12. Donation number labels must be re-checked independently to ensure that those on blood packs, sample tubes and donation records are identical.
13. 血袋及血液分離系統在被使用於收集血液或血漿前，應確實檢查有無破損或污染。另為確保其可追溯性，血袋及血液分離系統的批號亦應予以記錄。	13. Blood bag and apheresis systems should be inspected for damage or contamination before being used to collect blood or plasma. In order to ensure traceability, the batch number of blood bags and apheresis systems should be recorded.
可追溯性及收集後措施 （TRACEABILITY AND POST COLLECTION MEASURES）	
14. 於完全尊重隱密性的同時,應備有一套可追溯每一捐血路徑系統,可由前端的捐血者開始追溯,亦可由後端的最終產品開始追溯，包括客戶(醫院或健康照護專業人員)在內。辨識接受者的身分，通常是醫院或健康照護專業人員的責任。	14. While fully respecting confidentiality, there must be a system in place which enables the path taken by each donation to be traced, both forward from the donor and back from the finished medicinal product, including the customer (hospital or health care professional). It is normally the responsibility of this customer to identify the recipient.
15. 血液/血漿收集後的措施：應建立該收集機構與製造/分離廠間之相互通報系統的標準作業程序,以便捐血後有下列情形發生時可互相通知：	15. Post-collection measures: A standard operating procedure describing the mutual information system between the blood/plasma collection establishment and the manufacturing/fractionation facility should be set up so that they can inform each other if, following donation:
➢ 發現該捐血者不符合相關的捐血者健	➢ it is found that the donor did not meet

康標準；	the relevant donor health criteria;
➢ 先前病毒標記為陰性的捐血者，後來捐血時發現有任何病毒標記為陽性反應；	➢ a subsequent donation from a donor previously found negative for viral markers is found positive for any of the viral markers;
➢ 發現其病毒標記檢測未依議定的程序執行；	➢ is it discovered that testing for viral markers has not been carried out according to agreed procedures;
➢ 捐血者已罹有由某種病原體引起的傳染病，該等病原體(B 型肝炎、C 型肝炎、A 型肝炎及其他非 A 型、非 B 型、非 C 型等肝炎病毒、後天人類免疫缺乏病毒第 I 和第 II 型，及依現今知識已知的其他病原體) 可能藉由自血漿衍生的產品傳染；	➢ the donor has developed an infectious disease caused by an agent potentially transmissible by plasma-derived products (HBV, HCV, HAV and other non-A, non-B, non-C hepatitis viruses, HIV 1 and 2 and other agents in the light of current knowledge);
➢ 捐血者罹有庫賈氏症(CJD or vCJD)疾病；	➢ the donor develops Creutzfeldt-Jakob disease (CJD or vCJD);
➢ 血液或成分血的受血者發生輸血/輸注後的感染，且該感染牽涉或可追溯至該捐血者。	➢ the recipient of blood or a blood component develops post-transfusion /infusion infection which implicates or can be traced back to the donor.

在上述任何一種狀況發生時所應依循之程序，應列入標準作業程序中。回溯作業應包括追溯到最近一次陰性捐血前至少六個月之捐血紀錄。如果發生上述任何一種狀況時，則應毫無例外地執行批次文件的再評估。執行該批次撤回之必要性，應就所涉及的傳染病原體、合併量的大小、捐血與血清陽轉期間之時間、產品本質及其製造方法等因素謹慎考量。捐入合併血漿的捐血有受到後天人類免疫缺乏病毒，或 A、B 或 C 型肝炎病毒感染的跡象時，應將該情況提報許可該藥品之相關主管機關；關於自該牽連之合併血漿繼續製造或撤回該產品的可能性，亦應提出公司的觀點。	The procedures to be followed in the event of any of the above should be documented in the standard operating procedure. Look-back should consist of tracing back of previous donations for at least six months prior to the last negative donation. In the event of any of the above, a re-assessment of the batch documentation should always be carried out. The need for withdrawal of the given batch should be carefully considered, taking into account criteria such as the transmissible agent involved, the size of the pool, the time period between donation and seroconversion, the nature of the product and its manufacturing method. Where there are indications that a donation contributing to a plasma pool was infected with HIV or hepatitis A, B or C, the case should be referred to the relevant competent authority(ies) responsible for the authorization of the medicinal product and the company's view regarding continued manufacture from the implicated pool or of the possibility of withdrawal of the product(s) should be given.
生產及品質管制（PRODUCTION AND QUALITY CONTROL）	
16. 任何血液及血漿捐贈品或從其衍生之任何製品，其放行以供配送及/或分離前，應對下列特定傳染病的病原體標記，使用具有適當靈敏度及專一性，並經已確效的檢驗方法予以檢驗：	16. Before any blood and plasma donations, or any product derived there from are released for issue and/or fractionation, they should be tested, using a validated test method of suitable sensitivity and specificity, for the following markers of specific disease-transmitting agents:
➢ B 型肝炎病毒表面抗原(HBsAg)；	➢ HBsAg;
➢ 後天人類免疫缺乏病毒第 I 及第 II 型的抗體；	➢ Antibodies to HIV 1 and HIV 2;
➢ C 型肝炎病毒的抗體；	➢ Antibodies to HCV.
任何上述檢測中，發現任一重覆陽性的結果時，則不可接受該捐血。 (可於國家要求中另外追加檢測項目)	If a repeat-reactive result is found in any of these tests, the donation is not acceptable. (Additional tests may form part of national requirements).

17. 血液、血漿及半製品/中間產品之儲存場所，及從收集機構到製造廠，或不同製造場所間之運輸，其規定的儲存溫度應予以檢查並確效。這亦適用於該產品的運送。	17. The specified storage temperatures of blood, plasma and intermediate products when stored and during transportation from collection establishments to manufacturers, or between different manufacturing sites, should be checked and validated. The same applies to delivery of these products.
18. 初始之均質性合併血漿(例如：冷凍沉澱物分離後)，應使用經確效且具適當靈敏度及專一性之方法檢測，且對下列特定傳染病之病原體標記應呈陰性反應：	18. The first homogeneous plasma pool (e.g. after separation of the cryoprecipitate) should be tested using a validated test method, of suitable sensitivity and specificity, and found non reactive for the following markers of specific disease-transmitting agents:
➢ B 型肝炎病毒表面抗原（HBsAg）；	➢ HBsAg;
➢ 後天人類免疫缺乏病毒第 I 及第 II 型的抗體；	➢ Antibodies to HIV 1 and HIV 2;
➢ C 型肝炎病毒的抗體。	➢ Antibodies to HCV.
檢測結果經確認為陽性反應的合併血漿應予以拒用。	Confirmed positive pools must be rejected.
19. 由合併血漿所衍生的批次產品，必須使用具有適當靈敏度及專一性，且經確效的核酸擴增技術(NAT)檢測方法，檢測 C 型肝炎病毒 RNA 之結果為陰性，始可放行。	19. Only batches derived from plasma pools tested and found non-reactive for HCV RNA by nucleic acid amplification technology (NAT), using a validated test method of suitable sensitivity and specificity, should be released.
20. 病毒或其他傳染性病原體的檢測要求，應參照有關傳染性病原體的最新知識及適當可行的檢測方法。	20. Testing requirements for viruses, or other infectious agents, should be considered in the light of knowledge emerging as to infectious agents and the availability of appropriate test methods.
21. 儲存以供合併及分離之單一血漿袋的標籤，應符合相關藥典「人類血漿原料」個論的規定，且至少應載有捐血者之識別碼、收集機構的名稱及地址或負責製備之輸血服務機構的參考資料、容器批號、儲存溫度、血漿總體積或總重量、使用之抗凝血劑類型及收集及/或分離之日期等。	21. The labels on single units of plasma stored for pooling and fractionation must comply with the provisions of the European Pharmacopoeia (or other relevant pharmacopoeias) monograph "Human plasma for fractionation" and bear at least the identification number of the donation, the name and address of the collection establishment or the references of the blood transfusion service responsible for preparation, the batch number of the

	container, the storage temperature, the total volume or weight of plasma, the type of anticoagulant used and the date of collection and/or separation.
22. 為使血漿原料受到微生物學上或是外來異物之污染減到最低，血漿的解凍及合併應至少在 D 級潔淨區中執行，且操作者須穿著適當的服裝及戴上面罩及手套。用於打開血袋、合併及解凍的方法應定期予以監測，例如執行負荷菌之測試。所有其他開放性操作之工作室的潔淨度要求，應符合 PIC/S GMP 指引之附則 1。	22. In order to minimise the microbiological contamination of plasma for fractionation or the introduction of foreign material, the thawing and pooling should be performed at least in a grade D clean area, wearing the appropriate clothing and in addition face masks and gloves should be worn. Methods used for opening bags, pooling and thawing should be regularly monitored, e.g. by testing for bioburden. The cleanroom requirements for all other open manipulations should conform to the requirements of Annex 1 of the PIC/S guide to GMP.
23. 應建立適當方法以清楚區別業經與未經病毒去除或去活化過程的產品或半製品/中間產品。	23. Methods for clearly distinguishing between products or intermediates which have undergone a process of virus removal or inactivation, from those which have not, should be in place.
24. 病毒去除或病毒去活化方法之確效，不得在生產設施中執行，以避免例行製造受到確效所使用病毒污染之風險。	24. Validation of methods used for virus removal or virus inactivation should not be conducted in the production facilities in order not to put the routine manufacture at any risk of contamination with the viruses used for validation.
檢體的留存（RETENTION OF SAMPLES）	
25. 收集機構應負責將捐血的檢體盡可能地個別儲存，以利任何必要的回溯程序。每個合併血漿的檢體，應儲存在適當條件下，並至少保存至最長架儲期之最終產品末效日期後一年。	25. Where possible, samples of individual donations should be stored to facilitate any necessary look-back procedure. This would normally be the responsibility of the collection establishment. Samples of each pool of plasma should be stored under suitable conditions for at least one year after the expiry date of the finished product with the longest shelf-life.
拒用血液、血漿或半製品/中間產品的處置（DISPOSAL OF REJECTED BLOOD, PLASMA OR INTERMEDIATES）	

26. 應建立安全及有效處置血液、血漿或半製品/中間產品的標準作業程序。	26. There should be a standard operating procedure for the safe and effective disposal of blood, plasma or intermediates.

附則 15 驗證及確效（QUALIFICATION AND VALIDATION）

原則（PRINCIPLE）	
1. 本附則係說明適用於藥品製造之驗證與確效的原則。藥廠應辨識其所需執行之確效作業，以證明其特別操作之關鍵面的管制是 GMP 的要求。會影響產品品質的設施、設備及製程之重大變更，應進行確效。應使用風險評估方法以確定其確效的範圍與程度。	1. This Annex describes the principles of qualification and validation which are applicable to the manufacture of medicinal products. It is a requirement of GMP that manufacturers identify what validation work is needed to prove control of the critical aspects of their particular operations. Significant changes to the facilities, the equipment and the processes, which may affect the quality of the product, should be validated. A risk assessment approach should be used to determine the scope and extent of validation.
確效之規劃（PLANNING FOR VALIDATION）	
2. 所有確效活動均應予以規劃。確效計畫的關鍵因素應在確效主計畫書或在等同的文件中清楚界定並文件化。	2. All validation activities should be planned. The key elements of a validation programme should be clearly defined and documented in a validation master plan (VMP) or equivalent documents.
3. 確效主計畫書，應是一個簡短、簡明且清楚的摘要文件。	3. The VMP should be a summary document which is brief, concise and clear.
4. 確效主計畫書應包含至少下列資料：	4. The VMP should contain data on at least the following:
a) 確效策略；	a) validation policy;
b) 確效活動的組織架構；	b) organizational structure of validation activities;
c) 所需確效的設施、系統、設備與製程的摘要；	c) summary of facilities, systems, equipment and processes to be validated;
d) 文件格式：計畫書及報告使用的格式；	d) documentation format: the format to be used for protocols and reports;
e) 規劃及時程安排；	e) planning and scheduling;
f) 變更管制；	f) change control;
g) 參照現有文件。	g) reference to existing documents.
5. 如為大型計畫，可能需建立個別的確效主計畫書。	5. In case of large projects, it may be necessary to create separate validation master plans.
文件（DOCUMENTATION）	

6. 應建立書面計畫書，規定將如何執行驗證及確效。該計畫書應經審查及核准，並載明其關鍵步驟及允收標準。	6. A written protocol should be established that specifies how qualification and validation will be conducted. The protocol should be reviewed and approved. The protocol should specify critical steps and acceptance criteria.
7. 應制作交互參照之驗證及/或確效計畫書之報告，摘述取得的結果、評論觀察到之任何偏差及研擬必要的結論，包含為矯正缺失所需之變更的建議。對計畫書中已界定之計畫的任何變更，應備有其正當理由予以文件化。	7. A report that cross-references the qualification and/or validation protocol should be prepared, summarising the results obtained, commenting on any deviations observed, and drawing the necessary conclusions, including recommending changes necessary to correct deficiencies. Any changes to the plan as defined in the protocol should be documented with appropriate justification.
8. 完成滿意之驗證後，應以書面授權作成正式之放行，供下一步驟之驗證及確效。	8. After completion of a satisfactory qualification, a formal release for the next step in qualification and validation should be made as a written authorisation.
驗證（QUALIFICATION）	
設計驗證（Design qualification）	
9. 新的廠房設施、系統或設備之確效的首要要件可能是設計驗證(DQ)。	9. The first element of the validation of new facilities, systems or equipment could be design qualification (DQ).
10. 設計與 GMP 之相符性應予以證明並文件化。	10. The compliance of the design with GMP should be demonstrated and documented.
安裝驗證（Installation qualification）	
11. 新的或修改過之廠房設施、系統及設備應執行安裝驗證(IQ)。	11. Installation qualification (IQ) should be performed on new or modified facilities, systems and equipment.
12. 安裝驗證應包括，但不侷限於下列各項：	12. IQ should include, but not be limited to the following:
a) 設備、管路、支援設施及儀器裝置之安裝與現行工程圖及其規格的核對；	a) installation of equipment, piping, services and instrumentation checked to current engineering drawings and specifications;

b) 供應商之操作、工作說明書以及維護保養要求的收集與校對；	b) collection and collation of supplier operating and working instructions and maintenance requirements;
c) 校正要求；	c) calibration requirements;
d) 建造材質的確認。	d) verification of materials of construction.
操作驗證（Operational qualification）	
13. 操作驗證(OQ)應接續在安裝驗證後。	13. Operational qualification (OQ) should follow Installation qualification.
14. 操作驗證應包括，但不侷限於下列各項：	14. OQ should include, but not be limited to the following:
a) 從對製程、系統及設備的瞭解所開發的測試；	a) tests that have been developed from knowledge of processes, systems and equipment;
b) 包括操作上下限的一個條件或一組條件的測試，有時稱為「最差狀況」條件。	b) tests to include a condition or a set of conditions encompassing upper and lower operating limits, sometimes referred to as “worst case” conditions.
15. 成功之操作驗證應完成校正、操作及清潔程序、操作人員訓練及預防保養的要求。該驗證應容許廠房設施、系統及設備之正式「放行」。	15. The completion of a successful Operational qualification should allow the finalisation of calibration, operating and cleaning procedures, operator training and preventative maintenance requirements. It should permit a formal "release" of the facilities, systems and equipment.
性能驗證（Performance qualification）	
16. 性能驗證(PQ)應接續在成功的安裝驗證及操作驗證後。	16. Performance qualification (PQ) should follow successful completion of Installation qualification and Operational qualification.
17. 性能驗證應包括，但不侷限於下列各項：	17. PQ should include, but not be limited to the following:
a) 運用對製程、廠房設施、系統或設備的知識，使用生產原物料、合格替代品或模擬產品所開發出的測試；	a) tests, using production materials, qualified substitutes or simulated product, that have been developed from knowledge of the process and the facilities, systems or equipment;
b) 涵蓋操作上下限的一個條件或是一組條件的測試。	b) tests to include a condition or set of conditions encompassing upper and lower operating limits.

18. 雖然性能驗證(PQ)被描述為個別的作業活動，但在某些情況可能適合與操作驗證(OQ)一起執行。	18. Although PQ is described as a separate activity, it may in some cases be appropriate to perform it in conjunction with OQ.
既有(使用中)廠房設施、系統及設備的驗證（Qualification of established (in-use) facilities, systems and equipment）	
19. 應有證據支持及證實設備之操作參數與重要變數的極限。另，校正、清潔、預防保養、操作程序、操作者訓練程序及紀錄，應予以文件化。	19. Evidence should be available to support and verify the operating parameters and limits for the critical variables of the operating equipment. Additionally, the calibration, cleaning, preventative maintenance, operating procedures and operator training procedures and records should be documented.
製程確效（PROCESS VALIDATION）	
概述（General）	
20. 本章中所概述之要求與原則適用於藥品劑型的製造。這涵蓋新製程的初始確效、修改製程之後續確效及再確效。	20. The requirements and principles outlined in this chapter are applicable to the manufacture of pharmaceutical dosage forms. They cover the initial validation of new processes, subsequent validation of modified processes and revalidation.
21. 製程確效通常應在藥品運銷與販售前完成(先期性確效)。在例外情形，先期性確效不可行時，在例行生產中執行製程確效可能是需要的(併行性確效)。製程在執行一段時間後亦應予以確效(回溯性確效)。	21. Process validation should normally be completed prior to the distribution and sale of the medicinal product (prospective validation). In exceptional circumstances, where this is not possible, it may be necessary to validate processes during routine production (concurrent validation). Processes in use for some time should also be validated (retrospective validation).
22. 使用之廠房設施、系統及設備應完成驗證，且分析檢驗的方法應經確效。參與該確效工作的員工應已完成適當的訓練。	22. Facilities, systems and equipment to be used should have been qualified and analytical testing methods should be validated. Staff taking part in the validation work should have been appropriately trained.
23. 廠房設施、系統、設備及製程應定期評估，以確認其仍在確效狀態下持續運轉。	23. Facilities, systems, equipment and processes should be periodically evaluated to verify that they are still operating in a valid manner.

先期性確效（Prospective validation）	
24. 先期性確效應包括，但不侷限於下列各項：	24. Prospective validation should include, but not be limited to the following:
(a) 製程的簡要描述；	(a) short description of the process;
(b) 調查之關鍵性製程步驟的摘要；	(b) summary of the critical processing steps to be investigated;
(c) 使用之設備/廠房設施(包括測量/監測/記錄設備)及其校正狀態的清單；	(c) list of the equipment/facilities to be used (including measuring / monitoring / recording equipment) together with its calibration status
(d) 供放行用之最終產品的規格；	(d) finished product specifications for release;
(e) 合適時，分析方法的清單；	(e) list of analytical methods, as appropriate;
(f) 建議之製程中管制及其允收標準；	(f) proposed in-process controls with acceptance criteria;
(g) 合適時，執行之追加試驗，連同其允收標準及分析確效；	(g) additional testing to be carried out, with acceptance criteria and analytical validation, as appropriate;
(h) 抽樣計畫；	(h) sampling plan;
(i) 記錄及評估結果的方法；	(i) methods for recording and evaluating results
(j) 功能及職責；	(j) functions and responsibilities;
(k) 建議的時程表。	(k) proposed timetable.
25. 使用本界定的製程(包括特定的組成物)，可能可以在例行條件下生產一系列批次之最終產品。理論上，製程的操作次數及所做之觀察，應足以提供所要建立之變異與趨勢的正常範圍，並提供足夠的數據，以供評估。三個連續批次/操作在最終同意的參數內，構成該製程的確效，通常被認為是可接受的。	25. Using this defined process (including specified components) a series of batches of the final product may be produced under routine conditions. In theory the number of process runs carried out and observations made should be sufficient to allow the normal extent of variation and trends to be established and to provide sufficient data for evaluation. It is generally considered acceptable that three consecutive batches/runs within the finally agreed parameters, would constitute a validation of the process.
26. 供製程確效而製造的批次，應與預定之工業量產規模批次的批量相同。	26. Batches made for process validation should be the same size as the intended industrial scale batches.

27. 預定將確效批次販售或供應者，其生產條件應完全符合優良製造準則的要求，包括確效操作的滿意結果在內，以及可行時，符合上市許可之要求。	27. If it is intended that validation batches be sold or supplied, the conditions under which they are produced should comply fully with the requirements of Good Manufacturing Practice, including the satisfactory outcome of the validation exercise, and (where applicable) the marketing authorisation.
併行性確效（Concurrent validation）	
28. 例外的情形，未在例行生產前完成確效計畫，是可接受的。	28. In exceptional circumstances it may be acceptable not to complete a validation programme before routine production starts.
29. 執行併行性確效的決定，應證明其合理性，並予以文件化，且需經被授權人員核准。	29. The decision to carry out concurrent validation must be justified, documented and approved by authorised personnel.
30. 併行性確效的文件要求，與先期性確效的規定相同。	30. Documentation requirements for concurrent validation are the same as specified for prospective validation.
回溯性確效（Retrospective validation）	
31. 回溯性確效，僅對完善既定的製程才可接受。產品組成、操作程序或設備有新近變更時，則不適合採用回溯性確效。	31. Retrospective validation is only acceptable for well-established processes and will be inappropriate where there have been recent changes in the composition of the product, operating procedures or equipment.
32. 這些製程的確效應以歷史數據為基礎。所涉及的確效步驟需制定特定的計畫書及提報數據審查結果，以獲得結論及建議。	32. Validation of such processes should be based on historical data. The steps involved require the preparation of a specific protocol and the reporting of the results of the data review, leading to a conclusion and a recommendation.
33. 確效數據的來源應包括，但不侷限於批次製造與分/包裝紀錄、製程管制圖表、維修保養日誌、人員更換紀錄、製程能力研究及包含其趨勢圖表與儲存安定性的結果之最終產品數據。	33. The source of data for this validation should include, but not be limited to batch processing and packaging records, process control charts, maintenance log books, records of personnel changes, process capability studies, finished product data, including trend cards and storage stability results.

34. 選擇供回溯性確效的批次，應為審查期間生產的所有代表批次，包括不符合規格之任何批次在內，且應有足夠的批次數目，以證明製程的一致性。必要時，以留樣品來做追加試驗，以獲得對回溯性製程確效所需數據的數量或類型。	34. 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. Additional testing of retained samples may be needed to obtain the necessary amount or type of data to retrospectively validate the process.
35. 回溯性確效，通常應檢查取自 10 至 30 個連續批次的資料，以評估製程的一致性。有正當理由者，亦可檢查較少的批次。	35. For retrospective validation, generally data from ten to thirty consecutive batches should be examined to assess process consistency, but fewer batches may be examined if justified.
清潔確效（CLEANING VALIDATION）	
36. 為確認清潔程序的有效性，應執行清潔確效。選定產品殘留物、清潔劑及微生物污染之移轉限量(limits of carry over)的理論依據，邏輯上應以涉及的物質為基礎。該限量應為可達成且是可確認的。	36. Cleaning validation should be performed in order to confirm the effectiveness of a cleaning procedure. The rationale for selecting limits of carry over of product residues, cleaning agents and microbial contamination should be logically based on the materials involved. The limits should be achievable and verifiable.
37. 應使用對殘留物或污染物具靈敏度之經確效的分析方法。每種分析方法之最低檢測濃度，應足夠靈敏以檢測殘留物或污染物之既定允收標準。	37. 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.
38. 通常，僅對設備之產品接觸表面的清潔程序才需要確效，未與產品接觸的部分亦應予以考量。對於製造設備在使用與清潔間，以及在清潔與再使用間之時間間隔應予以確效。清潔的時間間隔與方法應予以確定。	38. Normally only cleaning procedures for product contact surfaces of the equipment need to be validated. Consideration should be given to non-contact parts. The intervals between use and cleaning as well as cleaning and reuse should be validated. Cleaning intervals and methods should be determined.

39. 對類似產品及製程的清潔程序，選擇類似產品與製程之代表性的範圍是可接受的。利用「最差狀況」作法，得執行單一確效試驗，該最差狀況應考量清潔程序之關鍵問題。	39. For cleaning procedures for products and processes which are similar, it is considered acceptable to select a representative range of similar products and processes. A single validation study utilizing a "worst case" approach can be carried out which takes account of the critical issues.
40. 為證明清潔方法係經確效，典型上，應執行該清潔程序連續三次，並顯示其成功。	40. Typically three consecutive applications of the cleaning procedure should be performed and shown to be successful in order to prove that the method is validated.
41. 「測試直到潔淨」不被認為是清潔確效之適當替代方法。	41. "Test until clean" is not considered an appropriate alternative to cleaning validation.
42. 欲移除的物質具劇毒或危害性時，得例外以模擬欲移除物之物化特性的產品取代。	42. Products which simulate the physicochemical properties of the substances to be removed may exceptionally be used instead of the substances themselves, where such substances are either toxic or hazardous.
變更管制（CHANGE CONTROL）	
43. 對原料、產品組成物、製程設備、製程環境(或場所)、生產或測試方法的變更，或對任何其他可能影響產品品質或製程之再現性的變更提出時，應備有書面程序描述要採取的措施。變更管制程序應確保產生足夠的支持數據，證明修正的製程可產生與核准規格一致之預期品質的產品。	43. Written procedures should be in place to describe the actions to be taken if a change is proposed to a starting material, product component, process equipment, process environment (or site), method of production or testing or any other change that may affect product quality or reproducibility of the process. Change control procedures should ensure that sufficient supporting data are generated to demonstrate that the revised process will result in a product of the desired quality, consistent with the approved specifications.

44. 可能影響產品品質或製程再現性的所有變更應提出正式申請、文件化並經核准。廠房設施、系統及設備的變更對產品可能之影響應予以評估，包括風險分析。再驗證及再確效的需求及範圍應予以決定。	44. All changes that may affect product quality or reproducibility of the process should be formally requested, documented and accepted. The likely impact of the change of facilities, systems and equipment on the product should be evaluated, including risk analysis. The need for, and the extent of re-qualification and re-validation should be determined.
再確效（REVALIDATION）	
45. 廠房設施、系統、設備及製程，包括清潔，均應定期評估，以確認其仍然有效。確效狀態無重大變更時，審核廠房設施、系統、設備及製程均符合規定之證據，即已滿足再確效要件。	45. Facilities, systems, equipment and processes, including cleaning, should be periodically evaluated to confirm that they remain valid. Where no significant changes have been made to the validated status, a review with evidence that facilities, systems, equipment and processes meet the prescribed requirements fulfils the need for revalidation.
術語彙編（GLOSSARY）	
與驗證及確效有關之術語的定義，在現行 PIC/S GMP 指引的術語彙編中未規定，而在本附則中使用者，規定如下：	Definitions of terms relating to qualification and validation which are not given in the glossary of the current PIC/S Guide to GMP, but which are used in this Annex, are given below.
變更管制 *變更管制是一個正式系統。在該系統下，由具有適當學識與經驗之合格代表人員，審核可能影響廠房設施、系統、設備或製程等確效狀態之擬提的或實際的變更。其目的在於決定所需採取之行動，以確保並文件化該系統是維持在已確效的狀態。*	***Change Control*** *A formal system by which qualified representatives of appropriate disciplines review proposed or actual changes that might affect the validated status of facilities, systems, equipment or processes. The intent is to determine the need for action that would ensure and document that the system is maintained in a validated state.*
清潔確效 *清潔確效是經文件化的證據，證明經核准的清潔程序將提供適合於藥品製造之潔淨程度的設備。*	***Cleaning Validation*** *Cleaning validation is documented evidence that an approved cleaning procedure will provide equipment which is suitable for processing medicinal products.*

併行性確效 *預定供販售產品之例行生產所執行的確效。*	***Concurrent Validation*** *Validation carried out during routine production of products intended for sale.*
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)*** *The documented verification that the proposed design of the facilities, systems and equipment is suitable for the intended purpose.*
安裝驗證 (IQ) *廠房設施、系統及設備經安裝或修改時，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)*** *The documented verification that the facilities, systems and equipment, as installed or modified, comply with the approved design and the manufacturer's recommendations.*
操作驗證 (OQ) *廠房設施、系統及設備經安裝或修改時，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)*** *The documented verification that the facilities, systems and equipment, 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，與廠房設施、系統及設備連結，能有效執行並具再現性之文件化的確認作業。*	***Performance Qualification (PQ)*** *The documented verification that the facilities, systems and equipment, as connected together, can perform effectively and reproducibly, based on the approved process method and product specification.*
製程確效 *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藥品之文件化的證據。*	***Process Validation*** *The documented evidence that the process, operated within established parameters, can perform effectively and reproducibly to produce a medicinal product meeting its predetermined specifications and quality attributes.*
先期性確效 *例行生產預定販售之產品前所執行的確效。*	***Prospective Validation*** *Validation carried out before routine production of products intended for sale.*
回溯性確效 *已上市的產品，以其累積的製造、檢驗及管制之批次數據為基礎的製程確效。*	***Retrospective Validation*** *Validation of a process for a product which has been marketed based upon accumulated manufacturing, testing and control batch data.*
再確效 *製程確效之重複執行，用以確保依變更管制程序導入之製程/設備的變更，對製程特性與產品品質無不利之影響。*	***Re-Validation*** *A repeat of the process validation to provide an assurance that changes in the process/equipment introduced in accordance with change control procedures do not adversely affect process characteristics and*

	product quality.
風險分析 *用以評估及描述一種設備或製程之功能性的關鍵參數之特性的方法。*	***Risk analysis*** *Method to assess and characterise the critical parameters in the functionality of an equipment or process.*
模擬產品 *一種與確效中產品之物理及化學的(可行時)特性(例如黏度、粒子大小、pH 值等)非常接近的物質。在許多情形，這些特性可藉由空白產品(placebo product)批次予以滿足。*	***Simulated Product*** *A material that closely approximates the physical and, where practical, the chemical characteristics (e.g. viscosity, particle size, pH etc.) of the product under validation. In many cases, these characteristics may be satisfied by a placebo product batch.*
系統 *為一組具有共同目的之設備。*	***System*** *A group of equipment with a common purpose.*
最差狀況 *一個或一套條件，包含在標準作業程序內之上限及下限作業極限及環境，當其與理想條件相比，有最大之產品或製程失敗的機會，然該條件未必引起產品或製程之失敗。*	***Worst Case*** *A condition or set of conditions encompassing upper and lower processing limits and circumstances, within standard operating procedures, which pose the greatest chance of product or process failure when compared to ideal conditions. Such conditions do not necessarily induce product or process failure.*

附則 19 對照樣品與留存樣品（REFERENCE AND RETENTION SAMPLES）

1. 範圍（SCOPE）	
1.1 藥品 GMP 指引（本指引）之本附則規定關於原料、包裝材料或最終產品之對照樣品，以及最終產品之留存樣品的取樣與保存的指導。	1.1 This Annex to the Guide to Good Manufacturing Practice for Medicinal Products ("the GMP Guide") gives guidance on the taking and holding of reference samples of starting materials, packaging materials or finished products and retention samples of finished products.
1.2 關於研究用藥品之特別要求規定於本指引的附則 13。	1.2 Specific requirements for investigational medicinal products are given in Annex 13 to the Guide.
1.3 本附則亦包含關於平行輸入/運銷藥品的留存樣品之取樣指導。	1.3 This annex also includes guidance on the taking of retention samples for parallel imported / distributed medicinal products.
2.原則（PRINCIPLE）	
2.1 樣品的留存是為了達成兩個目的：第一，為提供分析測試的樣品，第二，為提供完整最終產品的樣本。因此，樣品可以歸納成兩個類別：	2.1 Samples are retained to fulfil two purposes; firstly to provide a sample for analytical testing and secondly to provide a specimen of the fully finished product. Samples may therefore fall into two categories:
對照樣品（Reference sample）：在相關批次之架儲期間中倘若發生分析需要時，為分析目的而儲存之一個批次的原料、包裝材料或最終產品的樣品。	Reference sample: a sample of a batch of starting material, packaging material or finished product which is stored for the purpose of being analyzed should the need arise during the shelf life of the batch concerned.
在安定性允許時，應保存來自關鍵中間階段（例如需要分析測試與放行）的對照樣品，或運送到製造者控管外之中間產品的對照樣品。	Where stability permits, reference samples from critical intermediate stages (e.g. those requiring analytical testing and release) or intermediates that are transported outside of the manufacturer's control should be kept.
留存樣品（Retention sample）：來自一個批次之最終產品的完整包裝單元之樣品。這是為識別目的而儲存。例如，在相關批次之架儲期間中倘若發生需要時，用以辨識其外觀、包裝、標示、病人用說明書、批號、末效日期等。	Retention sample: a sample of a fully packaged unit from a batch of finished product. It is stored for identification purposes. For example, presentation, packaging, labelling, patient information leaflet, batch number, expiry date should the need arise during the shelf life of the batch concerned.
可能有例外情形，即使未留存完全相同的樣	There may be exceptional circumstances where

品亦能符合本要求。例如，為不同市場，包裝一個批次中之小數量或製造極為昂貴之藥品。	this requirement can be met without retention of duplicate samples e.g. where small amounts of a batch are packaged for different markets or in the production of very expensive medicinal products.
在許多情況中，最終產品之對照樣品與留存樣品會以完全相同的，亦即，以完整包裝單元的型態呈現。在此種情形中，對照樣品及留存樣品可視為得以互換。	For finished products, in many instances the reference and retention samples will be presented identically, i.e. as fully packaged units. In such circumstances, reference and retention samples may be regarded as interchangeable.
2.2 依第 7 與 8 節之規定，製造者、輸入者或批次放行者必須保存來自每批次之最終產品的對照及/或留存樣品；製造者並必須保存來自一個批次之原料（會有某些例外，參見下面 3.2 節）及/或中間產品的對照樣品。包裝廠應保存每批次之直接包裝材料及業經印刷之包裝材料的對照樣品。	2.2 It is necessary for the manufacturer, importer or site of batch release, as specified under section 7 and 8, to keep reference and/or retention samples from each batch of finished product and, for the manufacturer to keep a reference sample from a batch of starting material (subject to certain exceptions – see 3.2 below) and/or intermediate product. Each packaging site should keep reference samples of each batch of primary and printed packaging materials.
印刷之包裝材料作為最終產品之對照及/或留存樣品的一部分是可接受的。	Availability of printed materials as part of the reference and/or retention sample of the finished product can be accepted.
2.3 對照樣品及/或留存樣品可作為最終產品或原料批次的紀錄，例如當有劑型品質申訴、有關上市許可符合性的質疑、標示/包裝的質疑或藥品監視報告等情形時，可據以評定。	2.3 The reference and/or retention samples serve as a record of the batch of finished product or starting material and can be assessed in the event of, for example, a dosage form quality complaint, a query relating to compliance with the marketing authorization, a labelling/packaging query or a pharmacovigilance report.
2.4 樣品之可追溯性的紀錄應予以保存，並可供主管機關審閱。	2.4 Records of traceability of samples should be maintained and be available for review by competent authorities.
3.儲存期間（DURATION OF STORAGE）	

3.1 來自每一最終產品批次的對照樣品與留存樣品應保存至末效日期後至少一年。該對照樣品應裝在其最終直接包裝中或在與其上市產品直接容器相同材質所組成的包裝中【對於免疫製劑之外的動物用藥品，參見附則 4，第 8 及 9 段落】。	3.1 Reference and retention samples from each batch of finished product should be retained for at least one year after the expiry date. The reference sample should be contained in its finished primary packaging or in packaging composed of the same material as the primary container in which the product is marketed (for veterinary medicinal products other than immunologicals, see also Annex 4, paragraphs 8 & 9).
3.2 除非製造國（其主管機關是 PIC/S 會員）的法律要求一段較長的期間，原料樣品（製程中使用的溶劑、氣體或水除外），應保存至產品放行後至少兩年。依相關規格之記載原料之安定性期間較短者，該期間得以縮短。	3.2 Unless a longer period is required under the law of the country of manufacture (whose competent authority is a PIC/S Member), samples of starting materials (other than solvents, gases or water used in the manufacturing process) shall be retained for at least two years after the release of product. That period may be shortened if the period of stability of the material, as indicated in the relevant specification, is shorter.
包裝材料應保存至相關最終產品之架儲期間屆滿。	Packaging materials should be retained for the duration of the shelf life of the finished product concerned.
4.對照樣品與留存樣品的量（SIZE OF REFERENCE AND RETENTION SAMPLES）	
4.1 對照樣品應有足夠數量，至少在兩種時機，可依照經相關主管機關評估與核准的上市許可檔案，對該批次從事全項分析對照（analytical controls）。	4.1 The reference sample should be of sufficient size to permit the carrying out, on, at least, two occasions, of the full analytical controls on the batch in accordance with the Marketing Authorisation File which has been assessed and approved by the relevant Competent Authority / Authorities.
當需要這樣做時，在從事每套分析對照時，應使用沒有打開的包裝品。	Where it is necessary to do so, unopened packs should be used when carrying out each set of analytical controls.
對此要求提出的任何例外，皆應向相關主管機關證明其正當性，並為其同意。	Any proposed exception to this should be justified to, and agreed with, the relevant competent authority.
4.2 適用時，應遵循國家關於對照樣品之量的要求；必要時，留存樣品，亦同。	4.2 Where applicable, national requirements relating to the size of reference samples and, if necessary, retention samples, should be followed.

4.3 對照樣品對於從其抽樣之原料、中間產品或最終產品的批次應具有代表性。亦可以抽取其他樣品，用以監測製程中最易發生偏差的部份（例如，製程的起始與終端）。一個批次在兩個以上不同包裝作業包裝者，應從每一個個別包裝作業抽取至少一個留存樣品。對此要求建議之任何例外，應向相關主管機關證明其正當性並為其同意。	4.3 Reference samples should be representative of the batch of starting material, intermediate product or finished product from which they are taken. Other samples may also be taken to monitor the most stressed part of a process (e.g. beginning or end of a process). Where a batch is packaged in two, or more, distinct packaging operations, at least one retention sample should be taken from each individual packaging operation. Any proposed exception to this should be justified to, and agreed with, the relevant competent authority.
4.4 最後製造批次的末效期後一年內，可從事規格中規定之所有試驗，應確保所有必要的分析材料及設備仍然具備，或是容易獲得。	4.4 It should be ensured that all necessary analytical materials and equipment are still available, or are readily obtainable, in order to carry out all tests given in the specification until one year after expiry of the last batch manufactured.
5.儲存條件（STORAGE CONDITIONS）	
5.1 …	5.1…
5.2 儲存條件應依照上市許可規定（例如，視情形，以冷藏儲存）。	5.2 Storage conditions should be in accordance with the marketing authorisation (e.g. refrigerated storage where relevant)
6.書面協議（WRITTEN AGREEMENTS）	
6.1 上市許可之持有者與負責批次放行場所之法律主體不相同時，對照樣品/留存樣品之取樣及儲存的責任，應依照本指引第七章，在雙方的書面協議中界定。這也適用於，任何製造或批次放行活動非在對該批次負全部責任之場所從事的情形。且每個不同場所間關於對照樣品與留存樣品之抽取與保存的安排，應於書面協議中界定。	6.1 Where the marketing authorization holder is not the same legal entity as the site(s) responsible for batch release, the responsibility for taking and storage of reference/retention samples should be defined in a written agreement between the two parties in accordance with Chapter 7 of the PIC/S Guide to Good Manufacturing Practice. This applies also where any manufacturing or batch release activity is carried out at a site other than that with overall responsibility for the batch and the arrangements between each different site for the taking and keeping of reference and retention samples should be defined in a written agreement.

6.2 負責簽署放行一個批次供銷售之被授權人員，應確保能在所有合理的時間取得所有相關對照樣品與留存樣品。必要時，對於該取得之安排應以書面協議界定。	6.2 The Authorised Person who certifies a batch for sale should ensure that all relevant reference and retention samples are accessible at all reasonable times. Where necessary, the arrangements for such access should be defined in a written agreement.
6.3 最終產品之製造涉及一個以上廠區者，對於對照樣品與留存樣品之取用與存放位置的管制，備妥書面協議至關重要。	6.3 Where more than one site is involved in the manufacture of a finished product, the availability of written agreements is key to controlling the taking and location of reference and retention samples.
7.對照樣品－一般考量要點 （REFERENCE SAMPLES－ GENERAL POINTS）	
7.1 對照樣品是為了分析目的，因此，應可為具有確效方法之實驗室方便獲得。對使用於藥品之原料及包裝材料，是指最終產品之原製造場所。對於最終產品，是指原製造場所。	7.1 Reference samples are for the purpose of analysis and, therefore, should be conveniently available to a laboratory with validated methodology. For starting materials and packaging materials used for medicinal products, this is the original site of manufacture of the finished product. For finished products, this is the original site of manufacture.
8. 留存樣品－一般考量要點 （RETENTION SAMPLES－GENERAL POINTS）	
8.1 為確認非技術性屬性符合上市許可或國家法律，留存樣品應代表一個批次如其在運銷時之狀態的最終產品，並可能需要被檢查。留存樣品最好應儲存於負責簽署該最終產品批次之被授權人員所在的處所。	8.1 A retention sample should represent a batch of finished products as distributed and may need to be examined in order to confirm non-technical attributes for compliance with the marketing authorization or national legislation. The retention samples should preferably be stored at the site where the Authorised Person (AP) certifying the finished product batch is located.
8.2 …	8.2…
8.3 為使主管機關能隨時取得，留存樣品應儲存在被授權之製造者的廠房。	8.3 Retention samples should be stored at the premises of an authorised manufacturer in order to permit ready access by the Competent Authority.

8.4 當一個產品涉及一個以上的製造場所時，考量產品特性，製造/輸入/包裝/檢驗/批次放行其留存樣品之取用及儲存的責任，應界定於所涉各方間的書面協議中。	8.4 Where more than one manufacturing site is involved in the manufacture/importation/ packaging/testing/batch release, as appropriate of a product, the responsibility for taking and storage of retention samples should be defined in a written agreement(s) between the parties concerned.
9.平行輸入/平行運銷產品的對照樣品及留存樣品（ REFERENCE AND RETENTION SAMPLES FOR PARALLEL IMPORTED / PARALLEL DISTRIBUTED PRODUCTS）	
附註：本節僅在國家法律規範平行輸入/平行運銷之產品時適用。	Note: This section is only applicable if the national legislation deals with parallel imported / parallel distributed products.
9.1 未打開間接包裝時，因無或少有產品混雜的風險，只需要留存所使用的包裝材料。	9.1 Where the secondary packaging is not opened, only the packaging material used needs to be retained, as there is no, or little, risk of product mix up.
9.2 打開間接包裝時，例如，置換紙盒或病人用說明書時，因為在組裝過程中有產品混雜的風險，所以在每一包裝作業，應抽取一件含該產品之留存樣品。當有混雜發生時，能夠迅速識別誰應負責（原始製造者或是平行輸入組裝者）是重要的，因為這會影響任何衍生之回收程度。	9.2 Where the secondary packaging is opened, for example, to replace the carton or patient information leaflet, then one retention sample, per packaging operation, containing the product should be taken, as there is a risk of product mix-up during the assembly process. It is important to be able to identify quickly who is responsible in the event of a mix-up (original manufacturer or parallel import assembler), as it would affect the extent of any resulting recall.
10. 製造者關廠時之對照樣品及留存樣品（REFERENCE AND RETENTION SAMPLES IN THE CASE OF CLOSEDOWN OF A MANUFACTURER）	
10.1 製造者關廠，而讓與、吊銷或廢止其製造許可時，由該製造者製造之許多未屆效期批次之藥品可能還在市場上。為使該等批次繼續留在市場上，製造者應做出詳細的安排，將對照樣品及留存樣品（及相關的 GMP 文件）移轉到一個被授權的儲存場所。製造者應做到，使主管機關滿意該儲存的安排；必要時，該樣品並能夠易於取得及分析。	10.1 Where a manufacturer closes down and the manufacturing authorisation is surrendered, revoked, or ceases to exist, it is probable that many unexpired batches of medicinal products manufactured by that manufacturer remain on the market. In order for those batches to remain on the market, the manufacturer should make detailed arrangements for transfer of reference and retention samples (and relevant GMP documentation) to an authorised storage

	site. The manufacturer should satisfy the Competent Authority that the arrangements for storage are satisfactory and that the samples can, if necessary, be readily accessed and analysed.
10.2 製造者不能從事該必要安排者，得委任其他製造者。上市許可之持有者應負起對該委任及對主管機關提供所有必要資訊之責任。此外，有關提議之對照樣品與留存樣品的儲存安排之適當性，上市許可持有者應與任何未逾效期批次所在市場之每一國家的主管機關協商。	10.2 If the manufacturer is not in a position to make the necessary arrangements this may be delegated to another manufacturer. The Marketing Authorisation holder (MAH) is responsible for such delegation and for the provision of all necessary information to the Competent Authority. In addition, the MAH should, in relation to the suitability of the proposed arrangements for storage of reference and retention samples, consult with the competent authority of each country in which any unexpired batch has been placed on the market.

附則 20 品質風險管理（QUALITY RISK MANAGEMENT）

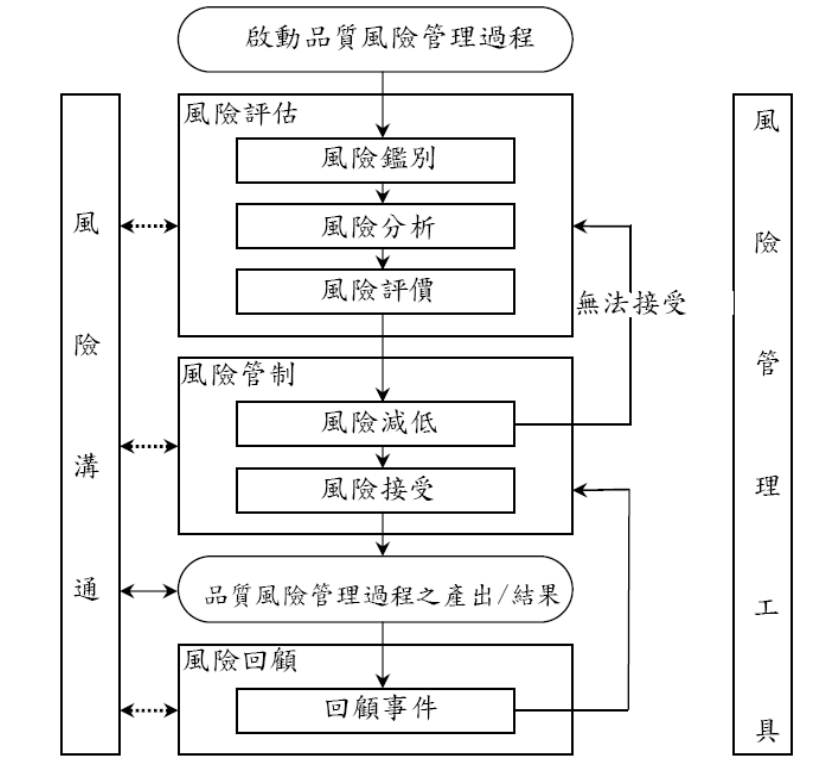
*本附則為自願性的/非強制性的。	* This Annex is voluntary.
序文和適用範圍 （FOREWORD AND SCOPE OF APPLICATION）	
1. 新的 GMP 附則 20 相當於 ICH Q9 關於品質風險管理的指引。它對於品質風險管理提供系統性方法之指引，以利遵守從 GMP 及其他品質之要求。當應用正式的品質風險管理方法時，它包括要使用之原理及可能使用之過程、方法和工具的選項。	1. The new GMP Annex 20 corresponds to ICH Q9 guideline on Quality Risk Management. It provides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

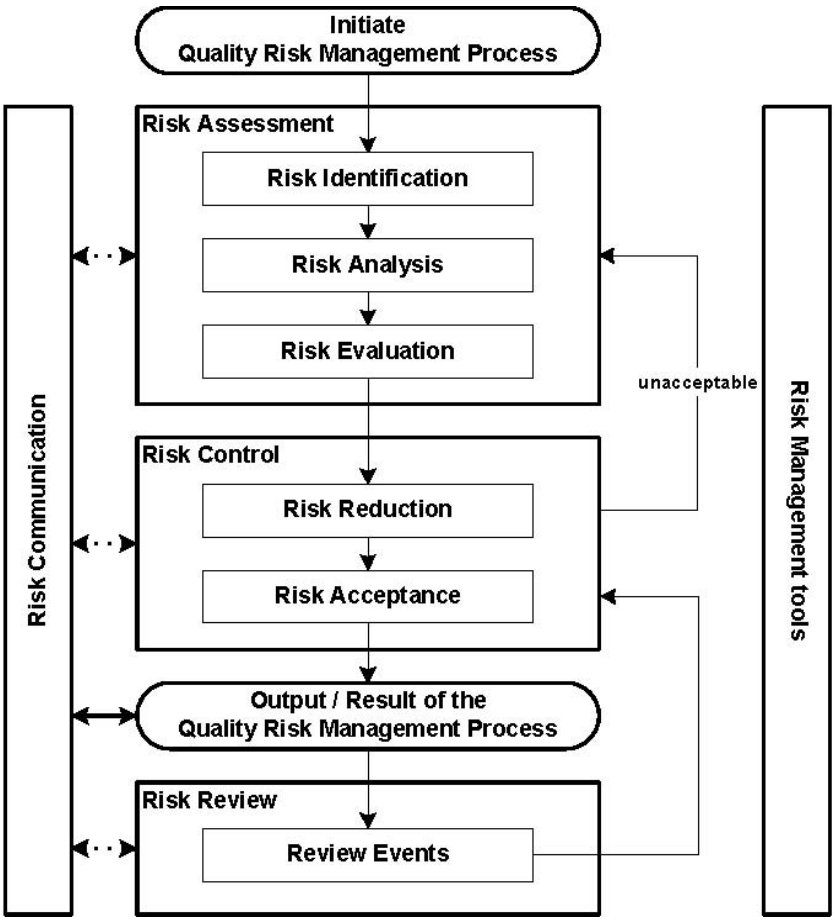
5. GMP 指引主要係針對製造廠，而 ICH Q9 指引則與其他品質指引具有關聯，並包括對主管機關之特定部門。	5. While the GMP guide is primarily addressed to manufacturers, the ICH Q9 guideline, has relevance for other quality guidelines and includes specific sections for regulatory agencies.
6. 然而，為了連貫性及完整性，已將 ICH Q9 指引完全轉為 GMP 附則 20。	6. However, for reasons of coherence and completeness, the ICH Q9 guideline has been transferred completely into GMP Annex 20.
1 前言（Introduction）	
7. 風險管理原則，除有效地被利用在包括財政、保險、職業安全、公共衛生、藥物監視在內之許多商業及政府的領域外，亦被管理這些產業的主管機關有效地利用。雖然目前在製藥產業有一些*品質風險管理*之使用的實例，但他們是有限的，而且尚未代表風險管理應提供之全部的貢獻。此外，製藥產業中已經認知品質系統的重要性，而且變得越來越明顯的是，品質風險管理是一個有效品質系統之重要構成要素。	7. *Risk management* principles are effectively utilized in many areas of business and government including finance, insurance, occupational safety, public health, pharmacovigilance, and by agencies regulating these industries. Although there are some examples of the use of *quality risk management* in the pharmaceutical industry today, they are limited and do not represent the full contributions that risk management has to offer. In addition, the importance of *quality systems* has been recognized in the pharmaceutical industry and it is becoming evident that quality risk management is a valuable component of an effective quality system.
8. 普遍瞭解的是，風險經界定為損害之發生機率及該損害之嚴重度的結合。然而，因為每一位利害關係人可能感受不同的潛在損害，可能將不同的機率置於每一損害的發生上，並且將不同的嚴重度歸屬於每一種損害上，所以在不同利害關係人（stakeholders）間難以達成風險管理之應用的共識。關於醫藥產品，雖然有各種不同的利害關係人，包含病人和執業醫師以及政府與產業在內，但經由品質風險管理以保護病人應被視為最重要。	8. It is commonly understood that *risk* is defined as the combination of the probability of occurrence of *harm* and the *severity* of that harm. However, achieving a shared understanding of the application of risk management among diverse *stakeholders* is difficult because each stakeholder might perceive different potential harms, place a different probability on each harm occurring and attribute different severities to each harm. In relation to pharmaceuticals, although there are a variety of stakeholders, including patients and medical practitioners as well as government and industry, the protection of the patient by managing the risk to quality should be considered of prime importance.

9. 藥品(醫藥製品)之製造及使用，包含其組成物在內，必定伴隨著若干程度的風險。其品質之風險只是其整體風險的一個構成部分而已。重要的是，要瞭解在產品的整個生命週期皆應維持產品品質，以將對於藥品(醫藥製品)之品質具有重要性的屬性，保持與臨床研究上所使用藥品的那些屬性一致。一個有效的品質風險管理方法，可以經由提供一個洞燭機先的方法，去確認和管制在開發及製造期間之潛在品質問題，以對病人進一步確保藥品的高度品質。此外，品質風險管理的使用，可以在品質問題發生時，改善其決策。有效的品質風險管理，可以幫助更好及具有更多情報的決策，可以就一個公司處理潛在風險的能力提供主管機關更大的保證，而且有利於影響主管機關監督的程度及等級。	9. The manufacturing and use of a drug (medicinal) product, including its components, necessarily entail some degree of risk. The risk to its quality is just one component of the overall risk. It is important to understand that product *quality* should be maintained throughout the *product lifecycle* such that the attributes that are important to the quality of the drug (medicinal) product remain consistent with those used in the clinical studies. An effective quality risk management approach can further ensure the high quality of the drug (medicinal) product to the patient by providing a proactive means to identify and control potential quality issues during development and manufacturing. Additionally, use of quality risk management can improve the decision making if a quality problem arises. Effective quality risk management can facilitate better and more informed decisions, can provide regulators with greater assurance of a company's ability to deal with potential risks and can beneficially affect the extent and level of direct regulatory oversight.
10. 本文件之目的是要對品質風險管理提供一個系統性的方法。它當作一個基礎文件或資源文件，獨立但支持其他 ICH 品質文件，並補充製藥產業及管制環境內既存的品管慣例、要求、標準及指引。它具體地提供關於品質風險管理原則及一些工具的指引。該指引能使主管機關及產業二者基於風險，對於跨越產品生命週期之藥物和醫藥產品的品質所作的決策更為有效且一致。它無意創造超過當前法規要求之任何新的期望。	10. The purpose of this document is to offer a systematic approach to quality risk management. It serves as a foundation or resource document that is independent of, yet supports, other ICH Quality documents and complements existing quality practices, requirements, standards, and guidelines within the pharmaceutical industry and regulatory environment. It specifically provides guidance on the principles and some of the tools of quality risk management that can enable more effective and consistent risk based decisions, both by regulators and industry, regarding the quality of drug substances and drug (medicinal) products across the product lifecycle. It is not intended to create any new expectations beyond the current

	regulatory requirements.
11. 使用一個正式的風險管理程序(使用受承認的工具及/或內部程序，例如，標準作業程序）既非總是適合的，也非總是必需的。使用非正式的風險管理程序（使用經驗上的工具及/或內部程序）亦得認定為可接受。	11. It is neither always appropriate nor always necessary to use a formal risk management process (using recognized tools and/ or internal procedures e.g. standard operating procedures). The use of informal risk management processes (using empirical tools and/ or internal procedures) can also be considered acceptable.
12. 品質風險管理之適當的使用，可以是有幫助的，但不得排除產業需遵守法規要求的義務，也不取代產業與主管機關間之適當溝通。	12. Appropriate use of quality risk management can facilitate but does not obviate industry's obligation to comply with regulatory requirements and does not replace appropriate communications between industry and regulators.
2 範圍（Scope）	
13. 本指引提供可適用於製藥品質之不同層面的品質風險管理之原則及工具範例。這些層面涵蓋藥物、藥品、生物產品及生技產品（包含藥品、生物產品及生技產品之原料、溶媒、賦型劑、包裝及標示材料的使用在內）的開發、製造、運銷，以及檢查和申請/審查程序之整個生命週期。	13. This guideline provides principles and examples of tools for quality risk management that can be applied to different aspects of pharmaceutical quality. These aspects include development, manufacturing, distribution, and the inspection and submission/review processes throughout the lifecycle of drug substances, drug (medicinal) products, biological and biotechnological products (including the use of raw materials, solvents, excipients, packaging and labeling materials in drug (medicinal) products, biological and biotechnological products).
3. 品質風險管理的原則（PRINCIPLES OF QUALITY RISK MANAGEMENT）	
14. 品質風險管理之二個主要原則是：	14. Two primary principles of quality risk management are:
• 品質風險之評估應以科學知識為基礎且最終連結到對病人的保護；以及	• The evaluation of the risk to quality should be based on scientific knowledge and ultimately link to the protection of the patient; and
• 品質風險管理過程之努力、正式性及文件制作的程度應與風險之層級相稱。	• The level of effort, formality and documentation of the quality risk management process should be commensurate with the level of risk.
4. 一般品質風險管理過程	

(GENERAL QUALITY RISK MANAGEMENT PROCESS)	
15. 品質風險管理是對藥物產品整個生命週期之品質風險的評價、管制、溝通及檢討之系統性的過程。品質風險管理的模式概述於圖 1。其他模式也可使用。該架構之每一構成部分的重點可能因個案而異，但健全的過程會將所有要素納入考慮，其詳細程度是與其特定風險相稱。	15. Quality risk management is a systematic process for the assessment, control, communication and review of risks to the quality of the drug (medicinal) product across the product lifecycle. A model for quality risk management is outlined in the diagram (Figure 1). Other models could be used. The emphasis on each component of the framework might differ from case to case but a robust process will incorporate consideration of all the elements at a level of detail that is commensurate with the specific risk.


啟動品質風險管理過程
風險評估
風險鑑別
風險分析
風險評價
無法接受
風險管制
風險減低
風險接受
品質風險管理過程之產出/結果
風險回顧
回顧事件
風險溝通
風險管理工具


Initiate
Quality Risk Management Process
Risk Assessment
Risk Identification
Risk Analysis
Risk Evaluation
unacceptable
Risk Control
Risk Reduction
Risk Acceptance
Output / Result of the
Quality Risk Management Process
Risk Review
Review Events
Risk Communication
Risk Management tools

16. 因為決策可能發生在過程中的任何一點，所以決策結節(decision nodes)未顯示在上圖中。基於支持如此決策之資訊，這些決策可能會因而回到先前的步驟並尋求進一步的資訊，調整風險模式或甚至終止風險管理程序。**註：**流程圖中之「無法接受」並非只指法令、立法或行政管制的要求，而且亦指回顧風險評價過程的必要性。	16. Decision nodes are not shown in the diagram above because decisions can occur at any point in the process. These decisions might be to return to the previous step and seek further information, to adjust the risk models or even to terminate the risk management process based upon information that supports such a decision. Note: "unacceptable" in the flowchart does not only refer to statutory, legislative or regulatory requirements, but also to the need to revisit the risk assessment process.
4.1 責任（Responsibilities）	
17. 品質風險管理活動，通常，但不是一直都由跨學科的團隊所從事。當組成團隊時，除了具有關於品質風險管理過程之知識的人員外，還應包含來自適當領域（例如，品質部門、業務開發、工程、法規事務、生產操作、銷售及行銷、法律、統計及臨床）的專家。	17. Quality risk management activities are usually, but not always, undertaken by interdisciplinary teams. When teams are formed, they should include experts from the appropriate areas (e.g. quality unit, business development, engineering, regulatory affairs, production operations, sales and marketing, legal, statistics and clinical) in addition to individuals who are knowledgeable about the quality risk management process.
18. *決策者*應該：	18. Decision *makers* should:
• 在其組織之不同職能與部門間負起協調品質風險管理的責任；而且	• take responsibility for coordinating quality risk management across various functions and departments of their organization; and
• 確保品質風險管理程序是經過界定、佈署及審查，並可獲得適當的資源。	• assure that a quality risk management process is defined, deployed and reviewed and that adequate resources are available.
4.2 引進品質風險管理程序（Initiating a Quality Risk Management Process）	
19. 品質風險管理過程應包含系統性決策程序，該過程經設計並可用於協調、幫助及改善基於科學所作風險之決策。使用於啟動及規劃一個品質風險管理過程之可能步驟包含如下：	19. Quality risk management should include systematic processes designed to coordinate, facilitate and improve science-based decision making with respect to risk. Possible steps used to initiate and plan a quality risk management process might include the following:
• 界定問題及/或風險疑問，包含確認風險之潛在性的相關假設在內；	• Define the problem and/or risk question, including pertinent

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

能性及損害之嚴重度的定性與定量過程。在有些風險管理工具中，檢測損害的能力（可檢測性）亦是風險估計中的因素。	the qualitative or quantitative process of linking the likelihood of occurrence and severity of harms. In some risk management tools, the ability to detect the harm (detectability) also factors in the estimation of risk.
23. ***風險評估***是將經辨識及分析的風險與已知的風險標準進行比對。風險評估是就所有三個基本問題考量其證據的強度。	23. ***Risk evaluation*** compares the identified and analyzed risk against given risk criteria. Risk evaluations consider the strength of evidence for all three of the fundamental questions.
24. 在執行有效之風險評價時，數據套組的健全性/耐用性是重要的，因為這決定產出（output）的品質。揭露不確定性（uncertainty）之假設及合理來源，將提高該產出之信心及/或幫助確認其限制。不確定性是由於過程的不完整知識及其預期或非預期之變異性的組合。不確定性之典型來源包括知識上的差距、製藥科學與製程瞭解上的差距、傷害的來源(例如過程的失敗模式、變異性的來源)，以及問題檢測的機率。	24. In doing an effective risk assessment, the robustness of the data set is important because it determines the quality of the output. Revealing assumptions and reasonable sources of uncertainty will enhance confidence in this output and/or help identify its limitations. Uncertainty is due to combination of incomplete knowledge about a process and its expected or unexpected variability. Typical sources of uncertainty include gaps in knowledge gaps in pharmaceutical science and process understanding, sources of harm (e.g., failure modes of a process, sources of variability), and probability of detection of problems.
25. 風險評價之產出是風險之定量估計或風險範圍之定性***描述***。當風險以定量表達時，使用數字表達其機率，或風險可以定性描述(例如「高」、「中」或「低」)表達。惟描述應盡可能界定其細節。有時可使用「風險分數」（risk score），以再進一步界定風險分級上的描述。在定量風險評價上，風險估計值指在假定之一套產生風險的情況下，提供一個特定後果的可能性。因此，逐一定量風險估計對於特別的結果是有用的。或者，有些風險管理工具使用一個相對風險計量（relative risk measure），以將不同層級嚴重度及機率組合成相對風險之一個	25. The output of a risk assessment is either a quantitative estimate of risk or a qualitative ***description*** of a range of risk. When risk is expressed quantitatively, a numerical probability is used. Alternatively, risk can be expressed using qualitative descriptors, such as “high”, “medium”, or “low”, which should be defined in as much detail as possible. Sometimes a "risk score" is used to further define descriptors in risk ranking. In quantitative risk assessments, a risk estimate provides the likelihood of a specific consequence, given a set of risk-generating circumstances. Thus,

整體估計值。在評分過程的中間步驟有時可以使用定量風險估計。	quantitative risk estimation is useful for one particular consequence at a time. Alternatively, some risk management tools use a relative risk measure to combine multiple levels of severity and probability into an overall estimate of relative risk. The intermediate steps within a scoring process can sometimes employ quantitative risk estimation.
4.4 風險管制 （Risk Control）	
26. ***風險管制***包括為***降低***及/或接受風險之決策制定。風險管制之目的是要將風險減到一個可以接受的程度。使用於風險管制之努力程度應與風險的重要性成正比。為瞭解/確認風險管制之最適化等級，決策者可使用不同的過程，包含成本效益分析在內。	26. ***Risk control*** includes decision making to ***reduce*** and/or accept risks. The purpose of risk control is to reduce the risk to an acceptable level. The amount of effort used for risk control should be proportional to the significance of the risk. Decision makers might use different processes, including benefit-cost analysis, for understanding the optimal level of risk control.
27. 風險管制可以聚焦於下列問題：	27. Risk control might focus on the following questions:
• 風險是否高於可接受的程度？	• Is the risk above an acceptable level?
• 可做什麼以減低或消除風險？	• What can be done to reduce or eliminate risks?
• 效益、風險及資源三者之適當的平衡是什麼？	• What is the appropriate balance among benefits, risks and resources?
• 是否由於管制經辨識之風險的結果，而導入新的風險？	• Are new risks introduced as a result of the identified risks being controlled?
28. 當品質風險超過規定的（可接受的）水準時，***風險減低***將焦點放在減輕或避免品質風險的過程上（參見流程圖1）。「風險減低」可能包括為減輕損害之嚴重度及機率所採取的行動。提高危害及品質風險之可檢測性的過程，亦可做為風險管制策略的一部分。風險減低措施之實施可能將新的風險導入系統中，或增加其他既有風險的嚴重性。因此，在實施風險減低過程後，應重新檢視風險評價，以確認及評估風險之任何可能的變更。	28. ***Risk reduction*** focuses on processes for mitigation or avoidance of quality risk when it exceeds a specified (acceptable) level (see Fig. 1). Risk reduction might include actions taken to mitigate the severity and probability of harm. Processes that improve the detectability of hazards and quality risks might also be used as part of a risk control strategy. The implementation of risk reduction measures can introduce new risks into the system or increase the significance of other existing risks. Hence, it might be appropriate to revisit the risk assessment to identify and evaluate any possible change in risk after implementing a risk reduction

	process.
29. ***風險接受***是對接受風險的一個決定。風險的接受可能是正式決定接受殘留風險，或可能是被動接受非特定殘留風險之決定。對於某些類型的損害，即使施行最好的品質風險管理，也不能完全消除風險。在這些情況中，可能同意其已經應用一個適當品質風險管理策略，且將品質風險降低至一個規定的（可接受的）水準。這個（規定的）可接受的水準受到多個參數影響，且應由不同個案之基礎決定之。	29. ***Risk acceptance*** is a decision to accept risk. Risk acceptance can be a formal decision to accept the residual risk or it can be a passive decision in which residual risks are not specified. For some types of harms, even the best quality risk management practices might not entirely eliminate risk. In these circumstances, it might be agreed that an appropriate quality risk management strategy has been applied and that quality risk is reduced to a specified (acceptable) level. This (specified) acceptable level will depend on many parameters and should be decided on a case-by-case basis.
4.5 風險溝通（Risk Communication）	
30. ***風險溝通***是在決策者與其他人員間關於風險及風險管理資訊的分享。各方都可以在風險管理過程的任何階段進行溝通（參見流程圖1：虛線箭頭）。品質風險管理過程之產出/結果應適當地溝通並且加以文件化（參見流程圖1：實線箭頭）。溝通可能包括那些有利害關係之各方間的溝通，例如主管機關與業者、業者與病人、在公司內、業界或主管機關內部等。所包含之資訊可能關於品質之風險的存在、性質、型式、機率、嚴重性、接受性、管制、處理、可檢測性或其它層面。不必就每一個風險的接受進行溝通。在業者與主管機關間，關於品質風險管理決策的溝通，可以透過法規及指引規範之既有管道進行。	30. ***Risk communication*** is the sharing of information about risk and risk management between the decision makers and others. Parties can communicate at any stage of the risk management process (see Fig. 1: dashed arrows). The output/result of the quality risk management process should be appropriately communicated and documented (see Fig. 1: solid arrows). Communications might include those among interested parties; e.g., regulators and industry, industry and the patient, within a company, industry or regulatory authority, etc. The included information might relate to the existence, nature, form, probability, severity, acceptability, control, treatment, detectability or other aspects of risks to quality. Communication need not be carried out for each and every risk acceptance. Between the industry and regulatory authorities, communication concerning quality risk management decisions might be effected through existing channels as specified in regulations and guidances.
4.6 風險檢討（Risk Review）	
31. 風險管理應是品質管理過程中持續進行	31. Risk management should be an ongoing part

的部分。檢討或監測事件的機制應予實施。	of the quality management process. A mechanism to review or monitor events should be implemented.
32. 風險管理過程的產出/結果應檢討並考慮採用新的知識及經驗。一旦啟動一個品質風險管理過程，則該過程應持續應用於可能衝擊原來品質風險管理決策之事件，不論是計畫性的(例如產品檢討、檢查、稽核、變更管制等之結果)或非計畫性的(例如調查失敗的根本原因、回收)，皆應繼續利用該過程。任何檢討的頻率應以風險之水準/程度為基礎。風險的檢討可能包含風險之接受決策的重新考慮(第4.4節)。	32. The output/results of the risk management process should be reviewed to take into account new knowledge and experience. Once a quality risk management process has been initiated, that process should continue to be utilized for events that might impact the original quality risk management decision, whether these events are planned (e.g. results of product review, inspections, audits, change control) or unplanned (e.g. root cause from failure investigations, recall). The frequency of any review should be based upon the level of risk. Risk review might include reconsideration of risk acceptance decisions (section 4.4).
5. 風險管理方法 （RISK MANAGEMENT METHODOLOGY）	
33. 品質風險管理係支持以科學的及實用的方法制定決策。藉由現行關於評價風險之機率、嚴重性及有時是檢測性之知識，提供文件化、透明且可再現的方法，以完成品質風險管理過程的步驟。	33. Quality risk management supports a scientific and practical approach to decision-making. It provides documented, transparent and reproducible methods to accomplish steps of the quality risk management process based on current knowledge about assessing the probability, severity and sometimes detectability of the risk.
34. 傳統上，對品質之風險，會以各種非正式的方式（經驗的及/或內部的程序），譬如觀察、趨勢及其他資訊的彙集為基礎加以評價及管理。該等方法可持續提供有用的資訊，而這些資訊可支持諸如申訴、品質缺陷、偏離及資源配置之處理的主題。	34. Traditionally, risks to quality have been assessed and managed in a variety of informal ways (empirical and/ or internal procedures) based on, for example, compilation of observations, trends and other information. Such approaches continue to provide useful information that might support topics such as handling of complaints, quality defects, deviations and allocation of resources.
35. 此外，製藥產業及主管機關可使用經公認之風險管理工具及/或內部程序（例如，標準作業程序）評價及管理風險。下述內容為這些工具當中的一些非詳細周全的清單（附則 1 與第 8 章提供進一步的細節）。	35. Additionally, the pharmaceutical industry and regulators can assess and manage risk using recognized risk management tools and/ or internal procedures (e.g., standard operating procedures). Below is a

	non-exhaustive list of some of these tools (further details in Annex 1 and chapter 8):
• 基本風險管理簡易方法（流程表、檢查單等）；	• Basic risk management facilitation methods (flowcharts, check sheets etc.)
• 失敗模式效應分析(FMEA)；	• Failure Mode Effects Analysis (FMEA)
• 失敗模式效應及關鍵性分析(FMECA)；	• Failure Mode, Effects and Criticality Analysis (FMECA)
• 缺失之樹狀分析(FTA)；	• Fault Tree Analysis (FTA)
• 危害分析及關鍵管制點(HACCP)；	• Hazard Analysis and Critical Control Points (HACCP)
• 危害操作性分析(HAZOP)；	• Hazard Operability Analysis (HAZOP)
• 事先危害分析(PHA)；	• Preliminary Hazard Analysis (PHA)
• 風險分級及篩選；	• Risk ranking and filtering
• 輔助性統計工具。	• Supporting statistical tools
36. 在原料藥及醫藥品品質相關之特定領域運用這些工具可能是適當的。品質風險管理方法及輔助性統計工具可合併使用(例如機率性的風險評價)。合併使用提供可促進靈活的應用品質風險管理原則。	36. It might be appropriate to adapt these tools for use in specific areas pertaining to drug substance and drug (medicinal) product quality. Quality risk management methods and the supporting statistical tools can be used in combination (e.g. Probabilistic Risk Assessment). Combined use provides flexibility that can facilitate the application of quality risk management principles.
37. 品質風險管理之嚴格性及正式性的程度應反映可利用的知識，並應與所要論述之問題的複雜性，及/或關鍵性相當。	37. The degree of rigor and formality of quality risk management should reflect available knowledge and be commensurate with the complexity and/ or criticality of the issue to be addressed.
6. 品質風險管理整合於產業及管制運作中 （INTEGRATION OF QUALITY RISK MANAGEMENT INTO INDUSTRY AND REGULATORY OPERATIONS）	
38. 當品質風險管理整合入品質系統中時，品質風險管理是一個支持基於科學及實用之決策的過程(參見附件II)。如同在前言中所概述，品質風險管理的適當使用並不免除業者需遵從主管機關要求的義務。然而，有效的品質風險管理可以促成更好及更明智的決策，可以就一個公司處理潛在風險之能力對主管機關提供更大的保證，以及可能影響直接管制監督的範圍及程度。此外，品質風險管理還可促使各方更好的使用資源。	38. Quality risk management is a process that supports science-based and practical decisions when integrated into quality systems (see Annex II). As outlined in the introduction, appropriate use of quality risk management does not obviate industry's obligation to comply with regulatory requirements. However, effective quality risk management can facilitate better and more informed decisions, can provide regulators with greater assurance of a

	company's ability to deal with potential risks, and might affect the extent and level of direct regulatory oversight. In addition, quality risk management can facilitate better use of resources by all parties.
39. 業者及法規人員在品質風險管理過程上之訓練，提供對制定決策過程更多的瞭解，並建立對品質風險管理結果的信心。	39. Training of both industry and regulatory personnel in quality risk management processes provides for greater understanding of decision-making processes and builds confidence in quality risk management outcomes.
40. 品質風險管理應整合入既有操作中，並適當地文件化。附件II提供情況範例。在其中，品質風險管理過程之使用可能提供以後在各種製藥操作，用得上的資訊。這些範例只是為說明之目的而提供，不得將之視為一個最終的或詳細周全的清單。這些實例無意在現行法規明訂之要求外，創造任何新的期待。	40. Quality risk management should be integrated into existing operations and documented appropriately. Annex II provides examples of situations in which the use of the quality risk management process might provide information that could then be used in a variety of pharmaceutical operations. These examples are provided for illustrative purposes only and should not be considered a definitive or exhaustive list. These examples are not intended to create any new expectations beyond the requirements laid out in the current regulations.
41. 業界及法規作業之範例（參見附件 II）：	41.Examples for industry and regulatory operations (see Annex II):
• 品質管理	• Quality management
42. 產業作業及活動範例（參見附件 II）：	42.Examples for industry operations and activities (see Annex II):
• 開發；	• Development
• 設施、設備及公用設施；	• Facility, equipment and utilities
• 物料管理；	• Materials management
• 生產；	• Production
• 實驗室管制及安定性試驗；	• Laboratory control and stability testing
• 包裝及標示。	• Packaging and labeling
43. 法規作業的範例（參見附件 II）：	43.Examples for regulatory operations (see Annex II):
• 檢查及評價活動	• Inspection and assessment activities

44. 雖然法規決策將持續在一個區域性的基礎上為之，但品質風險管理原則之普遍瞭解及應用可增進相互的信心，並在相同資訊的基礎上提升管制者間更為一致的決策。該協力合作，在整合及支持品質風險管理實務之政策及準則的發展上可能是重要的。	44. While regulatory decisions will continue to be taken on a regional basis, a common understanding and application of quality risk management principles could facilitate mutual confidence and promote more consistent decisions among regulators on the basis of the same information. This collaboration could be important in the development of policies and guidelines that integrate and support quality risk management practices.
7. 定義（DEFINITIONS）	
決策者 *具有資格及權能去做出適當且適時之品質風險管理決策的人。*	***Decision maker(s) –*** *Person(s) with the competence and authority to make appropriate and timely quality risk management decisions*
可檢測性 *發現或確定一個危害之存在、出現或事實的能力。*	***Detectability*** *-the ability to discover or determine the existence, presence, or fact of a hazard*
傷害 *對健康的損害，包含因產品品質或有效性之減失而導致的損害在內。*	***Harm –****damage to health, including the damage that can occur from loss of product quality or availability*
危害 *傷害的潛在來源 (ISO/IEC Guide 51)。*	***Hazard*** *- the potential source of harm (ISO/IEC Guide 51)*
產品生命週期 *產品從初始開發，經過上市直到產品終止之生命的全部階段。*	***Product Lifecycle –****all phases in the life of the product from the initial development through marketing until the product's discontinuation*
品質 *一個產品、系統或製程之一組固有性質符合要求的程度（參見 ICH Q6A 針對藥物原料和藥物產品之"品質"的定義）。*	***Quality –****the degree to which a set of inherent properties of a product, system or process fulfills requirements (see ICH Q6a definition specifically for "quality" of drug substance and drug (medicinal) products.)*
品質風險管理 *對藥品跨越產品生命週期之品質的風險為評價、管制、溝通及檢討之一個系統性的過程。*	***Quality risk management –****a systematic process for the assessment, control, communication and review of risks to the quality of the drug (medicinal) product across the product lifecycle*
品質系統 *一個系統之全部層面的總和，用以實施品質政策並確保符合品質目標。*	***Quality system –****the sum of all aspects of a system that implements quality policy and ensures that quality objectives are met*

要求 *病人或其代理人【例如，健康照護專業人員、主管機關及立法者】之明示或暗示的需求或期待。在本文件中，"要求"不但指稱法律、立法或管制的要求，而且亦指稱該等需求及期望。*	***Requirements*** *–the explicit or implicit needs or expectations of the patients or their surrogates (e.g. health care professionals, regulators and legislators). In this document, "requirements" refers not only to statutory, legislative, or regulatory requirements, but also to such needs and expectations.*
風險 *傷害之發生的機率及該傷害之嚴重度的組合(ISO/IEC Guide 51)。*	***Risk*** *–the combination of the probability of occurrence of harm and the severity of that harm (ISO/IEC Guide 51)*
風險接受 *接受風險的決策(ISO Guide 73)。*	***Risk acceptance*** *–the decision to accept risk (ISO Guide 73)*
風險分析 *與業經確認之危害所關聯的風險之估計。*	***Risk analysis*** *–the estimation of the risk associated with the identified hazards*
風險評價 *一個組織資訊之系統性過程，用以支持在風險管理過程中做出的風險決策。這包含危害之確認及與暴露於該等危害有關之風險的分析及評估。*	***Risk assessment*** *–a systematic process of organizing information to support a risk decision to be made within a risk management process. It consists of the identification of hazards and the analysis and evaluation of risks associated with exposure to those hazards.*
風險溝通 *在決策者與其他利害關係人間，關於風險及風險管理之資訊的分享。*	***Risk communication*** *–the sharing of information about risk and risk management between the decision maker and other stakeholders*
風險管制 *執行風險管理決策的行動(ISO Guide 73)。*	***Risk control*** *–actions implementing risk management decisions (ISO Guide 73)*
風險評估 *使用定量或定性尺度，比較估計之風險與已知之風險基準，以決定風險的重要性。*	***Risk evaluation*** *–the comparison of the estimated risk to given risk criteria using a quantitative or qualitative scale to determine the significance of the risk*
風險確認 *資訊之系統性使用，以藉由風險疑問或問題描述能確認傷害(危害)之潛在來源。*	***Risk identification*** *–the systematic use of information to identify potential sources of harm (hazards) referring to the risk question or problem description*
風險管理 *將品質管理政策、程序和實務系統性的應用於評價、管制、溝通及檢討風險的工作。*	***Risk management*** *–the systematic application of quality management policies, procedures, and practices to the tasks of assessing, controlling, communicating and reviewing risk*
風險減低 *為減少傷害之發生機率及該傷害之嚴重度所採取的行動。*	***Risk reduction*** *–actions taken to lessen the probability of occurrence of harm and the severity of that harm*

風險檢討 *考慮（如合適時）關於風險之新知識及經驗，以檢討或監測風險管理過程的產出/結果。*	***Risk review –****review or monitoring of output/results of the risk management process considering (if appropriate) new knowledge and experience about the risk*
嚴重度 *衡量危害之可能後果。*	***Severity –****a measure of the possible consequences of a hazard*
利害關係人 *可能影響或受風險影響，或感受其本身受風險影響之任何個人、團體或組織。決策者可能也是利害關係人。為本準則之目的，主要利害關係人是病人、健康照護專業人員、主管機關及業界。*	***Stakeholder –****any individual, group or organization that can affect, be affected by, or perceive itself to be affected by a risk. Decision makers might also be stakeholders. For the purposes of this guideline, the primary stakeholders are the patient, healthcare professional, regulatory authority, and industry*
趨勢 *指出一個變數之改變方向或比率的統計學術語。*	***Trend –****a statistical term referring to the direction or rate of change of a variable(s)*

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附件I：風險管理方法和工具 （Appendix I: Risk Management Methods and Tools）	
本附件之目的在於就可能被業界及主管機關使用於品質風險管理之一些主要工具，提供其一般的概觀及參考資料。這些參考資料是為幫助取得關於特定工具之更多知識及細節而納入。這不是一個詳細周全的清單。重點是沒有任何一件或一套工具可適用於品質風險管理程序之每一種情況。	The purpose of this appendix is to provide a general overview of and references for some of the primary tools that might be used in quality risk management by industry and regulators. The references are included as an aid to gain more knowledge and detail about the particular tool. This is not an exhaustive list. It is important to note that no one tool or set of tools is applicable to every situation in which a quality risk management procedure is used.
I.1 基本風險管理之簡易方法 （Basic Risk Management Facilitation Methods）	
一些藉由組織數據及促進決策之制定，以普遍用來建構風險管理之簡單技術是：	Some of the simple techniques that are commonly used to structure risk management by organizing data and facilitating decision-making are:
• 流程圖；	• Flowcharts
• 檢查單；	• Check Sheets
• 過程圖示；	• Process Mapping
• 原因和效應圖表（亦稱為石川圖或魚骨圖）。	• Cause and Effect Diagrams (also called an Ishikawa diagram or fish bone diagram)
I.2 失敗模式效應分析 （Failure Mode Effects Analysis (FMEA)）	
FMEA (參見 IEC 60812) 係就程序及其對結果及/或產品性能之可能的效應，提供潛在失敗模式的評估。失敗模式一旦建立，風險減低便可用以排除、圍堵、減少或控制該潛在失敗。FMEA 倚賴對產品及製程的瞭解。FMEA 在方法上將複雜程序的分析分解成可管理的步驟。對於總結失敗之重要模式、引起這些失敗的因素及這些失敗之可能效應，這是一個強而有力的工具。	FMEA (see IEC 60812) provides for an evaluation of potential failure modes for processes and their likely effect on outcomes and/or product performance. Once failure modes are established, risk reduction can be used to eliminate, contain, reduce or control the potential failures. FMEA relies on product and process understanding. FMEA methodically breaks down the analysis of complex processes into manageable steps. It is a powerful tool for summarizing the important modes of failure, factors causing these failures and the likely effects of these failures.
潛在的使用領域 （Potential Areas of Use(s)）	
FMEA 可用於安排風險優先順序及監測風險管制活動的效果。	FMEA can be used to prioritize risks and monitor the effectiveness of risk control activities.

FMEA 可應用於設備及設施，及可用於分析製造作業及其對產品或製程的影響。這可辨識使系統脆弱之因素/操作。FMEA 之產出/結果可用為設計或進一步分析或指引資源配置的基礎。	FMEA can be applied to equipment and facilities and might be used to analyze a manufacturing operation and its effect on product or process. It identifies elements/operations within the system that render it vulnerable. The output/ results of FMEA can be used as a basis for design or further analysis or to guide resource deployment.
I.3失敗模式，效應及關鍵性分析（Failure Mode Effects and Criticality Analysis，FMECA）	
FMEA 可加以延伸，納入結果之嚴重程度的調查、其個別之發生機率，以及其檢測性，轉變為失敗模式，效應及關鍵性分析（FMECA；參見 IEC 60812)。為執行這樣的分析，應建立產品或製程規格。	FMEA might be extended to incorporate an investigation of the degree of severity of the consequences, their respective probabilities of occurrence, and their detectability, thereby becoming a Failure Mode Effect and Criticality Analysis (FMECA; see IEC 60812). In order for such an analysis to be performed, the product or process specifications should be established.
FMECA 能確認在何處追加預防措施，可能將風險減至最低。	FMECA can identify places where additional preventive actions might be appropriate to minimize risks.
潛在的使用領域（Potential Areas of Use(s)）	
FMECA 在製藥產業之應用，應主要用於與製造過程有關之失敗及風險；然而，並不侷限於該應用。FMECA 之結果是每一失敗模式之相對風險"分數"。該分數在相對風險的基礎上，將這些模式分級。	FMECA application in the pharmaceutical industry should mostly be utilized for failures and risks associated with manufacturing processes; however, it is not limited to this application. The output of an FMECA is a relative risk “score” for each failure mode, which is used to rank the modes on a relative risk basis.
I.4 缺失之樹狀分析 （Fault Tree Analysis，FTA）	

FTA 工具(參見 IEC 61025)是假定一個產品或製程有功能性失效之方法。這個工具每次只評估造成系統(或子系統)失效的一個原因，但可將失效之數個原因以確認其為原因鏈的方式組合在一起。該結果以缺失模式樹的形式圖示之。在該模式樹中的每一層級，其缺失模式間的關連以邏輯運算符號（"及"、"或"等）描述之。FTA 有賴於專家對製程的瞭解，以確認原因的因素。	The FTA tool (see IEC 61025) is an approach that assumes failure of the functionality of a product or process. This tool evaluates system (or subsystem) failures one at a time but can combine multiple causes of failure by identifying causal chains. The results are represented pictorially in the form of a tree of fault modes. At each level in the tree, combinations of fault modes are described with logical operators (AND, OR, etc.). FTA relies on the experts' process understanding to identify causal factors.
潛在的使用領域 （Potential Areas of Use(s)）	
FTA 得用於建立導致失敗之根本原因的路徑。FTA 得用來調查申訴或偏離，以完全瞭解其根本原因，並確保其預定的改善將會完全解決該問題，而不會引起其他問題（亦即，解決了一個問題卻又引起另一個不同的問題）。缺失之樹狀分析是評估多重因素對於一個已知問題影響的有效工具。FTA 之產出包含可見的失敗模式描述。這對於風險評價及監測計畫的開發都有助益。	FTA can be used to establish the pathway to the root cause of the failure. FTA can be used to investigate complaints or deviations in order to fully understand their root cause and to ensure that intended improvements will fully resolve the issue and not lead to other issues (i.e. solve one problem yet cause a different problem). Fault Tree Analysis is an effective tool for evaluating how multiple factors affect a given issue. The output of an FTA includes a visual representation of failure modes. It is useful both for risk assessment and in developing monitoring programs.
I.5 危害分析及關鍵管制點 （Hazard Analysis and Critical Control Points，HACCP）	
HACCP 是為確保產品品質、可靠性及安全性之系統性、積極性及預防性的工具(參見 WHO Technical Report Series No 908, 2003 Annex 7)。這是一個結構化的方法。該方法應用技術和科學的原理，分析、評估、預防及管制由產品之設計、開發、生產及使用的危害所產生之風險或不良後果。	HACCP is a systematic, proactive, and preventive tool for assuring product quality, reliability, and safety (see WHO Technical Report Series No 908, 2003 Annex 7). It is a structured approach that applies technical and scientific principles to analyze, evaluate, prevent, and control the risk or adverse consequence(s) of hazard(s) due to the design, development, production, and use of products.
HACCP 包含下列 7 個步驟：	HACCP consists of the following seven steps:
(1) 對製程的每一個步驟執行危害分析，並確認其預防措施；	(1) conduct a hazard analysis and identify preventive measures for each step of the process;
(2) 決定關鍵管制點；	(2) determine the critical control points;
(3) 建立關鍵限量；	(3) establish critical limits;

(4) 建立一個監測關鍵管制點的系統；	(4) establish a system to monitor the critical control points;
(5) 建立當監測出關鍵管制點不在管制狀態時，應採取的矯正措施；	(5) establish the corrective action to be taken when monitoring indicates that the critical control points are not in a state of control;
(6) 建立系統，證實 HACCP 系統在有效運作中；	(6) establish system to verify that the HACCP system is working effectively;
(7) 建立一個保存紀錄之系統。	(7) establish a record-keeping system.
潛在的使用領域（Potential Areas of Use(s)）	
HACCP 可能用於確認和管理與物理學、化學及生物學上之危害(包括微生物學上的污染)相關聯的風險。當對產品及製程之瞭解足夠廣泛，以支持關鍵管制點的確認時，則 HACCP 最為有用。HACCP 分析的產出是風險管理資訊。不僅在製造過程上，且亦在其他生命週期的階段中，該資訊皆有助於關鍵管制點的監測。	HACCP might be used to identify and manage risks associated with physical, chemical and biological hazards (including microbiological contamination). HACCP is most useful when product and process understanding is sufficiently comprehensive to support identification of critical control points. The output of a HACCP analysis is risk management information that facilitates monitoring of critical points not only in the manufacturing process but also in other life cycle phases.
I.6 危害操作性分析 （Hazard Operability Analysis，HAZOP）	
HAZOP（參見 IEC 61882）係以假定風險事件是由於偏離設計或作業目的而引起之理論為基礎。這是一個系統性腦力激盪技術。該技術利用所謂"指引字語"來確認危害。"指引字語"（例如，"無"、"更多"、"異於"、"部分"等）應用於相關的參數（例如，污染、溫度）上，以幫助確認離開正常使用或設計目的之潛在偏離。這常常使用一組人員組成之團隊。這些人員具有涵蓋該製程或產品之設計及其應用的專門知識。	HAZOP (see IEC 61882) is based on a theory that assumes that risk events are caused by deviations from the design or operating intentions. It is a systematic brainstorming technique for identifying hazards using so-called “guide-words”. “Guide-words” (e.g., No, More, Other Than, Part of, etc.) are applied to relevant parameters (e.g., contamination, temperature) to help identify potential deviations from normal use or design intentions. It often uses a team of people with expertise covering the design of the process or product and its application.
潛在的使用領域（Potential Areas of Use(s)）	

HAZOP 可適用於原料及藥品之製造過程，包括委外生產與配方及上游供應商、設備和設施。這亦已使用於製藥工業，主要以評估製程安全性的危害。類似於 HACCP 之情況，HAZOP 分析之產出是一個對風險管理之關鍵作業的清單。這有助於製造過程中之關鍵點的定期監測。	HAZOP can be applied to manufacturing processes, including outsourced production and formulation as well as the upstream suppliers, equipment and facilities for drug substances and drug (medicinal) products. It has also been used primarily in the pharmaceutical industry for evaluating process safety hazards. As is the case with HACCP, the output of a HAZOP analysis is a list of critical operations for risk management. This facilitates regular monitoring of critical points in the manufacturing process.
I.7 事先危害分析 （Preliminary Hazard Analysis，PHA）	
PHA 是一個分析工具，該工具應用先前關於一個危害或失效之經驗或知識為基礎，以確認將來可能引起損害之危害、危害狀況及事件，並預測其在一定的活動、設施、產品或系統之發生機率。其工具包含：	PHA is a tool of analysis based on applying prior experience or knowledge of a hazard or failure to identify future hazards, hazardous situations and events that might cause harm, as well as to estimate their probability of occurrence for a given activity, facility, product or system. The tool consists of:
1) 確認風險事件發生的可能性，	1) the identification of the possibilities that the risk event happens,
2) 對健康可能造成之傷害或損害程度的定性評估，	2) the qualitative evaluation of the extent of possible injury or damage to health that could result and
3) 利用綜合事件之嚴重性及可能性將危害相對分級，以及	3) a relative ranking of the hazard using a combination of severity and likelihood of occurrence, and
4) 確認可能之改善措施。	4) the identification of possible remedial measures
潛在的使用領域（Potential Areas of Use(s)）	
當情況不允許使用一個更廣泛技術，則在分析既有系統或危害之優先順序時，PHA 可能是很有用的。這可用於產品、製程及設施之設計，亦可評估一般產品類型、次為產品分類及後為特殊產品之危害。PHA 是最普遍使用於一個計畫之開發的初期。那時候關於細部設計或作業程序都只有很少的資訊。因此，這常常會是進一步研究的一個前導。典型地，在 PHA 中確認之危害，將與像在本節中規定之其他風險管理工具一起，進一步加以評價。	PHA might be useful when analyzing existing systems or prioritizing hazards where circumstances prevent a more extensive technique from being used. It can be used for product, process and facility design as well as to evaluate the types of hazards for the general product type, then the product class, and finally the specific product. PHA is most commonly used early in the development of a project when there is little information on design details or operating procedures; thus, it will often be a precursor to further studies. Typically, hazards identified in the PHA are further assessed with

	other risk management tools such as those in this section.
I.8 風險分級及篩選（Risk Ranking and Filtering）	
風險分級及篩選是將風險比較與分級的工具。複雜系統之風險分級典型地需要對每一風險之多樣的定量和定性因素加以評估。這個工具包含視需要，將一個基本風險問題分解成許多構成要素，以捕捉在此風險中所涉及之因素。這些因素結合成一個單一的相對風險分數，而後可用以將風險分級。"篩選器"是以對風險分數進行加權或減去的形式存在，可用為將風險分級改變尺度或使風險分級合適於管理或政策目標。	Risk ranking and filtering is a tool for comparing and ranking risks. Risk ranking of complex systems typically requires evaluation of multiple diverse quantitative and qualitative factors for each risk. The tool involves breaking down a basic risk question into as many components as needed to capture factors involved in the risk. These factors are combined into a single relative risk score that can then be used for ranking risks. "Filters," in the form of weighting factors or cut-offs for risk scores, can be used to scale or fit the risk ranking to management or policy objectives.
潛在的使用領域（Potential Areas of Use(s)）	
風險分級及過濾可用於將製造場所排定優先順序，以供主管機關或工業界檢查/稽核。於風險組合與其需被管理的潛在後果之多樣化，且難以使用單一工具進行比較的情況時，風險分級方法尤其有效。當管理上需要在相同組織架構內，評估定量及定性評價之風險時，風險分級是有用的。	Risk ranking and filtering can be used to prioritize manufacturing sites for inspection/audit by regulators or industry. Risk ranking methods are particularly helpful in situations in which the portfolio of risks and the underlying consequences to be managed are diverse and difficult to compare using a single tool. Risk ranking is useful when management needs to evaluate both quantitatively-assessed and qualitatively-assessed risks within the same organizational framework.
I.9 輔助性統計工具 （Supporting Statistical Tools）	
統計工具可支持及促進品質風險管理。它們可進行有效的數據評價，幫助決定數據套組的重要性，並促成更可靠的決策。下面提供在製藥工業普遍使用之一些主要的統計工具清單：	Statistical tools can support and facilitate quality risk management. They can enable effective data assessment, aid in determining the significance of the data set(s), and facilitate more reliable decision making. A listing of some of the principal statistical tools commonly used in the pharmaceutical industry is provided:
(i) 管制圖，例如：	(i) Control Charts, for example:
- 允收管制圖 (參見 ISO 7966)；	-Acceptance Control Charts (see ISO 7966)
- 具有算術平均值和警告限量的管制圖 (參見 ISO 7873)；	-Control Charts with Arithmetic Average and Warning Limits (see ISO 7873)
- 累積總和圖 (ISO 7871);	-Cumulative Sum Charts (see ISO 7871)
- Shewhart 管制圖(參見 ISO 8258)；	-Shewhart Control Charts (see ISO 8258)

- 加權移動平均。	-Weighted Moving Average
(ii) 實驗設計（DOE）;	(ii) Design of Experiments (DOE)
(iii) 直方圖；	(iii) Histograms
(iv) Pareto 圖；	(iv) Pareto Charts
(v) 製程能力分析。	(v) Process Capability Analysis
附件II：品質風險管理的可能應用（Appendix II: Potential Applications for Quality Risk Management）	
本附件意在確認產業界及主管機構可能運用之品質風險管理的原則及工具。然而，特定風險管理工具之選擇完全取決於特定事實及情況。這些案例係為說明之目的而提供，並且只是建議可能運用之品質風險管理。本附件無意在超過現行法規之要求，創設任何新的期待。	This Appendix is intended to identify potential uses of quality risk management principles and tools by industry and regulators. However, the selection of particular risk management tools is completely dependent upon specific facts and circumstances. These examples are provided for illustrative purposes and only suggest potential uses of quality risk management. This Annex is not intended to create any new expectations beyond the current regulatory requirements.
II.1品質風險管理當作完整品質管理的一部分 （Quality Risk Management as Part of Integrated Quality Management）	
文件（Documentation）	
檢討對現行法規所期望的解釋與應用。	To review current interpretations and application of regulatory expectations
決定標準作業程序、準則等之需要性及/或開發其內容。	To determine the desirability of and/or develop the content for SOPs, guidelines, etc.
訓練與教育 （Training and education）	
以人員之教育、經驗及工作習慣，以及以先前訓練之定期評價(例如，其成效)為基礎，決定職前及/或持續訓練的適當性。	To determine the appropriateness of initial and/or ongoing training sessions based on education, experience and working habits of staff, as well as on a periodic assessment of previous training (e.g., its effectiveness)
確認使人員可靠地執行作業且對產品品質無不良衝擊所需的訓練、經驗、資格檢定及體能。	To identify the training, experience, qualifications and physical abilities that allow personnel to perform an operation reliably and with no adverse impact on the quality of the product
品質缺陷 （Quality defects）	
提供基礎，以辨識、評估及溝通可疑的品質缺陷、申訴、趨勢、偏離、調查、偏離規格結果等之潛在的品質影響。	To provide the basis for identifying, evaluating, and communicating the potential quality impact of a suspected quality defect, complaint, trend, deviation, investigation, out of specification result, etc.

促進風險之溝通及決定適當的行動，並會同主管機關處理重大的產品缺陷(例如，回收)。	To facilitate risk communications and determine appropriate action to address significant product defects, in conjunction with regulatory authorities (e.g., recall)
稽核/檢查 （Auditing/Inspection）	
界定內部與外部稽核的頻率及範圍，考慮諸如以下的因素：	To define the frequency and scope of audits, both internal and external, taking into account factors such as:
• 既有之法定要求；	• Existing legal requirements
• 公司或設施之整體狀態和歷史；	• Overall compliance status and history of the company or facility
• 公司之品質風險管理措施的健全性；	• Robustness of a company's quality risk management activities
• 場所之複雜性；	• Complexity of the site
• 製造過程之複雜性；	• Complexity of the manufacturing process
• 產品之複雜性及其治療上的重要性；	• Complexity of the product and its therapeutic significance
• 品質缺陷之次數及重要性(例如，回收)；	• Number and significance of quality defects (e.g, recall)
• 先前稽核/檢查之結果；	• Results of previous audits/inspections
• 建築物、設備、製程、關鍵人員之重大變更；	• Major changes of building, equipment, processes, key personnel
• 製造產品之經驗(例如頻率、數量、批數)；	• Experience with manufacturing of a product (e.g. frequency, volume, number of batches)
• 官方管制實驗室之檢驗結果。	• Test results of official control laboratories
定期檢討 （Periodic review）	
在產品品質檢討之內，選擇、評估及解釋數據之趨勢結果；	To select, evaluate and interpret trend results of data within the product quality review
解釋監測數據（例如支持再確效或變更抽樣之適當性的評價）。	To interpret monitoring data (e.g., to support an assessment of the appropriateness of revalidation or changes in sampling)
變更管理/變更管制 （Change management / change control）	
變更之管理是基於在藥劑開發上及製造期間所累積之知識及資訊；	To manage changes based on knowledge and information accumulated in pharmaceutical development and during manufacturing
評估變更對最終產品之可用性/可得性的影響；	To evaluate the impact of the changes on the availability of the final product
評估設施、設備、原物料、製程之變更或技術移轉對產品品質之影響；	To evaluate the impact on product quality of changes to the facility, equipment, material, manufacturing process or technical transfers

決定在變更實施前之適當行動，例如追加之測試、(再）驗證、(再）確效或與管理機構之溝通。	To determine appropriate actions preceding the implementation of a change, e.g., additional testing, (re)qualification, (re)validation or communication with regulators
持續改善 （Continual improvement）	
促進製程在產品生命週期全程之持續改善。	To facilitate continual improvement in processes throughout the product lifecycle.
II.2 品質風險管理作為受管理作業的一部分（Quality Risk Management as Part of Regulatory Operations）	
檢查及評價措施 （Inspection and assessment activities）	
協助資源配置，包含，例如檢查計畫及頻率，以及檢查和評價強度在內(參見"附件 II.1 的“稽核”段)；	To assist with resource allocation including, for example, inspection planning and frequency, and inspection and assessment intensity (see "Auditing" section in Annex II.1)
評估例如，品質缺陷、潛在回收及檢查結果之重要性；	To evaluate the significance of, for example, quality defects, potential recalls and inspectional findings
決定檢查後之後續措施的適當性及類型；	To determine the appropriateness and type of post-inspection regulatory follow-up
評估由業界提出之資訊，包含藥劑開發的資訊在內；	To evaluate information submitted by industry including pharmaceutical development information
評估所提出之變異或變更的影響；	To evaluate impact of proposed variations or changes
確認應在檢查者與評估者間溝通之風險，以幫助更佳瞭解風險將如何管制或已受管制【例如，參數放行、製程分析技術(PAT)】。	To identify risks which should be communicated between inspectors and assessors to facilitate better understanding of how risks can be or are controlled (e.g., parametric release, Process Analytical Technology (PAT)).
II.3品質風險管理作為開發的一部分 （Quality Risk Management as Part of Development）	
設計一個高品質產品及其製造過程，以一致地交付預定性能的產品（參見 ICH Q8）；	To design a quality product and its manufacturing process to consistently deliver the intended performance of the product (see ICH Q8)
提高涵蓋寬廣範圍之物料屬性(例如，粒子大小分佈、含水量、流動性質)之產品性能的知識、作業選項及製程參數；	To enhance knowledge of product performance over a wide range of material attributes (e.g. particle size distribution, moisture content, flow properties), processing options and process parameters

評估原料、溶劑、原料藥（API）起始物、原料藥（APIs）、賦型劑或包裝材料的關鍵屬性；	To assess the critical attributes of raw materials, solvents, Active Pharmaceutical Ingredient (API) starting materials, APIs, excipients, or packaging materials
建立適當的規格、確認關鍵製程參數，及建立製造管制(例如，使用得自藥劑開發研究的資料。該資料與品質屬性之臨床重要性及在操作期間管制其能力有關)；	To establish appropriate specifications, identify critical process parameters and establish manufacturing controls (e.g., using information from pharmaceutical development studies regarding the clinical significance of quality attributes and the ability to control them during processing)
減少品質屬性的變異性： ● 降低產品及原物料的缺陷； ● 降低製造的缺陷。	To decrease variability of quality attributes: • reduce product and material defects • reduce manufacturing defects
評估關於放大批量及技術移轉之進一步研究（例如，生體相等性、安定性）的需求：	To assess the need for additional studies (e.g., bioequivalence, stability) relating to scale up and technology transfer
使用“設計空間”的概念(參見 ICH Q8)。	To make use of the “design space” concept (see ICH Q8)
II.4 設施、設備和公用設施的品質風險管理 （Quality Risk Management for Facilities, Equipment and Utilities）	
設施/設備的設計 （Design of facility / equipment）	
當設計建築物及設施時，決定其適當的區域，例如：	To determine appropriate zones when designing buildings and facilities, e.g.,
● 物料及人員的動線；	• flow of material and personnel
● 使污染減至最低；	• minimize contamination
● 防蟲鼠措施；	• pest control measures
● 混雜的防止；	• prevention of mix-ups
● 開放設備相對於密閉設備；	• open versus closed equipment
● 潔淨室相對於隔離裝置技術；	• clean rooms versus isolator technologies
● 專用或隔離的設施/設備。	• dedicated or segregated facilities / equipment
對設備及容器，決定其適當接觸產品之材料(例如不銹鋼等級、墊圈、潤滑劑的選擇)；	To determine appropriate product contact materials for equipment and containers (e.g., selection of stainless steel grade, gaskets, lubricants)
決定適當之公用設施(例如，蒸汽、氣體、電源、壓縮空氣、加熱、通風及空調(HVAC)、水)；	To determine appropriate utilities (e.g., steam, gases, power source, compressed air, heating, ventilation and air conditioning (HVAC), water)

相關之設備，決定適當之預防性維護保養(例如必要之備用零件的清單)。	To determine appropriate preventive maintenance for associated equipment (e.g., inventory of necessary spare parts)
設施的衛生狀況 （Hygiene aspects in facilities）	
使產品免於受到環境之危害，包含化學、微生物學、物理學上的危害(例如，決定適當的服裝及更衣、衛生相關事項)；	To protect the product from environmental hazards, including chemical, microbiological, and physical hazards (e.g., determining appropriate clothing and gowning, hygiene concerns)
保護環境（例如人員及潛在的交叉污染）的免於受到與所製造之產品造成相關的危害。	To protect the environment (e.g., personnel, potential for cross-contamination) from hazards related to the product being manufactured
設施/設備/公用設施的驗證 （Qualification of facility/ equipment/utilities）	
決定設施、建築物、生產設備及/或實驗室儀器之驗證範圍及程度（包含適當的校正方法）。	To determine the scope and extent of qualification of facilities, buildings, and production equipment and/or laboratory instruments (including proper calibration methods)
設備的清潔及環境管制 （Cleaning of equipment and environmental control）	
以預定用途為基礎,區分影響及決策 (例如多重目的相對於單一目的，批次生產相對於連續生產)；	To differentiate efforts and decisions based on the intended use (e.g., multi- versus single-purpose, batch versus continuous production)
決定可接受的（規定的）清潔確效限量。	To determine acceptable (specified) cleaning validation limits
校正/預防性維護保養（Calibration/preventive maintenance）	
設定適當的校正及維護保養時程表。	To set appropriate calibration and maintenance schedules
電腦系統及電腦管制設備 （Computer systems and computer controlled equipment）	
選擇電腦硬體及軟體的設計(例如，模組的、故障耐受性)；	To select the design of computer hardware and software (e.g., modular, structured, fault tolerance)
決定確效的程度，例如，	To determine the extent of validation, e.g.,
● 關鍵性能參數的確認；	• identification of critical performance parameters
● 需求及設計的選擇；	• selection of the requirements and design
● 程式碼的回顧；	• code review
● 測試的程度及測試方法；	• the extent of testing and test methods
● 電子紀錄及簽章的可靠性。	• reliability of electronic records and signatures

II.5 品質風險管理作為原/物料管理的一部分 （Quality Risk Management as Part of Materials Management）	
供應商及合約製造商（受委託製造者）的評價及評估（Assessment and evaluation of suppliers and contract manufacturers）	
提供供應商及合約製造商（受委託製造者）一個廣泛的評估(例如稽核、供應商品質協議)。	To provide a comprehensive evaluation of suppliers and contract manufacturers (e.g., auditing, supplier quality agreements)
原料 （Starting material）	
評估與原料上之變異有關聯的差異及可能的品質風險（例如年齡、合成路徑）。	To assess differences and possible quality risks associated with variability in starting materials (e.g., age, route of synthesis).
原物料的使用 （Use of materials）	
決定使用待驗中的原物料是否適當(例如，為後續之廠內處理)；	To determine whether it is appropriate to use material under quarantine (e.g., for further internal processing)
決定退回物品之重製、再加工、使用的適當性。	To determine appropriateness of reprocessing, reworking, use of returned goods
儲存、物流和運銷條件 （Storage, logistics and distribution condition s）	
評估裝置之適當性，以確保適當儲存及輸送條件的維持(例如溫度、濕度、容器之設計)；	To assess the adequacy of arrangements to ensure maintenance of appropriate storage and transport conditions (e.g., temperature, humidity, container design)
結合其他 ICH 指引，決定在儲存或運輸條件上之差異對產品品質的影響【例如，冷鏈管理 (cold chain management)】；	To determine the effect on product quality of discrepancies in storage or transport conditions (e.g. cold chain management) in conjunction with other ICH guidelines
維護基礎設施（例如，確保正確裝運條件、暫時儲存、危害性原物料及受管制原物料之處理、海關報關/海關結關的能力）；	To maintain infrastructure (e.g. capacity to ensure proper shipping conditions, interim storage, handling of hazardous materials and controlled substances, customs clearance)
提供確保藥品之可得性的資訊（例如，供應鏈之風險分級）。	To provide information for ensuring the availability of pharmaceuticals (e.g., ranking risks to the supply chain).
II.6 品質風險管理作為生產的一部分 （Quality Risk Management as Part of Production）	
確效 （Validation）	
確認查證、驗證及確效措施之範圍及程度(例如分析方法、製程、設備及清潔方法)；	To identify the scope and extent of verification, qualification and validation activities (e.g., analytical methods, processes, equipment and cleaning methods
決定後續管理措施的程度(例如抽樣、監測及再確效)；	To determine the extent for follow-up activities (e.g., sampling, monitoring and re-validation)

區分關鍵性與非關鍵性製程步驟，以便於確效研究之設計。	To distinguish between critical and non-critical process steps to facilitate design of a validation study
製程中抽樣及測試 （In-process sampling & testing）	
評估製程中之管制測試的頻率及程度(例如證明在核准之管制條件下縮減測試的正當性)；	To evaluate the frequency and extent of in-process control testing (e.g., to justify reduced testing under conditions of proven control)
評估並證明結合參數放行及即時放行之製程分析技術（PAT）的使用之合理性。	To evaluate and justify the use of process analytical technologies (PAT) in conjunction with parametric and real time release
生產計畫 （Production planning）	
決定適當之生產計畫（例如，專用的、時段切換的及併行性的生產順序）。	To determine appropriate production planning (e.g., dedicated, campaign and concurrent production process sequences).
II.7 品質風險管理當作實驗室管制及安定性研究的一部分 （Quality Risk Management as Part of Laboratory Control and Stability Studies）	
偏離規格結果 （Out of specification results）	
在調查偏離規格結果期間中，用於確認可能的根本原因及矯正措施。	To identify potential root causes and corrective actions during the investigation of out of specification results
再驗期間/末效日期 （Retest period / expiration date）	
評估半製品/中間產物、賦型劑及原料之儲存與檢驗的適當性。	To evaluate adequacy of storage and testing of intermediates, excipients and starting materials
II.8 品質風險管理做為包裝與標示的一部分 （Quality Risk Management as Part of Packaging and Labelling）	
包裝設計 （Design of packages）	
設計外包裝以保護經直接包材包裝的產品(例如確保產品之真實性、標示之易讀性)。	To design the secondary package for the protection of primary packaged product (e.g., to ensure product authenticity, label legibility)
容器封蓋系統的選擇 （Selection of container closure system）	
決定容器封蓋系統之關鍵性參數。	To determine the critical parameters of the container closure system
標籤管制 （Label controls）	
基於不同產品標籤可能產生混雜，包含相同標籤之不同版本在內，設計標籤之管制程序。	To design label control procedures based on the potential for mix-ups involving different product labels, including different versions of the same label