第一章 质量管理

一、原则Principle

生产许可证持有厂家只能生产医药产品，以确保药品符合其预期的使用目的，符合销售许可证的要求，并不因药品安全性、质量或药效方面的问题而给患者带来风险。达到这一质量目标是高层管理者的责任，同时也需要公司各部门、各层次的职员以及公司的供应商和销售商的参与并承担义务。为了确保达到该质量目标，必须全面设计并正确贯彻实施包括GMP 与质量控制(QC)在内的质量保证(QA)体系。该体系应用文件明文规定并对其有效性加以监控。质量保证体系的所有部门都必须充分配备胜任的人员，适宜足够的厂房、设备及设施。与此同时，生产许可证持有者及受权人员具有另外的法律责任。

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. To achieve the quality objective in a reliable manner there must be a comprehensively designed and correctly implemented system of Quality Assurance incorporating Good Manufacturing Practice and thus Quality Control. It should be fully documented and its effectiveness monitored. All parts of the Quality Assurance system 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 Qualified Person(s).

1.1 质量保证、GMP 和质量控制的基本概念是内在相互联系的。这里叙述的主要目的是强调它们之间的关系以及药品生产和控制中的重要性。*The basic concepts of Quality Assurance, Good Manufacturing Practice and Quality Control 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.*

二、质量保证Quality Assurance

1.2 质量保证是一个宽泛的概念，它包括影响产品质量的所有问题，是确保药品质量符合预期使用目的而进行组织管理的总和。因此质量保证是由GMP 本规范之外的其他因素所组成。*Quality Assurance is a wide ranging concept which covers all matters which individually or collectively influence the quality of a product. It is the total sum of the organised arrangements made with the object 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.*

质量保证体系对于药品的生产而言，应保证：*The system of Quality Assurance appropriate for the manufacture of medicinal products should ensure that:*

(1) 药品的设计与开发应按照GMP 和GLP 的要求进行；*medicinal products are designed and developed in a way that takes account of the requirements of Good Manufacturing Practice and Good Laboratory Practice;*

(2) 生产和控制操作应有明确规定，并采用GMP； *production and control operations are clearly specified and Good Manufacturing Practice adopted;*

(3) 明确规定管理职责； *managerial responsibilities are clearly specified;*

(4) 安排生产、供应和使用正确的原、辅、包材料； *arrangements are made for the manufacture, supply and use of the correct starting and packaging materials;*

(5) 对中间产品进行必要的控制、进行其他任何过程控制和验证； *all necessary controls on intermediate products, and any other in-process controls and validations are carried out;*

(6) 按照规定的程序，正确地加工与核查成品； *the finished product is correctly processed and checked, according to the defined procedures;*

(7) 在受权人确认批产品按照销售许可证和其他与药品生产、检验和释放有关的法规要求进行生产和质量控制，并签发合格证之前，药品不得销售或供应； *medicinal products are not sold or supplied before a Qualified 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;*

(8) 尽可能对药品贮存、销售及随后的处理做出满意的安排，以保证药品在货架寿命期内的质量；*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;*

(9) 建立自检和/或质量审计程序，定期对质量保证体系的有效性和适用性进行评价。*there is a procedure for Self-Inspection and/or quality audit which regularly appraises the effectiveness and applicability of the Quality Assurance system.*

三、药品生产质量管理规范(GMP)Good Manufacturing Practice for Medicinal Products

1.3 GMP 是质量保证的一部分，它确保药品始终按照适合于其使用目的的质量标准进行生产和控制，并符合销售许可证的要求。

1.3 Good Manufacturing Practice is that part of Quality Assurance which ensures that 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.

GMP 涉及生产和质量控制，其基本要求如下：

Good Manufacturing Practice is concerned with both production and quality control. The basic requirements of GMP are that:

(1) 所有生产工艺应有明确规定，根据经验进行系统的审核，并证明能够始终如一地生产出符合质量标准的药品。*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;*

(2) 应对生产工艺的关键步骤和工艺的重要变更进行验证。*critical steps of manufacturing processes and significant changes to the process are validated;*

(3) 提供所有GMP 必需的设施，包括：*all necessary facilities for GMP are provided including:*

a. 资历合格并经过培训的人员；*appropriately qualified and trained personnel;*

b. 适宜的厂房和空间；*adequate premises and space;*

c. 合适的设备及配套设施；*suitable equipment and services;*

d. 正确的物料、容器和标签；*correct materials, containers and labels;*

e. 经批准的程序和指令；*approved procedures and instructions;*

f. 合适的贮存设施和运输设备。*suitable storage and transport;*

(4) 指令和程序应使用清楚明了的语言，并适用于所提供的设施。 *instructions and procedures are written in an instructional form in clear and unambiguous language, specifically applicable to the facilities provided;*

(5) 操作者应经过培训，以便按正确地按照程序进行操作。*operators are trained to carry out procedures correctly;*

(6) 生产过程中采用手工和/或记录仪填写记录，以证明已完成的所有生产步骤是按照确定的程序和指令要求进行的，产品达到预期的质量和数量。任何重要偏差都应详细记录和调查。*records are made, manually 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;*

(7) 采用合适的方式保存生产记录（包括销售记录），以便追溯各批产品的完整历史。*records of*

manufacture including distribution which enable the complete history of a batch to be traced, are retained in a comprehensible and accessible form;

(8) 应将产品销售(批发)中影响质量的风险减至最低限度。*the distribution (wholesaling) of the products minimises any risk to their quality;*

(9) 建立从销售或供应渠道收回任何一批产品的系统。*a system is available to recall any batch of product, from sale or supply;*

(10) 了解上市产品的用户投拆，调查质量缺陷的原因，并采取的相应的整改措施，以避免再次发生。*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 reoccurrence.*

四、质量控制(QC) Quality Control

1.4. 质量控制是GMP 的一部分，它涉及取样、质量标准和质量检验、机构、文件和放行程序，以确保进行必要的相关检验，在判定质量符合要求之前，物料不得使用，产品不得销售或供应。*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.*

质量控制的基本要求如下：*The basic requirements of Quality Control are that:*

(1) 有适宜的设施、经过培训的人员和批准的程序，以便对原辅料、包装材料、中间产品、待包装品和成品进行取样、检查、测试以及必要时按照GMP 要求对环境进行监测。*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;*

(2) 由质量部门批准的人员并使用已批准的方法对原辅料、包装材料、中间产品、待包装品和成品进行取样。*samples of starting materials, packaging materials, intermediate products, bulk products and finished products are taken by personnel and by methods approved by Quality Control;*

(3) 对检验方法进行验证。*test methods are validated;*

(4) 采用手工和/或记录仪进行记录，以证明规定的取样、检查和测试程序均已完成。详细记录出现的任何偏差，并进行调查。*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;*

(5) 成品应含有符合销售许可证规定的定性、定量要求的活性成分，应具有规定的纯度，包装在合适容器中，并正确加贴标签。*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;*

(6) 记录应包括检查结果以及物料、中间产品、待包装品和成品依照质量标准进行检验的评价结果。产品评价包括对有关生产文件的审核与评价以及对偏离规定程序的偏差的评价。*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 roduction documentation and an assessment of deviations from specified rocedures;*

(7) 任何一批产品在未经受权人按照销售许可证的要求审核并签发合格证之前，不得放行销售或供应。*no batch of product is released for sale or supply prior to certification by a qualified Person that it is in accordance with the requirements of the Marketing Authorisation;*

(8) 原料有充足的对照品，产品应保留以便用于将来必须的产品检验，除产品的大包装外，产品保留最终包装形式。*sufficient reference samples of starting materials and products are retained 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.

五、产品质量回顾Product Quality Review

1.5. 应对所有获得许可证的药品，包括那些仅供出口的药品，进行定期或滚动式的质量回顾以证明所用工艺的始终一致性，起始原料和成品现行质量标准的适当性，并重点反映出变化趋势以及产品和工艺的改进。产品质量回顾一般情况下每年进行一次，并形成文件，应考虑到以前所作的产品质量回顾并至少应包括以下内容：

1.5. 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. Such reviews should normally be conducted and documented annually, taking into account previous reviews, and should include at least:

(1) 对产品中所使用的原辅料进行质量回顾，特别是那些由新供应商提供的原辅料。*A review of starting materials and packaging materials used for the product, especially those from new sources.*

(2) 对关键的过程控制和成品的检验结果进行质量回顾。*A review of critical in-process controls and finished product results.*

(3) 对所有不符合质量标准的批次进行回顾。*A review of all batches that failed to meet established specification(s) and their investigation.*

(4) 对所有关键性的偏差或不符合项以及与之相关的调查、整改结果和预防措施的有效性进行回顾。*A review of all significant deviations or non-conformances, their related investigations, and the effectiveness of resultant corrective and preventative actions taken.*

(5) 对所有工艺或检验方法的变更进行回顾。*A review of all changes carried out to the processes or analytical methods.*

(6) 对销售许可证变更内容的申报/批准/拒绝批准的情况进行回顾，包括第三国（出口国）申报的资料。*A review of Marketing Authorisation variations submitted/granted/refused, including those for third country (export only) dossiers.*

(7) 对稳定性监测结果进行回顾。*A review of the results of the stability monitoring programme and any adverse trends.*

(8) 对所有与质量相关的退货、投诉、召回、调查进行回顾。*A review of all quality-related returns, complaints and recalls and the investigations performed at the time.*

(9) 对以前整改措施的适合性进行回顾。*A review of adequacy of any other previous product process or equipment corrective actions.*

(10) 对于新销售许可证和销售许可证变更，则对其执行情况进行回顾。*For new marketing authorisations and variations to marketing authorisations, a review of post-marketing commitments.*

(11) 相关设备和公用系统的验证状态，如暖通空调系统、水系统、压缩空气等。*The qualification status of relevant equipment and utilities, e.g. HVAC, water, compressed gases, etc.*

(12) 已进行验证的设备清单和再验证的日期。*A review of Technical Agreements to ensure that they are up to date.*

生产厂家和销售许可证的持有者，若不是同一主体时，应对产品质量回顾的结果进行评价，应评价是否应采取整改措施和预防措施或是否应进行再验证。进行整改的原因应形成文件。对于已同意的整改措施和预防措施应通过有效的方法适时完成。应有适用的管理程序，应在自检中对这些程序的有效性进行确认。

The manufacturer and marketing authorisation holder, where different, should evaluate the results of this review and an assessment should be made 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 selfinspection.

产品质量回顾可根据产品类型进行相应的科学分类，例如：固体制剂、液体制剂、无菌产品等。

Quality reviews may be grouped by product type, e.g. solid dosage forms, liquid dosage forms, sterile products, etc. where scientifically justified.

当生产厂家与销售许可证的持有者不是同一主体时，双方之间应签订技术协议详细说明在产品质量回顾中各自相应的职责。负责成品质量的受权人与销售许可证持有者应确保产品质量回顾适时进行，并且确保其结果的准确性。

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 Qualified 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.

第二章 人员
CHAPTER 2 PERSONNEL

一、原则Principle

良好的质量保证体系的建立和保持以及药品的正确生产都需要依靠人来完成，因此必须有足够的高素质人员来承担企业的全部工作和责任。应清楚地了解并记录各自的职责。所有人员均应了解与其有关的GMP 的原则，并接受其工作所需要的初步培训和继续培训，其中包括卫生学知识的培训。

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.

二、通则General

2.1. 生产厂应有足够数量的具有资格和实践经验的人员，任何一个人所担负的责任不应太多，以免出现质量隐患。*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. 生产厂应有组织机图，重要岗位的负责人应有明确的书面岗位职责，并有权履行其职责。他们职责可以委派给具有满意资历水平的副职人员代理。执行GMP 的有关人员的职责，不应有空缺或重叠。*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.*

三、关键人员Key Personnel

2.3. 关键人员包括生产部门负责人和质量控制部门负责人，如果其中至少一人不负责2001/83/ EC《指南》第22 条款中所描述的职责，则应指定受权人（QP）负责。通常，关键岗位人员应为全职人员。生产部门和质量控制部门的负责人不能兼任。在较大的生产厂里，有必要将2.5、2.6、2.7 条所列的一些职能委派给代理人。

2.3 Key Personnel include the head of Production, the head of Quality Control, and if at least one of these persons is not responsible for the duties described in Article 51 of Directive 2001/83/EC1, the Qualified 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. 受权人（QP）的职责在2001/83/EC《指南》第51 条款中有详细描述，概括如下：*The duties of the Qualified Person(s) are fully described in Article 51 of Directive 2001/83/EC, and can be summarised as follows:*

a) 对于在欧共体内生产的药品，受权人必须确保每批药品的生产和检验符合《指导》的条款和销售许可证(1)。*for medicinal products manufactured within the European Community, a Qualified Person must ensure that each batch has been produced and tested/checked in accordance with the directives and the marketing authorisation (2);*

b) 对于在欧共体之外生产的药品，受权人必须确保每批进口药品在进口国均经过第51 条款1(b)中规定的检查。*for medicinal products manufactured outside the European Community, a*

Qualified Person must ensure that each imported batch has undergone, in the importing country, the testing specified in paragraph 1 (b) of Article 51;

c) 受权人在产品放行前必须在记录或相应文件中证明每批产品符合第51 条款的规定。*a Qualified Person must certify in a register or equivalent document, as operations are carried out and before any release, that each production batch satisfies the provisions of Article 51.*

履行以上职责的人员必须符合《指南》第493 条款的要求，他们将始终如一、持续地在生产许可证持有者的的安排下履行他们的职责。其职责可以委派，但只能委派于其它质量受权人。*The persons responsible for these duties must meet the qualification requirements laid down in Article 493 of the same Directive, they shall be permanently and continuously at the disposal of the holder of the Manufacturing Authorisation to carry out their responsibilities. Their responsibilities may be delegated, but only to other Qualified Person(s).*

2.5. 生产部门的负责人应负以下职责：*The head of the Production Department generally has the following responsibilities:*

(1) 确保产品按适当的文件进行生产和贮存，以达到质量要求。*to ensure that products are produced and stored according to the appropriate documentation in order to obtain the required quality;*

(2) 批准与生产操作相关的规程，并确保其严格地执行。*to approve the instructions relating to production operations and to ensure their strict implementation;*

(3) 确保生产记录在送到质量控制部门前经受权人评估和签字。*to ensure that the production records are evaluated and signed by an authorised person before they are sent to the Quality Control Department;*

(4) 检查所属部门设施、设备的维护保养情况。*to check the maintenance of his department, premises and equipment;*

(5) 确保相关验证工作的进行。*to ensure that the appropriate validations are done;*

(6) 确保所属部门人员按照需要进行初级和继续的培训。*to ensure that the required initial and continuing training of his department personnel is carried out and adapted according to need.*

2.6. 质量控制部门负责人应负以下职责：*The head of the Quality Control Department generally has the following responsibilities:*

(1) 有权批准或拒绝原料、包装材料、中间产品、待包装产品和成品的使用或发放。*to approve or reject, as he sees fit, starting materials, packaging materials, and intermediate, bulk and finished products;*

(2) 评估批生产记录。*to evaluate batch records;*

(3) 确保所有必须检验项目的进行。*to ensure that all necessary testing is carried out;*

(4) 批准质量标准、取样规程、检验方法和其它质量控制程序。*to approve specifications, sampling instructions, test methods and other Quality Control procedures;*

(5) 批准和检查委托检验工作。*to approve and monitor any contract analysts;*

(6) 检查所属部门设施、设备的维护保养情况。*to check the maintenance of his department, premises and equipment;*

(7) 确保相关验证工作的进行。*to ensure that the appropriate validations are done;*

(8) 确保所属部门人员按照需要进行初级和继续的培训。*to ensure that the required initial and continuing training of his department personnel is carried out and adapted according to need.*

质量控制部门的其它责任在第六章中概述。*Other duties of the Quality Control Department are summarised in Chapter 6.*

2.7. 生产部门和质量控制部门的负责人同行对质量负有分别或共同的责任。关于国家法规方面的内容包括：*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:*

◆ 书面程序和其它文件（包括修订）的批准；*the authorisation of written procedures and other documents, including amendments;*

◆ 生产环境监控；*the monitoring and control of the manufacturing environment;*

◆ 工厂卫生；*plant hygiene;*

◆ 工艺验证；*process validation;*

◆ 培训；*training;*

◆ 物料供应商的批准和检查；*the approval and monitoring of suppliers of materials;*

◆ 合同生产厂的批准和检查；*the approval and monitoring of contract manufacturers;*

◆ 物料和产品贮存条件的确定和监控；*the designation and monitoring of storage conditions for materials and products;*

◆ 记录的保存；*the retention of records;*

◆ 检查对GMP 的执行情况；*the monitoring of compliance with the requirements of Good Manufacturing Practice;*

◆ 对影响产品质量的因素进行检查、调查和取样。*the inspection, investigation, and taking of samples, in order to monitor factors which may affect product quality.*

四、培训Training

2.8. 生产厂应对进入生产区或质量控制实验室的人员（包括技术、维护和清洁人员）以及那些从事的活动可能对产品质量产生影响的人员进行培训。*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. 对于新员工，除GMP 理论和操作的基础培训外，还应对他们进行与其岗位相关的职责培训，以及再培训，并定期评价培训的实际效果。培训应有计划，并根据情况由生产部门或质量控制部门负责人批准。应保存培训记录。*Besides 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. 对于在污染危险区（例如：洁净区或其它从事高活性、毒性、污染性和致敏性物料的区域）工作的人员，应给予特殊的培训。*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. 参观人员和未经过培训的人员不得进入生产区和质量控制区域。如果这种情况不能避免时，应事先告诉他们在进入上述区域时，特别要注意个人卫生并按规定穿戴防护服。对他们应严格监督。*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. 培训期间，应对质量保证的概念和有助于增进对其理解、执行的所有措施进行充分讨论。*The concept of Quality Assurance and all the measures capable of improving its understanding and implementation should be fully discussed during the training sessions.*

五、人员卫生Personnel Hygiene

2.13. 应建立详细的卫生规程，并使之适应工厂内的不同需要，它应包括与人员的健康、卫生行为、人员着装相关的程序。每一个进入生产和质量控制区域的人员都应了解并严格执行这些程序。卫生规程应由管理人员改进，并在培训时进行充分讨论。*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. 所有新招聘的人员都应接受身体检查。生产企业应确保有相关程序，以保证生产人员明白人员健康状况与产品质量密切相关。在第一次体检后，应根据工作和个人健康状况的需要，再次进行体检。*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. 应采取措施确保任何患有传染病及体表有外伤的人员不得从事药品生产操作。*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. 所有进入生产区的人员应穿着与生产操作相适应的防护服。*Every person entering the manufacturing areas should wear protective garments appropriate to the operations to be carried out.*

2.17. 禁止在生产区和贮存区饮食、咀口香糖和吸烟，或贮存食品、饮料、香烟和个人药品。通常，在生产区或其它任何可能影响产品质量的区域禁止任何不卫生的行为。*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. 生产操作人员的手不得直接接触未包装的产品以及任何与产品接触的设备部位。*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. 应指导人员使用洗手装置。*Personnel should be instructed to use the hand-washing facilities.*

2.20. 特殊药品（如：无菌制剂）的生产要求见附录。*Any specific requirements for the manufacture of special groups of products, for example sterile preparations, are covered in the annexes.*

第三章 厂房和设备
CHAPTER 3 PREMISES AND EQUIPMENT

一、原则Principle

厂房和设备的位置、设计、结构、改建和维护保养应适合于所进行的操作。为了避免交叉污染、灰尘或污垢以及其它影响产品质量的因素，厂房和设备的布局及设计应使产生误差的危险减至最低限度，并易于有效的清洁和维护保养。*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 crosscontamination, build up of dust or dirt and, in general, any adverse effect on the quality of products.*

二、厂房Premises

（一）通则*General*

3.1. 厂房的位置选择应在考虑保证生产的同时，可使对物料或产品产生污染的危险减至低的环境。*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. 厂房的维护工作应细致，以确保在维修和维护保养操作不会危及产品质量。应按照详细的书面操作规程对厂房进行清洁和必要的消毒。*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. 厂房应有适当的照明、温度、湿度和通风条件。这些条件不得对生产和贮存中的药品质量或设备的精准操作产生直接或间接的影响。*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. 厂房的设计和配备应能最大地防止昆虫和其它动物的侵入。*Premises should be designed and equipped so as to afford maximum protection against the entry of insects or other animals.*

3.5. 应采取措施防止未经准许的人员进入厂房。生产区、贮存区和质量控制区不得成为不在这些地方工作的人员的通道。*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.*

（二）生产区*Production Area*

3.6. 为了使由于交叉污染引起药品质量事故的危险减至最低限度，一些特殊药品[如：高致敏性物质（如：青霉素类）或生物制品（如：活微生物制品）的生产应采用专用设施。另外一些产品（如：某些抗生素、激素、细胞毒素、高活性药物和非医药用产品）的生产不应在同一设施中进行。在特殊情况下，这些产品的生产不得不使用同一设施时，可安排同一品种不同批次连续生产，但必须采取特殊的防范措施，并经过必要的验证。具有工业毒性的产品（如：杀虫剂和除草剂）的生产不得与药品生产使用同一厂房。

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. 厂房应按实际生产制造的顺序及所要求的洁净级别进行合理布局。*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. 生产区和中间贮存区应足够大，设备和物料的摆放应有固定有规律的位置，以使不同药品和药品成份之间混淆的危险减至最低限度、避免交叉污染、最大限度地减小生产操作和质量控制步骤的遗漏或差错。*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. 对于原料、内包装材料、中间体或待包装产品暴露放置的环境，其内表面（如：墙壁、地板和天花板）应光滑、无裂缝、接口严密、无可理性物质脱落、易于有效清洁和必要时的消毒。*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. 线管、照明设施、通风端和其它辅助设施在设计和安装时应避免出现不易清洁的凹陷处。对于这些设施的维护保养，应尽可能地在生产区外进行。*Pipework, 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. 排水管口的尺寸应适当，并有防倒流装置。水道应尽可能避免开放式，如必须为开放式时，应较浅，以便于清洁与消毒。*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. 选用适当的空调设备（包括温度以及必要的湿度和过滤装置），以保证生产区内通风良好，即适宜于产品和操作者，又不影响外部环境。*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. 原辅料的称量应在专门的称量间中进行。*Weighing of starting materials usually should be carried out in a separate weighing room designed for that use.*

3.14. 为了防止交叉污染并有利于清洁，对易产生粉尘的操作（如：干品的取样、称量、混合和生产操作和的包装），应有特殊措施。*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 crosscontamination and facilitate cleaning.*

3.15. 为了防止混批和交叉污染，包装车间应有特殊的设计和布局。*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. 生产区尤其是生产线的目检部位应有良好的照明设备。*Production areas should be well lit, particularly where visual on-line controls are carried out.*

3.17. 生产过程控制可以在生产区内进行，但不得对生产构成危险。*In-process controls may be carried out within the production area provided they do not carry any risk for the production.*

（三）贮存区*Storage Areas*

3.18. 贮存区的面积应足够大，以便于各种物料和产品（原辅料和包装材料、中间体、待包装品

和成品，待检产品，合格产品、不合格产品、退货产品或召回产品）有次序地分类存放。*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. 贮存区的设计或改建应确保良好的贮存条件，特别应清洁、干燥、并保持适宜的温度。如果需要特殊的贮存条件（如，温度、湿度），应提供，并定期检查和监控。*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. 收发货区应能保证物料和产品免受气候的影响。接收区的设计与装备应使物料外包装在贮存前得到必要的清洁。*Receiving and dispatch bays should protect materials and products from the weather. Reception areas should be designed and equipped to allow containers of incoming materials to be cleaned where necessary before storage.*

3.21. 待检品隔离贮存时，该区域必须有明显的标志并仅限于受权人员进入。任何系统取代物理隔离系统时，应有同等的安全性。*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. 原辅料的取样通常应在隔离的取样区内进行。如果取样是在贮存区进行，应采取适当措施，以防止污染或交叉污染。*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. 不合格、召回会退回的物料或产品应分区存放。*Segregated areas should be provided for the storage of rejected, recalled or returned materials or products.*

3.24. 高活性物料或产品应贮存于安全区内。*Highly active materials or products should be stored in safe and secure areas.*

3.25. 印字包装材料与药品的一致性是至关重要的，应特别注意这些材料的安全贮存。*Printed packaging materials are considered critical to the conformity of the medicinal product and special attention should be paid to the safe and secure storage of these materials.*

（四）质量控制区*Quality Control Areas*

3.26. 质量控制实验室一般应与生产区分开。这对生物检定、微生物检定、放射性同位素检定的实验室尤为重要，它们应有各自独立的实验室。*Normally, Quality Control laboratories should be separated from production areas. This is particularly important for laboratories for the control of biologicals, microbiologicals and radioisotopes, which should also be separated from each other.*

3.27. 控制实验室应设计合理，便于检验操作。实验室应有充足的空间，以防止混淆和交叉污染，应有适当的样品贮存和记录存放的场所。*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. 为保护灵敏仪器设备免受振动、电子干扰和湿度等因素影响，必要时应有各自单独的操作间。*Separate rooms may be necessary to protect sensitive instruments from vibration, electrical interference, humidity, etc.*

3.29. 从事特殊物品（生物制品或放射性样品）检验的实验室应有特别的要求。*Special requirements are needed in laboratories handling particular substances, such as biological or radioactive samples.*

（五）附助区*Ancillary Areas*

3.30. 休息和茶点实应与其它区域分开。*Rest and refreshment rooms should be separate from other areas.*

3.31. 更衣室、洗涤室和卫生间应便于人员进入，并与使用者的数目相适应。卫生间不能与生产区或贮存区直接相连。*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. 维修间应尽可能地与生产区分开。在生产区内存放的零配件和工具，应保存在专用的房间内或带锁的小柜中。*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. 动物房间应与其它区域严格分开，并有专门入口（动物进口）和空气处理设施。*Animal houses should be well isolated from other areas, with separate entrance (animal access) and air handling facilities.*

三、设备Equipment

3.34. 生产设备的设计、位置和维护应适合于药品生产。*Manufacturing equipment should be designed, located and maintained to suit its intended purpose.*

3.35. 维修和维护保养操作不应危及产品质量。*Repair and maintenance operations should not present any hazard to the quality of the products.*

3.36. 生产设备的设计应易于彻底清洁。设备清洁应遵循详细的书面程序。设备应存放在清洁干燥的环境中。*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. 选用的洗涤和清洁设备不应成为污染源。*Washing and cleaning equipment should be chosen and used in order not to be a source of contamination.*

3.38. 设备的安装不应发生差错或产生污染。*Equipment should be installed in such a way as to prevent any risk of error or of contamination.*

3.39. 使用的生产设备不应对产品质量有不良影响。设备中与产品直接接触的部分不应与产品发生化学反应、加成作用或吸附作用以至影响产品质量，发生任何质量事故。*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. 衡器和测量设备的范围和精密度应满足生产和控制的要求。*Balances and measuring equipment of an appropriate range and precision should be available for production and control operations.*

3.41. 对于测量、称量、记录和控制设备，应采用合适的方法在规定时间内进行校验和检查，并保存这些检测的记录。*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. 固定的管线应清楚地标识其内容物和流向。*Fixed pipework should be clearly labelled to indicate the contents and, where applicable, the direction of flow.*

3.43. 应根据书面规程对蒸馏水管、去离子水管和其它水管进行清洁。书面规程中应描述微生物污染的超标限度和应采取的措施。*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. 不合格的设备应尽可能地搬离生产区和质量控制区，或至少应有醒目的不合格标志。*Defective equipment should, if possible, be removed from production and quality control areas, or at least be clearly labelled as defective.*

第四章 文件
CHAPTER 4 DOCUMENTATION

一、原则Principle

好的文件是质量保证体系必不可少的基本组成部分。明确的书面文件可以避免口头交流产生的错误，并能追溯批产品的历史。必须有书面的准确的质量标准、生产处方、指令、规程和记录。文件的清晰度是至关重要的。*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.*

二、通则General

4.1. 质量标准：详细描述产品或在生产中使用的或获得的物料必需达到的要求。它是质量评价的基础。*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.*

生产处方、制造和包装指令：应阐明所使用的全部原材料以及所有的制造步骤和包装操作。*Manufacturing Formulae, Processing and Packaging Instructions state all the starting materials used and lay down all processing and packaging operations.*

规程：提供了进行某项具体操作的规定，如：清洁、着装、环境控制、取样、检验、设备操作等。*Procedures give directions for performing certain operations e.g. cleaning, clothing, environmental control, sampling, testing, equipment operation.*

记录：应提供每批产品的历史，包括产品的销售以及与成品质量相关的所有细节。*Records provide a history of each batch of product, including its distribution, and also of all other relevant circumstances pertinent to the quality of the final product.*

4.2. 文件应仔细地设计、起草、审核和分发，应符合生产和销售许可证档案中相关部分的要求。*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. 文件应由相关的受权人批准，签字并注明日期。*Documents should be approved, signed and dated by appropriate and authorised persons.*

4.4. 文件内容不应含糊不清，其标题、类别和目的应表述明确。文件管理应有序以便于检查。复印件应清晰、易读。由主文件复制工作文件时，应保证整个复制过程不得产生任何差错。*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. 文件应定期审查、修订，以保持其时效性。文件修订后，应有有效的系统防止过时文件的误用。*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. 文件不应为手写体。如果需要在文件中填写数据，填写时也要保证干净、清晰、不易擦掉。文件中应有足够的空间以便于填写数据。*Documents should not be handwritten; 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. 对任何填写内容的更改均应签字，并注明日期；更改后原内容应清晰可读，必要时应记录更改的原因。*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. 各项记录均应及时填写，以便追溯与药品生产相关的全部重要活动。记录至少应保留至成品

效期后一年。*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. 数据可通过电子数据处理系统、照相或其它可靠的方式记录，但应有可行的与所使用系统相关的详细规程，并应检查记录的准确性。如果文件是使用电子数据处理方式处理的，仅允许受权人登录电脑或修改数据，修改和删除均应记录；应用密码或其它方法限制上述行为，关键数据的输入结果应逐一检查核对。采用电子方式贮存的批记录，应用磁带、缩影胶片、纸或其它方式进行备份。尤其重要的是在批记录保存期间随时可以得到。*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.*

三、文件要求Documents required

质量标准***Specifications***

4.10.原辅料、包装材料和成品应有经过批准并注明日期的质量标准，有时中间产品或待包装产品也应有质量标准。*There should be appropriately authorised and dated specifications for starting and packagingmaterials, and finished products; where appropriate, they should be also available forintermediate or bulk products.*

A. 原辅料和包装材料质量标准***Specifications for starting and packaging materials***

4.11. 原辅料、内包装材料或印字包装材料的质量标准应包括下列内容： *Specifications for starting and primary or printed packaging materials should include, if applicable:*

a) 对物料的描述内容应包括：*a description of the materials, including:*

— 物料名称和内部编码；*the designated name and the internal code reference;*

— 可参考的药典专论；*the reference, if any, to a pharmacopoeial monograph;*

— 批准的供应商和物料的生产厂家(如果可能)；*the approved suppliers and, if possible, the original producer of the products;*

— 印字包装材料的样本。*a specimen of printed materials;*

b) 取样、检验或相关程序的说明；*directions for sampling and testing or reference to procedures;*

c) 可接受的定性、定量的限度要求；*qualitative and quantitative requirements with acceptance limits;*

d) 贮存条件和注意事项；*storage conditions and precautions;*

e) 复检前的最长贮存期。*the maximum period of storage before re-examination.*

B. 中间产品和待包装产品的质量标准***Specifications for intermediate and bulk products***

4.12. 如果中间产品和待包装产品是采购或发送的，或者中间产品的数据将用于对成品的评价，此时应有中间产品和待包装产品的质量标准。中间产品和待包装产品的质量标准应与原辅料或成品的质量标准相类似。*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.*

C. 成品质量标准***Specifications for finished products***

4.13. 成品质量标准应包括：*Specifications for finished products should include:*

a) 产品名称和编码（如需要）；*the designated name of the product and the code reference where applicable;*

b) 产品处方或处方代号；*the formula or a reference to;*

c) 剂型和包装的详细说明；*a description of the pharmaceutical form and package details;*

d) 取样、检验或相关程序的说明；*directions for sampling and testing or a reference to procedures;*

e) 可接受的定性、定量的限度要求；*the qualitative and quantitative requirements, with the acceptance limits;*

f) 贮存条件和注意事项（如需要）；*the storage conditions and any special handling precautions, where applicable;*

g) 货架寿命。*the shelf-life.*

四、生产处方和工艺规程Manufacturing Formula and Processing Instructions

每一批量的产品均应有经正式批准的生产处方和工艺规程。两者通常合并在一个文件中。*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. 生产处方应包括：*The Manufacturing Formula should include:*

a) 产品名称和与该产品质量标准相关的产品编码；*the name of the product, with a product reference code relating to its specification;*

b) 剂型、规格和批量；*a description of the pharmaceutical form, strength of the product and batch size;*

c) 所用原辅料清单，包括每一种物料的名称、编码（该编码对某一物料是唯一的）和用量；指出在工艺过程中消失的任何物料；*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) 产品最终收率的可接受限度，如果需要也应有中间产品收率的可接受限度。*a statement of the expected final yield with the acceptable limits, and of relevant intermediate yields, where applicable.*

4.15. 工艺规程应包括：*The Processing Instructions should include:*

a) 生产场所和使用的主要设备；*a statement of the processing location and the principal equipment to be used;*

b) 关键设备使用前的准备方法或方法代号。（如：清洁、装配、校正、消毒）；*the methods, or reference to the methods, to be used for preparing the critical equipment (e.g. cleaning, assembling, calibrating, sterilising);*

c) 生产各步骤的详细规程（如：物料的核查、预处理、加料顺序、混合时间、温度）；*detailed stepwise processing instructions (e.g. checks on materials, pre-treatments, sequence for adding materials, mixing times, temperatures);*

d) 过程控制项目及限度；*the instructions for any in-process controls with their limits;*

e) 必要时，应注明待包装产品的贮存要求，包括容器、标签以及特殊贮存条件的要求；*where necessary, the requirements for bulk storage of the products; including the container, labelling and special storage conditions where applicable;*

f) 应遵守的任何特殊预防措施。*any special precautions to be observed.*

五、包装规程Packaging Instructions

4.16. 对每一产品的包装规格和包装形式都应有正式批准的包装规程。包装规程通常包括或涉及以下内容：*There should be formally authorised Packaging Instructions for each product, pack size and type. These should normally include, or have a reference to, the following:*

a) 产品名称；*name of the product;*

b) 剂型和规格；*description of its pharmaceutical form, and strength where applicable;*

c) 包装规格按产品在最终包装容器内的数量、重量或体积表示；*the pack size expressed in terms of the number, weight or volume of the product in the final container;*

d) 一个标准批量产品所需全部包装材料的清单。包括包装材料的数量、尺寸和类型，以及与每一种包装材料的质量标准相关的编码或代号；*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) 适当的时候应给出印字包装材料的样本或复印件，样本上标示出产品批号和货架寿命的打印位置；*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) 需遵守的特殊预防措施，包括开机前仔细检查生产区域和设备以确定生产线的清洁；*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) 包装操作的描述，包括任何重要的辅助操作和使用的设备；*a description of the packaging operation, including any significant subsidiary operations, and equipment to be used;*

h) 控制控制的细节，包括取样和可以接受限度。*details of in-process controls with instructions for sampling and acceptance limits.*

六、批生产记录Batch Processing Records

4.17. 每批产品的生产都应有批生产记录。批生产记录应以现行的已批准的生产处方和工艺规程的相关部分为基础编写。记录的设计应避免发生书写错误，记录上应记录正在生产中的产品批号。*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.*

在任何生产操作开始之前，应有检查设备和工作场所无上批产品，无计划生产批所不需要的文件或物料，设备已清洁待用，并作记录。*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.*

生产过程中，每完成一项操作均应及时记录以下内容，并由生产操作的负责人确认签字，注明日期。*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) 产品名称；*the name of the product;*

b) 中间产品重要步骤开始的日期和时间，以及生产结束的日期和时间；*dates and times of commencement, of significant intermediate stages and of completion of production;*

c) 生产各阶段负责人的姓名；*name of the person responsible for each stage of production;*

d) 各重要生产步骤操作人员以及适当时复核人员的签名（如：称量）；*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) 批号和/或检验编号以及每种原辅料的实际称量数量。（包括加入回收料或返工料的批号和数量）；*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) 任何与生产相关的操作或事项和使用的主要设备；*any relevant processing operation or event and major equipment used;*

g) 生产过程控制记录、过程控制人员签名及过程控制的结果；*a record of the in-process controls and the initials of the person(s) carrying them out, and the results obtained;*

h) 生产各阶段的产品收率；*the product yield obtained at different and pertinent stages of*

manufacture;

i) 特殊问题的说明，包括对生产处方和工艺规程的偏差处理的细节，以及批准人的签名。*notes on special problems including details, with signed authorisation for any deviation from the Manufacturing Formula and Processing Instructions.*

七、批包装记录Batch Packaging Records

4.18. 每批产品或部分批产品的包装都应有批包装记录。批包装记录应以包装规程的相关部分为基础编写。记录的设计应避免发生书写错误，记录上应记录包装产品的批号和待包装品的数量，以及将得到的成品的批号和计划产量。*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.*

在任何包装操作开始之前，应有检查设备和工作场所无上批产品，无计划生产批所不需要的文件或物料，设备已清洁待用，并作记录。*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.*

生产过程中，每完成一项操作均应及时记录以下内容，并由包装操作的负责人确认签字，注明日期。*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) 产品名称；*the name of the product;*

b) 包装操作的日期和时间；*the date(s) and times of the packaging operations;*

c) 包装操作负责人的姓名；*the name of the responsible person carrying out the packaging operation;*

d) 各重要步骤操作人员的签名；*the initials of the operators of the different significant steps;*

e) 与包装规程一致性的检查记录，包括过程控制结果；*records of checks for identity and conformity with the packaging instructions including the results of in-process controls;*

f) 包装操作的详细情况，包括所使用的包装设备和包装线；*details of the packaging operations carried out, including references to equipment and the packaging lines used;*

g) 如有可能，对使用的印字包装材料应留样本，包括打印了批号、有效期和任何附加内容的包装材料样本；*whenever possible, samples of printed packaging materials used, including specimens of the batch coding, expiry dating and any additional overprinting;*

j) 任何特殊问题或异常情况的说明，包括对生产处方和工艺规程的偏差处理的细节，以及批准人的签名；*notes on any special problems or unusual events including details, with signed authorisation for any deviation from the Manufacturing Formula and Processing Instructions;*

h) 所有印字包装材料和待包装品的编码或鉴别号、发送量、使用量、销毁量或退库量以及成品的数量，以便进行物料平衡。*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.*

八、程序和记录Procedures and records

（一）接收*Receipt*

4.19. 应制定原辅料、内包装材料和印字包装材料的书面接收程序，每次到货接收应有记录。*There should be written procedures and records for the receipt of each delivery of each starting and primary and printed packaging material.*

4.20. 接收记录应包括：*The records of the receipts should include:*

a) 交货单和包装上的物料名称；*the name of the material on the delivery note and the containers;*

b) 内部使用的物料名称和/或物料编码（如果与a）项不同）；*the "in-house" name and/or code of material (if different from a);*

c) 接收日期；*date of receipt;*

d) 供应商名称和生产厂家名称（如果可能）；*supplier's name and, if possible, manufacturer's name;*

e) 生产厂家的批号或相关参考号；*manufacturer's batch or reference number;*

f) 接收的总数量和包装件数；*total quantity, and number of containers received;*

g) 接收编号；*the batch number assigned after receipt;*

h) 任何相关的说明（如：对包装状况）；*any relevant comment (e.g. state of the containers).*

4.21. 应制定原辅料、包装材料和其它物料的内部贴签、待检及贮存的书面操作规程。*There should be written procedures for the internal labelling, quarantine and storage of starting materials, packaging materials and other materials, as appropriate.*

（二）取样*Sampling*

4.22. 应制定书面的取样规程，包括取样受权人、取样方法和取样设备、取样量和为避免物料污染和影响物料质量所采取的预防措施（见第六章质量控制第13 条）。*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).*

（三）检验*Testing*

4.23. 应制定物料和生产各阶段产品的书面检验规程。规程中应阐明检验方法和检验使用的设备，并有检验记录（见第六章质量控制第17 条）。*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).*

（四）其它*Other*

4.24. 应制定物料和产品放行和拒收的书面规程，尤其是受权人按照2001/83/EC《指南》第51 条之要求批准放行供销售的成品。*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 Qualified Person(s) in accordance with the requirements of Article 51 of Directive 2001/83/EC1.*

4.25. 每批产品的销售应有记录，并予以保存，以便于必要时按批召回产品。（见第八章 投诉和产品召回）。*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. 对以下各项应分别制定书面规程，必要时应对以下各项所做工作和得到的结论进行记录。*There should be written procedures and the associated records of actions taken or conclusions reached, where appropriate, for:*

a) 验证；

b) 设备安装和校验；*equipment assembly and calibration;*

c) 维修、清洁和消毒；*maintenance, cleaning and sanitation;*

d) 人员情况，包括：培训、着装和卫生；*personnel matters including training, clothing, hygiene;*

e) 环境监控；*environmental monitoring;*

f) 昆虫预防；*pest control;*

g) 用户投诉；*complaints;*

h) 产品召回；*recalls;*

i) 退货。*returns.*

4.27. 主要的生产和检验设备应有明确的操作规程。*Clear operating procedures should be available for major items of manufacturing and test equipment.*

4.28. 主要设备或关键设备应有台帐，记录验证、校验、维护保养、清洁或维修等操作，并应包括操作人员的签名和日期。*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. 台帐中还应按时间顺序记录主要设备或关键设备的使用和产品的生产区域。*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 生产
CHAPTER 5 PRODUCTION

一、原则Principle

生产操作必须按规定的程序进行，必须符合GMP 的原则，以确保产品达到所要求的质量，并满足相关生产许可证和销售许可证的要求。*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.*

二、通则General

5.1. 应由有能力的人员进行生产操作和生产监督。*Production should be performed and supervised by competent people.*

5.2. 物料和产品的处理，如接收和待检、取样、贮存、贴签、发料、生产、包装和销售等应按照书面规程或指令进行，并作必要的记录。*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. 应对所有的进货进行检查，以确保到货的物料与订单相符。必要时对包装进行清洁，并贴签标明规定的内容。*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. 对包装破损及其它任何可能影响物料质量的问题应进行调查和记录，并报告质量控制部门。*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 物料和成品应在接受时或生产中应有效隔离，直至其被放行使用或发货。*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. 对于外购的中间产品和待包装产品，在接收时视同原辅料接收。*Intermediate and bulk products purchased as such should be handled on receipt as though they were starting materials.*

5.7. 所有物料和产品都应按生产厂家确定的合适的条件贮存，并有序保管，以便于分批存放和库存周转。*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. 应检查收率和数量平衡，确保差异未超出可接受的限制标准。*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. 不同产品的生产操作不得在同一房间内同时或连续地进行，除非能避免混淆或交叉污染。*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. 在生产的每一阶段，应保护产品和物料不受微生物和其它污染。*At every stage of processing, products and materials should be protected from microbial and other contamination.*

5.11. 使用干燥物料和进行干燥产品的生产时，应采取特殊的预防措施，避免粉尘的产生和飞扬，尤其是高活性和敏感性物质。*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. 在整个生产过程中，对所有物料、包装容器、主要设备和使用房间均应标识，或以其它方式

指明正在生产的产品或物料、规格和批号，必要时标明生产步骤。*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. 用于包装容器、设备或房间的标签应清晰、准确，并采用公司统一的格式。除在标签上使用文字外，使用颜色标明其状态（如，待验、合格、不合格、清洁等）很有益处。*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. 应对将产品从一个区域传送到另一个区域所使用的管线和设备接口进行检查，确保其正确连接。*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. 应尽量避免任何与规程或程序不符的偏差。如果有偏差发生，应得到指定人员的书面批准，必要时需质量控制部门参与。*Any deviation from instructions or procedures should be avoided as far as possible. If a deviation occurs, it should be approved in writing by a competent person, with the involvement of the Quality Control Department when appropriate.*

5.16. 生产区应仅限于经过批准的人员进入。*Access to production premises should be restricted to authorised personnel.*

5.17. 通常，应避免在药品生产区使用制药设备生产非药用产品。*Normally, the production of non-medicinal products should be avoided in areas and with the equipment destined for the production of medicinal products.*

三、生产过程中对交叉污染的预防

Prevention of cross-contamination in production

5.18. 应避免一种原辅料或产品被另一种原辅料或产品污染。由生产过程中的物料和产品、设备上的残留物和操作人员的服装产生的未经控制的尘埃、气体、蒸汽、喷雾、喷雾或生物可引起交叉污染的危险。污染程度因污染的类型和被污染的产品而有所不同，其中强致敏物、生物制剂（或生物体）、某些激素、细胞毒素、其它高活性物质等引起的污染是最危险的。注射剂、大量使用和/或长期使用的药品一旦污染可能是最严重的。*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. 为了避免交叉污染的发生，应采取适当的技术或管理措施，如：*Cross-contamination should be avoided by appropriate technical or organizational measures, for example:*

a) 在隔离区内进行生产（如：青霉素、活疫苗、活菌制剂和其它一些生物制品），或同品种不同批次的产品连续生产一定的周期，然后进行必要的清洁；*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) 提供适当的气闸排气；*providing appropriate air-locks and air extraction;*

c) 将再循环空气、或未经处理或处理不彻底的空气进入而引起的污染危险降至最低；*minimising the risk of contamination caused by recirculation or re-entry of untreated or insufficiently treated air;*

d) 在生产极具交叉污染危险的产品的区域穿戴防护服；*keeping protective clothing inside areas where products with special risk of crosscontamination are processed;*

e) 使用有效的清洁和防污染程序，因为未有效清洁的设备是一种常见的交叉污染源；*using cleaning and decontamination procedures of known effectiveness, as ineffective cleaning of equipment is a common source of cross-contamination;*

f) 使用“封闭系统”生产；*using “closed systems” of production;*

g) 检验设备上的残留物，使用设备清洁状态标志。*testing for residues and use of cleaning status labels on equipment.*

5.20 根据制定的程序定期检查预防交叉污染的措施及其有效性。*Measures to prevent cross-contamination and their effectiveness should be checked periodically according to set procedures.*

四、验证Validation

5.21. 验证是对GMP 的加强，应按制定的程序进行验证；验证结果和结论应有记录。*Validation studies should reinforce Good Manufacturing Practice and be conducted in accordance with defined procedures. Results and conclusions should be recorded.*

5.22. 当采用任何一种新的生产处方或制备方法时，应验证其在常规生产中的适宜程度。应证明使用所确定的工艺、原辅料和设备可得到始终符合质量标准的产品。*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. 对生产工艺的任何重大修改（包括可能影响产品质量和/或工艺冲现性的设备或物料的任何改变）应进行验证。*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. 应对工艺和程序定期进行关键的再验证，以确保其达到预期的结果。*Processes and procedures should undergo periodic critical re-validation to ensure that they remain capable of achieving the intended results.*

五、原料Starting materials

5.25. 原辅料的采购是一项重要的工作。采购人员应具有专业知识，并了解供应商的全部情况。*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. 原辅料只能从经过批准的供应商（在相关的质量标准中注明）处采购，如果可能，应直接从生产厂采购。建议与供应商讨论企业制定的原辅料质量标准。企业与供应商就有疑问的原辅料生产和控制方面的问题(包括物料处理、贴签和包装要求以及投诉和拒收程序)进行讨论是有益的。*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. 原辅料每次到货接收时，应对包装和封签的完好性进行以及交货单与供应上标签的一致性进行检查。*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. 如果一次到货的同一种物料由不同批次构成时，应对每一批次分别取样、检验和放行。*If one material delivery is made up of different batches, each batch must be considered as separate for sampling, testing and release.*

5.29. 贮存区的原辅料应有适当的标识（详见第5 章生产 第13 条）。标签至少应包括以下内容：*Starting materials in the storage area should be appropriately labelled (see Chapter 5, item 13). Labels should bear at least the following information:*

— 产品名称和内部编码；*the designated name of the product and the internal code*

reference where applicable;

— 接收批号；*a batch number given at receipt;*

— 内容物的状态（如：待检、检验中、合格、不合格）；*where appropriate, the status of the contents (e.g. in quarantine, on test, released, rejected);*

— 有效期或复检日期。*where appropriate, an expiry date or a date beyond which retesting is necessary.*

当库房完全适用计算机系统管理时，以上内容不一定要全部反映在标签上。*When fully computerised storage systems are used, all the above information need not necessarily be in a legible form on the label.*

5.30. 应制定适当的的程序或措施以确保对每一个包装的内容物进行鉴别。已取样的包装上应有取样标志（详见第六章质量控制 第13 条）。*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. 只有经质量控制部门检验合格，并在货架寿命期内的原辅料方可使用。*Only starting materials which have been released by the Quality Control Department and which are within their shelf life should be used.*

5.32. 原辅料应由指定的人员根据书面程序进行称量，以保证将正确的物料精准地称量，并置于洁净并正确贴签的容器内。*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. 对称量好的每一种原辅料，应逐一复核其重量或容积，并作记录。*Each dispensed material and its weight or volume should be independently checked and the check recorded.*

5.34. 为同一批次产品被好的各种原辅料应放在一起，并醒目标识。*Materials dispensed for each batch should be kept together and conspicuously labelled as such.*

六、生产操作：中间产品和待包装产品

Processing operations: intermediate and bulk products

5.35. 在任何生产操作开始前，确保工作区域和设备的清洁，并没有与本次操作无关的任何原辅料、产品、产品剩余物或文件。*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. 中间产品和待包装产品应保存在适宜的条件下。*Intermediate and bulk products should be kept under appropriate conditions.*

5.37. 关键工艺应经过验证（见本章验证）。*Critical processes should be validated (see "VALIDATION" in this Chapter).*

5.38. 进行必须的生产过程控制和环境控制，并作记录。*Any necessary in-process controls and environmental controls should be carried out and recorded.*

5.39. 任何与预期产量的明显偏差均应记录并进行调查。*Any significant deviation from the expected yield should be recorded and investigated.*

七、包装材料Packaging materials

5.40. 内包装材料和印字包装材料的采购、操作和控制应参照原辅料的有关规定执行。*The purchase, handling and control of primary and printed packaging materials shall be accorded attention similar to that given to starting materials.*

5.41 应特别注意印字包装材料。印字包装材料应贮存在适当安全的条件下，以避免未经许可的人员接近。裁切过的标签和其它印字包装材料应按分类置于密闭的包装容器内贮存和输送，以避免混淆。包装材料只能由受权人按照批准的书面程序发放使用。*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 authorized personnel following an approved and documented procedure.

5.42. 每次交付的或每一批次的印字包装材料或内包装材料应有编码或识别标记。*Each delivery or batch of printed or primary packaging material should be given a specific reference number or identification mark.*

5.43. 过期或作废的内包装材料或印字装材料应进行销毁，并有销毁记录。*Outdated or obsolete primary packaging material or printed packaging material should be destroyed and this disposal recorded.*

八、包装操作Packaging operations

5.44. 制订包装计划时，应特别注意使产生交叉污染、混淆或差错的危险降至最小限度。不同的产品不得在相邻的包装线上进行包装，除非对其进行物理隔离。*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. 在包装操作开始前，应确保工作区域、包装线、印刷设备和其它设备的洁净，并没有上一次使用的与本次操作无关的任何产品、物料或文件。应根据合适的检查清单逐项对包装线的清场情况进行检查。*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. 在每一包装工作台或包装生产线上应标明正在生产的产品的名称和批号。*The name and batch number of the product being handled should be displayed at each packaging station or line.*

5.47. 所有将要使用的产品和包装材料在送到包装车间时，应对其品种、数量以及是否与包装指令相符进行检查。*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. 灌装用的容器在灌装前应是洁净的。应注意避免和清除玻璃碎片和金属颗粒等污染物质。*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，灌封后应尽可能快地进行贴签。否则，应制定适当的程序以保证不会出现混淆或者贴错标签。*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. 应对任何印字操作（如：编号、有效期等；无论是另外进行还是在包装过程中进行）进行检查核对，并作记录。应特别注意手工打印操作，对其应定期进行检查复检。*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. 当使用裁切过的标签和不在线打印操作时应特别注意。通常，卷式标签由于裁切过的标签，因为卷式标签有助于避免混淆。*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. 应对任何电子读码器、标签记数器或类似装置进行检查，以保证其正确操作。*Checks should be made to ensure that any electronic code readers, label counters or similar devices are operating correctly.*

5.53. 包装材料上的打印或压痕内容应清晰、持久、不易擦掉或褪色。*Printed and embossed information on packaging materials should be distinct and resistant to fading or erasing.*

5.54. 包装过程中对产品的在线控制至少应包括对下列项目的检查：*On-line control of the product during packaging should include at least checking the following:*

a) 包装的外观；*general appearance of the packages;*

b) 包装是否完整；*whether the packages are complete;*

c) 使用的产品和包装材料是否正确；*whether the correct products and packaging materials are used;*

d) 加印的内容是否正确；*whether any over-printing is correct;*

e) 生产线上的监测装置功能正常与否。*correct functioning of line monitors.*

从包装线上取走的样品，不得再放回包装线。*Samples taken away from the packaging line should not be returned.*

5.55. 涉及到异常事件的产品只有在经过特别检查、调查和受权人的批准后才能重新纳入生产过程。对此类操作应详细记录。*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. 在待包装产品和印字包装材料的数量以及成品数量的平衡过程中发现任何明显或异常的偏差时，均应进行调查，做出合理说明后，方可放行。*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. 包装操作全部完成后，应将印有批号而没有用完的包装材料销毁，销毁应有记录。如果将未打印批号的包装材料退库，则应按书面程序规定执行。*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.*

九、成品Finished products

5.58. 成品在最终放行前，应按企业制定的贮存条件存放于待检区。*Finished products should be held in quarantine until their final release under conditions established by the manufacturer.*

5.59. 成品放行前需进行的成品和文件的审核，见第六章 质量控制。*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. 成品放行后，应在企业制定的贮存条件下贮存。*After release, finished products should be stored as usable stock under conditions established by the manufacturer.*

十、不合格、回收料和退货物料Rejected, recovered and returned materials

5.61. 不合格物料和产品应有醒目的标识，并单另存放在限制区。不合格物料和产品应退回给供应商，或进行必要的返工，或销毁。无论采取那种处理方式均应由授权人批准，并作记录。*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. 对不合格产品的返工应属例外情况。只有当返工不影响最终产品的质量，成品符合质量标准，并在对其可能产生的质量风险进行评估后按照所制定并经批准的程序进行时方可允许返工。返工应有记录。*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. 将符合质量要求的同一产品先前批次的部分或全部回收料在确定的生产工序加入正在生产的产品这一做法，应事先得到批准。回收料的使用应在对其可能存在的质量风险包括影响货架寿命的可能性）进行评估后，按照已确定的程序进行。回收料的使用应有记录。*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. 对于返工或加入回收料的成品，质量控制部门应考虑增加额外的检验项目。*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. 对于退货且曾在生产厂家控制以外的产品，应予以销毁，除非确信其质量符合要求；只有在质量控制部门根据书面程序评估后方考虑退货产品的重新销售、重新贴签或加入以后批次的产品中进行回收利用。评估时应考虑产品的性质、特殊贮存条件、产品状况和历史，以及成品发货至今的时间等因素。若对产品质量有任何疑问，即便通过基本的化学方法返工后可回收有效成份，也不适合于再发货或再使用。所采取的任何措施均应有相应的记录。*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 in 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 ingredient may be possible. Any action taken should be appropriately recorded.*

第六章 质量控制

一、原则Principle

质量控制涉及取样、质量标准和检验，以及组织机构、文件系统和发放程序，以确保进行了必要的相关检验，在判定质量合格之前，物料不得放行使用，或产品不得放行销售或供应。质量控制不仅限于实验室操作，还必须参与所有与产品质量有关的决定。质量控制独立于生产是获得满意质量控制的基础（参见第一章 质量管理）。*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).*

二、通则General

6.1. 每个生产许可证持有者应设立质量控制部门，该部门应独立于其它部门。部门负责人应具有一定的资质和经验，并管理一个或几个实验室。质量控制部门不需有充足的资源，以确保所有质量控制活动能有效、可靠地进行。*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. 质量控制负责人的主要职责见第二章 人员。质量控制部门作为一个整体还有其它职责，例如：所有质量控制程序的制定、验证和实施，保存物料和产品的样品，确保物料和产品包装正确标签，确保对产品稳定性的监测，参与有关产品质量投诉的调查等。所有的操作应完全按照书面的程序进行，并作必要的记录。*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. 成品的评价应涵盖所有相关的因素，包括生产条件，过程检验结果，对生产（包括：包装）文件的审核，评判成品是否符合成品质量，及对最终产品包装的检查。*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. 质量控制人员应有权进入生产区进行取样和必要时的调查。*Quality Control personnel should have access to production areas for sampling and investigation as appropriate.*

三、质量控制实验室规范Good Quality Control Laboratory Practice

6.5. 质量控制实验室的房屋设施和设备应符合第三章 厂房和设备 中对质量控制区域的一般要求和特殊要求。*Control laboratory premises and equipment should meet the general and specific requirements for Quality Control areas given in Chapter 3.*

6.6. 实验室的人员、设施和设备应与其工作性质和生产规模相适应。使用外部实验室应符合第七章 合同生产和检验 的原则，在有特殊原因时，可以委托外部实验室检验，但应在质量控制记录中说明。*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.

四、文件*Documentation*

6.7. 实验室文件应符合第四章 文件原则，其中质量控制文件十分重要，质量控制部门应制定以下文件：*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:*

- 质量标准；*specifications;*
- 取样程序；*sampling procedures;*
- 检验程序与记录（包括：检验单和/或实验室记录）；*testing procedures and records (including analytical worksheets and/or laboratory notebooks);*
- 检验报告和/或证书；*analytical reports and/or certificates;*
- 环境监控数据（如需要）；*data from environmental monitoring, where required;*
- 检验方法的验证记录（如需要）；*validation records of test methods, where applicable;*
- 仪器校验和设备维护保养规程和记录。*procedures for and records of the calibration of instruments and maintenance of equipment.*

6.8. 任何与批记录相关的质量控制文件应保存至产品有效期后一年，并至少保存到按2001/83/EC规范第53（3）条款要求签发证书后五年。*Any Quality Control documentation relating to a batch record should be retained for one year after the expiry date of the batch and at least 5 years after the certification referred to in Article 51(3) of Directive 2001/83/EC.*

6.9. 对于某些数据（如：分析检验结果、收率、环境控制等），建议以适当的方式保存记录，以便进行趋势评估。*For some kinds of data (e.g. analytical tests results, yields, environmental controls) it is recommended that records are kept in a manner permitting trend evaluation.*

6.10. 除了与批记录有关的文件外，其它原始数据，如实验室记录本和/或记录，应予以保留，并可供随时查阅。*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*

五、取样*Sampling*

6.11. 取样应按批准的书面程序进行，程序应包括以下内容：*The sample taking should be done in accordance with approved written procedures that describe:*

- 取样方法；*the method of sampling;*
- 所用设备；*the equipment to be used;*
- 取样量；*the amount of the sample to be taken;*
- 分样说明；*instructions for any required sub-division of the sample;*
- 样品瓶的类形和要求；*the type and condition of the sample container to be used;*
- 已取样容器的标识；*the identification of containers sampled;*
- 需注意的事项，特别是无菌物料或有害物料取样时；*any special precautions to be observed, especially with regard to the sampling of sterile or noxious materials;*
- 样品贮存条件；*the storage conditions;*
- 取样设备的清洁和贮存说明。*instructions for the cleaning and storage of sampling equipment.*

6.12. 样品应具有代表性。为了监测生产过程中最重要的环节，还可取其它样品（如：生产开始或结束时的样品）。*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. 样品瓶应贴标签，标明其内容物、批号、取样日期以及样品取自哪一包装容器。*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. 对照品与留样指南详见附录19。*Further guidance on reference and retention samples is*

given in Annex 19.

六、检验***Testing***

6.15. 应对分析检验方法进行验证，销售许可证上要求的任何检验项目均应按照批准的检验方法进行检验。*Analytical methods should be validated. All testing operations described in the marketing authorisation should be carried out according to the approved methods.*

6.16. 记录并复核检验结果，以确保其一致性。任何计算均应仔细复核。*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. 检验应有记录，检验记录应至少包括以下内容：*The tests performed should be recorded and the records should include at least the following data:*

a) 物料或产品的名称和剂型（如适用）；*name of the material or product and, where applicable, dosage form;*

b) 批号和生产厂家和/或供应商；*batch number and, where appropriate, the manufacturer and/or supplier;*

c) 相关质量标准和检验程序编号；*references to the relevant specifications and testing procedures;*

d) 检验结果（包括：观察与计算结果）和检验报告编号；*test results, including observations and calculations, and reference to any certificates of analysis;*

e) 检验日期；*dates of testing;*

f) 检验员签名；*initials of the persons who performed the testing;*

g) 复核人（检验和计算）签名；*initials of the persons who verified the testing and the calculations, where appropriate;*

h) 合格或不合格（或其它决定）的明确陈述，并有相关负责人的签字和日期。*a clear statement of release or rejection (or other status decision) and the dated signature of the designated responsible person.*

6.18. 所有过程控制，包括生产人员在生产区进行的检验，都应按照质量控制部门批准的方法进行检验，并记录结果。*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. 应特别注意实验室试剂、容量玻璃仪器和溶液、对照品和培养基的质量，并按照书面程序进行准备。*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. 长期使用的试剂应标明配制日期并有配制人签名。对于不稳定的试剂和培训基应在标签上标明其有效期和贮存条件。另外，容量分析用的标准溶液应注明最后一次标定的日期及最新的参数。*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 standardization and the last current factor should be indicated.*

6.21. 必要时，在检验所用物质（如：试剂和标准品）的包装上标明接收日期，使用和贮存应按说明书执行。在某些情况下，应于接收时或使用前对试剂进行鉴别试验和/或其它检验。*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. 用于物料或产品检验的动物，使用前应进行检疫。应通过有效方法进行饲养和控制，以确保其适用性。应对动物进行标识并作详细记录，以便了解其使用历史。*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.

七、产品的稳定性考察*On-going stability programme*

6.23. 产品销售后，应继续对其稳定性进行监测，以便发现任何影响相关包装产品的稳定性因素（如：杂质、溶出度曲线等）。*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. 对已销售产品继续进行稳定性考察的目的是为了在货架寿命期内对产品质量进行监测，并确定产品在标示的贮存条件下是否可以保持其质量符合质量标准。*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. 此条款主要适用于已包装的销售产品，但也应考虑对待包装的产品进行稳定性考察，例如：当待包装产品在包装前和/或从生产厂运至包装厂之前存放了一段时间，则应就存放时间对已包装产品在环境条件下质量稳定性的影响进行评价和考察。另外，也应考虑到在较长周期内贮存和使用的中间体。重组产品（reconstituted product）的稳定性考察在产品开发阶段进行，不必再对销售产品进行监测，但是，如果有关系，也可对重组产品进行稳定性监测。*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. 应根据第4 章通则的相关要求制定书面的稳定性考察方案，考察结果应形成报告。应根据第3 章通则和附录15 的相关规定对稳定性考察所用设备（稳定性考察箱）进行验证与维护。*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. 稳定性考察应进行至产品货架寿命结束时，考察方案应包括，但不限于，以下内容: *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:*

每一规格和不同批量产品的批次；*number of batch(es) per strength and different batch sizes, if applicable*

相关的物理、化学、微生物和生物检验方法；*relevant physical, chemical, microbiological and biological test methods*

可接受标准；*acceptance criteria*

检验方法的出处；*reference to test methods*

瓶盖形式描述；*description of the container closure system(s)*

检验周期（检验时间点）；*testing intervals (time points)*

对贮存条件的描述（除非另有经证明的合适条件，否则应采用标准要求的贮存条件，如，长期考察要求的ICH 贮存条件）；*description of the conditions of storage (standardised ICH conditions for long term testing, consistent with the product labelling, should be used)*

其它适用于药品的数据。*other applicable parameters specific to the medicinal product.*

6.28.销售产品的稳定性考察方案可以与销售许可证资料中提交的初始产品的长期稳定性考察方案

有所不同，但应有充分理由并在方案中予以说明（例如：检测周期，或可根据更新后ICH 要求进行的调整）。*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. 产品批次和检验频次应提供充足的数据以便于趋势分析。除非另有经证明的合适方法，每年所生产的每一规格产品和各种不同类型的内包装产品，其至少一批应进行相关的稳定性考察（除非一年内没有生产该产品）。对于通常要求进行动物试验并且没有其他稳定性检测方法可供选择的产品，相关技术应经过验证，设定检验周期时可考虑使用风险-利益方法。如有科学依据，可采用括号法和矩阵法的 设计原则。*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. 在某些情况下，应增加稳定性考察的批次。例如，在对工艺或包装进行任何重大更变或发生严重偏差后应进行稳定性考察，返工产品、重新加工产品或回收产品均应纳入稳定性考察。*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. 应将稳定性考察结果告知关键人员，特别是受权人。当稳定性考察未在半成品或成品生产场所进行时，相关方应签订一份书面协议。生产厂应有稳定性考察的结果，供相关权威部门审阅。*Results of on-going stability studies should be made available to key personnel and, in particular, to the Qualified 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. 对于不符合质量标准的结果或严重的非典型趋势应进行调查。应将任何已确认的不符合质量标准的结果或严重的不良趋势报告给相关权威部门。应根据本《指南》第八章的要求考虑可能对已销售产品产生的影响，并与权威部门进行磋商。*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. 对所有数据（包括稳定性计划的中期结论）的汇总应形成文字，保留，并定期进行回顾。*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 委托生产与委托检验
CHAPTER 7 CONTRACT MANUFACTURE AND ANALYSIS

一、原则Principle

为了避免因误解而造成产品质量或工作质量不佳，委托生产和委托检验的内容应正确无误地加以确定、经各方同意并严格控制。委托方与受托方必须签订书面合同，明确规定双方的职责。合同中必须清楚地阐述放行每一批产品供销售的受权人的全部职责。

注：本章主要介绍生产厂家对成员国负责发放销售许可证和生产许可证的主管部门的责任。不能以任何方式去影响合同委托方和受托方各自对客户的责任；应服从于共同体规定及成员国的法律。

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 Qualified Person releasing each batch of product for sale exercises his full responsibility.

Note: This Chapter deals with the responsibilities of manufacturers towards the Competent Authorities of the Member States 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; this is governed by other provisions of Community and national law.

二、通则General

7.1. 应有书面的委托生产和/或委托检验的合同，以及与之相关的技术方面的安排。*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. 委托生产和委托检验的所有安排（包括技术上的变更或其它安排）都应符合相关产品市场许可证的要求。*All arrangements for contract manufacture and analysis including any proposed changes in technical or other arrangements should be in accordance with the marketing authorization for the product concerned.*

三、委托方The Contract Giver

7.3. 委托方负责对受托方进行审核，看其是否能够按要求完成委托事项，能否通过合同保证执行本规范中GMP 的原则和指南要求。*The Contract Giver is responsible for assessing the competence of the Contract 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. 委托方应向受托方提供所有必要的资料，以便受托方按照销售许可证的要求和任何其它法规要求，正确无误地执行合同规定的操作。委托方应确保受托方充分了解与产品或操作有关的任何问题，这些问题可能对受托方的厂房、设备、人员、其它物料或产品造成危险等情况。*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. 委托方应确保受托方提供的所有产品和物料符合质量标准，或由受权人批准放行。*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 a Qualified Person.*

四、受托方The Contract Acceptor

7.6. 受托方必须有充足的厂房和设备、知识和经验丰富的合格人员，以便能够满意地完成委托方所委托的工作。委托生产只能由具有生产许可证的生产厂家承担。*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. 受托方应确保提供给他的所有产品或物料适合其用途。*The Contract Acceptor should ensure that all products or materials delivered to him are suitable for their intended purpose.*

7.8. 受托方在没有取得委托方的事先评价和同意之前，不得将根据合同委托给他的任何工作转让给第三方。受托方与第三方之间所达成的协议应确保有关生产和检验资料的内容与委托方和受托方之间所签署的合同中的相关内容一致。*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. 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. 受托方不得从事可能影响为委托方生产和/或检验的产品之质量的任何活动。*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.*

五、合同The Contract

7.10.委托方与受托方之间应签订合同，阐明各自对产品生产和检验的责任。合同中与技术有关的内容应由具备制药技术、检验分析和GMP 知识的人员起草。所有有关委托生产和检验的协议必须符合销售许可证的要求，并得到双方同意。*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.合同应明确受权人批准放行产品供销售的方法，确保每批产品的生产和检查符合销售许可证的要求。*The contract should specify the way in which the Qualified 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.合同应明确规定哪一方负责物料的采购、检验和放行；哪一方负责生产和质量控制（包括生产过程控制）；哪一方负责取样和检验。如果是委托检验，合同应明确受托方是否应去生产厂取样。*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.生产、检验和发货记录及标准品应由委托方保管，或可供委托方查阅。对与产品质量评价有关的用户投诉或怀疑质量有问题的任何记录，均应按委托方制定的缺陷产品/召回产品程序处理，并允许委托方查阅。*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.合同中应允许委托方参观受托方的工厂。*The contract should permit the Contract Giver to visit the facilities of the Contract Acceptor.*

7.15.就委托检验而言，受托方应清楚自己须接受主管当局的检查。*In the case of contract analysis, the Contract Acceptor should understand that he is subject to Inspection by the competent Authorities.*

第八章 投诉与召回
CHAPTER 8 COMPLAINTS AND PRODUCT RECALL

一、原则Principle

所有投诉和其它有潜在缺陷的产品之信息，必须按照书面程序细仔审阅。为了预防意外，并符合2001/83/EC 第28 条规定，应建立必要时快速有效地召回已知或怀疑有缺陷产品的系统。*All complaints and other information concerning potentially defective products must be reviewed carefully according to written procedures. In order to provide for all contingencies, and in accordance with Article 28 of Directive 75/319/EEC, a system should be designed to recall, if necessary, promptly and effectively products known or suspected to be defective from the market.*

二、投诉Complaints

8.1. 应指定一人负责投诉处理，并决定拟采取的措施。该负责人应有足够的人员予以协助。如果此人并非受权人，则应将任何投诉、调查或产品召回的情况告知受权人。*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 Qualified Person, the latter should be made aware of any complaint, investigation or recall.*

8.2. 对具有潜在产品缺陷的任何用户投诉，应制定书面规程，详细论述采取的处理措施，包括必要时召回产品的措施。*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. 对有关产品缺陷的任何用户投诉，应有所有原始资料和全面调查的记录。质量控制负责人通常应参与这类问题的调查研究。*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. 如发现或怀疑某批产品有缺陷，应考虑对其他批产品进行检查，已确定是否存在同样缺陷。特别应对含有返工产品的批次进行调查。*If a product defect is discovered or suspected in a batch, consideration should be given to checking other batches 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. 为投诉处理而做出的所有决定和采取的措施均应有记录，并编号以便与相应的批记录相关联。*All the decisions and measures taken as a result of a complaint should be recorded and referenced to the corresponding batch records.*

8.6. 投诉处理记录应定期复查，以便发现需要注意的特殊的或重复出现的问题，以及那些可能需要召回的产品。*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. 如果生产厂因生产中可能出现的错误、产品变质、或其它严重的质量问题，应将可能采取的措施报告主管当局。*The Competent Authorities should be informed if a manufacturer is considering action following possibly faulty manufacture, product deterioration, or any other serious quality problems with a product.*

8.8. 如果生产厂考虑对可能有生产缺陷的产品、变质产品、假冒产品或其它有任何严重质量问题的产品采取措施时，应通知主管当局。

三、召回Recalls

8.9. 应指定专人负责产品召回的实施与协调，同时应有足够的人员根据召回的紧急程度进行产品召回的各项工作。通常，该负责人应独立于市场销售系统。如果他不是受权人，则应将产品召回的情

况告知受权人。*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 Qualified Person, the latter should be made aware of any recall operation.*

8.10.为了组织召回行动，应制定书面程序，定期复核，必要时更新。*There should be established written procedures, regularly checked and updated when necessary, in order to organise any recall activity.*

8.11.产品召回应能随时快速启动。*Recall operations should be capable of being initiated promptly and at any time.*

8.12.如果因产品质量问题或怀疑产品质量问题而打算召回产品时，应立即通知产品销往国家的主管当局. *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.负责产品召回的人员应能随时得到销售记录，销售记录应包含批发商和直接客户的详细资料（包括：地址、工作时间内外的电话号码和/或传真号、销售产品的批号和数量），包括出品产品和样品。*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.召回产品在等待处理决定过程中，应有标识，并贮存在单独的安全区内。*Recalled products should be identified and stored separately in a secure area while awaiting a decision on their fate.*

8.15.应记录召回工作的进程，并写出最终的报告，包括销售量与召回数量的平衡。*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.对召回工作安排的有效性应经常进行评价。*The effectiveness of the arrangements for recalls should be evaluated from time to time.*

第九章 自查
CHAPTER 9 SELF INSPECTION

一、原则Principle

为了检查GMP 的执行情况，提出必要的整改措施，应进行自查。*Self inspections should be conducted in order to monitor the implementation and compliance with Good Manufacturing Practice principles and to propose necessary corrective measures.*

9.1. 应按照预定的计划，定期对人员情况、厂房、设备、文件、生产、质量控制、产品销售、投诉处理和产品召回、自查等内容进行自查，以证明它们与质量保证原则的一致性。*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. 自查应由公司指定的合格人员按照独立和详细的工作方式进行。由外部专家进行独立的检查也是有益的。*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. 所有的自查都应有记录。报告应包括自查中发现的所有问题以及必要时建议的整改措施。随后采取的措施也应有记录。*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.*