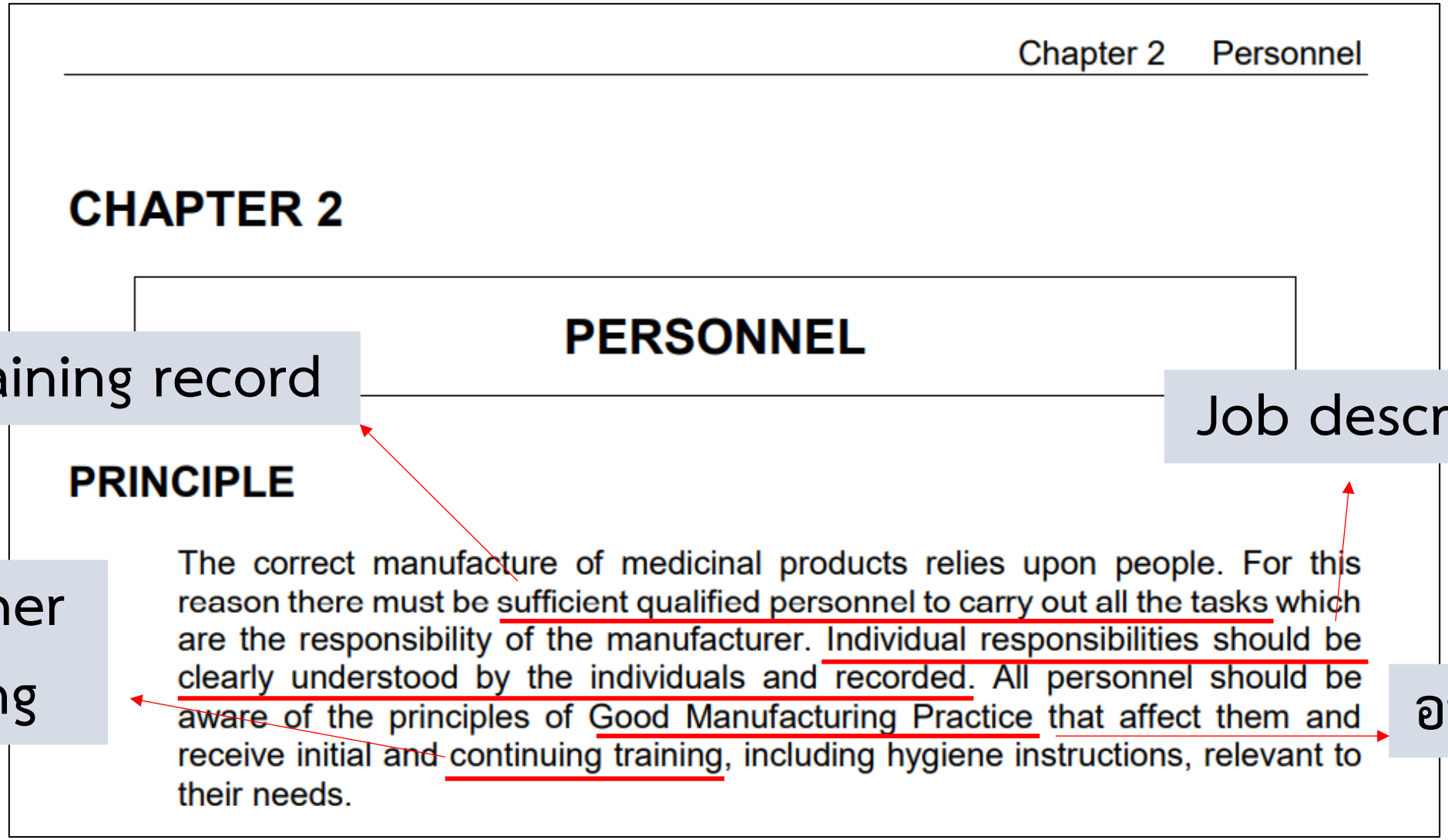
# GMP (PIC/S)

## chapter 2 and 3

# CHAPTER 2 PERSONNEL





## CHAPTER 2

## PERSONNEL

### PRINCIPLE

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.

Training record

Job description

Refresher training

อบรม GMP

# CHAPTER 2 PERSONNEL (Cont.)

Organization chart

**GENERAL**

2.1 The manufacturer should have an adequate number of personnel with the necessary qualifications and practical experience. Senior management should determine and provide adequate and appropriate resources (human, financial, materials, facilities and equipment) to implement and maintain the Pharmaceutical Quality System and continually improve its effectiveness. The responsibilities placed on any one individual should not be so extensive as to present any risk to quality.

2.2 The manufacturer must have an organisation chart in which the relationships between the heads of Production, Quality Control and where applicable Head of Quality Assurance or Quality Unit referred to in point 2.5 and the position of the Authorised Person(s) are clearly shown in the managerial hierarchy.

2.3 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.

2.4 Senior management has the ultimate responsibility to ensure an effective Pharmaceutical Quality System is in place to achieve the *quality objectives,* and, that roles, responsibilities, and authorities are defined, communicated and implemented throughout the organisation. Senior management should establish a quality policy that describes the overall intentions and direction of the company related to quality and should ensure continuing suitability and effectiveness of the Pharmaceutical Quality System and GMP compliance through participation in management review.

2.4 Additional requirement to develop and maintain a quality policy

# CHAPTER 2 PERSONNEL (Cont.)



## KEY PERSONNEL

2.5 Senior Management should appoint Key Management Personnel including the head of Production, the head of Quality Control, and if at least one of these persons is not responsible for the release of products the Authorised Person(s) designated for the purpose. Normally, key posts should be occupied by full-time personnel. The heads of Production and Quality Control must be independent from each other. In large organisations, it may be necessary to delegate some of the functions listed in 2.7, 2.8 and 2.9. Additionally, depending on the size and organisational structure of the company, a separate Head of Quality Assurance or Head of the Quality Unit may be appointed. Where such a function exists usually some of the responsibilities described in 2.7, 2.8 and 2.9 are shared with the Head of Quality Control and Head of Production and senior management should therefore take care that roles, responsibilities, and authorities are defined.

ให้หัวหน้าฝ่ายผลิต หัวหน้าฝ่ายควบคุมคุณภาพ และผู้มีหน้าที่ในการปล่อยผ่านผลิตภัณฑ์สำเร็จรูปในกรณีที่มีการแต่งตั้งเพิ่มเติม ตามที่ระบุใน Chapter 2 Personnel ของ Guide to Good Manufacturing Practice for Medical Products Part I เป็นเภสัชกรที่มีใบประกอบวิชาชีพเภสัชกรรม และเป็นตำแหน่งงานประจำเต็มเวลา

# CHAPTER 2 PERSONNEL (Cont.)

2.6 The duties of the Authorised Person(s) are described in the national requirements and can be summarised as follows:

a) An Authorised Person must ensure that each batch of medicinal products has been manufactured and checked in compliance with the laws in force in that country and in accordance with the requirements of the Marketing Authorisation;

b) The Authorised Person(s) must meet the qualification requirements laid down in the national legislation, they shall be permanently and continuously at the disposal of the holder of the Manufacturing Authorisation to carry out their responsibilities;

c) The responsibilities of an Authorised Person may be delegated, but only to other Authorised Person(s).

# CHAPTER 2 PERSONNEL (Cont.)

2.7 The head of Production generally has the following responsibilities:

(i) To ensure that products are produced and stored according to the appropriate documentation in order to obtain the required quality;

(ii) To approve the instructions relating to production operations and to ensure their strict implementation;

(iii) To ensure that the production records are evaluated and signed by an authorised person;

(iv) To ensure the qualification and maintenance of his department, premises and equipment;

(v) To ensure that the appropriate validations are done;

(vi) To ensure that the required initial and continuing training of his department personnel is carried out and adapted according to need.

# CHAPTER 2 PERSONNEL (Cont.)



2.8 The head of Quality Control generally has the following responsibilities:

(i) To approve or reject, as he/she sees fit, starting materials, packaging materials, intermediate, bulk and finished products;

(ii) To ensure that all necessary testing is carried out and the associated records evaluated;

(iii) To approve specifications, sampling instructions, test methods and other Quality Control procedures;

(iv) To approve and monitor any contract analysts;

(v) To ensure the qualification and maintenance of his/her department, premises and equipment;

(vi) To ensure that the appropriate validations are done;

(vii) To ensure that the required initial and continuing training of his department personnel is carried out and adapted according to need.

Other duties of Quality Control are summarised in Chapter 6.

2.9 Additional responsibility for QA/QC staff

# CHAPTER 2 PERSONNEL (Cont.)

2.9 The heads of Production, Quality Control and where relevant, Head of Quality Assurance or Head of Quality Unit, generally have some shared, or jointly exercised, responsibilities relating to quality including in particular the design, effective implementation, monitoring and maintenance of the Pharmaceutical Quality System. These may include, subject to any national regulations:

(i) The authorisation of written procedures and other documents, including amendments;

(ii) The monitoring and control of the manufacturing environment;

(iii) Plant hygiene;

(iv) Process validation;

(v) Training;

(vi) The approval and monitoring of suppliers of materials;

(vii) The approval and monitoring of contract manufacturers and providers of other GMP related outsourced activities;

(viii) The designation and monitoring of storage conditions for materials and products;

(ix) The retention of records;

(x) The monitoring of compliance with the requirements of Good Manufacturing Practice;

# CHAPTER 2 PERSONNEL (Cont.)



(xi) The inspection, investigation, and taking of samples, in order to monitor factors which may affect product quality;

(xii) Participation in management reviews of process performance, product quality and of the Pharmaceutical Quality System and advocating continual improvement;

(xiii) Ensuring that a timely and effective communication and escalation process exists to raise quality issues to the appropriate levels of management.

# CHAPTER 2 PERSONNEL (Cont.)

## TRAINING

2.10 The manufacturer should provide training for all the personnel whose duties take them into production and storage 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.

2.11 Besides the basic training on the theory and practice of the Pharmaceutical Quality System and 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.

2.12 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.

2.13 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.

2.14 The Pharmaceutical Quality System and all the measures capable of improving its understanding and implementation should be fully discussed during the training sessions.

# CHAPTER 2 PERSONNEL (Cont.)

## PERSONNEL HYGIENE

2.15 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.

2.16 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

# CHAPTER 2 PERSONNEL (Cont.)



manufacturer's knowledge. After the first medical examination, examinations should be carried out when necessary for the work and personal health.

2.17 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.

2.18 Every person entering the manufacturing areas should wear protective garments appropriate to the operations to be carried out.

2.19 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.

2.20 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.

2.21 Personnel should be instructed to use the hand-washing facilities.

2.22 Any specific requirements for the manufacture of special groups of products, for example sterile preparations, are covered in the annexes.

# CHAPTER 2 PERSONNEL (Cont.)

**CONSULTANTS**

2.23 Consultants should have adequate education, training, and experience, or any combination thereof, to advise on the subject for which they are retained.

Records should be maintained stating the name, address, qualifications, and type of service provided by these consultants.

Formal requirement to document consultant details and scope of works

# CHAPTER 3 PREMISES AND EQUIPMENT



## CHAPTER 3

## PREMISES AND EQUIPMENT

### PRINCIPLE

Premises and equipment must be located, designed, constructed, adapted and maintained to suit the operations to be carried out. Their layout and design must aim to minimise the risk of errors and permit effective cleaning and maintenance in order to avoid cross-contamination, build-up of dust or dirt and, in general, any adverse effect on the quality of products.

# CHAPTER 3 PREMISES AND EQUIPMENT (Cont.)

- Additional guidance on cross-contamination
- Quality risk management principles should be used to assess and control the risks.
- Dedicated facilities are required when:
  - The risk cannot be adequately controlled by operational and/ or technical measures
  - Scientific data from the toxicological evaluation does not support a controllable risk (e.g. allergenic potential from highly sensitizing materials such as beta-lactams) or Relevant residue limits, derived from the toxicological evaluation, cannot be satisfactorily determined by a validated analytical method.

# CHAPTER 3 PREMISES AND EQUIPMENT (Cont.)

## PREMISES

### General

3.1. Premises should be situated in an environment which, when considered together with measures to protect the manufacture, presents minimal risk of causing contamination of materials or products.

3.2. 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. 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. Premises should be designed and equipped so as to afford maximum protection against the entry of insects or other animals.

3.5. Steps should be taken in order to prevent the entry of unauthorised people. Production, storage and quality control areas should not be used as a right of way by personnel who do not work in them.

# CHAPTER 3 PREMISES AND EQUIPMENT (Cont.)

**Production Areas**

3.6 Cross-contamination should be prevented for all products by appropriate design and operation of manufacturing facilities. The measures to prevent cross-contamination should be commensurate with the risks. Quality Risk Management principles should be used to assess and control the risks.

Depending of the level of risk, it may be necessary to dedicate premises and equipment for manufacturing and/or packaging operations to control the risk presented by some medicinal products.

# CHAPTER 3 PREMISES AND EQUIPMENT (Cont.)



Dedicated facilities are required for manufacturing when a medicinal product presents a risk because:

i. the risk cannot be adequately controlled by operational and/ or technical measures,

ii. scientific data from the toxicological evaluation does not support a controllable risk (e.g. allergenic potential from highly sensitising materials such as beta-lactams) or

iii. relevant residue limits, derived from the toxicological evaluation, cannot be satisfactorily determined by a validated analytical method.

Further guidance can be found in Chapter 5 and in Annexes 2, 3, 4, 5 & 6.

3.7. Premises should preferably be laid out in such a way as to allow the production to take place in areas connected in a logical order corresponding to the sequence of the operations and to the requisite cleanliness levels.

3.8. 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.

# CHAPTER 3 PREMISES AND EQUIPMENT (Cont.)

3.9. Where starting and primary packaging materials, intermediate or bulk products are exposed to the environment, interior surfaces (walls, floors and ceilings) should be smooth, free from cracks and open joints, and should not shed particulate matter and should permit easy and effective cleaning and, if necessary, disinfection.

3.10 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. 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. 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 Weighing of starting materials usually should be carried out in a separate weighing room designed for such use.

3.14. In cases where dust is generated (e.g. during sampling, weighing, mixing and processing operations, packaging of dry products), specific provisions should be taken to avoid cross-contamination and facilitate cleaning.

# CHAPTER 3 PREMISES AND EQUIPMENT (Cont.)

Line clearance

Chapter 3 Premises and equipment

3.15. Premises for the packaging of medicinal products should be specifically designed and laid out so as to avoid mix-ups or cross-contamination.

3.16 Production areas should be well lit, particularly where visual on-line controls are carried out.

3.17. In-process controls may be carried out within the production area provided they do not carry any risk to production.

# CHAPTER 3 PREMISES AND EQUIPMENT (Cont.)

**Storage Areas**

3.18. Storage areas should be of sufficient capacity to allow orderly storage of the various categories of materials and products: starting and packaging materials, intermediate, bulk and finished products, products in quarantine, released, rejected, returned or recalled.

3.19. 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 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. 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. 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. Segregated areas should be provided for the storage of rejected, recalled or returned materials or products.

3.24. Highly active materials or products should be stored in safe and secure areas.

3.25. 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.


# CHAPTER 3 PREMISES AND EQUIPMENT (Cont.)

**Quality Control Areas**

3.26. 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. 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.

# CHAPTER 3 PREMISES AND EQUIPMENT (Cont.)



3.28. Separate rooms may be necessary to protect sensitive instruments from vibration, electrical interference, humidity, etc.

3.29. Special requirements are needed in laboratories handling particular substances, such as biological or radioactive samples.

**Ancillary Areas**

3.30. Rest and refreshment rooms should be separate from other areas.

3.31. Facilities for changing clothes and for washing and toilet purposes should be easily accessible and appropriate for the number of users. Toilets should not directly communicate with production or storage areas.

3.32. 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. Animal houses should be well isolated from other areas, with separate entrance (animal access) and air handling facilities.

# CHAPTER 3 PREMISES AND EQUIPMENT (Cont.)

## EQUIPMENT

3.34. Manufacturing equipment should be designed, located and maintained to suit its intended purpose.

3.35. Repair and maintenance operations should not present any hazard to the quality of the products.

3.36. Manufacturing equipment should be designed so that it can be easily and thoroughly cleaned. It should be cleaned according to detailed and written procedures and stored only in a clean and dry condition.

3.37. Washing and cleaning equipment should be chosen and used in order not to be a source of contamination.

3.38. Equipment should be installed in such a way as to prevent any risk of error or of contamination.

3.39. Production equipment should not present any hazard to products. Parts of 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. Balances and measuring equipment of an appropriate range and precision should be available for production and control operations.

3.41. Measuring, weighing, recording and control equipment should be calibrated and checked at defined intervals by appropriate methods. Adequate records of such tests should be maintained.

3.42. Fixed pipework should be clearly labelled to indicate the contents and, where applicable, the direction of flow.

# CHAPTER 3 PREMISES AND EQUIPMENT (Cont.)



3.43. Distilled, deionised 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. Defective equipment should, if possible, be removed from production and quality control areas, or at least be clearly labelled as defective.