Code of Practice for Licenced Manufacturers and Registered Authorized Persons

Pharmacy and Poisons Board of Hong Kong

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Contents

1. Background

Licensed Manufacturers

1.1 According to regulation 29(1) of the Pharmacy and Poisons Regulations (Cap. 138A, Laws of Hong Kong), no person shall manufacture any pharmaceutical product on any premises unless he is the holder of a licence to manufacture pharmaceutical products ("manufacturer licence") on those premises. Manufacture of pharmaceutical products includes secondary packaging, which means the labelling, re-labelling, cartoning, re-cartoning or adding additional information (including inserts) to pharmaceutical products which are already enclosed in the container in which they are to be sold or supplied.

1.2 The issuing authority for manufacturer licence is the Pharmacy and Poisons (Manufacturers Licensing) Committee ("the Committee") of the Pharmacy and Poisons Board ("the Board"). The various criteria that the Committee may consider in granting and renewing a manufacturer licence includes the following:

a. supervison of the manufacturing process by a registered pharmacist or a person approved by the Board;

b. proper labelling of pharmaceutical products manufactured;

c. suitable premises used in the manufacturing, testing, packing and despatch of pharmaceutical products;

d. adequate hygiene control of personnel and premises to avoid contamination of pharmaceutical products;

e. quality assurance of raw materials and finished products with retention of control samples and all related records; and

f. compliance with the current Good Manufacturing Practice (GMP) guide issued or adopted by the Board in respect of pharmaceutical products.

Registered Authorized Persons

1.3 Both the Pharmaceutical Inspection Co-operation Scheme's Guide to Good Manufacturing Practice for Medicinal Products ("PIC/S Guide to GMP") and the Hong Kong Guide to Good Manufacturing Practice for the Secondary Packaging of Pharmaceutical Products require that pharmaceutical products may not be sold or supplied unless a registered Authorised Person has certified that each batch of the products is produced and controlled in accordance with the requirements of the marketing authorisation and any other regulations relevant to the production, control and release of the products.

1.4 To ensure compliance with the required standards in the manufacture of pharmaceutical products, the registered Authorized Person employed by Licensed Manufacturers of pharmaceutical products ("Pharmaceutical Manufacturers"), including the registered Authorized Person employed by manufacturers to carry out only secondary packaging of pharmaceutical products ("Secondary Packaging Manufacturers"), who is referred to as the Quality Assurance Officer, must be suitably qualified, experienced and competent for the types of manufacturing and packaging operations undertaken by the company that he or she works for.

1.5 A system of registering Authorized Persons is established to ensure that only suitable persons will undertake this role.

2. Purpose of this Code of Practice

2.1 This Code of Practice sets out, in addition to those in the relevant GMP guide issued by the Board, the minimum standards, obligations and requirements to be followed by Licensed Manufacturers and registered Authorized Persons. Its purpose is to provide Licensed Manufacturers and registered Authorized Persons with practical guidance and directions for manufacturing of pharmaceutical products with a view to safeguarding the interest of the public.

2.2 Compliance with this Code is one of the conditions upon which the Committee issues a manufacturer licence as well as conditions of registration of Authorized Person. All Licensed Manufacturers and registered Authorized Persons must observe the standards set out in this Code and be aware of the consequences of non-compliance.

3. Scope

3.1 Part I of this Code of Practice applies to Licensed Manufacturers, including the Secondary Packaging Manufacturers.

3.2 Part II of this Code of Practice applies to registered Authorized Persons employed by the Pharmaceutical Manufacturers, including registered Authorized Persons employed by Secondary Packaging Manufacturers, namely the Quality Assurance Officer.

Part I

4. Obligations and Requirements for Licensed Manufacturers

Licensed Manufacturers of pharmaceutical products must ensure that the following obligations and requirements are met:

4.1 Pharmaceutical products are manufactured and packaged in a manner which will ensure that they are fit for their intended use, comply with the registered particulars and will not place patients at risk due to inadequate safety, quality or efficacy of the pharmaceutical products.

4.2 All manufacturing processes, packaging processes, and activities conducted on their licensed premises are carried out in a manner compliant with the relevant legislation, which include but are not limited to:

- the Import and Export Ordinance (Cap. 60);
- the Pharmacy and Poisons Ordinance (Cap. 138);
- the Dangerous Drugs Ordinance (Cap. 134);
- the Antibiotics Ordinance (Cap. 137);
- the Public Health and Municipal Services Ordinance (Cap. 132);
- the Undesirable Medical Advertisements Ordinance (Cap. 231); and
- the Trade Descriptions Ordinance (Cap. 362).

4.3 Pharmaceutical products are manufactured, packaged and tested in accordance with the conditions specified on the manufacturer licence.

4.4 All parts of the Quality Management System referred to in the current GMP guide issued by the Board are adequately resourced with competent personnel and suitable and sufficient premises, equipment and facilities.

4.5 Approval from the Committee has been obtained prior to any change in key personnel. The key personnel include the registered Authorized Person, Head of Production and Head of Quality Control, or, for Secondary Packaging Manufacturers, the Quality Assurance Officer and the Person in charge of secondary packaging.

4.6 Approval from the Committee has been obtained prior to any change in manufacturing premises that may affect the quality of the product.

4.7 An Authorized Person registered by the Board is employed to, inter alia, take responsibility for the quality of pharmaceutical products produced and packaged on the premises and to authorise the release for sale or distribution of each batch of finished pharmaceutical products, including certifying that each batch of product has been manufactured or packaged in compliance with the requirements of the current GMP guide issued by the Board in respect of pharmaceutical products and in compliance with the registered particulars for that product.

4.8 The registered Authorized Person is either:

a. appointed as a board member of the Licensed Manufacturer; or

b. invited to attend board meetings of the Licensed Manufacturer and allowed to speak on matters where safety, efficacy and quality issues of products are concerned and his/her remarks will be put on record.

The Licensed Manufacturer provide its registered Authorized Person with the necessary authority for and provide every support to the decisions of the registered Authorized Person made in the performance of his/her duties .

4.9 All key personnel have appropriate qualifications and experience as required by the Board.

4.10 Key personnel and company staff are provided with training necessary to enable them to undertake their respective duties in accordance with the GMP requirements and appropriate records of such training are maintained.

4.11 Any defect impacting on the quality of products released for sale or distribution, including products intended for markets other than Hong Kong, is documented.

4.12 Report to the Drug Office all serious adverse drug reactions in accordance with the Drug Office's "Guidance for Pharmaceutical Industry- Adverse Drug Reaction Reporting Requirements".

4.13 Report to the Drug Office any conditions or significant changes or deviations which may affect the quality, safety or efficacy of a pharmaceutical product, including significant changes to key personnel, facilities, equipment, systems, procedures, etc.

4.14 Report to the Drug Office upon commencement of a product recall, submit pertinent product information related to the recall and comply with the current Pharmaceutical Products Recall Guidelines issued by the Drug Office.

4.15 Any quality control testing required to be contracted out is contracted out to:

a. a Licensed Manufacturer certified as a GMP manufacturer by the Committee; or

b. a laboratory:

i. accredited in accordance with ISO 17025, or equivalent, for the tests required to be performed; or

ii. inspected by inspectors of the Drug Office and the result of the inspection has shown to the satisfaction of the Committee that the laboratory has complied with such parts of GMP relevant to the quality control testing to be contracted out.

4.16 Allow public officers authorised by the Chairman of the Board to carry out inspections and to take samples, photos and copies of documentation as may be necessary for the purpose of inspection and, where inspection referred to in section 4.15(b)(ii) is required, to make relevant arrangement with the laboratory for the inspection.

4.17 Not wilfully delay or obstruct authorised public officers in the carrying out of their duties during the course of inspection and investigation.

4.18 In case of suspected product quality defects, suspend distribution of or recall any defective products according to instruction of the Drug Office.

4.19 An order in writing issued by the purchaser has been obtained before the completion of the sale of Part I Poisons, Dangerous Drugs and Antibiotics. Electronic communications (such as e-mail), fax and mail are accepted forms of written order. The order in writing should be kept for at least two years from the date of issue of the order.

5. Consequence of breaching section 4 of this Code of Practice

5.1 Licensed Manufacturers found to have breached section 4 of this Code of Practice will be reported to the Committee for appropriate action.

5.2 Depending on the severity of individual case, the Committee may revoke the licence or suspend it for such period as it thinks fit, vary the licence condition(s) or issue a warning letter to the Licensed Manufacturer if, in its opinion, the Licensed Manaufacturer has failed to comply with section 4 of this Code of Practice.

5.3 Any Licensed Manufacturer aggrieved by a decision of the Committee may appeal to the Pharmacy and Poisons Appeal Tribunal against that decision.

Part II

6. Obligations and Requirements for Registered Authorized Persons

Registered Authorized Persons employed by Licensed Manufacturers in Hong Kong must ensure that the following obligations and requirements are met:

6.1 He or she is listed on the Register of Authorized Persons maintained by the Board.

6.2 Take responsibility for the quality of the pharmaceutical products manufactured or packaged on the premises of the manufacturer.

6.3 Authorise the release for sale or distribution of each batch of finished pharmaceutical products manufactured or packaged, including certifying before the release that each batch of the products has been manufactured or packaged in compliance with the requirements of the current GMP guide issued by the Board in respect of pharmaceutical products and in compliance with the registered particulars for the products.

6.4 Maintain a register (or equivalent document) as a record of product batches certified prior to batch release.

6.5 The appropriate senior management is made fully aware of any manufacturing and/or testing difficulties which may cast doubt on the certification of batches or which may post facto require a product recall and, where there is any aspect of manufacturer's Quality Management System which is not in compliance with the current GMP guide issued by the Board, such non-compliance is brought to the attention of the senior management and appropriate corrective measures are taken.

6.6 Authorised public officers are not wilfully delayed or obstructed in the carrying out of their duties during the course of inspection and investigation.

6.7 Keep knowledge, experience and competence up-to-date through continuing professional development.

Guidance on how some of the above obligations and requirements for registered Authorized Persons can be met is listed in Appendix A and Appendix B to this Code of Practice.

7. Consequence of breaching section 6 of this Code of Practice

7.1 Registered Authorized Persons found to have breached section 6 of this Code of Practice, or found to be incompetent, will be reported to the Committee for appropriate action.

7.2 Depending on the severity of individual case, the Committee may cancel or suspend the registration of an Authorized Person, vary the registration condition(s) or issue a warning letter to the registered Authorized Person, if, in its opinion, the registered Authorized Person is incompetent or not undertaking appropriate continuing professional development.

7.3 Any registered Authorized Person aggrieved by a decision of the Committee may appeal to the Pharmacy and Poisons Appeal Tribunal against that decision.

Appendix A: Duties of Registered Authorized Person relating to release of finished products

Each batch of finished product must be certified by a registered Authorised Person before being released for sale. The certification should **ensure** that the following requirements have been met:

(The meaning of the word "ensure" in this context is that the registered Authorized Person must be confident that various actions, which may not be under his/her direct control, have in fact been taken).

A.1 The licensing conditions of the manufacturer licence and the registered particulars of pharmaceutical product have been met for the batch concerned.

A.2 The current GMP guide issued by the Board have been followed in all manufacturing, packaging, testing and warehousing activities.

A.3 Critical manufacturing processes and quality control test methods have been validated.

A.4 All the necessary quality control checking and testing have been performed, and account has been taken of the manufacturing and packaging conditions including a review of the batch records.

A.5 Any changes or deviations in manufacturing, packaging or quality control have been processed in accordance with well-defined systems, including reporting of such changes or deviations to the Authorized Person before any product batch is released.

A.6 Any additional sampling, inspection, tests and checks have been carried out or initiated, as appropriate, to cover changes or deviations in manufacturing, packaging or quality control.

A.7 All necessary manufacturing, packaging and associated documentation have been completed and endorsed by suitably authorised staff trained in the concept of Quality Management and GMP.

A.8 Regular audits, self-inspections and spot checks have been carried out by experienced staff.

A.9 All relevant factors including any factor not specifically associated with the output batch directly under review (e.g. calibration and maintenance records, environmental monitoring, etc) have been considered.

A.10 The registered Authorized Person should recognise the need to consult other company's experts in a specific area so as to reinforce his/her knowledge on appropriate points when a doubtful situation arises (e.g. stability, unusual analytical results, process or equipment changes, potential environmental or microbiological risks, re-labelling, abnormal yields, cross contamination risks, etc.).

A.11 A register (or equivalent document) is maintained as a record of product batches certified by the registered Authorized Person prior to batch release.

A.12 Reference samples and/or retention samples of each product batch are retained for a period of time specified in the current GMP guide issued by the Board in respect of pharmaceutical products.

A.13 *[Not applicable to Quality Assurance Officer]* If the registered Authorized Person is not involved in the on-going stability testing program or the preparation of Product Quality Review ("PQR"), he or she should at least have access to the full results of such testing program and review (since the registered Authorized Person must consider the results of both as part of the release for sale/distribution process).

In considering how to perform the above duties, the registered Authorized Person should take into account the nature and size of the operations involved. For example, registered Authorized Person employed to work in a very small company manufacturing a limited range of products may have to take direct responsibility for some or all of the duties outlined above, whereas the registered Authorized Person working in larger organisations may have to be more dependent upon the knowledge and expertise of his/her colleagues in undertaking some or all of such duties.

In any event, it is of paramount importance that the registered Authorized Person must take steps, within a well-planned Quality Management System, to assure himself or herself that the tasks allocated are being performed satisfactorily. The duties of the registered Authorized Person depend very much upon a team effort wherein the individuals involved realise the position and responsibility of the registered Authorized Person and provide every support.

A registered Authorized Person who failed to discharge his/her duties relating to release of finished products may be subjected to disciplinary actions.

Appendix B: Continuing professional development (CPD)

B.1. Registered Authorized Persons have a personal and professional duty to keep up-to-date their knowledge and experience on the current state of pharmaceutical quality management, regulatory aspects and GMP standards, product manufacturing and control technology, and general work practices.

B.2. Records of continuing professional development should be kept to reflect the Registered Authorized Person's continued performance of professional duties.

B.3. In the event of a significant change in an Registered Authorized Person's professional responsibilities, for example changing employment from one with a company making only non-sterile oral solid dosage forms to one with a company making a wider range of products including sterile products; or from one with a company packaging oral solid dosage forms to one with a company packaging parenternal products requiring cold chain management, the registered Authorized Person and the senior management of the company involved should recognise the need for receiving additional training/education and demonstrate that adequate steps have been taken to receive or provide such additional training/education, which should have been undertaken before the registered Authorized Person commences his or her work in the new positions.

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