Report of the

Review Committee on
Regulation of Pharmaceutical Products in Hong Kong

Food and Health Bureau

December 2009

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Executive Summary

INTRODUCTION

In early 2009, a number of incidents concerning pharmaceutical products in Hong Kong had caused public concerns on drug safety. The Food and Health Bureau (FHB) and Department of Health (DH) took immediate measures to address the concerns, including the inspection of all local drug manufacturers. As a longer term measure, it was decided that a comprehensive review on the existing regime for the regulation of pharmaceutical products (western medicines) be conducted.

SETTING UP OF THE REVIEW COMMITTEE ON THE REGULATION OF PHARMACEUTICAL PRODUCTS IN HONG KONG

2. The Review Committee on the Regulation of Pharmaceutical Products in Hong Kong (Review Committee) chaired by the Permanent Secretary for Health with members from the pharmaceutical sector, medical profession, academia, patient groups and consumer representative was set up on 24 March 2009. In consideration of the wide range and complexity of the issues to be examined, the Review Committee set up two Sub Committees, one on drug manufacturing and another on drug distribution and procurement to examine the various issues in depth. A Task Force was also set up under the chairmanship of the Director of Health to provide expert advice to the Review Committee, and an Expert Group was set up to give advice on the microbiological hazards on drug manufacturing. The background of the review, the terms of reference, membership and work of the Review Committee, the two Sub Committees, the Task Force and the Expert Group are set out in Chapter 1 (and Annexes A to C) of this report.

PRESENT SITUATION

3. The current drug regulatory regime adopts a risk management, dual target and multi-pronged approach backed by the law. The dual targets are the pharmaceutical products and the pharmaceutical trade. Multi-pronged approach embraces legal requirements and administrative measures which provide the framework of the control system, education for the pharmaceutical sector to equip them with the necessary professional knowledge, promotion and publicity to remind the public of the importance of drug safety, and a penalty system to deter the pharmaceutical sector from malpractices. The control system starts at

the source of supply of drugs and follow through each point in the production line and the supply chain until the drug reaches its target patients. The framework of the regime is similar to those of many overseas jurisdictions, but the implementation details could differ from one place to another. Chapter 2 of the review report provides an overview of the existing regulatory regime.

UNDERLYING PRINCIPLES OF THE REGULATORY REGIME

4. The Review Committee agrees that the regulatory regime of the pharmaceutical sector should adhere to the following key principles and objectives:

(a) protecting public health and ensuring patient safety is the top priority;

(b) the regulatory regime should be able to maintain public confidence on the usage of drugs;

(c) the regulatory regime should be able to sustain and improve the standard of the pharmaceutical sector, but at the same time able to identify and address any bad practices;

(d) the regulatory regime should be fair, accountable, consistent and transparent; and

(e) the regulatory regime has to strike a fine balance between effective regulation and the challenges to the trade and the professionals.

5. The Review Committee agrees that while the Government has the responsibility to regulate, the pharmaceutical trade has the responsibility to comply with the prescribed requirements and standards, to enhance governance and the audit process. The pharmacist profession and all healthcare professionals have the responsibility to discharge their duties and uphold their high professional standards.

FINDINGS AND RECOMMENDATIONS OF THE REVIEW

6. With the above principles in mind, the Review Committee has examined in detail the existing regulatory regime. It considers that the framework and the rationale behind the existing regime is sound and while it should continue to be adopted, the coverage and depth of the regulatory

measures should be enhanced. The Review Committee is, however, mindful of the implementation details and considers that while changes should be made to enhance the effectiveness of the regime, various proposed new measures should have an implementation programme, taking into account the lead time required to acquire resources, train the personnel both within DH and in the trade, set up the system for the stakeholders to follow or adapt, and to take forward the legislative amendments. Nevertheless, proposals which are key to enhance drug safety should be implemented with priority. At the same time, the Review Committee believes that the pharmaceutical sector plays a pivotal role in protecting the integrity of the system by observing self-discipline and upholding the pharmacist professional standards.

7. The Review Committee has made a total of 75 recommendations, covering the following different aspects as summarised in the ensuing paragraphs (and Annexes D and E).

(a) Regulation of drug manufacturers and Good Manufacturing Practices (GMP) Scheme (Chapter 3)

(i) **To upgrade the current Hong Kong GMP standard to a higher international standard**: GMP is a quality assurance approach used by the drug manufacturing industry worldwide to ensure that products are consistently produced and controlled throughout the manufacturing process. The spirit of GMP emphasizes that the assessment of good quality should be based on scrutiny of the manufacturing processes and not by testing of the end product alone. Hong Kong is now adopting the GMP standard promulgated by the World Health Organization (WHO) in 1995. The Review Committee recommends that in about two years' time the GMP standard of Hong Kong be first upgraded to the standard promulgated by WHO in 2007, and in about another two years' time it should be upgraded to an even higher standard devised by the Pharmaceutical Inspection Cooperation Scheme, i.e. the PIC/S standard. The PIC/S standard includes a stricter control over the use of active pharmaceutical ingredients for drug manufacturing, more stringent qualification requirements for the position of the authorized person who oversees the entire drug manufacturing process, a more enhanced inspection and licensing arrangement, and a more comprehensive training framework for all levels of personnel involved in the GMP system. This recommendation should be implemented with priority.

(ii) **To introduce microbiological monitoring for non-sterile drugs during the manufacturing process**: In the light of the earlier incident of fungal contamination of drugs, the Review Committee recommends that local manufacturers be required to conduct microbiological tests for non sterile drugs. Drug manufacturers will be required to adopt a new model for microbiological monitoring, including the carrying out of microbiological tests on raw materials, limiting the time whereby the granules can be kept to not more than 48 hours, conducting microbiological tests on finished products and including microbiological testing in the stability studies of all products. If a manufacturer intends to adopt a longer holding time, he must provide the necessary data and evidence supporting the proposed holding time to DH for consideration. This recommendation should be implemented with priority.

(iii) **To tighten up the qualification of the Authorized Person (AP) by increasing the required number of years of industrial experience and imposing requirements on training**: A formal set of criteria regarding the qualifications of the AP will be set, alongside with the introduction of a structured training programme and a mechanism to ensure that APs will take responsibility for the quality, safety and efficacy of their drug products. In the meantime, the position of AP will still be required to be filled by pharmacist with relevant experience. In the long run when a licensing or listing system for APs and additional formal certified GMP training have been developed, consideration will be given to allowing additionally non-pharmacists with the required experience and training to assume the position of AP.

(iv) **To require all companies which undertake repackaging activities, including secondary repackaging in addition to primary repackaging, to have a manufacturing licence**: A new category of repackaging licence will be introduced for such purpose. This recommendation should be implemented with priority.

(b) Pre-market control of drugs (Chapter 4)

(i) **To require bioavailability and bioequivalence (BABE) studies for drug registration**: BABE refers to the therapeutic equivalence of the same pharmaceutical product manufactured by different manufacturers. BABE studies seek to assess whether a generic

drug produces the same therapeutic effect as the patent drug. This is particularly important for some drugs, such as antiepileptic drugs, where a reduced or excessive therapeutic effect could be harmful to the patient. The Review Committee recommends that BABE studies be required for drug registration. To allow time for the market to build up its capacity for carrying out the studies, the recommendation will be implemented in phases, starting with drugs where a reduced or excessive therapeutic effect could have undesirable consequences.

(ii) **To Change the term "Poison 毒藥" on drug labels**: The term "poison" in drug labels arouses unnecessary concern of the public regarding the safety of the drug. The Review Committee recommends that alternative terms be devised. One recommendation is to adopt the terms "prescription drugs 處方藥" and "drugs under supervised sale 監售藥". The Pharmacy and Poisons Board should consult the stakeholders on the most appropriate terms.

(iii) **DH to shorten the processing time for drug registration approval**: As a result of manpower constraints, the processing time for approval of registration of drugs, for change of particulars of registered drugs and for clinical trials are quite long. The Review Committee recommends that DH shortens the time by 40% - 50%.

(c) Regulation of importers/exporters, wholesalers and retailers (Chapter 5)

(i) **To require wholesalers handling non-poisons to apply for a licence:** At present, wholesalers of drugs which are non-poisons (e.g. vitamins) are not subject to licensing control. The Review Committee considers that patients' health would be affected if these drugs are not handled properly. The Review Committee recommends that DH requires all wholesalers of non-poisons to apply for a licence so that DH could impose licensing requirements on them.

(ii) **To require wholesalers to keep transaction records for Part II Poisons and non-poisons**: At present the law only requires wholesaler to keep transaction records for Part I Poisons. The Review Committee recommends that wholesalers also keep transaction records for all pharmaceutical products, including Part II Poisons and non-poisons. This will ensure that drugs are being

procured through a proper channel and the sources can be traced if problems arise.

(iii) **To introduce a Code of Practice for wholesalers, importers and exporters**: At present there are no guidelines governing the roles and responsibilities of wholesalers, importers and exporters on product quality, as opposed to the GMP compliance for manufacturers. The Review Committee recommends that a Code of Practice be introduced for wholesalers, importers and exporters to follow.

(iv) **To strengthen the control of the import and export of pharmaceutical products:** The Review Committee recommends DH to deploy a designated team to provide advice to the Customs and Excise Department (C&ED) at ports of entry and to undertake surveillance work.

(v) **To strengthen the tracking system for drugs imported for re-export purpose:** The Review Committee recommends DH to set up a record and tracking system so that export licence applicants are required to produce the relevant import licences of the imported drugs to be re-exported. This will enable DH staff to keep track of the amount imported and the amount intended to be exported to prevent illegal diversion of drugs imported for re-export purpose into the local market. In the long run, an electronic record system which is inter-operable with C&ED and the Trade and Industry Department should be a more efficient alternative. In addition, the weekly quota of post-shipment consignment checks of licence by C&ED will be increased, taking into account the workload of C&ED staff.

(vi) **To require retailers handling non-poisons to apply for a licence**: At present, retailers of non-poisons are not required to apply for a licence. Although non-poisons are drugs of lower risk, they will still affect public health if not being handled properly. The Review Committee recommends that retailers selling non-poisons be required to apply for a licence from DH.

(vii) **To require the presence of pharmacists during all business hours of pharmacies**: At present, a registered pharmacist has to be present in an Authorized Sellers of Poisons (ASPs), i.e. pharmacies, for not less than two-third of its opening hours. The Review Committee recommends that in the long run a registered

pharmacist should be present whenever an ASP is open for business. This will improve the professional services provided by pharmacists. To further enhance the role of pharmacists in the control of the storage and supply of drugs at ASPs, apart from the above proposal, heightened enforcement actions should be taken against non-pharmacists who have violated the law or interfered with the duties of pharmacists. The Review Committee noted that this recommendation should take into account the market operating conditions as well as the availability of sufficient pharmacists and cannot be implemented immediately.

(viii) **To include in the law the requirement for retailers to follow their Codes of Practice**: The existing Code of Practice for ASPs, i.e. pharmacies, has no legal status for enforcement, and there is no Code of Practice for Listed Seller of Poisons **(**LSPs), i.e. medicine companies, to follow with regard to the handling of drugs. The Review Committee recommends that a Code of Practice be devised for LSPs and the law be amended to require that both ASPs and LSPs have to follow their respective Codes of Practice.

(ix) **To empower the Pharmacy and Poisons Board (PPB) to revoke licences of ASPs**: At present the PPB can only stop renewing licences of ASPs at the beginning of each year, but has no authority to revoke the licence during the year. The Review Committee recommends giving such authority to the PPB so that the licence of an ASP can be revoked if it has committed a serious offence.

(x) **To require retailers and doctors to have written records for drug orders**: This is to ensure that there is proper record and checking mechanism to prevent errors during delivery of drugs which is necessary to protect the safety of patients. The Review Committee notes that the trade would need time to work out a system with the suppliers. In the long run, electronic record should be a more efficient alternative. The Review Committee also notes that the written record requirement is already recommended in the "Good Dispensing Practice Manual" issued by the Hong Kong Medical Association and the Hong Kong Medical Council has advised doctors to observe the Manual. The Hong Kong Doctors Union objects to the mandatory requirement of written order of drugs.

(d) Procurement and supply of pharmaceutical products in the public and private medical sectors (Chapter 6)

(i) **The Hospital Authority (HA) and DH to require suppliers to provide detailed information on the delivery documentation:** HA and DH will require supplier to provide information such as pack size and registration number in the delivery documents to enable more effective checking and verification of drugs received. This recommendation should be implemented with priority.

(ii) **HA and DH to check the quality of drugs**: Microbiological and chemical testings will be conducted to ensure drug quality. This recommendation should be implemented with priority.

(iii) **DH to encourage the private medical sector to follow the proposed set of guiding principles on drug handling**: DH will issue a set of guiding principles for all private hospitals. The principles include the selection, procurement, delivery and receipt, storage and repacking of drugs, staff training and auditing. This recommendation should be implemented with priority.

(e) Post-market control of drugs and Pharmacovigilance (Chapter 7)

(i) **DH to continue the extended coverage for the surveillance of high risk products in the market**: DH has increased the number of drug samples collected in the market for testing to over 2 000 in recent years. The Review Committee recommends DH to continue with such rigorous surveillance and the existing practice of reporting anomalies to the public. This recommendation should be implemented with priority.

(ii) **DH to enhance Pharmacovigilance activities**: Pharmacovigilance is the detection, assessment, understanding and prevention of adverse effects of drugs. DH will promote these activities through education, training and promotion among healthcare professionals and the trade and to foster a culture of awareness of pharmacovigilance.

(f) Risk communication, education and training (Chapter 8)

(i) **DH to set up a dedicated team for education and training**: At present there is no coordination amongst various organizations which provide public education programmes on drug safety. The

Review Committee recommends DH to set up a dedicated team to coordinate the efforts of various parties, to draw up guidelines on risk communication and to perform risk assessment in response to incidents and to recommend risk communication actions. This recommendation should be implemented with priority.

(ii) **DH to provide more information on drugs to the public**: Drug information in the existing DH's electronic compendium of pharmaceutical products are not comprehensive and user friendly enough. The Review Committee recommends that the content of the compendium be enhanced. The Review Committee also recommends the setting up of a designated website to promote drug safety. This recommendation should be implemented with priority.

(g) Penalty review (Chapter 9)

(i) **To strengthen the penalty on manufacturers**: The Review Committee recommends authorizing the Manufacturing Licensing Committee of the Pharmacy and Poisons Board to remove the authorized person when he breaches his duties and to stop the production of the manufacturer when the authorized person has been removed.

(ii) **To require the convicted person to bear the costs for analyzing exhibits in court cases**: The cost for analyzing exhibits in court cases could be substantial. The Review Committee recommends that the law be amended to require the convicted person to bear such costs in order to increase the deterrent effect.

(iii) **To provide the Court with more background information in prosecution cases:** DH should present more information to the Court to reflect the seriousness of the offence concerned for the Court to consider the penalty proportionate to the seriousness of the offence.

8. Chapter 10 of this report provides a general assessment on the resources implications of implementing the recommendations, while Chapter 11 summarizes the recommendations and concludes the work of the Review Committee. A glossary of terms is at *Annex F* for reference.

WAY FORWARD

9. The Review Committee has completed its task by giving recommendations on the measures to improve the existing regime. The Government will take follow up actions to implement these measures. The Food and Health Bureau will oversee the policy issues, and together with the Department of Health, will take forward the necessary legislative amendments, address the resource implications and requirements involved. The Department of Health and Hospital Authority will also be responsible for the implementation of the recommendations, consulting the stakeholders in the process. The implementation programme of the various recommendations is set out at *Annex D*. Some of the recommendations will be implemented subject to the passing of the relevant legislative amendments and may require a longer timeframe for implementation. A list of such recommendations is at *Annex E*.

10. Whilst the recommendations will be implemented in different phases, the Review Committee also recommends that a dedicated office on drugs should be set up to strengthen the regulatory role of the Government in enhancing drug safety in Hong Kong as a matter of priority . The office will plan and direct the implementation of measures relating to drug safety. DH will work closely with the pharmaceutical trade and all stakeholders to plan for the setting up of the office. In the long run, consideration will be given to expanding the office to be a "Centre for Drug Safety".

11. The Review Committee also notes that the Pharmacy and the Poisons Ordinance needs to be kept under regular review taking into account the changes in the operating environment of the pharmaceutical trade.

12. The Review Committee Chairman expresses her gratitude to all its Members, the pharmaceutical and medical sectors, academia, patient groups and consumer representative for their invaluable advice and unfailing support during the whole course of the review. The recommendations of the Review Committee will be implemented through the tripartite collaboration among the regulatory authority, the trade and consumers. All parties would need to maintain their heightened vigilance against any mal-practices. We believe that the key to the success in raising the standard of the pharmaceutical sector in Hong Kong lies in an effective regulatory regime, the commitment and determination of the professionals to practise to their highest standards and the trade to perform responsibly.

IN MEMORIAM

13. The Review Committee is very saddened that one of its Members, Ms Sandra CHOW, Chairperson of Care for your Health - Cardiac Patients Mutual Support Association, passed away in late-December 2009 just before the completion of this review. Ms CHOW had participated actively in all meetings of the Review Committee as well as its subcommittees and had contributed many useful and constructive ideas from the patients' perspective on a wide range of topics. The Chairman and all Members of the Review Committee would like to express their deepest condolences to Ms CHOW's family.

CHAPTER 1 INTRODUCTION

Overview

1.1 This chapter sets out the background of the review; the terms of reference and membership of the Review Committee on Regulation of Pharmaceutical Products in Hong Kong; and its work in the last nine months.

Background

1.2 In March 2009, a number of incidents concerning pharmaceutical products broke out in Hong Kong, causing public concerns and calling into question the adequacy and performance of the existing regime for the regulation and control of pharmaceutical products. A chronology of these drug incidents since March 2009 is at *Annex G*.

1.3 Immediate after these drug incidents, the Department of Health (DH) conducted an additional round of inspections to all the 25 drug manufacturers in Hong Kong for risk and microbiology safety assessment. Written advices were also issued to all manufacturers, importers/exporters, wholesalers, retailers and professional associations in the drug industry to remind them of the essential licensing requirements on drug safety.

1.4 The Government considered that in order to ensure patient safety, protect public health and restore public confidence, a comprehensive review on the existing regime for the regulation and control of pharmaceutical products was necessary to identify gaps and areas for improvement.

1.5 Against this background, the Secretary for Food and Health announced on 19 March 2009 the setting up of a Review Committee on Regulation of Pharmaceutical Products in Hong Kong (Review Committee), to be chaired by the Permanent Secretary for Health with members from the pharmaceutical sector, medical profession, academia, patient groups and consumer representative. The Review Committee was tasked to complete the review in six to nine months' time.

Membership and Terms of Reference of the Review Committee

1.6 The membership and terms of reference of the Review Committee, as adopted at its first meeting held on 3 April 2009, are at *Annex A*.

Work of the Review Committee

1.7 To facilitate in-depth examination of the wide range of drug issues, Members of the Review Committee formed two subcommittees on drug manufacturing, and drug distribution and procurement respectively. The membership of the two subcommittees is at *Annex B*. Besides, to support the work of the Review Committee, a Task Force was set up under DH to make proposals, through the engagement of overseas consultancy studies, on the updating of the Good Manufacturing Practices (GMP) scheme and on the enhancement of pharmacovigilance in Hong Kong. Furthermore, DH also formed an Expert Group to give advice on microbiological hazards on drug manufacturing, based on the trial run testing results in a local drug manufacturer, to the Task Force. The memberships and terms of reference of the Task Force and Expert Group are at *Annex C*. Recommendations from the Task Force were first deliberated at subcommittee level before they were put forward to the Review Committee for deliberation and endorsement.

1.8 During the review period from April to December 2009, the Review Committee held a total of five meetings to consider the work reports of its subcommittees and the findings and recommendations in the review report. In addition, the Subcommittee on Drug Manufacturing and the Subcommittee on Drug Distribution and Procurement both met on three occasions to conduct detailed examination on a wide range of drug issues.

1.9 In order to have a deeper understanding on the actual operation of local drug manufacturers, Members of the Review Committee visited the premises of two local drug manufacturers in Yuen Long in May 2009.

1.10 The Review Committee has examined all aspects of the current drug regulatory regime and the supply chain of pharmaceutical products, from manufacturing, distribution, import and re-export, procurement, supply of drugs and delivery to the public and private sectors, to control of pharmaceutical products, pharmacovigilance, penalty for non-compliance as well as risk communication, education and training. The Review Committee has also considered the additional resources requirements to implement all its recommendations.

1.11 In the course of the review, the Review Committee has sought and duly taken into account the views of its Members. The majority views of Members are taken before arriving at the final recommendations. Detailed recommendations of the Review Committee are set out in the ensuing chapters.

CHAPTER 2 EXISTING REGULATORY REGIME

Overview

2.1 This chapter states the objectives of the review, gives an overview on the existing regime for the regulation and control of pharmaceutical products in Hong Kong, and sets out the underlying principles of existing regulatory regime.

Objectives of the Review

2.2 The Review Committee intends to achieve the following objectives in this review -

(a) to protect public health and ensure patient safety as the top priority;

(b) to ensure that all pharmaceutical products supplied in Hong Kong fulfill a set of stringent safety and quality criteria in order to protect public health;

(c) to restore and maintain public confidence on the consumption and use of drugs;

(d) to sustain and upgrade the standard of Hong Kong drug manufacturing industry to international level; and

(e) to foster the development of Hong Kong pharmaceutical trade and industry and promote the trademark of Hong Kong.

2.3 While striving to improve the effectiveness of the existing regulatory regime, the Review Committee is mindful of the challenges to the trade and the professionals. Moreover, the proposed regulatory regime should be fair, accountable, consistent and transparent.

Existing Regulatory Regime

2.4 The existing drug regulatory regime adopts a risk management, dual target and multi-pronged approach backed by the law. The regime targets at both the pharmaceutical products and the pharmaceutical trade. Multi-pronged approach embraces legal requirements and administrative measures which

provide the framework of the control system; education for players in the pharmaceutical sector to equip them with the necessary professional knowledge; promotion and publicity to educate the public on safe use of drugs; and a penalty system to deter the pharmaceutical sector from malpractices.

2.5 The regulatory regime is risk and evidence based, starting at the source and following through each point in the production line and the supply chain until the drug reaches its target patients. A penalty system is in place with penalty for non-compliance of drug regulations proportional to the harm and impact that each mal-practice or defective drug products may cause to the patients and general public.

Legal Framework

2.6 Regulation of the pharmaceutical trade in Hong Kong is essentially provided for by the Pharmacy and Poisons Ordinance (Chapter 138) ("the Ordinance") and its regulations. Section 3 of the Ordinance provides for the establishment of a Pharmacy and Poisons Board for the enforcement of the Ordinance. Section 4A of the Ordinance further allows the Pharmacy and Poisons Board to establish executive committees to license various medicine dealers, to register pharmaceutical products and to approve clinical trials of drugs. The Review Committee notes that the Ordinance is subject to regular review taking into consideration changes in the operating environment and needs of the trade.

Pharmaceutical Trade

2.7 There are four levels of players in the drug supply chain, viz. manufacturers, importers/exporters, wholesalers and retailers (including the pharmacists overseeing the operations of the retailers). At present, there are 25 manufacturers, around 240 importers/exporters, 860 wholesalers and 3,800 retailers in Hong Kong. They are all subject to licensing control under the Ordinance.

Classification of Pharmaceutical Products

2.8 The Ordinance provides for a Poisons List which is divided into two parts: Part I and Part II respectively. Drugs included in Part I of the Poisons List are termed "Part I Poisons" while drugs included in Part II of the Poisons List are termed "Part II Poisons". "Part I Poisons" in general are drugs with more serious side effects which warrant enhanced supervision in handling, while "Part II Poisons" have less serious side effects. Drugs which are not

included in the Poisons List are commonly referred to as "non-poisons" by the traders.

2.9 Some Part I Poisons are further classified into the First Schedule and the Third Schedule with additional restrictions on their sale at retailers (the Second Schedule refers to drugs exempted as "poisons").

2.10 Currently, there are about 19,500 pharmaceutical products registered in Hong Kong, including 12,300 poisons and 7,200 non-poisons. Among the 12,300 poisons, 10,800 are Part I Poisons and 1,500 are Part II Poisons. Of the Part I Poisons, 400 are First Schedule Poisons and 10,400 are Third Schedule Poisons.

Two-tier Monitoring and Control of Pharmaceutical Products

2.11 It is stipulated under the Pharmacy and Poisons Regulations that all drugs in Hong Kong must be registered with the Pharmacy and Poisons Board before sale. In line with international practice, only products which are safe, efficacious and of good quality will be registered. To ensure proper control of the safety, efficacy and quality of drugs, Hong Kong has a two-tier monitoring and control system that is very similar to those in many other overseas drug authorities, comprising pre-market and post-market control.

Underlying Principles of Existing Regulatory Regime

2.12 Since there are over 19,000 pharmaceutical products registered in Hong Kong, it is impossible for the Government to conduct regular tests on each of the drug items, given that each item is also produced at different time. As with the practice in other overseas drug authorities, the primary responsibility falls on the pharmaceutical trade, in particular the drug manufacturers, to ensure that the pharmaceutical products they produce or supply to the patients are safe, efficacious and of good quality. Specifically, local manufacturers are required to comply with the Good Manufacturing Practices (GMP) which is a quality assurance approach used by the drug manufacturing industry worldwide to ensure that products are consistently produced and controlled according to appropriate quality standards. GMP emphasizes on self-inspection and quality audits. The Government's role is more on monitoring of the pharmaceutical trade in compliance with the licensing requirements, and education of the public on drug safety.

2.13 The Review Committee notes that government oversight plus self-regulation by the trade is an internationally accepted mode of regulatory regime

in advanced countries, and has proven to be sound and effective. It also underlines the importance of enhancing corporate governance of players in the drug supply chain. The Review Committee agrees that the basic principles of the existing regulatory regime in Hong Kong are in order and should be maintained. However, improvements should be made to expand its coverage and depth of the implementation details.

CHAPTER 3 REGULATION OF DRUG MANUFACTURERS AND ENHANCEMENT TO THE GOOD MANUFACTURING PRACTICES SCHEME

Overview

3.1 This chapter describes the current licensing system for drug manufacturers in Hong Kong and sets out the Review Committee's findings and recommendations on areas for improvement.

Current Licensing System for Drug Manufacturers

3.2 Drug manufacturing is defined under the Ordinance as "the preparation of pharmaceutical products for sale or distribution, but shall not include the individual dispensing on a prescription or otherwise of any pharmaceutical products". To ensure that drugs produced are safe, efficacious and of good quality, drug manufacturers must first obtain a licence. The licensing authority is the Pharmacy and Poisons (Manufacturers Licensing) Committee ("the Manufacturers Licensing Committee") under the Pharmacy and Poisons Board.

Licensing Requirements

3.3 The licensing requirements to be met in awarding a manufacturer licence and during licence renewal include –

(a) the manufacturing process under the supervision of registered pharmacist;

(b) proper labelling of drugs manufactured;

(c) adequate hygiene control of personnel and premises to avoid contamination of drugs; and

(d) quality assurance of raw materials and finished products with retention of control sample and all related records.

Since 2002, compliance with the Good Manufacturing Practices (GMP) has become an additional important licensing condition.

Good Manufacturing Practices

3.4 GMP is a quality assurance approach used by the drug manufacturing industry worldwide to ensure that products are consistently produced and controlled according to appropriate quality standards. Most countries have adopted the GMP guidelines promulgated by the World Health Organization (WHO), although countries such as the United States, European Union and Australia have drawn up their national GMP guidelines which are recognized to be of a standard higher than the WHO guidelines. The spirit of the GMP emphasizes that the assessment of "good quality" should be based on scrutiny of the manufacturing process and not by testing of the end products alone.

3.5 A GMP manufacturer should have adequate premises, spaces, laboratories, personnel, storage facilities and transport. The personnel should be appropriately qualified and trained. All the manufacturing processes must be validated and clearly defined, systematically reviewed and shown to be capable of consistently manufacturing pharmaceutical products of the required quality and complying with their specifications. Instructions and procedures are required to be written in clear and unambiguous language, specifically applicable to the facilities provided. Records must be made during manufacture to show that all the steps required by the defined procedures and instructions have in fact been taken and that the quantity and quality of the product are as expected. Any significant deviations must be fully recorded and investigated. In addition, appropriate materials, containers and labels must be used.

3.6 GMP specifies the recruitment of three key personnel in the manufacturer, namely the Authorized Person (AP) responsible for product release, head of production and head of quality control. In the Hong Kong context, the AP position must be filled by a registered pharmacist with at least one year of relevant experience in pharmaceutical manufacturing or quality control. As regards the other two heads, they must have at least one year of relevant experience if they have a pharmacy degree; two years of relevant experience if they have a higher diploma in pharmacy-related subjects; or three years of relevant experience if they have a degree in a relevant science subject. In addition, any change in the three key personnel must be approved by the Manufacturers Licensing Committee.

3.7 Of the 25 licensed manufacturers in Hong Kong, 24 are GMP certified to perform the manufacturing of various kinds of medicines. The remaining one is GMP certified to perform the packaging of pharmaceutical products only, which is regarded as part of a manufacturing process by leading drug regulatory authorities.

Processing of Licence Applications

3.8 Upon receipt of a licence application, DH inspectors will first study and assess the information in the application carefully. If the applicant has met the licensing requirements on paper, DH will inform the applicant to proceed with site preparation, staff recruitment and training; and then conduct on-site inspection. When DH is satisfied that the applicant has fulfilled all licensing conditions, a report will be put up to the Manufacturers Licensing Committee for decision. A licence is valid for one year and is renewable annually.

Monitoring and Inspections

3.9 To ensure compliance with the licensing requirements, licensed manufacturing premises are regulated by means of GMP inspections conducted by two DH inspectors at least once a year. Each inspection lasts for two days. During the inspection, all different GMP aspects will be audited for compliance against a checklist and product samples will be taken for analysis.

3.10 For minor non-compliance with any licensing conditions, the manufacturer will be verbally reprimanded and instructed to remedy the situation. For more serious non-compliance, the case will be submitted to the Manufacturers Licensing Committee which may revoke the licence or suspend it for such period as it thinks fit. If non-compliance with the law is found, prosecution action will be initiated. Convicted persons are liable to a maximum penalty of $100,000 and two years' imprisonment. The Manufacturers Licensing Committee may take further disciplinary action against the licensee after conviction, including the issue of a warning letter and further revocation or suspension of licence.

Consultancy Study on Hong Kong's GMP

3.11 Since Hong Kong's GMP has been in use since 2002 and may need updating in content, DH commissioned an overseas GMP expert from Australia in May 2009 to conduct a consultancy study on Hong Kong's GMP in the light of the latest practices in leading world drug regulatory authorities. The overseas consultant has made a number of recommendations, which were discussed first in the DH Task Force before putting forward to the Review Committee for consideration.

Microbiological Hazards on Drug Manufacturing

3.12 The Europharm drug incident has revealed the microbiological hazards in drug manufacturing. Shortly after the incident, DH set up an Expert Group, with Professor YUEN Kwok Yung, Head of the Department of Microbiology of University of Hong Kong as an expert advisor, to identify and evaluate microbiological hazards in the drug production process; and then propose an enhanced model for microbiological monitoring in drug manufacturing in Hong Kong. The Expert Group formulated an enhanced model and tested out this enhanced model in Europharm Laboratoires Company Limited. Based on the trial-run results, the Expert Group has refined the model and recommended that the model be implemented in all drug manufacturers in Hong Kong.

3.13 Under the proposed model, microbiological tests should be performed on all batches of high risk raw materials, prior to the use of the batch, and every six months thereafter, until the batch is used up. The holding time of granules prior to tabletting should be as short as possible, with an upper limit of not more than 48 hours. If a manufacturer intends to adopt a holding time beyond 48 hours for any product, the holding time to be adopted for that product must be supported by validation studies data. Furthermore, manufacturers should establish a more stringent in-house microbial limit for each product. Full microbial limit tests should be performed on every batch of every finished product before release for sale. Microbiological testing should also be included in the stability study programmes of all pharmaceutical products.

Findings and Recommendations

I. GMP Consultant's Recommendations

3.14 The Review Committee has considered and **endorsed the majority of the GMP consultant's recommendations** as follows –

(a) Upgrade of Hong Kong GMP Standards

3.15 It is recommended that DH should upgrade Hong Kong's current GMP licensing standards by a phased approach to PIC/S (Pharmaceutical Inspection Co-operation Scheme[1]) standards over a period of about four years to reflect changes in industry technology and to be on par with international best practice.

[1] The Pharmaceutical Inspection Co-operation Scheme is an international agreement between pharmaceutical regulatory authorities of different countries or territories which provide an active and constructive co-operation in the field of GMP. This is to be achieved by developing and promoting harmonized GMP standards and guidance documents; training competent authorities, in particular inspectors; assessing (and reassessing) inspectorates; and facilitate co-operation and networking for competent authorities and international organisations. There are currently 37 participating authorities including the majority European Union countries, Australia, Singapore, etc.

During the transition period, Hong Kong's GMP licensing standards should first be upgraded to 2007 WHO standards in about two years' time.

3.16 It is recommended that DH commissions a consultant to assist local drug manufacturing industry in progressing towards the PIC/S standards. Furthermore, DH should adopt international GMP guidance documents for implementation by the industry, develop an information website and set up an industry liaison group with industry participation.

(b) Control over Imported Drugs

3.17 It is recommended that DH should require imported drugs to comply with the same standards once local drugs attained the PIC/S standards, i.e. they should have GMP certificates issued by PIC/S member countries. For drugs of other places without recognized GMP certificates, their manufacturing premises must be inspected by either DH inspectors or a third party approved by the Pharmacy and Poisons Board to certify that their GMP standards is equivalent to the PIC/S standards before they could be allowed to import into Hong Kong.

(c) Control over the Use of Active Pharmaceutical Ingredients and Testing Laboratories

3.18 It is recommended that DH strengthens the control of the use of Active Pharmaceutical Ingredients (APIs) and contract laboratories by local manufacturers. For APIs not produced by manufacturers certified to have PIC/S standards, APs should be responsible for inspection of the manufacturing premises of APIs to certify the quality of APIs as well as retention of the inspection reports for DH examination. Besides, only laboratories licensed by DH or accredited by a third party in lieu could be used by local manufacturers for product testing. In this connection, DH should work out with relevant experts the licensing requirements and inspection checklist for contract laboratories.

(d) Tightening up the Qualification Requirements for AP and other positions

3.19 To ensure that the APs and the heads of production and quality control are capable of discharging their duties, the Review Committee **recommends** strengthening their experience requirement as follows –

- for AP: from at least <u>one</u> year of relevant working experience to at least <u>three</u> years;

- for the heads of production and quality control: from at least one year to at least two years for pharmacy degree holders and from at least two years to at least three years for holders of higher diploma in pharmacy-related subjects.

For degree holders of a relevant science subject, the Review Committee recommends no change to the three years' experience requirement to be eligible as the head of production or quality control.

3.20 The Review Committee considers that it is part of PIC/S requirements as well as a worldwide trend that the AP or equivalent position of manufacturers is filled by the most qualified person in possession of the relevant knowledge and experience dependent on the product characteristics and manufacturing needs of individual manufacturer. In many developed countries, the APs are not necessarily pharmacists. The Review Committee **recommends** that a formal set of criteria regarding the qualifications of the AP be set, a licensing or listing scheme to be established, alongside with the introduction of a structured training programme and a mechanism to ensure that APs will take responsibility for the quality, safety and efficacy of their drug products. The tightening up of the entry requirements of AP will raise the product manufacturing and quality control standards of local manufacturers.

3.21 In the meantime, the position of AP will still be required to be filled by pharmacist with relevant experience. The Review Committee notes that a pharmacist acting as AP is bound by both the responsibilities of AP as laid down under GMP and the disciplinary mechanism of the Pharmacy and Poisons Board against his professional status. Such a "double gate-keeping mechanism" is desirable for the protection of public health.

3.22 In the longer run, the Review Committee **recommends** empowering the Pharmacy and Poisons Board to maintain an AP register and remove any AP from the register should he be found incompetent to perform the AP role. The Pharmacy and Poisons Board should adhere to the usual open and transparent procedures in taking disciplinary actions against an AP and allow the AP concerned to make representations. The Review Committee also **recommends** DH to consult the Department of Justice (DoJ) on the feasibility of including the registration mechanism of APs in the Pharmacy and Poisons Ordinance.

3.23 When the above registration system for APs is in place and additional formal certified GMP training has been developed, consideration will be given to allowing non-pharmacists with the required experience and training to assume the position of AP.

3.24 The Review Committee **recommends** DH to liaise with the University Grants Committee and the universities offering pharmacy courses with a view to launching Master degree course(s) in drug manufacturing similar to the one being developed by the Chinese University of Hong Kong as soon as possible. DH should then monitor the supply of graduates from these courses and draw up an implementation timetable in consultation with the manufacturing industry for allowing non pharmacists to be APs.

(e) DH Inspection and Licensing Processes

3.25 It is **recommended** that DH upgrades the inspection and licensing processes to PIC/S standards in one year's time, including the establishment of an internal quality management system in line with the PIC/S requirements. In addition, the inspection reports should model on the PIC/S risk-rating and evidence-based report format. The portion of GMP-related duties of DH inspectors should be raised from the current 20% to not less than 50% of their work and the number of inspections should increase. While most of the inspections to manufacturing premises should remain announced, some unannounced inspections should be introduced. Further, one of the two inspectors in the inspection team should be retained for subsequent inspections to facilitate effective follow-up on irregularities identified.

3.26 DH should arrange the necessary training to staff and provide additional manpower support to implement the GMP consultant's recommendations in this regard.

3.27 The Review Committee also notes that DH inspectors do not have expertise on every aspects of drug manufacturing process. The Review Committee therefore **recommends** that DH sets up a multi-disciplinary GMP inspection team with professionals of other related disciplines like biochemists, chemists, engineers, microbiologists, etc. dependent on the production environment of manufacturers.

(f) Training Programme

3.28 It is **recommended** that structured, practical and continuous training programmes be developed for all levels of players in the GMP system including DH inspectors, APs, production and quality control heads, and shop floor level workers. Specifically, training programme for APs should be mandatory with content approved by DH. Training records for different levels of staff of manufacturers should be kept for auditing by DH as part of GMP inspections.

II. Invitation of AP to attend Board Meetings of Manufacturers

3.29 The Review Committee has also discussed the pros and cons of requiring AP to be a board member of manufacturers. On the pros side, the Review Committee notes that by sitting on the board, the status of AP can be elevated and the AP can ensure that his authority in respect of product quality and release will not be interfered with. Besides, the AP being a professional can help to ensure that decisions of the board will not be made on commercial interests alone. Furthermore, the AP can draw the board's attention to product quality issues and guide the board to take a proactive approach in avoiding drug incidents, instead of just playing a gate-keeping role.

3.30 On the other hand, the Review Committee notes that under GMP, the AP already has the final authority in respect of product release and even the board cannot interfere with the decisions of AP in this regard. If the AP is on the board, he will be diverted by business considerations and may compromise his professional role in respect of product quality control. Besides, AP being a pharmacist may not be able to undertake the business responsibilities of a board member, nor is it fair for AP to bear the business liabilities of a board member.

3.31 The Review Committee also notes that according to research of DH, there are no countries mandating manufacturers to put the AP or equivalent on the board of directors. It may constitute an unreasonable interference to the business decisions of manufacturers. From the perspective of good corporate governance, it is more important to establish a communication channel between AP and the management.

3.32 Taking into consideration the pros and cons, the Review Committee **recommends** DH state in the licensing condition that local manufacturers should either (a) appoint the AP as a board member; or (b) invite the AP to attend board meetings and allow the AP to speak and have his remarks put on record where safety, efficacy and quality issues of products are concerned. The recommendation should be put on trial for two years and then reviewed.

3.33 To further protect the authority of APs, the Review Committee **recommends** that a code of practice (COP) be introduced to govern the conducts of both the manufacturers and the APs. DH should prepare the COP in consultation with the industry and other stakeholders. The COP should state, inter alia, that AP has ultimate responsibility on product safety and that AP is required to certify every batch of finished products in compliance with GMP standard and registered particulars before release for sale. Compliance with COP should be a licensing condition.

III. Enhanced Model for Microbiological Monitoring of Pharmaceutical Products manufactured in Hong Kong

3.34 The Review Committee has considered the proposed model by the Expert Group on better monitoring of pharmaceutical products manufactured in Hong Kong, and **recommends** that all local manufacturers be required as a licensing condition to implement the proposed model in order to better guarantee safety and quality of finished products. The enhanced microbiological monitoring model covers raw materials, granules, finished products and stability studies.

Raw Materials

3.35 Manufacturers should perform microbiological tests on all batches of high risk raw materials prior to the use of the batch, and every six months thereafter, until the batch is used up. If a manufacturer wishes to test in other time intervals, it has to provide justifications for approval by DH.

Granules

3.36 Manufacturers are required to limit the holding time for in-process granules to not more than 48 hours before tabletting. If a manufacturer intends to adopt a holding time beyond 48 hours for any product, it must first seek approval from DH with support of validation studies data.

Finished Products

3.37 Manufacturers should set a more stringent in-house alert level for microbial burden of each product to be two times one $\log_{10}$ value lower than the pharmacopoeial limits, as compared with the common practice of one $\log_{10}$ lower value. If a manufacturer intends to adopt other alert level, it must first seek approval from DH with justifications.

3.38 Manufacturers are required to conduct full microbial limit tests on every batch of every finished product before release for sale. If the test results of five successive batches of a product meet the in-house standards, manufacturers are allowed to reduce the testing to every 5^{th} batch. However, at a minimum, manufacturers should still perform one batch test every six months. If any test result shows deviation from the longitudinal trend of previous results, manufacturers must conduct investigation, record the investigation result in writing and take all necessary remedial measures to restore the test result within the in-house standards.

Stability Studies

3.39 Manufacturers should include microbiological testing in the stability study programmes of all pharmaceutical products.

Chapter 4 PRE-MARKET CONTROL OF DRUGS

Overview

4.1 This chapter provides an overview of the existing regime for the pre-market regulation and control of drugs in Hong Kong and presents the Review Committee's findings and recommendations on enhancing the existing regime.

The Existing Pre-market control

4.2 Under the Pharmacy and Poisons Ordinance, Cap. 138 ("the Ordinance"), a Pharmacy and Poisons Board is established to implement the provisions of the Ordinance. As stipulated under the Pharmacy and Poisons Regulations, all pharmaceutical products in Hong Kong must be registered with the Board before sale. The licensing authority is the Pharmacy and Poisons (Registration of Pharmaceutical Products and Substances: Certification of Clinical Trial/Medicinal Test) Committee ("the Registration Committee") under the Board. Apart from the registration of pharmaceutical products, the Registration Committee is also responsible for the issuance of clinical trial certificates for the clinical trial of new pharmaceutical products.

Definition of "pharmaceutical product"

4.3 The Ordinance defines "pharmaceutical product" as "any substance or mixture of substances manufactured, sold, supplied or offered for sale or supply for use in -

(a) the diagnosis, treatment, mitigation, alleviation or prevention of disease or any symptom thereof;

(b) the diagnosis, treatment, mitigation, alleviation of any abnormal physical or physiological state or any symptom thereof;

(c) altering, modifying, correcting or restoring any organic function,

in human beings or in animals".

4.4 Some products are exempted from registration. They are -

(a) products manufactured in Hong Kong for export only;

(b) products imported for re-export only;

(c) products imported by a manufacturer for reprocessing into other pharmaceutical products; and

(d) products imported only for the use of a particular patient or animal, under the direction of a registered doctor, dentist or veterinarian (commonly referred to as "named patient" use).

Registration of Pharmaceutical Products

4.5 Pre-market control refers to the assessment of safety, efficacy and quality of pharmaceutical products, which are products containing new chemical entities, generic versions of drugs, or products that required re-registration before they are released to market.

4.6 DH will access the information on the product's composition, specification, analysis results, stability data, label and insert, as well as a visual inspection of the product sample. Evidence that the product is available for sale in the country where the product is manufactured is required. Specifically for quality assurance, the product has to be manufactured by manufacturer with GMP certificate issued by the relevant competent authority.

4.7 When there are changes in product name, dose form and/or name and quantity of all its active ingredients of a product, the products need to be re-registered under the Pharmacy and Poisons Regulations. Any change in a drug's other registered particulars, including the pack size and manufacturer, requires the approval of the Registration Committee.

4.8 Apart from satisfying the requirements of safety, efficacy and quality, a pharmaceutical product must also comply with the relevant labelling requirements for registration approval purpose.

4.9 When a product's safety, efficacy and quality has been proven to the satisfaction of the Registration Committee of the Board, and its packaging, insert and labelling have also been found to meet the relevant requirements, the product can be registered. A registration certificate bearing the name of the drug as well as the registration number will be issued. The certificate is valid for five years and renewable on expiration.

4.10 Registered pharmaceutical products are subject to continuous monitoring in respect of their safety, efficacy and quality. If there is new evidence that a registered product no longer meets any of the three criteria, the

Registration Committee may deregister it. The sale and possession for the purpose of sale of unregistered products are both criminal offences and are subject to a maximum penalty of $100,000 and two years' imprisonment on conviction.

Assessment of Generic Drugs

4.11 Apart from the quality assurance through the GMP certification of manufacturers, an additional quality concern of generic drugs or multisource pharmaceutical products is bioavailability and bioequivalence (BABE), or the conformance to the same appropriate standards of quality, efficacy and safety as those required of the innovator's product. Proof of BABE is particularly important for some drugs, such as antiepileptic drugs, where difference in BABE from the innovator's product may result in undesirable consequences when the two products are interchanged.

Clinical Trials of New Pharmaceutical Products

4.12 Drug safety and efficacy are mainly demonstrated through clinical trial results. As such, clinical trials are conducted to allow safety and efficacy data to be collected for new drugs. Some public and private hospitals are involved in clinical trials of new pharmaceutical products. They are mostly multi-centre studies, sponsored by multi-national pharmaceutical manufacturers. The Ordinance requires sponsors to apply for clinical trial certificate, which is issued by the Registration Committee on the basis that the centres comply with good clinical practices (GCP). GCP provides for an acceptable standard of ethics on human experimentation, sound justification of the trial, informed consent, the design of the trial protocol, methodology of data analysis and the review by an independent Ethics Committee. A clinical trial certificate is valid for not more than two years.

Findings and Recommendations

4.13 The Review Committees finds that the existing registration approval criteria that products must be safe, efficacious and of good quality are in line with international registration requirements. There are, however, rooms for improvement and the Review Committee makes recommendations in the following areas -

(a) Bioavailability and Bioequivalence (BABE) Studies

4.14 The Review Committee **recommends** that DH and the Board require BABE studies as registration requirement for pharmaceutical products to enhance quality of generic drugs. The implementation will be by phases starting from April 2010. The first phase will include antiepileptic drugs where a comparatively small difference in the absorption of the drug by the human body may lead to undesirable consequences. The Board will prepare the implementation timeline and DH will pursue with the local universities to facilitate the carrying out of BABE studies.

(b) Labelling of Pharmaceutical Products

4.15 The Review Committee **recommends** that DH and the Board replace the word "Poison 毒藥" which is required under the Pharmacy and Poisons Ordinance to be labelled on pharmaceutical products classified as poisons with other terms to alleviate the unnecessary concern of consumers that the products might be harmful and unsuitable for use or consumption. The terms "prescription drugs 處方藥" and "drugs under supervised sale 監售藥" have been suggested for drugs with different level of control in their supply. The Board will conduct consultation with stakeholders on the choice of the most appropriate terms to be used and seek advice from the Department of Justice.

(c) Wording in the Certificate of Registration of Pharmaceutical Products

4.16 The Review Committee finds that the registration certificate (copy at Annex *H*) is issued based on the product having satisfied the registration criteria of safety, efficacy and quality. However, the certificate bears the phrase "to be marketed for use within Hong Kong". This is undesirable as DH is not in a position to assess whether the product has infringed any intellectual property rights which may render it not proper for sale in Hong Kong. The Review Committee **recommends** that DH and the Board delete the phrase "to be marketed for use within Hong Kong" on the certificate of registration of pharmaceutical products. The revised certificate will more accurately reflect that the product only satisfies the safety, efficacy and quality criteria for registration but not other commercial requirements.

(d) Validity of Clinical Trial Certificate

4.17 The validity of a clinical trial certificate is only two years, which is often too short for the completion of a clinical trial. The Review Committee **recommends** that DH and the Board extend the validity of clinical trial certificate from not more than two years to not more than five years so that the applicant does not need to apply for a certificate again if the trial lasts more than two years.

(e) Timeliness of Registration Approval

4.18 The Review Committee finds that because of manpower constraint, DH has a long processing time for approval of applications for registration of pharmaceutical products, approval of applications for change of particulars of registered products and applications for clinical trials. The Review Committee **recommends** that DH shortens the time-frame for processing these applications by 40% to 50% to enhance the business competitiveness of Hong Kong and facilitate the pharmaceutical trade.

CHAPTER 5 REGULATION OF IMPORTERS/EXPORTERS, WHOLESALERS AND RETAILERS

Overview

5.1 This chapter provides an overview of the existing regulatory regime for the other three levels of players in the drug supply chain, viz. importers/exporters, wholesalers, and retailers; and presents the Review Committee's findings and recommendations on areas for improvement.

Importers/Exporters, Wholesalers and Retailers

5.2 As provided in the Pharmacy and Poisons Ordinance (the Ordinance), importers/exporters and wholesalers can only resell drugs to retailers, hospitals, clinics and other authorized persons, while retailers can sell drugs direct to members of the public. Depending on the types of drugs being handled, these two levels of traders are issued with different kinds of licences.

Existing Regulatory Regime for Importers/Exporters and Wholesalers

5.3 There are around 240 importers/exporters licensed to deal with the import/export of pharmaceutical products not classified as poisons, and 860 wholesalers licensed to deal with import/export, and wholesale within Hong Kong, of all pharmaceutical products whether or not classified as poisons.

Types of Licences for Importers/Exporters and Wholesalers

5.4 Under section 28A of the Ordinance, for a company importing or exporting drugs not classified as poisons into or out of Hong Kong, a Certificate of Registration as an Importer and Exporter (IE) is required.

5.5 Under regulation 26 of the Pharmacy and Poisons Regulations, for a company handling import and export and/or wholesaling in drugs classified as poisons under the Ordinance, a Wholesale Poisons Licence (WPL) is required.

5.6 In addition, holders of either IE or WPL importing or exporting drugs of any classification must also obtain beforehand an Import Licence (IL) or Export Licence (EL) for each consignment as appropriate under the Import and Export (General) Regulations. While the licensing authority for ILs and ELs is vested in the Director-General of Trade and Industry (DGTI), the DGTI has delegated

the power for issue of ILs and ELs in relation to drugs to DH. In practice, DH will only issue ILs and ELs for either registered drugs or unregistered drugs imported for re-export purpose only.

5.7 No licence is required for a company trading in drugs of non-poisons inside Hong Kong, provided that the drugs are registered.

5.8 To summarize, the licensing requirements for traders are as follows –

Traders	Licence required
Wholesalers of poisons	WPL
Importers and exporters of poisons	WPL
Wholesalers of non-poisons	Nil
Importers and exporters of non-poisons	IE
Importers and Exporters of all pharmaceutical products	IL or EL for each consignment

Processing of Licence Applications

5.9 IE and WPL are issued by the Wholesale Licences and Registration of Importers & Exporters Committee (IE Committee) under the Pharmacy and Poisons Board. General licensing conditions include suitable premises and adequate knowledge of the person-in-charge in the pharmaceutical trade.

5.10 Any company can apply for an IE or WPL. Upon receipt of an application, DH inspector will conduct an unannounced pre-licensing inspection at the premises for the purposes of assessing the suitability of premises for the storage of drugs to be handled and conducting interview with the person-in-charge of the proposed pharmaceutical business regarding his knowledge and experience in the pharmaceutical trade. After an applicant has satisfied the licensing conditions, the application will be referred to the IE Committee for decision, which may also impose additional conditions, such as restricting the applicant to deal with drugs mentioned in the application form only. An IE or WPL is valid for not more than one year and is renewable annually.

Licensing Requirements

5.11 Wholesalers are required to keep proper records of all transactions involving Part I poisons in the format specified in the Ordinance, including the name of the drug, date of transaction, to whom the drug is sold, quantity, etc. The objective is to ensure that the drugs are sold to persons authorized to handle them and to ensure traceability of drugs in case of product recall. Every

transaction must be supported by the relevant documents signed by the purchaser. The record and the signed documents must be kept for two years.

5.12 In addition, wholesalers are required to devise and maintain a recall mechanism so as to ensure comprehensive and speedy recall of their products at various levels whenever required. The recall mechanism is a key area for consideration when relevant licences are renewed. To facilitate wholesalers in devising their own recall mechanism, DH has issued a set of recall guidelines since 2000.

Monitoring and Inspections

5.13 Importers/exporters and wholesalers are monitored by DH by means of unannounced inspections. Each licensed premises is inspected about once a year on average. During inspections, transaction records with the relevant supporting documents, storage conditions of the premises, and the labelling of the pharmaceutical products are audited. If non-compliance with the law is found, prosecution action will be initiated. Convicted persons are liable to a maximum penalty of $100,000 fine and two years' imprisonment. The Committee may also issue a warning letter, revoke or suspend the licence for such period as it thinks fit after the licensee has been convicted of an offence. For failure to comply with the licensing requirements, the dealers will be instructed to rectify the situation.

5.14 Import and export control of drugs is conducted by staff of the Customs and Excise Department (C&ED) at various control points to ensure all pharmaceutical products have the required IL or EL. C&ED also conducts post-shipment consignment checks on a specified number of licences referred weekly by DH. The current weekly quota is 18 as agreed between C&ED and DH, in consideration of the staff resources of C&ED deployed for such purpose.

5.15 DH has adopted a risk-based approach towards import and export control of drugs. For Part I Poisons and antibiotics, importers/exporters and wholesalers are required by the Ordinance to keep records of all transactions (purchasing and supplying) with supporting documents. DH inspectors will cross check with the ILs and ELs and examine the records and supporting documents of these high risk pharmaceutical products during inspections of importers/exporters and wholesalers to detect any local sale of unregistered Part I poisons or antibiotics. For lower risk drugs classified as Part II poisons and non-poisons such as vitamins and medicated shampoos, DH has implemented market surveillance to detect any unregistered drugs being offered for sale in the local market.

Findings and Recommendations

5.16 The Review Committee identifies a number of areas for improvement in the existing regulatory regime for importers/exporters and wholesalers, and the recommendations are set out in the following paragraphs.

Licensing on Wholesalers of Non-poisons

5.17 The Review Committee notes that wholesalers of drugs which are non-poisons (e.g. stomach antacids, paracetamol and multivitamins) are not subject to inspection and licensing control at present. As a result, wholesaler may not maintain an accurate record on the transaction of these non-poisons. The Review Committee considers this situation undesirable, as non-poisons, though less dangerous, could also endanger patient health if they are not stored and handled properly. It is essential to monitor their quality and maintain a complete record to facilitate recall, if necessary. Moreover, wholesalers of non-poisons usually handle drugs in large quantity and are therefore an important link in the supply chain and an important player of drug quality maintenance.

5.18 The Review Committee **recommends** that DH requires all wholesalers of non-poisons be subject to inspection and licensing control. Although non-poisons are of lower risk, it is still important that wholesalers who handle them have the required storage facilities to protect drug quality, and that they maintain complete transaction records to facilitate recalls when necessary.

Keeping of Transaction Records

5.19 The Review Committee notes that existing record-keeping requirements under the law apply to transactions of Part I poisons only. There are no such requirements for Part II poisons or non-poisons, thus creating difficulties in the event of a drug recall. In addition, the existing transaction record form does not contain information such as registered pack size and batch number which is useful for monitoring and recall purposes.

5.20 The Review Committee **recommends** that DH requires all wholesalers to keep transactions records of all pharmaceutical products, including Part II poisons and non-poisons in the same manner as for Part I poisons. DH should take the opportunity to review the transaction record form with a view to providing more comprehensive information on the quality and whereabouts of the drugs concerned. The Review Committee further **recommends** that DH requires wholesalers to keep samples of each batch of drugs handled to facilitate investigation when needed.

Secondary Packaging of Pharmaceutical Products

5.21 The Review Committee finds that importers/exporters and wholesalers are currently permitted to perform secondary packaging of pharmaceutical products (i.e. packaging activities which do not expose the drug to air such as putting bottles of drugs into carton boxes, putting strip-packed tablets into carton boxes, labelling of bottles or carton boxes, etc.). The Review Committee considers this situation undesirable as problems such as wrong labelling or wrong content of carton boxes may arise in the secondary packaging process. As a matter of fact, some of the drug incidents occurred in early 2009 were caused by wrong packaging.

5.22 The Review Committee **recommends** that primary and secondary packaging should only be carried out by a licensed manufacturer who complies with the GMP requirements. A new category of secondary packaging licence will be introduced for such purpose. The Review Committee is aware of the impact of the recommendation on the business operation of importers/exporters and wholesalers, and suggests that an appropriate transition period be provided to help importers/exporters and wholesalers prepare for the change.

Introduction of a Code of Practice

5.23 The Review Committee finds that at present there are no guidelines governing the roles and responsibilities of importers/exporters and wholesalers on product quality, as compared with GMP for compliance by manufacturers. For instance, importers/exporters and wholesalers are not required to obtain from their overseas suppliers relevant quality control documents, such as batch release certificates, to ascertain product quality. Besides, there is no guidance for them to report adverse drug reactions of their imported drugs to DH. The Review Committee considers this situation unsatisfactory, as import of substandard drugs or poor handling of drugs by importers/exporters and wholesalers will affect public health. It is also unfair to local manufacturers who have to follow GMP requirements in respect of product manufacturing and quality control.

5.24 The Review Committee **recommends** that DH introduces a code of practice for importers/exporters and wholesalers detailing their roles and responsibilities, including the requirement of batch release certificate, the reporting of adverse drug reactions, points to note in storage and transportation of drugs, etc. DH should draft such a code of practice in consultation with DoJ and the wholesale industry, and include the code of practice in the licensing conditions for importers/exporters and wholesalers, so that sanctions could be imposed by the Pharmacy and Poisons Board for any non-compliance with the

code of practice. DH should also organize briefing sessions to help staff of importers/exporters and wholesalers familiarize with the content of the code of practice.

Inspections and Enforcement

5.25 The Review Committee finds the current inspection frequency of once a year on average to premises of importers/exporters and wholesalers insufficient, taking into account the large volume of drug items handled by importers/exporters and wholesalers and their risk to public health.

5.26 The Review Committee **recommends** that DH strengthens the monitoring of importers/exporters and wholesalers by means of more frequent and more detailed inspections, especially after the introduction of a code of practice. DH should review the existing inspection guidelines and checklists to enhance the quality of inspections.

Checking of Pharmaceutical Products at Ports of Entry

5.27 At present, pharmaceutical products entering into Hong Kong are checked by the Customs and Excise Department (C&ED) at various ports of entry. C&ED has to contact DH if they have any doubts about a particular consignment as they do not possess expertise about pharmaceutical products. The Review Committee notes that there is no dedicated DH team on the spot to check the imported products, which undermines the effectiveness of dealing with problematic pharmaceutical products when they arrive at Hong Kong.

5.28 The Review Committee **recommends** that DH sets up a dedicated team of pharmacist inspectors to advise C&ED on pharmaceutical imports at various ports of entry, such as whether the imported products require registration, or whether the imported products fit the description in the import licence.

Import and Export Control of Drugs

5.29 The Review Committee notes that there is at present no record and tracking system in place to trace if drugs imported into Hong Kong for re-export purpose are indeed exported, thus creating a loophole for the illegal sale of imported unregistered drugs in local market. The Review Committee **recommends** that DH sets up a record and tracking system as a matter of priority. When pharmaceutical products are imported for re-export purposes, DH would record the name and amount of the products. When the products are due for re-export, DH would check the information against the import licence to ensure that all the products are re-exported without being sold in Hong Kong.

5.30 The Review Committee further **recommends** that DH prescribes in the licensing conditions for ILs for the products for re-export that the importer should not sell unregistered imported drugs in Hong Kong and must re-export the products within a specified period of time, say one year.

5.31 The Review Committee acknowledges that the weekly quota of 18 for post-shipment consignment checks of licences is agreed between C&ED and DH in consideration of the workload of C&ED staff. Nevertheless, the Review Committee notes that this weekly quota has remained unchanged for many years while the numbers of ILs and ELs have been on an increasing trend in recent years. The Review Committee **recommends** that DH conducts joint review with C&ED to determine a new weekly quota which represents a statistically significant sample size of the ILs and ELs population.

5.32 The Review Committee notes that many drug exporters choose to export the products by mail. The daily average of such mail parcels of drugs is around 700. The Review Committee considers that the monitoring of export of drugs by mail should be stepped up and **recommends** that DH requires exporters who chose to export products by mail to clear their products at designated post offices where C&ED staff are present. DH will include the requirement in the ELs. DH will also discuss with C&ED and Post Office on the implementation arrangements.

5.33 The Review Committee also notes that there is no electronic record system among DH, C&ED and TID to facilitate the tracking of imported and exported drugs. The Review Committee **recommends** that DH develops an electronic record system to facilitate the tracing and tracking of imported unregistered drugs intended for re-export.

Existing Regulatory Regime for Retailers

5.34 There are a total of around 3,800 retailers, including 500 authorized sellers of poisons and 3,300 listed sellers of poisons. They are licensed to deal with retail business of drugs.

Types of Licences for Retailers

5.35 "Authorized Sellers of Poisons" (ASPs), commonly known as "dispensaries" or "pharmacies" (藥房), are authorized to sell Part I Poisons, Part II Poisons and non-poisons. The Ordinance requires that registered pharmacists should be present at the premises of ASPs to supervise the sale of poisons. The

name, certificate of registration and working hours of the pharmacist must be displayed in a conspicuous location inside the ASP. Besides, sale of First Schedule Part I Poisons should be recorded and kept in a "poisons book", while doctor prescription is required for sale of Third Schedule Part I Poisons. Both the sales record in the "poisons book' and the doctor prescription records have to be kept for two years and are subject to DH inspection. Furthermore, First and Third Schedules Part I Poisons must be stored in a locked receptacle away from customers' access within the ASP premises.

5.36 "Listed Sellers of Poisons" (LSPs), commonly known as "medicine companies" (藥行), are only allowed to sell Part II Poisons and non-poisons only. Moreover, they do not have the service of a registered pharmacist.

Licensing Requirements for ASPs

5.37 Under the Ordinance, the Pharmacy and Poisons Board will issue an ASP licence if it is satisfied that the applicant is a fit and proper person and the premises is suitable to conduct the retail sale of poisons. In addition, the premises have to be under the personal control of a registered pharmacist, which is defined as being present for not less than two-third of the opening hours of the premises.

5.38 Apart from the legal requirements, ASPs should comply with the "Code of Practice for Authorized Sellers of Poisons" and "Guidelines on the Labelling of Dispensed Medicines" promulgated by the Pharmacy and Poisons Board.

Processing of ASP Applications

5.39 Upon receipt of an ASP application, DH inspector will search the Company Registry for company profile of the applicant and interview the owner or person in charge of the applicant company as well as the registered pharmacist to ascertain if they have sufficient knowledge and experience and are "fit and proper" to conduct the retail sale of poisons. One or more unannounced on-site inspections will then be conducted for the purposes of assessing the suitability of the premises. Furthermore, DH inspector will conduct a criminal record search of all persons involved in the daily operation of business. The Board will refuse the application if any of the persons involved has had two convictions in the past three years related to any specified drug offences.

5.40 ASP licences are valid till the end of each year. At the beginning of each year, the Pharmacy and Poisons Board may renew the certificates upon application. In considering the renewal applications, the Board will assess if

any person involved in the daily operations of the ASP has had two convictions in the past three years in the same manner as in the assessment of a new applications.

Licensing Requirements for LSPs

5.41 The licensing requirements of LSPs are similar to that of ASPs, which include the suitability of the premises for the sale of pharmaceutical products and the fitness and properness of the persons involved in the business operation.

5.42 Unlike ASPs who can purchase pharmaceutical products in bulk packs and dispense to customers, LSPs cannot dispense prescriptions. LSPs must sell pharmaceutical products in their original packages as received from suppliers.

Processing of LSP Applications

5.43 The Pharmacy and Poisons (Listed Sellers of Poisons) Committee of the Pharmacy and Poisons Board (LSP Committee) is responsible for the licensing of LSPs. Upon receipt of an LSP application, DH inspector will make an unannounced inspection at the premises of the applicant for the purpose of assessing the suitability of the premises and interviewing the persons involved in the daily business operation to ascertain if they are "fit and proper" to conduct the retail sale of Part II Poisons and non-poisons.

5.44 The inspection report will be submitted to the LSP Committee for consideration. The LSP Committee will refuse the application if any person involved in the daily business operation has had two or more convictions over the past three years, or one conviction over the past three years related to specified drug offences.

5.45 Same as ASP licences, LSP licences are valid till the end of each year and the LSP Committee may renew the certificates upon application at the beginning of each year. In considering the renewal applications, the LSP Committee will assess if any person involved in the daily operations of the LSP has had two convictions in the past three years or one conviction over the past three years related to specified drug offences in the same manner as in the assessment of a new application.

Monitoring of ASPs and LSPs

5.46 ASPs and LSPs are monitored by means of unannounced inspections by DH inspectors, test-purchases to detect any incidents of illegal sale of medicines, and prosecution of offenders. During an inspection, issues related to the

licensing conditions of the particular licensee and compliance with the statutory requirements will be audited. If the retailer is found to have breached a licensing condition, the case will be referred to the Pharmacy and Poisons Board for consideration. If non-compliance with the law is found, either during an inspection or during a test-purchase, prosecution action will be initiated. Convicted persons are liable to a maximum penalty of a $100,000 fine and two years' imprisonment. Following a conviction, further actions will be taken by the Disciplinary Committee of the Pharmacy and Poisons Board. The outcome may be the issue of a warning letter against the retailers concerned, or suspension of the licence for a period of time.

5.47 Inspections are conducted about twice a year per premises on average, with a higher frequency for retailers with a poor track record of law compliance.

Findings and Recommendations

5.48 The Review Committee identifies a number of areas for improvement in the existing regulatory regime for retailers, and makes the recommendations as set out in the following paragraphs.

Regulation of Retailers of Non-poisons

5.49 The Review Committee notes that retailers of pharmaceutical products classified as "non-poisons" are not subject to any licensing control. Consequently, there are no means to know their exact number and whereabouts. While the Review Committee acknowledges that non-poisons are drugs of lower risk, they will still pose risk to public health if they are not handled properly.

5.50 The Review Committee **recommends** that retailers of non-poisons also be subject to DH licensing and inspection control. The licensing requirements should be similar to that of LSPs while the licence period may be longer and the DH inspection may be less frequent in view of the lower risk of non-poisons to public health as compared with LSPs.

Duration of Presence of Pharmacist in ASPs

5.51 The Review Committee notes that the Ordinance only requires a registered pharmacist to be present in an ASP for not less than two-third of its opening hours. This means that for the remaining one-third opening hours, members of the public cannot have access to the professional services of

pharmacist. It also weakens the pharmacist's supervision over the sale of Part I Poisons at ASP.

5.52 The Review Committee **recommends** DH amends the Ordinance to the effect that a registered pharmacist should be present in an ASP whenever it is open for business. This will improve the professional services provided by pharmacists at ASPs (i.e. community pharmacists). The Review Committee, however, acknowledges that the implementation of this recommendation requires consideration of the market operating conditions and availability of sufficient pharmacists. The Review Committee urges DH to set a clear policy direction in this regard and draw up an implementation timetable. DH should liaise with the University Grants Committee with a view to offering more places in the pharmacy programmes of universities.

5.53 To enhance the role of pharmacists in the control of the storage and supply of drugs at ASPs, the Review Committee further **recommends** that heightened enforcement actions be taken against those non-pharmacists who violate and interrupt the pharmacists' performance of their duties at ASPs.

5.54 One Member of the Review Committee proposes and another Member supports a proposal that ASPs should either be fully owned or majority owned by pharmacist who should hold a minimum of 51% share of an ASP. After very thorough discussion, the majority of the Members of the Review Committee consider that this proposal is not immediately workable and that the views of the owners and operators of ASPs should also be taken into account. Furthermore, this proposal will have implications in relation to the anti-competition law being introduced. Other than these two members, the rest of the Review Committee members do not support this proposal.

Storage of Part I Poisons at ASP Premises

5.55 The Review Committee notes that while all Part I Poisons have to be sold under the supervision of pharmacists at ASPs according to the Ordinance, only First and Third Schedules Part I Poisons are required to be stored in a locked receptacle. Other Part I Poisons can be stored in any part of the premises. This provides an opportunity for these poisons to be sold to customers by other staff when the pharmacist is not present.

5.56 The Review Committee **recommends** that DH requires all Part I Poisons be stored in locked receptacle in the premises of an ASP and that only the pharmacist should hold the key to the locked receptacle in order to ensure that the pharmacist has complete control over the sale of Part I Poisons in the premises of an ASP.

Code of Practice

5.57 The Review Committee notes that the code of practice for ASPs has no legal status at present. The Review Committee also notes that there is no code of practice for LSPs and thus are no guidelines for staff at LSPs to follow in storage and handling of drugs.

5.58 The Review Committee **recommends** that a provision in the Pharmacy and Poisons Ordinance be added for the issuance and revision of the code of practice for ASPs to give a legal status to the code to enhance monitoring on the operation of ASPs. The Review Committee also **recommends** that DH drafts a code of practice to provide detailed guidance for staff at LSPs in storage and handling of drugs. The code of practice for LSPs should also enjoy the same legal status as ASPs.

Revocation of Licences for ASPs

5.59 The Review Committee notes that at present the Pharmacy and Poisons Board can renew the licences for ASP at the beginning of each year. However, the Pharmacy and Poisons Board has no authority to revoke the licence of an ASP when the ASP concerned has committed a serious drug offence. The Board can only revoke the ASP licence for a certain period of time or do not renew its licence upon expiry in extreme situation.

5.60 The Review Committee **recommends** giving the Pharmacy and Poisons Board the authority to revoke the licence of an ASP at any time. However, before making such a decision, the Pharmacy and Poisons Board should provide an opportunity for the ASP concerned to make representations to defend itself.

Convictions affecting Applications for Issue and Renewal of ASP and LSP licences

5.61 The Review Committee notes that the Pharmacy and Poisons Board would refuse an ASP or LSP application if any person involved in the daily business operation has had two convictions in the past three years related to the sale of any drug of abuse, the possession or sale of any counterfeit drugs, or the possession or sale of any unregistered pharmaceutical products. However, the sale of Third Schedule Part I Poisons without doctor prescription which is the most common misconduct of ASPs is not taken into account. The Review Committee also considers that other types of convictions of the licensees should be taken into account when considering the issuance and renewal of ASP and LSP licences.

5.62 The Review Committee **recommends** that the sale of Third Schedule Part I Poisons without doctor prescription be considered as a conviction record for the refusal of ASP or LSP applications. DH should also evaluate what other drug offences should be included based on their public health impact.

Inspections and Enforcement

5.63 The Review Committee finds the current inspection frequency of twice a year on average to premises of ASPs and LSPs insufficient, as they provide drugs direct to the customers and mal-practices of some ASPs are often found.

5.64 The Review Committee **recommends** that DH strengthens the monitoring of ASPs and LSPs by means of more frequent and more detailed inspections.

Purchase of Drugs from Licensed Traders only

5.65 The Review Committee notes that there is at present no requirement for wholesalers of "non-poisons" to have licence. In this connection, during DH inspections, it was often found that some drugs, in particular those "non-poisons", being sold at ASPs are of unknown origin. The quality of these drugs is in doubt because it is uncertain whether the quality, means of transportation and storage conditions are appropriate for the drugs concerned. Moreover, as the source of these drugs is unknown, difficulties will arise in the event of drug recall.

5.66 The Review Committee **recommends** that DH requires ASPs and LSPs to purchase drugs from licensed traders only after the recommendation in paragraph 5.18 above that wholesalers of non-poisons be subject to inspection and licensing control has been implemented. This is to ensure product quality and to facilitate product recall if necessary.

Written Orders of Drugs by ASPs, LSPs and Private Doctors

5.67 The Review Committee notes that there is at present no requirement for ASPs or LSPs to place orders for drugs in writing only. The same also applies to private doctors, even though it is stated as a recommended practice in the "Good Dispensing Practice Manual" published by the Hong Kong Medical Association.

5.68 The Review Committee agrees that written drug orders serve two major purposes. First, it contributes to building up a complete set of record in the drug

supply chain all the way from the primary source to the patients. It thus facilitates the tracing of source of drugs in the event of drug recall. It also deters the sale of unregistered drugs and purchase of drugs from unregistered traders as these unlawful acts do not have the support of written orders.

5.69 Second, it facilitates ASPs, LSPs and private doctors to verify if the drugs delivered are actually the drugs ordered. Since there is always a time gap between the ordering and delivery of drugs, a written drug order can assist the receiving staff, who may not be the ordering staff, to verify if the correct drugs are delivered. Furthermore, verbal order for drugs is prone to errors, as many drug names are similar and misunderstanding will easily arise.

5.70 The Review Committee acknowledges the concerns and difficulties of ASPs and some private doctors in complying with the written drug order requirement. In particular, for ASPs who may have to place over 100 drug orders daily, the amount of manpower and efforts involved may be quite significant, while many ASPs only have a few staff members and a limited storage area for the written records.

5.71 The Review Committee considers that protection of public health is of the top priority. Placing drug orders in writing contributes to building up a complete set of drug movement record, reducing errors in drug delivery and receipt, and combating illegal sale of drugs. The Review Committee also considers that ASPs and private doctors should not have great difficulties to comply with the requirement. The Review Committee suggests manufacturers and wholesalers design a standard procurement form for use by their clients in order to save their efforts. In fact, many advanced countries, for example in Europe, are already following this practice which has proved to be very convenient and easy to use.

5.72 In the light of the above considerations, the Review Committee recommends that all orders for drugs should have written records. DH should include this requirement in the licensing conditions for ASPs and LSPs, and in parallel, add in the licensing conditions of manufacturers and wholesalers that they can only supply drugs to ASPs, LSPs and private doctors with the support of written orders. The Review Committee is also pleased to note that the Hong Kong Medical Association and the Pharmaceutical Distributors Association of Hong Kong are supportive of this recommendation. Furthermore, it is noted that the written order practice is already recommended in the "Good Dispensing Practice Manual" issued by the Hong Kong Medical Association which should be observed by all doctors as advised by the Hong Kong Medical Council.

5.73 The Review Committee notes the objection of Hong Kong Doctors Union to the mandatory requirement of written order for drugs which is only supported by one other member. The rest of the other members support this recommendation.

Sale of Pharmaceutical Products in Original Packing by ASPs

5.74 The Review Committee notes that ASPs are currently permitted to purchase pharmaceutical products in bulk packs and then repack them into smaller packs for the purpose of dispensing them to customers. However, this "repacking" process could pose risk of contamination or mix-up of drugs, thus endangering public health.

5.75 The Review Committee **recommends** that ASPs only sell pharmaceutical products in their original packing to avoid human errors in the repacking process, save in the case of a doctor prescription drug which is required by law to be dispensed in exact quantity in accordance with the prescription and in the case of pharmacist dispensing drugs to patients according to their need with proper labelling. This recommendation is also in line with the worldwide trend of increasing use of drugs in their original packing. The Review Committee, however, understands that the manufacturers and wholesalers need time to adjust the pack sizes of their products to meet market demand. The Review Committee suggests DH draw up an implementation timetable for the recommendation with an appropriate transition period in consultation with the manufacturing and wholesale industry.

Keeping of Transaction Records

5.76 The Review Committee notes that there is no requirement at present for ASPs and LSPs to keep record of every transaction involving pharmaceutical products. This hinders the tracing of source of drugs in the event of drug recall.

5.77 The Review Committee **recommends** that DH requires ASPs and LSPs to keep all the supporting documents including drug orders and sales invoices related to every purchase of all pharmaceutical products, and the documents should be kept as long as the expiry date of the pharmaceutical product concerned for DH inspection if necessary. DH should add this requirement as a licensing condition.

CHAPTER 6 PROCUREMENT AND SUPPLY OF PHARMACEUTICAL PRODUCTS IN THE PUBLIC AND PRIVATE MEDICAL SECTORS

Overview

6.1 This chapter sets out the Review Committee's findings and recommendations on procurement and supply of pharmaceutical products in the public medical sector including DH and the Hospital Authority (HA), after detailed examination of their existing procurement system. The Review Committee makes recommendations to further ensure the safety of drugs supplied by DH and HA.

6.2 This chapter also sets out (a) a set of guiding principles being practised in private hospitals and (b) the current practices of solo or joint private medical practitioners, in the procurement and supply of pharmaceutical products. It then presents the Review Committee's findings and recommendations on areas for improvement to the drug procurement system in the private medical sector.

The Existing Procurement and Supply System

Procurement System of DH

6.3 DH follows a strict set of procurement procedures which are in accordance with the Supplies and Procurement Regulations (SPR) promulgated by the Government Logistics Department.

6.4 There are two routes for procurement, namely by supplies contracts and by direct purchase, and are determined based on the total value of the purchase. In accordance with SPR, purchase value of over HK$50,000 procurement is by tendering procedures. Drugs the consumption of which does not exceed $50,000 per year are procured by direct purchase and DH would invite quotations from a list of potential suppliers of the drug.

Procurement System of HA

6.5 The Hospital Authority prescribes a wide spectrum of pharmaceutical products for patients in its hospitals and clinics. The procurement system is in compliance with the requirements of the Government Procurement Agreement of the World Trade Organization.

6.6 There are three levels of procurement procedures. Purchase exceeding $1 million per year are purchased through tendering procedures. Purchase between $50,000 and $1 million per year are purchased using standing quotations. Standing quotations are arranged through tendering procedures, but without quantity commitment; and more than one standing quotations can be set up for the same item. Purchase which does not exceed $50,000 per year, procurement is conducted by direct purchase. HA headquarters maintain item-specific list of approved suppliers, from which hospitals and clinics can make direct purchase of individual items.

Quality Requirements

6.7 Whichever procurement procedures are used, the drug must satisfy the quality requirements required by DH and HA. Suppliers are required to provide documentation evidence to support the quality of the drug on the areas of manufacturing and quality control; product characteristics including, where applicable, comparative clinical data either in the form of bioequivalence study reports or clinical trial reports; and sales data. These documents may include GMP certificate of the manufacturer; registration status, composition and certificate of analysis of a batch of the drug.

Storage and Inventory Monitoring System

6.8 DH has a computer system to monitor drug inventory, stock levels and expiry dates of drugs and to handle requisitions for drugs by clinic dispensaries. After the drugs are procured in accordance with SPR, suppliers will deliver the drugs to the dispensaries. Upon delivery, the clinic dispensers will examine the drugs against the orders in accordance with the procedures in the Good Dispensing Practice Manual issued by DH.

6.9 HA has a set of guidelines on the storage of pharmaceutical products in respect of the corresponding storage conditions required by individual products. Goods are stored in a way to facilitate the implementation of the "first in first out" practice.

6.10 HA requests the Government Laboratory to undertake the testing for the first introduction of a generic drug purchased from a supplier. Regarding auditing of inventory, samples of contract items are tested by the School of Pharmacy of the Chinese University of Hong Kong once in each contract cycle, which is usually for two years.

Findings

6.11 The Review Committee finds that the drug procurement system of both DH and HA follows a strict set of procedures which are in line with international standards.

6.12 Both procurement systems are determined based on the total value of the purchase. Whichever route of procurement is used, the Review Committee finds that quality of drug, which is the most important element is ensured via the quality requirements set out in details by both DH and HA.

6.13 The Review Committee further finds that both DH and HA utilize a computer system to monitor the drug inventory, stock levels and expiry dates of drugs and to handle requisitions for drugs by different clinic dispensaries and hospitals. In DH, dispensing of drugs and stock management are guided by the Good Dispensing Practice Manual available since 1999.

Recommendations

6.14 The Review Committee finds that there are rooms for improvement in the receipt and the handling of drugs after delivery. The Review Committee makes the following recommendations –

(a) The Review Committee **recommends** that both DH and HA conduct post-delivery surveillance including microbiological and chemical testing to ensure drug quality. This is to be conducted regularly in accordance with standard operating procedures for transparency.

(b) The Review Committee **recommends** that both DH and HA require the suppliers to provide additional information, such as pack size and registration number, etc. in the delivery documents to enable more effective physical checking and verification of drugs received.

(c) The Review Committee **recommends** that both DH and HA provide additional training to staff and monitor the workflow in the repacking activities in drug dispensing to minimize errors.

(d) The Review Committee **recommends** that DH imposes new requirement on suppliers to keep samples of each batch of drugs that are still within the expiration period to facilitate investigation when needed.

(e) The Review Committee **recommends** that DH upgrades its central

inventory monitoring computer system to enhance the traceability of drugs.

(f) The Review Committee **recommends** that DH works with the trade associations to enrich the database of registered pharmaceutical products so as to provide more detailed information to the public on registration details of products, e.g. pack-size, labelling, legal classification, etc.

(g) The Review Committee **recommends** that HA requires suppliers to provide evidence that their products are either registered or are exempted from registration under the law.

(h) The Review Committee **recommends** that HA requires suppliers to provide microbiological test results for high risk drug items and batch release certificates on all drugs supplied to HA to ensure safety and quality.

(i) The Review Committee **recommends** that HA uses multiple sources for the supply of high risk products with high usage volume to ensure continuity of supply in case problems arise with one supplier.

(j) The Review Committee **recommends** that HA establishes a Drug Quality Assurance Office to enhance quality monitoring of products, performance management of manufacturers and suppliers and quality incident management as well as to monitor the implementation of all improvement initiatives.

(k) The Review Committee **recommends** that HA enhances the current electronic system, such as exploring the use of RFID, bar coding, wireless data transmission, etc. to enable product traceability and effective stores management.

(l) The Review Committee **recommends** that HA requires suppliers to provide drugs in suitable pack sizes as far as possible to reduce the need for repacking.

Guiding Principles for Drug handling in Private Hospitals

6.15 There are currently 13 private hospitals in Hong Kong, each with its own drug procurement and supply system. After consulting among themselves and making reference to relevant guidelines drawn up by DH and HA, as well

as international hospital management and accreditation practices, the private hospitals have put in place the following set of guiding principles for compliance. The principles encompass the selection, procurement, delivery and receipt, storage and repacking of drugs. Staff training and auditing are also important elements during the drug handling process.

Selection of Drugs

6.16 A drug formulary should be set up which enables members of the healthcare team to focus on a limited choice of carefully selected drugs for specific medical conditions rather than on all the available drugs in the market. It helps prevent medication errors. Drug selection and formulary management is usually carried out through the professional expertise of the pharmacists of individual institutions. Some private hospitals also involve a multi-disciplinary committee of medical and administrative personnel to ensure that the safest, most efficacious and least costly medications are stocked.

6.17 Drugs selected include both patent and generic drugs. The purchase pattern follows such sequence: patent drug, generic drug registered in developed countries, generic drugs from other sources. Selected drugs must fulfill all the quality requirements. For generic drugs, bioequivalence and bioavailability data shall be submitted to prove their equivalence with patent drugs. Drugs similar in appearance are avoided in order to minimize dispensing errors. Blister packaging of drugs are preferred over loose tablets as blister packs are more convenient to dispense and offer assurance of product integrity. Oral liquid medicines with smaller pack sizes are preferred over bulk bottles to minimize errors resulting from the repacking process.

Procurement of Drugs

6.18 Procurement of drugs should be done in a timely manner and in reasonable quantity in order to minimize interruption in supply while at the same time to avoid overstocking. All procurement activities should be performed by qualified staff under the supervision of pharmacists.

Receipt of Drugs

6.19 Drugs should only be received and handled by staff with relevant training. During the receipt process, all essential information such as brand name and chemical name, strength, dosage form, Hong Kong registration number, etc. of the drug should be checked against the purchase order. The expiry date, pack size, product appearance and storage condition of drug should also be audited. Should there be any non-conformity in product appearance,

pack size, volume, etc. of the delivered product, it should be quarantined pending clarification from the supplier.

Storage of Drugs

6.20 All drugs should be stored according to conditions described on the package/label with respect to temperature, humidity, light, etc. Temperatures of drug storage areas should be properly controlled and monitored by keeping temperature log. The principle of "First-in First-Out" should be properly followed. Stock rotation is vital to use stocks with shorter shelf lives first and to facilitate the identification of soon-to-expire or expired products. Regular check on expiry date should be conducted for all storage locations to ensure timely removal and replacement of near expiry or expired products. A disposal record of expired products should be maintained.

Repacking of Drugs

6.21 Ready-for-use drugs should be used whenever possible to minimize the need for repacking or compounding. To facilitate dispensing, repacking of bulk purchase drugs into smaller packs is commonly practised. All staff engaged in repacking must be adequately trained and must follow a set of standard repacking procedures, including environmental control measures.

Staff Training

6.22 All staff involved in procurement and stock management should be well qualified and well trained, and should have the knowledge in all pertinent principles and guidelines.

Auditing

6.23 Internal audits on compliance of established procedures and guidelines relating to procurement, inventory receipt, storage and repacking should be conducted periodically to identify areas that need reinforcement or improvement.

Drug Handling by Solo or Joint Private Medical Practitioners

6.24 Private medical practitioners are subject to the code of professional conduct promulgated by the Hong Kong Medical Council, the registration body of medical practitioners in Hong Kong. The code states that doctors are advised

to observe the provisions of the Good Dispensing Practice Manual issued by the Hong Kong Medical Association.

6.25 Private medical practitioners can work in solo or joint practices. In the case of the former, the medical practitioner concerned will be solely responsible for the procurement and supply of drugs. In the case of the latter, one of the medical practitioners in the joint practice will be responsible for all the drugs handled in the clinic.

Findings and Recommendations

6.26 The Review Committee considers the guiding principles on drug handling as practised by private hospitals in order and serves as a useful reference for the private medical sector. Many guiding principles can be equally applied to the settings of Managed Care Organizations (MCOs) and private medical practitioners in solo or joint practices in spite of the difference in scale of operation.

6.27 The Review Committee **recommends** that DH issues a set of guiding principles as set out in paragraphs 6.16 to 6.23 above for the private medical sector and encourage private hospitals, MCOs and private medical practitioners in solo or joint practices to follow the set of guiding principles as far as practicable.

6.28 The Review Committee also considers it desirable for private hospitals to widen the use of information technology in drug handling to enhance efficiency and reduce the chance of human errors.

6.29 The Review Committee **recommends** that DH encourages private hospitals to develop an automated inventory management system and bar-coding system for pharmaceutical products. Private hospitals can devise a computer system for better control on the inventory and drug dispensing, while the use of bar-coding can also be integrated in the drug dispensing and administration activities within the hospital to ensure that the correct drug is being given to the patient. Furthermore, in designing the automated inventory management system, private hospitals can introduce a bar-coding system coding individual product with information on (a) the manufacturer (including repacker or relabeller), (b) the specific strength, dosage form and formulation, and (c) the packaging configuration (pack size and type). If all products are coded in a structured manner, problematic drugs, manufacturers or suppliers can be traced more easily when necessary.

CHAPTER 7 POST-MARKET CONTROL OF DRUGS AND PHARMACOVIGILANCE

Overview

7.1 This chapter provides an overview of the existing framework of post-market control on pharmaceutical products, including pharmacovigilance; and sets out the Review Committee's findings and recommendations on areas for improvement.

Post-market Control on Pharmaceutical Products

7.2 Post-market control is commonly used interchangeably with pharmacovigilance, although theoretically pharmacovigilance covers a wider scope. Pharmacovigilance is defined by the WHO as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other quality problems concerning drugs on supply in the market. The health authorities could then base on the findings to take appropriate actions in accordance with the level of hazard to public health.

7.3 Pharmacovigilance has developed into robust systems by many health authorities around the world. In the Hong Kong context, DH has been utilizing the following channels to identify hazards related to drug safety.

(a) Drug Surveillance Programme

7.4 Registered drugs in Hong Kong are subject to a mixture of random and risk-based sampling for chemical, microbiological (for sterile products only) testing and checks for packaging insert and labelling requirements. On average, about 2,100 samples are taken by DH for various tests each year. In 2008, this figure reached an all-time high of 2,335 due to a number of hospitalizations arising from the consumption of male sexual enhancement products. DH will notify the manufacturers or importers concerned of any failed results, and direct them to recall the affected batches of drugs from the market, to explain the failure, and to suggest preventive measures.

(b) Adverse Drug Reaction (ADR) Reporting Programme

7.5 Since 2005, healthcare professionals in practice including doctors, dentists, traditional Chinese medicine practitioners and pharmacists have been

encouraged to report to DH uncommon signs and symptoms under normal dose of drugs.

(c) Toxicovigilance Programme

7.6 This is a collaborative programme between DH and HA. When HA encounters any patient suspected to have been affected by the consumption of harmful products (e.g. traditional Chinese medicines or health products adulterated with western drug ingredients, herbal tea made with harmful ingredients or ingredients of the wrong identity), it will refer the case to DH for follow-up investigation. DH will announce cases with public health implications to healthcare professionals, the general public and overseas health authorities as appropriate. In 2007 and 2008, 20 and 101 such reports were received by DH respectively.

(d) Monitoring Drug Information of Overseas Authorities

7.7 DH has a dedicated team of staff screening websites of WHO, the European Medicines Agency and the national drug regulatory authorities of the Mainland, Australia, Canada, Macao, Singapore, United Kingdom, United States, etc. daily for any drug safety related information for follow-up actions.

(e) Hotline

7.8 DH also encourages members of the public and healthcare professionals to report any drug related problems to its Pharmaceutical Service Hotline.

Follow-up on ADR Reports

7.9 Drug hazards can be classified into the following three categories: (a) a quality defect, such as over-dosing or under-dosing of an active ingredient of the product; (b) a safety issue arising from the use of the product, such as bacterial or fungal contamination; or (c) a compliance issue, such as non-compliance of package size with the registered version.

7.10 Depending on the classification and extent of hazards, DH will disseminate the hazard assessment outcome in the form of product recalls or announcements of precautionary and warning messages through the media.

7.11 DH will also issue letters about drug incidents and product recalls to doctors, pharmacists and their professional associations, as well as public and private hospitals. Members of the general public could then receive the risk

message during their encounters with these healthcare professionals.

7.12 If necessary, DH will require the registration holder of the concerned product to amend the indications, dosage and administration, contraindications, warnings or precautions sections of the product label and package insert.

Recall of Pharmaceutical Products

7.13 When the safety or quality of a drug has been compromised and poses public health concern, or when a drug violates the registration requirements, DH will instruct the manufacturer or wholesaler concerned to recall the product. Manufacturers and wholesalers are required by the Pharmacy and Poisons Ordinance to devise and maintain a recall mechanism to ensure comprehensive and speedy recall of the affected product. DH has also issued a set of drug recall guidelines to facilitate recall. Retailers are expected to cooperate and immediately remove the affected products from display shelves and return them to the suppliers.

Consultancy Study on Hong Kong's Pharmacovigilance System

7.14 To upgrade Hong Kong's pharmacovigilance system to international standard, DH commissioned an overseas pharmacovigilance expert from Australia in May 2009 to conduct a consultancy study on the current practices of pharmacovigilance in Hong Kong in the light of the latest practices in leading world drug regulatory authorities. The overseas consultant has made a number of recommendations, which was discussed first in the DH Task Force before putting forward to the Review Committee for consideration.

Findings and Recommendations

I. Pharmacovigilance Consultant's Recommendations

7.15 The Review Committee has considered and **endorsed the pharmacovigilance consultant's recommendations** focusing on different subjects as follows –

General

7.16 It is recommended that DH establishes a pharmacovigilance advisory body comprising medical practitioner, pharmacist, pharmacologist and

academia to review DH assessments of the ADR reports received, to advise DH on action on specific cases, to serve as an editorial advisory board of the pharmacovigilance bulletin and to assist DH in the promotion of pharmacovigilance activities.

7.17 It is recommended that DH sets up a dedicated team to promote pharmacovigilance work among professionals, education institutions and the industry; handle ADR reports received; disseminate information; and support the pharmacovigilance advisory body.

Communications

7.18 It is recommended that DH produces a regular pharmacovigilance bulletin for distribution to all doctors, dentists and pharmacists. The Review Committee also **recommends** that DH produces a user-friendly version of pharmacovigilance bulletin for reference of the general public.

7.19 It is recommended that DH includes an ADR report form in mails to doctors and pharmacists, enhances DH website such that doctors and pharmacists could subscribe and receive emails from DH on ADR as soon as they are released and encourage the use of electronic reporting of ADRs. DH should also enhance the existing electronic interface between doctors and DH and develop additional electronic interface for dentists and pharmacists to facilitate ADR reporting.

Drug Industry

7.20 It is recommended that DH establishes guidelines for the drug industry on their responsibilities to report ADRs, to educate and encourage them to report ADRs and to develop a culture of awareness of pharmacovigilance. DH should also meet with the drug industry on a regular basis to promote ADR reporting.

Existing Pharmacovigilance Activities

7.21 It is recommended that DH should require the drug industry to report any actions taken by overseas drug regulatory authorities on any drugs as a consequence of safety issues. It is also recommended that DH requires manufacturers to inform DH if they have committed to the request of European Union or United States to develop an EU Risk Management Plans (RMP) or US Risk Evaluation and Mitigation Strategies (REM) as a condition for approving a new drug. DH should state these requirements in the guidelines.

7.22 It is recommended that DH reviews ADR reports within three working days.

Liaison and Training

7.23 It is recommended that DH should establish liaison with overseas health authorities, such as Australia, Japan, Malaysia, New Zealand and Singapore for exchange of ADR information as well as providing training on pharmacovigilance to staff. DH should source pharmacovigilance training courses organized by WHO and other authorities and arrange staff to attend these courses.

Review on the Improved Pharmacovigilance Measures

7.24 It is recommended that DH reviews the progress and effectiveness of the development and implementation of the improved pharmacovigilance measures in two years' time.

II. Other Recommendations of the Review Committee

Sampling of Pharmaceutical Products for Analysis

7.25 In addition to the pharmacovigilance consultant's recommendations, the Review Committee considers that the sampling of pharmaceutical products for analysis in DH's drug surveillance programme should be enhanced. The Review Committee **recommends** that, as a first step, the heightened surveillance in 2008 against high risk products by taking over 2,000 samples from the market for testing be continued. DH should also maintain the existing practice of reporting anomalies to the public. The Review Committee further **recommends** that, in the next step, DH sets up a dedicated team of pharmacists to handle the increased sampling of high risk products.

Drug Recall Strategies

7.26 The Review Committee has made reference to the practices of advanced countries including the United States, United Kingdom, Canada and Australia in drug recall and public alert strategies. The Review Committee notes that it is a common practice of these countries to classify drug safety hazards into different levels in accordance with the degree of risk, and then deploy the corresponding public alert strategies. When a product is found to have less serious side effects, revision of the product insert and post of updated information on related websites may be sufficient, and product recall may not be necessary. However,

when a product is found defective, e.g. microbial and chemical contamination, and non-compliance of specifications or registration particulars, product recall will be initiated. If the case is serious, e.g. serious adverse drug reactions, the product concerned will be recalled immediately and an urgent public alert will be issued.

7.27 The Review Committee notes that unlike these countries, Hong Kong does not have a risk-based drug recall and public alert strategy. The Review Committee **recommends** that DH adopts a risk-based approach in drug recall and public communication. Specifically DH should revise the recall guidelines to include, but not limited to, the following information –

(a) the different stages of recall procedures;
(b) the classification of the recall;
(c) the level of the recall;
(d) the strategy of the recall including the dissemination of information to the public;
(e) the responsibilities of the trade, including refund; and
(f) the monitoring of all follow up actions, including the effectiveness of the recall.

7.28 To widen the dissemination network of the drug recall message, the Review Committee also **recommends** that DH informs the Consumer Council on every drug recall incident at consumer level.

Refund Mechanism for drug recall

7.29 The Review Committee notes that unlike other commodities such as electrical products, there is no refund mechanism in the recall guidelines issued by DH.

7.30 The Review Committee **recommends** that DH includes a refund mechanism in the recall guidelines requiring manufacturers and wholesalers to provide refund details to consumers at retail level in the event of drug recall. DH should consult the Consumer Council and draw reference from the practice in other trades when drafting the refund mechanism in the recall guidelines.

CHAPTER 8 RISK COMMUNICATION, EDUCATION AND TRAINING

Overview

8.1 This chapter provides an overview of the existing framework of risk communication on drug safety, including education and training; and presents the Review Committee's findings and recommendations on the enhanced measures for effective risk communication.

Existing Framework of Risk Communication

8.2. Risk communication is a process of exchange of risk information among all stakeholders in order to make them aware of the risks identified, and ensure the risk assessment results are clearly received and understood. In respect of drug safety, stakeholders include the whole drug industry and its practitioners, healthcare professionals in both the public and private sectors, patients and the general public.

8.3 The risk communication strategy of DH on drug safety is an integral part of the post-market control of drugs. Risks are divided into two levels: those related to drug safety and those related to the safe use of drugs.

Risks related to Drug Safety

8.4 DH has implemented various measures to identify and assess the potential hazards of registered drugs, including the drug surveillance programme, adverse drug reaction reporting programme, toxicovigilance programme, intelligence obtained through monitoring of overseas authorities, and drug incident reports in the media and from the patients.

8.5 Hazards on drug safety can be a quality defect affecting one or all batches of the product, presence of an undeclared drug substance in the product or a newly-discovered side effect. Upon receipt of the hazard report, DH would assess the risk and impact of the hazard, and then use the appropriate means to disseminate the drug recall message to the public. Dissemination channels include issue of press statements, holding of press conferences, distribution of information leaflets to the public, announcements of public interest in electronic media, etc., depending on the gravity of case.

8.6 Doctors and pharmacists are important stakeholders along the line of risk communication due to their services provided to the public. DH would therefore issue letters about drug incidents and product recalls to doctors, pharmacists and their professional associations, as well as private and public hospitals. The general public could then also receive the message during their encounter with these healthcare professionals.

Risks related to Safe Use of Drugs

8.7 On the perspective of safe use of drugs, HA and healthcare professionals have been playing an active role. Information about drug indication, side effects, contra-indications, drug interaction, etc. is disseminated to patients during doctor consultations and counselling to patients at pharmacies.

8.8 As a registration body for drugs, DH publishes certain essential registration information on the electronic compendium of registered drugs on its website. The primary objective is to facilitate healthcare professionals to check whether a drug is registered or not.

Education and Training Programmes for the Pharmaceutical Industry

8.9 DH conducts regular education and training programmes to the pharmaceutical industry. Topics covered include information on various traders' licences, information on registered drugs on the website of DH, classification of drugs, requirements for drug registration, requirements for approval of change of particulars of registered drugs, undesirable medical advertising, etc.

8.10 After the drug incidents in March 2009, DH organized a number of seminars for the management of different levels of the drug supply chain including manufacturers, wholesalers and importers/exporters to remind them of the required standards under the GMP and all the legal and licensing requirements, as well as the importance of internal audit and corporate governance during the drug manufacturing process.

Findings and Recommendations

8.11 The Review Committee identifies a number of areas for improvement in the existing framework for risk communication, and makes the recommendations as outlined in the following paragraphs.

Setting Up of a Dedicated Team in DH for Education and Training

8.12 The Review Committee finds that apart from DH, HA, Consumer Council and some pharmaceutical associations have been organizing various public education programmes on drug safety, yet there is no co-ordination among these programmes, leading to duplication of efforts.

8.13 The Review Committee **recommends** that DH sets up a dedicated, multi-disciplinary team for education and training. The team should collaborate with and co-ordinate efforts of the academia, Consumer Council and relevant professional bodies in the provision of education and training programmes on drug safety. Other functions of the team should include –

(a) drawing up guidelines and protocols for hazard identification and risk communication in the manufacturing process;

(b) performing risk assessment in response to any incident related to drug manufacturing and recommending risk communication actions accordingly;

(c) assisting training institutions to organize educational and training activities for the pharmaceutical industry; and

(d) producing education and training materials.

Organization of More Training Programmes with Focus on Quality Control

8.14 The Review Committee notes that the focus of training programmes organized by DH prior to the drug incidents in March 2009 was on drug registration requirements, and the target group was the management of manufacturers, wholesalers and importers/exporters.

8.15 The Review Committee **recommends** that DH should continue to organize seminars with additional focus on quality control. In addition to the management at different levels of the drug supply chain, DH should also organize continuous training programmes for front-line staff, including manufacturing workers and workers involved in handling of drugs at the importer, wholesaler and retailer levels. Training content should cover checking of supplies, appropriate drug storage conditions, stock control, keeping of records, etc.

Enhancement of the Content of "Compendium of Pharmaceutical Products" on DH Website

8.16 The Review Committee notes that DH's electronic compendium of registered pharmaceutical products currently only includes the product brand-name, the active ingredients, the product registration number and the name and address of the registrant. This scope of information does not meet the rising demand of users. The Review Committee also finds that some drug information is not user-friendly. For instance, the list of pharmaceutical products is available in English only.

8.17 The Review Committee **recommends** that the content of the compendium be enhanced to provide more information for the general public, healthcare professionals and the drug industry, including product classification (i.e. Part I or Part II Poison or non-poison), whether the product has to be prescribed by doctors only, Chinese name of product if available, images of approved packaging, address of the manufacturer, country where the product is manufactured, product registration expiry date, etc. Any product recall and approved changes to registered particulars of drugs should also be highlighted in the compendium to alert the general public.

Setting Up of a Designated Website to promote Drug Safety

8.18 The Review Committee observes that, in spite of its wide public health implications, there is no designated website of DH on the subject of drug safety, and information on the subject is scattered in different parts of DH website. This is not convenient for the public to access useful drug information.

8.19 The Review Committee **recommends** DH to set up a designated website on drug safety to provide a better platform for information dissemination and exchange, while the revamped electronic compendium of pharmaceutical products as well as other information related to the work of DH pharmaceutical service should also be migrated to this designated website. The information database should be enriched to provide more patient-oriented advice, drug alerts and other useful drug information to the public, the pharmaceutical industry and the healthcare professionals. The revamped website should be more user-friendly, facilitating the public's quick search of information. Hyperlinks to websites of relevant professional bodies and organizations should also be included. The Review Committee further **recommends** that DH establishes a focus group comprising user representatives from the Consumer Council, public and private hospitals, community pharmacists, patient groups, etc. to work out the prototype of the enhanced website and its contents.

Enhancement of Drug Information accompanying Dispensed Medicines

8.20 The Review Committee finds that except for the basic information on frequency and method of use of drug, drug information for medicines dispensed to patients at hospitals and clinics is rather limited.

8.21 The Review Committee **recommends** that more information on drugs and patient-oriented advice, such as uses, side effects and precautions, be provided when dispensing drugs to patients at hospitals or clinics, either on the drug label or in an accompanying leaflet to educate the public on safe use of the drug concerned.

CHAPTER 9 PENALTY REVIEW

Overview

9.1 This chapter sets out the Review Committee's findings on the existing penalty system under the Pharmacy & Poisons Ordinance (Cap. 138) for manufacturers, importers, wholesalers and retailers of pharmaceutical products in Hong Kong and the recommendations on enhancing the existing system for better deterrent.

The Pharmacy and Poisons Ordinance ("the Ordinance")

9.2 The Pharmacy and Poisons Ordinance, Cap. 138 (the Ordinance) provides the principal framework for the regulation of pharmaceutical products and traders. A penalty system is in place for any infringement of the provisions of the legislation. As a general rule of justice, penalty must be set proportional to the harm and impact that the offence may cause to general public and the society.

Existing Penalty System

The Maximum Penalties under the Ordinance

9.3 Under the Ordinance, the maximum penalties imposed are a fine of $100,000 and imprisonment of two years. DH has conducted a review of the existing penalty system under the Ordinance in consultation with the Department of Justice (DoJ). DoJ is of the opinion that the current maximum penalty of $100,000 fine and two years' imprisonment imposed by the Ordinance sufficient for summary convictions of the offences in the Ordinance. However, DH found that, based on past conviction records, 60% of the penalty imposed by the Court in recent years were on the low end of $5,000 or below.

9.4 According to DoJ, sentencing in any individual case is at the discretion of the Court concerned which is dependant on the circumstance of the case. As such, prosecution should always present to the Court the gravity of the case by including more aggravating factors in the brief facts of the case, such as the nature of the drugs, abuse potential, public interest, etc to reflect the seriousness of the offence concerned. This would provide the Court with more background knowledge in considering the imposition of a penalty proportionate to the seriousness of the offence.

Retailers, Importers and Wholesalers

9.5 DH also found that the Court imposed light penalties on traders of pharmaceutical products in cases regarding illegal possession of Part I Poisons. According to the conviction records of DH, the penalty imposed by the Court in these cases was on the low end of $5,000 or below.

Manufacturers

9.6 Under the current regulatory regime, it is a licensing requirement for the manufacturer to fully implement the GMP. GMP requires the appointment of an authorized person (AP) responsible for product release to ensure quality. In Hong Kong, the Manufacturers Licensing Committee has the authority to individually assess the suitability of an AP for a particular manufacturer especially taking into consideration the complexity of the products produced by the manufacturer. Penalty system on the manufacturers is in place such as revocation of the licence when there is non-compliance with the GMP.

Practice in other Countries

9.7 In Australia, every manufacturer licensed by the licensing authority, the Therapeutic Goods Administration (TGA), must appoint an AP. Curriculum vitae and other relevant information regarding the AP's education and experience must be provided to TGA for assessment. The TGA has the right to reject the AP nominated by the licensee if they believe that the AP is not sufficiently qualified or experienced. Regulatory action could be taken against the manufacturer if the AP breaches his duties. TGA has the authority to direct manufacturer to remove the AP (such power has not been exercised so far).

9.8 In UK, the Medicines and Healthcare products Regulatory Agency (MHRA) of the UK Department of Health acting on behalf of the Licensing Authority, has given authority to three Professional Bodies [the Institute of Biology, Royal Pharmaceutical Society of Great Britain and Royal Society of Chemistry – known collectively as the Joint Professional Bodies (JPB)] to operate an assessment which seeks to determine and certify the eligibility of the applicant for nomination as a Qualified Person (equivalent to AP) on a manufacturer's licence. The JPB is responsible for maintaining a register of AP. The AP is named in the manufacturer's licence and the acceptance of AP on a manufacturer's licence is a matter for the licensing authority (MHRA). MHRA could request the removal of AP from the AP register. Furthermore, it is a

statutory requirement that if an AP fails to discharge its duties, MHRA could notify the licence holder that such person shall not be permitted to act as AP.

9.9 In Canada, the power to appoint and dismiss AP vested in the manufacturer. AP and their qualification are GMP requirements. Non-compliance with the GMP requirements may lead to suspension of licence by the Minister of Health.

9.10 In Singapore, the manufacturer is responsible for assessment of the suitability of AP. The Licensing authority, Health Sciences Authority (HSA) may choose not to approve the nomination or change of AP if there are justifications that the nominee is unfit to carry out the duties as described in the GMP standard. If the competency and or integrity of the AP are concluded as questionable, HSA may consider taking regulatory actions including suspension of the manufacturer's licence.

Findings and Recommendations

9.11 The Review Committees finds that even though the current controls on manufacturers, retailers, importers and wholesalers are in place, there have been criticisms from the public that the penalties imposed by the Ordinance are not commensurate with the seriousness of the offences. The Review Committee makes the following recommendations in this regard –

(a) The Review Committee notes that the current maximum penalty under the Ordinance is a fine of $100,000 and imprisonment of two years. Nevertheless, for serious offence leading to the loss of life, the prosecution authority may also charge the manufacturer concerned with manslaughter under another ordinance. Moreover, the victims of drug incidents can make civil claims against the manufacturer concerned.

The Review Committee **recommends** that DH includes more aggravating factors in the facts of the case submitted to the Court, such as the nature of the drugs, abuse potential, public interest, etc. to reflect the seriousness of the offence concerned for the Court to impose an appropriate sentence. DH will track the sentencing of the Court as a first step by gathering the data on sentencing of each case after the implementation of the enhancement strategies to look for any further weaknesses of the current law for review of the maximum penalty at the next stage.

(b) The Review Committee notes that at present the Manufacturers Licensing Committee does not have the authority to remove an incompetent AP. The Review Committee **recommends** that DH strengthens the current GMP standard by adding different annexes to GMP guidelines. The annexes will include guidelines to strengthen the control on the eligibility of the AP with reference to their qualification and previous experience, to explicitly state the duties and responsibilities of AP, to authorize the Manufacturers Licensing Committee to remove AP when he breaches his duties and to stop the production of the manufacturer when the AP had been removed.

(c) The Review Committee notes that the analytical costs on exhibits in some prosecution cases were quite substantial and it was unfair for the taxpayers to bear such costs. The Review Committee **recommends** that the Ordinance be amended to include provision for the Court to order the convicted person to pay the analytical costs incurred by the Government to increase the deterrent effect.

CHAPTER 10 RESOURCES IMPLICATIONS AND ESTABLISHMENT OF A DEDICATED OFFICE ON DRUGS

Overview

10.1 This chapter sets out the additional manpower requirements in implementing all the recommendations of the Review Committee to enhance the regulatory regime on pharmaceutical products in Hong Kong, and outlines the proposed establishment of a dedicated office on drugs to strengthen DH's capacity in drug regulation.

Additional Manpower Requirements

10.2 The Review Committee notes that additional staff will be required to improve existing services including shortening of processing time for drug registration and related applications, monitoring of side effects reports on approved clinical study programmes, enhancement of inspections to drug traders including local manufacturers, importers/exporters, wholesalers and retailers, etc. The Review Committee also notes that many new policy initiatives have staff implications, including licensing of wholesalers and retailers of non-poisons, setting up of a dedicated team for pharmacovigilance and risk communication, inspections of overseas and Mainland drug manufacturers without a PIC/S certificate, liaison with overseas and Mainland State and Provincial drug regulatory authorities, etc.

10.3 Apart from pharmacist grade staff, the Review Committee agrees that professionals from other disciplines including medical officers, scientific officers, engineers, environmental hygienists and veterinary officers should be included in the multi-disciplinary inspection team to enrich the technical basis for regulatory enhancement, while information officers should be available in the pharmacovigilance and risk communication team to assist in the publicity of drug alert and other drug education messages.

10.4 To tie in with the increased professional manpower and the expanded scope of responsibilities, the Review Committee also agrees that the administrative, information technology and technical support should be enhanced correspondingly. The Review Committee understands that DH will go through the established procedures in seeking additional staff resources with detailed justifications for the posts to be created.

Establishment of a Dedicated Office on Drugs

10.5 The Review Committee notes that the drug regulatory functions of DH are principally carried out through its Pharmaceutical Service (PS). Apart from serving as a law enforcement agency over legislations concerning drugs, PS also provides for the procurement, manufacturing and dispensing of drugs at the clinics of DH. PS is now headed by a Chief Pharmacist (CP) at Directorate One (D1) level and supported by 7 Senior Pharmacists (SPs) and 41 Pharmacists. In addition, there are 61 dispensers and some 50 other administrative and information technology supporting staff. The existing organization chart of PS is at *Annex I*. CP reports to the Assistant Director (Special Health Services), who has to look after other services of DH, such as port health, electronic health record management, health care voucher, radiation health and narcotics etc.

10.6 The Review Committee has made reference to overseas practices and observes that the drug regulatory authorities of advanced countries, including the Therapeutic Goods Administration of Australia, Health Canada of Canada, Healthcare Products Regulatory Agency of the United Kingdom, and the Health Sciences Authority of Singapore are all independent government departments or agencies. The Review Committee also notes that in the Hong Kong context, the Centre for Health Protection (CHP) was set up in 2004 while the Centre for Food Safety (CFS) was set up in 2006 with the objectives of enhancing the prevention and control of communicable diseases and enhancing food safety regulation respectively.

10.7 If the manpower proposals in this chapter are implemented in full, the staff strength of PS will be increased significantly from around 160 to more than 350. In addition, all the other recommendations in this review will also expand the scope of responsibilities of PS. The Review Committee considers that the present organizational setup of PS could no longer enable it to discharge its enhanced role on drug regulation effectively. The Review Committee **recommends** to DH that a dedicated office on drugs be established to strengthen the organizational capacity in drug regulation. This is in line with the practice in advanced countries on drug regulation and local practice in respect of prevention and control of communicable disease and food safety regulation. More importantly, it demonstrates to the general public the Government's strong determination and long-term commitment in ensuring drug safety, protecting public health and restoring public confidence in the use of drugs.

10.8 Having regard to the size and scale of operation when the office commences operation, the Review Committee considers it prudent at the setup stage to have a dedicated head at Directorate 2 Level to oversee the office's operation, make day-to-day management and professional decisions, and formulate strategic plans on drug regulation. The head will report to the Deputy Director of Health and ultimately the Director of Health who will focus on the strategic missions of the office. The statutory authority of the Director of Health vested under the Pharmacy and Poisons Ordinance will remain unchanged, and the Director of Health will still be the Chairman of the Pharmacy and Poisons Board.

10.9 The dedicated office will consist of three functional divisions. The Pharmacovigilance, Risk Communication and Quality Management Division will be responsible for pharmacovigilance matters; monitoring of undesirable medical advertisements; risk analysis, management and communication; international affairs and training; the development and maintenance of a drug information management system and a dedicated website on drug safety; and providing administrative, information technology and technical support to the operation of the office. The Inspection and Licensing Division will be responsible for the licensing and compliance inspection of all drug traders including manufacturers, wholesalers, importers/exporters and retailers; undertaking preparatory works in the journey towards the attainment of PIC/S membership; and the conduct of inspections to overseas and Mainland drug manufacturers without a PIC/S certificate in future. Lastly, the Pharmaceuticals Registration and Business Development Division will be responsible for processing of drug registration and related applications; import and export control of drugs; providing drug procurement, manufacturing and dispensing services to clinics of DH; maintenance of drug information; and organization of training programmes for the pharmaceutical trade and public education programmes on drug safety.

10.10 Having regard to the increased number of pharmacists and senior pharmacists, the addition of professionals of other disciplines comparable to the senior pharmacist level, and the expanded scope of responsibilities, the Review Committee **recommends** that the Inspection and Licensing Division and the Pharmaceuticals Registration and Business Development Division both be headed by a Chief Pharmacist at Directorate 1 level. As for the Pharmacovigilance, Risk Communication and Quality management Division, due to its importance in terms of the public health perspective, the Review Committee **recommends** that it be headed by a Principal Medical Officer at Directorate 1 level. The proposed organization of the office is at *Annex J*.

10.11 In the long run, consideration will be given to expanding the scope of the dedicated office to cover other therapeutic products. The dedicated office could transform into a "Centre for Drug Safety".

CHAPTER 11 SUMMARY OF RECOMMENDATIONS

Overview

11.1 This chapter gives a summary on all the recommendations and concludes the work of the Review Committee.

Summary of Recommendations

11.2 The Review Committee has made a total of 75 recommendations as follows. Recommendations which can be implemented with existing resources are marked with an "＊" while recommendations which will be implemented when new resources are available are marked with an "＃".

Regulation of Drug Manufacturers

Recommendation 1# – to upgrade Hong Kong's current GMP licensing standards by a phased approach to PIC/S standards over a period of fours years. (paragraphs 3.15 – 3.16 above)

Recommendation 2# – to require imported drugs to comply with the same standards once local drugs attained the PIC/S standards. (paragraph 3.17 above)

Recommendation 3# – to strengthen the control of the use of Active Pharmaceutical Ingredients (APIs) and contract laboratories by local manufacturers. (paragraph 3.18 above)

Recommendation 4* – to strengthen the experience requirement for existing APs from at least one year of relevant working experience to at least three years; and for the heads of production and quality control from at least one year to at least two years for pharmacy degree holders and from at least two years to at least three years for holders of higher diploma in pharmacy-related subjects. (paragraph 3.19 above)

Recommendation 5# – to draw up a set of qualification requirements of Authorized Persons (APs), to establish a licensing or listing scheme and to liaise with the universities for offering a structured training programme for APs. (paragraph 3.20 above)

Recommendation 6# – to empower the Pharmacy and Poisons Board to maintain an AP register and remove any AP from the register should he be found incompetent to perform the AP role. (paragraph 3.22 above)

Recommendation 7* – to increase the number of inspections to local manufacturers. While most of the inspections to manufacturing premises should remain announced, some unannounced inspections should be introduced. Further, one of the two inspectors in the inspection team should be retained for subsequent inspections to facilitate effective follow-up on irregularities identified. (paragraph 3.25 above)

Recommendation 8# – to set up a multi-disciplinary GMP inspection team with professionals of other related disciplines like biochemists, chemists, engineers, microbiologists, etc. for effective auditing of manufacturers with diversified production environment. (paragraph 3.27 above)

Recommendation 9# – to develop structured, practical and continuous training programmes for all levels of players in the GMP system including DH inspectors, APs, production and quality control heads, and other workers. (paragraph 3.28 above)

Recommendation 10* – to state in the licensing conditions that local manufacturers should either (a) appoint the AP as a board member; or (b) invite the AP to attend board meetings and allow the AP to speak and have his remarks put on record where safety, efficacy and quality issues of products are concerned. This recommendation should be put on trial for two years and then reviewed. (paragraphs 3.29 – 3.32 above)

Recommendation 11# – to introduce a code of practice to govern the conducts of the manufacturers and the APs. (paragraph 3.33 above)

Recommendation 12* – to require all local manufacturers to adopt the enhanced microbiological monitoring model covering raw materials, granules, finished products and stability studies. (paragraphs 3.34 – 3.39 above)

Pre-market Control of Drugs

Recommendation 13# – to require BABE studies as registration requirement for pharmaceutical products to enhance quality of generic drugs. The implementation should be by phases starting in April 2010. It will begin with antiepileptic drugs, which have a narrow therapeutic index where a comparatively small difference in the absorption of the drug by the human body may lead to undesirable consequences. (paragraph 4.14 above)

Recommendation 14* – to replace the term "Poison 毒藥", as required to be labelled on pharmaceutical products classified as poisons, with other terms to alleviate the unnecessary concern of consumers that the products might be harmful and unsuitable for use or consumption. (paragraph 4.15 above)

Recommendation 15* – to delete the phrase "to be marketed for use within Hong Kong" on the certificate of registration of pharmaceutical products. (paragraph 4.16 above)

Recommendation 16* – to extend the validity of clinical trial certificate from not more than two years to not more than five years. (paragraph 4.17 above)

Recommendation 17# – to shorten the time-frame for processing applications for registration of pharmaceutical products, change of particulars of registered products and clinical trials by 40% - 50%. (paragraph 4.18 above)

Regulation of Importers/Exporters and Wholesalers

Recommendation 18# – to require all wholesalers of non-poisons to be subject to inspection and licensing control. (paragraphs 5.17 – 5.18 above)

Recommendation 19# – to require all wholesalers to keep transactions records of all pharmaceutical products, including Part II poisons and non-poisons in the same manner as for Part I poisons, and to require wholesalers to keep samples of each batch of drugs handled to facilitate investigation when needed. (paragraphs 5.19 – 5.20 above)

Recommendation 20* – to require both primary and secondary packaging be carried out by a licensed manufacturer. (paragraphs 5.21 – 5.22 above)

Recommendation 21* – to introduce a code of practice for importers/exporters and wholesalers detailing their roles and responsibilities, including the requirement of batch release certificate, the reporting of adverse drug reactions, proper storage and transportation of drugs, etc. (paragraphs 5.23 – 5.24 above)

Recommendation 22# – to strengthen the monitoring of importers/exporters and wholesalers by means of more frequent and more detailed inspections, especially after the introduction of a code of practice. (paragraphs 5.25 – 5.26 above)

Recommendation 23# – to set up a dedicated team of pharmacist inspectors to advise C&ED staff on pharmaceutical imports at various ports of entry. (paragraphs 5.27 – 5.28 above)

Recommendation 24# – to set up a record and tracking system by requiring EL applicants to produce the ILs of the imported drugs to be re-exported. (paragraph 5.29 above)

Recommendation 25# – to prescribe in the licensing conditions for ILs for the products for re-export that the importer should not sell unregistered imported drugs in Hong Kong and must re-export the products within a specified period of time, say one year. (paragraph 5.30 above)

Recommendation 26# – to conduct a joint review with C&ED to determine a new weekly quota for post-shipment consignment checks of licences which should be a statistically significant sample size of the ILs and ELs population. (paragraph 5.31 above)

Recommendation 27# – to require exporters who chose to export products by mail to clear their products at designated post offices. DH should include the requirement in the ELs and discuss with C&ED for the introduction of a daily quota on outgoing mail parcels of drugs for verification of content and endorsement by C&ED. (paragraph 5.32 above)

Recommendation 28# – to develop an electronic record system among DH, C&ED and TID to facilitate the tracking of imported and exported drugs. (paragraph 5.33 above)

Regulation of Retailers

Recommendation 29# – to require all retailers of non-poisons to be subject to licensing and inspection control. (paragraphs 5.49 – 5.50 above)

Recommendation 30# – in the longer term after taking into account the market operating conditions and the availability of sufficient pharmacists, to require the presence of a registered pharmacist whenever an ASP is open for business. Heightened enforcement actions should be taken against those non-pharmacists who violate and interrupt the pharmacists' performance of their duties at ASPs. (paragraphs 5.51 – 5.54 above)

Recommendation 31* – to require all Part I Poisons be stored in locked receptacle in the premises of an ASP and that only the pharmacist should hold the key to the locked receptacle. (paragraphs 5.55 – 5.56 above)

Recommendation 32* – to add a provision in the Pharmacy and Poisons Ordinance for the issuance and revision of the code of practice for ASPs in order to give a legal status to the code to enhance monitoring on the operation of ASPs; and to introduce a code of practice for LSPs which should enjoy the same legal status as the code for ASPs. (paragraphs 5.57 – 5.58 above)

Recommendation 33* – to give the Pharmacy and Poisons Board the authority to revoke the licence of an ASP at any time after the ASP has been convicted of serious drug offence. (paragraphs 5.59 – 5.60 above)

Recommendation 34* – to tighten the licensing conditions for the refusal or renewal of ASP or LSP applications. DH should evaluate what type of drug offences should be included based on their public health impact. (paragraphs 5.61 – 5.62 above)

Recommendation 35# – to strengthen the monitoring of ASPs and LSPs by means of more frequent and more detailed inspections. (paragraphs 5.63 – 5.64 above)

Recommendation 36* – to require ASPs and LSPs to purchase drugs from licensed traders only. (paragraphs 5.65 – 5.66 above)

Recommendation 37* – to require that all orders for drugs to have written records. (paragraphs 5.67 – 5.73 above)

Recommendation 38* – to require ASPs to sell pharmaceutical products in their original packing, save in the case of a doctor prescription drug which is required by law to be dispensed in exact quantity in accordance with the prescription and in the case of pharmacist dispensing drugs to patients according to their need with proper labelling. (paragraphs 5.74 – 5.75 above)

Recommendation 39* – to require ASPs and LSPs to keep all the supporting documents including drug orders and sales invoices related to every purchase of all pharmaceutical products, and the documents should be kept as long as the expiry date of the pharmaceutical product concerned for DH's inspection if necessary. (paragraphs 5.76 – 5.77 above)

Regulation of Drug Procurement

Recommendation 40# – both DH and HA to conduct post-delivery surveillance including microbiological and chemical testing to ensure drug quality. (paragraph 6.14(a) above)

Recommendation 41* – both DH and HA to require the suppliers to provide additional information, such as pack size and registration number, etc. in the delivery documents to enable more effective physical checking and verification if drugs received are legally conforming. (paragraph 6.14(b) above)

Recommendation 42# – both DH and HA to provide additional training to staff and monitor the workflow in the repacking activities in drug dispensing to minimize errors. (paragraph 6.14(c) above)

Recommendation 43* – to impose a new requirement on suppliers to keep samples of each batch of drugs that are still within the expiration period to facilitate investigation when needed. (paragraph 6.14(d) above)

Recommendation 44# – to upgrade DH's central inventory monitoring computer system to enhance the traceability of drugs. (paragraph 6.14(e) above)

Recommendation 45# – DH to enrich the database of registered pharmaceutical products so as to provide more detailed information to the public on registration details of products, e.g. pack-size, labelling, legal classification, etc. (paragraph 6.14(f) above)

Recommendation 46* – HA to require suppliers to provide evidence that their products are either registered or are exempted from registration under the law. (paragraph 6.14(g) above)

Recommendation 47* – HA to require suppliers to provide microbiological test results for high risk drug items and batch release certificates on all drugs supplied to HA to ensure safety and quality. (paragraph 6.14(h) above)

Recommendation 48* – HA to use multiple sources for supply of high risk products with high usage volume. (paragraph 6.14(i) above)

Recommendation 49# – HA to establish a Drug Quality Assurance Office to enhance quality monitoring of products, performance management of manufacturers and suppliers and quality incident management as well as to monitor the implementation of all improvement initiatives. (paragraph 6.14(j) above)

Recommendation 50# – HA to enhance the current electronic system, such as exploring the use of RFID, bar coding, wireless data transmission, etc. to enable product traceability and effective stores management. (paragraph 6.14(k) above)

Recommendation 51* – HA to require suppliers to provide drugs in suitable pack sizes as far as possible to reduce the need for repacking. (paragraph 6.14(l) above)

Recommendation 52* – DH to issue a set of guiding principles on drug procurement for the private medical sector and encourage private hospitals, MCOs and private medical practitioners in solo or joint practices to follow this set of guiding principles as far as practicable. (paragraphs 6.26 – 6.27 above)

Recommendation 53* – DH to encourage private hospitals to develop an automated inventory management system and bar-coding system for pharmaceutical products. (paragraphs 6.28 – 6.29 above)

Pharmacovigilance

Recommendation 54* – to establish a pharmacovigilance advisory body to review DH assessments of the ADR reports received, advise DH on action on specific cases, serve as an editorial advisory board of the pharmacovigilance bulletin and assist DH in the promotion of pharmacovigilance activities. (paragraph 7.16 above)

Recommendation 55[#] – DH to set up a dedicated team to promote pharmacovigilance work among professionals, education institutions and the industry; handle ADR reports received; disseminate information; and support the pharmacovigilance advisory body. (paragraph 7.17 above)

Recommendation 56* – DH to publish a regular pharmacovigilance bulletin for distribution to all doctors, dentists and pharmacists, and a user-friendly version of the bulletin for reference of the general public. (paragraph 7.18 above)

Recommendation 57[#] – DH to include an ADR report form in mails to doctors and pharmacists, enhance DH website such that doctors and pharmacists could subscribe and receive emails from DH on ADR as soon as they become known, encourage the use of electronic reporting of ADRs, and develop additional electronic interface for dentists and pharmacists to facilitate ADR reporting. (paragraph 7.19 above)

Recommendation 58[#] – DH to publish guidelines for the drug industry on their responsibilities to report ADRs, to educate and encourage them to report ADRs and to develop a culture of awareness of pharmacovigilance. (paragraph 7.20 above)

Recommendation 59* – to require the drug industry to report any actions taken by overseas drug regulatory authorities on any drugs as a consequence of safety issues and require manufacturers to inform DH if they have committed to the request of European Union or United States to develop an EU Risk Management Plans (RMP) or US Risk Evaluation and Mitigation Strategies (REM) as a condition for approving a new drug. (paragraph 7.21 above)

Recommendation 60* – DH to review ADR reports within three working days. (paragraph 7.22 above)

Recommendation 61* – DH to establish liaison with overseas health authorities for exchange of ADR information as well as providing training on pharmacovigilance to staff. (paragraph 7.23 above)

Recommendation 62# – DH to review the progress and effectiveness of the development and implementation of the improved pharmacovigilance measures in two years' time. (paragraph 7.24 above)

Recommendation 63# – DH to continue the heightened surveillance against high risk products sold in the market and set up a dedicated team of pharmacists to handle increased sampling of high risk products. (paragraph 7.25 above)

Recommendation 64* – to adopt a risk-based approach in drug recall and public communication. Specifically DH should revise the recall guidelines to include the different stages of recall procedures, the classification of the recall, the level of the recall, the strategy of the recall including the dissemination of information to the public, the responsibilities of the trade including refund, and the monitoring of all follow up actions, including the effectiveness of the recall. (paragraphs 7.26 – 7.27 above)

Recommendation 65* – DH to inform the Consumer Council on every drug recall incident at consumer level to widen the dissemination network of the drug recall message. (paragraph 7.28 above)

Recommendation 66* – DH to add a refund mechanism in the recall guidelines requiring manufacturers and wholesalers to provide refund details to consumers at retail level in the event of drug recall. (paragraphs 7.29 – 7.30 above)

Risk Communication

Recommendation 67# – to set up a dedicated, multi-disciplinary team to oversee education and training. The team should collaborate with and co-ordinate efforts of the academia, Consumer Council and relevant professional

bodies in the provision of education and training programmes on drug safety. (paragraphs 8.12 – 8.13 above)

Recommendation 68[#] – to continue organizing seminars with additional focus on quality control for the management at different levels of the drug supply chain as well as front-line staff. (paragraphs 8.14 – 8.15 above)

Recommendation 69[#] – to enhance the content of "Compendium of Pharmaceutical Products" on DH website to provide more information about each registered drug. (paragraphs 8.16 – 8.17 above)

Recommendation 70[#] – to set up a designated website on drug safety to provide a better platform for information dissemination and exchange. (paragraphs 8.18 – 8.19 above)

Recommendation 71* – to establish a working group to work out the prototype of the enhanced website and its contents. (paragraph 8.19 above)

Recommendation 72[#] – to require that more information on drugs and patient-oriented advice be provided along with drugs dispensed to patients at hospitals or clinics. (paragraphs 8.20 – 8.21 above)

Penalty System

Recommendation 73* – to include more aggravating factors in the facts of the case submitted to the Court to reflect the seriousness of the offence concerned for the Court to impose an appropriate sentence. (paragraph 9.11(a) above)

Recommendation 74* – to amend the Pharmacy and Poisons Ordinance to include provision for the Court to order the convicted person to pay the analytical costs incurred by the Government to increase the deterrent effect. (paragraph 9.11 (c) above)

Manpower Requirements

Recommendation 75[#] – to expand DH's Pharmaceutical Service into a dedicated office on drugs to strengthen DH's regulatory role in enhancing drug safety. In the long run, consideration will be given to expanding the office to be a "Centre for Drug Safety". (paragraphs 10.5 – 10.11 above)

Way Forward

11.3 The Review Committee has now completed its task. The Review Committee is pleased that the Government has accepted all its recommendations. In particular, the establishment of a dedicated office on drugs and the raising of Hong Kong's GMP licensing standards to PIC/S standards will become major milestones in the enhancement of Hong Kong's drug safety standard.

11.4 The next step is for the Government to join hands with the pharmaceutical sector in implementing the recommendations. The Food and Health Bureau will oversee the policy issues, introduce the necessary legislative amendments and seek the required resources, while DH, HA and the pharmaceutical sector will be responsible for implementation of the recommendations. The Review Committee would like to appeal to the pharmaceutical sector that it is their primary responsibility to practise to their highest professional standards and strive for continuous service improvement. With the joint efforts of all parties, the Review Committee is confident that the standards of the pharmaceutical industry in Hong Kong will be enhanced and public confidence on the use of drugs will be raised.

11.5 The Chairman of the Review Committee would like to thank all the members of the Committee, the pharmaceutical sector, the medical sector, patient groups and the consumer representative for their contributions to the deliberations of the Review Committee. Members have been most generous with their time and they contributed constructively to all discussions and debates at the meetings in this comprehensive review resulting in a total of 75 recommendations. The Food and Health Bureau and the Department of Health look forward to working with all stakeholders to implement these recommendations under the same spirit of cooperation.

Review Committee on
Regulation of Pharmaceutical Products in Hong Kong
Food and Health Bureau
December 2009

Annex A

Review Committee on
Regulation of Pharmaceutical Products in Hong Kong

Membership

Chairman	**:**	Ms Sandra LEE Permanent Secretary for Health
Vice Chairman	**:**	Dr LAM Ping-yan Director of Health
Official Members	**:**	Dr Gloria TAM Deputy Director of Health
		Mr Anthony CHAN Chief Pharmacist, Department of Health
		Dr CHEUNG Wai Lun Director (Cluster Services), Hospital Authority
		Ms Anna LEE Chief Pharmacist, Hospital Authority
Non-Official Members	**:**	Ms Sabrina CHAN Executive Director, Hong Kong Association of the Pharmaceutical Industry
		Ms Iris CHANG President, The Practising Pharmacists Association of Hong Kong

Ms Celine CHENG
President,
The Hong Kong Pharmaceutical Manufacturers Association Ltd.

Ms Sandra CHOW
Chairperson,
Care for your Heart – Cardiac Patients Mutual Support Association
(up to late December 2009)

Mr William CHUI
Vice President,
The Society of Hospital Pharmacists of Hong Kong

Mr Benjamin KWONG
President,
The Pharmaceutical Society of Hong Kong

Dr Alan LAU
Chairman,
Hong Kong Private Hospitals Association

Mr Andy LAU
Chairman,
Alliance for Renal Patients Mutual Help Association

Ms Connie LAU
Chief Executive,
Consumer Council

Mr LAU Oi Kwok
Chairman,
Hong Kong General Chamber of Pharmacy Ltd.

Professor Kenneth LEE
Professor, School of Pharmacy
The Chinese University of Hong Kong

Dr TSE Hung Hing
President,
Hong Kong Medical Association

Ms Tina YAP
Chairman,
The Pharmaceutical Distributors Association of Hong Kong

Dr YEUNG Chiu Fat
President,
Hong Kong Doctors Union

Secretary : Ms Shirley LAM,
Principal Assistant Secretary for Health,
Food and Health Bureau

Terms of Reference

1. To comprehensively review the existing regime for the regulation of pharmaceutical products in Hong Kong with a view to ensuring patient safety, protecting public health and enhancing the standard and performance of the pharmacy profession and the pharmaceutical industry.

2. To make proposals to enhance the control of the supply chain of pharmaceutical products, covering manufacturers, importers, wholesalers and retailers.

3. To make proposals to enhance the control of pharmaceutical products, including –

   (a) reviewing the Good Manufacturing Practice (GMP) Scheme for safety and quality assurance;

(b) strengthening the enforcement mechanism, including effective penalty system, for GMP compliance; and

(c) tightening the pre-market and post-market control of pharmaceutical products.

4. To recommend measures to enhance the standard and performance of the pharmaceutical industry, including strengthening the governance and internal audit system of manufacturers, and the establishment of a robust microbiological vigilance system in the manufacturing process.

5. To make proposals for legislative amendments, if required, in support of the enhanced regulatory framework.

6. To review the mechanism for the procurement and supply of pharmaceutical products in the Hospital Authority and the Department of Health, including post-delivery verification, storage and auditing of the products.

7. To propose a code of practice to private hospitals and private medical practitioners on procurement and supply of pharmaceutical products.

Annex B

Memberships of the Two Subcommittees under the Review Committee on Regulation of Pharmaceutical Products in Hong Kong

Subcommittee on Drug Manufacturing

Chairman	:	Dr Gloria TAM Deputy Director of Health
Official Members	:	Mr Anthony CHAN Chief Pharmacist, Department of Health
		Ms Anna LEE Chief Pharmacist, Hospital Authority
Non-Official Members	:	Ms Sabrina CHAN Executive Director, Hong Kong Association of the Pharmaceutical Industry
		Ms Iris CHANG President, The Practising Pharmacists Association of Hong Kong
		Ms Celine CHENG President, The Hong Kong Pharmaceutical Manufacturers Association
		Ms Sandra CHOW Chairperson, Care for your Heart – Cardiac Patients Mutual Support Association (up to late December 2009)

Mr William CHUI
Vice President,
The Society of Hospital Pharmacists of Hong Kong

Mr Benjamin KWONG
President,
The Pharmaceutical Society of Hong Kong

Mr Andy LAU
Chairman,
Alliance for Renal Patients Mutual Help Association

Professor Kenneth LEE
Professor, School of Pharmacy
The Chinese University of Hong Kong

Dr TSE Hung Hing
President,
Hong Kong Medical Association

Ms Tina YAP
Chairman,
The Pharmaceutical Distributors Association of Hong Kong

Dr YEUNG Chiu Fat
President,
Hong Kong Doctors Union

Secretary : Ms Linda WOO
Chief Pharmacist (Health) Special Duties, Food and Health Bureau

Subcommittee on Drug Distribution and Procurement

Chairman	:	Mrs Susan MAK Deputy Secretary for Food and Health (Health)
Official Members	:	Mr Anthony CHAN Chief Pharmacist, Department of Health
		Dr CHEUNG Wal Lun Director (Cluster Services), Hospital Authority
		Ms Anna LEE Chief Pharmacist, Hospital Authority
Non-Official Members	:	Ms Sabrina CHAN Executive Director, Hong Kong Association of the Pharmaceutical Industry
		Ms Iris CHANG President, The Practising Pharmacists Association of Hong Kong
		Ms Celine CHENG President, The Hong Kong Pharmaceutical Manufacturers Association
		Ms Sandra CHOW Chairperson, Care for your Heart – Cardiac Patients Mutual Support Association (up to late December 2009)

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The Society of Hospital Pharmacists of Hong Kong

Mr Benjamin KWONG
President,
The Pharmaceutical Society of Hong Kong

Dr Alan LAU
Chairman, Hong Kong Private Hospitals Association

Mr Andy LAU
Chairman,
Alliance for Renal Patients Mutual Help Association

Ms Connie LAU
Chief Executive, Consumer Council

Mr LAU Oi Kwok
Chairman, Hong Kong General Chamber of Pharmacy

Professor Kenneth LEE
Professor, School of Pharmacy
The Chinese University of Hong Kong

Dr TSE Hung Hing
President,
Hong Kong Medical Association

Ms Tina YAP
Chairman,
The Pharmaceutical Distributors Association of Hong Kong

Dr YEUNG Chiu Fat
President,
Hong Kong Doctors Union

Secretary : Ms Shirley LAM
Principal Assistant Secretary for Health, Food and Health Bureau

Annex C

Task Force on Enhancement of Regulation of Pharmaceutical Products in Hong Kong

Membership

Chairman : Dr LAM Ping-yan
Director of Health

Members : Dr TING Tai Lun
Government Chemist

Dr Gloria TAM
Deputy Director of Health

Dr Heston KWONG
Assistant Director of Health
(Special Health Services)

Dr KAM Kai Man
Consultant Medical Microbiologist,
Department of Health

Mr Anthony CHAN
Chief Pharmacist, Department of Health

Secretary : Ms Linda WOO
Chief Pharmacist (Health) Special Duties,
Food and Health Bureau

Terms of Reference

(a) To propose measures to enhance the regulation of pharmaceutical products in Hong Kong.

(b) To update Hong Kong GMP Scheme by incorporating, among others, the principles of Hazard Analysis and Critical Control Point.

(c) To propose measures to enhance pharmacovigilance in Hong Kong.

Expert Group on the Microbiological Hazards on Drug Manufacturing

Membership

Convenor	**:**	Dr Heston KWONG Assistant Director of Health (Special Health Services)
Expert Advisor	**:**	Professor YUEN Kwok Yung Head, Department of Microbiology, University of Hong Kong
Members	**:**	Dr LIM Wei Ling, Wilina Head, Public Health Laboratory Services Branch, Department of Health
		Mr Joseph LEE Pharmacist (Inspection & Licensing), Department of Health

Terms of Reference

(a) To identify and evaluate microbiological hazards in the drug production process.

(b) To propose a mechanism for microbiological monitoring of drug manufacturing process using Europharm Laboratories Co. Ltd. as a case study.

(c) To propose a model for microbiological monitoring in drug manufacturing in Hong Kong, making reference to the Europharm case.

Annex D

(A) Implementation Plan for Review Committee Recommendations with Existing Resources

	Implementation timeframe / Tasks	2010	2011	2012	2013
I	**Regulation of Manufacturers**				
i	Appoint external advisor to GMP audit team				
ii	Develop stratetgy for communication and liaison with industry				
iii	Introduce microbiological monitoring model				
iv	Stipulate detailed requirement of AP, Head of Production & Quality Control				
v	Introduce new licensing condition to have manufacturers to invite AP to attend board of governors' meetings involving safety, efficacy and quality matters				
II	**Enhancement of Pre-Market Control**				
i	Set up expert advisory group on BABE				
ii	Shorten the approval period of clinical trial applications				
III	**Regulation of Wholesalers, Importer/Exporters and Retailers**				
i	Trade consultation				
ii	Prepare Code of Practice for wholesalers, importer/exporters and retailers				
iii	Tightening up licensing conditions				
iv	Revise DH inspection report forms & implement				
v	Introduce new licence for secondary packaging				
vi	Require to keep written records of orders by retailers and doctors				
vii	Research on electronic record system for import/export of drugs including conducting feasibility study				

	Implementation timeframe / Tasks	2010	2011	2012	2013
IV	**Enhancement of Drug Procurement**				
i	Set up contractual agreement between purchasers and suppliers to keep samples of each batch of drugs that are still within the expiry period				
ii	Set up working group with the trade on enriching the registered drug database				
iii	HA to improve on drug procurement				
iv	Prepare guiding principles on drug procurement for private medical sector				
v	Encourage private hospitals to develop automated inventory management system				
V	**Enhancement of Pharmacovigilance and Risk Communication**				
i	Establish a pharmacovigilance advisory body				
ii	Produce a pharmacovigilance bulletin				
iii	Establish liaisons with International Society of Pharmacovigilance and other pharmacovigilance counterparts				
iv	Establish a working group on enhancement of drug information				
v	Update recall guidelines				
vi	Improve on public communication adopting a risk-based approach including informing relevant stakeholders, such as Consumer Council, etc.				
vii	Seek assistance from expert for upgrade of the computer system of DH and the provision of information technology support for enhancement of drug information				
VI	**Raising of Penalty**				
i	Provide the Court with more aggravating factors in the brief facts of each case to reflect the seriousness of the case				
ii	Review the sentencing of each court case				

Annex D

(B) Implementation Plan for Review Committee Recommendations with New Resources

	Implementation timeframe (After allocation of required resources) / Tasks	1/2 year	1 year	2 years	4 years	6 years
I	**Regulation of Manufacturers (Transition to WHO (2007) GMP standard then to PIC/S GMP standard)**					
i	Develop training programmes for DH and trade					
ii	Set up multidisciplinary GMP inspection team					
iii	Initiate HK membership of PIC/S					
iv	Impose PIC/S standard API and contract laboratories licensing requirement					
v	Introduce structured training for AP					
II	**Enhancement of Pre-Market Control**					
i	Require BABE studies as registration requirement for generic drugs by phases					
ii	Shorten the approval period of applications for registration and change of registered particulars					
III	**Regulation of Wholesalers, Importer/Exporters and Retailers**					
i	Enhance inspection based on risk assessment					
ii	Establish an inspection team to advise C&ED on import and export of drugs					
iii	Devise a system to enhance the import/export control of drugs					
iv	Increase the quota sent to C&ED for consignment check					
IV	**Enhancement of Drug Procurement**					
i	Enhance vigilance using risk-based approach in post-delivery surveillance including microbiological and chemical testing					
ii	Enhance training to staff on compliance with Good Dispensing Practice including repacking activities					
iii	Upgrade the central inventory monitoring computer system					
V	**Enhancement of Pharmacovigilance and Risk Communication**					
i	Set up a dedicated team to promote pharmacovigilance work					
ii	Develop electronic ADR reporting interfaces for healthcare providers					
iii	Establish ADR reporting guidelines and impose new requirements for industry					
iv	Set up a dedicated, multi-disiplinary team for public education					
v	Launch the dedicated drug safety website					
VI	**Establishment of a Centre for Drug Safety**					

Annex D

(C) Implementation Plan for Review Committee Recommendations requiring Legislative Amendments

	Implementation timeframe / Tasks (Preparation of Draft Drafting Instructions)	2010	2011
I	**Enhancement of Pre-Market Control**		
i	Replace the word "poison" with other suitable words after consultation with trade by the Pharmacy and Poisons Board		
ii	Delete the words "to be marketed for use within Hong Kong" on the registration certificate		
iii	Lengthen the validity of clinical trial certificate to "not more than 5 years"		
II	**Regulation of Wholesalers, Importer/Exporters and Retailers**		
i	Introduce new licences for wholesale and retail of non-poisons		
ii	Introduce new requirement to maintain record of transactions of Part II poisons & non-poisons		
iii	Empower PPB to revoke ASP licence after ASP convicted of serious drug offence		
iv	Require to keep Part I poisons in locked receptacles		
v	Require the presence of pharmacists during all business hours of ASPs		
III	**Tightening of Penalty**		
i	Require the convicted persons to pay the analytical costs		

Annex E

Recommendations Requiring Legislative Amendments

The implementation of some recommendations of the Review Committee requires amendments to the existing Pharmacy and Poisons Ordinance (Cap 138). This Annex sets out the legislative amendments required.

2. We will work with the Department of Justice (DoJ) to prepare the legislative amendments. The trade and other stakeholders will be consulted before the legislative proposals are submitted to the Legislative Council.

Regulation of Wholesalers

(a) **Requiring wholesalers handling non-poisons to apply for a licence:** At present, wholesalers of drugs which are non-poisons (e.g. vitamins) are not subject to licensing control. The Review Committee considers that patients' health would be affected if these drugs are not handled properly. The Review Committee recommends that the Department of Health (DH) require all wholesalers of non-poisons to apply for a licence so that DH could impose licensing requirements on them. Cap 138 will have to be amended to introduce the licensing requirements.

(b) **Requiring wholesalers to keep transaction records for Part II Poisons and non-poisons**: At present the law only requires wholesaler to keep transaction records for Part I Poisons. The Review Committee recommends that wholesalers also keep transaction records for all pharmaceutical products, including Part II Poisons and non-poisons. Cap 138 will have to be amended to introduce this requirement.

(c) **Introduction of a Code of Practice for wholesalers**: At present there are no guidelines governing the roles and responsibilities of

wholesalers on product quality, as opposed to the Good Manufacturing Practices (GMP) compliance for manufacturers. The Review Committee recommends that a Code of Practice be introduced for wholesalers. Cap 138 will be amended to stipulate that wholesalers will have to follow the Code of Practice when applying for a licence from DH.

Regulation of Importers and Exporters

(d) **Introduction of a Code of Practice for importers and exporters**: As in the case of wholesalers, at present there are no guidelines governing the roles and responsibilities of importers and exporters on product quality. The Review Committee recommends that a Code of Practice be introduced for importers and exporters. Cap 138 will be amended to stipulate that importers and exporters will have to follow the Code of Practice when applying for a licence from DH.

Regulation of Retailers

(e) **Requiring retailers handling non-poisons to apply for a licence**: At present, retailers of non-poisons are not required to apply for a licence. Although non-poisons are drugs of lower risk, they will still affect public health if not being handled properly. The Review Committee recommends that retailers selling non-poisons be required to apply for a licence from DH. Cap 138 will be amended to introduce the licensing requirement.

(f) **Providing legal status for the Code of Practice for Authorized Sellers of Poisons (ASPs) and introducing a Code of Practice for Listed Seller of Poisons (LSPs)**: The Code of Practice for ASPs has no legal status at present, and there is no Code of Practice for LSPs to follow with regard to the handling of drugs. The Review Committee recommends that a provision in Cap 138 be added to stipulate that both ASPs and LSPs have to follow their respective Code of Practice.

(g) **Requiring the presence of pharmacists during all business hours of pharmacies**: At present, Cap 138 requires a registered pharmacist to be present in an ASP for not less than two-third of its opening hours. The Review Committee recommends that a registered pharmacist be present whenever an ASP is open for business. This will improve the professional services provided by pharmacists to the public. Cap 138 will need to be amended to this effect.

(h) **Requiring Part I Poisons be stored in locked receptacles**: At present only Part I Poisons in the First and Third Schedules of Cap 138 are required to be stored in a locked receptacle. The Review Committee recommends that all Part I Poisons have to be stored in locked receptacle to ensure that the pharmacist has complete control over the sale of Part I Poisons. Cap 138 has to be amended to this effect.

(i) **Empowering the Pharmacy and Poisons Board (PPB) to revoke licences of ASPs**: At present the PPB can only stop renewing licences of ASPs at the beginning of each year, but has no authority to revoke the licence during the year. The Review Committee recommends giving such authority to the PPB so that the licence of the ASP can be revoked if it has committed a serious offence.

Pre-market control of drugs

(j) **Changing the term "Poison 毒藥" on drug labels**: The term "poison" in drug labels arouses unnecessary concern of the public regarding the safety of the drug. The Review Committee recommends DH and the PPB consider other alternative terms. The term is currently specified in the law and therefore legislative amendment is required.

(k) **Delection of the phrase "to be marketed for use within Hong Kong" on the certificate of registration of pharmaceutical**

products: DH issue the certificate of registration based on the quality, efficacy and safety of drugs, having no regard to whether the product infringes any intellectual property rights (IPR). The Review Committee recommends deleting the phrase "to be marketed for use within Hong Kong" as DH is not in a position to confirm whether the drug can be sold in the market from the angle of IPR. As the phrase is stipulated in the law, legislative amendment is required.

(l) **Extending the validity of clinical trial certificate from not more than 2 years to not more than 5 years**: It is now stipulated in the law that the validity of clinical trial certificate is not more 2 years. The Review Committee recommends amending the law to extend the period to not more than 5 years so that many clinical trials lasting more than 2 years can continue without the need to apply again for a certificate.

Penalty

(m) **Requiring the convicted person to bear the costs for analyzing exhibits in court cases**: The cost for analyzing exhibits in court cases could be substantial. The Review Committee recommends that the law be amended to require the convicted person to bear such costs in order to increase the deterrent effect.

Annex F

Glossary of Terms

Active Ingredient

The therapeutically active component in a medicine's final formulation that is responsible for its physiological action.

Active Pharmaceutical Ingredient (API)

Any substance or mixture of substances intended to be used in the manufacture of a pharmaceutical dosage form and that, when so used, becomes an active ingredient of that pharmaceutical dosage form. Such substances are intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease or to affect the structure and function of the body.

Adverse Drug Reaction

A response to a medicine which is noxious and unintended, and which occurs at doses normally used in man. It concerns the response of a patient, in which individual factors may play an important role, and that the phenomenon is noxious (an unexpected therapeutic response, for example, may be a side effect but not an adverse reaction).

Alert Limit

Established criteria giving early warning of potential drift from normal conditions which are not necessarily grounds for definitive corrective action but which require follow-up investigation.

Authorized Person

The person recognized by the regulatory authority as having the necessary basic scientific and technical background and experience as well as the responsibility for ensuring that each batch of finished product has been manufactured, tested and approved for release in compliance with the laws and regulations in force in that place.

Batch

A defined quantity of starting material, packaging material, or product processed in a single process or series of processes so that it is expected to be homogeneous.

Batch Number

A distinctive combination of numbers and/or letters which uniquely identifies a batch on the labels, its batch records and corresponding certificates of analysis, etc.

Batch Records

All documents associated with the manufacture of a batch of bulk product or finished product. They provide a history of each batch of product and of all circumstances pertinent to the quality of the final product.

Bioavailability

The rate and extent at which the active pharmaceutical ingredient or active moiety is absorbed from a pharmaceutical dosage form and becomes available at the site(s) of action.

Bioequivalence

Two pharmaceutical products are bioequivalent if they are pharmaceutically equivalent or pharmaceutical alternatives and their bioavailabilities, in terms of peak (Cmax and Tmax) and total exposure (area under the curve (AUC)), after administration in the same molar dose under the same conditions, are similar to such a degree that their effects can be expected to be essentially the same.

Chemical Test

Test to identify the chemical content of the product to assess its quality.

Clinical Trial

A planned study in humans designed to investigate or report upon the efficacy/effectiveness and/or safety of a therapeutic good.

Computerised System

A system including the input of data, electronic processing and the output of information to be used either for reporting or automatic control.

Contamination

The undesired introduction of impurities of a chemical or microbiological nature, or of foreign matter, into or on to a starting material or intermediate during production, sampling, packaging or repackaging, storage or transport.

Drug or ***Medicine***

Pharmaceutical product, used in or on the human body for the prevention, diagnosis or treatment of disease, or for the modification of physiological function.

Expiry Date

The date given on the individual container (usually on the label) of a product up to and including which the product is expected to remain within specifications, if stored correctly. It is established for each batch by adding the shelf-life to the date of manufacture.

Finished Product

A finished dosage form that has undergone all stages of manufacture, including packaging in its final container and labelling.

Generic Product

Pharmaceutical product, usually intended to be interchangeable with the

innovator product, which is usually manufactured without a licence from the innovator company and marketed after expiry of the patent or other exclusivity rights.

Good Manufacturing Practices (GMP)

That part of quality assurance which ensures that pharmaceutical products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing authorization.

Hazard

A factor, an agent or a situation that endangers or poses a potential threat to human health.

Innovator Pharmaceutical Product

Generally the pharmaceutical product which was first authorized for marketing (normally as a patented product) on the basis of documentation of efficacy, safety and quality according to requirements at the time of the authorization. When a substance has been available for many years, it may not be possible to identify an innovator pharmaceutical product.

Labelling

Process of identifying a pharmaceutical product including the following information, as appropriate: name; active ingredient(s), type and amount; batch number; expiry date; special storage conditions or handling precautions; directions for use, warnings and precautions; names and addresses of the manufacturer and/or the supplier.

Manufacture

All operations of purchase of materials and products, production, quality control, release, storage and distribution of pharmaceutical products, and the related controls.

Manufacturer

A person or company who manufactures pharmaceutical products. It produces the product, or engages in any part of the process of producing the product or of bringing the product to its final state, including engaging in the processing, assembling, packaging, labelling, storage, sterilising, testing or releasing for supply of the product or of any component of ingredient of the product as part of that process.

Microbiology

A branch of science that refers to microbes of all of types, including bacteria, viruses, rickettsia, protozoa, fungi and prions. Derived words (such as microbiological) have a similar meaning.

Model

A pattern or replica of the same tests or behaviours.

Multisource (generic) Pharmaceutical Product

Pharmaceutically equivalent or pharmaceutically alternative products that may or may not be therapeutically equivalent. Multisource pharmaceutical products that are therapeutically equivalent are interchangeable.

New Chemical (or Biological) Entities

Active ingredients that have not previously been authorized for marketing as a drug for use in humans in the country in question.

Pack Size

The size of the products in terms of the quantity contained in the container (e.g. volume in a multi-use container) and/or the number of items in the primary/unit pack (e.g. number of tablets in a bottle).

Pharmaceutical Inspection Co-operation Scheme (PIC/S)

An recognized arrangement between Regulatory Authorities in the field of GMP of medicinal products for human or veterinary use. It aims at harmonizing GMP inspection procedures, training to inspectors, facilitating co-operation and networking between competent authorities and mutual confidence.

Pharmaceutical Product

Any material or product intended for human or veterinary use presented in its finished dosage form or as a starting material for use in such a dosage form, that is subject to control by pharmaceutical legislation in the exporting state and/or the importing state.

Primary Packaging

Product packaging that is in direct contact with the product, e.g. blister packaging.

Procedures

Description of the operations to be carried out, the precautions to be taken and measures to be applied directly or indirectly related to the manufacture of a medicinal products.

Procurement

The process of purchasing or otherwise acquiring any pharmaceutical product. It means the pre-selection of products and manufacturers through a procedure of qualification and continuous monitoring thereafter.

Product Recall

Product recall is a process of withdrawing or removing a pharmaceutical product from the pharmaceutical distribution chain because the safety, efficacy and quality of the products could not be assured. The recall might be initiated by the manufacturer, importer, distributor or a

responsible agency.

Production

All operations involved in the preparation of a pharmaceutical product, from receipt of materials, through processing, packaging and repackaging, labelling and relabelling, to completion of the finished product.

Quality Assurance

A wide-ranging concept covering all matters that individually or collectively influence the quality of a product. It is the totality of the arrangements made with the object of ensuring that pharmaceutical products are of the quality required for their intended use.

Quality Control

Quality control covers all measures taken, including the setting of specification, sampling, testing and analytical clearance, to ensure that starting materials, intermediates, packaging materials and finished pharmaceutical products conform with established specifications for identity, strength, purity and other characteristics.

Quality System

An appropriate infrastructure, encompassing the organizational structure, procedures, processes and resources, and systematic actions necessary to ensure adequate confidence that a product (or services) will satisfy given requirements for quality.

Quarantine

The status of starting or packaging materials, intermediates, or bulk or finished products isolated physically or by other effective means while a decision is awaited on their use, rejection or reprocessing.

Registration Certificate

A legal document issued by the competent drug regulatory authority that establishes the registration status of the product.

Risk

The probability of harm or injury. It is most correctly applied to the predicted or actual frequency of occurrence of an adverse event of a drug or other hazard.

Risk Assessment

A systematic process of analysing information to estimate the likelihood of adverse effects that may result from exposure to a specific health hazards.

Risk Communication

The sharing of information about identification and control process of health hazards and decision of action between the decision maker and relevant stakeholders.

Secondary Packaging

Product packaging that is not in direct contact with the product, e.g. carton box packaging.

Shelf-life

The period of time during which a pharmaceutical product, if stored correctly, is expected to comply with the specification as determined by stability studies on a number of batches of the product. The shelf-life is used to establish the expiry date of each batch.

Side Effect

Any unintended effect of a pharmaceutical product occurring at doses

normally used in man, which is related to the pharmacological proprieties of the drug.

Specification

A list of detailed requirements with which the products or materials used or obtained during manufacture have to conform. They serve as a basis for quality evaluation.

Stability

The ability of a pharmaceutical product to retain its chemical, physical, microbiological and biopharmaceutical properties within specified limits throughout its shelf-life.

Stability Tests

A series of tests designed to obtain information on the stability of a pharmaceutical product in order to define its shelf-life and utilization period under specified packaging and storage conditions.

Stakeholder

Any individual, group, or organization that can affect, be affected by, or perceive itself to be affected by an action or decision. Decision makers might also be stakeholders. Stakeholders can include the patient, healthcare professional, regulatory authority, and industry.

Standard Operating Procedure (SOP)

An authorized written procedure giving instructions for performing operations.

Sterile Product

Product which is free from germs or microorganisms

Supplier

Person or company providing pharmaceutical products on request. Suppliers include distributors, manufacturers or traders.

Tabletting

The process of compacting granules into tablets.

Tender

A procedure for procuring pharmaceutical products which puts a number of suppliers into competition. Purchasing is done on the basis of quotations submitted by the suppliers in response to a public notice.

Transparency

Defining policies and procedures in writing and publishing the written documentation; and giving reasons for decisions to the public.

Trial-run

The testing of a new measure in a fixed period to ascertain if the new measure achieves its intended outcomes before putting the new measure into mass production.

Validation

Action of proving, in accordance with the principles of Good Manufacturing Practice that any procedure, process, equipment, material, activity or system actually leads to the expected results.

Annex G

Chronology of Drug Incidents since March 2009

Date	Details of Incident
6 March	The University of Hong Kong announced that four batches of Allopurinol tablets produced by a local manufacturer, Europharm Laboratoires Co. Ltd. were contaminated with Rhizopus microsporus. HA announced replacement of the drug for affected patients from 8 March 2009. On 9 March, DH ordered Europharm to recall all Allopurinol tablets from the market as laboratory analysis of the samples of the affected four batches of Allopurinol confirmed the presence of Rhizopus. DH investigation revealed that during the production process, there was prolonged storage of granules prior to tabletting. Europharm voluntarily stopped production and distribution of all products.
11 March	DH instructed Marching Pharmaceutical Ltd., a local manufacturer, to recall a total of 216 pharmaceutical products as the label expiry dates of these products were not substantiated by laboratory data. On 12 March, the Manufacturers Licensing Committee of the Pharmacy and Poisons Board suspended the licence of the company for one month. The case had also been reported to the police as during the course of DH investigations, certain irregularities in the documents submitted by the company were found.
16 March	DH investigation found that part of the pharmaceutical products, metformin tablets packed in 50x10's blister, supplied to HA by a local manufacturer, Christro Pharmaceuticals Ltd., was not registered with DH. HA announced replacement of the drug for affected patients from 17 March 2009.
19 March	DH investigation found that Unipharm Trading Company, a licenced wholesaler with no drug manufacturing licence, conducted unlicensed packaging of Amitriptyline tablets. DH ordered the company to recall the product.

Date	Details of Incident
20 March	DH investigation found that the expiry dates of two batches of Cosalgesic tablets imported by Unipharm Trading Company had been tampered. The correct expiry dates of the concerned batches should be May 2009 and June 2009 respectively, but they had been changed to June 2010. DH would report the case to the police for investigation. Unipharm initiated product recall at consumer level.
22 March	HA announced that staff of Yaumatei Jockey Club General Out-patient Clinic dispensed expired cough medicine, Promethazine Co Linctus, to around 10 out of 250 patients prescribed with this drug during 1 February to 20 March. HA made arrangements for replacement of the drug for affected patients.
	DH received report from HA that the actual volume of two batches of "Water for injections" imported by Luen Cheong Hong Ltd., a licenced wholesaler, exceeded the volume of 100 ml on the product label by 30 ml. The product was manufactured by the Indonesian subsidiary of a Japanese company, Otsuka. Luen Cheong Hong initiated product recall from HA. The product was not available in private market.
27 March	In response to media enquiries, HA replied that a leukemia female patient in Prince of Wales Hospital received two doses of 4 grams of Cytarabine instead of the correct quantity of 2 grams on 24 March on the first day of a five-day chemotherapy treatment. Staff later became aware of the mistake and doctor immediately assessed the patient; the patient was in stable condition.
2 April	DH investigation found that Mentholatum Pain Patch supplied by Mentholatum (Asia Pacific) Ltd., a licensed wholesaler, was unregistered. Mentholatum applied for registration of the product in 2005 but the application was yet to be approved. DH instructed Mentholatum to recall the product at retail level. There was however no immediate safety or quality concern over the use of the product.

Date	Details of Incident
4 April	DH investigation found that a product named Viscotears supplied by Novartis Pharmaceuticals (Hong Kong) Ltd., a licenced wholesaler, was not yet registered. DH instructed Novartis to recall the product from the market. There was however no immediate safety or quality concern over the use of the product.
6 April	DH investigation found that the registration of a product named Cortiphenol H Eye ointment 2.5g supplied by Novartis Pharmaceuticals (Hong Kong) Ltd. had been expired in December 2007. DH instructed Novartis to recall the product from the market. There was however no immediate safety or quality concern over the use of the product.
	Hind Wing Company Ltd., a licensed wholesaler, initiated a consumer-level recall of two batches of Dithrasal ointment, Dithrasal ointment and Dithrasal ointment 2%, as they were found containing a higher than permitted level of 1,8 dihydroxyanthraquinone (DHAQ) by the Australian drug authority.
	DH investigation found that five pharmaceutical products supplied by Main Life Corporation Ltd., a licensed wholesaler, were unregistered. DH instructed Main Life to recall the products from the market. There was however no immediate safety or quality concern over the use of the product.
11 April	Tung Wah Hospital announced that during a routine check of Phenobarbitone tablets before issuing to the ward on 8 April, it was discovered that Phenobarbitone 60 mg tablets were pre-packaged instead of the intended Phenobarbitone 30 mg tablets on 17 March, resulting in the intake of double dosage of the medication by 6 in-patients. One of the concerned patients passed away on 10 April while the remaining 5 patients were in stable condition.
18 April	In response to media enquiries, HA replied that staff of Lady Trench General Out-patient Clinic mixed up diabetes tablets with drugs for controlling high blood pressure for

Date	Details of Incident
	at least 63 diabetes patients on 17 April.
21 April	DH investigation found that the product insert of Funginox Solution imported by Deltpharm Ltd., a licenced wholesaler, contained unregistered indications and treatment duration. DH instructed Deltpharm to recall the product from the market. There was however no immediate safety or quality concern over the use of the product.
22 April	The pharmacy of Kennedy Town Jockey Club Clinic found black spots on some tablets in a bottle of diuretic drug (Frusemide 40 mg) supplied by Vickmans Laboratories Ltd., a licensed wholesaler, on 15 April. HA Head Office carried out a random check on other batches of Frusemide 40mg and found out that some tablets of another batch also had black spots. According to initial findings, the black spots were confirmed as contamination by fungal species asperigillus. HA announced replacement of the drug for affected patients from 8 March 2009. The Manufacturers Licensing Committee suspended the license of Vickmans with immediate effect for non-compliance with GMP standards on 22 April. DH also instructed Vickmans to conduct a consumer level recall of the product.
28 April	Pfizer Corporation Hong Kong Ltd., a licenced wholesaler, recalled a product Lignocaine HCl Injection 1% from the market as one bottle in a ten-bottle pack of the product was found to be labeled as Sodium Chloride Intravenous Infusion 0.9%. The product was manufactured and packed in Australia, without further repackaging after import into Hong Kong.
6 May	In an internal review, Zuellig Pharma Ltd., a licensed wholesaler, found that Milupa GES 45 Oral Rehydration Salts Sachet was not registered. The product was manufactured in Germany and was once registered in Hong Kong from 1989 to 2004. However, the registration holder did not renew the product registration

Date	Details of Incident
	after its expiry in 2004. Zuellig initiated a recall of the product.
7 May	DH investigation found that the registration of a drug Povidone-iodine Prep Pad imported by Luen Cheong Hing Ltd., a licenced wholesaler, had expired in October 2008, but Luen Cheong Hong was still selling the product. DH instructed Luen Cheong Hong to recall the product from the market. There was however no immediate safety or quality concern over the use of the product.
	During a DH investigation, Hitpharm Pharmaceutical Company Ltd., a licensed wholesaler, was found selling 46 pharmaceutical products in unapproved sales packages with unapproved label information. DH instructed Hitpharm to recall the unregistered products from the market.
2 September	DH investigation found that Jacobson Medical (Hong Kong) Ltd., a licensed wholesaler, had sold the product Tylenol in unapproved sales packages with unapproved label information. Jacobson initiated a recall of the product. There was however no immediate safety or quality concern over the use of the product.
28 September	DH investigation found that a series of 17 pharmaceutical products imported by Dragon Link (International) Trading Company Ltd., a licensed wholesaler, contained 10mg of the mineral manganese instead of 5mg as per the product label. Dragon Link initiated a recall of the affected products.

Annex H

No.04 1

FORM 7
表格 7

[reg. 36(5).]
〔第36(5)條〕

PHARMACY AND POISONS ORDINANCE
藥劑業及毒藥條例

(Chapter 138)
(第138章)

CERTIFICATE OF DRUG/PRODUCT REGISTRATION
藥品/製品註冊證明書

It is hereby certified that... .....
現證明

.....
(Name and Address)
(姓名或名稱及地址)

has been issued with a permit No. HK— ..... authorizing.....
已獲發編號爲 的許可證，准許將

.....(Name of drug/product) to be marketed for use
(藥品/製品名稱)在市場出售以供

within Hong Kong.
在香港使用。

2. This certificate will be valid until..... and thereafter
本證明書的有效期至 年 月 日止，

for periods of five years at a time on renewal and subject to the payment of the registration fee.
之後在註冊費繳付後，每次續期的有效期爲5年。

3. No change in the formulation and commercial presentation of this product shall be made
在註冊有效期內，未經藥劑業及毒藥管理局批准，

during the effectivity of this registration without the approval of the Pharmacy and Poisons Board.
不得更改該製品的合成方式及商業外觀。

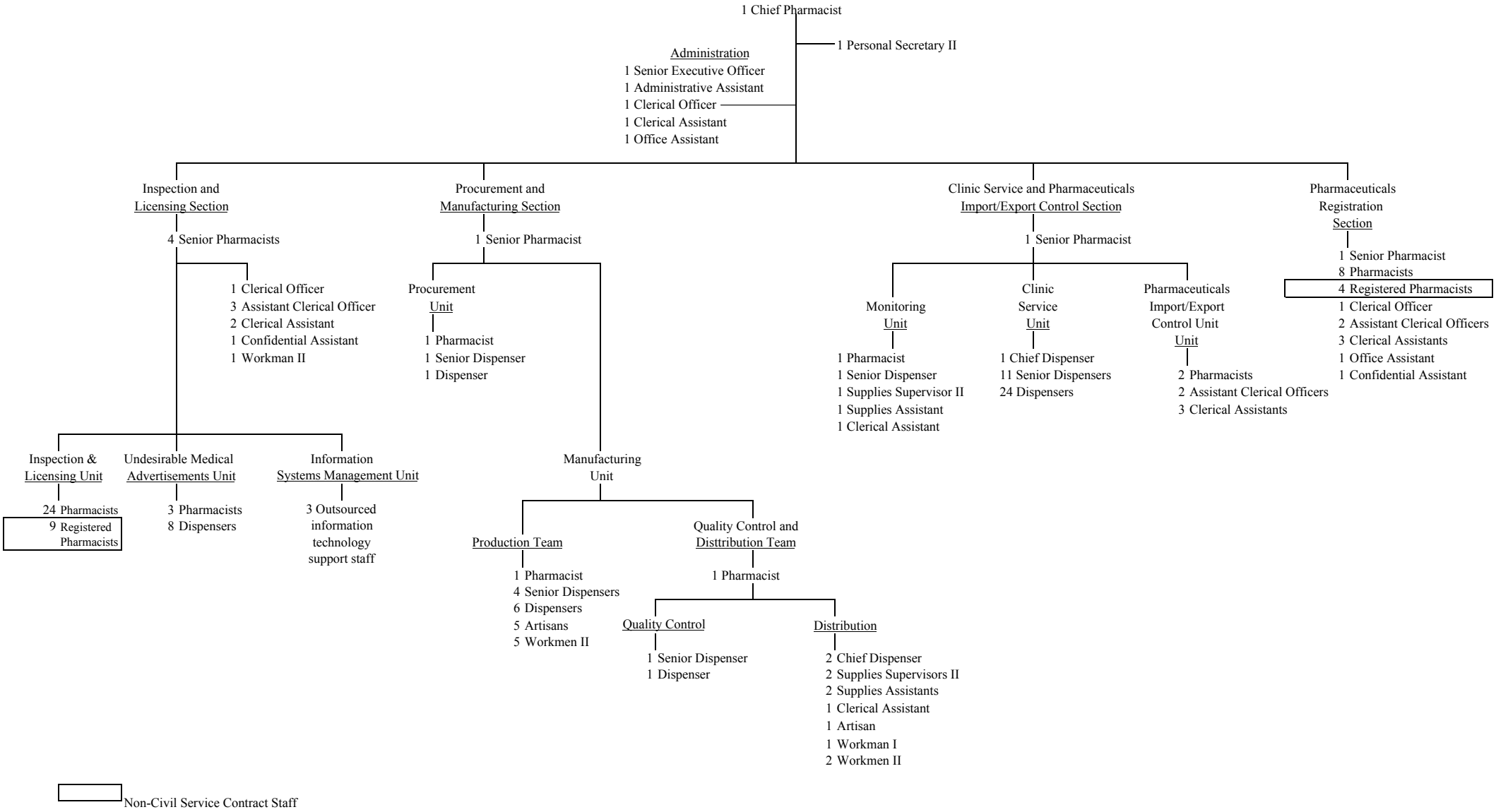
HONG KONG.
香港

(代行)
....
for *Pharmacy and Poisons Board*
藥劑業及毒藥管理局

..... (Date)
(日期)

CLASSIFICATION ON DATE OF ISSUE:
DH 1519(S)

Existing Organization Chart of Pharmaceutical Service



Proposed Organization of the Dedicated Office on Drugs