For Discussion
on 18 November 2013

Legislative Council Panel on Health Services

Legislative Proposals to Enhance the Regulation of Pharmaceutical Products in Hong Kong

PURPOSE

This paper briefs Members on the legislative amendments proposed by the Administration to the Pharmacy and Poisons Ordinance (Cap. 138) ("PPO") and its subsidiary legislation in response to the recommendations put forth by the Review Committee on the Regulation of Pharmaceutical Products in Hong Kong ("Review Committee"). The legislative proposals will also clarify and update the relevant provisions to ensure the consistency with the regulatory framework for pharmaceutical products in Hong Kong.

BACKGROUND

(A) Existing Regulatory Regime

2. Regulation of pharmaceutical products is essentially governed by the PPO and implemented through a multi-pronged system with the dual target of (a) control of the trade; and (b) control of the pharmaceutical products. Section 3 of the PPO provides for the establishment of a Pharmacy and Poisons Board ("the Board") for enforcement of the PPO. Section 4A of the PPO further allows the Board to establish executive committees to register pharmaceutical products and license pharmaceutical dealers.

3. Under the multi-pronged approach, there are legal requirements and administrative measures providing for 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 follows through each point in the production line and the supply chain until the drug reaches its target patients.

Control of the Trade

4. There are four levels of players in the drug supply chain, viz. manufacturers, importers, wholesalers of poisons, retailers of poisons (including the pharmacists overseeing the operations of the retailers). They are all subject to licensing control under the PPO.

5. All pharmaceutical **manufacturers** must first obtain the required licence from the Pharmacy and Poisons (Manufacturers Licensing) Committee of the Board. As of October 2013, there were 24 licensed Good Manufacturing Practice[1] ("GMP") pharmaceutical manufacturers. The requirements for approving and renewing the manufacturer's licence include –

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

(b) proper labelling of the drugs manufactured;

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

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

(e) quality assurance of raw materials and finished products with retention of control samples and all the related control records of these different processes; and

(f) for new application, compliance with the "Guide to Good Manufacturing Practice for Medicinal Products" and its

[1] GMP is a quality assurance approach used by the drug manufacturing industry worldwide to ensure that products are consistently produced and controlled according to quality standards appropriate to the products' intended use. Most countries have adopted the GMP guidelines promulgated by the World Health Organization ("WHO"), although countries such as the United States, the European Union and Australia have drawn up their national GMP guidelines which are similar to the WHO guidelines. There is consensus amongst leading drug regulatory authorities that the purpose of GMP is to diminish risks inherent in any pharmaceutical production. 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 pharmaceutical goods produced.

annexes (where applicable) published by the Pharmaceutical Inspection Cooperation Scheme ("PIC/S") (existing licensees are required to comply with this PIC/S Guide by 2015).

6. As regards **importers/exporters and wholesalers** of drugs, depending on the nature of the drugs being handled, different types of licences are required. For company importing or exporting drugs not classified as poisons under the PPO, a Certificate of Registration as an Importer and Exporter ("IE Certificate") is required. For company handling import and export, and/or wholesaling in drugs classified as poisons under the PPO, a Wholesale Poisons Licence ("WPL") is required. As of October 2013, about 720 WPLs and about 94 IE Certificates have been issued by the Pharmacy and Poisons (Wholesale Licences and Registration of Importers & Exporters) Committee of the Board. No licence is required for company trading in pharmaceutical products of non-poisons within Hong Kong, provided that the pharmaceutical products concerned are registered with the Board. General licensing conditions for the wholesalers and importers/exporters include the suitability of the premises and the adequate knowledge of the person-in-charge in the pharmaceutical trade.

7. For **retailers**, as of October 2013, a total of around 4 500 retailers [around 590 authorized sellers of poisons ("ASP") and 3 920 listed sellers of poisons ("LSP")] have been permitted to deal with retail sale of pharmaceutical products. ASP, commonly known as pharmacy, is authorized to sell pharmaceutical products including those classified as poisons. The Board will issue a certificate of registration of premises to an ASP if it is satisfied that the applicant is a fit and proper person, and that the premises is suitable to conduct the retail sale of poisons listed either in Part I or Part II of the Poisons List Regulations (Cap. 138B) ("PLR"). In addition, the premises have to be under the personal control of a registered pharmacist who is required by the PPO to be present at the premises and exercise control and supervision over the persons employed therein for not less than two-third of the opening hours of the premises. LSP licence is required for company conducting retail sale of pharmaceutical products classified as Part II poisons under the PLR. Such companies are commonly known as medicine companies. The Pharmacy and Poisons (Listed Sellers of Poisons) Committee of the Board issues licence to LSP on the basis of the suitability of the premises and the fitness and properness of the person involved in the business operation.

Control of Pharmaceutical Products

8. Under the PPO, all pharmaceutical products must be registered with the Board before sale in Hong Kong. In line with international practice, only pharmaceutical products which are safe, efficacious and of good quality will be registered. Safety and efficacy are mainly demonstrated through clinical trial studies. Assurance of product quality is achieved through the licensing conditions for local pharmaceutical manufacturers to comply with the GMP requirements or, in the case of imported pharmaceutical products, the certification of compliance with the GMP requirements by the corresponding overseas authorities. To date, some 19 000 pharmaceutical products are registered in Hong Kong. Around 70% are imported while the rest are manufactured locally.

Two-tier Monitoring and Control System

9. To ensure proper control of the safety, efficacy and quality of pharmaceutical products, Hong Kong has a two-tier monitoring and control system that is very similar to those in many other overseas authorities, comprising pre-market and post-market controls.

10. **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 require re-registration before they are released into market. When there are changes in product name, dose form and/or any name or quantity of its active ingredients of a product, the product will need to be re-registered under the Pharmacy and Poisons Regulations (Cap. 138A) ("PPR").

11. To complement licensing of the trade and inspections of licensed premises described above, the Department of Health ("DH") also has in place a series of **post-market control** programmes to monitor the safety, efficacy and quality of marketed pharmaceutical products. Besides, manufacturers and wholesalers are required by law to devise and maintain a recall mechanism so as to ensure comprehensive and speedy recall of their products at various levels whenever required. As regards retailers, they are expected to cooperate with the manufacturers and wholesalers when the latter initiates any recall, by immediately removing the products concerned from display shelves and returning them to the manufacturer or wholesaler concerned.

(B) Recommendations of the Review Committee

12. In the light of a number of incidents concerning pharmaceutical products in Hong Kong in early 2009, the Review Committee, chaired by the Permanent Secretary for Food and Health (Health) of the Food and Health Bureau and comprising members from the pharmaceutical sectors, medical profession, academia, patient groups and consumer representatives, was set up in March 2009 to conduct a comprehensive review on the existing regime for the regulation of pharmaceutical products.

13. After examining in detail the existing regulatory regime, the Review Committee considers that while the framework and the rationale behind the existing regime is sound and should continue to be adopted, the coverage and depth of the regulatory measures should be enhanced. In December 2009, the Review Committee issued a report and made a total of 75 recommendations covering the following aspects:

- Regulation of drug manufacturers and GMP Scheme;
- Pre-market control of drugs;
- Regulation of importers/exporters, wholesalers and retailers;
- Procurement and supply of pharmaceutical products in the public and private medical sectors;
- Post-market control of drugs and pharmacovigilance;
- Risk communication, education and training; and
- Penalty review.

14. The recommendations of the Review Committee have been accepted by the Administration and are being implemented progressively, beginning with those which do not require additional resources. Among the 75 recommendations, 16 recommendations require amendments to be made to the existing PPO and its subsidiary legislation (see **Annex A**). To assess the impacts of the proposed legislative amendments to pharmaceutical dealers, the Administration commissioned a consultant to conduct a Regulatory Impact Assessment ("RIA"). Having considered the RIA result concluded in January 2013 and views expressed by the relevant stakeholders, the Administration has decided to propose

legislative amendments to PPO and its subsidiary legislation to implement most of the recommendations in Annex A which are conducive to enhancing the regulatory regime without causing significant impact to the relevant parties. For the remaining recommendations in Annex A, the Administration would monitor the situation and formulate appropriate implementing measures in due course.

15. Apart from the abovementioned 16 recommendations, the Administration has taken steps to implement the remaining 59 recommendations. The implementation progress of the remaining recommendations is summarised in **Annex B**.

PROPOSED LEGISLATIVE AMENDMENTS

(A) General Provisions

16. We propose to revise the definition of the word "pharmaceutical product" in accordance with the definition adopted by the European Union so as to align with the international practice. To provide guidance and enhance monitoring for the conduct of the activities of different licensed traders (including manufacturers, wholesalers and retailers) and registered pharmacists, we propose to empower the Board to promulgate corresponding Code of Practice ("COP") for these licensed traders and registered pharmacists. The Board will also be empowered to impose licensing conditions; revoke or suspend licence; suspend such directions; or issue warning letter to the relevant licence/registration holders upon non-compliance of the COP, licensing conditions or relevant drug-related offences.

17. Since the Assistant Director (Drug) of the DH, who is a registered pharmacist, has replaced the Chief Pharmacist of the DH to be the head of the drug regulatory agency in Hong Kong, the membership of the Board as stipulated in the PPO will be revised accordingly. In order to ensure the continuity of the work of the Board and its committees, the Assistant Director (Drug) will serve as a member of the Board and its Examination Committee.

(B) Regulation of Manufacturers

18. The definition of "manufacture" will be revised to explicitly include both primary and secondary packaging[2], such that these activities should only be carried out by a licensed manufacturer who complies with the GMP requirements. To minimise the impact on the trade, certain secondary packaging activities which do not affect the safety, efficacy and quality of the products will be exempted from licensing control. Furthermore, ASP will no longer be allowed to manufacture pharmaceutical products at the registered premises unless the ASP holds a manufacturer's licence.

19. The Board will be empowered to set out the qualification requirements of authorized person ("AP"), who is responsible for the quality of pharmaceutical products; maintain a register of AP, and remove any AP from the register should the AP be found incompetent to perform the role of an AP.

20. Manufacturers will be required to label the container of each pharmaceutical product with batch number and expiry dates. Manufacturers will also have to ensure the finished product will conform to the registered particulars of the registered pharmaceutical products. All the relevant manufacturing records should be completed at the time when the manufacturing process is being carried out.

(C) Regulation of Wholesalers

21. In addition to the regulation of wholesale of poisons (see paragraph 6 above), we propose to impose licensing control on wholesalers of non-poisons. We also propose to merge the registration of importers/exporters of pharmaceutical products with the licensing of wholesalers of poisons and subject the licensees to the same set of control. Furthermore, wholesalers will be required to keep transaction records for all pharmaceutical products (including both poisons and non-poisons). The records should include additional details such as registered pack size and batch number of products.

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[2] "Primary packaging" refers to product packaging that is in direct contact with the product (e.g. blister packaging), and "secondary packaging" refers to 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.

(D) Regulation of Retailers

22. The definition of ASP will be revised to reflect the usage in the legislation as entity that carries on the retail sales of poisons. Apart from poisons listed in the First Schedule of PPR, we propose that all poisons listed in Part I of PLR (which will be merged into PPR under our proposal) will also be required to be stored in locked receptacles at the registered premises of an ASP. To heighten control, we propose to tighten up the regulation of the ASP by providing for the direction of Disciplinary Committee to, at the conclusion of a disciplinary inquiry of an ASP convicted of drug related offence, disqualify the ASP and remove its premises from the register of premises, if it is in the public interest to do so, and for such direction to take effect immediately.

23. Registered pharmacist employed by an ASP will be required to be present whenever the ASP is opened for business. Considering the current manpower supply of registered pharmacists, the implementation of this proposed provision will take effect at a later stage (i.e. effective from a date to be announced in the Gazette).

(E) Pre-market Control of Drugs

24. Possession or use of pharmaceutical products for the purpose of conducting clinical trial in accordance with clinical trial certificate issued, or for the treatment of a particular patient by registered medical practitioners, will be exempted from the registration requirement for pharmaceutical products (see paragraph 8 above). Regarding the applicant for registration of pharmaceutical product manufactured in Hong Kong, at the moment, only local licensed GMP manufacturers who manufacture the pharmaceutical product can apply for registration. We propose also to allow licensed wholesalers who have contracted out the manufacturing to licensed GMP manufacturers to apply for registration of pharmaceutical products.

25. For the sake of convenience and clarity, the PLR will be repealed and its contents will be migrated to the PPR in the form of a schedule. In addition, in order to enhance the efficiency to impose suitable control on pharmaceutical products and poisons, we propose that adjustments to the Schedules to the PPR, which includes the First, Second and Third Schedules and the Poisons List to be migrated from PLR to the PPR under the proposed legislative amendments, should be made by means of

negative vetting, as opposed to positive vetting as required under the existing provisions, by the Legislative Council ("LegCo").

26. We propose to empower the Board to require holders of certificate of drug registration to submit updated information for renewal of drug registration. In considering the application for registration of imported pharmaceutical product, if the applicant/importer is unable to provide evidence of compliance with GMP standard adopted by the Board and hence requests the Board to conduct inspection of the manufacturing site of the overseas manufacturer, the Board will also be empowered to recover from the applicant/importer, the cost incurred for GMP inspection conducted at the overseas manufacturing site to ensure its GMP compliance.

27. It is proposed to extend the validity of clinical trial certificate from two years to not more than five years, so that the applicant does not need to apply for a certificate again if a trial lasts more than two years. In addition, it is proposed that any person who conducts a clinical trial without a clinical trial certificate will be subject to penalty upon conviction.

(F) Labelling of Poisons

28. To avoid confusion that the products might be harmful and unsuitable for use or consumption, we propose to replace the word "Poison 毒藥", as required under the PPO to be labelled on pharmaceutical products classified as poisons, by "Prescription drug 處方藥物" or "Drug under supervised sale 監督售賣藥物" depending on the sale restriction.

(G) Special Provisions with respect to Institutions

29. Taking into account the requests and practical operation of the Hospital Authority, drugs supplied by institutions as interpreted under the PPO to out-patients will be labelled with instructions for use in either English or Chinese. Besides, poisons on the First Schedule of the PPR will no longer be required to be stored in locked receptacle solely reserved for the storage of such poisons.

(H) Recovery of Conviction-related Expenses

30. To increase the deterrent effect, the Court will be empowered to order recovery of all expenses incidental to the taking, examination and analyses of any sample of drugs in respect of which the conviction is based from the defendant.

CONSULTATION

31. During the RIA mentioned in paragraph 14 above, the consultant concerned conducted a series of stakeholder consultations. Also, a public opinion survey was conducted by the University of Hong Kong to gauge the sentiments of the general public towards the proposed changes. In general, the general public and the relevant stakeholders support the proposals to enhance the regulatory regime for pharmaceutical products, although some dealers expressed concerns about the likely impact of the proposed changes on their operations.

WAY FORWARD

32. We plan to introduce the relevant legislative amendments into the LegCo in the first quarter of 2014.

Food and Health Bureau
November 2013

Annex A

Summary on the Recommendations of
the Review Committee on the Regulation of Pharmaceutical Products in Hong Kong ("Review Committee")
which Require Amendments to the Pharmacy and Poisons Ordinance ("PPO")

No.[1]	Details of recommendation	The Administration's response to the recommendation
6	Empower the Pharmacy and Poisons Board to maintain an Authorized Person ("AP") register and remove any AP from the register should the AP be found incompetent to perform the role of an AP.	The Administration will implement the recommendation through legislative amendments.
11	Introduce a code of practice ("COP") to govern the conducts of the manufacturers and the APs.	The Administration will implement the recommendation through legislative amendments.
14	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.	The Administration will implement the recommendation through legislative amendments.
15	Delete the phrase "to be marketed for use within Hong Kong" on the certificate of registration of pharmaceutical products.	The Administration will implement the recommendation through legislative amendments.
16	Extend the validity of clinical trial certificate from "not more than two years" to "not more than five years".	The Administration will implement the recommendation through legislative amendments.

[1] Denotes the number of the recommendations put forward by the Review Committee as appeared in its report issued in December 2009.

No.[1]	Details of recommendation	The Administration's response to the recommendation
18 & 29	All wholesalers and retailers of non-poisons shall be subject to inspection and licensing control.	Due to (i) the significant impact to the large number of direct sellers of non-poisons; and (ii) the significant cost to trade arising from to the wide range of products involving huge volume, the Administration considers it not appropriate to impose licensing control on retailers of non-poisons.
19	All wholesalers are required to (i) keep transactions records of all pharmaceutical products, including Part II poisons and non-poisons in the same manner as for Part I poisons; and (ii) keep samples of each batch of drugs handled to facilitate investigation when needed.	The Administration proposes to implement (i). For (ii), as additional space is required for sample retention and keeping samples of expensive drugs is costly, the Administration does not consider it necessary to implement (ii) if traders can provide samples within specified period upon request. Moreover, manufacturers of registered drugs must reach Good Manufacturing Practice ("GMP") standards and must keep drug samples under GMP requirements.
20	Require secondary packaging be carried out by a licensed manufacturer.	The Administration will implement the recommendation through legislative amendments.
21	Introduce a COP 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.	The Administration will implement the recommendation through legislative amendments.
30	Registered pharmacist should be present at authorized seller of poisons ("ASP") whenever an ASP is open for business.	The Administration proposes to implement this recommendation at a later stage when there are sufficient pharmacists available.

No.[1]	Details of recommendation	The Administration's response to the recommendation
31	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.	The Administration will implement the recommendation through legislative amendments.
32	Add a provision in the PPO for the issuance and revision of the COP for ASPs in order to give a legal status to the COP to enhance monitoring on the operation of ASPs; and to introduce a COP for listed sellers of poisons ("LSP") which should enjoy the same legal status as the COP for ASPs.	The Administration will implement the recommendation through legislative amendments.
33	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.	The Administration will implement the recommendation through legislative amendments.
34	Tighten the licensing conditions for the refusal or renewal of ASP or LSP applications. Department of Health should evaluate which types of drug offences should be included based on their public health impact.	The Administration will implement the recommendation through legislative amendments.
74	Amend the PPO 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.	To increase the deterrent effect, the Administration will propose legislative amendment to empower the Court to recover all expenses incidental to the taking, examination and analyses of any sample of drugs in respect of which the conviction is based from the defendant.

Annex B

Summary on the Progress of the Implementation of the Recommendations by the Review Committee on the Regulation of Pharmaceutical Products in Hong Kong ("Review Committee")

The Department of Health ("DH") has been actively implementing the 75 recommendations of the Review Committee to raise the standards of the pharmaceutical industry and enhance the regulation of pharmaceutical products. Accordingly, the Steering Committee on the Regulation of Therapeutic Products, chaired by the Deputy Director of Health of the DH, was established in the DH on 20 January 2010 to oversee the implementation of the recommendations of the Review Committee. Seven working groups were also established to oversee the implementation progress.

2. Among the 75 recommendations put forward by the Review Committee, 16 recommendations require amendments to the existing Pharmacy and Poisons Ordinance (Cap. 138) and it subsidiary legislation.

3. For the rest of the recommendations, 35 recommendations have already been implemented, including the setting up of a Drug Office in the DH and headed by Assistant Director (Drug) in September 2011; raising the requirements of microbiological monitoring in the process of drug manufacturing by local drug manufacturers; stepping up inspection on drug manufacturers and traders; shortening the processing time for application for drug registration; enhancing the tracking of import and export of unregistered drugs; implementing enhanced pharmacovigilance measures including regular publication of pharmacovigilance bulletin; adopting a risk-based approach in drug recall and public communication as well as the provision of more information on drug safety on the website of the Drug Office.

4. Another six recommendations which are related to Hospital Authority's measures to ensure the continuity of supply, safety and quality of drugs procured and to improve the storage and inventory monitoring system have also been implemented.

5. The remaining 18 recommendations are being implemented, five of which are related to the upgrade of the Hong Kong Good

Manufacturing Practice standard to PIC/S standard[1] so as to be on par with international best practice. In this regard, DH has commissioned a two-year consultancy starting from August 2012 which would be completed in August 2014.

6. Five of the remaining recommendations are related to the preparation of Code of Practice ("COP") for various groups of licensed traders. The COP for licensed manufacturers and wholesalers are being drafted, whereas the drafting of the COP for licensed retailers has been completed.

7. The rest of the recommendations are on-going, including the enhancement of the drugs database on the DH website; the implementation of BABE studies[2] as registration requirement for pharmaceutical products by phases; promotion of pharmacovigilance activities and review of the effectiveness of the improved pharmacovigilance measures etc.

[1] PIC/S standard refers to the standard promulgated in the "Guide to Good Manufacturing Practice for Medicinal Products" and it annexes (where applicable) published by the Pharmaceutical Inspection Cooperation Scheme.

[2] BABE refers to "bioavailability and bioequivalence", and is 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.