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.