

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.