

**Third Meeting of
the Business Facilitation Advisory Committee**

***Agenda Item 2 : Follow-up Actions in Response to the
Concerns and Proposals from the Hong Kong
Association of the Pharmaceutical Industry***

Purpose

This paper reports on the follow-up actions in response to the concerns and proposals from the Hong Kong Association of the Pharmaceutical Industry (HKAPI).

Background

2. At the meeting of the Business Facilitation Advisory Committee (BFAC) in February, the HKAPI raised the following concerns:

- (a) non-transparent policy concerning the Hospital Authority's Drug Formulary;
- (b) lack of linkage between pharmaceutical patents and drug registration;
- (c) outdatedness of the Undesirable Medical Advertisements Ordinance (UMAO) and related Codes of Practice on Advertising Standards issued by the Broadcasting Authority; and
- (d) delay in registration of new pharmaceutical products.

3. At its meeting in June, the BFAC considered the Administration's response to the HKAPI's concerns and proposals. While the BFAC generally accepted the Administration's response to the first two concerns, it requested the Administration to explore further improvement opportunities to address the last two concerns.

The UMAO and related Codes of Practice

4. The UMAO prohibits/regulates the advertisement of medicines, surgical appliances, or treatment for prevention of or treatment of certain

diseases or bodily conditions, and those of orally-consumed products in respect of health claims. On the other hand, the Broadcasting Authority (BA) has issued the Codes of Practice on Advertising Standards for radio and television that specifically disallow the airing through the electronic media of advertisements for pharmaceutical products included in Part I of the Poisons List in the Pharmacy and Poisons Ordinance (Cap 138). The HKAPI considered that the restriction on the advertising of western pharmaceutical products through the electronic media was unfair and outdated as compared with the United States.

5. The Administration has explained that the UMAO is intended to protect the public from being induced by advertisements to seek improper self-medication or treatment, regardless of whether such claims are in relation to evidenced-based pharmaceutical products. The Administration considers it important to regulate relevant health claims to protect members of the public and does not have immediate plans to review the provisions in the UMAO at this stage.

6. The Codes of Practice on Advertising Standards are administered by the Television and Entertainment Licensing Authority (TELA). To provide a forum for exchange of views, the Secretariat arranged a meeting for the HKAPI and the TELA in August. The HKAPI presented to the TELA its concerns on the current restrictions of medicinal advertisements and suggested relaxing advertisements for pharmaceutical products through the electronic media.

7. The meeting enhanced the mutual understanding between the HKAPI and the TELA. The TELA suggested to the HKAPI that the TV licensees might put up a case for the consideration of the BA if they support the HKAPI's appeal for relaxation in medicinal advertisements on television.

Delay in registration of new pharmaceutical products

8. For registration of a pharmaceutical product containing new chemical entities (NCEs), a “secondary review¹” approach is adopted in Hong Kong. The eligibility of an application depends on the availability of

¹ The terms “primary review” and “secondary review” are used by the HKAPI in one of their submissions to the BFAC. Very briefly, “primary review” means a full review on the safety, efficacy and quality of the drug by scrutinising all the preclinical (i.e. animal) studies, clinical studies, and manufacturing and quality control documentation. “Secondary review” means approval of drugs based on the reviews conducted by one or more of the reference drug regulatory authorities (e.g. US or EU).

two Certificates of Pharmaceutical Product (CPPs) issued by reference countries². The Department of Health (DH) conducts the initial review and verification of the CPPs and supporting documents. The Pharmacy and Poisons Board (PPB) and its Registration Committee (RC) and Poisons Committee (PC) will then consider giving approval to the registration and the proper classification to control its sale. The NCE will have to be included into the Poisons List under Cap 138 through legislative amendments prior to the registration of the product in question. After gazettal, the applicant will sign an undertaking on reporting requirements before obtaining the registration certificate.

9. Some years ago, two CPPs were required before a NCE application would be accepted by the DH for processing. Since December 2004, the DH has started processing an application upon receipt of one CPP³. We note, on average, this can reduce the overall application time by about a month.

10. From experience, there is on average a time lag of six to nine months between the second CPP and the first CPP of a new product. The trade suggested that a requirement of only one CPP to support a new product registration would allow earlier introduction of the drug to the market and better address the need of the patients. Under regulation 36 (1A)(a)(iii) of the Pharmacy and Poisons Regulations, drugs not yet registered in Hong Kong can still be used for the purpose of treatment by a doctor, dentist or veterinarian, of a particular patient or animal. To source a new drug for a patient, a doctor has to fill out an application form for the required import licence, provide medical information about the drug and submit a letter stating why the drug is required and the quantity to be imported. On average there are 100 cases where new drugs are imported on a name basis each month.

11. The Retail Task Force suggested to the RC under the PPB to review its requirement on the number of CPPs. The RC has deliberated on the requirement and decided to maintain the status quo on the following grounds:

² In July 2005, in view of the industry's concern that overseas authorities often take one to two months to issue a CPP on application, the requirement for submitting CPPs was removed. Instead any official evidence of a drug's approval in the reference country (e.g. a certified true copy of the registration certificate or approval letter) is accepted.

³ Before December 2004, the RC had required two CPPs to be available before accepting applications. It was only at its meeting of 13 December 2004 that the RC decided to accept applications with only one CPP. That decision was communicated to the HKAPI by a letter dated 20 December 2004.

- (a) The RC noted that in a survey of five neighbouring countries/territories (including Singapore and South Korea) which adopted the “secondary review” procedure, all require two to three CPPs from reference countries;
- (b) The RC also noted that in recent years, there had been a number of products which had been registered in one country only but had soon to be withdrawn due to the emergence of serious, often fatal, side effects before they could pass the required assessments and become registered in a second country; and
- (c) The RC also noted that the list of reference countries (recognised for acceptable CPPs) has been expanding gradually to 30 countries now.

12. The requirement of a second CPP serves to reduce the risk in adverse side effects which may take some time to observe after the drug has been generally available in the first country. Should a patient need an unregistered drug, it can be made available by a doctor on individual application to the DH. The application can now be approved in a day, but the doctor may need to expend time in preparing the application. The trade has explicit request for removing the two-CPP requirement. To facilitate the access to new drugs by doctors and patients, we **recommend** that consideration be given to gauge the latest opinion of the general public and the health professionals in this regard.

Review findings

13. Apart from the proposal to relax the CPP requirement, members of the BFAC have also indicated that there should be a further effort to identify other scope for speeding up the registration process. The Secretariat has followed up on this and reviewed 97 applications for NCE registration that were approved in the past three years. The registration procedure and review findings on the average processing times are depicted at **Annex I**. The major observations are:

- (a) The average elapsed time for issuing a registration certificate was 8.8 months;

- (b) The DH spent an average of 3.5 months to process the application before submission to the RC meeting;
- (c) About 2.4 months was required for the three meetings of the RC, PC and PPB to approve the registration;
- (d) The legislative procedure to include a NCE in the Poisons List took 2.4 months; and
- (e) 0.5 month was required to complete the administrative paperwork before issue of the registration certificate.

The PPB to meet on one CPP

14. If the requirement for two CPPs is to remain unchanged, we should look at the possibility of completing as much of the procedure as possible before the second CPP is made available. In fact, as mentioned in para 9, the DH has started processing of applications lodged with only one CPP since December 2004. We suggest that **this concept of processing with one CPP should be extended to the approval procedure under the PPB.** The PPB and its related committees may examine an application on the basis of one CPP and if satisfied, may grant approval in principle to the product. When the second CPP is available, the DH will verify the product attributes prescribed by the second CPP and proceed with the legislative procedure if it is in order. If there are any questions or uncertainties, the application can be referred back to the PPB for consideration.

15. Past experience shows that there is close to 25% of all cases where the second country approves a drug with details of approval (e.g. indications, precautions) different from those of the first country of approval. Such cases need to be considered in detail, and the proposal above would mean that the three bodies of the PPB would have to re-consider a quarter of their approvals in principle. In the light of the need to refer the second CPP back to the PPB, the DH considered that the proposal could hamper the work of the professional members on the PPB and affect the efficiency in processing applications, i.e. the PPB would need to reconsider 25% of the applications (or an additional 25% workload) if such approval in principle arrangement is implemented. On the other hand, the proposal may advance the consideration of an application by the PPB by five months and shorten the overall registration process by four months for 75% of the cases.

Minimise the need for clarification

16. The DH has been organising twice a year briefings/seminars for the trade in which specific requirements for registration are explained. Despite the effort, out of the 3.5 months in preparing for the RC meeting, the DH still had to spend 2.2 months on waiting information required for clarification. The three main items requiring clarification are “package insert/actual sales pack” (37.7%), “shelf life/stability test data” (19.8%) and “manufacturer-related information such as Good Manufacturing Practices (GMP) Certificate” (5.0%) (details are at **Annex II**). To minimize the need for clarification, we recommend that the DH should **review and trim the supporting details for the registration requirements at Annex III** to a bare minimum, and to **provide more comprehensive guidelines**.

17. Much clarification work is spent on verifying the product labelling and package insert of a product against its CPPs that may contain various information of the product presented on different packaging used in the issuing countries. It can be assumed that if a product is to be marketed in Hong Kong in the same packaging as that covered in its CPP, the DH can adopt a form of curtailed checking limited to fundamentals such as indications. Upon satisfactory checking, additional labels (e.g. registration number and warnings in Chinese) could be applied to the packaging. We recommend that the DH should consider setting up **a fast-track processing path for products that will be marketed in packaging matching their CPPs**.

Shorten the time lapse for the RC, PC and PPB meetings

18. At present, the three meetings of the RC, PC and PPB for NCE product registration are scheduled quarterly in consecutive months. The PPB has agreed to increase the meeting frequency from four to five times a year and to schedule the meetings so as to avoid the Legislative Council’s summer recess. The PPB has adopted circulation of papers as the means to give endorsement to the PC’s recommendation in October. This can shorten the process by two weeks to a month. Considerations have been given to extending the practice of circulation of papers to the RC and PC. However, in view of the interactive nature of the discussion, the practice of circulation of papers may not be appropriate for the RC and PC. Nonetheless, we recommend that the DH should **look out for opportunities to increase the frequency of the RC, PC and PPB meetings** to tie in with the receipt of every application.

Rationalise the legislative process for NCE drugs

19. The legislative procedure to include a NCE into the Poisons List takes 2.4 months. To shorten the overall processing time, we recommend revamping Cap 138 **to delegate authority to the Director of Health to maintain the Poisons List** without referral to the Legislative Council. In the short-term, the HWFB is piloting an arrangement whereby preparatory work for law drafting would commence immediately after the PC made a recommendation to the PPB for endorsement.

Advance the undertaking by an applicant

20. Currently, most of the final paperwork before registration is started after the completion of the legislative process. These tasks cover the signing of undertaking and payment of registration fee. An average of two weeks can elapse before the issue of the registration certificate. We recommend that **the signing of the undertaking be completed prior to the gazettal** so that the registration certificate can be issued on the gazettal date upon payment of the registration fee. The DH might need to alert the applicant of the gazettal date in advance. This will eliminate the time now spent before issuing the registration certificate.

Set up regular discussion forum with the trade

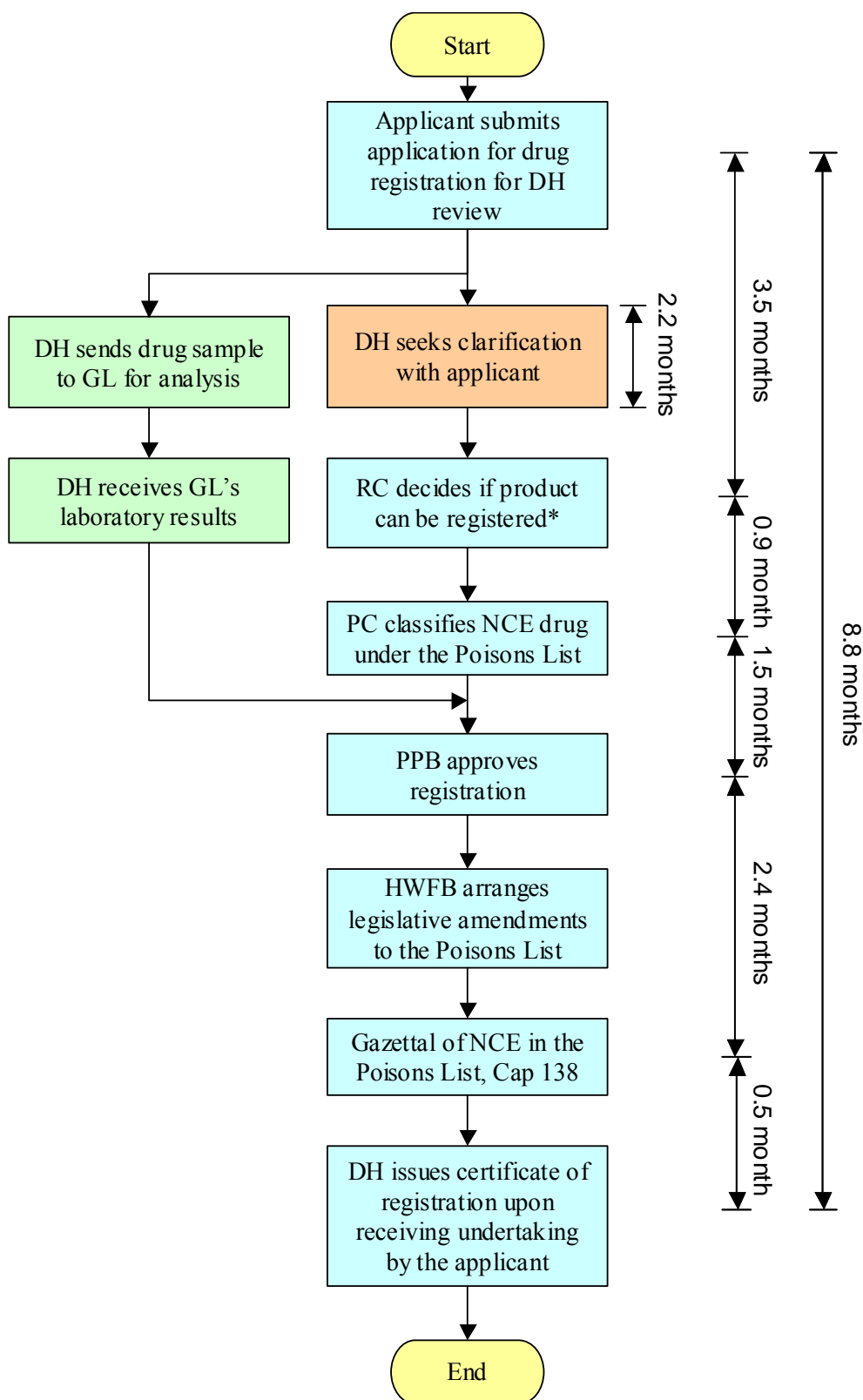
21. It is essential for the DH to grasp the concern and issues of the pharmaceutical industry in order to maintain an efficient registration system. We recommend that **a regular discussion forum be established** for exchanging views with the trade.

Way forward

22. We estimate that the overall processing time can be reduced if the above proposals are taken on board. Members are invited to note the actions taken at paras. 4 to 7 and to give views on the recommendations at paras. 12, 14 and 16 to 21.

Economic Analysis and Business Facilitation Unit,
Financial Secretary's Office
November 2006

Processing of application for registration of drugs containing new chemical entities (NCE)



* At least two Certificates of Pharmaceutical Product (CPPs) are required before application is passed to the RC for consideration. The average time to obtain the second CPP was 5.6 months.

Abbreviations:

DH Department of Health

GL Government Laboratory

PPB Pharmacy and Poisons Board

PC Poisons Committee under the PPB

HWFB Health, Welfare and Food Bureau

NCE New chemical entities

RC Registration Committee under the PPB

Annex II

Occurrence of subjects requiring clarification with applicants

<u>Subject</u>	<u>Percentage</u>
1. Package insert/actual sales pack	37.7%
2. Shelf-life/stability test data	19.8%
3. Good Manufacturing Practices (GMP) Certificate of the manufacturer; information on manufacturing facilities and practice	5.0%
4. Indications	3.8%
5. Reference standard	3.8%
6. Dosage	3.0%
7. Clinical data	2.3%
8. Others (e.g. molecular structure and Chinese name of the active ingredient)	24.6%
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Total:	100%

Items supporting applications for NCE product registration

- detailed qualitative and quantitative composition of the finished product, issued by the manufacturer;
- specifications issued by the manufacturer showing compliance with one or more of the following, unless otherwise justified: Pharmacopeia of the People's Republic of China, British Pharmacopeia, European Pharmacopeia, International Pharmacopeia, Japanese Pharmacopeia and/or United States Pharmacopeia;
- a certificate of analysis of a representative batch of the finished product, issued by the manufacturer or the company performing the analysis;
- method of analysis of the product;
- a certified true copy of the manufacturer's licence;
- certified true copy of Good Manufacturing Practices (GMP) Certificate of the manufacturer;
- the original or a certified true copy of free sale certificate (i.e. certificate of pharmaceutical product) of the product issued by the country of origin and other countries;
- product samples for laboratory analysis;
- one set of original or prototype sales pack (outer carton) and container label of each pack size of the product, complying fully with the appropriate labelling requirements;
- clinical and scientific documentation substantiating the safety and efficacy of the product;
- a quantity (about 1 to 2 grammes) of the drug ingredient for laboratory analysis and expert reports on clinical documentation, chemical, biological and pharmaceutical evaluation and pharmacological and toxicological evaluation;
- information on manufacturing facilities and practice of overseas manufacturers; and

- stability test data
 - real time stability studies at a combination of 30 °C /65% RH. Alternatively, stability studies performed at a combination of 25°C/60% RH with appropriate labelling of storage conditions in Chinese and English. Other temperature-humidity conditions could be adopted where justified; or
 - accelerated stability study data at a combination of 40±2°C/75±5%RH for 6 months.