LCQ19: Vetting and approval of applications for registration of pharmaceutical products

â€‹Following is a question by the Hon Shiu Ka-fai and a written reply by the Secretary for Food and Health, Professor Sophia Chan, in the Legislative Council today (July 14):

Question:

Under the Pharmacy and Poisons Ordinance (Cap. 138) and the relevant regulations, pharmaceutical products must meet the standards of safety, efficacy and quality and be registered with the Pharmacy and Poisons Board (the Board) before they may be sold or distributed in Hong Kong. The Board currently adopts a "secondary review" approach in vetting and approval of applications for registration of pharmaceutical products containing new chemicals or biological entities (collectively referred to as "new drugs"). Applicants are required to submit to the Board documentary proofs of registration of the new drugs and certificates of free sale issued by the drug regulatory authorities of at least two recognised countries (consisting of a total of 32 countries including Australia, Canada, European Union (EU) member states, Japan, Switzerland and the United States (US)), as well as other relevant documents. In this connection, will the Government inform this Council:

(1) of the respective justifications for the Board to adopt the secondary review approach in vetting and approval of applications for new drug registration and to specify the aforesaid 32 countries as recognised countries; whether it has reviewed if such arrangements are in line with the present circumstances; if so, of the details; if not, the reasons for that;

(2) whether the secondary review approach is applicable to applications for registration of drugs containing only new combinations, dosage strengths or forms of registered pharmaceutical ingredients;

(3) whether the Board will consider accepting, apart from the documentary proofs issued by the drug regulatory authorities of the 32 recognised countries, certificates of assessment issued by the drug regulatory authorities/qualified scientific research institutes or universities in Hong Kong and on the Mainland; if so, of the details; if not, the reasons for that;

(4) whether the existing legislation on new drug registration requires that the registration of a new drug will be approved only if the manufacturer of the new drug owns the relevant drug patents; if so, of the reasons for that; if not, whether the ownership or non-ownership of the relevant drug patent by the manufacturer of a new drug has any impact on the registration of the new

drug; if so, of the details; and

(5) as some members of the pharmaceutical trade have relayed that EU and countries such as US and Japan have long implemented a "drug marketing authorisation holder" system (and so has China since the middle of last year) to separately process applications for marketing authorisation and manufacturing authorisation for drugs, so that research and development institutions and natural persons who do not have the corresponding production qualification will be able to produce drugs and obtain drug marketing authorisation through the approach of cooperation or entrustment, so as to encourage them to actively conduct researches and develop drugs, whether the Government will consider introducing a similar system; if so, of the details; if not, the reasons for that?

Reply:

President,

In Hong Kong, pharmaceutical product is mainly regulated by the Pharmacy and Poisons Ordinance (Cap. 138) (the Ordinance) and the Pharmacy and Poisons Regulations (Cap. 138A) (the Regulations). Pharmaceutical products must satisfy the criteria of safety, efficacy and quality for registration with the Pharmacy and Poisons Board (the Board) before they can be sold or supplied in Hong Kong. The Board also sets out the requirements of supporting documents, reports and evidence for the registration of pharmaceutical products. The Drug Office of the Department of Health is responsible for providing technical and executive supports to the Board and its Committees.

After consulting the Department of Health, the reply to the Hon Shiu Ka-fai's question is as follows:

(1), (2) and (3) According to the Guidance Notes on Registration of Pharmaceutical Products/Substances (Guidance Notes) (Note 1) as promulgated by the Board, applicant of registration of pharmaceutical products is required to submit sufficient information in accordance with the Guidance Notes to substantiate the safety, efficacy and quality of the pharmaceutical product, including complete master formula, specification, certificate of analysis and method of analysis, manufacturer licence, certificate showing the manufacturer's compliance to Pharmaceutical Inspection Co-operation Scheme (PIC/S) Good Manufacturing Practice (GMP) (i.e. PIC/S GMP certificate), free sale certificate issued by the drug regulatory authority of the country of origin, sale package, related scientific documentation or references, and stability test data.

As pharmaceutical product containing new chemical or biological entities (NCEs, i.e. contain active ingredients which have not been registered in Hong Kong) generally has not been used widely, applicant of registration of such product is required to provide additional documents as stated in the Guidance Notes, that include the expert evaluation report on the safety, efficacy and quality of the NCEs, and documentary proof of registration of the pharmaceutical products issued by at least two drug regulatory authorities of

recognised countries (Note 2) (e.g. free sale certificate) (the above approval system is also referred to as "secondary evaluation"), in order to provide supporting evidence that the product has been rigorously evaluated before placing in market.

The "secondary evaluation" approach adopted in Hong Kong for approving pharmaceutical products is mainly used to process applications for registration of pharmaceutical products containing NCEs. It relies on approvals from competent drug regulatory agencies or authorities of recognised countries which have conduced primary evaluation (Note 3). The drug regulatory agencies or authorities of recognised countries have fully complied with the technical standards and requirements promulgated by the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) (Note 4).

The Board reviews the drug regulatory mechanism and registration requirements from time to time while upholding the principle of ensuring the relevant standards of safety, efficacy and quality of pharmaceutical products. For example, having considered the special circumstances (e.g. a medicine is registered in only one recognised country due to differences in regional epidemiology or due to public health emergency) in December 2017 and July 2020, the Board amended the relevant registration requirement that, in the case there is no evidence of registration approval in two or more recognised countries, but:

(i) there is a local unmet medical need of the product for public health emergency, communicable diseases or matters of public health importance, including in the areas of tuberculosis, emerging and/ or re-emerging infectious diseases (e.g. avian influenza, chicken pox, Ebola, COVID-19, etc.), or antimicrobial resistance; and

(ii) the product for the public health emergency, communicable diseases or matters of public health importance is promulgated by international health agencies, including the World Health Organization (WHO), World Organisation for Animal Health, etc.;

then the application together with submitted supporting justification, document and expert report may also be accepted by the Board for evaluation and approval on a case by case basis.

(4) and (5) The Regulations have already been amended in 2015 to stipulate that if the pharmaceutical product is manufactured in Hong Kong, the person responsible for obtaining registration of the product must be the licensed manufacturer of the pharmaceutical product, or the licensed wholesale dealer contracting with the licensed manufacturer. If the pharmaceutical product is manufactured outside Hong Kong, the person responsible for obtaining registration must be the licensed wholesale dealer who imported the pharmaceutical product, or the Hong Kong branch, subsidiary, representative, agent or distributor of the overseas manufacturer of the pharmaceutical product. Therefore, the current Regulations do not mandate the applicant of registration to be the manufacturer of pharmaceutical product.

The drug registration system in Hong Kong is established for the protection of public health and the drug registration system does not deprive patent owners of any protection under Patents Ordinance (Cap. 514). As there is already a well-established patent protection system in Hong Kong, the drug registration system focuses on the safety, efficacy and quality aspects of drugs. The Board therefore does not take into consideration the factor of patent right when deciding on an application for registration of a pharmaceutical product. Nevertheless, as advised in the Guidance Notes, applicant of registration should not overlook the issue of infringement of patent rights. To ensure that a pharmaceutical product would not infringe any patent right, the applicant is advised to refer to the Patent Ordinance and consult its lawyer if there is any doubts on the issue.

Note 1: Please see the full text of the Guidance Notes at: www.drugoffice.gov.hk/eps/do/en/doc/guidelines_forms/guid.pdf?v=1gx6ql.
Note 2: There are 32 recognised countries, including Australia, Canada, Members States of the European Union, United Kingdom, Japan, Switzerland and the United States. The drug regulatory authorities of the said countries are members of the Stringent Regulatory Authority (SRA) as designated by the WHO, and are also members of the ICH that have implemented all relevant ICH guidance.
Note 3: Primary evaluation is generally conducted by highly developed and large scale drug regulatory authorities (e.g. SRAs as designated by the WHO). It involves the assessment of primary data and information of all pre-clinical studies (i.e. animal testing), clinical studies, manufacturing and quality control in order to fully evaluate the safety, efficacy and quality of a medicine. By taking reference to the primary evaluation conducted in other countries, it requires multidisciplinary assessment including the professional assessment and evaluation from chemistry, microbiology, toxicology, pathology, statistics and different clinical specialities, which involves a vast amount of human and hardware resources (e.g. independent and accredited laboratories).
Note 4: The ICH plays a unique role in bringing together the regulatory authorities and pharmaceutical industry to discuss scientific and technical aspects of drug registration. ICH regulators are required to implement the final Guidelines to ensure that the medicines that were developed and registered are safe, effective and of high quality.