Business Facilitation Advisory Committee
Wholesale and Retail Task Force

New Mechanism for
Registration of New Drugs in treating serious or rare diseases ("1+" Mechanism) and the measure of using Hong Kong-registered drugs in the Greater Bay Area

Purpose

This paper aims to brief members on the new mechanism (i.e. the "1+" mechanism) for the registration of pharmaceutical products containing New Chemical or Biological Entities[1] ("NCE products") for life-threatening or severely-debilitating diseases in Hong Kong and to provide update on the list of Hong Kong-registered drugs being used in the Greater Bay Area (the "GBA").

Background

2. Under the Pharmacy and Poisons Ordinance (Cap. 138), pharmaceutical products must meet the criteria of safety, efficacy, quality and be registered with the Pharmacy and Poisons Board of Hong Kong (the "Board") before they can be sold or supplied in Hong Kong.

3. An applicant of registration containing NCE products is required to submit documents in accordance with the "Guidance Notes on Registration of Pharmaceutical Products Containing a New Chemical or Biological Entity" ("Guidance Notes") promulgated by the Board. In accordance with the Guidance Notes, applicants for registration of NCE products are required to provide, among others, documentary proof for registration approval of the products issued by the drug regulatory authorities in two or more of the reference countries in order to provide supporting evidence that the product has been rigorously evaluated before placing in the market (i.e. the "secondary evaluation" approach).

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[1] i.e. containing active ingredients which have not been registered in Hong Kong

4. The Board reviews the registration requirements of drug regulation from time to time, including the update of the list of reference countries. Since 1 November 2022, the regulatory authorities of Brazil, Mainland China, Korea and Singapore were included in the list of reference places for registration of drugs containing NCEs. The current list comprises 36 reference countries[2]. To enhance the existing drug regulatory regime, the Chief Executive's 2023 Policy Address announced the new "1+" mechanism as endorsed by the Board for registration of NCE products which came into effect on 1 November 2023. Under this mechanism, applications for registration of NCE products beneficial for life-threatening or severely-debilitating diseases that are supported with local clinical data and scope of application recognised by local relevant expert are required to submit evidence of approval from the drug regulatory authority of one of the reference countries (instead of two).

5. The "1+" mechanism serves to facilitate the registration of new drugs from different parts of the world that meet local unmet medical needs and allow patients' early access to new drugs. The new mechanism could attract more drug development and clinical trials to be conducted in Hong Kong, and the requirements of local clinical data and recognition by relevant expert for application for registration (the "+" under the "1+" mechanism) ensures that all the pharmaceutical products approved for registration fulfil the stringent requirements of safety, efficacy and quality. It also strengthens the local capacity of drug evaluation and enhances the development of relevant software, hardware and expertise, which is an important step in progressing toward a "primary evaluation"[3] approach in the long run.

[2] Currently, the 36 reference countries include Australia, Brazil, Canada, China, 26 European Union countries, Japan, Republic of Korea, Singapore, Switzerland, the United Kingdom and the United States.
[3] "Primary evaluation" 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.

Criteria and Requirements for "1+" Mechanism

6. Under the new "1+" mechanism, applications for registration of NCE products that cannot provide the official evidence of registration approval in two or more of the listed reference countries may still be accepted for evaluation on a case-by-case basis, provided that:

(i) there is a local unmet medical need of the product for life-threatening or severely-debilitating disease(s);

(ii) the product is approved with orphan drug designation, breakthrough therapy designation, priority review designation, or equivalent, and marketed in any of the reference countries; and

(iii) there are local clinical data (e.g. clinical studies, case reports, case series, real-world data, etc.) of the product related to the proposed indication(s) and posology.

7. Apart from the general documents required in the Guidance Notes, applications for registration of NCE products under the "1+" mechanism are subjected to additional requirements which include supporting justification, expert report, etc. as set out in the updated Guidance Notes. Please see **Annex** for the additional information to be provided by applicants for the registration of NCE products under the "1+" mechanism.

8. Applications for registration under the "1+" mechanism will be submitted to the Expert Group on Drug Registration ("Expert Group") set up under the Board, if necessary, for preliminary advice on whether they are eligible to be evaluated under the "1+" mechanism. Applications that fulfil the relevant additional pre-registration documentary requirements may be accepted for evaluation on a case-by-case basis. Accepted applications will then be put forward to the Expert Group for advice and comments on the safety, efficacy and quality of the product, as well as the proposed risk management submitted by applicants before submission to the Pharmacy and Poisons (Registration of Pharmaceutical Products and Substances: Certification of Clinical Trial/Medicinal Test) Committee

("Registration Committee") for consideration.

9. After considering the comments from the Expert Group and subject to submission of a complete application, the Registration Committee may grant conditional approval for the application for registration.

Implementation of the "1+" Mechanism

10. The Drug Office of the Department of Health ("DH"), as the professional and executive arm of the Board, provides input and support in the implementation of the enhanced drug regulatory regime of the new "1+" mechanism. Actions and facilitation measures taken so far include the following:

(i) The updated Guidance Notes endorsed by the Board have been uploaded to the website of the Board (www.ppbhk.org.hk) and Drug Office (www.drugoffice.gov.hk);

(ii) To inform various stakeholders on the implementation details of the new "1+" mechanism, the Drug Office has issued relevant press releases and letters to the stakeholders on 26 October 2023 and handled relevant enquiries and potential applications from the trade. Since the implementation of the new mechanism, the Drug Office has received and followed up 129 enquiries involving 57 companies (as of 17 March 2024); and

(iii) The Drug Office has also proactively approached the pharmaceutical trade and invited the submission of applications for registration under the "1+" mechanism for suitable products, and conducted four online briefing seminars in November 2023 (with attendance of 175 participants) to explain the arrangements for the "1+" mechanism.

11. Under the "1+" mechanism, two new drugs for cancer treatment

have already been approved for registration in Hong Kong, which are oral target therapy products with different strengths indicated for metastatic colorectal cancer. In addition, several pharmaceutical companies have expressed interest in applying for registration under the "1+" mechanism. Applications would be submitted to the Board once the necessary information is available.

Enhancements of "1+" mechanism

12. With a view to being on a par with international regulatory practices to achieve timeliness, predictability, transparency, clarity and efficiency in the management of drug evaluation and paving the way for conducting primary evaluation of new drug applications, the Board has also recently endorsed the following measures for enhancing the "1+" mechanism which will come into effect on 1 May 2024:

(i) A pilot run of a "stop-clock" mechanism that serves to set a target timeline for processing of applications for registration of NCE products under the "1+" mechanism would be established in order to facilitate the management of both dossier submission and timely review;

(ii) To pave the way for building the capacity within the local regulatory framework in carrying out primary evaluation of applications for registration of NCE products, the Expert Group will be expanded in providing expert opinion in the evaluation of scientific evidence substantiating the safety, efficacy and quality of an NCE product under application and associated risk management along its product lifecycle; in anticipation of the lack of local expertise in specific areas and to further strengthen the local regulatory regime to a level on a par with international standard, international experts with relevant academic background and ample experience in drug evaluation will join the Expert Group; and

(iii) To facilitate the timely processing of registration of drugs for life-threatening or severely-debilitating diseases with local unmet medical needs whilst avoiding unnecessary delay in handling ineligible applications, a refuse-to-file mechanism for applications under the "1+" mechanism at the screening stage will be established[4].

The measure of using Hong Kong-registered drugs in the GBA (the "Measure")

13. As a facilitation measure for Hong Kong residents working and living in the GBA to seek healthcare services, National Medical Products Administration announced the Work Plan for Regulatory Innovation and Development of Pharmaceutical and Medical Device in the Guangdong-Hong Kong-Macao Greater Bay Area (the "Work Plan") in November 2020. It allows designated healthcare institutions operating in the GBA to use Hong Kong-registered drugs with urgent clinical use, and medical devices used in Hong Kong public hospitals with urgent clinical use, subject to the approval of the People's Government of Guangdong Province.

14. The Government has been maintaining close liaison and discussion with the Guangdong Provincial Medical Products Administration ("GDMPA") to implement the Measure at the University of Hong Kong-Shenzhen Hospital (HKU-SZH) on a trial basis. GDMPA commenced the Measure at the HKU-SZH on a trial basis in January 2021, which was completed on 31 July 2021.

15. In August 2021, GDMPA and the Health Commission of Guangdong Province announced "Guangdong Province - Guangdong-Hong Kong-Macao Greater Bay Area Interim Regulations on the Administration of Imported Pharmaceuticals and Medical Devices for Urgent Clinical Needs in China" and the relevant policy documents to extend the implementation of the Measure in the nine cities in the GBA.

[4] An application which does not fulfill the criteria and requirements specified under paragraphs 6 and 7 above would be refused to file. The refusal, however, does not preclude the submission of an application for registration under the requirements stated in paragraph 3.

The Measure has gradually extended from Shenzhen to cover other designated healthcare institutions in the GBA. The first batch of 5 designated hospitals included the HKU-SZH, Modern Hospital Guangzhou, Guangzhou United Family Hospital, C-MER (Zhuhai) Dennis Lam Eye Hospital and Zhongshan Chenxinghai Hospital. The second batch of 14 designated hospitals included The First Affiliated Hospital of Sun Yat-sen University, Guangdong Provincial People's Hospital, Shenzhen Qianhai Shekou Free Trade Zone Hospital, Hengqin Branch of Zhuhai People's Hospital, Dongguan Songshan Lake Tungwah Hospital, etc.

16. As at 16 January 2024, 28 drugs and 28 medical devices have been allowed to be used in the designated healthcare institutions in the GBA through the Measure.

17. The HKSAR Government will continue to closely collaborate and communicate with the GDMPA on the Measure with a view to expanding the directory of drugs and medical devices as soon as possible, and extending the arrangement gradually to cover more designated healthcare institutions in the GBA.

18. Members are invited to note the content of this paper.

Department of Health
April 2024

Annex

Additional information to be provided by applicant for registration of NCE products for life-threatening or severely-debilitating diseases under "1+" mechanism

- Justifications for non-compliance with the registration requirement for approval in at least two reference countries and documentary evidence showing the product fulfils the requirements under the new mechanism;

- An assessment report prepared by a local expert with fellowship or equivalent qualification and has at least five years of experience in the field relevant to the product. The report should include a review of the following:
    - the global and local epidemiology of the disease(s);
    - international and local treatment paradigms of the disease(s);
    - local unmet medical need of the disease(s);
    - how the product could address the local unmet medical need; and
    - safety and efficacy of the product.

  The expert should also submit evaluation report(s) on the local clinical data of the product related to the proposed indication(s) and posology (e.g. clinical studies, case reports, case series, real-world data, etc.);

- Assessment report(s), post-authorisation requirement(s), and/or licensing condition(s) issued and imposed by the drug regulatory authority which granted the approval of the product in the reference country;

- Periodic safety update report(s), summary safety report(s), or equivalent, if available; and

- Post-registration development plan (e.g. global regulatory planning of the product, planned and ongoing efficacy and safety studies, local clinical studies, real-world evidence studies).