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By email only: del.questions-leppp@hc-sc.gc.ca

Dear Ms. De Silva,

On behalf of Innovative Medicines Canada (IMC) and its membership, I am writing with respect to the proposed plan for the future use and availability of the drug establishment licence (DEL) and good manufacturing practices (GMP) regulatory flexibilities which were released for comments on March 2, 2023.

IMC is the national association representing the voice of Canada's innovative pharmaceutical industry. The association advocates for policies that enable the discovery, development, and delivery of innovative medicines and vaccines to improve the lives of all Canadians and supports the members' commitment to being a valued partner in the Canadian healthcare system. The association represents companies which support 107,000 high-quality, well-paying jobs in Canada and invest $2.4 billion in R&D every year. Collectively, our members contribute $15.9 billion per year to Canada's knowledge-based economy.

IMC and its members welcomed the efforts by Health Canada to simplify the DEL and GMP framework during the pandemic. We would encourage Health Canada to continue to take a risk-based approach and to rely on GMP compliance through the supply chain, as demonstrated specifically during the last few years where those flexibilities were being used, as the removal of some of those flexibilities is under consideration. Given the lack of evidence of any quality concerns for products that utilized those flexibilities and which allowed drugs to reach patients more readily in Canada, IMC believes that these flexibilities should continue to apply in the normal course as opposed to being only used in response to emergency situations and drug shortages.

In addition, IMC encourages Health Canada to align its performance standards for review of the DEL with other jurisdictions. For instance, the timelines imposed by the Therapeutic Goods Administration in Australia are between 30 days (MRA) and 120 days (sterile/biotech). Similar

timelines could be implemented in Canada. We would also recommend the harmonization of expectations for companies conducting activities related to the sterilization of components.

IMC and its members would be happy to meet with Health Canada to continue the dialogue on the implementation of the revised performance standards for DEL processing as discussed at previous meetings, in addition to the currently proposed plan for DEL and GMP flexibilities.

IMC's specific comments on each of the regulatory flexibilities in the proposed plan, as well as the NERBY extension new Form 0559, are set out below:

I- Extending new evidence requirement by date (NERBY) for foreign buildings

Due to the multiyear COVID-19 pandemic there is still a significant backlog for Health Authority inspections. For instance, USA FDA will have, at minimum, an estimated 13,000 inspection backlog by the end of 2023, and EMA has extended validity of GMP certificates until the end of 2023.To avoid numerous requests for extensions being submitted or drug shortages, it is recommended that the earliest Fixed Transition NERBY date be one year from the date Health Canada's changes to the flexibilities takes effect, i.e., no earlier than August 1, 2024 and with consideration be given to continued monitoring of trusted partners' risk-based approach to setting inspection schedules (i.e., manufacturing sites versus low risk activities).

Consideration should also be given for sites with NERBY dates between July 2023 and December 2023, given that the pandemic started in 2020 and many sites had their last inspection in 2019. Should the proposal be implemented as written, based on our members' initial feedback, we anticipate there will be many extension requests or requests for foreign inspections. The regulatory burden for filing the level of information required for these requests will be significant.

II- Extending foreign evidence validity period

Based on the What We Heard report, most respondents indicated that this flexibility should be adopted as a normal regulatory practice and not just for emergency or drug shortage situations. Similar to Health Canada, inspection cycles of foreign regulators should take a risk-based approach. The GMP validity should be aligned with foreign authorities' inspection cycles and processing considerations. Lower risk activities such as secondary packaging, testing, and sterilization of packaging materials are likely to be inspected less frequently. Japan, as a leading member in ICH and a core member in the Pharmaceutical Inspection Co-operation Scheme (PIC/S), has a validity period of 5 years for GMP evidence. IMC would request that Health Canada require GMP evidence from PIC/S health authority inspections every 5 years similar to what Japan has implemented and also consider inspection of more than 5 years for

low-risk activities such as sterilization of packaging as these are not considered GMP activities in other jurisdictions and are already covered under International Organization for Standardization (ISO).

III- Accepting corporate/consultant audit reports to demonstrate GMP compliance of foreign buildings

IMC recommends that this flexibility remain across all inspection activities and sites when no other health agency report is available, including Health Canada, to allow a more agile and risk-based approach.

IV- Deferral of confirmatory testing

IMC is highly supportive of the complete removal of confirmatory testing based on risk-based approach, including but not limited to reliance on trusted partners through DEL activities, compliance history of the site and the product, and the ability to apply Terms and Conditions should concerns arise.

If Health Canada intends to maintain confirmatory testing requirement, it is recommended that all flexibilities be implemented no earlier than August 1, 2024, after which the current confirmatory testing should revert to current GMPs rather than introducing a more stringent requirement of needing to be completed within three months. A three-month timeframe would introduce logistical challenges and additional costs for most member companies.

V- Modified identity testing

As stated above, IMC is highly supportive of the removal of identity testing based on a risk-based approach, including but not limited to reliance on trusted partners through DEL activities, compliance history of the site and the product, and the ability to apply Terms and Conditions should concerns arise.
Should Health Canada's intention be to maintain an identity testing requirement, the concept of Unique Identifier (UID) should be expanded to include flexible attributes and it should be the responsibility of the importer to justify the uniqueness of the product.

VI- Deferring low-risk investigations for drugs with a shortage concern

IMC supports a risk-based approach and encourages Health Canada to maintain this flexibility, since it could potentially help to alleviate drug shortages.

VII- Using electronic signatures that are not fully validated

For companies who have not had the chance to implement a validated e-signature system or repository, the implementation date would not provide sufficient time to remove this flexibility and revert to a validated e-signature or repository.

VIII- NERBY extension new Form 0559

Prior to the pandemic, the current GUI-0080 form was sufficient to cover all the requirements needed to submit for an extension to the NERBY date (section 6). Consequently, it is unclear why Health Canada is proposing new Form 0559 which contains more detailed information (e.g., Section 4: GMP information) but also requests information that has been provided to Health Canada to approve/review via other channels (e.g. SNDS, Notifiable Changes, Annual Notification, YBPR, and APQR).The new form increases the regulatory burden on companies for no apparent benefit. In addition, Health Canada will need to review multiple forms submitted in accordance with this new requirement. We therefore recommend requests for extension follow the current GUI-0080 and would encourage Health Canada not introduce new Form-0559. The current attestation should be sufficient to allow continued use of the foreign sites. As noted above, we recommend that Health Canada delay the implementation of the current proposal for NERBY dates and allow the 5-year acceptance of evidence which will greatly reduce the number of NERBY extension requests from the industry.

IMC thanks Health Canada for the open dialogue and opportunity to provide feedback on this proposal.

Please do not hesitate to contact IMC should you have any questions or comments.

With Kind Regards,

Declan Hamill
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