

Provisional Translation (as of April 2023)\*

PFSB/ELD Notification No. 0331-1

March 31, 2022

To: Directors of Prefectural Health Departments (Bureau)

From:

Director, Pharmaceutical Evaluation Division,  
Pharmaceutical Safety and Environmental Health Bureau,  
Ministry of Health, Labour and Welfare

Director, Medical Device Evaluation Division,  
Pharmaceutical Safety and Environmental Health Bureau,  
Ministry of Health, Labour and Welfare

Director, Safety Division, Pharmaceutical Safety and  
Environmental Health Bureau, Ministry of Health, Labour  
and Welfare

#### Notification on Handling of In Vitro Diagnostics and Medical Device Products Aiming for Drug-agnostic Companion Diagnosis

The handling of in vitro companion diagnostics (hereinafter referred to as "CDx") and corresponding therapeutic products has been described in the "Notification on Approval Application for In Vitro Companion Diagnostics and Corresponding Therapeutic Products" (PFSB/ELD Notification 0701-10, by the Director of the Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour and Welfare, dated July 1, 2013).

From the viewpoint of further promotion of personalized medical therapy, we have determined to handle CDx and corresponding therapeutic products as follows in order to enable selecting of therapeutic products reasonably and promptly utilizing test results of CDx to improve patient access to therapeutic drugs. Please inform the relevant

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\* This English version of the Japanese Notification is provided for reference purposes only. In the event of any inconsistency between the Japanese original and the English translation, the former shall prevail.

industries under your jurisdiction.

#### 1. Scope of the notification

This notification is applied to CDx approved under Article 23-2-5, Paragraph 1 of the Act on Quality, Efficacy and Safety Assurance of Pharmaceuticals and Medical Devices (Act No. 135 of 1960), which meet all of the following requirements (hereinafter referred to as "drug-agnostic CDx").

- (1) More than one CDx product with the same intended use (i.e. the target disease (cancer type in the case of malignant tumors), biomarker and specimen type) is approved.
- (2) Therapeutic product(s) for which each CDx product is approved to be used as aid in identifying the eligible patients for treatment is (are) different.
- (3) It is considered scientifically reasonable to use the test results of any of the CDx products interchangeably to identify the eligible patients for treatment with relevant therapeutic products.

#### 2. Procedures for changing conventional CDx to drug-agnostic CDx

##### (1) Proposal of candidate products

The marketing authorization holder of a CDx product which is considered to be a candidate product meeting the requirements of Article 1 above or the relevant academic societies etc. is recommended to submit a proposal by filling out the necessary information in the attached form to the Medical Device Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, Ministry of Health, Labour and Welfare (hereinafter referred to as "MHLW" ) by e-mail or mail, upon agreement with the relevant marketing authorization holders (hereinafter referred to as "MAHs") of the other CDx to confirm the eligibility for drug-agnostic CDx. The proposer(s) should consult Pharmaceuticals and Medical Devices Agency (hereinafter referred to as "PMDA") in advance on the propriety of the proposal for the drug-agnostic CDx candidate, as necessary.

#### Mail address

1-2-2 Kasumigaseki, Chiyoda-ku, Tokyo 100-8916, Japan

Medical Device Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, Ministry of Health

Person in charge of Drug-agnostic CDx Candidate Product

## (2) Procedure for changing conventional CDx to drug-agnostic CDx

Upon accepting the proposal at MHLW, PMDA will assess its eligibility for each requirement of Article 1 above and compile the evaluation report. Then the MAH will submit an application for partial change of the designated drug-agnostic CDx product on the report requested by the MHLW's administrative notice. The MAHs would be requested by an administrative notice to amend the intended use of the CDx product by filing the application for partial change approval. The intended use will be amended to be used as aid in identifying eligible patients for treatment with multiple relevant therapeutic products, and this is not limited to the specific corresponding therapeutic products. It is necessary to amend the package insert to provide additional caution statements etc. as well. For filing of a new application of the follow-on CDx product to drug-agnostic CDx, its intended use should be the same as that of approved drug-agnostic CDx.

## 3. Application for approval of the new therapeutic products relevant to CDx

An application for partial change of an approved drug-agnostic CDx is not required, in association with an application of the new therapeutic product which the CDx would be used as aid in identifying the eligible patients for the treatment, If it can be adequately explained that the CDx is able to identify the eligible patients. For example, the CDx has been used the pivotal clinical trial of the product for companion diagnosis.

The MAH of the CDx should consult PMDA on the strategy of an application using drug-agnostic CDx at the time of planning a pivotal study for the application for approval etc. as necessary.