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Hisashi Ietsugu, President
Japan Association of Clinical
Reagents Industries (JACRI)
Isao Ikeda, Chairman
IVD (in-vitro diagnostics) Committee
The American Medical Devices and
Diagnostics Manufacturers' Association (AMDD)
Isao Ikeda, Chairman
Medical Diagnostics Committee
European Business Council in Japan (EBC)

Attention:

Yusuke Nakamura
Director, Office of Medical Innovation Cabinet Secretariat of the Japanese Government
Hirayama Yoshinobu
Councillor for Pharmaceutical Safety Minister's Secretariat
Haruo Akagawa
Director, Evaluation and Licensing Division Pharmaceutical and Food Safety Bureau
Ministry of Health, Labour and Welfare
Kazunari Asanuma
Director, Office of Medical Devices Evaluation Pharmaceutical and Food safety Bureau
Ministry of Health Labour and Welfare
Mitsuaki Kamata
Director, Economic affairs Division Health Policy Bureau Ministry of Health Labour and Welfare
Hidehito Sekino
Director, Office for Medical Device Policy Health Policy Bureau Ministry of Health Labour and Welfare
Yasuhiro Suzuki
Director, Medical Economics Division Health Insurance Bureau Ministry of Health Labour and Welfare
Masami Sakoi
Policy Planning Director, Medical Economics Division Health Insurance Bureau
Ministry of Health Labour and Welfare
Tatsuya Kondo
Chief Executive, Pharmaceuticals and Medical Devices Agency
Hideo Utsumi
Executive Director and Director (Center for Product Evaluation)
Pharmaceuticals and Medical Devices Agency

Proposal on Infrastructuring Companion Diagnostic Agents to Promote Personalized Medicine

Introduction

In order for each individual patient to achieve the best clinical outcome, it is important to select the medical treatment most appropriate for each patient. Today, with the progress of life science, personalized medicine is becoming available which enables selection of regimen/agents appropriate for each patient by examining biomarkers such as genes and proteins of a patient before drug administration. Personalized medicine is expected to spread more in the future for improvement of quality and safety of medical practices as well as effective use of financial medical resources.

To realize such personalized medicine in pharmacotherapy, companion diagnostics (hereafter referred to as "CoDx"), i.e. test drugs of biomarkers to predict the effect and safety of agents as well as to optimize dosing, are essential. Our mission of diagnostic agent companies is to develop and market CoDx as in-vitro diagnostic products and contribute to facilitate personalized medicine in collaboration with pharmaceutical companies. For the provision of medical care based on the new concept, the processes of development, clinical evaluation, approval by the pharmaceutical affairs bodies, and entry in the NHI Reimbursement Price List/insurance coverage of new drugs and in-vitro diagnostic products needed for those new drugs are required to progress simultaneously so that the pharmaceutical products and CoDx will be provided to the clinical settings without time lag. However, because there is no structure to link CoDx development and pharmaceutical products, infrastructuring of CoDx development is prime issue to promote appropriate use of pharmaceutical products which require CoDx (hereafter referred to as "pharmaceutical product-CoDx") in clinical settings.

Therefore we propose the followings for infrastructuring related to approval by the pharmaceutical affairs bodies/insurance reimbursement of CoDx which is essential for realizing personalized medicine. In addition, we request that a setting for continuous exchange of opinions between the government and the industry will be established in order to facilitate improvement in the processe of CoDx development/approval review.

We expect that this proposal will help to realize and spread effective and safe

medical practices, which will bring well-being of each patient.

1. Requirements for regulatory application and developmental/approval process of CoDx

In order to provide CoDx, which has close relation with the efficacy/safety of pharmaceutical products and therefore, as precondition, should be used together with the products, we suggest construction of new developmental/approval criteria and process of *in vitro* diagnostic products which are linked to regulatory review of pharmaceutical products.

(1) Constructing framework for implementation of collaborative trials (clinical studies) of pharmaceutical products and CoDx

To enable verification of clinical diagnostic efficacy of CoDx simultaneously in a clinical study of pharmaceutical product-CoDx, we propose that framework should be constructed in collaboration with pharmaceutical companies from the developmental stage of a clinical study such as consultation.

(2) Review of in-vitro diagnostic products in conjunction with pharmaceutical products and simultaneous approval

In principle, regarding pharmaceutical product-CoDx, it is expected that CoDx is developed simultaneously with the development of the pharmaceutical product and each product is approved by the pharmaceutical affairs bodies at the same time. In addition, for the conduct of efficient review, we propose that the system should be linked to review pharmaceutical product in conjunction with CoDx: for example, for CoDx which is developed simultaneously with the pharmaceutical product, the clinical efficacy as a CoDx should be reviewed during the pharmaceutical product review; the quality of the reagent and its basic performance should be reviewed during the in-vitro diagnostic product review.

(3) Development of pharmaceutical requirements including equivalence tests

When an in-vitro diagnostic product is not developed at the time of pharmaceutical product development, a clinical study of a pharmaceutical product will be performed

using LDT (Laboratory Developed Test*). If an in-vitro diagnostic product is developed after the pharmaceutical product development and application for regulatory approval is made, the equivalence with the LDT used in the clinical study of the pharmaceutical product will be of importance. Therefore, it is proposed that pharmaceutical requirements such as equivalence tests necessary for review of CoDx should be developed.

* Tests conducted at laboratories of medical institutions and registered clinical laboratories using techniques developed uniquely at their sites. Tests will be performed using reagents not approved by the regulatory authorities.

2. About insurance reimbursement of in-vitro diagnostic products used for CoDx

For future growth of personalized medicine, CoDx plays an important role. To facilitate CoDx development and appropriate implementation in clinical settings, optimizing insurance reimbursement of CoDx as well as developing systems in which a pharmaceutical product and CoDx will be covered by insurance at the same time are essential elements. The current processes for application of insurance coverage differ between pharmaceutical products and specimen tests, which may pose the issue of causing time lag of insurance coverage timing. In addition, the following problems of technological innovations and developmental efforts of diagnostic agent companies not being reflected on evaluation in the current medical fee payment system of specimen tests are pointed out: the structure of the current medical fee payment system of specimen tests makes it difficult to directly reflect technologies of in-vitro diagnostic products and their clinical efficacy on reimbursement pricing; regarding genetic tests, some testing methods not approved by the pharmaceutical affairs bodies (LDT) are entered on the insurance price list, and the testing fees of unapproved testing methods and approved testing methods are the same.

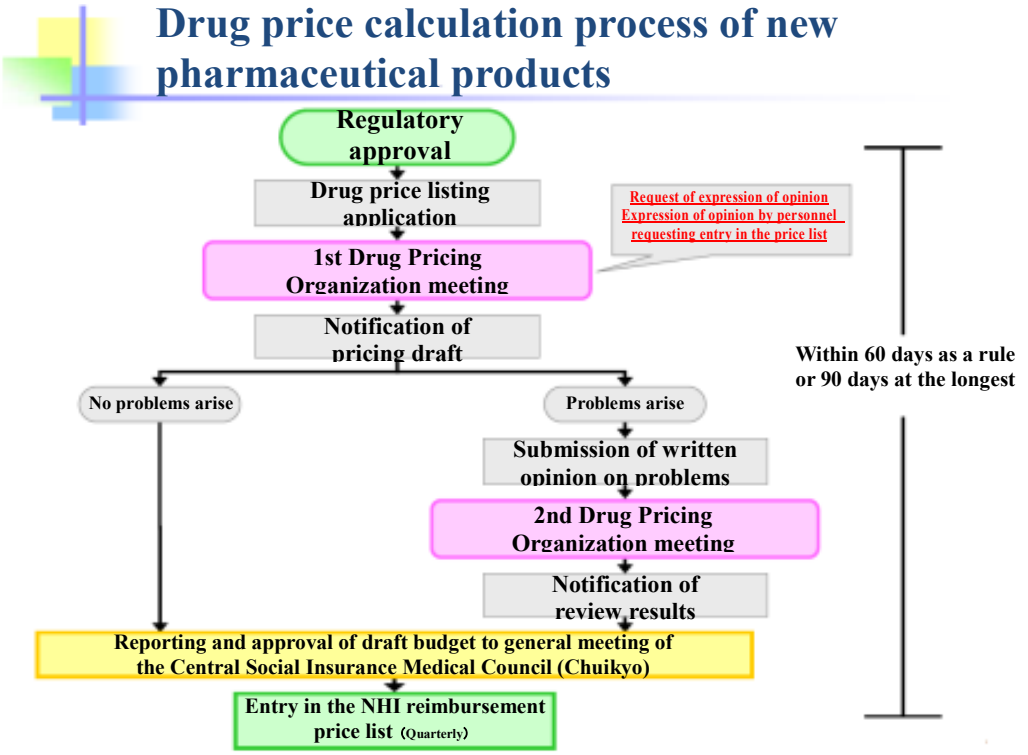
Based on these challenges of the medical fee payment system related to specimen tests, to promote CoDx, we will make the following proposals.

(1) Constructing insurance coverage review process of CoDx that are synchronized with pharmaceutical products review

[1] When the drug price of a pharmaceutical product is listed and marketed, CoDx

should also be covered by insurance and marketed at the same time. For this purpose, we propose that insurance coverage of CoDx will also be reviewed in the same process as the drug price listing of the corresponding pharmaceutical product (see the attached figure) in order to obtain insurance coverage simultaneously after approval by the pharmaceutical affairs bodies.

[2] We propose that CoDx will be subject to quarterly point allocation and item listing same as new drugs, instead of the current system of specimen tests in which new items are listed at the time of two-yearly medical fee payment revision and during the revision of the points, similar insurance coverage are applied.



(2) Establishing insurance point allocation system to encourage development and spread of CoDx approved by the pharmaceutical affairs bodies

[1] We propose to newly establish an insurance point allocation system which adds incentive for technological innovations of testing and product development which are not clearly defined under the current insurance coverage review.

[2] Regarding CoDx which promotes effective use of pharmaceutical agents and, at the same time, can exert effects on medical economy, we request to allocate

insurance points which reflect the value on medical economy.

[3] We request to establish a system which supports development/introduction of CoDx approved by the pharmaceutical affairs bodies by allocating insurance points, which are different from those of testing methods not approved by the regulatory authorities. At the same time, we request that unapproved testing methods of the same items covered by insurance will be removed immediately from the insurance coverage when the in-vitro diagnostic products approved by the pharmaceutical affairs bodies become under insurance coverage.