Executive Summary

The Development of Clinical Management Guide for Temporary Approval of New Health Technology

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The results of the new health technology assessment revealed that the “research phase technology” that lacks scientific evidence to evaluate safety and efficacy cannot be introduced to the medical market in reality as it cannot be included as national health insurance coverage and noncoverage. Research phase technologies are washed out without a second chance for marketing unless additional clinical evidence to verify the safety and efficacy is accumulated for the re-performance of the new health technology assessment. It serves to protect the people’s health rights and the purpose of the system in which only health technology whose safety and efficacy are verified is introduced to the medical market. However, some argue that it regulates market introduction of therapeutic (diagnostic) methods for rare diseases and intractable diseases for which the urgency of clinical introduction is recognized but whose accumulation of scientific evidence for safety and efficacy is difficult. Health technology (performance), unlike drug and medical devices, is a licensed activity without the concept of property, such as patents, and it is difficult to secure the evidence with which to assess the corresponding health technology without a national level of support for research because investment of social capital for safety and efficacy of performance is difficult.

Therefore, the need for a system for the early adoption and development of

promising health technologies on a national level must be recognized, and the adoption of a “Temporary Approval of the New Health Technology System” in which health technologies without replaceable technology or a therapeutic (diagnostic) method for rare diseases that cannot be misused according to the results of the new health technology assessment are introduced to the market with the “approval for the temporary new health technology” under the condition that it is for the generation of evidence, and the new health technology assessment is re-performed once that evidence is generated. The technologies to be selected may have to be limited to those determined as research phase technology (II-b class research phase technology) during the new health technology assessment because of the lack of evidence to determine the efficacy despite the recognized need for clinical support or urgent introduction to the practice.

This research was conducted to provide the requirements for managing the process of evidence generation so that scientific evidences generated from the Temporary Approval of the New Health Technology System may be managed systematically during the re-performance of the new health technology assessment and objective information that satisfies the scheduled criteria may be provided. For this purpose, first, we intended to design the performance system and detailed procedures to manage the process that can verify whether a certain level of health technology that has been approved as the temporary new health technology is provided in real time. Second, we intended to provide legal evidences for system adoption and enforcement and develop the guideline required to manage the performance process. Third, we intended to obtain a social consensus through communication with various groups concerned with the deduced performance system and legal evidences.

The principles, regulations, and guidelines related to the process management of clinical researches in Korea and abroad were investigated and reviewed to conduct this research with special focus on the corresponding guideline of similar international systems that conduct health technology assessment based on the evidence generated while permitting procedures of research phase technology without enough clinical evidence for a certain period. The performance process system for the temporary new health technology was prepared based on the analyzed data, and the necessary bill and guideline were developed after reviewing the laws for enforcing the system. With

this, prepared research outcomes, such as enactment and revision of laws, and a detailed guideline were presented, and a system-briefing session was held to gather opinions of the specialists.

Similar regulatory data investigated in Korea include Addendum 2 of 3 of the Pharmaceutical Affairs Act enforcement regulation, “Good Clinical Practice,” and Addendum 2 of 2 of the Medical Appliances Act enforcement regulation, “Good Clinical Practice for Medical Appliances,” and the role and responsibility of individuals and organizations related to clinical researches are legally regulated. The common characteristics and process management procedure of general clinical researches were discovered in keeping with the purpose of the Temporary Approval of the New Health Technology System that targets to produce evidence for the assessment of the new health technology unlike clinical researches on drugs and medical appliances with the purpose of economic benefits through commercial sales.

Also, the review of the guidelines of the “International Conference on Harmonization-Good Clinical Practice (ICP-GCP),” “Nuremberg Code,” and the “Belmont Report,” which affect the safety and welfare of clinical research subjects around the world, including Korea, revealed that they clearly define the responsibility and function of an organization’s “Institutional Review Board” and include a detailed explanation about the investigator, the sponsor, and the clinical research protocol. The essential clauses on the safety and voluntariness of the subject (patient) were specially referred to for the development of the process management guideline for the temporary new health technology performance.

Foreign countries that perform evidence-based health technology assessments to determine the range of benefits and insurance coverage of health technology have clinical researches with conditional payment generation along with the policy of permitting marketing of drug and health technology and procedure (test) of health technology. The United States permits insurance coverage of the health technologies without enough evidence or with low-quality research under the condition that is to generate quality evidence in order to support early market introduction of a promising new health technology. Centers for Medicare and Medicaid Services (CMS) is enforcing Coverage with Evidence Development (CED) to provide an official permit for the insurance coverage of promising drug, bio drug, medical appliance, diagnostic

method, and procedure that do not satisfy Medicare's determination criteria. Coverage is provided with limitation to patients who satisfy the criteria of clinical researches proposed by National Institutes of Health (NIH), and the final decision about the coverage is made after the accumulation of research results. If selected as the National Coverage Determination (NCD), the NCD report that describes the corresponding approval criteria and the range of benefits, method and characteristics of procedure, indication, coverage limitation, criteria of subject selection, etc., of the corresponding health technology is announced to approve the clinical research. In addition, if selected as CED, the public notification (plan) that describes the decision summary, contents of final decision, coverage status of corresponding health technology, and results of health technology assessment are announced.

In the United Kingdom, if a promising health technology does not have sufficient evidence for efficacy under the supervision of the National Institute for Health and Clinical Excellence (NICE), it is determined as Only in Research (OIR) and the use of national medical service is recommended based on the assessment outcomes. Once started from subject selection and selected as "research recommendation" in NICE, the research is selected as either a Health Technology Assessment programme (HTA programme) or NIHR Evaluation, Trials and Studies Coordinating Centre (NETSCC) program according to the criteria of the National Institute of Health Research (NIHR), and clinical research is then conducted in accordance with each program.

In Japan, the new health technology expected of its safety and efficacy despite lack of evidence through an "Advanced Health Technology Support System" is classified as advanced health technology A and B (A: health technology not accompanying the use of unapproved or out-of-indication drugs or medical appliances according to the Pharmaceutical Affairs Act, B: health technology accompanying the use of unapproved or out-of-indication drugs or out-of-indication medical appliances according to the Pharmaceutical Affairs Act) of the assessed treatment. Advanced health technology A is reviewed in the aspect of safety, efficacy, efficiency, social validity, need for future insurance adoption, etc., of the corresponding technology through a meeting of advanced medical specialists, and the corresponding technology can be performed in medical institutions if a certain institution criteria that can be safely performed is satisfied. As for the advanced health technology B, if the review of the safety and

efficacy, as well as the possibility of performance in the applying medical institution, are assessed and judged appropriate in the advanced health assessment meeting, it is assessed in the aspect of the efficiency, social validity, need for future insurance adoption, etc., in a meeting of advanced health specialists and its performance in certain medical institutions is approved.

In Ontario, Canada, a system called Conditionally Funded Field Evaluation (CFFE) in which the government selects technologies with potential but currently lacking evidence in relation to efficiency, and supports clinical researches as a part of an evidence-generation support system of health technology when determining coverage, wherein a part is covered conditionally. The conducting institution, OHTAC, completed 10 performance assessments by 2008, and currently 25 researches are being conducted.

In major European countries like Germany, Italy, the Netherlands, France, and Sweden, the effectiveness of health technologies is assessed by selecting health technologies with high uncertainty as coverage items during a certain period and decides on coverage based on the accumulated evidence through a conditional coverage system suitable for the coverage system of each managing government.

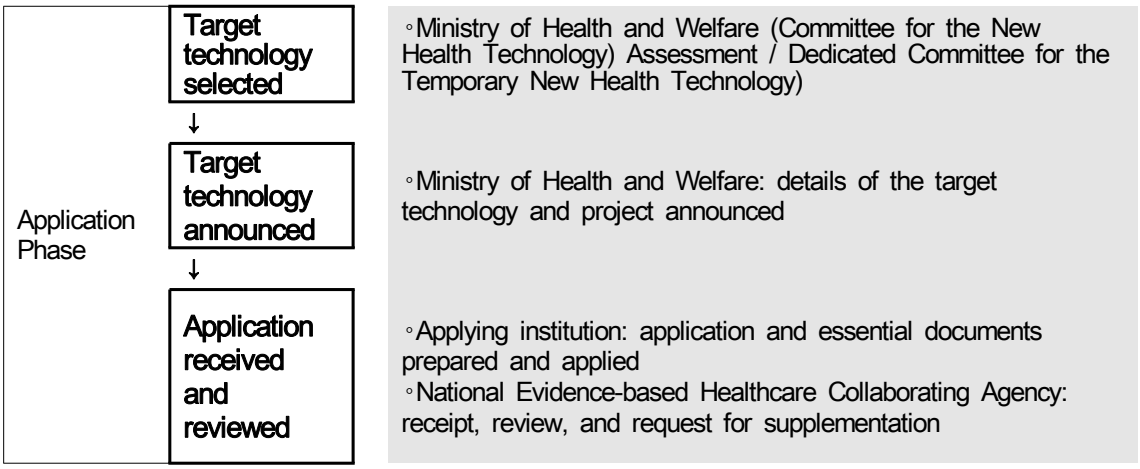
Opinions of specialists, such as the Korea Organization for Patient Group, Consumers, and Medical Ethics, were collected when developing the performance system and guideline of evidence-generation process management of the temporary new health technology based on the research results that analyzed clinical research management guideline in Korea and abroad, and it was recognized that the adoption of a system like the “Prior Approval System” is needed for medical performance, such as drugs. It was also recognized as a positive system that can prevent illegal recommendation to patients prior to the assessment of promising new health technology because of lack of evidence, and that active intervention of the government is required. Moreover, it was confirmed that an ethical review is to be held most important for the management process to secure the safety and rights of patients and provide efficient health technology, and that the patient informed consent form must be standardized and objectified in accordance with Korean and international ethics guidelines, and that there is a need to clarify the evidence of confidentiality of the patient’s personal record through verifiable informed consent procedure and

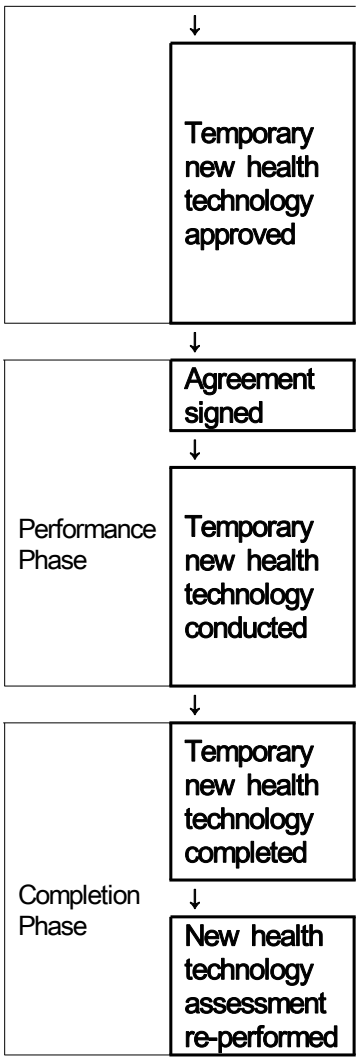
notification procedure.

The role and function of Contract Research Organizations (CRO) required in the process of performing the Temporary Approval of the New Health Technology System was discussed with Korean CROs, and it is anticipated that the input of patient case report form, uniformity with source data, etc., will require strict management of the conducting institution during the process prior to performance, and it is judged that the classification of roles with associated organizations including inspection will have to be clear because it would be a research to provide clinical evidence of the performance itself.

Responsible personnel of CMPT, which is the conditional coverage system-performing institution, were consulted, and it was confirmed that the CED performance system is currently performed after selecting Research Coordinating Centers (RCC) for each item, and that as for the composition of the research budget, only the CED research fee is paid by CMTP and the fees for clinical research procedures are paid by the investigators.

Based on the process management-related standards of clinical researches in Korea and abroad, and analysis and review of cases, the performance system of the evidence-generation process management of the temporary new health technology prepared in this research was designed to be classified into the application phase, performance phase, and completion phase, and the details, subjects, and functions of each phase as follows.





◦Dedicated Committee for the Temporary New Health Technology: medical consultation of the subcommittee reviewed → health technology reviewed in accordance with the review criteria → applying institution and principal doctor in charge reviewed → temporary new health technology reviewed → Committee for the New Health Technology Assessment introduced
◦The Temporary New Health Technology is decided by the Ministry of Health and Welfare

◦Agreement signed: National Evidence-based Healthcare Collaborating Agency ↔ conducting institution

◦Conducting institution: medical care (noncoverage) within acknowledged range, medical data electronic input, and written interim report
◦IRB of the conducting institution: monitoring
◦Dedicated Committee for the Temporary New Health Technology: regular and occasional visits for inspection and review of interim review result

◦Conducting institution: preparation of results report (within three months after completion)
◦Dedicated Committee for the Temporary New Health Technology: review of final result → introduction of a Committee for the New Health Technology Assessment

◦Committee for the New Health Technology Assessment: assessment re-performed based on medical evidence generated from the Temporary Approval of the New Health Technology System

Performance System for the Temporary Approval of the New Health Technology System

In order to provide legal evidence for the detailed performance system to be proposed, we intend to create a new clause related to the enforcement regulation, “Regulations on the Assessment of the New Health Technology,” and establish detailed performance regulations. Major revisions of the “Regulations on the Assessment of the New Health Technology” include adding the process of the Temporary Approval of the New Health Technology and adding a clause to assess the target technologies for the Temporary Approval of the New Health Technology by expanding the targets of the assessment of the new health technology by the Committee for the New Health Technology Assessment, and including it in the committee review items. Contents about the Dedicated Committee for the Temporary

New Health Technology were added as a part of the specialists' assessment committee under the Committee for the New Health Technology Assessment for the composition of a committee that can conduct a professional review on the temporary new health technology. In addition, clauses of "Procedures of the Assessment of the Temporary New Health Technology" and "Management of the Temporary New Health Technology Procedure" were newly founded. Each clause were proposed along with the comparison table of the current clause and the revision plan, and the purpose, aim, and evidence of the revision were described.

Enactment (plan) of "Regulations on Acknowledgement and Enforcement of the Temporary New Health Technology" to regulate the specifics including detailed procedures of acknowledging and enforcing the temporary new health technology will be proposed in the order of 1) submission and supplementation of application, 2) acknowledgment procedure and announcement of result, 3) revision procedure, 4) organization of the specialists' committee and subcommittee, 5) enforcement standards, and 6) enforcement process, and the purpose, aim, and evidence of the enacted will be proposed, and the cases of each country and the evidence of the enactment of other existing ordinances will be analyzed and suggested.

Detailed requirements and procedures not described in the revised plan of rules and regulations will be developed and proposed as a separate guideline.

First, the "Management Guideline for Protection of Patients' Human Rights" will be developed as a separate guideline in order to protect patients participating in the temporary new health technology because the patients' rights should be protected the most. For this purpose, only the minimum standards will be suggested for the inclusion in the patient information sheet, and standardized indemnification by laws were prepared to prevent disadvantage to patients participating in the performance.

Second, the "Report of Conflict of Interest and Management Guideline" was prepared with reference to the report of conflict of interest in clinical research institutions in and outside Korea to be referred to when the IRB of each conducting institution checks and it manages the conflict of interest of the participating research staff including the principal investigator arising from conducting temporary new health technology. By developing and suggesting an "Open Report of the Conflict of Interest" that can be innately applied in the process of the temporary new health technology,

management of the temporary new health technology performance will be strictly free of conflict of interest on a national level.

Third, the opinion-making organization IRB was utilized to develop “Authorship and Proprietorship of Research Outcomes Management Guideline” in accordance with Research Planning and Management Guideline Section 2, Clause 7 of National Evidence-based Healthcare Collaborating Agency to protect the authorship, proprietorship, and management of research results generated during and after performing the temporary new health technology.

In addition, audit contents of the reviewer were developed for fair and objective review of the applying institutions in accordance with the standards and audit items determined in advance, and the announcement (plan) was prepared as “Bronchial Thermoplasty” as an example to announce health technologies acknowledged as the temporary new health technology.

It is expected that objective and clear clinical evidence, which the government wants, of new health technologies acknowledged temporarily will be provided while protecting the safety of patients if an active and systematic national level of support is secured and an objective and detailed management system is established based on the research results. In addition, health technologies provided to the patients are expected to maintain a certain level of quality, and may contribute to the re-performance process of assessing the new health technology because the objectivity and transparency of the generated evidence can be secured. Providing an opportunity to select medical technologies currently unavailable to the patients will contribute to the protection of health rights, and it is expected to be of positive effects on the fostering of the new health technology on a national level and on the early adoption of promising health technologies.

For the Temporary Approval of the New Health Technology to be successfully adopted using announcements, regulations, and guidelines deduced from researches, the principal investigators must conduct researches in accordance with the approved protocol, and the Dedicated Committee for the Temporary New Health Technology will have to perform a strict process management. In addition, issues that may occur during the process of acknowledging the temporary new health technology and issues that require social agreement and discussion will have to be resolved through

opinions of specialists and sufficient discussion between the concerned parties and ultimately be determined by the policy arbiter. To operate the Temporary Approval of the New Health Technology System efficiently and increase its application, data established through evidence generation will have to be released within limits of not interfering with personal information, and the research outcomes will have to be shared with countries performing health technology assessment through international cooperation in order to discuss improvements to be made on this system. However, the evidence generated after performing the Temporary Approval of the New Health Technology System may be lacking to go through a new health technology assessment despite much effort, and the safety and efficacy may not be proven during the re-performance of the new health technology assessment. At this point, we will have to take the difficulties of prediction of various cases into consideration, and need to prepare specific procedures and standards through future researches.

new health technology, research phase health technology, temporary approval, clinical trial management