Provisional translation

Fiscal 2022

Application Guidelines

for Moonshot Research and Development program

Project Manager (PM)

(3rd Application)

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Division of Moonshot Research and Development Program,
Office of Project Management

Japan Agency for Medical Research and Development
(AMED)

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Chapter 1. Introduction

These Application Guidelines specify provisions for the solicitation of applications for the post of project manager (“PM”) for a major groundbreaking research and development program, which is administrated by the Japan Agency for Medical Research and Development (hereinafter referred to as “AMED”).

1.1 Program Overview

1.1.1 Current status of Program

In January 2020, the Council for Science, Technology and Innovation (“CSTI”) made the decision to promote ambitious, moonshot R&D projects (so-called “moonshots”) to be founded on innovations beyond the reach of conventional technologies, with a view to creating disruptive innovations of Japanese origin. Initiatives are underway by the Cabinet Office and corresponding ministries and agencies with six goals in mind. In July 2020, the Health and Medical Care Strategies Promotion Headquarters identified Moonshot Goal #7 “Realization of sustainable care systems to overcome major diseases by 2040, for enjoying one’s life with relief and release from health concerns until 100 years old” for the health and medical care sectors (“MS Goal #7”).

Pursuant to this MS Goal #7 and based on R&D concepts specifying sectors and domains in which challenging R&D activities are to be promoted by the Cabinet Office (CAO), the Ministry of Education, Culture, Sports, Science and Technology (MEXT), the Ministry of Health, Labour and Welfare (MHLW), and the Ministry of Economy, Trade and Industry (METI), AMED will promote R&D activities to achieve the ambitious groundbreaking goals for future society, identifying social issues that present significant challenges and seeking to find solutions that would have epochal impact

For references purposes, “The basic approach for the Moonshot Research and Development Program” is attached as Appendix 1.

In order to carry out the moonshot R&D projects program ("the Program"), AMED has appointed Dr. Toshio Hirano, President of the National Institutes for Quantum and Radiological Science and Technology, as the moonshot program director ("PD") for MS Goal #7, and has solicited applications for the post of project manager ("PM"), who will be responsible for proposing and managing R&D projects aimed at achieving the MS Goal #7 and realizing its concepts as shown by the figure below (please also refer to Appendix 3 “Moonshot goal of health and medical field”). The keyword of the FY2020 solicitation of applications was "chronic inflammation”, and five suitable PMs for moonshot projects were selected*.

* https://www.amed.go.jp/en/program/list/18/03/001.html

Another disease that must be tackled in order to achieve MS Goal #7 is cancer. Efforts for bringing about a "the society with zero-cancer"*[2] are extremely important. Research is being conducted around the world with the aim of beating cancer. The U.S.-Japan Competitiveness and Resilience (CoRe) Partnership, announced in a Japan-U.S. joint statement on April 16, 2021, includes research cooperation in the cancer field. As indicated in Appendix 6, "Supplementary information to the 3rd applications from the PD," this application is seeking a PM to manage innovative research and development that is novel, innovative, and takes feasibility into consideration, from the perspective of chronic inflammation, a keyword for MS Goal

#7. From the perspective of promoting research and development collaboration based on the above Japan-U.S. joint statement, this application will require a partnership with researchers in U.S.-based research institutions.

*2 A society where people can overcome cancer for enjoying one's life with relief and release form health concerns until 100 years old (Appendix 5 "R&D concept for Moonshot Goal #7")

1.1.2 Project goals and results

The MS Goal #7 and R&D concepts to be addressed by applications solicited under this Program:

(1) MS Goal #7

The Goal of this Program is "Realization of sustainable care systems to overcome major diseases by 2040, for enjoying one's life with relief and release from health concerns until 100 years old."

Three R&D Targets defined to achieve the MS Goal #7 are as follows:

Target 1: Realization of a society where everyone can prevent diseases spontaneously in daily life.

Target 2: Realization of medical networks accessible for anyone from anywhere in the world.

Target 3: Realization of drastic improvement of QoL without feeling load.

For more information, refer to "Moonshot goal of health & medical field" attached hereto as Appendix 3 and "Moonshot Goal #7" attached hereto as Appendix 4.

(2) R&D concept

The R&D concepts set forth examples of R&D activities and the direction of such R&D activities to achieve the MS Goal #7. For more information, refer to "R&D Concept for Moonshot Goal #7" in Appendix 5.

1.2 Program Structure

1.2.1 Program Implementation Systems

(1) Overall system

AMED will supervise overall Program operations. The program director ("PD") appointed by AMED will be responsible for overall program management to achieve the MS Goal and realize the concepts.

Under the PD's direction, the selected PMs will implement R&D projects to achieve the MS Goal #7 and related concepts.

(2) Roles of the PD

The major responsibilities of the PD appointed to achieve the MS Goal #7 and realize the R&D concepts are as follows:

1. Build a strategic portfolio (a management plan summarizing policies regarding project structures (mixes) and resource allocation) and promote R&D activities in a challenging and systematic way, with the achievement of the MS Goal #7 and realization of the R&D concepts in mind.
2. To build a strategic portfolio, adopt several projects using different research methods selected in light of the innovative and ambitious nature of the R&D activities envisioned and the scope of future socioeconomic consequences.
3. Continually monitor R&D activities under the portfolio, reappraise the portfolio according to the status of research activities, and exercise unified direction and supervision over the PMs, who in turn are responsible for administering each project.
4. Take the lead in portfolio reappraisals based on evaluations by outside experts and advice from the strategy's promotion council.

(3) Roles of the PMs

To achieve the MS Goal #7 and realize the R&D concepts, the PMs will, on their own authority and responsibility under the PD's direction, promote the redirection of individual R&D themes within the projects based on the status of R&D activities, including accelerating or extending the project timeframe and spinning off results, demonstrating both agility and flexibility. The PMs' duties include the following:

1. Under the direction of the PD, refine a proposed project during an open call to improve it, draw up a R&S plan (target setting of R&D projects, preparation of R&D details and implementation schedule, establishment of an R&D system to implement the project, and formulation of a plan to allocate research funding to participating R&D institutions in the project), and strategically implement the project.
2. Properly manage intellectual property and information, and actively and strategically promote international cooperation.
3. Objectively evaluate the research content, seek sponsors from private enterprises if R&D is at the phase at which private funding can be used, and try to draw on private funding. In addition, conduct bi-directional communication activities (public dialogue on science and technology) to explain the research activities to society.
4. Develop a data management plan (DMP)*[1] that defines the data to be managed, and also aggregate metadata about the data to be managed from researchers based on DMP and submit

the metadata to AMED. In addition, with system such as the Research Data Infrastructure System, store and share the data to be managed, and publish the data to the extent necessary[*2].

*1 For the data management plan, refer to Chapter 7.

*2 Metadata is not the data itself. The term refers to descriptive information concerning data characteristics, including data title, description, manager and location, contact details, and policies on data storage, sharing and public release.

(4) Roles of contributing participants

Contributing participants will implement their respective R&D assignments in the R&D projects as instructed by the PM to achieve the MS Goal #7 and realize the concepts.

(5) U.S. Partnership researcher

Principal Investigator (PI)-level researchers being affiliated with a US research institute and receiving or will receive R&D funding in the U.S. in the future and who will conduct collaborative research related to this R&D.

* Regarding (1) through (3) above, refer to “Guidelines for Operation and Evaluation of the Moonshot R&D Program (Goal #7)” attached hereto as Appendix 2.

1.2.2 Roles of the Principal Institution and Subsidiary Institutions

R&D projects in this Program will be implemented by the principal institution and also subsidiary institutions if required.

(1) *Principal institution* refers to the institution with which the PMs are affiliated, serving as the principal role of project management. The principal institution will conclude a contracted R&D agreement directly with AMED and seek to ensure the effective and efficient undertaking of PMs’ activities. Its primary obligation will be to support PMS’ activities. The principal institution must be a domestic research institution as described in Chapter 2.

(2) *Subsidiary institution* refers to the institution(s) with which contributing participants are affiliated. The subsidiary institution(s) will implement R&D assignments as instructed by the PMs. In principle, subsidiary institutions will pursue R&D activities based on agreements concluded with the principal institution.

Chapter 2. Application Requirement

2.1 Applicant qualifications

Pursuant to “Guidelines for Operation and Evaluation of the Moonshot R&D Program (Goal #7)” (attached hereto as Appendix 2), the nationality of applicants for PMs are not considered. However, PMs are principally based in Japan after being appointed. Furthermore, the applicant must belong to (or have the prospects of belonging to) organizations that meet the following requirements throughout the course of the R&D project implementation period, even if, during the course of the R&D project, PMs reach retirement age and the end of their term of office, so PMs are transferred to another organization, etc. The detailed conditions are as set forth below.

2.1.1 Requirements for the Principal Institution and Subsidiary Institutions

The principal and subsidiary institutions with which the PMs and contributing participants are affiliated must be domestic institutions meeting requirements (1) through (5) below. If a researcher unaffiliated with a particular research institution or affiliated with a research institution outside Japan is selected as PMs, they will be required to establish an affiliation with an institution meeting the requirements below by the date on which the agreement is concluded or a date designated by AMED. If no such affiliation is established, the selection will be canceled. In addition, to confirm the capacity and competence of the principal institution and subsidiary institutions to fulfill the contracted R&D agreement, the institutions may be required to submit reference materials describing major activities, assets, liabilities, and other financial data during the review process.

The institutions with which contributing participants are affiliated may be either domestic institutions meeting requirements (1) through (5) below or overseas institutions meeting requirements (2) through (5) below.

(1) “Research Institute” refers to institution with the characteristics shown in (a)–(h) below.

(a) National facilities or other organizations[*2] (limited to institutions/facilities where PIs are employed in an educational position, a research position, a medical care position[*3], a welfare service position[*3], a designated position[*3], or a fixed-term contract researcher position).

(b) Research institutes, etc., affiliated with local governments.

(c) Universities as prescribed under the School Education Act (Law No. 26 of 1947) or universities affiliated research institutes, etc. (including inter-university research institute corporations).

(d) R&D divisions or research laboratories, etc. of private enterprises.

(e) Special private corporations, general incorporated associations, general incorporated foundations, public interest incorporated associations, or public interest incorporated foundations (hereinafter referred to as “special private corporations, etc.”) whose main activity is research.

(f) Independent administrative corporations as prescribed under Article 2 of the Act on General Rules for Incorporated Administrative Agencies (Act No. 103 of 1999, partially amended on June 13, 2014) or local incorporated administrative agencies as prescribed under Article 2 of the Act on

Local Incorporated Administrative Agencies (Act No. 118 of 2003) whose main activity is research.

(g) Non-profit, charitable technology research associations[*4].

(h) Other institutions deemed appropriate by the President of AMED.

*1 Refers to a research institute, an inspection and certification institute, an educational and training facility, a medical and rehabilitation facility, a reformatory and internment facility, and a work facility affiliated with a government organization as prescribed by the Cabinet Office and under Article 3 Paragraph 2 of the National Government Organization Act.

*2 Limited to persons affiliated with a hospital or an institution that conducts research.

*3 Experimental research institutes affiliated with local governments.

*4 Technology Research Association as prescribed under the Technology Research Association Act (Law No. 81 of 1961).

(2) In the case that the project is selected, the research institute's facilities and equipment can be used for carrying out the project.

(3) In the case that the project is selected, the research institute can carry out administrative procedures such as contract procedures.

(4) In the case that the project is selected, the research institute is capable of responsibly handling any intellectual property (IP) rights (including patents and copyright, etc.) and R&D data generated through implementation of this program.

(5) The research institute can continue to promote R&D even after this program has concluded and can support researchers in relation to this program.

2.1.2 Research Implementation System

An applicant should assume that the research institution with which the applicant is or will be affiliated is the principal institution and that projects will be implemented under a research implementation system involving the principal institution and other multiple research institutions, including prospective subsidiary institutions. In addition, it should be noted that those subsidiary institutions are not allowed to outsource the research or operation containing any element of the R&D projects to other institutions (Re-subcontracting) as this program requires both principal institution and the subsidiary institutions to take place the R&D activities in an integrated manner. Furthermore, excepting for the U.S. partnership researcher defined in Chapter 1, collaborative research system is unacceptable under the moonshot R&D system in principle.

Nevertheless, the portfolio created by the PD before the conclusion of the contracted R&D agreement following PM selection may result in changes in the research implementation system.

Note 1: Regarding the present MS Goal #7, the same individual may propose one project as a PM and participate in another proposed project as a contributing participant. However, in the case that those proposals are nominated as candidates for adoption both for this time and for the 2nd solicitation of applications which will be conducted at the same time, AMED may make certain adjustments, such as reducing the R&D funds or rejecting that individual's participation as contributing participant pursuant to Chapter 5 "Eliminating Unreasonable Redundancy or Excessive Concentration of Research Funds".

Note 2: Regarding the present MS Goal #7, the same researcher may be named as contributing participants in two or more proposed projects. However, if two or more proposals in which the same researcher is named as contributing participants are selected, AMED may make certain adjustments, such as reducing R&D funds or rejecting the researcher's participation in one or more R&D project themes for which his/her participation is proposed.

2.2 Important Items Regarding Applications

2.2.1 Contracted R&D Agreements

In implementing selected R&D projects, as a general rule a contracted R&D agreement shall be concluded between the research institution carrying out the R&D project and AMED. Please read Chapter 8 for more information.

2.2.2 Cross-ministerial Research and Development Management System (e-Rad)

The Cross-ministerial Research and Development Management System (hereinafter referred to as "e-Rad"*) is a system that makes available online the series of processes relating to management of solicitation-based research funding systems at individual ministries and agencies (receipt of application => selection => management of selected projects => application to register research achievements and accounting reports). In submitting an application, please be sure to carefully read the program outline, the outline of R&D projects for which applications are being solicited, and other information provided and thoroughly consider the kinds of results your proposed R&D project can produce before completing the proposal documents. For details, please refer to Chapter 5.

* "e-Rad" is the acronym for the Cross-ministerial Research and Development Management System, composed of the first letters of Research and Development, preceded by the "e" of electronic.

2.2.3 Security Trade Control (Countermeasures to Technology Leakage Overseas)

At research institutes, a large quantity of cutting-edge research is carried out. At universities in particular, with the increase in international students and foreign researchers due to internationalization, there is an increasing risk of cutting-edge research and/or research materials/equipment flowing out of Japan and being misused for the development/production of weapons of mass destruction or for other improper uses. For this reason, it is imperative that in carrying out various type of research activities—including contracted R&D under this program—research institutes implement systematic measures to ensure that research accomplishments that could be used for military purposes do not fall into the hands of persons suspected of being involved in the development of weapons of mass destruction or with terrorist organizations or other concerning activities.

In Japan, export regulations* are enforced in accordance with the Foreign Exchange and Foreign Trade Act (Law No. 228 of 1949) (hereinafter referred to as the "Foreign Exchange Act"). Accordingly, in the case that a person wishes to export (provide) goods or technology prescribed under the Foreign Exchange Act, generally they are required to obtain the permission of the Minister of Economy, Trade and Industry. Please

be sure to comply strictly with all laws, guidelines, and directives, etc., issued by the Japanese government, beginning with the Foreign Exchange Act. In the case that R&D is carried out in infringement of relevant laws or guidelines, in addition to the imposition of punishments and penalties according to legislation, the allocation of R&D funds may be suspended and the decision to allocate R&D funds may be cancelled.

* Currently, under Japan's security export control system, there are two types of regulations based on international agreements: (1) a system under which the permission of the Minister of Economy, Trade and Industry must generally be obtained in the case that a person wishes to export (provide) goods (technology) with specifications or functions above a certain level—mainly carbon-fiber and numerically controlled machine tools, etc.—("List Control"), and (2) a system under which the permission of the Minister of Economy, Trade and Industry must generally be obtained in the case that a person wishes to export (provide) goods (technology) to which List Control do not apply and which fulfill certain conditions (use, demand, inform conditions) (Catch-all Regulations).

Not only the export of goods but also the provision of information is subject to regulations under the Foreign Exchange Act. When providing List Control technology to a foreign national (non-resident of Japan) or outside of Japan, permission must be received in advance. "Provision of technology" includes not only the provision of blueprints/designs, specifications, manuals, samples, prototypes, and other technological information via paper, e-mail, CD, DVD, USB flash drive, or other storage medium but also the provision of operational knowledge through technological guidance or skills training and technological support at seminars, etc. There are cases in which large amounts of technological exchange that could be subject to regulation under the Foreign Exchange Act may be included in joint research activities or when international students are involved.

On the Ministry of Economy, Trade and Industry website, details regarding security trade control are provided. Please refer to the following for further details (in Japanese).

- Ministry of Economy, Trade and Industry: Security Trade Control (general)
  https://www.meti.go.jp/policy/anpo/
- Ministry of Economy, Trade and Industry: Handbook for Security Trade Control
  https://www.meti.go.jp/policy/anpo/seminer/shiryo/handbook.pdf
- Center for Information on Security Trade Control
  http://www.cistec.or.jp/
- Guidance for Management of Sensible Nuclear Technology (SNT) in Relation to Security Trade Control (for universities/research institutes)
  https://www.meti.go.jp/policy/anpo/law_document/tutatu/t07sonota/t07sonota_jishukanri03.pdf

2.2.4 Stringent Implementation of United Nations Security Council Resolution 2321

In response to North Korea's nuclear test of September 2016 and its repeated ballistic missile launches, on November 30, 2016 (local time in New York) the United Nations Security Council (hereinafter referred to as "the UN Security Council") adopted Resolution 2321, substantially adding and bolstering sanction measures against North Korea. With regard to this, on February 17, 2017 the Japanese Ministry of

Education, Culture, Sports, Science and Technology (MEXT) issued to all relevant organizations its Directive Regarding the Stringent Implementation of United Nations Security Council Resolution 2321 (MEXT No.98 of FY2017) .

Paragraph 11 of the Resolution suspended not only scientific and technical cooperation regulated by the Foreign Exchange and Trade Act but also all cooperation other than for the purpose of medical exchanges. It is vital that research institutions take care to stringently implement the Resolution in the course of all research activities including the relevant contracted research.

Please see below for the United Nations Security Council Resolution 2321 (2016):

- https://www.undocs.org/S/RES/2321(2016)

2.2.5 Active participation and achievement by young researchers

In line with the common intent of programs funded by public research funding AMED broadly promotes the nurturing and fostering of researchers who will shoulder the future of Japan and who through which R&D accomplishments will be put to use for the good of society. Subsequently, it is desirable that enthusiastic efforts are made to assign young researchers in AMED programs.

"Young researchers" are those to whom all of the following apply.

Males who are under 40 years old as of April 1, 2022 (i.e. who were born on or after April 2, 1982); females who are under 43 years old as of April 1, 2022 (i.e. who were born on or after April 2, 1979); or those who acquired their doctorate less than 10 years ago. However, for those who have taken pre- or post-natal leave or child-rearing leave, the age restriction (under 40 years old for males and 43 years old for females) may be extended by the number of days they took the leave.

2.2.6 Data sharing

With regard to the treatment of data arising from the accomplishments of R&D in the medical field, the importance of data sharing between researchers is recognized as the data is also useful to researchers sharing the same awareness of problems. At the same time, in the case of data arising from R&D implemented through public funding, because of its highly public nature and considerable public benefit moves are afoot to attempt to expand the possibility of their secondary use through registration with repositories and timely release. Moreover, in order to aim for the practical application of R&D there is a need to share detailed and accurate clinical information and genome information among not only academic research bodies such as universities and research institutions but also the industrial sector, including private corporations that will make industrial use of such data, to cooperate and develop new diagnostic and treatment methods.

At AMED, whenever contracted R&D agreements are concluded the submission of a data management plan (hereinafter referred to as “DMP”) by research institutions is made obligatory. In addition, the AMED Basic Policy on Handling of R&D Data that compiles the definition of R&D data and policy regarding the treatment etc. of R&D data, and the Guidelines on AMED Research Data Utilization* that

compiles the specific management guidelines have been formulated, and are available on the AMED website. For the details regarding submission of DMPs, please refer to Chapter 7.

Furthermore, the contracted R&D agreements with AMED in principle prohibit the research institutions, etc. from disclosing or providing to third parties any type of R&D data generated, acquired or collected in connection with R&D supported (contracted or assisted) by AMED. However, in cases in which it is permitted according to the AMED guidelines mentioned above, or when the prior consent of AMED has been obtained, it is possible to disclose or provide data to third parties.

In addition, R&D data is categorized into the four types of “unrestricted openly shared data,” “restricted openly shared data,” “restricted closed shared data,” and “unshared data,” while data other than data that it would be inappropriate to divulge to third parties is in principle designated as either unrestricted openly shared data or restricted openly shared data, and is required to be published. Furthermore, even if certain data falls under the categories of either unrestricted openly shared data or restricted openly shared data it is permitted to share it only with specific third parties for the duration of the period when it is treated as restricted closed shared data prior to release. For further details please refer to the Guidelines on AMED Research Data Utilization*

*https://www.amed.go.jp/koubo/datamanagement.html (in Japanese)

It should be noted that with regard to the sequence data for which the use of restricted closed shared data are promoted through the establishment of Controlled Sharing of Genome and Clinical Datasets (CANNDs),* a large-scale genome analysis platform, it has become necessary from the perspective of sequence quality assurance to submit a genome analysis protocol when whole-genome analysis is conducted.

Human whole-gene analysis is permitted only when, regardless of whether it is contracted out or not, the samples used in the whole-genome analysis in question and the results of the analyses in question (including data derived during those processes) are not taken outside of Japan, including after the research is completed. (Excluding cases in which AMED discusses the matter with researchers for an appropriate reason and after consultation with the relevant ministries and agencies exceptional permission is given by AMED.)

*AMED report material: CANNDs Implementation Plan, March 6, 2021
https://www.kantei.go.jp/jp/singi/kenkouiryou/genome/genome_dai5/siryou3-1.pdf

2.2.7 Conditions for Submitting R&D Proposals for Clinical Trials (Investigator-Initiated Trials/Company-Initiated Trials) and/or Clinical Studies (Including Some Nonclinical Studies)

AMED promotes research with a view to practical application. In particular, for research undertaking medical investigator-initiated trials or clinical studies with a view to creating innovative drugs or medical devices, or nonclinical studies aimed at conducting such trials/studies*, researchers are required to prepare and submit appropriate materials to AMED at the time of submitting the R&D proposal as well as on the commencement and at each development stage of the investigator-initiated trial or clinical study. The

materials that are required to be submitted, centered on the main materials that need to be submitted at the time the research proposal is submitted, are summarized as follows (please refer to the table provided separately). However, the table provided separately may not apply to some research. In this regard, AMED shall consult with PD, PS, and PO of the R&D projects about the respective research content and request the preparation and submission of appropriate materials at an appropriate time.

* “Nonclinical studies” refer mainly to pharmacological tests conducted in or after the final stage of candidate drug selection, toxicity tests, and pharmacokinetic studies.

(1) Schedule (road map)

Please prepare a schedule (road map) enabling understanding of the entire R&D process, from formulation of the R&D proposal to approval of products such as new drugs, medical devices, and regenerative medicine (out-licensing to a company) and/or exits such as the addition of new indications, clearly showing where the proposed research is positioned within this schedule.

(2) Investigator-initiated Trial/Clinical Study Implementation Plan

For development/practical application research aimed at receiving approval for products such as new drugs, medical devices, and regenerative medicine (licensing to businesses) and/or exits such as the addition of new indications (including some nonclinical studies), is most desirable that the Investigator-initiated Trial/Clinical Study Implementation Plan has been formulated at the time the R&D proposal is submitted, and it is required that the relevant plan clearly shows the overall study schedule as well as achievable milestones. Furthermore, a Protocol Concept* is required at the time the R&D proposal is submitted, regardless of whether the Investigator-initiated Trial/Clinical Study Implementation Plan has been completed.

* There are cases in which it may be difficult to submit a completed Investigator-initiated Trial/Clinical Study Implementation Plan when the plan for implementing the investigator-initiated trial or clinical study is at the concept stage amongst researchers or within the research institution. In such cases, researchers must submit a Protocol Concept that includes the following items. For Protocol Concepts, please provide information regarding the purpose of the R&D (including important evaluation items); background to or basis for the study plan (basis for subjects, standard treatments for subjects, and treatment plan formulation); patient selection criteria; measurement of effects and measurement criteria; statistical items (mainly analysis and judgement criteria, computation/basic for setting of target number of cases, registration period, follow-up period); and research implementation system.

(3) Regulatory Science Strategy Consultation etc.

Clinical studies (trials) aimed at applying for approval for creating new drugs must be conducted in accordance with ordinances on Good Clinical Practice (GCP). Even if the research is at the nonclinical study stage, safety testing with a view to the creation of new drugs needs to be implemented after reliability has been assured in accordance with Good Laboratory Practice (GLP). Furthermore,

regarding materials required for applying for approval—including for regenerative medicine products and medical devices—testing must be carried out based on sufficient understanding.

In addition, as a condition of their selection, R&D projects moving into the practical application stage (R&D projects that are within the target scope* of the regulatory science strategy consultation, etc. conducted by the PMDA), must be implemented in accordance with the R&D plans that are agreed on based on PMDA regulatory science strategy consultation (face-to-face advice) conducted in advance. Research institutions that have already undergone regulatory science strategy consultation, etc. (face-to-face) before project selection may engage in consultation again as necessary during the R&D period. While applicants are not required to engage in regulatory science strategy consultation, etc. (face-to-face) before applying in response to this solicitation of applications, it is preferred that they do so and reflect the results of the consultation in their research plans.

* Please refer to "2. Consultation Categories and Target Scope" in the Implementation Guidelines Regarding Regulatory Science Strategy Consultation (dated March 16, 2017)

(4) Involvement of biostatistics specialists/clinical study statisticians/biostatisticians

When conducting an investigator-initiated trial/clinical study, the basis for setting the number of cases to be studied plays an extremely important role in the success of the trial/study. The involvement of biostatisticians is essential for the overall planning of studies and analysis (especially desirable of the biostatistician has experience participating in clinical studies or trials), and it is desirable that the involvement of biostatistics specialists/clinical study statisticians/biostatisticians in the research is stated clearly at the time the application is submitted. Even if the R&D proposal is at the concept stage, information about the involvement of biostatisticians needs to be provided.

(5) Intellectual property officer and strategies leading to intellectual property/achievements

For investigator-initiated trials/clinical studies aimed at receiving approval for products such as new drugs, medical devices, and regenerative medicine (licensing to businesses), information must be provided at the time of R&D proposal submission with regard to the involvement in the R&D of an intellectual property officer (persons responsible for matter related to intellectual property) and strategies leading to intellectual property/achievements as follows. (In the case that intellectual property is owned by a company, please provide information to the extent possible.)

(A) Status of own technology

- Has a patent application been submitted? (In the case that a patent application has been submitted, please provide information about the technology content and patent application number, including for joint patents)
- Is submission of a patent application planned? (What kind of technology/achievements? When is the application to be submitted?)

(B) Status of related technology developed by others (please provide information to the extent possible at the time of R&D proposal submission)

- Results of surveys of patents acquired by others (please provide survey key words and patent database information)
- Relationship to the seeds for which the application has been submitted (restricted to cases in which self-generated technology is used)

(C) Policies related to licensing of research achievements to businesses (practical application)

- Is the research institute already collaborating with a company/business? (If so, please provide information on the intellectual property content and policies regarding future intellectual property utilization)
- Is the research institute planning to collaborate with a company/business? (What technology/achievements? When is intellectual propertization to be carried out? How are the technology/achievements to be utilized?)

(6) Status of collaboration with companies/businesses

In obtaining approval for products such as new drugs, medical devices, and regenerative medicine (licensing to businesses), collaboration with companies/businesses is important. In the case that the research institute has licensed trial results to a company/business as at the time of R&D proposal submission, or in the case of business seeds, please provide information regarding the status of collaboration with the company/business, including methods for procuring investigational drugs and obtaining safety information.

(7) Ascertaining and reporting adverse events

Please ensure that when an investigator-initiated trial or clinical study is implemented it obeys all laws/ordinances, ethical guidelines and notifications, try to ascertain any information about adverse events etc. related to the clinical trial or research, and appropriately report any adverse events in line with laws/ordinances etc.

(8) The number of clinical trial plan in jRCT

In order to carry out clinical research, it is necessary to register the clinical research with Japan Registry of Clinical Trials (jRCT) in accordance with the standards for clinical research prescribed under the Clinical Research Act. Regarding R&D proposals that incorporate clinical research, please include the “number of clinical trial plan” issued when registering clinical research plan information with jRCT in the R&D Proposal. Please note that in the case that the jRCT registration for the proposed project’s clinical research plan has not been completed by the time the R&D proposal is submitted, after the project has been adopted, please report the “number of clinical trial plan″ to AMED before the commencement of the relevant clinical research. For further details regarding the Ordinance for Enforcement of the Clinical Trials Act, please see the Ministry of Health, Labour and Welfare's website*.

* About the Clinical Trials Act (Ministry of Health, Labour and Welfare website)

https://www.mhlw.go.jp/stf/seisakunitsuite/bunya/0000163417.html

Chapter 3. R&D themes for which applications are being solicitated

The R&D project for which applications are being solicited is as follows. For an overview of this entire program, please refer to Chapter 1; for application/selection implementation methods, please refer to Chapter 4.

3.1 Scaled of R&D funds, R&D period, number of projects to be selected, etc.

#	R&D field	R&D funds required (excluding indirect expenses)	R&D implementation period envisioned	Number of adopted themes envisioned
1	Moonshot Goal #7: The research and development towards “The society with zero-cancer” through the Japan-U.S. Partnership.	No upper or lower limits are set per proposal.	Five years in principle But until fiscal year 2030 at the latest	0 ~ 1 (not fixed)

Note 1: Since there are no specified upper or lower limits per proposal, the applicant should calculate the estimated necessary budgets for the themes. Nevertheless, fund availability is limited as follows:

Available funds (approximate): 2 billion yen per proposal per five years (excluding indirect expenses).

As a condition attached to selection, changes may be requested with regard to implementation plans, including the R&D budget and research implementation system. The proposed R&D expenses may need to be changed accordingly.

Note 2: If the decision to continue the project beyond year 5 is made based on evaluations, the maximum R&D period will be until fiscal year 2030 at the latest.

Note 3: The same applicant may file applications for more than one R&D theme under public solicitation programs. However, information on the R&D themes proposed at the same time must be provided in the applicable field of the R&D proposal to indicate the absence of unreasonable overlapping or excessive concentration of research funds. For more information, please refer to Chapter 5.

Note 4: More than one R&D project may not be proposed by a single proposer for this 3rd application of FY2022. However, this does not preclude an applicant from applying to be the PMs for 2nd application of FY2022, which opens at the same time. Also, this does not preclude an applicant from applying both the MS Goal related solicitations from a funding agency other than AMED and the present MS Goal #7 related AMED’s solicitations.

Note 5: Both Japanese and English shall be the governing language for the purposes of this application. If there is any discrepancy between Japanese version and English version, Japanese version will take precedence.

Note 6: Please refer to Appendix 6 “Supplemental Information to the 3rd application from PD”.

- Important notes

1) Research projects must have a clear roadmap to their final objectives.

2) In order to clarify these objectives, on the R&D proposal, indicate in detail the scientific results the research is expected to produce together with the scientific, social, and economic benefits that these results will provide.

3) Pay attention to the following when creating the R&D proposal.

- Include a detailed but succinct overview of the research based on an understanding of the purpose of the moonshots and the objectives of the themes being solicited. The overview must include the objectives of the research, its features and what makes it original, the potential for achieving the intended results, the results that are expected, etc.
- Include a comparison of the ideas/originality that led to the proposal by PMs and the issues which past research directions have been unable to address.
- Create a roadmap to achieving the overall objectives of the research. In the roadmap, indicate the targets and achievement points that will serve as research milestones to be achieved for each research (development) item, and succinctly indicate how they are linked to each research (development) item.
- With relation to the future concepts following the conclusion of the research, indicate any envisioned future ripple effects, impact, etc.
- Include an organization diagram that clearly indicates the roles and relationships of mutual cooperation between PMs, co-investigators, U.S. Partnership researcher, collaborating companies, primary subcontractors, etc.

4) The research must appropriately involve Patient and Public Involvement* ("PPI"). If the research is deemed not to require PPI, the R&D proposal must include an explanation of the reasons for arriving at this conclusion.

* https://www.amed.go.jp/content/000055212.pdf (in Japanese)

5) In the event that information and communications technologies (ICT) including AI are used in the creation of evidence, ensure this is done in conjunction with the appropriate specialists required for the execution of research.

6) It is preferable that any biostatisticians involved in the research cooperation system are either in possession of certified trial statistician qualification such as Senior Trial Statistician conferred by the Biometric Society of Japan etc. or in possession of certification conferred by the Japan Statistical Society and have accumulated experience as a clinical study statistician (for example, five or more clinical studies).

7) It is preferable that any epidemiologists involved in the research cooperation system are professionals with certified qualifications as a (certified) professional conferred by an academic society.

3.2 Overviews of R&D project

3.2.1 Timeframe of R&D project

The timeframe of the R&D project under this Program is initially projected to be five years from the time of the PM selection. Depending on the results of the Year 3 evaluation, the project timetable may be revised (accelerated or extended) or the project terminated.

Evaluations will take place not just in Year 3, but in Year 5 and whenever the PD deems evaluations appropriate. The evaluation results at these timepoints may lead to schedule revisions or to project termination. If the decision is made to extend the project beyond five years, the project timeframe will be until fiscal year 2030 at the latest.

3.2.2 Scope of Program Funds

The most optimal amount of funds required per a PM at the time of its proposal shall be indicated depending on the proposed R&D project. Initial R&D project funds required will be determined by the PD with the cooperation of outside experts during the post-selection project elaboration phase.

3.2.3 Details of R&D themes

Based on the intentions of the PD, who wishes for research to be carried out in unison with MS Goal #7, this application seeks a PM to manage tasks related to the creation of a "the society with zero-cancer" from the perspective of chronic inflammation, a keyword for MS Goal #7. The priority will be given to proposals with the potential to produce synergistic effects for MS Goal #7 as a whole and to maximize the results of MS Goal #7. Proposals with innovations that apply to one of the three targets are, of course, welcome, but we also welcome bold proposals whose innovations span multiple targets, or which are linked to other targets, and are not bound by conventional frameworks. Furthermore, for these moonshots, proposals must include research and development in conjunction with researchers in U.S.-based research institutions from the perspective of research cooperation in the cancer field based on the Japan-U.S. joint statement of April 16, 2021 (U.S.-Japan Competitiveness and Resilience (CoRe) Partnership). This will require collaboration with Principal Investigator-level researchers who are currently receiving research and development funding in the U.S., or who will receive it in the future, so applicants must submit a document indicating its intention to participate in the research (Form 3). While the solicitation of applications is being conducted partly in order to support the advancement of the U.S.-Japan CoRe Partnership, but this does not preclude the participation of researchers from other regions, such as Asia or Europe, in the research group.

Note: When themes are selected as R&D projects, research can be carried out conditionally until Japan-U.S. cooperation has been deemed to have begun.

Chapter 4. Schedule, Review Methods etc.

4.1 Timeframe of acceptance of Proposal and schedule of actual selection

As of the start of the solicitation process, the Program timetable up to the actual selection shall be as follows.

Timeframe of acceptance of proposal and schedule of actual selection (Please be aware of notes 1 to 11 below).	
Timeframe of acceptance of proposal	**From March 7, 2022 (Monday) to noon of May 10, 2022 (Tuesday) (no late submission accepted)**
Document review	From mid-May 2022 to early-June 2022 (tentative)
Hearing	Late-July 2022 (tentative)
Notification of selection results	Mid-October 2022 (tentative)
Start of R&D (conclusion of agreements)	December 15, 2022 (Thursday) (tentative)

Note 1: Please note that no documents will be accepted beyond their submission deadlines.

Note 2: AMED may refuse to accept incomplete applications and applications that are not in order.

Note 3: After receiving a proposal, AMED may contact the PMs by email or telephone to perform confirm administrative matters. If you are contacted, please reply promptly using the method indicated by AMED (proposals may be disqualified if no response is received).

Note 4: Interviews may be conducted via the web.

Note 5: In principle, notification of a hearing will be issued by email to the PMs of the relevant theme at least one week in advance. (This notification will not be sent to applicants not required to attend the hearing and will not be sent at all if no hearing takes place, in which case applicants should wait for a selection results notice.) Updated information on hearing details and timetable, if any, will be posted as part of solicitation information on the AMED website set forth in Chapter 5. AMED will not answer individual questions regarding who is required to attend the hearing.

Note 6: The PM may be notified by email of inquiries arising during the document review process. Responses to such inquiries shall be made promptly by the methods designated by AMED and by the deadlines designated by AMED at the time of the inquiry's notification.

Note 7: The hearing will be done for the PM, in principle. The hearing date may not be changed.

Note 8: Following the hearing, appropriate administrative follow-up may be undertaken with the PMs. Responses to such follow-up efforts must be made promptly by the methods designated by AMED.

Note 9: The methods used to conduct interviews may be changed, or the interviews themselves may be cancelled, due to unforeseen circumstances such as infectious disease epidemics or societal disturbances caused by disasters. If interviews are cancelled, the document screening period may be extended.

Note 10: The PMs of research themes selected as candidates may be requested to revise their proposals' objectives, implementation plans, implementation organizations, etc., based on screening results. Selection terms may also be added due to changes in R&D expense totals. In the event of changes such as these, the viability of the proposals may be reexamined.

Note 11: The “Tentative Date” has been set in consideration of the time period required for formulating an optimal R&D plan at the time of submitting the proposal with a view to the timing of the commencement of R&D, and to enabling researchers to make the preparations they can between the time of the decision to adopt the project and the time the contracted R&D agreement is concluded so that R&D can commence as swiftly as possible after conclusion of the agreement, and does not guarantee conclusion of a contracted R&D agreement, as is the case with regard to the handling of all other items stipulated in these Application Guidelines. In order to conclude the contracted R&D agreement on the “Tentative Date”, the cooperation and efforts of research institutes, etc. regarding the formulation and/or revision of R&D plans (including R&D funds and R&D systems) are required. AMED will also endeavor to coordinate with the PD of a project as swiftly as possible to ensure that the contracted R&D agreement can be concluded as early as possible.

4.2 Method for Reviewing Proposal Documents

4.2.1 Review Method

For the purpose of R&D theme selection, preliminary theme evaluations (reviews) will be performed by evaluation committee members chosen by the AMED President from outside experts to evaluate the needs, objectives, and validity of the plans and to determine budget allocation pursuant to Appendix 2 “Guidelines for Operation and Evaluation of the Moonshot R&D Program (Goal #7)”. The theme evaluation committee will perform the evaluations on the predetermined items. AMED will select PMs and themes based on the committee’s evaluations and consultations with the PD and advice from the strategy’s promotion council.

Furthermore, as Japan-U.S. cooperation is a mandatory element of this 3rd application, researchers from U.S.-based research institutions (international reviewers) will take part in the screening process. Applicants must therefore submit a "(Form 4) Check Sheet for security trade control" when submitting their proposals. See Chapter 2 for details regarding security export control.

(a) Reviews shall be conducted in private by a Project Evaluation Panel established by AMED.

(b) The theme evaluation committee will undertake document reviews and, if necessary, interviews (hearings) about the submitted proposal documents* and evaluate them through discussions.

*PMs may be required to submit additional reference or other materials during the review process.

(c) During the selection process, PMs may be required to modify the objectives, implementation plans, implementation systems, or other aspects based on the review results* or be set selection conditions involving changing the amount of expenses. In such cases, the validity of the plans may be re-examined.

*If PMs are selected, the objectives and other aspects modified will be among the metrics in interim and ex post evaluations. For the management and evaluation of selected themes, refer to Chapter 9.

(d) Following the reviews, AMED will notify PMs of the selection results and related decisions, if any. Note that AMED will not respond to any inquiries regarding the status of the ongoing selection process.

(e) The members of the theme evaluation committee are bound by the confidentiality obligations prohibiting them from leaking or mishandling any confidential information obtained in connection with their positions, even after they leave such positions.

(f) The names of the selected R&D themes and PMs will be announced at the AMED website and elsewhere later. The names of all evaluation committee members for AMED will be announced once in every fiscal year. (Refer to Chapter 6 for more information of online announcements, etc.)

(g) From the standpoint of conducting fair and transparent evaluations, management of conflict of interest for Project Evaluation Panel members shall be implemented in accordance with AMED's "By-Law Regarding the Treatment of Conflict of Interest Management for Members of the Research & Development (R&D) Project Review Panel". In the case that any of the following items apply to a Project Evaluation Panel member, they are required to report to AMED that they are subject to management of conflict of interest and generally shall not be involved in evaluation of the relevant project. However, in the case that the Project Evaluation Panel Chair recognizes that participation by the Project Evaluation Panel member in question is especially necessary for ensuring the scientific validity of the evaluation and that their ability to make appropriate and transparent decisions as part of the evaluation is not impaired, the Project Evaluation Panel member may participate in the evaluation of the relevant project.

1) The evaluatee is a family member/relative of the Project Evaluation Panel member.
2) The evaluatee is affiliated with the same department at a university, the National Research and Development Agency, or a national research institution or other research institute or business enterprise as the Project Evaluation Panel member.
3) The evaluatee has worked closely with the evaluator on a joint research project within the past three years including the fiscal year in which the Project Evaluation Panel evaluation is conducted.
4) The Project Evaluation Panel member and evaluatee have a close teacher-disciple relationship wherein one provided guidance and instruction regarding the other's doctoral thesis.
5) The evaluatee has received economic benefits from the Project Evaluation Panel member within the past three years, including the fiscal year in which the Project Evaluation Panel evaluation is conducted, of more than one million yen.
6) The Project Evaluation Panel member is in a direct competitive relationship with the evaluatee.
7) Other serious conflicts of interest are recognized to exist.

(h) Program applicants and persons intending to apply for the program are prohibited from lobbying AMED executive officers, Program Director (PD) or evaluators regarding evaluations or project selection.

(i) Documents etc. regarding management of R&D from the perspective of verifying the appropriateness of R&D management, AMED may in future require submission of the materials regarding drugs*1, regenerative medicine etc.*2 and medical devices*3. In addition, inquiries may be made regarding the content of these materials as necessary. Please refer to the following web pages for more details.

*1 https://www.amed.go.jp/koubo/iyakuhin_check.html

*2 https://www.amed.go.jp/koubo/saisei_check.html

*3 https://www.amed.go.jp/koubo/medical_device_check.html

(j) Use of the results of previous AMED Mid-term Reviews and Ex-Post Evaluations about related projects in the course of the program there may be cases in which, from among research expenses received in the past by applicants, reviews are conducted of the submitted proposal documents based on the Mid-term Reviews and Ex-Post Evaluations of R&D projects put to use to create the current project proposal the current proposed project.

4.2.2 Review Items and Viewpoints

Proposal documents in this Program will be reviewed mainly from the following viewpoints for the purpose of selecting the theme(s):

(A) PMs have expert knowledge and a wide human network such as relevant researchers inside and outside Japan, to promote cutting-edge research.

(B) PMs have management and leadership skills such as the ability to establish an optimal R&D system, and nimbly review the system according to the status of progress.

(C) The project targets and contents proposed by PMs (hereinafter referred to as proposal details) are challenging and based more on bold ideas than existing proposals and comprise innovative proposals from which a substantial impact on future industry and society is expected.

(D) From the perspective of technical feasibility and practical use of its R&D results in society, there are appropriate scenarios (hypothesis for success) for achieving the MS Goal #7 by 2040 which can be clearly explained.

(E) The proposals contain top-level R&D capabilities, knowledge, and ideas, regardless of whether they come from inside or outside Japan.

(F) The proposals should be synergistically effective for whole MS Goal #7 projects and maximize the results of MS Goal #7.

(G) Proposals must involve cooperation with Principal Investigator-level researchers from U.S.-based research institutions. The research and development must be likely to produce synergistic effects through Japan-U.S. cooperation.

4.3 Enhancement of AMED Theme Evaluations

With the aim of enhancing the Project Evaluation Panel and conducting even more appropriate evaluations, AMED is endeavoring to secure panel members with a high degree of knowledge in specialized fields and

paying careful attention to membership diversity from the perspectives of age, gender, and affiliated institution.

For this reason, in the case that a R&D project is adopted under this program, AMED may request that researchers provide their cooperation as AMED Project Evaluation Panel members.

Chapter 5. Preparing proposal and submitting method

5.1 Preparing proposal

5.1.1 Proposal documents required for application

No.	Required / Optional	Required proposal documents	Remarks
1	Required	(Form 1) R&D proposal	Both in Japanese and in English required
2	Required	(Form 2) Data sheet of the researcher's number and the budget	Either in Japanese or in English required
3	Required	(Form 3) Letter of Intent	In English only
4	Required	(Form 4) Check sheet for security trade control	Either in Japanese or in English required
5	Required	Biography of U.S. Partnership researcher	Free format. In English only.
6	Optional	Records of ex-ante interviews/face-to-face advice with Pharmaceuticals and Medical Devices Agency (PMDA)	In Japanese only
7	Optional	Materials related to clinical study, etc.	In Japanese only
8	Optional	Self-monitoring/self-evaluation results related to animal experiments	In Japanese only

(Note) Please do not include Form 2 in the proposal documents but submit it in Excel format as a reference. Forms 3, 4 and the biographies of the U.S. Partnership researchers also should be not included in the proposal, but should be submitted as PDF files for reference.

5.1.2 Methods for Obtaining Proposal Forms, Etc.

Please download forms for proposal documents and other materials necessary for application from the "Calls for Applications" page on the AMED website.

https://www.amed.go.jp/koubo/

5.1.3 Proposal Document Format and Notes for Preparation

(1) Preparation of Proposal Documents

Please be careful about the following items when inputting information into the Proposal Form. The Research proposal (Form 1) and the abstract must be prepared in both Japanese and English. In the case that information required on the Research Proposal is missing, the application may be ineligible for review.

(A) Regarding formats prescribing word limits or page limits, please be sure to comply with the set limits.
(B) Regarding letter/character size when inputting information, please use 10.5 point generally.
(C) As a general rule, all alphanumeric characters in the Japanese-language version must be single-byte characters. ((E.g.) Postal codes, telephone numbers, numbers of people, etc.) All letters, numbers, symbols, etc., in the English-language version must be single-byte characters.
(D) Please number the pages of proposal documents with numbers placed centrally at the bottom of each page.
(E) Proposal documents may be prepared in color, but please ensure that the documents' content can be understood even when the documents are photocopied in black-and-white.

(2) Compliance with laws/ordinances and ethical guidelines

R&D plans must comply with laws, ministerial ordinances, and ethical guidelines. Refer to Chapter 11 for more information.

(3) Approval of R&D Project Proposals by Affiliated Research Institutions

Before submitting proposal documents, PMs must obtain approval from the principal institution (i.e., the research institution with which the PMs are affiliated—presumably the institution that would conclude a R&D agreement with AMED). The principal institution's approval must be obtained for all subsidiary institutions named as candidates for undertaking the R&D work.

(4) Revision of Proposal Content

In selecting R&D projects for adoption, due to budget restrictions and other reasons, it may be necessary to request applicants to revise their submitted research proposal plans. Furthermore, in implementing awarded R&D projects, please note that the expenditure/implementation period allocated to the project may need to be changed due to budget restrictions in the future.

(5) Ineligible Project Proposals

The following R&D projects are ineligible for funding under this program.

1) Proposals that aim simply to purchase ready-made facilities and equipment.
2) Proposals that envision covering the costs necessary for procuring equipment with funding from this program when covering these procurement costs with funding from another source would be appropriate.

5.2 Required Documents Apart from R&D Proposals

(1) Records of face-to-face advice with Pharmaceuticals and Medical Devices Agency (PMDA)

In the case that the applicant has already undergone ex-ante interviews with PMDA under their “regulatory science consultation” program or other consultation services, a summary of the interview must be submitted with the R&D proposal (free format; the summary may be provided by the academic institution), and if the applicant has already undergone face-to-face advice, a record of the face-to-face advice or separate sheet (consultation content) such be submitted with the R&D proposal.

Note: R&D projects that progress to the practical application stage (R&D projects within the scope of the “Regulatory science strategy consultation” program or other consultation services) must as a general rule undergo face-to-face advice being adopted as a condition of the contracted R&D agreement at each time a clinical trial is initiated. Although is it not compulsory for the applicant to have undergone face-to-face advice at the time of application, it is desirable that face-to face consultation is undertaken and the consultation results are reflected in the R&D plan.

(2) Materials related to clinical study, etc

For research undertaking investigator-initiated trials or clinical studies with a view to creating innovative drugs or medical devices, or nonclinical studies aimed at conducting such trials/studies*1, applicants are required to submit a trial plan and protocol*2 (including information such as aims, subjects, selection criteria, exclusion criteria, number of cases, observation content, intervention content, statistical methods, and research system) and other materials related to the clinical study (free format; a draft may be submitted if the trials have not been implemented at the time of application).

*1 Does not include clinical research that is not aimed at creating new drugs or medical devices or that differ from normal processes for evaluating/approving new medical technology.

*2 In the course of protocol creation please refer to the following as necessary. (As they are for illustrative purposes, they do not provide all-encompassing coverage of clinical trials.)

- Center for Clinical Trials, Japan Medical Association (procedural manuals on the creation of protocols and clinical report forms (CRF)
  http://www.jmacct.med.or.jp/clinical-trial/enforcement.html
- Japan Medical Association Ethical Review Board (sample retrospective observational study protocols)
  http://rinri.med.or.jp/kaisaibi_shinsashinseisho/files/youshiki_rei2.docx
- Translational Research Center for Medical Innovation, Foundation for Biomedical Research and Innovation at Kobe (guidelines on the creation of investigator-initiated clinical trial protocols “randomized controlled trials”)
  https://www2.tri-kobe.org/support/download/protocol_summary2.pdf

(3) Self-monitoring/self-evaluation results related to animal experiments

With regard to research institutes conducting animal experiments using animal species specified under the Fundamental Guidelines for Proper Conduct of Animal Experiments and Related Activities in Academic Research Institutions (Public Notice of the Ministry of Education, Culture, Sports, Science

and Technology (MEXT) No. 71 of 2006) and Fundamental Guidelines for Proper Conduct of Animal Experiments and Related Activities in Implementing Agencies under the Ministry of Health, Labour and Welfare (Notification by Director, Health Science Division, Minister's Secretariat, Ministry of Health, Labour and Welfare on June 1, 2006), based on these fundamental guidelines, research institutes may be required to submit a copy of the results of their most recently implemented self-monitoring/self-evaluation related to the research institute's conformance with these fundamental guidelines.

(4) Reference and other materials related to R&D management

Such materials may be requested about pharmaceuticals to confirm the propriety of research management. Other related inquiries may be made, where deemed necessary.

5.3 How to the Proposal Documents

Please submit proposal documents via e-Rad by the deadline. It should be noted that web access increases shortly before the deadline and errors sometimes occur, so allow yourself plenty of time for submission. Applications will not be accepted if the proposal documents are not submitted by the deadline. In order to amend proposal documents that have already been submitted, you need to carry out "Retrieval" procedures before the application deadline and then re-submit the amended documents. For details regarding retrieval procedures, please refer to the Operation Manuals for Researchers. Please note that submitted proposal documents cannot be replaced after the application deadline.

Note 1: The e-Rad system is available for use between 00:00 and 24:00 on weekdays and public holidays. Please note that the operation of the e-Rad site is sometimes suspended during operating hours due to maintenance or inspections. In the event that e-Rad is to be temporarily shut down, notice will be posted in advance on the e-Rad portal site.

Note 2: Please upload data files for proposal documents in a PDF format (e-Rad has a feature for converting Word and Ichitaro (Japanese document) files to PDF format. It is not necessary to use this feature for PDF conversion, but if you do use them, be sure to refer to user' manual (Quick Guide for Researchers). If you use foreign-language letters or special characters, the text may be garbled, and so please be sure to check the content of the converted PDF file on the system.).

Furthermore, please do not include Form 2 in the proposal documents but submit it in Excel format as a reference. Forms 3, 4 and the biographies of the U.S. Partnership researchers also should be not included in the proposal, but should be submitted as PDF files for reference.

Note 3: The maximum size of single files that can be uploaded is 15MB.

5.3.1 Checking Acceptance Status on e-Rad

Verifying the acceptance of proposal documents can be done by viewing the "Manage submitted proposals" screen on the e-Rad. Proposal documents whose application status has not changed to "Processing (Funding Agency) /Application in progress" or "Accepted" by the deadline will become invalid. In the event that although a researcher has submitted the proposal documents prior to the deadline and

acknowledgment has been given by the clerical affairs supervisor their status has not changed to “Processing (Funding Agency) /Application in progress” or “Accepted,” please contact the division in charge of this program. Note that in the event that there is a fault in the e-Rad system during the application period, there may be Notices from Funding Agencies or Notices from System Administrator displayed on the screen after logging in to e-Rad, or related information displayed on the top page of the AMED website, so please check these details.

Application Status	Application Type (status) Displayed
(1) Application submitted	The application type (status) will change to “**Processing (Research institution) /Application in progress**,” which indicates that the acknowledgement by the research institution is still unfinished. (Application to the program is not complete at the point that the PI submits the application to their affiliated research institution via e-Rad. Be sure to undergo procedures to obtain approval of the submission of the R&D project from your affiliated research institution) In the event of difficulties in the procedures for the acknowledgement by the research institution please consult with the division in charge of this program.
(2) Procedures for acknowledgement by the research institution completed	The application type (status) will change to “**Processing (Funding Agency) /Application in progress**.”
(3) Accepted by the funding agency (AMED)	The application type (status) will change to **"Accepted**."

5.3.2 Important notes regarding e-Rad

(1) Registration of research institute

In the case that researchers are applying for the program through a research institute, the “Principal Institution” (the research institute with which the PI is affiliated) and “Subsidiary Institution” (a research institute other than the Principal Institution with which a Co-Investigator is affiliated) must be registered with e-Rad prior to the time of application as a general rule. For information regarding how to register research institutes, please refer to the e-Rad portal site.

Please appoint one person within the research institution to serve as a clerical affairs supervisor for e-Rad matters and download the research institution registration application form from the e-Rad portal site and then fill out and submit it by postal mail. Registration may require several days, so please allow leeway of two weeks or more for carrying out registration procedures. Please note that once you have registered with e-Rad, there is no need for you to register again for R&D programs or projects under the jurisdiction of other ministries or agencies. (If you have already registered with e-Rad for R&D programs or projects under the jurisdiction of other ministries or agencies, there is no

need for you to register again.) In the case that you are not affiliated with a specific research institute at the time of application or are affiliated with a research institute outside of Japan, please separately contact the department or office responsible for the relevant program before submitting your application by April 6, 2022.

(2) Registration of researcher information

PMs, applicants, and the co-Investigators participating in the research must register their researcher information and obtain a login ID and password.

The research institute should register information for researchers who are affiliated with it.

Please note that researcher information registered previously for a scientific research grant is already registered in the e-Rad system. Please check your researcher number and input additional information regarding your affiliated research institution. Information for researchers who are not affiliated with a research institute shall be registered by e-Rad system operation managers at the Ministry of Education, Culture, Sports, Science and Technology (MEXT). Please refer to the e-Rad portal site for the necessary procedures

(3) Important notes regarding input.

When PMs also serve as co-investigators, these roles are to be indicated separately within the proposal, but in e-Rad, enter the combined totals for the PM plus co-investigator in the direct expenses, indirect expenses, effort, and other fields. In the "Role" section, enter "PM." Enter data for co-investigators in the order of the co-investigator numbers indicated on the R&D proposal.

5.3.3 Contact for inquiries regarding e-Rad operation

For inquiries regarding how to operate the e-Rad, please contact the e-Rad portal site's Help Desk. (Please refer to Chapter 14.) Please be sure to check the portal site and see the "Frequently Asked Questions" page before contacting the Help Desk. Please note that the Help Desk cannot answer any inquires whatsoever regarding the content of the Call for Applications, application review status, or acceptance/rejection of applications.

5.4 Eliminating Unreasonable Redundancy or Excessive Concentration of Research Funds

5.4.1 Measures to prevent unreasonable duplication

In the case that a researcher is unnecessarily being allocated competitive research funds from the national government and/or multiple independent administrative agencies (including hereinafter national research and development agencies) for the same R&D project (name or content of the research receiving competitive research funds) being conducted by the same researchers, and if any of the following applies, the R&D project may be eliminated from eligibility for review, the decision to adopt the R&D project may be cancelled, or the amount of funds reduced (hereinafter referred to as "Cancellation of decision to adopt,

etc.”). Although there are no restrictions on submitting applications for other competitive research funds at the stage of applying for this program, please notify AMED staff in charge of this program promptly in the case that your R&D project is adopted by another competitive research funding program. If this is not reported, there is the possibility that the decision to adopt the R&D project under this program will be cancelled.

(A) Applications are submitted simultaneously for multiple competitive research funding programs, etc. that are essentially the same (including if the projects overlap to a considerable degree; the same shall apply hereinafter) and multiple R&D projects are adopted on an overlapping basis.

(B) Applications are repeatedly submitted for R&D projects that are essentially the same as an R&D project that has already been adopted and been allocated competitive research funds, etc.

(C) There is duplication regarding the use of research funds amongst multiple R&D projects

(D) Other equivalent cases

5.4.2 Measures to prevent excessive concentration

Even if the content of the R&D proposal submitted for this program differs from the content of R&D being implemented under another competitive research funding program, in the case that the overall research funds allocated to the relevant researcher or research group (hereinafter referred in this item as “Researchers, etc.”) in the relevant fiscal year exceeds the limit that can be used effectively and efficiently and cannot be used completely within the R&D period, and any of the following apply, the decision to adopt the R&D project under this program may be cancelled.

Accordingly, in the case that a proposal document for an R&D project is submitted to and adopted by another competitive research funding program after an application documents for the R&D project has been submitted to this program, or if changes are made to the information provided on the application documents, please report this promptly to the AMED staff in charge of this program. If this is not reported, there is the possibility that the decision to adopt the R&D project under this program will be cancelled.

(A) Excessive research funds are allocated in comparison to the researcher’s abilities or research methods

(B) Excessive research funds are allocated in comparison to the effort allocated to the relevant R&D project (percentage of the researcher’s overall work time* that is needed for implementing the relevant research)

(C) Unnecessarily expensive research equipment is purchased

(D) Other equivalent cases

*Based on the Council for Science, Technology and Innovation’s definition of “effort”: the percentage of researchers’ time exclusively spent for the R&D activities concerned against the researcher’s annual working hours. Researchers’ total working hours refer to not only the time spent in research activities but also total substantive working hours, including educational/clinical activities and administrative duties.

5.4.3 Provision of information related to application content to eliminate unreasonable duplication/excessive concentration

In order to eliminate unreasonable duplication/excessive concentration, information related to parts of the application content (or awarded project/program content) may be provided within the necessary extent, to the persons in charge of other competitive research funding programs, including other government ministry/agency programs, via e-Rad. Furthermore, in the case that information is requested for checks being conducted under other competitive research funding programs, information may be provided in this way.

5.4.4 Status of application for and acceptance of other competitive research funds, including those from other ministries and agencies

Applicants may be required to provide information in proposal documents regarding the status of application and/or acceptance under other competitive research funding programs, including other government ministry/agency programs (name of program, name of R&D project, project implementation period, budget amount, effort, etc.) In the case that the information provided is factually inaccurate, the R&D project application may be rejected, the decision to adopt the R&D project may be cancelled, or the amount of funds allocated to the R&D project may be reduced.

Chapter 6. Handling of Information

6.1 Handling of Information Contained in Proposal Documents

6.1.1 Purpose of Use of Information

In addition to reviewing R&D project proposals as part of the selection process, information included in proposal documents regardless of whether they are accepted or not, shall be used in analysis of research trends or macro analysis that contributes to the operation of the AMED program management, such as the creation of new programs; in the procedures regarding contracted R&D funds; for research support purposes as described in Chapter 13.

It should be noted that in order to prevent the rights and interests of the researchers submitting research proposals or their affiliated institutions from being unfairly infringed, the information in question acquired shall be used solely for the work detailed above.

In addition, with regard to the information included in proposal documents regardless of whether they are accepted or not, AMED shall manage it in line with laws and ordinances related to the management of corporate documents, protection of personal information and disclosure of information, and the AMED regulations the confidentiality of secret information included in proposal documents shall be strictly maintained to ensure that the rights and interests of the researchers submitting research proposals or the research institutions to which they are affiliated are in no way unfairly infringed. For details, please refer to the Ministry of Internal Affairs and Communications website*.

* Public records and achieve management system (Cabinet Office)
https://www8.cao.go.jp/chosei/koubun/index.html (in Japanese)
Act on Protection of Personal Information etc. (Personal Information Protection Commission (PPC))
https://www.ppc.go.jp/personalinfo/ (in Japanese)
Information disclosure system (Ministry of Internal Affairs and Communications)
https://www.soumu.go.jp/main_sosiki/gyoukan/kanri/jyohokokai/index.html (in Japanese)

6.1.2 Necessary Disclosure/Provision of Information

(A) The information related to individual selected research themes (name of project, name of R&D theme, research institutions/positions/names of those involved in research indicated in the participant list, e-Rad theme/researcher/research institution numbers, budget amounts, implementation periods, research overviews/summaries, and contracted R&D result reports (disclosed information))*1 will be organized and categorized and may be disclosed on the AMED website, AMED's R&D theme database (AMEDfind), and public databases, etc. (such as World RePORT*2) operated by a research funding agency, etc., which is collaborating with AMED under a collaboration agreement, etc.

(B) With regard to all projects for which applications have been submitted, information requiring micro analysis will be analyzed by AMED and the analysis results provided to related government ministries and agencies as well as funding agencies, etc., and made public, and may also be posted on funding information databases, etc.*3

(C) The information registered on e-Rad will be utilized for the appropriate evaluation of R&D conducted with government funding, and the planning and formulation of efficient and effective comprehensive strategies, and policy on allocation of funds. Accordingly, the Council for Science, Technology and Innovation (CSTI) and related government ministries and agencies call for thoroughness in registering accomplishment information about academic papers and patents etc., and account records on e-Rad, in order to connect the output/outcome information with the input by solicitation-type research funding programs. For this reason, even after the relevant project has been selected, researchers are requested to input into e-Rad the R&D accomplishment information for each fiscal year (academic papers, patents, etc.) as well as accounting report information and information on actual disbursement of indirect costs related to competitive funding. Information required for micro-analysis including research R&D accomplishment information and accounting report information will be provided to the Cabinet Office.

(D) Within the scope necessary for eliminating unreasonable duplication/excessive concentration, some information included in proposal documents, etc., may be provided via e-Rad to divisions in charge of other competitive research funding programs, including other government ministries or agencies (including the provision of personal information used when computerized data processing and management is contracted out to an external private enterprise). Similarly, information may also be provided in the event that it is necessary to check for duplicate applications to other competitive research funding programs.

*1 This information will be treated as “information expected to be made public” as stipulated in Article 5, Paragraph 1, Item (a) of the Act on Access to Information Held by Independent Administrative Organs (Act No. 140 of 2001). Furthermore, the same shall apply to items designated for public disclosure in the R&D proposal and the above-mentioned items shown on the Contracted Items Sheet that is to be completed if the relevant R&D project is adopted.

*2 “World RePORT” is a database for international collaborative research supported by research funding agencies in major countries. Its purpose is the visualization of international research collaboration carried out by various countries, which was previously difficult to verify. Managed and operated by the United States’ National Institutes of Health (NIH), the database currently records information for twelve research funding agencies around the world, including the NIH, the UK’s Medical Research Council (MRC), the Bill & Melinda Gates Foundation (BMGF), the European Commission (EC), the Canadian Institutes of Health Research (CIHR), and the Wellcome Trust.

*3 “Databases, etc.” includes World RePORT, ERP and other databases.

Chapter 7. Points to Note Between Selection and Conclusion of the Agreement

7.1 Cancellation of Decision to Adopt R&D Project

The research institution implementing the R&D project must in principle, and pursuant to the stipulations of 8.1.1., conclude a contracted R&D agreement with AMED within 90 days of notification of the adoption decision (the contracted R&D agreement conclusion deadline).

The adoption of projects may be cancelled in the event that any of the following reasons for cancellation of adoption apply, even after adoption. Furthermore, in the event that despite of the existence of any of the following reasons for cancellation, they were not found out in advance and the agreement was concluded it is possible for the contract to be cancelled ex post facto.

(A) The requisite documents requested by AMED are not submitted by the contracted R&D agreement conclusion deadline.

(B) Conditions that were set for adoption of the R&D project ultimately have not been fulfilled.

(C) The R&D project does not fulfill the conditions for application.

(D) It has been discovered that during the R&D period restrictions on the application to/eligibility for participation in AMED R&D programs will be placed on researchers scheduled to participate in the R&D project in question.

(E) The planned PI or Co-Investigators of the R&D project are among persons under formal investigation for misconduct etc., and AMED does not approve their participation.

(F) In addition to the above, when it is not possible to conclude the agreement before the R&D agreement conclusion deadline due to reasons attributable to the research institution implementing the R&D project (including the event that there are violations of Representation and Warranty and matters to be observed as stipulated in the agreement).

7.2 Representation and Warranties regarding Researchers Investigated/Found to Have Engaged in Misconduct

Please note that in concluding contracted R&D agreements, AMED requires Principal Institutions to provide representation and warranty about items (A) through (C) below.

(A) PMs and the contributing participants have not been found by the research institution to have carried out misconduct in accordance with Japanese Government guidelines for responding to misconduct1 or AMED Regulations for Responding to Misconduct in Research Activities, but excluding, however, persons regarding whom restrictions have not been placed regarding application to/eligibility for participation in competitive research funding programs, etc. implemented by the national government or independent administrative agencies based on the findings of the research institution, or whose period of restriction on application to/eligibility for participation in competitive research funding programs, etc. implemented by the national government or independent administrative agencies has ended)*2.

(B) In the case that persons who are the subject of a formal investigation (hereinafter referred to as the “formal investigation”) being conducted by the research institution in accordance with Japanese Government guidelines for responding to misconduct or AMED Regulations for Responding to Misconduct in Research Activities are affiliated with the research institution in question and either the PI or Co-Investigator (if there is a subcontractor, including the Co-Investigator or equivalent person affiliated with the subcontractor) for the R&D Plan, AMED has been notified of the relevant target person by the day before the contracted R&D agreement will be concluded and AMED’s consent has been obtained with regard to handling of the relevant target person(s).

(C) The research institute is strictly complying with and implementing each of the items that research institutes are required to implement as research institute system improvements as prescribed under Japanese Government guidelines for responding to misconduct.

*1 The “Japanese Government guidelines for responding to misconduct” referred to in this section is a blanket term for all the various policies and guidelines concerning response to misconduct formulated by the Japanese Government.

*2 With regard to (a) above, in the case that a research institute with which AMED has concluded a contracted R&D agreement also concludes a contracted agreement with a third-party institute (from AMED’s perspective, a subcontracted agreement. Hereinafter, the third-party institute shall be referred to as the “subcontracted institute”), please note that of the researchers affiliated with the Subcontractor, the relevant research institute is also required to provide representation and warranty for the “Co-Investigator” (or person in an equivalent position).

7.3 Preparations for Concluding Agreement

Following the adoption of an R&D project, the research institution implementing the R&D project shall be required to prepare the following (A) to (C) in order to enable procedures for concluding the contracted R&D agreement with AMED to proceed quickly and smoothly. Documents required for the agreement (plan forms etc.) shall be provided separately after projects have been adopted.

One overall R&D Plan is to be prepared for each R&D project based on the R&D proposal at the time of selection of the project. It is to be centered on the proposed R&D concept for the entire project implementation period, and should include the basic plan, R&D content, R&D system, and budget plan. (This plan will be used as one of the basic documents used when considering budget allocation each fiscal year, conducting a Mid-term Review and an Ex-Post Evaluation, and managing project progress.) One R&D Plan is to be prepared for each agreement when concluding R&D agreements each fiscal year. (Please note that some parts of R&D Plans will be requested to be submitted in English.)

(A) Prepare an Overall R&D Plan, R&D Plan and other documents required for the agreement

(B) Obtain an estimate for the expenditures needed for the administrative plan

(C) Organize accounting regulations, contracted research regulations, and rules for employee inventions, etc.

7.4 Data Management Plan (DMP) submission

With regard to awarded projects, PM is requested to submit* a DMP to AMED when they conclude a contracted R&D agreement after adoption. Successful applicants will be separately informed regarding the requisite documents (forms) after adoption.

- The data etc. arising from R&D programs using public funds are a form of assets of the general public, and one of AMED's roles is to ascertain the location of data that is currently unknown, collect it, secure its quality, assess its significance, store and use it in an appropriate and fair manner.
- By ascertaining the types of R&D data, where they are stored, the person in charge of managing the data, the data usage and sharing plan policy, and the location of the human resources related to the data through DMPs, AMED seeks to strengthen its management and catalytic functions, and to the greatest extent possible be of use in encouraging collaboration between different R&D projects, and avoiding duplicated R&D.
- The DMP is a document recording what sort of data arises from what R&D project and who is managing it.
- It is requested that DMPs include the program year, program name and R&D project name, a general term for the data and data sets deriving from the project, an explanation of the R&D data, the affiliation and name of the data scientist and repository and any other requisite details.
- Please complete the DMP in strict accordance with the Guidelines on AMED Research Data Utilization and the Guide for Completing DMPs. (The Guidelines on AMED Research Data Utilization explain the obligation of submitting DMPs, and functions and role etc. of the plans, so please refer to them.)
- With regard to the DMP content that can be made public or information that the content is statistically processed these may be made public along with other project information. Please refer to Chapter 10 for details of the utilization of DMP.
- Please refer to the following for further details.

  https://www.amed.go.jp/koubo/datamanagement.html (in Japanese)

Chapter 8. Concluding Contracted R&D Agreements

8.1 Conclusion of Contracted R&D Agreements

8.1.1 Agreement Conditions

With regard to awarded R&D projects, a contracted R&D agreement must be concluded between the research institution implementing the R&D project and AMED. The research institution implementing the R&D project becomes able, through the conclusion of an agreement, to receive contracted R&D funds from AMED and implement the adopted R&D project. The contracted R&D agreements are single-year agreements in accordance with the principles of the accounting period of the national government. AMED will provide successful applicants with details of the documents required for the agreement and the procedures after adoption.

The contracted R&D agreements shall, in principle, be concluded within 90 days of notification of adoption (the contracted R&D agreement conclusion deadline). As stated above in 7.1 above, in the event that the required documents are not submitted prior to the contracted R&D agreement conclusion deadline, or the conditions decided at the time the R&D project was adopted have not been fulfilled based on the opinions of the Project Evaluation Panel, PS, PO, etc., take adequate care as the agreement cannot be concluded even if it is for an adopted R&D project, and the adoption decision may be rescinded.

Even after the contracted R&D agreement has been concluded, in the case that unavoidable circumstances arise due to budget restrictions, the R&D plan may be revised or suspended (including early conclusion of projects due to achievement of R&D plans).

The PM etc., shall check on the R&D progress status, and the contracted R&D agreement may be changed or cancelled part-way through the fiscal year due to revisions to the R&D plan or other reasons.

It should be noted that, with regard to Principal Institutions and Subsidiary Institutions that are national facilities or other institutions (general term for national facilities or other institutions or public test and research institutions run by local government), only in the case that the relevant institution or the PI or Co-Investigator affiliated with the relevant institution makes a request based on reasonable grounds and following discussion with AMED shall a payment method of the R&D grant being paid by AMED to the PI or Co-Investigator of the relevant institution be adopted. (In such cases, payment will be in accordance with the Guidelines for Handling of R&D Grants prescribed by AMED.) If this is the case, administration related to R&D grant accounting shall be entrusted to the head of the relevant institution. Furthermore, in the case that the need to carry out the research content at the Principal Institution and the Subsidiary Institution in an integrated manner under the R&D plan is recognized and the Subsidiary Institution is not a national facility or other institution, approval may be given under this program for the R&D to be subcontracted. However, even in the case that the R&D is subcontracted, as a general rule project accounting shall be performed by the subcontractor and the subcontractor shall be required to undergo government inspection and auditing by AMED in response to requests from AMED.

8.1.2 Administrative Procedures Regarding Conclusion of Agreements

Please carry out the necessary administrative procedures based on the AMED “Administration Manual for Contracted R&D Agreement.”*

*https://www.amed.go.jp/keiri/index.html (in Japanese)

8.1.3 Ensuring the R&D Timeframe through the End of the Fiscal year

To enable R&D to be conducted through the end of the fiscal year, the Contracted R&D Accomplishments Report should be submitted to AMED no later than the 61st day from the final day of the contracted R&D period. Each research institution should work to put in place the necessary in-house mechanisms needed to ensure that research can be conducted throughout the entire research period, through the end of the fiscal year.

8.1.4 Determination of Contracted R&D Funding Amount

Contracted R&D funding amounts are determined based on examination of the Contracted R&D Accomplishments Report, which is required to be submitted in accordance with the Contracted R&D Agreement following the conclusion of the contracted R&D agreement period. During this examination, if any funds provided for research purposes are found to have been used fraudulently or for purposes not recognized as contracted R&D activities, the return of all or part of the funds may be demanded. Furthermore, the person(s) conducting the research who used the funds fraudulently may be excluded from any agreements with AMED for a certain period of time, depending on the extent of the fraud. See Chapter 12 for details.

8.2 Scope and Payment of Contracted R&D Funds

8.2.1 Scope of Contracted R&D Funds

In accordance with the governmental ministries’ and agencies’ expenditure table used in common for the competitive funds, items of expenditure have been set as follows for the program. For details, please refer to the AMED’s “Administration Manual for Contracted R&D Agreement”*[1].

The principal institution’s expenses related to project management by PMs qualify as direct expenses. (Such expenses may include expenses related to the development of the environment needed by PMs to carry out activities effectively and efficiently; expenses related to systems development, such as expenses incurred for the PMs’ assistants; expenses related to the progress management of R&D activities by contributing participants in the principal or other institutions; and expenses related to cooperation between research institutions.)

Currently, improvements regarding the systems for competitive research funds are being promoted, with the 6th Science, Technology, and Innovation Basic Plan, the Integrated Innovation Strategy 2020 and the Comprehensive Package for Research Competitiveness Enhancement and Young Researcher Support. Based on this, under this program the direct costs can cover personnel costs for PIs and Co-Investigators

as well as expenses for entrusting other persons with PIs' work other than research and development ordinarily performed by PIs at their affiliated institutions (buyout expenses).

	Main item	Definition
Direct costs	Costs of goods (equipment/supplies)	Research facilities/equipment/prototypes, software (ready-made goods), book purchasing costs, purchasing costs for reagents/materials/consumables for use in research
	Travel costs	Travel costs of R&D participants, travel costs for invited participants such as external experts
	Personnel costs/ services costs	Personnel costs: personnel costs for researchers, etc., employed to conduct the relevant contracted R&D Service costs: expenditure for services such as lecture requests, guidance/advice, test subjects, interpretation/translation, and unskilled labor.
	Other	Costs for implementing the relevant contracted R&D other than the above. Examples: R&D results publication costs (academic paper contribution costs, academic paper offprint costs, website production costs, etc.), conference costs, equipment leasing costs, Equipment repair costs, printing costs, subcontract costs, licensing fee, amount equivalent to consumption tax related to untaxed transactions, etc.
Indirect costs*2	Expenditure used by research institutes as necessary costs for managing the research institutes during implementation of the relevant R&D, paid at a fixed percentage of direct costs (with a 30% rule of thumb) as an allowance.	

*1 https://www.amed.go.jp/keiri/index.html (in Japanese)

*2 The ratio of indirect expenses in this Program is set at 30% for universities and 10% for private sector entities (for SMEs, 20%). Excluded are researchers affiliated with national facilities or institutions (except for National Institute for Education Policy Research). Indirect expenses will also be allocated to subsidiary institutions (except for national facilities and institutions) based on allocated direct expenses.

8.2.2 Appropriation of Contracted R&D Funds

Please calculate costs required for conducting the R&D and record the total amount. As a general rule, calculation and recording of costs should be performed in accordance with the AMED "Administration Manual for Contracted R&D Agreement."*

* https://www.amed.go.jp/keiri/index.html

Note 1: Contracted R&D agreements for researcher-initiated trials or clinical studies under AMED shall employ "Contract management method using value per procedure (VPP) charts in clinical trials or clinical studies."

In the case that an awarded R&D project is recognized as being subject to this management method, if the research institution has created a system for registering cases for clinical trials/clinical studies in accordance with newly prescribed internal consignment regulations (Regulations for Handling Contracted R&D in Researcher-initiated Trials and Clinical Studies (tentative title), the head of the research institution can request case registration from other medical institutions in a kind of outsourcing method. For more details please refer to the section entitled “Management of medical institution expenses for investigator-initiated trials or clinical studies,” which can be found on the AMED website under “Management of research expenses.”2 Facilities where there is a sufficient administrative support system for clinical trials/clinical studies may continue using their current management method for the foreseeable future.

* https://www.amed.go.jp/program/kenkyu_unyo.html (in Japanese)

Note 2: In place of the supercomputer joint use service that will be taken out of service in FY2021, it will be possible to use the supercomputers prepared by the Biobank–Construction and Utilization biobank for genomic medicine Realization (B-Cure) (Platform Program for Promotion of Genome Medicine/Large-scale Genome Analysis Infrastructure Project) for certain purposes and under certain conditions. For more details please consult the CANNDs secretariat at this email address: cannds“AT”amed.go.jp (Change “AT” to @ when inputting the address.)

8.2.3 Encouragement of Shared Use of Research Equipment

From the perspective of the efficient use of contracted R&D funds and the effective use of research equipment, joint use of research equipment and combining research funds for multiple projects based on certain requirements are permitted. Details should be confirmed with the AMED “Administration Manual for Contracted R&D Agreement.”*

* https://www.amed.go.jp/keiri/index.html

8.2.4 Payment of Contracted R&D Funds

As a general rule payment of contracted R&D funds shall be made each quarter in even (one-quarter) installments of the total amount for direct and indirect costs for the entire fiscal year.

8.2.5 Diversion of Costs Between Items

When the diverted amount for each cost item (main item) does not exceed fifty percent (50%) of direct costs (or five million yen (JPY 5,000,000), if the amount equal to fifty percent (50%) of direct costs is less than five million yen (JPY 5,000,000)) for that fiscal year, the amount may be diverted without approval from AMED on the assumption that the diversion is appropriate and consistent with the R&D plan. For details, please refer to the AMED “Administration Manual for Contracted R&D Agreement.”*

* https://www.amed.go.jp/keiri/index.html

8.2.6 Provision of Documentary Evidence (Receipts, etc.) for Indirect Costs

You should prepare documentary evidence of appropriate expenditure, from the standpoint of ensuring transparency of use as noted in the “Common guidelines relating to the expenditure of indirect costs for competitive fund” (revised on October 1, 2021 at the liaison meeting of relevant Ministries on competitive fund) and retain it for a period of five years following the year of the completion of the R&D project. A Report on Indirect Cost Expenditures must be prepared for the expenditure of indirect costs for each fiscal year and submitted by June 30 of the following year. For details, please refer to the AMED “Administration Manual for Contracted R&D Agreement.”*

* https://www.amed.go.jp/keiri/index.html

8.2.7 Carry-over of contracted R&D funds

In the course of the program, in the case that it becomes difficult to ensure completion of contracted R&D fund payments within the relevant fiscal year due to difficulty in implementing preliminary surveys or deciding research methods for the R&D, various conditions related to the R&D plan, weather-related issues, difficulty in procuring materials, or other unavoidable reasons, the contracted R&D funds may be carried-over to the end of the next fiscal year maximum with the approval of the Minister of Finance. For details, please refer to the AMED “Administration Manual for Contracted R&D Agreement."*

* https://www.amed.go.jp/keiri/index.html

8.3 Handling of Acquired Goods

8.3.1 Ownership of Acquired Goods

Ownership of goods, etc. acquired by Universities and Research Institutions*1, through direct costs (hereinafter referred to as “Acquired Goods”) shall revert to the university, etc.

Ownership of acquired goods by Companies, etc.*2, shall revert to AMED in the case of goods with an acquisition cost of 500,000 yen or more (consumption tax included) and has a service life of one year or more, but the relevant acquired goods may be used free-of-charge for the purpose of contracted R&D by the contractor until the conclusion of the contracted R&D period. Companies, etc. shall, throughout the contracted R&D period, manage the relevant acquired goods properly with the due diligence of a prudent manager.

*1 “Universities and research institutions” include:

(i) Incorporated educational institutions such as national university corporations, public university corporations, and private universities

(ii) Public research institutions such as national research institutes, public research institutes, and independent administrative corporations

(iii) Organizations with a public nature, such as public-service corporations, that are recognized by AMED.

*2 “Companies, etc.” is a general term for research institutes other than “universities, etc.

8.3.2 Handling of Acquired Goods after the Completion of the R&D Period

For the purpose of continued application of the relevant R&D, as a general rule Companies etc., may continue to borrow free-of-charge tangible property and whose ownership has reverted to AMED for the duration of its useful life* and the tangible property may be transferred to the Companies etc., for a fee upon the evaluation of AMED after its service life has passed, provided that this shall not apply in either case in the event that AMED uses or disposes of the relevant acquired goods.

With regard to acquired goods that are treated as consumables, no specific leasing agreement or other procedures will be implemented, but the contractor shall manage the relevant acquired goods properly with the due diligence of a prudent manager until their use is finished (resale of acquired goods for profit is not permitted).

* The duration of useful life shall be the number of years stipulated in Appended Table 6 “Useful Life Table of Depreciable Assets for R&D of the Ministerial Order on Useful Life of Depreciable Assets” (Ministry of Finance Order No. 15 of 1965). (Four years for tools, appliances and equipment.)

8.3.3 Disposal of Radioactive Waste

It is the responsibility of the research institute to dispose of contaminated property and/or radioactive waste generated through implementation of the R&D project.

Chapter 9. Progress management for the selected R&D project

9.1 Progress management for the R&D project

The PD will perform progress management for all selected R&D projects. In doing so, important research data (including experiments) on which the R&D project proposal is based may be verified from the perspective of progress management, even if the relevant research was conducted prior to conclusion of the contracted R&D agreement.

A Contracted R&D Result Report, serving as an appendix to the Contracted R&D Accomplishments Report, is required to be submitted each fiscal year for all awarded R&D projects according to the contracted R&D agreement.

It should be noted that in implementing progress management, exit strategies shall be realized through the implementation of project progress meetings, questionnaires (documents to be completed with details on R&D progress status), hearings (interviews for individual projects), and site visits (confirming the actual status of R&D at the facility carrying out the research). Please also note that, upon referral to the R&D Plan and depending on the progress status, review of the project plan or cancelation (early conclusion) of the project may be carried out.

In addition, R&D projects progressing to the practical application stage (R&D projects that are within the target scope of the “Regulatory Science Strategy Consultation” program, etc. conducted by the Pharmaceuticals and Medical Devices Agency (PMDA)) are required as a condition of their selection to implement an R&D plan regarding which consensus was reached upon consultation (face-to-face advice) such as the PMDA's "Regulatory Science Strategy Consultation." Furthermore, based on appropriate information management, the research institution shall consent to AMED attending various kinds of consultation under the “Regulatory Science Strategy Consultation” program, etc., during the R&D period. The research institution shall also share records of face-to-face advice and other related information with AMED.

For research undertaking clinical trials or clinical studies with a view to creating innovative drugs or medical devices, etc., or research consisting of nonclinical studies with the same aims*, Conducted during the R&D period, research institutions are required to submit materials related to clinical studies such as their protocols (including information such as the clinical studies' aims, targets, selection criteria, exclusion criteria, number of cases, observation content, intervention content, statistical methods, and research system).

* This does not include research that is not aimed at developing new drugs or medical devices, new medical technology evaluations, or research that differs from normal approval processes.

9.2 Mid-Term Reviews and Ex-Post Evaluations

In the Program, outside evaluations will be conducted by a project evaluation committee composed of outside experts in the 3rd and 5th years after the start of R&D. If the decision is made to continue the project beyond 5th years after the start of R&D, outside evaluations will also be performed in 8th years after the

start of R&D and FY2030. Outside evaluations may be sought and implemented for any projects whenever deemed necessary.

AMED itself will perform self-evaluations in the fiscal years during which no outside evaluations are performed.

Depending on the results of these evaluations, AMED may revise (move up or move back) or cancel the project (conclude the project early), based on the holistic judgment of the PD and/or other parties.

9.3 Presentations at Achievement Report Meetings

As part of the Program achievement reporting process, PMs for the selected theme may be required to give public presentations or internal achievement report meetings organized by AMED. In addition, follow-up and achievement deployment investigations may include, where necessary, requests for presentations after the fiscal year in which the theme is completed. Cooperation in this respect is requested.

Chapter 10. Handling of R&D Achievements

Regarding the handling of R&D accomplishments, research institutes are obligated under contracted R&D agreements to strictly comply with items regarding R&D accomplishment reporting, intellectual property (IP) and usage of R&D accomplishments.

10.1 Indicating Reference Numbers in Paper Acknowledgments

When publicizing the R&D accomplishments made under this program, please be sure to state that the accomplishments are due to AMED support and include the grant number for acknowledgements in the acknowledgements section. For more details please check the AMED “Administration Manual for Contracted R&D Agreements*.

* https://www.amed.go.jp/keiri/index.html (in Japanese)

10.2 Submitting and releasing R&D results reports and DMPs (updated at the end of the R&D project)

Research institutions shall submit a Contracted R&D Result Report that summarizes the research accomplishments of the R&D project, serving as an appendix to the Contracted R&D Accomplishments Report, and a DMP (the latest version upon conclusion of R&D). Please note that the deadline for submission is within 61 days from the end of the term of the contracted R&D project or from the conclusion/cancellation/discontinuance of the contracted R&D project, whichever comes first. In the case that the Contracted R&D Result Report is not submitted by the deadline, it shall be deemed that the contracted R&D agreement has not been fulfilled, so please be sure to strictly comply with the submission deadline. It should be noted that some parts of the Contracted R&D Result Report may be required to be submitted in English.

A part of the items in the Contracted R&D Result Reports and outline of accomplishments will be treated as publicly open information. As it will be published at appropriate times on the AMED website please be careful to indicate parts that are not to be made public in the section “Non-Disclosure Items” in the report form with regard to information prior to patent applications, unpublished information about the details of patents being applied for, knowhow and other confidential sales information and any other undisclosed information.

Moreover, with regard to final Result Reports produced at the end of R&D projects that have lasted for several years, the content under the section of “Items for Disclosure” in the report compiled by the PI upon Ex-Post Evaluation will be published at appropriate times on the AMED website.

Furthermore, from the perspective of the use of R&D data through data sharing, with the objective of introducing R&D data generated, acquired or collected in connection with R&D supported (contracted or assisted) by AMED to universities, companies and other research institutions that are considering its use, AMED plans to publish on its website the parts that it is possible to make public of the DMP (the latest

version upon conclusion of R&D project). The undisclosed data will be appropriately managed by AMED, and in some cases AMED might, where necessary, make enquiries to PIs in order to confirm details.

10.3 Attribution of R&D Achievements

With regard to patent rights, copyrights and other intellectual property (IP) relating to R&D accomplishments, these can revert to the research institutes under the condition that the requirements provided for in Article 17 of the Industrial Technology Enhancement Act (Act No.44 of 2000, the Bayh-Dole Act. The Japanese version of the Bayh-Dole Act) are satisfied. The purpose of the Bayh-Dole Act is to invigorate R&D activities through the reversion of IP rights to research institutes so that the results of these R&D activities can be used efficiently in business activities. Under this program, it is expected that research institutes themselves will make the maximum effort to achieve practical application of their research accomplishments, and for this reason the Bayh–Dole Act has been applied. For details regarding conditions, please refer to contracted items prescribed under the contracted R&D agreement at the time the agreement is concluded. In the case of participation by a foreign research and development organization, etc., at least 50% of the intellectual property rights obtained through the research must belong to AMED. Furthermore, please consult with AMED in advance in the event that R&D accomplishments or intellectual property rights relating to R&D accomplishments are succeeded from a domestic subsidiary to an overseas parent company.

10.4 Measures to Advance the Practical Applications of R&D Achievements

Research institutes are requested to maintain a strong sense of awareness that they are in a position in which they must try their best to use the accomplishments of the R&D entrusted to them by AMED in order to make a contribution to society, implement them and put them to practical use, and take the requisite measures towards this goal. In particular, they are requested to make the maximum use of inventions, knowhow, data and other IP, while in accordance with AMED's IP policy* ensuring that appropriate measures have been implemented within the research institute’s funding sources such as appropriating indirect costs, and costs for obtaining IP rights in order to ensure appropriate protection and utilization of patent rights and other IP rights on a global scale.

AMED’s Department of Intellectual Property provides consistent support for maximizing and achieving the practical application of R&D accomplishments that have reverted to the research institutes, so do not hesitate to contact the Medical IP Desk (For details, please refer to Chapter 13.).

* https://www.amed.go.jp/chitekizaisan/chizai_policy.html

10.5 IP Educational Materials for Medical Researchers

IP educational materials for medical researchers are provided on the AMED website* as a reference for considering strategies for submitting applications for, obtaining patent/IP rights for, and utilizing R&D accomplishments that have reverted to research institutes. Researchers are strongly recommended to peruse these IP educational materials prior to carrying out research.

* https://www.amed.go.jp/chitekizaisan/chizai_kyouzai.html (in Japanese)

10.6 Securing Open Access to R&D Achievements

Having secured the necessary IP rights, research institutes are requested to cooperate in ensuring open access to research accomplishments (including data etc. acquired) as far as possible.

10.7 Data Handling

With regard to the data created, obtained or collected in connection with R&D supported (contracted or assisted) by AMED, or data (R&D data) produced through the processing etc. of data as a result of a contracted R&D agreement in which AMED is the assignor, please treat it in pursuance with the Contracted R&D Agreements, the AMED Basic Policy on Handling of R&D Data and the Guidelines on AMED Research Data Utilization.*

* https://www.amed.go.jp/koubo/datamanagement.html (in Japanese)

Chapter 11. Obligations of Research Institutes in Implementing this Program

11.1 Compliance with Laws and Ordinances

In implementing this program, research institutes must be observant of the fact that their research is being funded with public funds and strictly comply with related national government laws and ordinances, endeavoring to ensure that the program is implemented fairly and efficiently. Research institutes shall be required to take measures to prevent misconduct*1, fraudulent use*2, and fraudulent receipt*3 (hereinafter referred to collectively as “Misconduct, etc.”).

*1 “Misconduct” refers to the fabrication, falsification, or plagiarism of data or survey results, etc. included in research accomplishments published through submission to a journal, etc. (hereinafter referred to as an “Academic paper, etc.”) by a researcher, either willfully or through gross negligence of the fundamental duty of diligence that researchers bear in carrying out their research activities. The definitions of each of the above terms is as follows.

(i) Fabrication: creation of data or research accomplishments that do not exist.

(ii) Falsification: manipulation of research materials, equipment, or processes and changing results obtained from data or research activities to results that are untrue.

(iii) Plagiarism: appropriation of the ideas, analysis methods, data, research accomplishments, academic papers, or terminology of another researcher without the approval of the relevant researcher or appropriate acknowledgement.

*2 “Fraudulent use” refers to the use of public R&D funds, either willfully or through gross negligence, for a purpose other than that for which it was intended, or in a manner that infringes the content of the grant decision or conditions for use of the public R&D funds (including, but not limited to, purposes or uses other than those stated in the R&D plan, or use of R&D funds that infringes laws, ordinances, regulations, notifications, or guidelines, etc.)

*3 “Fraudulent receipt” refers to a researcher receiving public R&D funds through falsehoods or other unfair means.

*Under the above definitions, “researcher” refers to a researcher, technician, research assistant, or other person conducting research activities using public R&D funds, or a person engaged in work subsidiary to these research activities.

11.2 Management Responsibility for Executing Contracted R&D funds

The contracted R&D funds shall be executed by the research institution in accordance with the contracted R&D agreement. For this reason, research institutions shall abide by the principles stipulated under “Competitive research funding, etc. should be managed at the responsibility of the research institution,” and research funds shall be managed under the responsibility of research institutions. Moreover, researchers participating in this program should be fully aware of the fact that AMED contracted R&D

funds are provided by precious tax paid by the general public, and are obligated to execute funds fairly, appropriately, and efficiently.

11.3 Participation in/Completion of Responsible Conduct of Research (RCR) Education Program

As part of measures to prevent misconduct from occurring, AMED requires all researchers participating in the Program to participate in and complete a responsible conduct of research (RCR) education program. Accordingly, research institutions shall implement RCR education for researchers and report to AMED on the status of participation. Please note that in the case that a researcher does not complete a RCR education program, execution of contracted R&D funds may be suspended until completion of the RCR education program is confirmed.

11.3.1 Persons Required to Participate in RCR Education Program/Program(s) to be Undertaken/Educational Materials

Research institutions, etc., should ensure that researchers who are deemed to be substantially participating in research activities that are being conducted using research funding provided by AMED undergo training using one of following programs/materials.

● A Casebook for Responsible Research Conduct (AMED) (in Japanese)
● Collection of Close Calls Related to Research Integrity (AMED) (in Japanese)
● APRIN e-Learning Program (eAPRIN) (in Japanese)
● For the Sound Development of Science: The Attitudes of a Conscientious Scientist (Japan Society for the Promotion of Science Editing Committee “For the Sound Development of Science”) (in Japanese)
● Programs implemented by research institutes whose content is deemed to be equivalent to the that of the above programs (in Japanese)

Furthermore, the Clinical Research Act stipulates that the “Kenkyusekinin Ishi” (Principal Investigator) and “Buntankenkyu Ishi” (Co-Investigator) must undergo sufficient education and training regarding research-related ethics and the knowledge and skills of the research methods required for implementation of the research in order to carry out the relevant clinical research appropriately in accordance with their required responsibilities. Researchers required to undergo training must undertake one of the following training programs.

(1) Training conducted by a Clinical Research Core Hospital for persons working in the clinical research field*
(2) Training that is recognized by the research institution as being equivalent to the above (including training conducted by facilities other than a Clinical Research Core Hospital)

Note 1: Simply participating in academic meetings does not qualify as education/training.

Note 2: Certain quality-assured e-learning programs such as APRIN e-learning program (eAPRIN), Clinical Research e-Training Center (Center for Clinical Trials, Japan Medical Association), Introduction to Clinical Research (ICRweb) may also be acceptable for (b), but it is essential that the Principal Research Physician undergoes thorough training and understands the training content.

See the "Clinical Research Core Hospital" section of the following website for information on research conducted by Clinical Research Core Hospitals.

https://www.mhlw.go.jp/stf/seisakunitsuite/bunya/chiken.html (in Japanese)

11.3.2 Period to Participate in RCR Education Program

As a general rule, persons required to participate in the RCR education program are requested to endeavor to do so prior to the conclusion of the agreement for the initial fiscal year of the R&D project., and should continue to participate in the RCR education program as appropriate thereafter. (Previous participation in the RCR education program may also be valid.)

11.3.3 Roles of research institutions, etc. - reporting on the status of research ethics training

Research institutions shall ensure that persons required to undergo research ethics training who are affiliated with their institution (included subcontracted institutions) undergo the R&D ethics education using the programs/materials listed above. They shall compile information on researchers' R&D ethics education status and submit a report on the status of their training using the form prescribed by AMED. This report shall be submitted by e-mail to AMED (Department of Research Integrity and Legal Affairs - Research Integrity and Shared Societal Issue Section). (No seal needs to be affixed.)

Information regarding where and how to submit reports is to be posted on the "The Responsible Conduct of Research (RCR) Education Program" page under "Research Integrity" on the AMED website (see the URL below) around March 2022.

In addition, if there are any persons who have experience of participating in symposiums, seminars or workshops and so on regarding research integrity held by AMED, or have experience of completing educational materials/programs created under the Research and Development Program for Enhancement of Research Integrity, please report these, as far as you know, using the form specified by AMED and along with the status of RCR education.

● Subject of report	Persons required to undergo research ethics training in programs commencing in/after FY2022
● Deadline of submission	Within 182 days of the date upon which the agreement is concluded.
● Documents to be submitted	"Report on the Status of Participation in R&D Education Programs" (Please download the form from the AMED website.)
● URL	https://www.amed.go.jp/kenkyu_kousei/kyoiku_program.html (in Japanese)

11.4 Conflict of Interest Management

In order to ensure the fairness and reliability of research, in accordance with AMED's "Regulations for Managing COI in Research Activities" and Article 21 of the Ordinance for Enforcement of the Clinical Research Act, the situation regarding conflict of interest for researchers involved in R&D projects shall be managed appropriately and reported.

In the case of research institutes conducting R&D under the AMED program, in the case that AMED determines that the conflict of interest of the PI or Co-Investigator of a project is not being managed appropriately, AMED may instruct the research institute to improve the situation or suspend provision of R&D funds, as well as require the research institute to return all or part of the R&D funds already paid.

11.4.1 Conflict of Interest Management in Accordance with AMED's Regulations Regarding Conflict of Interest (COI) Management in Research Activities

(1) Target Persons

PMs or co-Investigators of R&D projects. Projects on the List of Non-R&D Projects on the AMED websites Research Integrity page's "COI Management in R&D" are excluded as targets.

(2) Requests for COI Reviews

Prior to the conclusion of a contracted R&D agreement for the relevant R&D project each fiscal year, target persons shall report to the COI Committee regarding matters related to economic interests and then comment regarding reviews concerning conflict of interest in the R&D project.

11.4.2 Conflict of Interest Management in Accordance with Article 21 of the Ordinance for Enforcement of the Clinical Research ACT

Please carry out conflict of interest management in accordance with relevant laws and ordinances.

11.4.3 Submission of Reports on the State of COI Management

Each research institution, etc. should prepare a Report on the State of COI Management, and submit it to AMED within 61 days after the end of each fiscal year or the conclusion of the contracted R&D project. The Reports on the State of COI Management are to be posted on the AMED website*.

Information including the forms of the Report on the State of COI Management, where and how to submit reports is to be posted on the "Conflict of Interest (COI) Management in R&D" page under "Research Integrity" on the AMED website*.

* For details regarding conflict of interest management, please refer to the AMED website below.

- Regulations for Managing COI in Research Activities
- Regulations Q&A/ Reports on the State of COI Management

  https://www.amed.go.jp/kenkyu_kousei/riekisohan_kanri.html (in Japanese)

11.5 Compliance with Laws/Ordinances and Ethical Guidelines

In the case that implementation of the proposed R&D concept involves research requiring procedures based on laws/ordinances and/or ethical guidelines (such as R&D requiring the consent/cooperation of another party; R&D requiring care in handling personal information; and R&D requiring measures regarding bioethics/safety measures), research institutions must undertake the necessary procedures for obtaining the approval of both internal and external ethics committees.

Please note that, in the case that R&D is carried out in infringement of related laws, ordinances and guidelines that must be complied with, in addition to the imposition of punishments and penalties according to legislation, the R&D may be suspended, the contracted R&D agreement cancelled, and/or the decision to adopt the R&D project cancelled.

Furthermore, in the case that the R&D plan includes R&D or surveys requiring the consent/cooperation of another party or social consensus, research institutes must take appropriate measures with regard to the handling of the guarantee of human rights and interests.

Within 61 days after the end of each fiscal year or the conclusion of the contracted R&D project, research institutions shall report to AMED regarding the status of ethical reviews by research institutes concerning related laws/ordinances and policies as an item shown in the Contracted R&D Accomplishments Report.

Regarding R&D related to life sciences in particular, the main laws and ordinances prescribed by government ministries and agencies are as follows. In addition, there are also laws and ordinances that pertain to certain R&D content, so please check the latest revision of laws/ordinances, etc.

- Act on Regulation of Human Cloning Techniques (Act No. 146 of 2000)
- Act on Prevention of Infectious Diseases and Medical Care for Patients Suffering from Infectious Diseases (Act No. 114 of 1998)
- Law Concerning the Conservation and Sustainable Use of Biological Diversity through Regulations on the Use of Living Modified Organisms (Law No. 97 of 2003)
- Act on the Safety of Regenerative Medicine (Act No. 85 of 2013)
- Clinical Research Act (Act No. 16 of 2017)
- Ordinance for Enforcement of the Clinical Research Act (Ordinance of the Ministry of Health, Labour and Welfare (MHLW) No. 17 of 2018)
- Ministerial Ordinance on Good Clinical Practice for Drugs (Ordinance of the Ministry of Health and Welfare No. 28 of March 27, 1997)
- Ministerial Ordinance on Good Clinical Practice for Medical Devices (Ordinance of the Ministry of Health, Labour and Welfare (MHLW) No. 36 of 2005)
- Ministerial Ordinance on Good Clinical Practices for Regenerative Medical Products (Ordinance of the Ministry of Health, Labour and Welfare (MHLW) No. 89 of 2014)
- Ministerial Ordinance on Good Laboratory Practice for Nonclinical Safety Studies of Drugs (Ordinance of the Ministry of Health, Labour and Welfare (MHLW) No.21 of 1997)

- Ministerial Ordinance on Good Laboratory Practice for Nonclinical Safety Studies of Medical Devices (Ordinance of the Ministry of Health, Labour and Welfare (MHLW) No.37 of 2005)
- Ministerial Ordinance on Good Laboratory Practices for Nonclinical Safety Studies of Regenerative Medical Products (Ordinance of the Ministry of Health, Labour and Welfare (MHLW) No.88 of 2014)
- Guidelines on the Handling of Specified Embryos (Public Notice of the Ministry of Education, Culture, Sports, Science and Technology (MEXT) No. 31 of 2019)
- Guidelines on the Derivation of Human Embryonic Stem Cells (Public Notice of the Ministry of Education, Culture, Sports, Science and Technology (MEXT) and the Ministry of Health, Labour and Welfare (MHLW) No. 4 of 2019)
- Guidelines on the Handling of Human Embryonic Stem Cells (Public Notice of the Ministry of Education, Culture, Sports, Science and Technology (MEXT) No. 68 of 2019)
- Guidelines for Human Embryonic Stem Cell Distributing Institutes (Public Notice of the Ministry of Education, Culture, Sports, Science and Technology (MEXT) No. 69 of 2019)
- Guidelines on Research Involving the Production of Germ Cells from Human iPS Cells or Human Tissue Stem Cells (Public Notice of the Ministry of Education, Culture, Sports, Science and Technology (MEXT) No. 88 of 2010)
- Ethical Guidelines for Research on Assisted Reproductive Technology Treatment Involving the Production of Human Fertilized Embryos (Public Notice of the Ministry of Education, Culture, Sports, Science and Technology (MEXT) and the Ministry of Health, Labour and Welfare (MHLW) No. 2 of 2010, partially revised on July 30, 2021)
- On the Approach of Research and Development Using Human Tissues Obtained from Surgery (Report of the Health Science Council, the Ministry of Health and Welfare, 1998)
- Ethical Guidelines for Medical and Health Research Involving Human Subjects (Public Notice of the Ministry of Education, Culture, Sports, Science and Technology (MEXT), and Ministry of Health, Labour and Welfare (MHLW) No. 1 of 2017)
- Policies on Clinical Research Involving Gene Therapy (Public Notice of the Ministry of Health, Labour and Welfare (MHLW) No. 344 of 2015)
- Fundamental Guidelines for Proper Conduct of Animal Experiments and Related Activities in Academic Research Institutions (Public Notice of the Ministry of Education, Culture, Sports, Science and Technology (MEXT) No. 71 of 2006); Fundamental Guidelines for Proper Conduct of Animal Experiments and Related Activities in Implementing Agencies under the Ministry of Health, Labour and Welfare (Notification by Director, Health Science Division, Minister's Secretariat, Ministry of Health, Labour and Welfare (MHLW) on June 1, 2006; partially revised on February 20, 2015); and Fundamental Guidelines for Proper Conduct of Animal Experiments and Related Activities in Implementing Agencies under the Ministry of Agriculture, Forestry and Fisheries (Notification by the Director-General of the Secretariat, Agriculture, Forestry and Fisheries Research Council, Ministry of Agriculture, Forestry and Fisheries (MAFF) on June 1, 2006)
- Guidelines on Opportunities for Acquisition of Genetic Resources and on Fair and Equitable Distribution of the Profits Generated through their Use (Public Notice of the Ministry of Finance (MOF), the Ministry of Education,

Culture, Sports, Science and Technology (MEXT), the Ministry of Health, Labour and Welfare (MHLW), the Ministry of Agriculture, Forestry and Fisheries (MAFF), the Ministry of Economy, Trade and Industry (METI), and the Ministry of Environment (MOE) No. 1 of 2017)

*Please refer to the following websites for details regarding bioethics and ensuring safety.

・MEXT's Life Sciences Forum "Initiative on Bioethics and Biosafety"
https://www.lifescience.mext.go.jp/bioethics/index.html

・Regarding Guidelines on Research (Ministry of Health, Labour and Welfare (MHLW))
https://www.mhlw.go.jp/stf/seisakunitsuite/bunya/hokabunya/kenkyujigyou/i-kenkyu/index.html

11.6 Obligation to Take Action with Regard to System Maintenance, etc.

All research institutions must strictly comply with the items required to be implemented by research institutions in accordance with the Guidelines for Responding to Misconduct, etc. in Research Activities with regards to Programs relating to Cabinet Budgets for Japan Agency for Medical Research and Development (formulated on March 1, 2017 by Office for Japan Agency for Medical Research and Development, Cabinet Office) and the Guidelines for Responding to the Misuse of Research Funds with regards to Programs relating to Cabinet Budgets for Japan Agency for Medical Research and Development (formulated on March 1, 2017 by Office for Japan Agency for Medical Research and Development, Cabinet Office).

Chapter 12. Countermeasures to Misconduct, Fraudulent Use, and Fraudulent Receipt

12.1 Reporting of and Cooperation in Investigations of Misconduct, Fraudulent Use, and Fraudulent Receipt

In the case that a complaint (including criticism from external organizations such as the media or the Board of Audit) related to misconduct, fraudulent use, or fraudulent receipt (hereinafter collectively referred to as "misconduct") by a research institution in relation to this program (if there is a subcontractor, including in cases that researchers or others at the subcontractor engaged in this program are suspected to have committed Misconduct, etc. in in this program), the research institution shall swiftly report to AMED that it will be commencing a preliminary investigation into the matter in accordance with the Guidelines on the Handling of Improprieties in Research Activities in Programs Funded by Cabinet Office Budgets at the Japan Agency for Medical Research and Development (established March 1, 2017; AMED office within Cabinet Office), Guidelines on the Handling of Inappropriate Use of Research Expenses for Programs Funded by Cabinet Office Budgets at the Japan Agency for Medical Research and Development (established March 1, 2017; AMED office within Cabinet Office, and the AMED Regulations for Responding to Misconduct in Research Activities.

In the event that it is deemed necessary for the research institution to conduct a formal investigation, an investigative committee must be established and the policy, targets, and methods of the investigation discussed with AMED.

Note that in this case, AMED may order the accused and/or the research institution to suspend use of research funds under this program as a temporary measure during the formal investigation if necessary.

Furthermore, the research institution must submit to AMED a final report including the investigation outcome, cause of the misconduct, status of management/auditing of other competitive research funding in which the people involved in the misconduct are also involved, and plan for preventing recurrence by the deadline prescribed under the AMED Regulations for Responding to Misconduct in Research Activities. For details regarding items that should be incorporated into the final report, please refer to the Guidelines on the Handling of Improprieties in Research Activities in Programs Funded by Cabinet Office Budgets at the Japan Agency for Medical Research and Development (established March 1, 2017; AMED office within Cabinet Office), Guidelines on the Handling of Inappropriate Use of Research Expenses for Programs Funded by Cabinet Office Budgets at the Japan Agency for Medical Research and Development (established March 1, 2017; AMED office within Cabinet Office), and the AMED Regulations for Responding to Misconduct in Research Activities.

In the case that it is confirmed that misconduct has occurred even partially and even before the investigation has been completed, the research institution must swiftly recognize this fact and report it to AMED, as well as submit an investigation progress report and/or interim investigation report, even if the investigation has not yet concluded.

Please note that, except in the case that there is a legitimate reason, such as hindering the investigation, the research institution must submit materials pertaining to the relevant case to AMED and respond to AMED's perusal of these materials and on-site investigations.

In the case that that research institution extends the deadline for submission of the final report, AMED may take measures against the research institution such as reducing indirect costs by a certain percentage or suspending execution of contracted R&D funds.

12.2 In the Event that Misconduct, Fraudulent Use, or Fraudulent Receipt is Discovered

In the case that misconduct takes place under this program, the following measures will be taken against the relevant research institution and researcher(s) in accordance with the Guidelines on the Handling of Improprieties in Research Activities in Programs Funded by Cabinet Office Budgets at the Japan Agency for Medical Research and Development (established March 1, 2017; AMED office within Cabinet Office), Guidelines on the Handling of Inappropriate Use of Research Expenses for Programs Funded by Cabinet Office Budgets at the Japan Agency for Medical Research and Development (established March 1, 2017; AMED office within Cabinet Office), and the AMED Regulations for Responding to Misconduct in Research Activities.

12.2.1 Cancellation of contracted R&D agreement

In the case that AMED recognizes that misconduct has taken place under this program, AMED shall cancel the contracted R&D agreement with the relevant research institute and demand the return of all or part of the contracted R&D funds from the research institute. In the event that contracted R&D funds are returned, the relevant research institute will be required to pay interest calculated in accordance with the number of days from the date of the receipt of contracted R&D funds until the date of return. The interest will be determined by AMED within the scope of 10.95% per annum for the contracted R&D funds (if a portion of the amount has been returned already, the already returned amount will be subtracted from the balance for the remaining time). Furthermore, AMED may not provide contracted R&D funds to the relevant research institute for the next fiscal year or thereafter.

12.2.2 Restrictions on applications and eligibility for participation

Researchers who are found to have carried out misconduct under this program or who are recognized as having been involved in or responsible for the misconduct shall have their application to and eligibility for participation in AMED programs restricted in accordance with the degree of misconduct as shown in the table below. Furthermore, in the case that misconduct is recognized to have taken place under this program and restrictions are placed on the researcher's application to and eligibility for participation in AMED programs, the related government ministries and agencies will be informed of an outline of the misconduct in question (name of the researcher responsible for misconduct, program name, research institution, research project, budget amount, fiscal year of research, details of the misconduct and details of measures

taken against them etc.). In this way competitive research funding programs provided by related government ministries/agencies may similarly be restricted in some cases.

[In the case of misconduct]

The period of restriction deemed appropriate in consideration of the misconduct and its nature, on or after the day that the misconduct is recognized, and between one year and ten years from the fiscal year in which the day on which the misconduct is recognized or the next fiscal year.

<table>
<tr><th colspan="3">Category of misconduct according to involvement</th><th>Degree of misconduct</th><th>Period deemed appropriate</th></tr>
<tr><td rowspan="5">Person Involved in the Misconduct</td><td colspan="2">1.Especially malicious individual who intentionally engages in misconduct from the outset of the research</td><td></td><td>10 years</td></tr>
<tr><td rowspan="3">2. Author of academic paper, etc. related to research in which there has been misconduct.</td><td rowspan="2">The author responsible for the academic paper in question (supervisor, first author, or other position of responsibility deemed equivalent)</td><td>The impact on the advancement of research in the relevant field or society is large, and the maliciousness of the misconduct is deemed to be high.</td><td>5-7 years</td></tr>
<tr><td>The impact on the advancement of research in the relevant field or society is small, and the maliciousness of the misconduct is deemed to be low.</td><td>3-5 years</td></tr>
<tr><td>Author other than that listed above</td><td></td><td>2-3 years</td></tr>
<tr><td colspan="2">3. An individual involved in misconduct other than that stipulated in 1 or 2</td><td></td><td>2-3 years</td></tr>
<tr><td colspan="3">An author responsible for academic papers, etc. related to research in which there has been misconduct but who was not involved in the misconduct (supervisor, first author, or other position of responsibility deemed equivalent)</td><td>The impact on the advancement of research in the relevant field or society is large, and the maliciousness of the misconduct is deemed to be high.</td><td>2-3 years</td></tr>
</table>

	The impact on the advancement of research in the relevant field or society is small, and the maliciousness of the misconduct is deemed to be low.	1-2years

[In the case of fraudulent use/fraudulent receipt]

The period of restriction deemed appropriate in consideration of the content etc. of the fraudulent use/fraudulent receipt, on or after the day that AMED decides upon the measures, and between one year and ten years from the fiscal year in which the day on which AMED decides upon the measures or the next fiscal year.

<table>
<tr><th>Researchers involved in fraudulent use or receipt whose applications will be restricted</th><th colspan="2">Severity of fraudulent use</th><th>Period of application restriction</th></tr>
<tr><td rowspan="4">1. Researcher who perpetrated fraudulent use and conspiring researchers</td><td colspan="2">(1) Personal diversion of funds for private benefit</td><td>10 years</td></tr>
<tr><td rowspan="3">(2)
Other than (1)</td><td>i) The researcher’s actions are deemed to have a large social impact and be highly malicious.</td><td>5 years</td></tr>
<tr><td>ii) Those other than i) and iii)</td><td>2 to 4 years</td></tr>
<tr><td>iii) The researcher’s actions are deemed to have a small social impact and be slightly malicious.</td><td>1 year</td></tr>
<tr><td>2. Researchers who received competitive research funds, etc. through falsehoods or other dishonest means and conspiring researchers</td><td colspan="2"></td><td>5 years</td></tr>
<tr><td>3. Researchers not directly involved in fraudulent use but who use the research funds in a manner infringing duty of diligence</td><td colspan="2"></td><td>Maximum of two years and minimum of one year depending on the severity of</td></tr>
</table>

		infringement of diligence by the researcher with duty of diligence

Note 1: In the following cases, the offender shall be given a reprimand without imposing restrictions on eligibility for participation.

- In Case 1, the researcher's actions are deemed to have a small social impact and be slightly malicious, and the funding amount used fraudulently is small.
- In Case 3, the researcher's actions are deemed to have a small social impact and be slightly malicious.

Note 2: Regarding Case 3, the period will be determined in the light of the magnitude of the violation of the duty of diligence.

12.2.3 Restrictions on researchers' subject to restrictions on applications and eligibility for participation in other competitive research fund programs

With regard to researchers who have been found to have carried out misconduct under research funding programs (including but not limited to competitive research funds, etc. and management expenses grants) (including programs for which new applications are solicited in FY2021 or later, and programs completed in or before FY2020) other than this program, which are under the jurisdiction of the national government or an independent administrative agency and are government-financed either wholly or in part, and whose application to and eligibility for participation in these programs has been restricted, application to and eligibility for participation as PI or Co-Investigator in this program shall also be restricted for the duration of the restrictions imposed. In the case that the relevant researcher's application to or participation in this program becomes known after adoption by another program, adoption by the relevant program may be cancelled. Furthermore, in the case that the relevant researcher's participation in this program becomes known after the conclusion of the contracted R&D agreement, the relevant agreement may be cancelled.

12.2.4 Suspected misconduct within any other competitive research fund program

In the case that there is a complaint, etc., that a researcher, etc. participating in this program is suspected of perpetrating misconduct under another competitive research funding program (including completed programs), the research institution with which the relevant researcher, etc. (if there is a subcontractor, including researchers or others at the subcontractor engaged in this program) is affiliated is obligated to report to AMED that a formal investigation of the relevant misconduct allegations has been implemented. Please note that, on receipt of this report, AMED may order the temporary suspension of usage of contracted R&D funds if deemed necessary.

Furthermore, in the case that the research institute to which the relevant researcher is affiliated fails to make the above report, the contracted R&D agreement may be cancelled

12.2.5 Public announcement of misconduct

In the case that the measures and/or restrictions prescribed in 12.2.1 and 12.2.2 above are implemented under this program, an outline of the misconduct in question (program name, research institution, fiscal year of research, details of the misconduct and details of measures taken against them) shall as a general rule be publicly disclosed in accordance with the Guidelines on the Handling of Improprieties in Research Activities in Programs Funded by Cabinet Office Budgets at the Japan Agency for Medical Research and Development (established March 1, 2017; AMED office within the Cabinet Office), Guidelines on the Handling of Inappropriate Use of Research Expenses for Programs Funded by Cabinet Office Budgets at the Japan Agency for Medical Research and Development (established March 1, 2017; AMED office within Cabinet Office), etc. In addition, the misconduct may be similarly disclosed by the related government ministries/agencies.

12.3 Registration with AMED RIO Network

To promote research integrity activities in an efficient manner, it is essential for AMED and the research institution or research institutions among themselves to exchange information and work together. Accordingly, to promote efficient research integrity activities nationwide, the RIO Network was established in FY 2017 to provide a venue where the Research Integrity Officers (RIO) of research institutions which are allocated research funds from AMED can easily exchange information. Detailed information on the RIO Network is provided on the website*.

The officers in charge of R&D ethics education and the officers in charge of promoting compliance (collectively referred to as “Research Integrity Officers” or RIO) who are participating in AMED programs should become members of the RIO Network.

There is a space on the “Breakdown of Expenses, etc. and Contracted Items Sheet,” which is submitted when the contract is concluded, for entering information about the officers in charge of R&D ethics education and the officers in charge of promoting compliance, so be sure to fill in this information. AMED will register Research Integrity Officers with the RIO Network. When registering personnel other than the above who are engaged in research integrity related tasks with the RIO Network, please do so in accordance with the instructions on the AMED RIO Network website.

*https://www.amed.go.jp/kenkyu_kousei/rionetwork.html (in Japanese)

Chapter 13. Others

While these items do not impact evaluations under each program unless noted as a special condition, AMED requires grant program participants to proactively endeavor to adhere to comply with each of these items due to their importance. Research institutions and researchers are asked to gain a thorough understanding of the purposes of these items and comply with these in carrying out their R&D.

Moreover, to ensure that the results of these efforts contribute to the improved implementation of AMED programs in the future, not only may they be used in analysis of research trends, but also the analysis results may be publicized in a form that does not identify the R&D project (E.g.: published by program rather than individual project). Accordingly, it is required that this information is included in Contracted R&D Accomplishments Reports.

13.1 Promoting Dialogue and Cooperation with Society

In accordance with the “Promotion of the 'Dialogue on Science and Technology with Citizens' (A Basic Course of Action)” (decided by the Minister of State for Science and Technology Policy and the Executive Members of the Council for Science and Technology Policy on June 19, 2010), requires not only that science and technology results are returned to the general public, but also that the content and results of R&D activities be explained to society and the general public in an easy-to-understand manner from the standpoint that it is imperative to take the stance of obtaining the general public’s understanding and support as well as promoting science and technology in order to generate outstanding science and technology results without pause, further advancing Japan’s science and technology. The 5th Science and Technology Basic Plan (decided by a Cabinet Decision on January 22, 2016) demands that science and technology and society, which have traditionally worked at cross purposes, need to have a deeper relationship in order to facilitate dialogue and cooperation, or “co-creation,” between a diverse range of stakeholders, including researchers, citizens, media, industry, and policymakers. From this perspective, there is a need for initiatives to explain research activity contents and their results and accomplishments in a comprehensible manner to society and the general public, and to promote dialogue and cooperation with many stakeholders. In response to this, research institutions are requested to hold public meetings and symposia, about their R&D accomplishments and continuously post their R&D accomplishments on the Internet, and eagerly involve themselves in round table meetings etc. that include the participation of a wide spectrum of stakeholders.

Reference: Regarding the Promotion of Dialog with Citizens on Science and Technology (basic initiative guidelines).

https://www8.cao.go.jp/cstp/stsonota/taiwa/taiwa_honbun.pdf (in Japanese)

Reference: The 5th Science and Technology Basic Plan

https://www8.cao.go.jp/cstp/kihonkeikaku/5honbun.pdf (in Japanese)

13.2 Promoting the Patient and Public Involvement (PPI) in Medical Research/Clinical Studies

AMED's mission is to approach each patient individually, staying close and providing support for LIFE (being alive, living each day, living life) while ensuring the practical application of research results in the medical field as quickly as possible and delivering these results to patients and their families. In view of this mission, AMED is promoting initiatives that promote Patient and Public Involvement (PPI)*1 in medical research and clinical studies. These efforts are expected to generate research results that are even more beneficial to patients, etc., as well as lead to smoother implementation of research and improved protection of clinical trial subjects. For these reasons, AMED requests that program participants proactively incorporate PPI into medical research and clinical studies.

*1 AMED's definition of "Patient and Public Involvement (PPI) in Medical Research/Clinical Studies"

As part of the medical research/clinical study process, researchers are endeavoring to incorporate the knowledge and opinions of patients and members of the general public. Here, "Patient and Public" includes patients, patients' families, former patients (survivors), and future patients.

Reference: AMED's "Patient/Public Involvement (PPI) in Medical Research/Clinical Studies"

https://www.amed.go.jp/ppi/index.html

13.3 Health Risk Information

In accordance with requests from the Ministry of Health, Labour and Welfare, AMED requires researchers to report information obtained in the process of conducting research that could seriously threaten the lives and/health of members of the general public (hereinafter referred to as "Health risk Information") to the Ministry of Health, Labour and Welfare using the prescribed form*1. For details such as contact information, please refer to the AMED Administration Manual for Contracted R&D Agreement in Japan Agency for Medical Research and Development*2.

The health risk information provided is evaluated together with other information by the Ministry of Health, Labour and Welfare and used in considering necessary responses to the relevant health risk. Providing this information does not place responsibility on the researcher, so please provide a broad range of information.

*1 https://www.mhlw.go.jp/file/06-Seisakujouhou-10600000-Daijinkanboukouseikagakuka/kenkoukiken.doc (in Japanese)

*2 https://www.amed.go.jp/keiri/index.html (in Japanese)

13.4 Smoothing Utilization of Research Tool Patents

With regard to research tool patents, please endeavor to handle research tool patents appropriately in accordance with the Guidelines for Facilitating the Use of Research Tool Patents in the Field of Life Sciences (Council for Science and Technology Policy (now the Council for Science, Technology and Innovation), March 1, 2007.

13.5 Measures Related to the IP Strategic Program

The “IP Strategic Program” is a program formulated every year by Intellectual Property Strategy Headquarters in accordance with the Intellectual Property Basic Act (Act No. 122 of 2002) with the aim of promoting strengthening of IP strategies. As the Intellectual Property Strategic Program 2014 (Intellectual Property Strategy Headquarters on July 4, 2014*1), sets forth the strategic utilization of certification in order to further invigorate international standardization activities, AMED is also to promote R&D with a view to international standardization/certification.

Accordingly, in the case that a public research institute under this program carries out R&D with the potential to lead to international standardization/certification, the research institute is requested to undertake R&D with a view to international standardization, such as considering support when instigating certification activities for incorporating formulation of standards for certification into individual R&D plans and including the participation of certification organizations in R&D activities.

*1 Excerpted from the Intellectual Property Strategic Program 2014
https://www.kantei.go.jp/jp/singi/titeki2/kettei/chizaikeikaku20140704.pdf (in Japanese)
First pillar: Building up a global IP system for enhancing industrial competitiveness
4. Efforts for international standardization and certification
(2) Measures to be taken in the future
(Promoting international standardization strategies in specific strategic fields*2)
・With regard to international standardization strategies in specific strategic fields (with the fields selected based on market scale and growth potential, expandability of the field, Japan’s superiority in the field, and the significance of international standardization), the Government of Japan will take the lead in international discussions and facilitate voluntary efforts made by interested parties (short term and medium term) (Cabinet Secretariat, Cabinet Office, MIC, MEXT, Ministry of Health, Labour and Welfare [MHLW], MAFF, METI, Ministry of Land, Infrastructure, Transport and Tourism [MLIT], Ministry of the Environment [MOE]).

*2 “Specific strategic fields”: (1) Advanced medical technology, (2) Water, (3) Next generation vehicles, (4) Railways, (5) Energy management, (6) Digital content, (7) Robots.

13.6 IP Consultation Support through AMED IP Consultants and AMED IP Liaisons

In order to encourage the practical application of R&D accomplishments obtained from AMED projects implemented, AMED provides a free-of-charge IP consultation service run by AMED IP Consultants and AMED IP Liaisons*1 covering IP strategy and licensing strategies. Furthermore, as one facet of this IP consultation service, when requested we also provide a free service to formulate precise IP strategies for R&D accomplishments through investigating the available literature, etc.

In addition, the AMED IP Liaison visits research institutions throughout the nation and in conjunction with the AMED IP Consultants help to create a system enabling consultation at an early stage regarding

appropriate out-licensing of R&D accomplishments obtained. Specifically, the AMED Liaison provides 1) IP strategy advice aimed at appropriate out-licensing at the early stages of R&D, 2) investigations of the available literature, markets research and support for technical seeds evaluation, and 3) guidance for the creation of appropriate PR sheets on R&D accomplishments for exhibitions and business negotiations.

If you wish to receive the support mentioned above, please contact AMED's Medical IP Desk*2. Please refer to the website2 below for information regarding the Medical IP Desk.

*1 AMED IP Liaisons: https://www.amed.go.jp/chitekizaisan/chizai_riezon.html (in Japanese)

*2 Medical IP Desk: https://www.amed.go.jp/chitekizaisan/medical_ip_desk.html (in Japanese)

13.7 Seeds/Needs Matching Support System "AMED ぷらっと® / AMED plat"

In April 2018, AMED launched the "AMED ぷらっと® / AMED plat" private information network system, the purpose of which is to match at the earliest possible stage the R&D seeds information of universities and other academia with corporate needs information, providing support aimed at achieving early practical application and commercialization of R&D results in the medical field. This enables research seeds to be showcased to staff in charge of in-licensing at multiple companies, facilitating university-company collaboration at an early stage. In order to achieve this it is requested that you proactively register research seeds in the medical field in the AMED ぷらっと® / AMED plat system. Note that you should refer to the AMED ぷらっと® / AMED plat website* regarding details about the launch of use of the AMED ぷらっと® / AMED plat.

* AMED ぷらっと® / AMED plat WEB SITE

https://www.amed.go.jp/chitekizaisan/amed_plat.html

13.8 Support from the AMED Drug Discovery Support Network/Department of Innovative Drug Discovery and Development

In order to link the accomplishments of outstanding basic research by universities, etc. to the practical application of drugs, AMED's Department of Innovative Drug Discovery and Development (hereinafter referred to as the "iD3") functions as headquarters for constructing a nationwide "Drug Discovery Support Network" comprising the Institute of Physical and Chemical Research (RIKEN), National Institutes of Biomedical Innovation, Health and Nutrition (NIBIOHN), National Institute of Advanced Industrial Science and Technology (AIST), and other institutions. Network activities include providing continuous support for practical application related to drug discovery research, mainly from the applied study stage through to the preclinical development stage, as well as out-licensing to a company.

The iD3 provides a wide range of consultation services for researchers undertaking drug discovery research as part of programs implemented by the Department, as well as gathers, examines, and evaluates information regarding promising R&D seeds; formulates R&D plans (including exit strategies) aimed at IP strategies for individual R&D seeds and out-licensing to drug companies; provides technological support for applied research (exploratory study, optimization study, etc.) and nonclinical studies (conforming to GLP

(Good Laboratory Practice)); provides introduction and contracted support of CROs (Contract Research Organizations) and CMOs (Contract Manufacturing Organizations), etc.; and facilitates out-licensing process to drug companies.

In this way, the iD3 is a department that specializes in providing advice on technological projects related to practical application to researchers at universities, etc., engaged in drug discovery research, as well as support for formulating R&D strategies aimed at out-licensing to drug companies. For this reason, R&D projects that are related to drug development may receive active support from the iD3 in coordination with the division in charge of this program.

Accordingly, information regarding applications for R&D projects related to drug development shall be provided to the Drug Development Department, regardless of whether or not the project is adopted under this program (please refer to Chapter 6.). Furthermore, the iD3 provides the above-mentioned support based on requests by researchers on the premise of maintaining confidentiality and protecting IP rights that have reverted to the researcher.

In the same way, with regards to the applied R&D projects related to drug development that is or was supported by the iD3, AMED provides the information on the support content to the division in charge of this program.

Please refer to Chapter 14 for references related to support provided by the AMED Drug Discovery Support Network and the iD3.

13.9 Support for Research Seeds and R&D through Translational and Clinical Research Core Centers

AMED is building a system to consistently link the accomplishments of basic research conducted by academia etc. with practical application at Translational and Clinical Research Core Centers (Centers for Advancing Translational Research and Clinical Research Core Hospitals).

In order to support the development of drugs and medical devices, the Translational and Clinical Research Core Centers secure human resources specialized in pharmaceutical affairs, biostatistics, project management, intellectual property, as well as provide biomarker evaluation equipment, cell processing facilities, and management centers securely handling clinical study data, supporting processes from the basic research stage through clinical studies, clinical trials, and practical application of research seeds generated by Translational and Clinical Research Core Centers and other research institutions. Furthermore, the Translational and Clinical Research Core Centers run programs to foster the young human resources taking on R&D into drugs and medical devices and medical entrepreneurs, and host seminars and symposia for those aiming to achieve practical application in medical fields.

The various services, consultations and shared facilities provided by the Translational and Clinical Research Core Centers are not restricted to within its centers and hospitals, but can also be used by a wide range of researchers ranging from those of external research institutions to corporate researchers including those of ventures. (There are charges for part of the support business and services according to the regulations of each organization.) For programs in which disbursement of Academic Research

Organization (ARO) support expenses as research expenses is approved, those wishing the support of Translational and Clinical Research Core Centers when planning and implementing research aimed at the practical application of medical seeds are requested to refer to the contact points provided in the List of Translational and Clinical Research Core Centers* provided below.

* List of Translational and Clinical Research Core Centers

https://www.amed.go.jp/program/list/16/01/001_ichiran.html (in Japanese)

13.10 Registering Researcher Information on researchmap

researchmap* is the largest database in Japan serving as a list of researchers in the nation. It enables researchers to publicize their registered accomplishments over the Internet. In addition, researchmap links in with e-Rad and many university databases of researchers, and since the information registered on it can be used on other systems it makes it unnecessary for researchers to repeatedly input information in multiple application forms about accomplishments and applications on various databases. The information registered on researchmap is effectively used in governmental and other science and technology policy making research and for statistical purposes, and those carrying out projects under this program are therefore requested to cooperate by registering with researchmap.

* https://researchmap.jp/?lang=en

13.11 Deposit of Developed Resources in Domestic Resource Centers

It is strongly recommended that after using bioresources developed under this program and publishing the research accomplishments obtained via academic papers, etc., the persons implementing this program are to deposit*1 the relevant bioresources in domestic resource centers*2, and make them broadly available for researchers' use.

*1 "Deposit": Procedure for permitting the use (storage/provision) of resources at domestic resource centers etc. listed in 1 above without transferring various rights related to the relevant resources. By prescribing conditions for provision within the deposit consent form, it is possible to add conditions regarding restrictions on use of resources and citation in academic papers, etc., for users receiving the relevant resources.

*2 Domestic public centers conducting deposit, storage and provision such as The National Bioresource Project (NBRP), RIKEN BioResource Research Center, National Institutes of Biomedical Innovation, Health and Nutrition, universities, etc.

13.12 Cooperation with Databases

(1) Publishing Data from the National Bioscience Database Center

The National Bioscience Database Center (NBDC) (https://biosciencedbc.jp/en/) was established in April 2011 in the Japan Science and Technology Agency in order to promote the integrated use of the life science database that has been created through the efforts of many research institutions. "The State of Progress and Future Direction of the Life Science Database Integration Project" that was

published on January 17, 2013, states that an expansion of the programs eligible to receive data and databases will be implemented with the Center playing a central role.

Based on this, you are asked to cooperate with the provision of data to the Center with regard to the following types of data and databases resulting from this program.

No.	Type of data	Publication platform	Publication platform URL
1	Outline of the database created for publication	Integbio Database Catalog	https://integbio.jp/dbcatalog/
2	Copies of data concerning results published in academic papers, or other means, or copies of the database created for publication.	Life Science Database Archive	https://dbarchive.biosciencedbc.jp/
3	Data or databases concerning humans from 2 above	NBDC Human Database	https://humandbs.biosciencedbc.jp/

(2) Registering with the Patient Registry Database Search System

By using a disease registry system (patient registry) in clinical development the Clinical Innovation Network (CIN) aims to vitalize clinical development of drugs and medical devices in Japan, and is a project led by the Ministry of Health, Labour and Welfare in which the environmental preparations are made by an industry-government-academia alliance. Through the promotion of the use of a disease registry system (patient registry) the National Center for Global Health and Medicine creates an information search system regarding the patient registries in existence in Japan as a part of support for efficient clinical development of drugs and medical devices, and makes this available to the general public (https://cinc.ncgm.go.jp/). Those working on R&D projects related to patient registries and cohort studies (not including clinical trials and intervention studies) who have yet to register with the system are requested to do so.

(3) Other

With regard to specimen storage and genome analysis, R&D projects are required to actively use existing research bases, and AMED may in some cases provide guidance regarding/matching with the most suitable research bases. Accordingly, please cooperate in the event that AMED requests that the R&D project provides data to various databases designated by AMED, including in response to the above.

13.13 Improvement of Incentives for Doctoral Students

Under the 6th Science, Technology, and Innovation Basic Plan (Cabinet decision of March 26, 2021), aiming to increase three-fold the number of doctoral students receiving the amount equivalent to living expenses (equivalent to about 30% of all doctoral students receiving the amount equivalent to living expenses) was cited as a numerical target in order to attract excellent students and working adults from Japan and overseas, and enhance the financial support of graduate students and in particular doctoral students. In addition, the Basic Plan states that in order to promote the payment of salaries to doctoral students at an appropriate level for research assistants (RA) from competitive research funds and joint research funds, the government will formulate rules for the payment of RA expenses relating to employment and remuneration for RAs at each business and university, and implement them sequentially from FY2021, and urges the expansion of the employment of doctoral students as RA at universities and research and development agencies, and the improved treatment of doctoral students.

In addition, the Guidelines on Employment and Fostering of Postdoctoral Students (formulated on December 3, 2020, by MEXT's Council for Science and Technology's Committee on Human Resources) state as follows with regard to doctoral students:

> While being students, doctoral students also have the facet of being researchers, and improving the environment for research activities and employment status is an important responsibility of universities as the fosters of researchers. (…) It is particularly vital that the contributions of doctoral students are appropriately evaluated by setting wages appropriate to the nature and content of work and the payment of salaries corresponding to the amount of time they have spent on work. (…) It is essential that universities, etc. budget as direct costs the requisite expenses in the event that they employ RAs when applying for competitive research funds, and that they conduct reviews and so on of their internal regulations in order to enable the payment to RAs of an acceptable level of wages.

In the light of that fact, in this program the doctoral students requisite for the execution of the research should be enthusiastically employed as RAs, etc. At the same time, unit costs fitting to the nature and content of their work should be set, and it is requested that doctoral students be paid a salary in accordance with the time they spend working under appropriate work management. It is also requested that when applying for this program applications are made with a funding plan paying due consideration to the salary levels of the above-mentioned doctoral students.

Points to Note

- Under the 6th Science, Technology, and Innovation Basic Plan the amount equivalent to living expenses of doctoral students is set as a minimum of 1.8 million yen per year. Furthermore, in order that excellent doctoral students can apply themselves to their research without feeling any financial concerns, the Basic Plan states the wide-sweeping expansion of those receiving around 2.4 million yen per year, equivalent to the stipend paid through the JSPS Research Fellowship for Young Researchers (Doctoral Course Students (DC)) program.

- With regard to the employment of doctoral students in order to execute research projects, the Guidelines on Employment and Fostering of Postdoctoral Students state that “Considering the average salary of assistant professors without tenure who are employed in competitive research funds etc., it is thought that the payment of an hourly wage of around 2,000 yen to 2,500 yen would be a standard amount.”
  * Considering the average salary of assistant professors without tenure who are employed in competitive research funds etc., it is thought that the payment of an hourly wage of around 2,000 yen to 2,500 yen would be a standard amount. (The August 2020 bulletin edition of the Survey on The Employment Status of Instructional Staff Members at Research Universities calculates the hourly wage of doctoral students by dividing the median value of the monthly salaries of assistant professors without tenure (between 400,000 and 450,000 yen) by a 19- to 20-day shift (excluding holidays etc.) of seven and three-quarter hours to eight hours, and subtracting 20% in consideration of the recipients’ status as doctoral students.)
- Research institutions are requested to decide by themselves the specific amounts and period the doctoral students will be paid. Salary payments of either a higher or lower amount than the salary level indicated above are permissible.
- When employing a doctoral student as an RA pay consideration to ensuring they do not work excessive hours and allow the doctoral students to maintain a balance with their own research and studies.

13.14 Securing Autonomous Stable Research Environments for Young Researchers

Since both “Improving and Reforming Research Capability 2019” (formulated on April 23, 2019 by MEXT) and “Development of Science and Technology Innovation Policy Towards the Creation of Knowledge-intensive Value: Towards a Nation that Leads the World in Achieving Society 5.0 (final summary)” (formulated on March 26, 2020, by MEXT’s Council for Science and Technology’s Comprehensive Policy Special Committee) points out that with regard to fixed-term positions such as specially appointed faculty members and postdoctoral fellows short-term appointments may hinder their career development, and securing tenures of five years or more is important.

In addition, with regard to national university corporations and inter-university research institute corporations, the “Guidelines on Personnel Salary Management Reform at National University Corporations etc.: Towards the Creation of Personnel Salary Management that are Attractive and Contribute to Improving Education and Research Capabilities” (formulated on February 25, 2019 by MEXT) state that “In order to achieve the twin perspectives of fostering young researchers and stable employment, even in the cases of fixed tenures, by using expenses with a high degree of freedom such as indirect costs and donations, it is to be hoped that certain terms of employment of between five to ten year are secured, and systems that maintain flexibility while incorporating researcher-fostering perspectives are designed and promoted.”

In the light of all of the above, in the event that young researchers such as specially appointed faculty members and postdoctoral fellows are employed in this program please strive to secure tenures of the length of the R&D period, having checked with the persons in charge of personnel and accounts in the

relevant department, and also make an effort to, as far as possible, secure tenures of five years or more through the utilization of other external funding such as indirect expenses, basic expenses and donations.

13.15 Research Activities Conducted at Their Own Initiative by Young Researchers Engaged

In line with the Implementation Guidelines Concerning Research Activities Conducted at Their Own Initiative by Young Researchers Employed for Project Implementation Using Competitive Research Funds (revised on December 18, 2020 at the Liaison Meeting of Relevant Ministries on Competitive Research Fund), and with regard to the certain degree (set at a ceiling of 20%) of effort made by young researchers who are engaged in this program and whose personnel costs are paid by this program, in the event that the PI etc. judge that the young researcher's own initiative does not obstruct the R&D in question but at the same time contributes to it, the consent of their institution of affiliation is obtained it is possible to allot that effort to activities that contribute to research activities conducted at their own initiative or improvements in research and management capabilities. For more details, please refer to the Administration Manuals and Forms* in the Program Administrative Procedures (Forms and other documents) section of the AMED website.

* https://www.amed.go.jp/keiri/index.html (in Japanese)

13.16 Support for Diverse Career Path for Young Researchers

According to the Basic Policy on Support for Diverse Career Paths for Young Postdoctoral Fellows to Be Employed through MEXT Public Research Funds (formulated on December 20, 2011 by MEXT's Council for Science and Technology's Personnel Committee), "The public research institutions and their representatives should eagerly involve themselves in the support of young postdoctoral researchers in order to secure for these young people a variety of career paths inside and outside of Japan." Furthermore, the 6th Science, Technology, and Innovation Basic Plan (Cabinet decision of March 26, 2021) also cites targets for the "expansion of career paths for doctoral researchers to the industrial sector" and "promotion of human resource mobility." In addition, the Guidelines on Employment and Fostering of Postdoctoral Students (formulated on December 3, 2020, by MEXT's Council for Science and Technology's Committee on Human Resources) state: "It is essential that doctoral human resources with sophisticated professionalism and excellent research capabilities are active in a variety of places including venture businesses and global corporations, and that they create innovation. Initiatives towards the diversification of career paths after the completion of post-doctoral terms are imperative." In response to this statement, those involved in the projects adopted by this program are requested to pursue positive initiatives to secure a variety of potential career paths for young researchers such as specially appointed professors and postdoctoral fellows employed using the competitive research funds, funding from other research projects, solicitation-based education and research funds aimed at universities, or other public research funds. In addition, please consider the use of indirect costs for the funding of these initiatives.

Chapter 14. Contacts

If you have any questions regarding these application guidelines, inquire via the contact addresses provided in the table below*1,2. Any changes in the information provided here are to be posted on the AMED website under “Collaborative Calls Information*3. Check the website for updates.

Do not contact the PD directly about the details of public solicitations or reviews.

*1 Make inquiries by email, wherever possible (Change the “AT” in the following addresses to @).

*2 Be careful to dial the correct telephone number. Unless otherwise noted, telephone inquiry services are available from 10:00 to 12:00 and from 13:00 to 17:00 on weekdays.

*3 https://www.amed.go.jp/koubo/

Content of inquiry	Contact address
R&D projects being solicited; review; how to fill in proposal documents (Please specify the title of e-mail with “Inquiry for the 3rd application”.)	Division of Moonshot Research and Development, Office of Project Management, AMED E-mail: moonshot"AT"amed.go.jp
Misconduct/fraudulent use/fraudulent receipt	Division of Research Integrity, Social Co-Creation and Legal Affairs, Department of Research Integrity and Project Management, AMED E-mail: kouseisoudan"AT"amed.go.jp
Management of conflict of interest/research ethics education programs	Division of Research Integrity, Social Co-Creation and Legal Affairs, Department of Research Integrity and Project Management, AMED E-mail: kenkyuukousei"AT"amed.go.jp
RIO Network	Division of Research Integrity, Social Co-Creation and Legal Affairs, Department of Research Integrity and Project Management, AMED E-mail: rionetwork"AT"amed.go.jp
Medical IP Desk (Contact point for medical IP consultation)	Division of Intellectual Property, Department of Intellectual Property and Technology Transfer, AMED E-mail: medicalip"AT"amed.go.jp
Support provided by the AMED Drug Discovery Support Network/Department of Innovative Drug Discovery and Development	East Japan Office, Department of Innovative Drug Discovery and Development, AMED8F Muromachi Chibagin Mitsui Bldg, 1-5-5 Nihonbashi-Muromachi, Chuo-ku, Tokyo 103-0022, Japan Tel: +81-3-3516-6181 E-mail: id3navi"AT"amed.go.jp
How to use the e-Rad system	e-Rad Portal Site Help Desk Before telephoning, please check the “Frequently Asked Questions (FAQ)” page. →After checking the FAQ page, log in to e-Rad (https://www.e-rad.go.jp/contact.html) so that you can check the operation manual, then dial: Tel: 0570-066-877 (NAVI-DIAL) or +81-3-6631-0622 (direct line) if the NAVI-DIAL service is unavailable. Operating hours: 9:00–18:00 (weekdays) *Excludes Saturdays, Sundays, public holidays, or Year-end/New Year holidays (December 29 – January 3)
Bioscience Database	Japan Science and Technology Agency (JST) National Bioscience Database Center (NBDC) Tel: 03-5214-8491 E-mail: nbdc-kikaku"AT"jst.go.jp

Appended Table

Summary of Submission Timing and Content of All Types of Information Material Required at AMED (Drugs)

	New drugs, etc.			New indications		Clinical study under ethical guidelines Clinical research under the Clinical Research Act
	Nonclinical study	Investigator-initiated clinical trial		Investigator-initiated clinical trial		
		Phase I (Safety)	From Phase II on	Phase I (Safety)	From Phase II on	
Schedule	When making R&D proposal, submit a schedule indicating the process steps and milestones up to approval.	Same as on the left	Same as on the left	Same as on the left	Same as on the left	When making R&D proposal, submit a schedule indicating the process steps and milestones up to attaining objectives.
Clinical Trial Implementation Plan	When making R&D proposal, submit a protocol concept statement or clearly state submission timing in Milestones.	When making R&D proposal, submit a Clinical Trial Implementation Plan or a a Clinical Trial Implementation Plan Outline, and submit a Clinical Trial Implementation Plan before implementing the trial.	Same as on the left	When making R&D proposal, submit a Clinical Trial Implementation Plan or a a Clinical Trial Implementation Plan Outline, and submit a Clinical Trial Implementation Plan before implementing the trial.	Same as on the left	When making R&D proposal, submit a Clinical Study Implementation Plan or an Implementation Plan Outline, and submit a Clinical Study Implementation Plan before implementing the study.
Regulatory Science Strategy Consultation (Face-to-face advice)	Consultation geared to research phase and content (face-to-face advice) is to be sought as a rule in the first or second year after adoption. It is not essential at the time of application, but it is desirable to have had a consultation. If you have a record of already implemented consultation (in the case of an advance interview, a summary prepared by the academia side is acceptable), then submit it.	Consultation geared to research phase and content (face-to-face advice) is to be sought as a rule after adoption and before clinical trial initiation. It is not essential at the time of application, but it is desirable to have had a consultation. If you have a record of already implemented consultation (in the case of an advance interview, a summary prepared by the academia side is acceptable), then submit it.	Same as on the left	Same as on the left	Same as on the left	-
Main substance of consultation	● Nonclinical study sufficiency ● Quality and standards, specifications of trial drug, etc.	Clinical trial design	● Clinical data package ● Clinical trial design	● Clinical trial design	● Clinical data package ● Clinical trial design	–
Record of involvement of biostatistician recorded in the R&D Proposal	-	Necessary to make note of whether or not there is involvement. If there is involvement, make note of it in a comment regarding clinical trial design. If there is no involvement, make note of the reason there is not.	Same as on the left	Same as on the left	Same as on the left	Same as on the left
Necessity for biostatistician involvement	Not necessarily needed.	Should have involvement in some cases.	Should have involvement.	Should have involvement in some cases.	Should have involvement.	Should have involvement in some cases.
Intellectual property	Make note of status and strategy regarding intellectual property, etc.					Not needed
Items regarding status of intellectual property, etc., recorded in the R&D Proposal	Status of own technology, status of relevant technology belonging to others, policy on corporate out-licensing (practical application) of research results					
Collaboration with corporations	Make note regarding status of collaboration.					
Status of trial drug procurement	Make note regarding status of trial drug (including comparison drugs) procurement.	Same as on the left	Same as on the left	Same as on the left	Same as on the left	–

Summary of Submission Timing and Content of All Types of Information Material Required at AMED (Medical Devices)

	Unapproved medical device (including expanded purpose of use)				Approved medical device (use within scope of approval)
	Nonclinical study	Investigator-initiated clinical trial		Clinical study under ethical guidelines Specified clinical research	Clinical study under ethical guidelines Specified clinical research
		Exploratory clinical trial	Clinical trial (pivotal test)		
Research objectives	● Acquisition of production and marketing approval (including expanded purpose of use)				● Build up new evidence (Establish standard treatment, establish procedure, etc.)
Schedule	When making R&D proposal, submit a schedule indicating the process steps and milestones up to acquisition of approval. (Also make concise note of listing for reimbursement under insurance and establishment as standard treatment.)	Same as on the left	Same as on the left	When making R&D proposal, clearly state how test is positioned and submit a schedule indicating exit strategy (future clinical trial implementation scheduling, corporate collaboration, production and marketing approval, listing for insurance).	When making R&D proposal, submit a schedule indicating how the evidence obtained is to be used together with steps and milestones leading to that use.
Implementation Plan	When making R&D proposal, submit a protocol concept statement or clearly state submission timing in Milestones.	When making R&D proposal, submit a Clinical Trial Implementation Plan or a Clinical Trial Implementation Plan Outline, and submit a Clinical Trial Implementation Plan before implementing the trial.	Same as on the left	When making R&D proposal, submit a Clinical Study Implementation Plan or a Clinical Study Implementation Plan Outline, and submit a Clinical Study Implementation Plan before implementing the study. When making R&D proposal, also submit information materials relating to nonclinical study.	When making R&D proposal, submit a Clinical Study Implementation Plan or a Clinical Study Implementation Plan Outline, and submit a Clinical Study Implementation Plan before implementing the study.
Consultation with regulatory authorities, etc.	Seek PMDA consultation geared to research phase and content in a timely manner. If you have a record of already implemented consultation at the time of application (in the case of an advance interview, a summary prepared by the academia side is acceptable), then submit it.	Same as on the left	Same as on the left	In addition to the left, when consultation with regulatory authorities is underway regarding the following, make a note of the status of consultations. ● Device procurement ● Utilization of advanced medical care system When consultations are underway with committees, etc., within the facility, make a note of the status of those consultations.	When consultation with regulatory authorities is underway regarding the following, make a note of the status of consultations. ● Utilization of advanced medical care system
Main substance of consultation	● Whether clinical trial is needed or not needed ● Nonclinical study sufficiency	● Clinical trial design	● Clinical trial design ● Clinical data package		
Record of involvement of biostatistician recorded in the R&D Proposal	–	Make note as to whether or not there is involvement. If there is involvement, make note of it in a comment regarding clinical trial design. If there is no involvement, make note of the reason there is not.	Same as on the left	Same as on the left	Same as on the left
Necessity for involvement of biostatistician	Not necessarily needed.	Should have involvement in some cases.	Should have involvement.	Should have involvement in some cases.	Should have involvement in some cases.
Intellectual property	Make note of status and strategy regarding intellectual property, etc.				Make note of status of intellectual property, etc., as necessary.
Items relating to status of intellectual property, etc. recorded in the R&D Proposal	Status of own technology, status of relevant technology belonging to others, policy on corporate out-licensing (practical application) of research results				-
Collaboration with corporations	Make note regarding status of collaboration where applicable	Make note regarding the following in the event that collaboration has taken place: ● Whether or not there is a joint research agreement or memorandum ● System for managing safety information ● Response and responsibility in event of malfunction			If there is collaboration, make note of its status.
Status of procurement or provision of trial device	Make note regarding procurement status of trial medical device (including comparison devices).				-

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