FY2020

Research Program on the challenges of Global Health issues

Application Guidelines

January 2020

Division of International Collaboration

Department of International Affairs

Japan Agency for Medical Research and Development (AMED)

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Ⅰ. Introduction

These Application Guidelines specify the conditions and solicitation details regarding the R&D projects being solicited under [Grant program title], which is administered by the Japan Agency for Medical Research and Development (hereinafter referred to as "AMED").

1. Program Outline

(1) Current Status of Program

In addition to conventional issues such as maternal and child health and infectious diseases, global health issues nowadays include new issues facing fragile states, such as lifestyle diseases and the aging of society, and responses to increasing health and medical service needs and diversification are necessary. Not only the World Health Organization (WHO) but also the United Nations General Assembly and major international meetings such as the G7 treat health issues as major agenda topics, and the importance of such issues within the international community is increasing more and more. In addition, under Sustainable Development Goals (SDGs), new goals in the field of health are being set and international initiatives are being further strengthened. In Japan, government policies and strategies related to international development of international healthcare and medical services have been formulated one after the other in recent years, including Healthcare and Medical Strategy and the Investments for the Future Strategy 2018. The purpose for formulating these policies and strategies is to enable Japan to contribute to global health initiatives, and they advocate the promotion, through cooperation with international organizations, of such measures as Universal Health Coverage (UHC), health security, and international development related to health and medical services. Within our limited financial resources, Japan is being asked to take a leadership role in formulating/implementing international policies in the health field as well as strengthening international technology cooperation, thereby contributing effectively and efficiently to international health and its international development as well as maintaining and strengthening Japan's existence within international society.

(2) Program Direction

In FY2020, with the aim of improving health and medical services by resolving issues in low- and middle-income countries, the program will promote international joint clinical studies for evaluating the effectiveness, safety, and efficiency of drugs, medical devices, and medical technologies, etc., that have not been introduced into or widely spread within the target countries. Furthermore, working in collaboration with the Global Alliance for Chronic Diseases (GACD), the program will promote R&D aimed at preventing cancers that are also spreading in low- and middle-income countries. Based on the knowledge acquired, attention will be focused on the practical application and implementation of new diagnostic, treatment, and prevention methods in the target countries.

(3) Program Objectives and Accomplishments

In order to achieve SDGs in low- and middle-income countries, this R&D program aims at the practical application of medical technologies that are needed by the target countries. Furthermore, the program aims to verify the effectiveness of cancer prevention and diagnostic methods in these countries and formulate implementation strategies for such methods. The results obtained are to be used in the setting of standards by the World Health Organization (WHO) and other international organizations, as well as the formulation of health and medical service measures in each country.

2. Program Structure

(1) Program Implementation System

In accordance with the "Plan for Promotion of Medical Research and Development*", a Program Supervisor (hereinafter referred to as "PS") and Program Officer (hereinafter referred to as "PO") are assigned to the Program to ensure efficient utilization of competitive research funds, etc. and generation of excellent research accomplishments.

The PS and PO have complete knowledge and understanding of the progress status of the program overall and provide the necessary guidance and advice to ensure that the program runs smoothly. Furthermore, research institutes and researchers are obligated to cooperate with the PS and PO. Based on the guidance and advice provided by the PS and PO, R&D plans may be revised, or projects cancelled (including early conclusion of projects due to achievement of R&D plans) as deemed necessary.

*https://www.kantei.go.jp/jp/singi/kenkouiryou/senryaku/suishinplan_henkou.pdf

(The next Plan for Promotion of Medical Research and Development for FY2020 onwards is currently under examination.)

(2) Roles, etc. of Principal Institutions and Subsidiary Institutions

Under this program, R&D projects shall be implemented by Principal Institutions or, if necessary, Subsidiary Institutions

(a) "Principal Institution" refers to the research institute with which the R&D Principal Investigator (PI) is affiliated and that is their main place of research; [1] which has concluded a direct contracted R&D agreement with AMED;[2] and which is the research institute, etc., in Japan referred to in the next item "II. Application Requirements 1. Eligible Applicants".

(b) "Subsidiary Institution" refers to a research institute, etc. other than the Principal Institution with which a Co-Investigator is affiliated and that is their main place of research[1] and which has concluded a subcontracted R&D agreement with the Principal Institution.

(c) "PI" refers to a researcher (one person) who is affiliated with the Principal Institution and who takes responsibility for formulating an R&D implementation plan and compiling the research accomplishments for the R&D project for which the application is being submitted during the implementation period.

(d) "Co-Investigator" refers to a researcher who is affiliated the Principal Institution or a Subsidiary Institution and who shares implementation of R&D items with the PI and takes responsibility for carry out the relevant R&D items.

(e) "Representative Investigator" refers to either the PI or the Co-Investigator affiliated with the Principal Institution or a Subsidiary Institution who is the representative researcher (one person) for the relevant research institution. (E.g.: the PI is the R&D Representative for the Principal Institution.)

[1]If the affiliate institution and the main place of research differ, please contact us.

[2]For details regarding contracted R&D agreements with institutions under this program, please refer to Chapter V.

Ⅱ. Application Requirements

1. Eligible Applicants

Eligible Applicants for this program shall be researchers affiliated with a research institute in Japan that fulfills the conditions shown in (1)–(5) below and that is their main place of research,[1] and who take responsibility for formulating an R&D implementation plan and compiling the research accomplishments for the R&D project for which the application is being submitted ("R&D Principal Investigator" (PI)).

(1) "Research Institute" refers to institution with the characteristics shown in (a)–(h) below.
- (a) National facility or other organization[2] (limited to institutions/facilities where the PI is employed in an educational position, research position, medical care position[3], welfare service position[3], or designated position[3], or as a fixed-term contract researcher).
- (b) Research institute, etc., affiliated with a local public body.
- (c) University as prescribed under the School Education Act (Law No. 26 of 1947) or university affiliated research institute, etc. (including inter-university research institute corporations).
- (d) R&D division or research laboratory, etc. of a private enterprise
- (e) A special private corporation, general incorporated association, general incorporated foundation, public interest incorporated association, or public interest incorporated foundation (hereinafter referred to as a "special private corporation, etc.") whose main activity purpose is research.
- (f) An independent administrative corporation 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 agency as prescribed under Article 2 of the Act on Local Incorporated Administrative Agencies (Act No. 118 of 2003) whose main activity purpose is research.
- (g) Non-profit, charitable technology research associations[4]
- (h) Other institution deemed appropriate by the President of AMED.

[1]If the affiliate institution and the main place of research differ, please contact us.
[2]Refers to a research institute, inspection and certification institute, educational and training facility, medical and rehabilitation facility, reformatory and internment facility, or 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
[3]Limited to persons affiliated with a hospital or institution that conducts research.
[4]With regard to technologies used in industrial activities, mutual associations providing finance, human resources, and facilities in which the association members autonomously conduct joint research.

(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 is able to 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.) generated through implementation of this program.
(5) The research institute is capable of continuing to promote R&D even after this program has concluded, and can support researchers in relation to this program.

In the case that a researcher who is not affiliated with a designated research institute, etc. or is affiliated with a research institute, etc. outside of Japan is selected as the PI, the researcher may apply for this program if they are able to become affiliated with a research institution in Japan and create a system for conducting research by the date the contracted R&D agreement is concluded or the date designated by AMED. However, in the case that the above conditions are not met by the date the contracted R&D agreement is concluded or the date designated by AMED, as a general rule the decision to adopt the R&D project shall be cancelled.

Furthermore, in order to confirm the research institute's ability to fulfill the contracted R&D agreement, at the time of the application review, the Principal Institution or Subsidiary Institution may be required to submit materials regarding the content of major projects undertaken by the institution and its finances (assets, debts, etc.).

2. Important Items Regarding Application

(3) 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 institute carrying out the R&D project and AMED.

*For details, please refer to Chapter V.

(4) 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 IV.

* "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.

(5) Registration with Japan Registry of Clinical Trials (jRCT)

Due to the promulgation of the Clinical Research Act (on April 1, 2018), registration with the Japan Registry of Clinical Trials (jRCT) database maintained by the Ministry of Health, Labour and Welfare and disease reporting, etc. are required when conducting clinical researches. Be sure to take the appropriate steps in compliance with the Act.

Clinical research initiated after the Clinical Research Act goes into effect should not be redundantly registered in the databases of Japanese clinical research registration institutions other than the jRCT. If the research has already been registered in the database of another clinical research registration institution in accordance with the "Ethical Guidelines for Medical and Health Research Involving Human Subjects," please take the appropriate action in accordance with laws and regulations, etc.

Please refer to Chapter IX. 16. for information on compliance with the Clinical Research Act.

(6) 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, as a general rule 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

Ⅲ. Application/Selection Implementation Methods

1. Outline of R&D Projects for Which Applications Are Being Solicited

The outline of the R&D projects for which applications are being solicited included in these Application Guidelines is as follows. For details regarding individual R&D projects being solicited, please refer to Chapter XI.

#	Field/R&D Projects Being Solicited	Scale of R&D funds (excluding indirect costs)	Period in which R&D is Scheduled to be Implemented	Planned Number of New Awarded Projects
1	International Joint Clinical Study for Promoting Overseas Utilization of Drugs, Medical Devices, and Medical Technologies in Order to Improve Health and Medical Services in Low- and Middle-Income Countries	1st and 2nd year Around 7.700.000yen per year for each project (excluding indirect costs) 3rd and 4th year Around 23.100.000yen per year for each project (excluding indirect costs)	Max. of 4 years FY2020 – FY2024	Around 0～4 projects （※1）
2	Global Alliance for Chronic Diseases (GACD) collaborative call: Primary and Secondary Prevention of Cancer in Low- and Middle-Income Countries	Around 7.700.000yen per year for each project (excluding indirect costs)	Max. of 4 years FY2020 – FY2024	Around 0～4 projects

（※1） AMED will conduct a mid-term evaluation two years after starting the project and will choose 1~2 projects which can proceed to 3rd and 4th years.

- “Scale of R&D Funds” is an approximate estimate guide.
- “Scale of R&D Funds” and “Planned Number of New Awarded Projects” may change depending on the situation regarding budget appropriation following the commencement of applications. In the event that there is a significant change, it is possible that acceptance of applications submitted for some of all of the R&D projects being solicited or adoption of projects may be cancelled.
- Although applicants may submit applications for multiple R&D projects being solicited, in order to show that there is no unreasonable duplication or excessive concentration of research funds (for details refer to Chapter V. 9 (5)), they must be sure to list information for all the other R&D projects for which applications are being submitted simultaneously in the relevant R&D Proposal column.

2. Preparation and Submission of R&D Proposals

(1) 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/

(2) Period of Acceptance of Proposals

- **Solicitation Theme#1:** International Joint Clinical Study for Promoting Overseas Utilization of Drugs, Medical Devices, and Medical Technologies in Order to Improve Health and Medical Services in Low- and Middle-Income Countries

January 20, 2020 (Mon) – April 10, 2020 (Fri) [12:00] (Japanese Standard Time) (Observe strictly.)

- **Solicitation Theme#2:** Global Alliance for Chronic Diseases (GACD) collaborative call: Primary and Secondary Prevention of Cancer in Low- and Middle-Income Countries
  Submission to **e-Rad:** January 20, 2020 (Mon) – April 30, 2020 (Thu) [17:00] (Japanese Standard Time) (Observe strictly.)
  Submission to **GACD common submission portal:** January 20, 2020 (Mon) – May 1, 2020 (Fri) 2:00] (UTC) (Observe strictly.)

Note 1: Procedures for registering with e-Rad can only be carried out during e-Rad system operating hours.
Note 2: For all R&D proposals, applications received after the deadline will not be accepted
Note 3: After the period of acceptance of proposal documents has ended, AMED may contact the PI by e-mail or telephone, etc., to confirm administrative details. Please respond to such requests for confirmation promptly using the methods designated by AMED (if AMED does not receive a response, the proposal in question may be ineligible for review.)
Note 4: If not completed correctly, proposal documents may not be accepted.

(3) Submission of Proposal Documents

Please submit proposal documents via e-Rad by the deadline. Applications will not be accepted if the proposal documents are not submitted by the deadline. When completing (inputting) the R&D proposal documents, please following the guidelines provided in this item and on the R&D Proposal (Form 1) and be sure that all the information you are required to provide is correct. Please note that submitted proposal documents cannot be replaced after the application deadline.

(a) Points to note in using the e-Rad

An e-Rad operating manual is available for reference or downloading from the e-Rad portal site (https://www.e-rad.go.jp/). Please read and agree to the e-Rad usage regulations before submitting your application.

1) Operating hours
The e-Rad system is available for use between 00:00 and 24:00 on weekdays and public holidays.

Note: During the above system operating hours, the e-Rad system by be temporarily shut down for maintenance or inspection. In the event that e-Rad is to be temporarily shut down, notice will be posted in advance on the e-Rad portal site.

2) 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 as early as possible before submitting your application.

3) Registration of researcher information
The PI, an applicant, and the Co-Investigator 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

(b) Points to note regarding submission of documents via the e-Rad

1) File type

The data file for filled-out application forms can only be submitted in PDF format. e-Rad has a feature for converting Word and Ichitaro (Japanese document) files to PDF format. You may also download a PDF conversion software program and use it on your PC to convert the file. It is not necessary to use this feature or software 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.

2) File capacity

The maximum size of single files that can be uploaded is 10MB.

3) Uploading proposal documents

Please convert proposal documents to PDF format before uploading.

4) Consent of affiliated institute

Application to the program is not complete at the point that the PI submits the application to their affiliated research institute via e-Rad. Be sure to undergo procedures to obtain approval of the submission of the R&D project from your affiliated research institute.

5) Checking acceptance status

Verifying the acceptance of proposal documents can be done by viewing the "Manage submitted proposals" screen on the e-Rad. After the researcher submits the application form, 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. When the acknowledgement procedures of the research institution have been completed the application type (status) will change to "Processing (Research institution) /Application in progress". When accepted by the Funding Agency (AMED) it will be displayed as "Accepted". Application documents whose application status has not changed to "Processing (Funding Agency) /Application in progress" or "Accepted" by the end of the acceptance period will become invalid. In the event that although a researcher has submitted the application documents prior to the end of the acceptance period and acknowledgment has been given by the clerical affairs supervisor their status remains unchanged as "Awaiting approval from research institution," please contact the division or office in charge of the program. Note that in the event that there is a fault in the e-Rad system during the application period (faults sometimes arise when there is heavy access immediately prior to the end of the submissions deadline) 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.

6) Amendment of proposal documents after submission

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.

7) Other

Details about points to note and content other than that shown above are posted as required on the e-Rad portal site (Researchers' Page), so please check this information.

(c) 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 X.) 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.

(4) Methods for Obtaining, Preparing, and Submitting Proposal Forms Prescribed by GACD (**Solicitation Theme#2**)

Proposal documents are to be prepared in English using uniform methods and formats prescribed by GACD. Please refer to the GACD website for the necessary application documents as well as information on how to prepare proposal documents.

Please submit the proposal documents before the application deadline via the GACD Common Submission Portal and the e-Rad. Applications will not be accepted if the proposal documents are not submitted by the deadline through both portals. Please note that submitted proposal documents cannot be replaced after the application deadline.

(5) Schedule

The schedule from application to selection of projects for the program shown below is current as at the time that the call for applications opens. For details on how reviews are carried out, refer to Chapter III. 3.

<table>
<tr><th>#</th><th>Name of Field/R&D Projects Being Solicited</th><th>Solicitation Period</th><th>Document Review</th><th>Interview (hearing)</th><th>Notification of selection</th><th>Commencement of R&D</th></tr>
<tr><td rowspan="2">1</td><td rowspan="2">International Joint Clinical Study for Promoting Overseas Utilization of Drugs, Medical Devices, and Medical Technologies in Order to Improve Health and Medical Services in Low- and Middle-Income Countries</td><td rowspan="2">Jan 20, 2020 (Mon) – Apr 10, 2020 (Fri)</td><td colspan="2">(a) Review by the Evaluation Panel on “the research program on the challenges of Global Health issues”.</td><td rowspan="2">End of May, 2020</td><td rowspan="2">Early June, 2020</td></tr>
<tr><td>Apr~May, 2020</td><td>Middle of May, 2020</td></tr>
<tr><td rowspan="2">2</td><td rowspan="2">Global Alliance for Chronic Diseases (GACD) collaborative call: Primary and Secondary Prevention of Cancer in Low- and Middle-Income Countries</td><td rowspan="2">Jan 20, 2020 (Mon) – Apr 30, 2020 (Thu)</td><td>May, 2020</td><td>Early June, 2020</td><td rowspan="2">November, 2020</td><td rowspan="2">December 2020</td></tr>
<tr><td colspan="2">Review by GACD Joint International Peer Review
July ~ October, 2020</td></tr>
</table>

- **Solicitation #1; International Joint Clinical Study for Promoting Overseas Utilization of Drugs, Medical Devices, and Medical Technologies in Order to Improve Health and Medical Services in Low- and Middle-Income Countries**

Document review	Middle of April-Middle of May 2020
Interview (hearing)	Middle of May 2020 (*Implemented as necessary.)

Note 1: In the case that a hearing is conducted, the PI for the relevant project shall as a general rule be contact by e-mail no later than one week before the hearing is to take place. (In the case that the project is not eligible for a hearing or hearings themselves are not being conducted, the PI will not be contacted. Please wait to receive your Notification of Selection/Rejection.) In the case that there is a change in information regarding the implementation or scheduling of hearings, this will be posted on the Application Information page on the AMED website listed in Chapter III.2. (1), so

please refer to this page for details. Note that we cannot answer questions regarding the eligibility of individual projects for hearings.

Note 2: The PI may be sent via e-mail a list of "Matters of Inquiry" that have arisen through the document review process. Please respond promptly to these "Matters of Inquiry" by the deadline designated by AMED at the time of inquiry via the method designated by AMED.

Note 3: As a general rule, the hearing shall be attended by the PI. The date and time of the hearing cannot be changed.

Note 4: Following the hearing, administrative matters may be confirmed with the PI as necessary. Please respond swiftly to the relevant checks via the method specified by AMED.

Notification of Selection/Rejection End of May 2020

Note: The PI of a project that has been selected as a candidate project for adoption may be required to revise the project's objectives, implementation plan, and/or implementation system in accordance with the review results, and conditions for adoption, including changes to the total R&D funding amount may be added. In such cases, the appropriateness of the plan may be reconsidered.

Commencement of R&D Project (Contracting, Etc.) (tentative date) Early of June 2020

Note: 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 PS/PO of a project as swiftly as possible to ensure that the contracted R&D agreement can be concluded as early as possible.

- **Solicitation #2; Global Alliance for Chronic Diseases (GACD) collaborative call: Primary and Secondary Prevention of Cancer in Low- and Middle-Income Countries**

Document review by the Evaluation Panel on "the research program on the challenges of Global Health issues". Middle of May-End of May 2020

Interview (hearing)by the Evaluation Panel on "the research program on the challenges of Global Health issues". Early of June 2020 (*Implemented as necessary.)

Document review by the GACD Joint International Peer Review July- October 2020

Note 1: In the case that a hearing is conducted, the PI for the relevant project shall as a general rule be contact by e-mail no later than one week before the hearing is to take place. (In the case that the project is not eligible for a hearing or hearings themselves are not being conducted, the PI will not be contacted. Please wait to receive your Notification of Selection/Rejection.) In the case that there is a change in information regarding the implementation or scheduling of hearings, this will be posted on the Application Information page on the AMED website listed in Chapter III.2. (1), so please refer to this page for details. Note that we cannot answer questions regarding the eligibility of individual projects for hearings.

Note 2: The PI may be sent via e-mail a list of "Matters of Inquiry" that have arisen through the document review process. Please respond promptly to these "Matters of Inquiry" by the deadline designated by AMED at the time of inquiry via the method designated by AMED.

Note 3: As a general rule, the hearing shall be attended by the PI. The date and time of the hearing cannot be changed.

Note 4: Following the hearing, administrative matters may be confirmed with the PI as necessary. Please respond swiftly to the relevant checks via the method specified by AMED.

3. Method for Reviewing Proposal Documents

(1) Review Method

In accordance with AMED's "Regulations Regarding the Evaluation of R&D Projects", in selecting R&D projects under this program, ex-ante evaluations (reviews) shall be conducted by evaluators (reviewers) comprising external experts appointed by the President of AMED in order to determine the necessity of the R&D project, appropriateness of project objectives and plans, and budget allocation.

Review for the Soliciattion theme#1 is conducted by the Evaluation Panel on "the research program on the challenges of Global Health issues". Review for the Soliciattion theme#2 is conducted by the GACD Joint International Peer Review in addition to the Evaluation Panel on "the research program on the challenges of Global Health issues".

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

(b) The Project Evaluation Panel shall evaluate project proposals by conducting a document review of the content of the submitted proposal documents and conducting interviews (hearings) as necessary* and deliberating on the project content.

*During the review process, the PI may be required to provide additional materials, etc.

(c) In deciding projects for adoption, the PI of a project may be required to revise* the project's objectives, implementation plan, and/or implementation system in accordance with the review results, and conditions for adoption, including changes to the total R&D funding amount may be added. In such cases, the appropriateness of the plan may be reconsidered.

*In the case that the project is adopted, the objectives, etc., revised at this stage shall be used as evaluation indicators when a Mid-term Review and an Ex-Post Evaluation are carried out. Please refer to Chapter VI. for information regarding the management and evaluation of awarded projects.

(d) Following completion of reviews, AMED will send notification of selection/rejection to the PI of the project. Note that we cannot answer questions regarding the progress status of the selection process.

(e) Project Evaluation Panel members are obligated to maintain confidentiality regarding any secret information learned during the course of performing their evaluation duties, including after these duties have concluded, in order to prohibit leakage or misappropriation of this information.

(f) The names of the R&D projects adopted for the program (awarded projects) and the name of the PI will be published at a later date on the AMED website. Furthermore, as a general rule, the names of all evaluators (reviewers) shall be published by AMED once each year. (For details about publication on the AMED website, please refer also to Chapter IV.)

(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 as a general rule 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), PS, PO, 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.

(2) Review Criteria and Perspectives in Evaluating Projects on "the research program on the challenges of Global Health issues"

In selecting projects for this program, reviews of proposal documents shall be carried out from the following perspectives. In the case that a proposal is submitted for an R&D project that designates a subsidiary institution, evaluations shall also examine the necessity of the subsidiary institution for carrying out the R&D and the competency of the subsidiary institution to carry out the R&D.

(a) Compatibility with the program's purpose
- Is the project compatible with the program's purpose and aims, etc.?
- Can the project be expected to make proposals/recommendations for governments of developing countries and international organizations to promote the resolution of health issues?
- Can the project contribute to efforts by the Japanese Government to promote the resolution of global-scale health issues?

(b) Appropriateness of the plan
- Are the overall content and aims of the plan clear?
- As the plans for each fiscal year detailed and realizable?

(c) Technological significance and predominance
- Are the current technological level and previous performance of the research institute sufficient?
- Does the project proposal have originality and novelty?
- Does the project respond to needs in the field of global-scale health issues?
- Does the project contribute to the generation of new technologies or the utilization of new technologies in addressing global-scale health issues?
- Does the project contribute to progress in the field of global-scale health issues?

(d) Implementation system
- Has an R&D system centered on the applicant been organized appropriately?
- Has a sufficient collaboration network within Japan been constructed?

Has a sufficient collaboration network been constructed with overseas researchers/research organizations, supporters/support organizations, and government officials/government organizations, including persons/organizations related to the target developing country?

(e) Costs
- Are the breakdown of costs and spending plan appropriate?

(f) Items stipulated under other programs

- With regard to global-scale health issues, is the project proposal based on worldwide trends?
- With regard to global-scale health issues, is the project compatible with global guidelines and strategies, etc., formulated by the World Health Organization or other organizations, and does it contribute to constructive reforms?
- Is the project appropriate for the current situation in the target developing country?
- Does the project have appropriate strategies for publishing research achievements?

(g) Overall evaluations

Overall evaluations will be carried out in consideration of (a) – (f) above and the following items.

- Is the project plan in compliance with laws and ordinances related to bioethics or safety measures?
- Are the efforts of the applicant appropriate?

(3) GACD Joint International Peer Review

Based on uniform evaluation standards prescribed by GACD, the Joint International Peer Review shall evaluate the quality, appropriateness, feasibility, and impact, etc., of the proposal content.

(a) Reviews shall be conducted in private by a Joint International Peer Review Panel comprising reviewers selected by GACD.

(b) The Joint International Peer Review Panel shall evaluate project proposals by conducting a document review of the content of the submitted proposal documents and deliberating on the content in the panel meeting.

(c) GACD Joint International Peer Review Criteria

- **Relevance and Quality of Project**
  - There is sound evidence that stakeholders, such as decision-makers and service delivery partners, have been actively involved in the research process including the selection and adaptation of the intervention and the research design; and
  - There will be demonstrable engagement with the public and/or patient and community groups or other relevant stakeholder groups.

- **Quality of Team**
  - The multidisciplinary team members have a high-quality track record in fields related to the proposed implementation research and the team has the right balance of expertise given the goal(s) of the research project;
  - There is evidence that the research will be jointly managed by researchers from HICs and LMICs, where applicable;
  - Early career investigators are part of the team and a strong training plan for research capacity-building is included;
  - There is sound evidence that stakeholders, such as decision-makers and service delivery partners, have been actively involved in the research process including the selection and adaptation of the intervention and the research design; and
  - There will be demonstrable engagement with the public and/or patient and community groups or other relevant stakeholder groups.

- **Feasibility of Project**
  - Major scientific, technical or organizational challenges have been identified, and realistic plans to tackle them are outlined;
  - Proposed intervention strategies are relevant to the socio-political, cultural, policy and economic contexts of the study settings and the proposal demonstrates understanding of the contextual factors (e.g. health systems, intersectoral policy, governance, leadership) affecting implementation, indicating how those factors and their impact will be analyzed;
  - Inequities and equity gaps, including age and gender, have been taken into account;
  - Appropriate measures of evaluation have been included. Projects that are able to track long-term clinical, public health, policy and/or health system outcomes are expected;
  - There is a clear governance plan, including evidence of ultimate accountability, shared strategic leadership, transparency in decision making, management of conflicts of interest, clearly defined roles/responsibilities/contributions, demonstrating that all key participants are highly engaged and committed;

- There is an appropriate collaboration plan, including but not limited to communication and coordination, management and administration, conflict prevention/resolution, quality improvement, budget and resource allocation and publication approach among team members.

- **Potential Impact**
  - The expected impacts, as listed in the scope above, are identified;
  - The project demonstrates alignment with international and/or national commitments to advance primary and/or secondary cancer prevention strategies;
  - The project appropriately leverages existing programs and platforms (e.g. research, data, delivery platforms), if relevant;
  - There is potential for sustaining intervention at scale; and
  - There is potential for the translation of the findings into different settings

4. Promotion of Selection of 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.

Ⅳ. Preparation of Proposal Documents and Cautions

1. Handling of Information Contained in Proposal Documents

(1) Purpose of Use of Information

In addition to reviewing R&D project proposals as part of the selection proves, information included in proposal documents, etc., shall also be used by contracted R&D fund administration organizations and for research support purposes as described in IX.

Furthermore, information included in proposal summaries shall also be used in analysis of research trends that contributes to the operation of the AMED program or in macro analysis, such as the creation of new programs. In accordance with laws related to the protection of personal information possessed by independent administrative corporations and other organizations, the confidentiality of secret information included in proposal documents shall be strictly maintained to ensure that the rights and interests of the applicant are in no way unfairly infringed. For details, please refer to the Ministry of Internal Affairs and Communications website. *

* "Introduction of legal systems for the protection of personal information by government organizations/independent administrative corporations, etc." (Ministry of Internal Affairs and Communications)
http://www.soumu.go.jp/main_sosiki/gyoukan/kanri/horei_kihon.html

(2) Necessary Disclosure/Provision of Information

(a) Information related to each adopted project (program title, R&D project title, PI's affiliated institution/position/name, e-Rad project/researcher/research institution number, budget amount, R&D period, research outline/abstract or Contracted R&D Accomplishments Report (public information))[1] may be sorted, classified, and made public on AMED's website, the AMED R&D projects database (AMEDfind), and public databases operated by funding agencies, etc., providing cooperation under an agreement, etc., with AMED (World RePORT,[2] etc.). In addition, 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] 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.

[1]Information shall be treated as "information expected to be made public" as per the stipulations of Article 5, Item (i) (a) of the Act on Access to Information Held by Independent Administrative Agencies (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]What is "World RePORT"?

"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), European Commission (EC), Canadian Institutes of Health Research (CIHR), and the Wellcome Trust. https://worldreport.nih.gov/app/#!/about

[3]"Databases, etc." includes World RePORT, ERP and other databases.

(b) 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 systems, etc.

2. Proposal Document Format and Notes for Preparation

(1) Proposal Document Format

The proposal document form shall be the "R&D Proposal". Please complete each item simply and clearly. With regard to the acceptance period for proposal documents and submissions, please refer to Chapter III.

(2) Preparation of Proposal Documents

Applications are to be submitted via e-Rad. In preparing proposal documents, please also refer to the Points to Note shown in (3). If not completed correctly, proposal documents may not be accepted.

Please be careful with regard to the following items when inputting information into the Proposal Form.

(a) As a general rule, the Research Proposal (Form 1) is to be prepared in Japanese and English, but 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.

(b) With regard to formats prescribing word limits or page limits, please be sure to comply with the set limits.

(c) With regard to letter/character size when inputting information, please use 10.5 point as a general rule.

(d) As a general rule, please use half-width letters when inputting alphanumeric characters. (E.g. post codes, telephone numbers, and numbers of people.)

(e) Please number the pages of proposal documents with numbers placed centrally at the bottom of each page.

(f) 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.

(3) Notes on Preparing Proposals

(a) Compliance with laws and ordinances/ethical guidelines, etc.

In preparing R&D proposals, be sure to comply with relevant laws and ministerial ordinances/ethical guidelines prescribed by government ministries and agencies. For details, please refer to Chapter V. 4 (4).

(b) Approval of R&D Project Proposals by Organizations

In submitting proposal documents, the PI must obtain the approval of the Principal Institution (research institute with which the PI is affiliated, and which is to conclude a direct contracted agreement with AMED). Furthermore, in the case that multiple research institutes jointly submit an R&D proposal for carrying out research, the approval of the heads of all the research institutes must be obtained.

(c) 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.

(d) 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.

(4) Required Documents Apart from R&D Proposals

(a) Records of ex-ante interviews/face-to-face advice with 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; 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. For details, please refer to the Points to Note provided for projects being solicited under Chapter XI.

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 within one to two years of the project being adopted as a condition of the contracted R&D agreement (please refer to Chapter IV. 1. for details regarding the period in which the consultation should be undertaken). 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.

(b) 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). For details, please refer to the Points to Note provided for R&D projects being solicited under Chapter XI.

[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")

(c) 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.

(d) Documents etc. regarding management of R&D

（医薬品文例）

The "Items for Checking Related to Research Management (Drugs)", which was notified as "Items for Checking Related to Research Management for Drug Development" on December 27, 2017, on the AMED website, are to be implemented.

Applicants who apply for [R&D Area XX, proposed project that fall into Proposal Category XX (←事業課で修正")] are required to submit an "Items for Checking Sheet". Please download the "Items for Checking Sheet" from the "Items for Checking Related to Research Management for Drug Development" page on the AMED website below, complete the "Items for Checking Sheet", and submit the sheet together with the other proposal documents via e-Rad. With regard to specific tasks to be performed in preparing the "Items for Checking Sheet", please refer to "Items for Checking Related to Research Management (Drugs)", "Explanatory Materials for Applicants", and "Instructions for Completing the 'Items for Checking Sheet' for Applicants", which are available from the same website. In addition, inquiries may be made regarding the content of "Items for Checking Sheet" as necessary.

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

Ⅴ. Conclusion of Contracted R&D Agreements

1. Conclusion of Contracted R&D Agreements

(1) Agreement Conditions

With regard to awarded R&D projects, R&D projects a one-fiscal-year contracted R&D agreement shall be concluded between the research institution implementing the R&D project* and AMED in accordance with the principle of the accounting period of the national government. Successful applicants shall receive detailed information from AMED following project selection.

In concluding contracted R&D agreements, in the case that the conditions decided at the time the project was adopted have not been fulfilled based on the opinions of the Project Evaluation Panel, PS, and PO, etc., and agreement is not reached regarding both the content of the agreement (including expenditure estimates) and method, an agreement will not be concluded even for an awarded R&D project.

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

The PS or PO, 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.

*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 research institutes), 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 the 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 subcontracted institution and the subcontracted institution shall be required to undergo government inspection and auditing by AMED in response to requests from AMED.

(2) Preparations for Concluding Agreement

Following the adoption of an R&D project, the research institution implementing the R&D project shall be required to carry out the following to enable procedures for concluding the contracted R&D agreement to proceed quickly and smoothly.

(a) Preparation of an Overall R&D Plan, R&D Plan and other documents required for the agreement

(b) Obtain an estimate for the expenditure needed under the administrative plan

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

*One Overall R&D Plan is to be prepared for each R&D project based on the R&D proposal at the time of adoption of the project. Centered on the proposed R&D concept for the entire project implementation period, please include the basic plan, R&D content, R&D system, and budget plan. This plan shall be used as a base material for 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 contracted R&D agreements for each fiscal year are concluded.

Other documents required for the agreement (plan forms etc.) shall be provided separately after projects have been adopted.

(3) 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

(4) Ensuring the Research Period 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 as calculated from the last day the Contracted R&D execution period. Each research institute should work to put in place the necessary mechanism in-house to ensure a research period up through the end of the fiscal year is secured.

(5) 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 for the relevant fiscal year. During this examination, in the case that expenditure for research purposes is found to have been used fraudulently or for purposes not recognized as contracted R&D activities under the Contracted R&D Agreement, all or part of the expenditure may be required to be returned. 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. (Please refer to V. 8. (2).)

2. Scope and Payment of Contracted R&D Funds

(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]

	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

[2] Implemented when AMED concludes a contracted R&D agreement with a national university corporation, inter-university research institute corporation, independent administrative corporation, special corporation, special private corporation, general incorporated association, general incorporated foundation, public interest incorporated association, public interest incorporated foundation, private enterprise, or private university, etc., and does not apply in the case that the researcher is affiliated with a national facility or other institution (excluding the National Institute for Educational Policy Research). The fixed percentage will not exceed 30%. With regard to Subsidiary Institutions (excluding national facilities or other institutions) also, indirect costs are allocated in accordance with direct costs.

(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."*

Please note that payment by note, netting, and factoring are not accepted.

* 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 researcher-initiated 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 institute has created a system for registering cases for trials/clinical research 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 institute can request case registration from other medical institutions in a kind of outsourcing method. For details, please refer to AMED "Operation of Research Funds: Management of Medical Institution Expenditure for Researcher-initiated Trials and Clinical Studies" (https://www.amed.go.jp/program/kenkyu_unyo.html). Facilities where there is a sufficient administrative support system for trials/clinical research may continue using their current management method for the foreseeable future.

Note 2: In order to mitigate the expenses involved in the use of computers and aim for effective cost management to accelerate research, AMED provides all R&D projects with a joint service for using the Tohoku University Tohoku Medical Megabank Organization's supercomputer at a special rate. Those planning to use this service should calculate the costs by referring to the Tohoku University Tohoku Medical Megabank Organization Supercomputer Usage Fee Rules (https://sc.megabank.tohoku.ac.jp/wp-content/uploads/2019/04/uses_fee_20190401.pdf).

(3) 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.

(4) 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

(5) 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 May 29, 2014 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

3. Carryover 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 deciding preliminary surveys or 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

4. Obligations of Research Institutes in Implementing this Program

(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. In particular, 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.

(2) Participation in/Completion of Research Ethics Education Program

As part of measures to prevent misconduct from occurring, AMED requires all researchers participating in this program to take and complete a research ethics education program. Research institutes shall implement research ethics education for researchers and report to AMED on the status of participation. (For details, please refer to Chapter V. 6. and the AMED website.)

Furthermore, in the case that a researcher does not fulfill their obligation to undergo the research ethics education despite AMED's urging, the research institute may be directed by AMED to suspend all or part of the contracted R&D funding. In this case, research institutes must suspend contracted R&D funding as directed by AMED and not recommence funding until directed to do so.

(3) 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. For details, please refer to Chapter V. 7. and the AMED website.

(4) 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.

With regard to 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. 106 of 2006)
- 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)
- 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. 2 of 2014)
- Guidelines on the Distribution and Utilization of Human Embryonic Stem Cells (Public Notice of the Ministry of Education, Culture, Sports, Science and Technology (MEXT) No. 174 of 2014)
- Guidelines on the Research on Producing 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 Human Genome/Gene Analysis Research (Public Notice of 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) No. 1 of 2013)
- 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 Practice 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 Practice for Nonclinical Safety Studies of Regenerative Medical Products (Ordinance of the Ministry of Health, Labour and Welfare (MHLW) No.88 of 2014)
- Ordinance for Enforcement of the Clinical Research Act (Ordinance of the Ministry of Health, Labour and Welfare (MHLW) No. 17 of 2018)
- 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)
- Ethical Guidelines for Assisted Reproductive Technology Studies Involving 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)
- 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

(5) Management Responsibility for Executing Contracted R&D Funds

The contracted R&D funds shall be executed by the research institute in accordance with the contracted R&D agreement. For this reason, research institutes shall abide by the principles stipulated under "Competitive research funding should be managed at the responsibility of the research institution", and research funds shall be managed under the responsibility of research institutes.

(6) Response Obligations Regarding System Maintenance, etc.

All research institutes must strictly comply with the items required to be implemented by research institutes in accordance with the Guidelines for Management and Audit of Public Research Funds at Research Institutions (implementation standards) (formulated on March 31, 2014; finally revised on February 23, 2017; decided by Director, Health Science Division, Minister's Secretariat, Ministry of Health, Labour and Welfare (MHLW)) and the Guidelines for Responding to Misconduct in Research Activities in the Field of Health, Labour and Welfare (formulated on January 16, 2015; finally revised on February 23, 2017)

5. Obligations of Researchers Participating in Research Activities under this Program

(1) Fair and Appropriate Execution of Contracted R&D Funds

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.

(2) Application Procedures

When lodging an application for this program, the researcher who is to participate in this program must make the appropriate arrangements, such as explaining the research to and receiving approval for the research from the research institute that is to conduct the R&D project in advance.

(3) Participation in/Completion of Research Ethics Education Program

In order to prevent fraudulent use, fraudulent receipt, and misconduct, researchers participating in this program are required to complete a research ethics education program. (Please refer to Chapter V. 6. for details.) Please note that in the case that a researcher does not complete a research ethics education program, execution of contracted R&D funds may be suspended until completion of the research ethics education program is confirmed.

6. Participation in Research Ethics Program

(1) Persons Required to Undergo Ethics Training/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) (only in Japanese)
- APRIN e-Learning Program (eAPRIN)
- "For the Sound Development of Science: The Attitude of a Conscientious Scientist" (Japan Society for the Promotion of Science Editing Committee "For the Sound Development of Science")
- Programs implemented by research institutes whose content is deemed to be equivalent to the that of the above programs

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.

(a) Training conducted by a Clinical Research Core Hospital for persons working in the clinical research field.

(b) 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.

(2) Research Ethics Training Period

As a general rule, persons required to undergo research ethics training shall undertake this training within the first fiscal year of the R&D period and should continue to undertake ethics training as appropriate thereafter. (Training undertaken previously may also be valid.)

(3) Role of Research Institutes

Research institutes shall ensure that persons required to undergo research ethics training as listed in (1) above who are affiliated with their institution (included a subcontracted institution) undergo the R&D ethics education using one of the programs/materials listed in (1) above, and shall report on their training status to AMED.

(4) Reporting Research Ethics Training Status

Research institutes shall compile information on researchers' R&D ethics education status and submit a report on the status of training on the form prescribed by AMED by e-mail to AMED (Department of Research Integrity and Legal Affairs). (Seal need not be affixed.)

Subject of report: Persons required to undergo research ethics training in programs commencing in/after FY2020
Deadline for submission: May 31, 2021
Documents to be submitted: "Report on the Status of Participation in R&D Ethics Education Programs" (Please download the form from the AMED website)
URL: https://www.amed.go.jp/kenkyu_kousei/kyoiku_program.html
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 (refer to URL shown above) around March 2020.

(5) Inquiries

For inquiries related to R&D ethics education programs, please send an e-mail to [kenkyuukousei"AT"amed.go.jp] (Change "AT" to @ when inputting the address.)

7. COI Management

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

(a) Target Persons

PI or Co-Investigator 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.

(b) 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.

(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.

(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.
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 (refer to URL shown above) around March 2020.
https://www.amed.go.jp/kenkyu_kousei/riekisohan_kanri.html

(4) Inquiries

For inquiries related to conflict of interest management, please send an e-mail to [kenkyuukousei"AT"amed.go.jp] (Change "AT" to @ when inputting the address.)

*For details, please refer to the following websites
- 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

8. Countermeasures to Misconduct, Fraudulent Use, and Fraudulent Receipt

① Guidelines for Responding to Misconduct in Research Activities in the Field of Health, Labour and Welfare (No. 0116-1, decided by Director, Health Science Division, Minister's Secretariat, Ministry of Health, Labour and Welfare (MHLW) on January 16, 2015; finally revised on February 23, 2017)
② Guidelines for Management and Audit of Public Research Funds at Research Institutions (implementation standards) (decided by Director, Health Science Division, Minister's Secretariat, Ministry of Health, Labour and Welfare (MHLW) on March 31, 2014; finally revised on February 23, 2017)

(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 institute in relation to this program, the research institute shall swiftly report to AMED that it will be commencing a preliminary investigation into the matter in accordance with the Guideline ①, Guideline ② and AMED Regulations for Responding to Misconduct in Research Activities.

In the event that it is deemed necessary for the research institute to conduct such an 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 complainee and/or the research institute to suspend use of research funds under this program as a temporary measure during the investigation if necessary.

Furthermore, the research institute 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 Guideline ①, Guideline ② and 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 institute 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 institute 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 institute extends the deadline for submission of the final report, AMED may take measures against the research institute such as reducing indirect costs by a certain percentage or suspending execution of contracted R&D funds.

(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 institute and researcher(s) in accordance with Guideline ①, Guideline ② and AMED Regulations for Responding to Misconduct in Research Activities.

(a) 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.

(b) Restrictions on applications to 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 that the restrictions will be implemented on the researcher's application and eligibility for participation in research. In this way 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.

Category of misconduct according to involvement		Degree of misconduct	Period deemed appropriate
Person	1. Especially malicious individual who		10 years

<table>
<tr><td rowspan="4">Involved in the Misconduct</td><td colspan="2">intentionally engages in misconduct from the outset of the research</td><td></td><td></td></tr>
<tr><td rowspan="3">2. Author of academic paper, etc. related to research in which there has been misconduct</td><td>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" rowspan="2">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>
<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>1–2 years</td></tr>
</table>

[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.

Content of usage of research funds	Period deemed appropriate
1. The degree of fraudulent use of research funds is deemed to have a small social impact and be slightly pernicious	1 year
2. The degree of fraudulent use of research funds is deemed to have a large social impact and be highly pernicious	5 years
3. Cases other than 1 or 2 that are deemed to have a social impact or be pernicious	2–4 years
4. Cases in which research funds were used for personal economic gain, regardless of 1 through 3	10 years
5. Cases in which the relevant project was adopted as an R&D project through falsehoods or other dishonest means	5 years
6. Cases in which the person is not directly involved in fraudulent use of research funds but uses the research funds in a manner that infringes duty of diligence	1–2 years

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

・In 1–4, the person's actions are deemed to have a small social impact and be slightly pernicious, and the funding amount used fraudulently is small.

・In 6, the person's actions are deemed to have a small social impact and be slightly pernicious.

Note 2: With regard to 6 above, periods will be decided upon with due consideration of the extent of violation by the researchers with duty of diligence.

(c) Restrictions on researchers whose application to and eligibility for participation in other R&D funding programs has been restricted

With regard to researchers who have been found to have carried out misconduct under R&D funding programs other than this program that are under the jurisdiction of the national government or an independent administrative corporation 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 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 the program becomes known after the conclusion of the contracted R&D agreement, the relevant agreement may be cancelled.

(d) Cases in which it is suspected that misconduct has occurred under another R&D funding program

In the case that there is a complaint, etc., that a researcher participating in this program is suspected of perpetrating misconduct under another R&D funding program, the research institute with which the relevant researcher is affiliated is obligated to report to AMED that an 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.

(e) Disclosure of misconduct

In the case that the measures and/or restrictions prescribed in (a) and (b) above are implemented under this program, the content of the relevant measures shall as a general rule be publicly disclosed in accordance with [Guideline name] (month, day, year); [Guideline name] (month, day, year); and AMED Regulations for Responding to Misconduct in Research Activities. In addition, the misconduct may be similarly disclosed by the related government ministries/agencies.

(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 following website:

* https://www.amed.go.jp/kenkyu_kousei/rionetwork.html

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.

9. Points to Note between Selection and Conclusion of Agreement

(1) Cancellation of Decision to Adopt R&D Project

Following adoption of the R&D project, the decision to adopt the R&D project may be cancelled in the following cases.

- Documents required by AMED to be submitted are not submitted by the submission deadline.
- A researcher/researchers involved in the relevant R&D project have had their application to/eligibility for participation in AMED R&D programs restricted for a certain period of time.
- An investigation has been opened into allegations of misconduct.
- Conditions that were set for adoption of the R&D project ultimately have not been fulfilled.
- It is discovered that the R&D project does not fulfill the conditions for solicitation, etc.

(2) Representation and Warranty for Researchers Undergoing Investigation/Researchers Discovered to Have Undertaken Misconduct

Please note that in concluding contracted R&D agreements, AMED requires Principal Institutions to provide representation and warranty with regard to items (a) through (c) below.

(a) The "PI" or person in an equivalent position (as the person in charge of the R&D under this program), and the "Co-Investigator" or person in an equivalent position (as the person sharing R&D items with the PI for the project) have not been found by the research institute to have carried out misconduct in accordance with Japanese Government guidelines for responding to misconduct* 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 implemented by the national government or independent administrative corporations based on the findings of the research institute, or whose period of restriction on application to/eligibility for participation in competitive research funding programs implemented by the national government or independent administrative corporations has ended).

(b) In the case that persons who are the subject of an investigation (hereinafter referred to as the "Investigation") being conducted by the research institute 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 institute in question and either the R&D PI or Co-Investigator (if there is a subcontracted institute, including the Co-Investigator or equivalent person affiliated with the subcontracted institute) for the R&D Plan, AMED has been notified of the relevant target persons 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 persons.

(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.

*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).

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

(3) Submission of R&D Plans and Reports

With regard to awarded projects, please note that some parts of the R&D Plan and reports may be required to be submitted in English.

(4) Submission of Data Management Plans

With regard to awarded projects, the PI is requested to submit* a data management plan to AMED when they conclude a contracted R&D agreement after adoption.

* With regard to R&D projects conducted using public funds in which there is a need to sort and systemize (make databases) of data, the submission of a data management plan helps to strengthen management and catalytic functions by enabling AMED to ascertain the location of research data, and is useful in the joint promotion of different R&D projects to the furthest extent possible, and also helps to avoid duplicative research.
* It is requested that data management plans 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. A separate form will be sent to successful applicants in due course.
* The name and affiliation of the data scientist may be published along with other project details unless the data scientist wishes to remain anonymous.
* AMED website https://www.amed.go.jp/koubo/datamanagement.html

(5) Elimination of Unreasonable Duplication or Excessive Concentration of Research Funds

(a) Measures to prevent unreasonable duplication

In the case that a researcher is unnecessarily being allocated competitive research funds, etc. from the national government and/or multiple independent administrative corporations for the same R&D project (name or content of the research receiving R&D funds) being conducted by the same researchers and 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.").

- 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.
- 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.
- There is duplication regarding the use of research funds amongst multiple R&D projects
- Other equivalent cases

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.

(b) 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 research period, and any of the following apply, the decision to adopt the R&D project under this program may be cancelled.

- Excessive research funds are allocated in comparison to the researcher's abilities or research methods
- 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)
- Unnecessarily expensive research equipment is purchased
- 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.

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.

(c) Provision of information related to application content in order 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.

(d) Status of application and/or acceptance under other competitive research funding programs, including other government ministry/agency programs

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.

Ⅵ. Management and Evaluation of Awarded Projects

1. Project Management

A Contracted R&D Accomplishments Report is required to be submitted each fiscal year for all awarded projects according to the contracted R&D agreement. Furthermore, the PS and PO shall manage progress of the project. 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.

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 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 moving into 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)), as required to undergo face-to-face advice as a general rule in the first or second year[1, 2] after adoption of the R&D project under this program as a condition of adoption. Furthermore, based on appropriate information management, the research institute shall consent to AMED attending various kinds of consultation interviews under the "regulatory science strategy consultation" program etc. during the R&D period and share face-to-face advice records and related information with AMED.

[1]Regarding R&D projects involving clinical studies (trials), face-to-face advice must be undergone prior to the commencement of the clinical trials. R&D that have already undergone face-to-face advice prior to adoption of the R&D project may undergo face-to-face advice again during the R&D period as necessary.

[2]Although it is not compulsory for the R&D project to have undergone face-to-face advice at the time of application to this program, it is desirable that face-to-face advice be undergone and the results of the consultation reflected in the R&D plan.

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[3] during the R&D period, research institutes are required to submit materials related to clinical studies such as a protocol (including information such as aims, subjects, selection criteria, exclusion criteria, number of cases, observation content, intervention content, statistical methods, and research system).

3 Does not include clinical research that is not aimed at developing new drugs or medical devices or that differs from normal processes for evaluating/approving new medical technology.

2. Evaluation

Under this program, awarded projects whose planned project period is five years or longer shall undergo a Mid-term Review by the "Project Evaluation Panel" at around the third year after the R&D commences to rigorously evaluate the degree to which the R&D plan is being achieved and R&D accomplishments, etc.* Awarded projects whose planned project period is less than five years are not required to undergo a Mid-term Review as a general rule, but in the case that it becomes necessary to conduct a Mid-term Review in the course of implementing the program, a Mid-term Review shall be conducted by the "Project Evaluation Panel". Furthermore, in the case that it is deemed necessary, R&D projects under this program shall undergo a Mid-term Review, regardless of the timing.

Based on evaluation results, AMED may cancel (conclude early) a project in accordance with the overall decision of the PS and PO, etc.

In addition, all awarded projects are to undergo Ex-Post Evaluations at an appropriate time following the conclusion of the R&D project. Based on the evaluation results, it may be decided to extend for one year the R&D period of projects that can be expected to lead to practical application and that should be continued developmentally. Moreover, a follow-up evaluation may be carried out after a certain period of time after conclusion of the project if deemed necessary.

*"Five years" refers to five fiscal years.

3. Presentations at Accomplishments Report Meeting

As part of achievements reporting under this program, the PI of an awarded project shall be required to make a public or closed-door presentation at an Accomplishments Report Meeting held by AMED. In addition, as part of follow-up evaluations and examinations of further development of project accomplishments, the PI of an awarded project may be requested, if necessary, to make a presentation in or after the fiscal year in which the project was completed, so please cooperate with this request.

Ⅶ. Handling of R&D Accomplishments

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

1. Submission and Publication of R&D Accomplishments Reports

Research institutions shall submit a R&D accomplishments report summarizing the research accomplishments of the R&D project. Please note that the deadline for submission of reports is within 61 days from the end of the term of the contracted R&D agreement or from the conclusion/cancellation/discontinuance of the contracted R&D, whichever comes first. In the case that the R&D accomplishments 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.

A part of the items in the R&D accomplishment 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 reporting 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 accomplishment 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 reporting form compiled by the PI upon Ex-Post Evaluation will be published at appropriate times on the AMED website.

2. Attribution of R&D Accomplishments

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. 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.

3. Measures towards the Practical Application of R&D Accomplishments

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 IX. 6.).

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

4. 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

5. Securing Open Access to R&D Accomplishments

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.

6. Handling of Data

With regard to the data etc. acquired from the results of R&D, please ensure that it is handled in pursuance with the “handling of data” section that is planned to be included in the contracted R&D agreements from FY2020 onwards.

Ⅷ. Handling of Acquired Goods

7. 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.[2]

Ownership of acquired goods by Companies, etc.,[3] 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]The submission of contracted research regulations etc. will be necessary in the event that goods acquired using contracting expenses are made the property of a university.

[3]"Companies, etc." is a general term for research institutes other than "universities, etc."

8. Handling of Acquired Goods after Completion of 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 service 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).

9. 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.

Ⅸ. Other

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.

1. Promotion of Dialogue and Cooperation with Citizens and 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), the Council for Science and Technology Policy (now the Council for Science, Technology and Innovation) 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/output/20100619taiwa.pdf

2. Promotion of 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. Moreover, for the time being it is envisages that among the areas of medical research and clinical studies the PPI initiative will mainly focus on investigator-initiated trials, intervention studies, observational studies (non-intervention studies) with human subjects.

[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

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. 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
[2] https://www.amed.go.jp/keiri/index.html

4. Registration of 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.
Note that there is a link from researcher names on the AMED funding for innovation database (AMEDfind) website to researchmap.

* https://researchmap.jp/

5. 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.

6. 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
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, Labor 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

7. 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 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. Please refer to the website[2] below for information regarding the Medical IP Desk.

1 AMED IP Liaisons: https://www.amed.go.jp/chitekizaisan/chizai_riezon.html

2 Medical IP Desk: https://www.amed.go.jp/chitekizaisan/medical_ip_desk.html

8. Seeds/Needs Matching Support System

In April 2018, AMED launched the "AMED ぷらっと®/AMEDplat " 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® /AMEDplat system. Note that you should refer to the AMED ぷらっと® /AMEDplat website* regarding details about the launch of use of the AMED ぷらっと® /AMEDplat.

*AMED ぷらっと® /AMEDplat website: https://www.amed.go.jp/chitekizaisan/amed_plat.html

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

In order to link the results of outstanding basic research by universities to the practical application of drugs, AMED's Department of Innovative Drug Discovery and Development (hereinafter referred to as the "Drug Development Department") 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 business derivation.

The Drug Development Department 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 collaboration with drug companies; provides technological support for applied research (exploratory study, optimization study, etc.) and nonclinical studies (conforming to GLP (Good Laboratory Practice)); introduction and contracted support of CROs (Contract Research Organizations) and CMOs (Contract Manufacturing Organizations), etc.; and procedures for collaboration with drug companies.

In this way, the Drug Development Department 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 collaboration with drug companies. For this reason, R&D projects that are related to drug development may receive active support from the Drug Development Department in coordination with the relevant departments/offices.

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 IV. 1.). Furthermore, the Drug Development Department 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 Drug Development Department, AMED provides the information on the support content to the department in charge of the program.

Please refer to Chapter X. for references related to support provided by the AMED Drug Discovery Support Network and the Drug Development Department.

10. Enhancement of AMED Project 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 pace 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.

11. Deposit of Resources to the National Bioresource Project (NBRP) and Use of Resources Developed by NBRP

As a general rule, 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[3] the relevant bioresources (limited to bioresources targeted by the NBRP[1]) to the NBPR Centers,[2] making these resources broadly available for researchers' use in order to contribute to research in the life science field. Use of bioresources that have already been prepared at NBRP is recommended from the standpoint of efficient project execution, etc.

[1] NBRP: https://www.amed.go.jp/program/list/04/01/002.html

[2] List of the NBRP Centers: http://nbrp.jp/center/center.jsp

[3] "Deposit": Procedure for permitting the use (storage/provision) of resources in the NBRP 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.

12. Cooperation with Databases

(1) Regarding Publicizing of Data from the National Bioscience Database Center

The National Bioscience Database Center (NBDC) (https://biosciencedbc.jp/) 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 2above	NBDC Human Database	https://humandbs.biosciencedbc.jp/

(2) Regarding 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. Regarding the 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

14. Responding to the Implementation of the Clinical Research Act

As the Clinical Research Act went into effect (on April 1, 2018), a number of new actions became necessary in order to conduct clinical research, such as registration with the Japan Registry of Clinical Trials (jRCT) database established by the Ministry of Health, Labour and Welfare and the reporting of diseases and the like. Please take the appropriate action to ensure compliance with the Act.

Clinical research initiated after the Clinical Research Act goes into effect should not be redundantly registered in the databases of Japanese clinical research registration institutions other than the jRCT. If the research has already been registered in the database of another clinical research registration institution in accordance with the "Ethical Guidelines for Medical and Health Research Involving Human Subjects," please take the appropriate action in accordance with laws and regulations, etc.

For more details of responding to the implementation of the Clinical Research Act please refer to the Ministry of Health, Labour and Welfare (MHLW) website.*

* Regarding the Clinical Research Act (Ministry of Health, Labour and Welfare website)
https://www.mhlw.go.jp/stf/seisakunitsuite/bunya/0000163417.html

15. Research Support through Translational and Clinical Research Core Centers

For the "Project of Translational and Clinical Research Core Centers", AMED is integrating various R&D programs—including the "Translational Research program: Strategic Promotion for practical application of Innovative medical Technology (TR-SPRINT) promoted by MEXT, "Comprehensive program for improving infrastructure to promote clinical application of innovative medical seeds", and "Research grant for Clinical Application of Innovative medical seeds promoted by MHLW"—with the aim of creating a centralized project implementation system.

The project seeks to construct a system at translational research support centers, clinical research core hospitals, and other academia enabling innovative basic research to be linked integratedly to practical application and commercialization, and comprises projects aimed at strengthening center functions (including securing/training human resources); multiple infrastructure development projects aimed at creating networks; and R&D projects providing support for investigator-initiated trials and translational research aimed at nurturing and achieving the practical application of research seeds.

In order to support the development of drugs and medical devices, the Translational Research and Clinical Trials 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.

For programs for which disbursement of Academic Research Organization (ARO) support expenses as research expenses is approved, if the support of a Translational Research and Clinical Trials Core Center in planning and carrying out research for the practical application of academia-generated medical seeds is desired, please refer to the list* of contacts for Translational Research and Clinical Trials Core Centers.

* List of contacts for Translational Research and Clinical Trials Core Centers
https://www.amed.go.jp/program/list/05/01/001_ichiran.html

Ⅹ. References

If you should have any questions regarding the content of these application guidelines, please make inquiries via the contact addresses provided in the table below.[1, 2] In addition, in the case that any information provided here changes, these changes shall be posted in the AMED website under "Collaborative Calls Information",[3] so please check the website for updates.

[1]Please make inquiries by e-mail as far as possible (Change "AT" to @ when inputting the address.)

[2]Be careful to dial the correct telephone number. Unless otherwise stated, telephone inquiry services are available 10:00–12:00 and 13:00–17:00 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	AMED Department of International Affairs Tel: +81-3-6870-2215 E-mail: chikyukibo "AT" amed.go.jp
Misconduct/fraudulent use/fraudulent receipt	AMED Department of Research Integrity and Legal Affairs E-mail: kouseisoudan "AT"amed.go.jp
Management of conflict of interest/research ethics education programs	AMED Department of Research Integrity and Legal Affairs E-mail: kenkyuukousei"AT"amed.go.jp
RIO Network	AMED Department of Research Integrity and Legal Affairs E-mail: rionetwork"AT"amed.go.jp
Medical IP Desk (Contact point for medical IP consultation)	AMED Department of Research Integrity and Legal Affairs E-mail: medicalip"AT"amed.go.jp
Support provided by the AMED Drug Discovery Support Network/Department of Innovative Drug Discovery and Development	AMED Department of Innovative Drug Discovery and Development East Japan Office 8F 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

XI. R&D Projects Being Solicited

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

1. R&D project being solicited 1

（１） Title of the R&D project being solicited

International Joint Clinical Study for Promoting Overseas Utilization of Drugs, Medical Devices, and Medical Technologies in Order to Improve Health and Medical Services in Low- and Middle-Income Countries

（２） Objectives

International development of the excellent medical technology that Japanese health and medical services possess will not only bring about economic effects for Japan but also be an important measure leading to the promotion of UHC in low- and middle-income countries, which is one of the SDGs, and to international contributions to the strengthening and improvement of healthcare systems in developing countries. With the aim of achieving these objectives, international joint clinical research is being carried out proactively around the world amidst efforts to secure reliability in, increase the efficiency of, and standardize the development of medical devices and drugs.

The objective of this R&D project being solicited is, through international joint clinical studies, the practical application of prevention, diagnosis, and treatment methods that have already been verified as effective in developed countries but have not yet diffused in the target countries in order to improve the situation regarding diseases (emerging/re-emerging infectious diseases, lifestyle diseases, maternal and child health, etc.) issues that are major public health issues on an international scale, thereby contributing to the enhancement of global healthcare. In concrete terms, we are seeking proposals for international joint clinical studies that assess and verify the effectiveness, safety, risks and benefits, and administration/usage methods for drugs, medical devices, and medical technologies related to prevention, diagnosis, and treatment regarding patients in low- and middle-income countries. Furthermore, through this research, projects should also examine local adaptability, medical service costs, and sustainability as well as strategies aimed at future practical application and commercialization.

（３） R&D content being solicited

The R&D is to comprise international joint clinical studies conducted in low- or medium-income countries with the aim of practical application of drugs, medical devices, medical technologies, etc., * that contribute to the improvement of health and medical services in low- and medium-income countries.

*Targets consist of drugs, medical devices, medical technologies, etc., that have already been verified as effective in developed countries but have not yet put to practical use (diffusion or implementation) in low- and middle-income countries.

Project implementation system

- Japanese academia and businesses (including venture businesses) are to collaborate and establish joint research teams with academia in the countries in which the research is to be conducted and present a proposal for international joint clinical research.
- International joint clinical research is to be carried out targeting patients in low- and middle-income countries. The research is to be led by medical practitioners who have a Japanese medical practitioner's license and medical practitioners from the joint research organization who have a medical practitioner's license issued by the country in which the research is to be conducted.

（４） Support following selection

Awarded projects are able to receive the following support as necessary.

- Support in elaborating clinical research protocols and managing clinical research progress

- Provision of information related to the health ministry and regulatory authority in the country in which the research is to be carried out.

（５） Accomplishments being sought

1) First stage: first and second year of the project

Review of related laws and regulations of the country in which the research is to be carried out; conclusion of international joint research agreement; elaboration of clinical research protocols; preparation of informed consent form; approval of the project by ethics review boards (both in Japan and the country in which the research is to be carried out); assurance of import/export of medical devices and drugs, etc.; and formulation of strategies for practical application/commercialization of the drugs, medical devices, medical technologies, etc. in low and medium income countries (surveys regarding local adaptability, medical service costs, sustainability, etc.)

2) Second stage: Third year onwards*

Implementation of clinical study, analysis of results, formulation of strategies for practical application, etc.

* Mid-term Reviews of the first stage accomplishments are to be conducted toward the end of the second year and R&D projects to be further pursued in the third year onwards narrowed down to one or two projects.

（６） Examples of the practical application of the research achievements, which is the ultimate objective of this R&D project being solicited

- Approval of the drugs, medical devices, medical technologies, etc. by the regulatory authority of the target country
- Establishment of treatment protocols and formulation of clinical guidelines for the target country based on the research achievements
- Use of the drugs, medical devices, medical technologies, etc., in the target country
- Acquisition of WHO Prequalification
- Inclusion in WHO guidelines
- Inclusion in WHO compendium etc.

Conditions for selection

In order to be selected, a project must fulfill all of the criteria prescribed in 1)–9) below.

① The research implementation system for the project can be determined to be highly capable of carrying out the project in the target country.

② When submitting the R&D proposal, it is possible to include documents showing the consent of the head(s) of the joint research organization(s) in the target country and the head(s) of related government organization(s).

③ The needs of low- and middle-income countries, including the country in which the research is to be carried out, have been clarified through literature reviews and preliminary surveys, etc. The proposed project can be expected to contribute to the improvement of health and medical service issues in low- and middle-income countries.

④ The proposal is in compliance with international standards and the target country's laws and regulations regarding bioethics and safety measures.

⑤ The project comprises a clinical study or clinical studies that will lead in the future to the practical application of drugs, medical devices, medical technologies, etc., and the project's value to the international community, concept originality, scientific validity, target diseases, and possibility of achieving results are clear.

⑥ At the time of submission of the R&D proposal, it is possible to simultaneously submit clinical study protocols (including information regarding objectives, subjects, inclusion criteria, exclusion criteria, number of cases, observation content, intervention methods/content, analytical methods, statistical methods, evaluation items such as outcomes and endpoints, and research system).

⑦ The research cooperation system includes experts in biological statistics.

⑧ In the case of development research, R&D Principal Investigators (PIs) undergo ex-ante interviews or face-to-face advice provided by the PMDA prior to submitting the R&D proposal, and submit with the proposal a record of consultation showing that the PMDA does not deny the project's developmental policy. If the

R&D PIs consult with an overseas regulatory authority other than that PMDA, documentation detailing the content of the advice received is submitted with the proposal.

⑨ With regard to clinical research that is to commence after selection, a schedule has been formulated that take efficiency and practicability into consideration.

In addition to the common criteria prescribed above, projects to which the following criteria apply shall be given priority in the selection process. If the following items apply to your project, please include details about the relevant content in your R&D plan.

⑩ The project plan provides a roadmap leading up to practical application.

⑪ It is desirable that the project develops drugs, medical devices, medical technologies, etc., for which medical needs in low and middle income countries are high but development and diffusion are lagging.

2. R&D project being solicited 2

（１）Title of the R&D project being solicited

Global Alliance for Chronic Diseases (GACD) collaborative call: Primary and Secondary Prevention of Cancer

（２）Details

The solicitation process for this R&D project is conducted in English under the uniform philosophies, objectives, details, and project reviews, etc. which are shared among GACD member agencies. Cancer is one of the most important public health issues in the world, with some 30,000,000 people predicted to die from cancer every year up to the year 2030, 75% of whom will die in low- and medium-income countries. It is also estimated that between 30% and 50% of all cancers are preventable. One-third of cancer deaths worldwide are caused by behavioral risk factors such as smoking or drinking alcohol, diet, obesity, and lack of exercise. Cancer deaths due to smoking comprise approx. 22% of the total, while approx. 25% of cancers occurring in low- and medium-income countries are thought to be caused by infectious diseases (HPV and HBV) that can be prevented through vaccinations.

Although evidence-based health and medical intervention is spreading in many developed countries, effective interventions have not been identified in low- and medium-income countries; the current situation is that health and medical intervention is not being sufficiently utilized due to implementation-related issues. This solicitation therefore seeks proposals for projects aiming to conduct intervention research using evidence-based health intervention/medical technologies that will contribute to the prevention of primary and secondary cancer and can be expected to prove effective in low- and medium-income countries. R&D proposals are also required to formulate strategies to implement the relevant interventions on behalf of groups of people. For concrete details regarding projects being solicited, please refer to the website shown below. Also, please note that target countries for this research shall comprise low- and medium-income countries; research related to vulnerable populations in developed countries is outside the scope of this call for proposals.

For detailed information about calls for proposals, please to refer to GACD's call text.
https://www.gacd.org/funding/calls-for-proposals/gacd-cancer-call

（３）Project implementation system

- Japanese academia and businesses (including venture businesses) are to collaborate.
- Joint research teams are to be established with academia in the country in which the research is to be conducted and intervention research targeting residents and patients in the target country carried out. The research is to be led by medical practitioners who have a Japanese medical practitioner's license and medical practitioners from the joint research organization who have a medical practitioner's license issued by the country in which the R&D is to be conducted.

（４）Conditions for selection

Points to note when preparing R&D proposals (In addition to the criteria stipulated by GACD, the following criteria must also be met.)

1) The research implementation system for the project can be determined to be highly capable of carrying out the project in the target country.

2) When submitting the R&D proposal, it is possible to include documents showing the consent of the head(s) of the joint research partner organization(s) in the target country and the head(s) of related government organization(s).
3) The needs of low- and medium-income countries, including the country in which the research is to be carried out, have been clarified through literature reviews and preliminary surveys, etc. The proposed project can be expected to contribute to the improvement of health and medical service issues in low- and medium-income countries.
4) The proposal is in compliance with international standards and the target country's laws and regulations regarding bioethics and safety measures.
5) The research cooperation system clearly involves experts in biological statistics and epidemiology, and it is desirable that these experts be involved from the proposal planning stage.
6) Research protocols (including information regarding objectives, subjects, inclusion criteria, exclusion criteria, number of cases, observation content, intervention methods/content, analytical methods, statistical methods, evaluation items such as outcomes and endpoints, and research system) are clearly stated in detail in the research plan.
7) A scheme of the implementation of the relevant interventions is shown.

（５）Accomplishments being sought

The following activities are to be carried out with the aim of achieving the expected impact of the call text.

1) First Year
Review of related laws and regulations of the country in which the research is to be carried out; conclusion of international joint research agreement; elaboration of clinical research protocols; preparation of informed consent form; approval of the project by the Ethics Review Board; assurance of import/export of medical devices and drugs, etc.

2) Second year onwards
(In addition to research topics continued from the first year) implementation of intervention research and analysis the results, formulation of strategies for implementation of achievements in low- and medium-income countries, and their implementation.

（６）Ultimate research achievements (the objective of this R&D project being solicited)

- Present strategies for future implementation of achievements
- Incorporate research achievements in health and medical policies of the target country, establish treatment protocols, formulate clinical guidelines
- Incorporate research achievements in WHO guidelines and other international standards etc.

3. Conditions for Submitting R&D Proposals for Investigator-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 with regard to 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[1] 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.

[1]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, with regard to materials required for applying for approval—including for regenerative medicine products and medical devices—testing must be carried out based on sufficient understanding.

R&D projects moving into the practical application stage (R&D projects that are within the target scope of the "regulatory science strategy consultation" or other PMDA consultation services[2]), are required to undergo "regulatory science strategy consultation" or other consultation services (face-to-face advice) provided by the Pharmaceuticals and Medical Devices Agency (PMDA) as a general rule in the first or second year[3] after adoption of the R&D project under this program as a condition of adoption. R&D projects that have already undergone face-to-face advice etc. prior to adoption of the R&D project may undergo regulatory science strategy consultation etc. again during the R&D period as necessary. Although it is not compulsory for the R&D project to have undergone face-to-face advice etc. at the time of application to this program, it is desirable that regulatory science strategy consultation be undertaken, and the results of the consultation reflected in the R&D plan.

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

[3]R&D projects targeting clinical studies (trials) are required to undergo consultation "prior to the commencement of the clinical trial".

(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. With regard to 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.

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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