[Translation]

FY2024 Strengthening Program for Pharmaceutical Startup Ecosystem: 4th Call for Proposal from Pharmaceutical Startups

Briefing Session of Call for Proposal

March 4, 2024

Department of Intellectual Property and Technology Transfer
Japan Agency for Medical Research and Development

About this document

- This document provides an overview of the FY2024 "Strengthening Program for Pharmaceutical Startup Ecosystem / 4th Call for Proposal from Pharmaceutical Startups".

- Before applying, please make sure to confirm the information in the main body of the Application Guidelines.

- If there are any discrepancies between this document and the Guidelines, the Guidelines shall prevail.

- The Guidelines and other materials may be revised during the Application period. In this case, they will be posted on the Application Information page on the AMED website*.

*the Application Information page on the AMED website
https://www.amed.go.jp/koubo/19/02/1902B_00047.html

- The parts written in red in this document are changes from the previous call for proposals.

Before Applying (Notes)

- The researcher (the "Principal Investigator" applying for the Subsidy and the " Co-Investigator" participating in the Subsidized Project) and the research institution (Business Operator and Contractor) must be registered in e-Rad (The Cross-Ministerial Research and Development Management System) by the time of application. Please refer to the e-Rad portal site for the registration procedure (see slide 34).

- Please allow at least two weeks for the e-Rad registration procedure, as it may take several days. (If you have already registered for programs under the jurisdiction of another ministry or agency, you do not need to register again.)

- Before preparing your proposal, please be sure to read the Innovative Research and Development Promotion Fund Subsidy (*kakushinteki kenkyukaihatsu suishin kikin hojokin*) Guidelines, the Appendix to the Subsidy Grant Decision Notification, the Administration Manual for Subsidized Project (including the Supplementary Version), the FAQs, and the Registration Agreement, which will be posted on the Application Information page on the AMED website*.

  *the Application Information page on the AMED website

  https://www.amed.go.jp/koubo/19/02/1902B_00047.html

Before Applying (Notes)

- If you have not yet decided to receive the prescribed investment from a Registered VC , please first request the Registered VC to consider investing in your company, and then conduct activities to receive the investment. The contact information of the Registered VCs is posted on the program website*.

- Please note that the investment is made to a Pharmaceutical Startup that is determined to be worthy of investment by the intention of the Registered VC, and AMED is not involved in the decision-making process of the Registered VC.

*the program website
https://www.amed.go.jp/program/list/19/02/005.html

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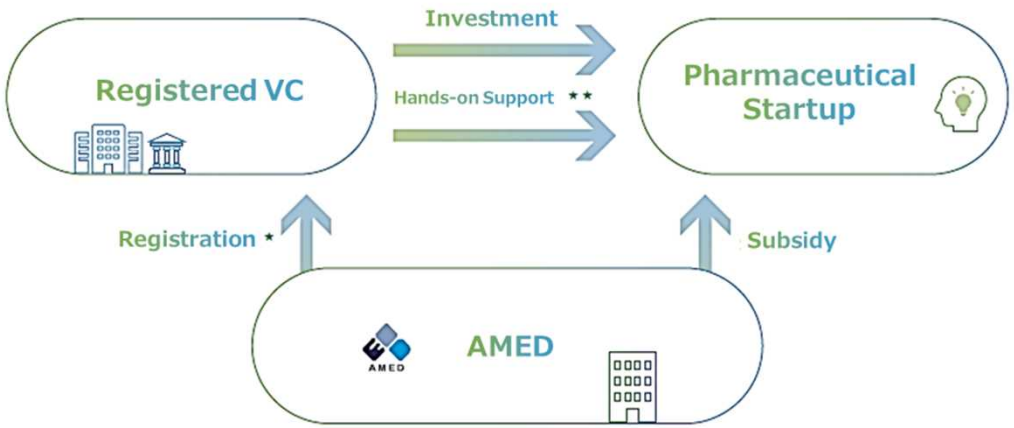
1. About Our Business

1-1 Background and Business Objectives

- To solve the shortage of large-scale development funds, this program supports pharmaceutical startup development and commercialization, especially those engaged in pre-clinical study, Phase 1 clinical study, Phase 2 clinical study or exploratory clinical study, on the condition that they also receive funding from venture capital firms registered by AMED (hereinafter referred to as “Registered VC”) specializing in drug development and providing hands-on business management and commercialization support.
- In particular, to achieve sufficient sales and growth of pharmaceutical startup, we will actively support plans to commercialize in overseas markets in addition to Japan. Pharmaceutical startups that are Japanese subsidiaries of foreign corporations established to raise funds overseas or commercialize in overseas markets are also eligible for support.



* Registration ----- Registration of VCs with track records of investment and support, etc. in the drug discovery field

** Hands-on Support ---- Support according to the growth stage of Pharmaceutical Startups from the perspectives on management, development and technology, and regulatory affairs

1-2 Outline of the Call for Proposal

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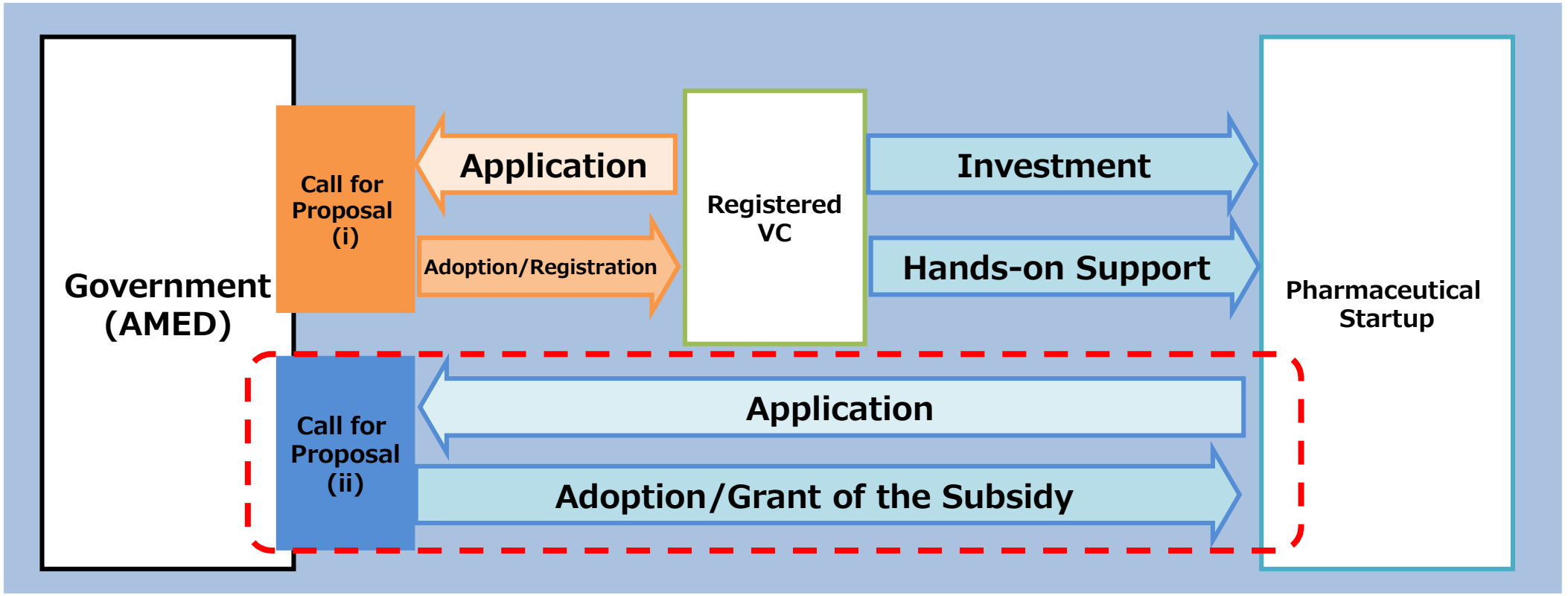
- The call for proposal will be carried out in two stages.
  - Call for Proposal for VC Registered by AMED ((i)Call for Proposal for VC), and Call for Proposal from Pharmaceutical Startups invested by Registered VC ((ii)Call for Proposal of Pharmaceutical Startups)
- This call is the (ii)Call for Proposal for Pharmaceutical Startups (dotted red line frame)



1-3 Program Structure

（1）Program Implementation System

- AMED will assign a Program Supervisor (PS) and a Program Officer (PO).
- The PS and PO have knowledge and understanding of the progress status of this program overall and provide the necessary guidance and advice to ensure that this program runs smoothly. Furthermore, Business Operator and Principal Investigator are obligated to cooperate with the PS and PO.

（2）Roles of Business Operator, Contractors, and Registered VCs, etc.

- The "Business Operator" is the organization to which the Principal Investigator belongs. A Pharmaceutical Startup that, in principle, is the main place of implementation for the Principal Investigator, receives the Subsidy directly from AMED, takes the main entity to commercialize the Subsidized Project, and is responsible for carrying out the Subsidized Project until the end of the Subsidized Project period, and has established a system for this purpose.
- The “Contractor" refers to the organization to which the Co-Investigator belongs, excluding the Business Operator. The "Contractor" refers to a research institution, etc., which concludes a contract agreement with the Business Operator and implements the Subsidized Project by sharing the implementation items in the Subsidized Project Plan. If you wish to consider an overseas institution or company as a Contractor, please consult AMED in advance. Contract in this project refers to outsourcing that includes research and development elements, that is, contract that has the potential to create new intellectual property. Furthermore, even if intellectual property is generated, if it is not assigned to the contract, it is considered just outsourcing.
- The “Registered VC" refers to a venture capital firm registered by AMED to invest in the Business Operator and provide hands-on management and commercialization support.

2. About Call for Proposal

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2-1 Target technology / Phase

- This program will support the development of innovative technologies for vaccines and therapeutic drugs for infectious diseases, as well as pharmaceuticals for diseases other than infectious diseases. However, proposals regarding the expansion of indications for drugs already on the market are not eligible.
- Pre-clinical study, Phase 1 clinical study, Phase 2 clinical study or Exploratory clinical study will be covered.
- Non-clinical studies will be conducted on the condition that there is a final development candidate to proceed to the clinic.
- You must have filed a domestic or foreign patent application for the final development candidate product. However, if you have not filed an application at the time of application for strategic reasons, please provide details of your strategy (development strategy, intellectual property strategy, business strategy, pharmaceutical strategy, etc.) in your proposal.

2-2 Scale of Expenses Covered by Subsidy・Subsidized Project Period・Planned Number of Adoptions

Field	Scale of Expenses Covered by Subsidy (Including indirect costs and Registered VC investment)	Subsidized Project Period	Planned Number of Adoptions
#1 Innovative technological development for development of infectious disease vaccines and therapeutic drugs.	[amount of money] (upper limit) 10 billion yen (Accept even if the upper limit is exceeded) ※AMED Subsidy covers up to 2/3 of the expenses.	Up to September 2031 (Set for each Adopted Project)	Around [0–15(number of projects)]
#2 Innovative technological development for development of pharmaceuticals etc. for diseases other than infectious diseases.			

- ”Pharmaceuticals, etc." includes pharmaceuticals and regenerative medicine products.
- If investors includes multiple Registered VCs, they can be added to the investment amount as Lead Registered VCs and follower Registered VCs. Applicants can choose whether or not to count as a follower Registered VC.
- If all Stage Gate Evaluations stipulated in the Subsidized Project Plan are passed, the Subsidized Project period will be up to September 2031.
- The retroactive period is from November 8, 2022 (the date of the Cabinet decision on the supplementary budget for 2022) until the time of application.
- Depending on the results of the review, the Expenses Covered by Subsidy listed in the proposal may be reduced or the Subsidized Project period may be shortened.

2-3 Objectives/Achievements at the end of Subsidized Project Period

- This program aims to complete Phase 2 clinical trial or exploratory clinical trial (POC acquisition) in the Subsidized Project period. In addition, it will be reviewed whether the business development plan after the completion of the Subsidized Project has been properly considered (the plan is for commercialization including overseas markets).

- In the following cases, in principle, the Subsidized Project will be terminated early after review by AMED.
  - If the Phase 2 clinical trial or exploratory clinical trial completion (POC acquisition) is achieved in the middle of the Subsidized Project period.
  - Business Operator or parent company of business operator* makes an initial public offering (IPO) and ceases to be a private.
  - If the business operator or the parent company of business operator* conducts a corporate merger and acquisition (M&A), and the Registered VC that received the investment, or an association or other fund managed by the Registered VC, ceases to be a shareholder. (in the case of transfer of shares, securities that can be requested or acquired for delivery of shares, or rights similar to these).
  - In addition, when AMED determines that the Subsidized Project should be terminated early.

*The term "parent company" here refers to the "foreign corporation that is 100% the parent company of the pharmaceutical startup" (requirements for "2.1 eligible Applicants" J).

3. Eligibility and Application Requirements

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3-1 Eligible Applicants

Eligible Applicants for this program shall be the person (Principal Investigator) belonging to a Pharmaceutical Startup in Japan that fulfills the conditions shown in A)–E) below and who will be their main place of implementation of the Subsidized Project, and who take responsibility for the formulation of the Subsidized Project Plan and compiling the results with for the Subsidized Project for which the application is being submitted.

A) The company must be an unlisted company.

B) Private companies registered in Japan that have a base of operations in Japan for their business activities, including technological development related to their business activities. However, it is also possible to have a base for drug development and business activities outside of Japan and use the Subsidy to conduct technological development outside of Japan.

C) The applicant must have an internal control and governance system that enables accurate execution of business activities. (After adoption or the start of the subsidized project, AMED staff or experts dispatched by AMED may check internal control and governance systems, etc., based on the status of administrative processing and system development.)

D) The applicant must have an appropriate management system and processing capability for accounting and other administrative work related to the Subsidized Project.

E) The applicant must be a corporation*1 that satisfies either the capitalization criteria or the number of employees criteria stipulated in the Small and Medium-seized Enterprise Basic Act, etc., and must not fall under the category of a deemed large corporation*2.

For F)、G)、H), *1 and *2, please refer to the Application Guidelines.

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3-1 Eligible Applicants

In addition, we require that either of the following I) and J) be satisfied.

I) Within the retroactive period, the applicant has received an investment* of 1/3 or more of the Expenses Covered by Subsidy in the proposal from a Registered VC (must include the Lead) or has decided to receive an investment in the future.

J) The foreign corporation that is the 100% parent company of the pharmaceutical startup must have received investment* from a Registered VC (must include the Lead) within the retrospective period or has decided to receive investment in the future. Moreover, with respect to all or part of the investment received by the foreign parent corporation from a Registered VC, a Japanese subsidiary company, which is a pharmaceutical startup that will be the implementing agency of the subsidized project, will receive an investment* of 1/3 or more of the Expenses Covered by Subsidy in the proposal. (The form of funding does not matter.) The amount of those funds that can be transferred to AMED's dedicated account will be counted as subsidized expenses.

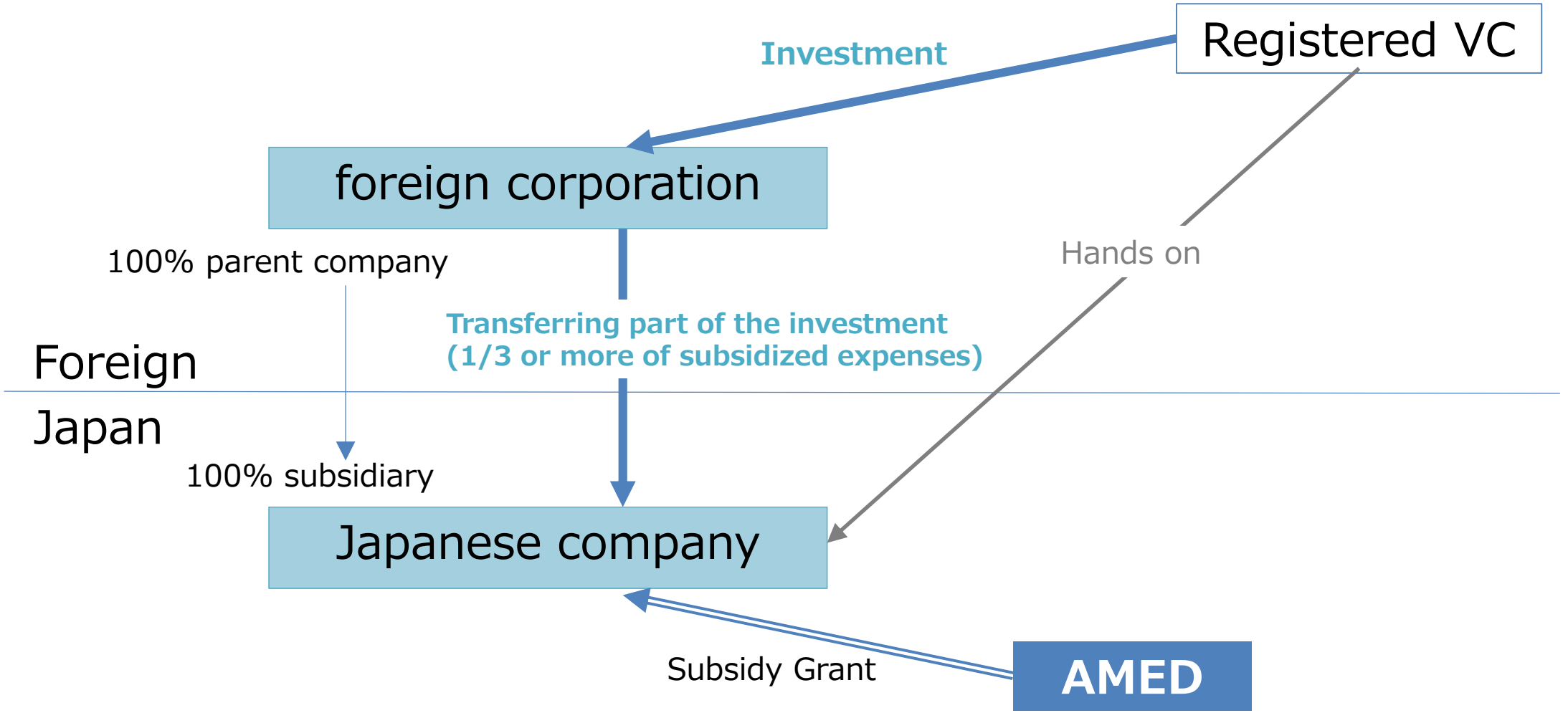
If you wish to make a proposal based on requirement J), please consult AMED in advance (this is a formal confirmation, and acceptance or rejection will be determined based on the review in accordance with "5.2.2 Evaluation Items and Perspectives").

If the proposal based on requirement J) is adopted, a tripartite contract will be concluded between the parent company, subsidiary, and AMED (the parent company will also be jointly and severally liable for the subsidiary's obligations regarding the subsidized business).

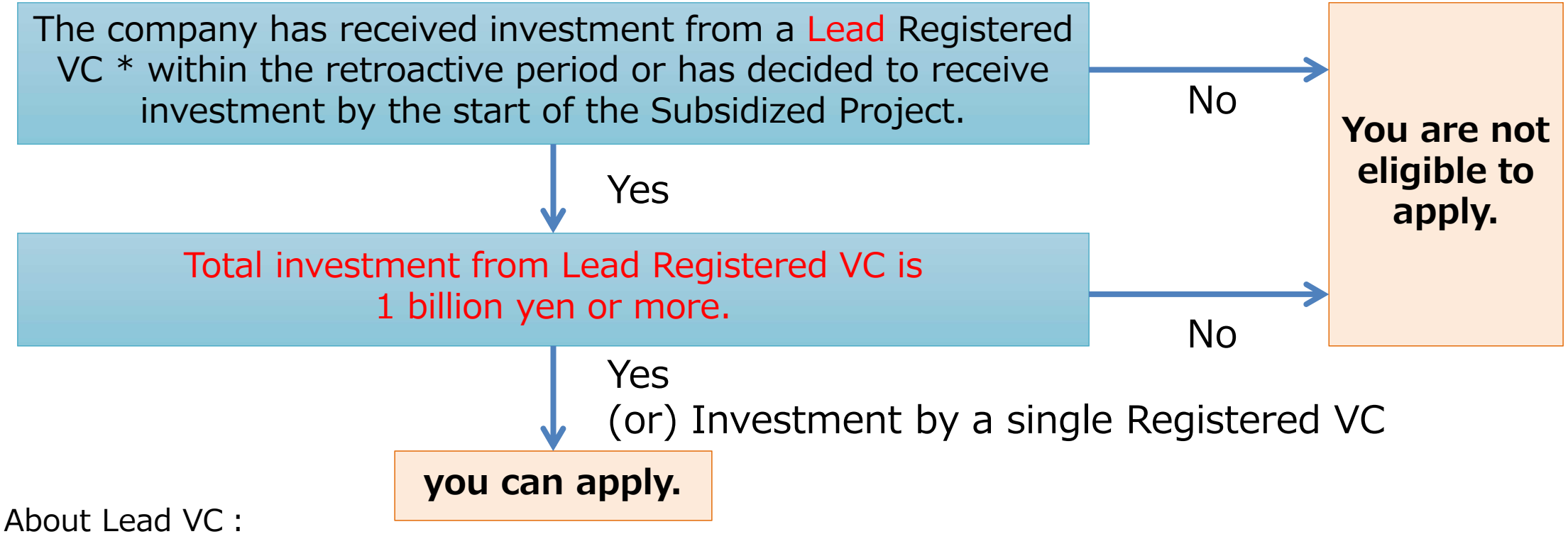
*For details, please check the Application Guidelines.

(Reference) Supplementary for Eligible Applicants

Requirement J)



(Reference)
Supplementary information on eligibility requirements



※About Lead VC :

The VC that has invested the largest amount among the investors (excluding operating companies such as pharmaceutical companies) in the fundraising after the start date of the retroactive period (see Slide 12) and plays a Leading role in fundraising and hands-on activities will be considered as the Lead VC. However, even if the VC does not have the largest amount among the investors (excluding business companies such as pharmaceutical companies), it may be recognized as the Lead VC. If applicable, please describe the reasons why the VC can be judged as a Lead VC in Item 8-3-2 of the [Form 1] Subsidized Project Proposal.

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3-2 Other requirements, etc.

- Only one proposal per Pharmaceutical Startup should be submitted to this Call for Proposal. Each proposal must include only one drug discovery pipeline (multiple pipelines cannot be proposed at the same time).

- This program will provide support for drug discovery pipelines. Platform-type Pharmaceutical startups are also eligible to apply if they have a specific drug discovery pipeline.

- A proposal will be created so that the investment amount by the Registered VC will be 1 billion yen or more, including the investment before the start date of the retroactive period (see slide 12) and the investment from the start date of the retroactive period throughout the entire subsidy project period. However, only the expenses incurred during the subsidized project period out of the contributions made after the start date of the retroactive period are eligible for subsidy.

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3-2 Other requirements, etc.

- Among the Registered VCs that pharmaceutical startup receive support from, the Lead Registered VCs must provide consistent support from the time of application to the end of the subsidized project. Generally, changes to the Lead Registered VC during the subsidized project period are not permitted, but if there is another Registered VC who will take over the Lead, the replacement may be approved as a result of the review. However, for both the Lead Registered VC who initially applies and the Registered VC who takes over the Lead, the total amount of investment prior to the start of the retroactive period and the total amount of investment from the start of the retroactive period through the entire subsidized project period must be at least 1 billion yen.

- A pharmaceutical startup that is an affiliated company of a business company, etc. cannot make a proposal with a VC that is an affiliated company of the business company, etc. as the Lead certified VC.

- If a pharmaceutical company receives investment from a VC and becomes a consolidated subsidiary and falls under the category of a deemed large company, the pharmaceutical company will not be able to make a proposal.

4. Preparation and submission of proposal documents

4-2 Necessary Proposal Documents

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【Form1】 Subsidized project proposal
"Proposal document check sheet"
"Submission document file name"

No.	Mandatory/Optional	Proposal documents	Submission format
1	Mandatory	【Form1】Subsidized Project Proposal	PDF
2	Mandatory	【Form2】Breakdown of expenses･Subsidy item sheet (Corporations, etc.)	Excel
3	Mandatory	【Form2 separate sheet】Breakdown of expenses for the entire subsidized Project period	Excel
4	Mandatory	【Form3】List of Subsidized Project Participants	Excel
5	Mandatory	【Form4】Cash flow table check sheet	Excel
6	Mandatory	【Form5】Confirmation of investment intention or investment report and its attachments	PDF
7	Required if applicable	Human Whole Genome Sequence Analysis Protocol Form	Optional
8	Required if applicable	Materials etc. regarding management of R&D	PDF
9	Mandatory	Patent specification or patent publication, etc.	PDF
10	Optional	Patent search reports, patent maps, etc.	PDF
11	Mandatory	PMDA consultation record, Clinical trial plan and protocol, Excerpts from clinical trial brochure, etc.	PDF
12	Mandatory	Certificate of Registered Matters (Certificate of Historical Matters) ※ Within 3 months	PDF
13	Mandatory	Financial statements required to be attached to corporate tax returns	PDF
14	Optional	Other attachments	PDF

※Please download forms 1 through 5 of the proposal documents prepared by AMED from the Application Information page on the AMED website. https://www.amed.go.jp/koubo/19/02/1902B_00047.html

4-2 Necessary Proposal Documents

【Form1】 Subsidized project proposal

Please pay particular attention to the following points when preparing the Subsidized Project Proposal.

- **“2 Technology Overview”**

  Please submit existing materials with evidence and data applicable to items 2-1 through 2-4 as “No. 14 Other attachments" in the proposal documents (e.g., materials submitted for due diligence by the VC, etc.).

- **“7-1 Target Product Profile（TPP）of Outline of Business Plan”**

  Please describe the target product profile in terms of "indications/target patients," "mechanism of action (including modalities), " "dosage & administration," "efficacy," "safety," "pharmacokinetics," etc.

- **Lead VC for "8-3-2 Actual/planned investments since the start of the retrospective period".**

  When proposing as a Lead VC when you have not made the largest investment (excluding pharmaceutical companies and other operating companies), please provide reasons why you can be judged as a Lead VC.

- **"9-2 Evaluation of target proposers (Pharmaceutical startup)“**

  As a registered VC, please describe in detail how you evaluated target proposer (pharmaceutical startup) in terms of technology and commercialization after checking the instructions.

4-2 About Stage Gate Settings

- In this program, Stage Gate Evaluation will be conducted by the Project Evaluation Panel, which will rigorously evaluate the progress of the Subsidized Project Plan and the achievement targets set in advance.

- Stage Gate Evaluations must be set at the time of the next round of funding from a Registered VC. Stage Gate Evaluations should also be set at the time of important technical milestones, etc..

- In the Subsidized Project Proposal, please state the end of the year and month, the target to be achieved, and the Expenses Covered by Subsidy in each stage*. The period for each stage should be within four(4) business years, with a quarter-by-quarter basis.

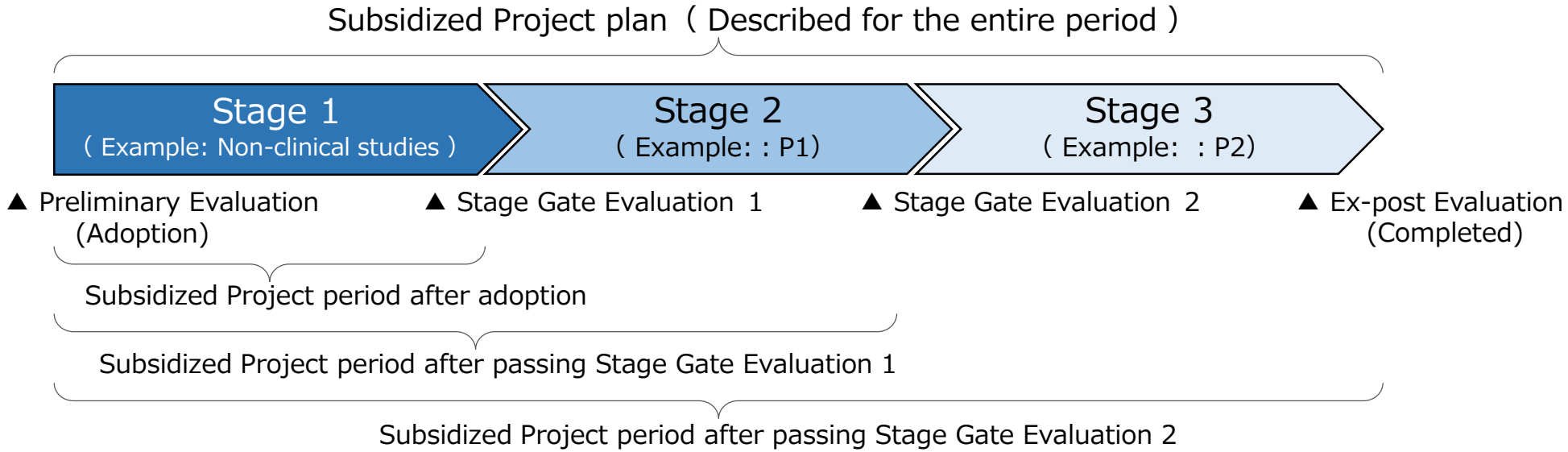
- After the project proposal is adopted, the details described in the Subsidized Project Proposal will be reflected in the Subsidized Project Plan based on the results of the preliminary evaluation by the Project Evaluation Panel, and the Subsidized Project Plan will be finalized in consultation with the Pharmaceutical startup, PS, PO, and AMED.

*Stage: The period from the Grant Decision after adoption or after passing the Stage Gate Evaluation to the Grant Decision after passing the next Stage Gate Evaluation or the end of the Subsidized Project period.

4-2 About Stage Gate Settings

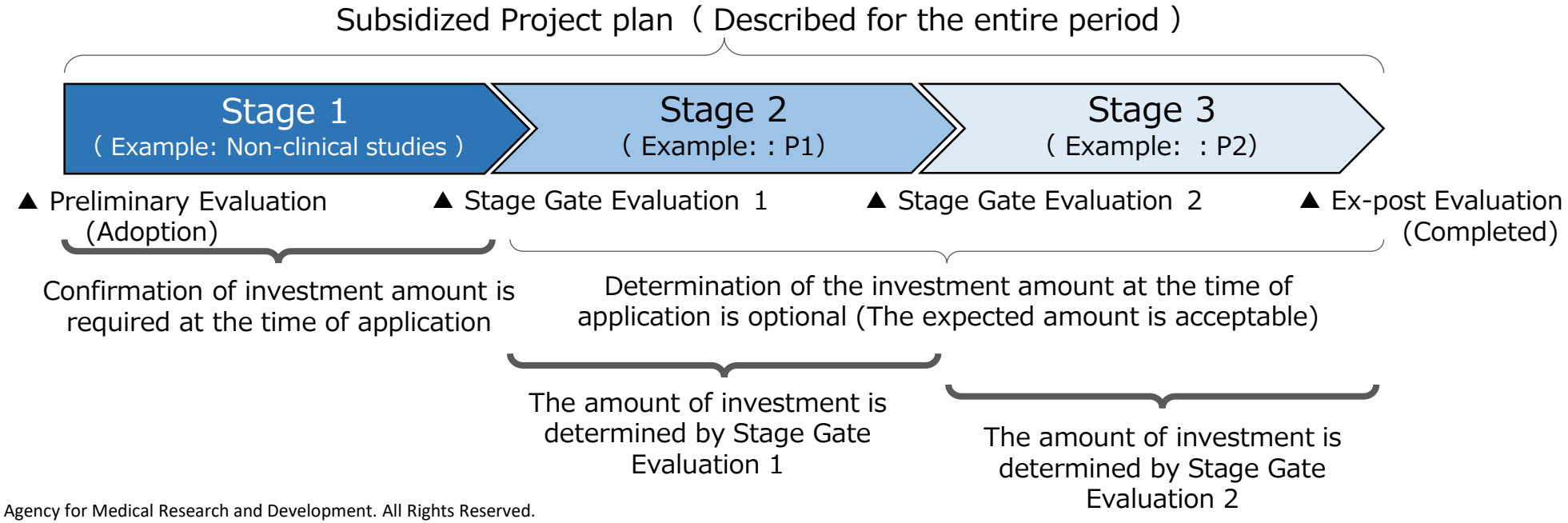
- After passing the Stage Gate Evaluation, the Grant Decision will be made by adding Expenses Covered by Subsidy and Subsidized Project period for the next stage according to the plan modification procedure. The Subsidy and periods for the subsequent stages will not be finalized until the Grand Decision after passing next Stage Gate Evaluation.

- As a general rule, the total amount of Expenses Covered by Subsidy for the entire period will be limited to the total amount of Expenses Covered by Subsidy as stated in the Subsidized Project Plan prepared after the adoption of the project.



4-2 About Stage Gate Settings

- Regarding the commitment of investment amount by Registered VC (Confirmation of Investment intention, investment report), it is possible to apply if there is a commitment of investment amount for Stage 1.
- For investments in Stage 2 and later, it is possible to apply if the planned amount is stated. The commitment of investment amount (confirmation of investment intention, investment report) will be confirmed at the time of Stage Gate Evaluation.



4-3 Scope of Expenses Covered by Subsidy

Project costs		These costs are directly necessary for the Subsidized Project and consist of the following four main items: “Costs of goods,” “Travel costs," "Personnel costs and services costs," and "Others". If Contract costs are to be recorded, please record them separately from the four main cost items.
Main items (4 Classifications)	Mid-range items (6 Classifications)	
(1) Costs of goods	Equipment and fixtures	Equipment, fixtures, prototypes, software (off-the-shelf), etc. for the Subsidized Project with an acquisition cost of 100,000 yen or more and a useful life of one year or more
	Consumables Fee	Items for the Subsidized Project that do not fall under equipment and fixtures, books, reagents and materials for research, consumables, etc.
(2) Travel costs	Travel costs	Travel costs listed in the “List of the Subsidized Project Participants” [Plan Form 3] pertaining to the participants in the Subsidized Project, travel costs for outside experts and other persons eligible for invitation
(3) Personnel costs ·services costs	Personnel costs	Personnel costs for researchers, etc., employed to conduct the Subsidized Project
	Services costs	Expenditure for services such as lecture requests, guidance/advice, test subjects, interpretation/translation etc.
(4) Other	Other	Costs for implementing the Subsidized Project other than the above. (e.g.) Subcontracting costs for testing, inspection work, animal breeding, etc. (including subcontracting to CMO/CDMO, CRO, etc.), costs for presenting the results of the Subsidized Project (paper submission fees, reprinting costs, website creation costs, etc.), meeting costs, transportation costs, equipment leasing costs, equipment repair costs, printing costs, software licensing costs, etc.
Indirect costs		Indirect costs: costs that are paid by AMED and used by the Business Operator as an allowance for a certain percentage (up to 10%) of the Project costs and necessary for the management, etc. of the Business Operator associated with the implementation of the Subsidized Project.
Contract costs		Costs for entrusting part of the Subsidized Project to a third party Up to 10% of indirect costs may be charged to the contractor (30% in the case of domestic universities, etc.). Contract costs= direct costs + indirect costs

4-4 Payment of Subsidy, attribution of acquired goods, etc.

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Payment of Subsidy

・If the first stage (Stage 1) is for multiple years, the Subsidy Grant Decision will be made for those multiple years.　In principle, the Subsidy, the total amount of Project costs, Indirect costs, and Contract costs, for each fiscal year written in the Subsidized Project Plan will be divided into four equal amounts and be paid to the dedicated account for the Subsidized Project.
Please refer to Slide 44 for the dedicated account (savings account (non-interest-bearing type)).

Attribution of acquired goods

・The ownership of goods, etc. (acquired goods) acquired by Expenses Covered by Subsidy shall belong to the Business Operator. However, there are restrictions on the handling of such items, including their disposal and movement. For details, please confirm them in the "Common Version" of the Explanation of Administrative Procedures for Subsidized Projects.

Contract costs

・ If AMED approves, a part of the Subsidized Project can be entrusted to a third party. Up to 10% of the direct costs may be charged to the contractor as the indirect costs. In accordance with the "Common Guidelines for the Execution of Indirect Costs of Competitive Funds," the maximum amount of indirect costs for contract to a university etc. is 30% of the direct costs. Please consult AMED in advance when considering overseas institutions or companies as contractors.

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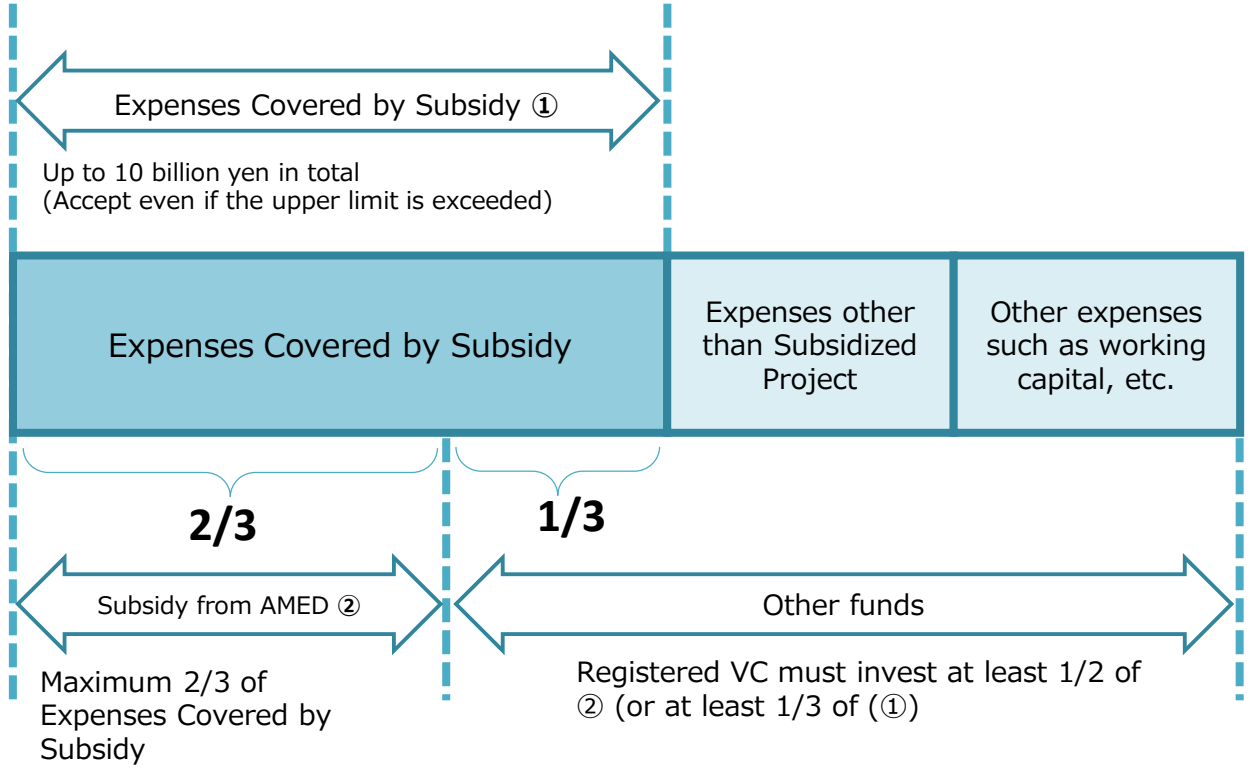
(Reference) Points to keep in mind for financing

- Expenses Covered by Subsidy are those costs for practical application development that are necessary to promote commercialization and directly required for practical application development and used exclusively for the Subsidized Project (general-purpose items and items used for other than the Subsidized Project are not eligible for subsidy), as shown on Slide 27.

- Therefore, the subsidy from AMED and the investment from the VC in the Subsidized Project may not be sufficient to cover all the necessary costs for the business development of the Business Operator. It is necessary to make an overall financing plan that takes into account the costs for general-purpose products and working capital etc., which are not allowed to be allocated for in the Subsidized Project.

- The figure on the right schematically illustrates the necessary costs. Please apply for this program after properly estimating necessary costs and making reasonable financing plan for the entire operation of the Subsidized Project.



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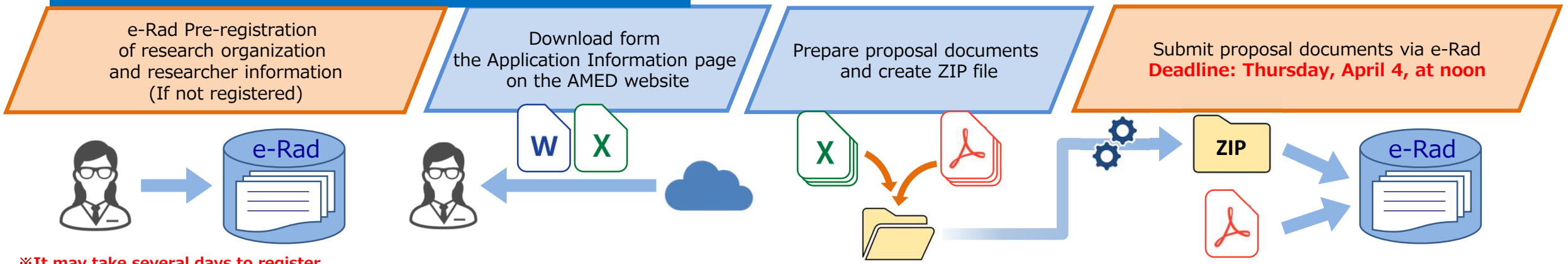
【Form1】Subsidized project proposal
"Proposal document check sheet"
"Submission document file name"

4-5 How to Submit Proposal Documents

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

Procedure for Preparation and Submission of Proposal Documents



※It may take several days to register.
Please allow at least two weeks for registration procedures. (see slide 31)

※PDF and ZIP files should be 15MB or less (per file)

4-6 e-Rad Input Notes

- Please enter only Stage 1 for the period and amount of expenses in e-Rad. Also, please enter only the AMED grant amount, not Expenses Covered by Subsidy.
- Upload the【Form 1】Subsidized Project Proposal to the "Application information file”.
- The e-Rad registration information of Principal Investigator will be used as the contact and document delivery address during the review process, so please be sure to update it with the latest information.
- In the "Research purpose" and "Research summary" sections of the basic information, please enter "Refer to "2. Abstract" in the summary of the Subsidized Project Proposal." No writing is required for this column.

4-7 Confirmation of Submission Status on e-Rad

- You can confirm the acceptance of proposal documents from the e-Rad "Manage Submitted Research Projects" screen.
- Proposal documents that are not in the "Funding Agency Processing" status by the end of the acceptance period will be considered invalid. If your application has been submitted by the researcher and approved by the administrative representative of the research institution by the end of the acceptance period, but has not reached these statuses, please contact the section in charge of this program (see Slide 53).

Application status	Display of application type [status]
①After application	The type of application [status] will be "**Research Institution Processing**". This indication means that approval by the research institution has not yet been completed. (The application to this program is not completed when the Principal Investigator submitted an application to the research institute via e-Rad. Please be sure to follow the approval procedures of your institution.) In addition, if you find it difficult to obtain institutional approval, please consult with the section in charge of this program ~~project~~ (see slide 51).
②After the completion of approval by research institute	The application type [Status] will be "**Funding Agency Processing**".
③ Accepted by the funding agency AMED	The application type [Status] will be "**Accepted**".

4-8 Notes on the Use of e-Rad

（1） Pre-registration of research institutions

- At the time of application, it is necessary that the “Business Operator" and “Contractor" have been registered with e-Rad by the time of application. Please refer to the e-Rad portal site for information on how to register your research institution.

- Please appoint one administrative representative for e-Rad at your research institution, download the application form for registration from the e-Rad portal site, and apply for registration according to the contents of “How to apply for registration of the research institution". It may take several days to register. Please allow at least two weeks for registration procedures.

（2） Pre-registration of Researcher Information

- The “Principal Investigator” who applies and the “Co-Investigator” who participates in the Subsidized Project must register their researcher information and obtain a login ID, password, and researcher number. Please note that if you belong to multiple institutions or if you change institutions, you may need to change the institution you belong to when you apply.

- This project is subject to security trade control requirements. Please check the necessary measures from "Notices from the system administrator" etc. on the e-Rad top page. We also ask that you check and respond in advance to any other system improvements or associated procedures.

4-9 Contact Details for Inquiries about How to Use e-Rad

- Inquiries on how to use e-Rad are accepted at the help desk on the e-Rad portal site.
- In addition to the portal site, please carefully check the "Frequently Asked Questions and Answers (FAQ) Page" before contacting the help desk or AMED.
- The help desk cannot respond to any inquiries regarding the content of the Application Guidelines, Review Status, or Acceptance/Rejection.

The help desk on e-Rad portal site

Before calling, please check the Frequently Asked Questions and Answers (FAQ) page.
https://www.e-rad.go.jp/contact.html

Then, please log in to e-Rad and contact us while you can check the operation manual.
Tel: 0570-057-060 (navidial), 03-6631-0622 (direct line) if unavailable

Hours: 9:00-18:00 (weekdays)
※Excluding Saturdays, Sundays, national holidays and Year-end and New Year's holidays (December 29 to January 3)

5. Review

5-1 Call for Proposals Period and Selection Schedule

Period of acceptance of proposal documents	**From Friday, February 16,2024 to Thursday, April 4,2024, at noon (JST) (Observe strictly)**
Document Review	From middle April 2024 to late April 2024 (tentative)
Hearing Review	Monday, May 13,2024, Thursday, May 16,2024, Saturday, May 18,2024 (tentative)
Notification of selection/rejection	Middle June 2024 (tentative)
Subsidized Project start date (Subsidy Grant Decision date)	Early August 2024 (tentative)

- Please note that all proposal documents will not be accepted after the deadline.
- In principle, we will contact Principal Investigator for which the hearing review is to be conducted by e-mail at least one week before the hearing review.
- In principle, the participants of the hearing review are Principal Investigator, the management of Business Operator, and the Registered VC (Lead Registered VC). If the business operator falls under the requirement J) of "3.1 Eligible Applicants", AMED may determine the necessity and request the presence of other relevant persons.The hearing review schedule cannot be changed.

※For other precautions, please refer to the Application Guidelines.

5-2 Evaluation Items and Perspectives

Evaluation Items	Perspectives
Ⅰ. Compatibility with the program's purpose	i -1. The proposal is to be compatible with the purpose and goals of the program. i -2. Satisfies each of the requirements i -3. The evidence of novelty, innovativeness, or originality, and the evidence reproducible. i -4. In the case of non-clinical testing, a final development candidate is obtained for clinical advancement. i -5. Patents for final development candidates have been filed in Japan and overseas. If it is not strategically filed, there is a valid reason. i -6. The business plan includes a plan for returning the results to Japan (funds, technology, employment, domestic investment, human resource development, etc.; especially the practical application of the results domestically).*In particular, if the applicant falls under the requirement J) of "3.1 Eligible Applicants ", the following points will also be considered when reviewing the return of results to Japan. ・The plan for returning the results to Japan (funds, technology, employment, domestic investment, human resource development, etc.) is concrete and has a high possibility of realization. ・The plan is to conduct research and development in Japan (or to collaborate with CDMOs and CROs in Japan, or domestic pharmaceutical companies, etc.). ・The business plan is to launch the pipeline in Japan within the Subsidized Project Period or after the Subsidized Project Period ends. If this is not the case, there is a rational reason why the product cannot be marketed domestically.

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5-2 Evaluation Items and Perspectives

Evaluation Items	Perspectives
Ⅱ. Superiority and effectiveness of technology, etc	ii-1. Competing domestic and overseas technologies and products have been surveyed, and superiority has been confirmed. ii-2. Evidence for quality, efficacy, and safety is established. The evidence is robust. ii-3. The technological issues for commercialization to be resolved are clarified, and concrete solutions for them are presented ii-4. Entry barriers are appropriately constructed, such as securing the necessary intellectual property. ii-5. Actions have been taken or are being considered for intellectual property that may require action or be an obstacle.

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5-2 Evaluation Items and Perspectives

Evaluation Items	Perspectives
Ⅲ. Development plans and goals	iii-1. A development roadmap for achieving the ultimate goal has been embodied. iii-2. It is clear that the procurement of development funds by this Subsidized Project can promote practical development. iii-3. The timing of stage gates and objectives in all Subsidized Project periods are set appropriately and concretely, and the plan for their realization is clear. iii-3-1. The regulatory plan is adequate and meets the requirements of regulatory authorities. iii-3-2. Principle verification of technology seeds has progressed to a certain extent, and the necessary preparations for starting clinical trials have been completed or are expected to be completed soon. iii-3-3. Exploratory content such as basic research is not included in the Subsidized Project Plan. iii-4. The total amount, breakdown, and expenditure plan of Expenses Covered by Subsidy, including contractors and subcontractors, are effective and efficient for implementing the Subsidized Project Plan. iii-5. An appropriate implementation system centered on the Business Operator and Principal Investigator has been established. iii-5-1. The division of roles is clear, and an appropriate collaboration system has been established. iii-5-2. The CMO/CDMO, CRO, etc. are in place to supplement the functions that the Business Operator lacks. iii-6. A plan that complies with laws and regulations regarding bioethics and safety measures. iii-7. Efforts of Principal Investigator are appropriate. There isn't unreasonable duplication/excessive concentration.

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5-2 Evaluation Items and Perspectives

Evaluation Items	Perspectives
Ⅳ. Business plan	iv-1. Business development after the completion of the Subsidized Project is properly considered (It needs to be planed for commercialization including overseas markets) iv-2. Market trends are analyzed, and commercialization strategies, including overseas, are specifically and appropriately considered. iv-2-1. The medical needs that the product meets are clear and have marketability. iv-2-2. The target market is clarified, and a strategy to acquire the market that satisfies profitability is specifically considered. iv-3. Concrete and appropriate intellectual property strategies and differentiation strategies are established, and competitive superiority is secured. iv-4. Have a specific funding plan up to commercialization iv-5. Possess the technical and management base (personnel, system, financial base, etc.) to work on the Subsidized Project
Ⅴ. Support plan by Registered VC	v-1. The investment from Registered VC in the first stage has already been implemented / is expected to be implemented with certainty, and the investment plan in the subsequent stages has been materialized v-2. Appropriate support system from Registered VC v-3. Appropriate support plans from Registered VC (Introduction of human resources for overseas expansion, support plans for overseas pharmaceutical approval, etc.)

6. Points to keep in mind after the adoption

6-1 Preparation for Subsidy Grant Decision

In the case of "(A) Pharmaceutical startup that have not received investment by the time of application" in 4.2 (5) of the Application Guidelines.

- The adoption of the proposal is conditional upon the investment of at least 1/3 of Expenses Covered by Subsidy described in the proposal being made by Registered VC within 30 days of the grant decision date, and a report on the investment being submitted. Other conditions may be attached on a case-by-case basis.

- After that, as soon as AMED confirms that the above conditions have been fulfilled, the Subsidy will be transferred to the applicant through the prescribed procedures. After the date of notification of the Grant Decision, costs can be recorded, and the Subsidized Project can begin. Failure to fulfill the above conditions will result in the cancellation of the Adoption.

- The amount of the investment transferred to the dedicated account (savings account (non-interest-bearing type)) for this Subsidized Project, which will be opened after the adoption of the project, will be deemed the Registered VC investment portion of Expenses Covered by Subsidy.

6-1 Preparation for Subsidy Grant Decision

In the case of "(B) Pharmaceutical startup that received investment by the time of application" in 4.2 (5) of the Application Guidelines

- The amount of capital contribution received during the retroactive period (see slide 12) and transferred to the dedicated account (savings account (non-interest-bearing type)) for this Subsidized Project to be opened after the adoption of the grant will be deemed Registered VC contribution for Expenses Covered by Subsidy.

- If there are no problems with conditions, etc., we will notify the Business Operator of the Grant Decision after the prescribed procedures. The project can be started after the date of notification of the Grant Decision (costs incurred prior to that date cannot be included). In addition, new conditions may be attached at the time of Subsidy Grant Decision.

6-2 Dedicated Account

- After the adoption, the Business Operator is required to open a dedicated account (savings account (non-interest-bearing type)) to be used only for this project in order to clearly distinguish and manage other funds and Expenses Covered by Subsidy.

- Please manage Expenses Covered by Subsidy, including the portion of Registered VC investment, in this account and do not mix other funds.

- In the case of either (A) a Pharmaceutical startup that has not received investment by the time of application and (B) a Pharmaceutical startup that received investment by the time of application, as described in Section 4.2 (5) of the Application Guidelines, the Business Operator must submit a copy of the bank book to confirm the payment into the account.

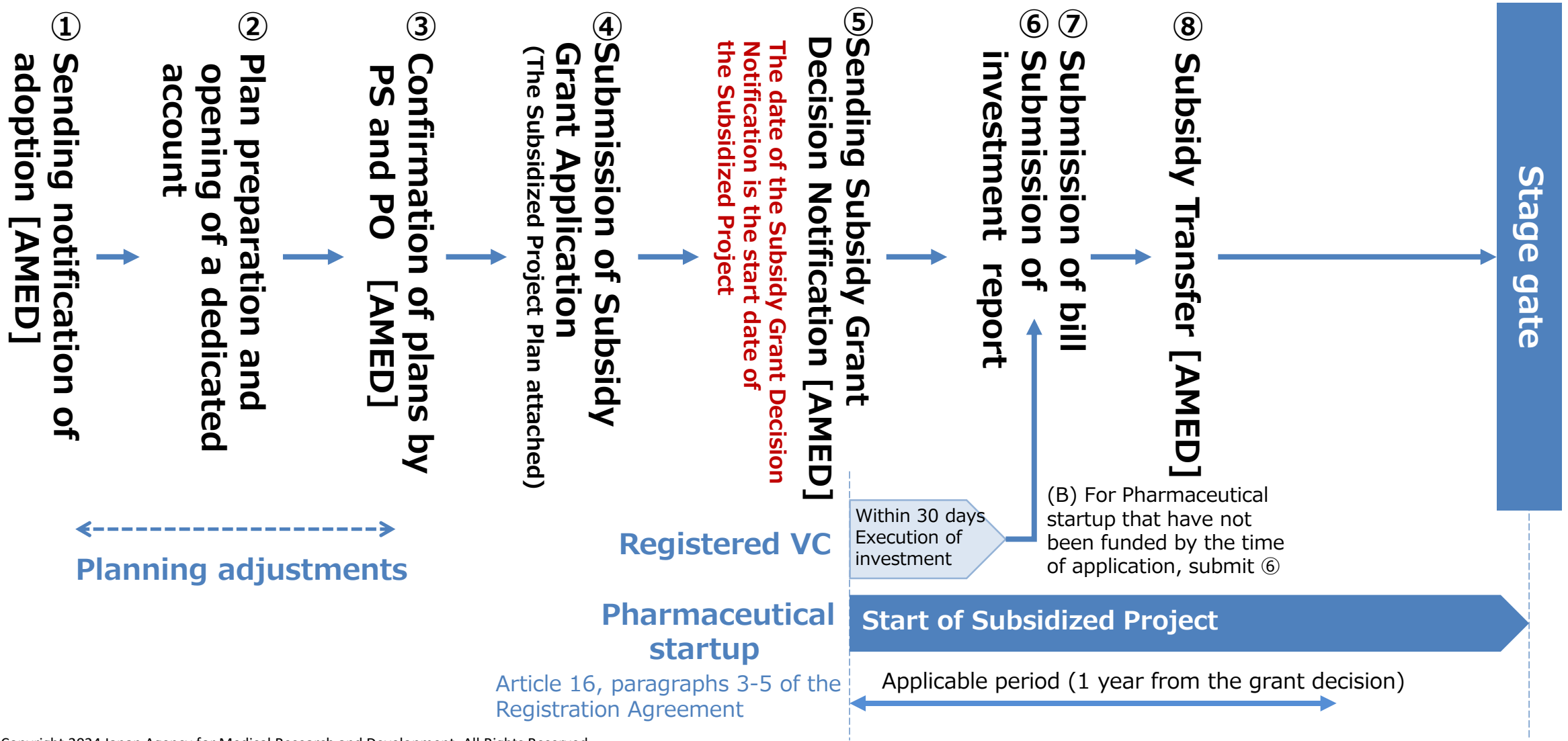
6-3 Conditions, etc., for the Subsidy Grant

- Upon receiving a Subsidy Grant Decision, Business Operator will receive a Subsidy from AMED and will be able to implement the adopted Subsidized Project.

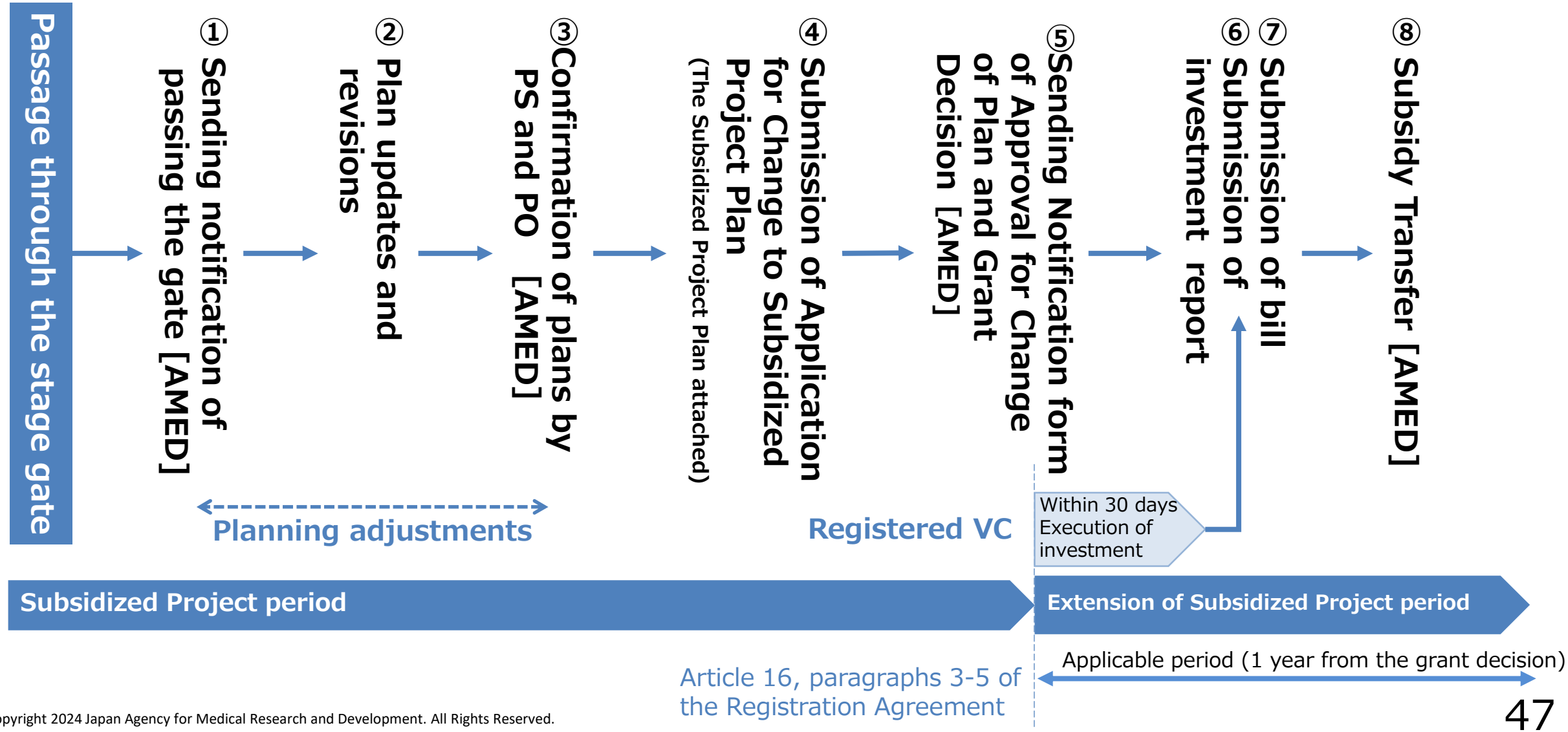
- The Subsidized Project period will be multiple years, and the Grant Decision will be made on a stage-by-stage basis, taking into consideration the progress of the Subsidized Project based on the results of the Stage-Gate Evaluation by the Project Evaluation Panel (see Slides 24-26). AMED will inform the Business Operator of the details of the procedures such as documents required for the Subsidy Grant, after the adoption.

- Please be aware that the Subsidy Grant Decision may be revoked if the conditions attached at the time of the adoption decision based on the opinions of the Project Evaluation Panel, PS, PO, etc. are not fulfilled.

(Reference) Flow after adoption



(Reference) Flow after Stage Gate Evaluation



6-4 Accounting Process

- Appropriate cost accounting is required for this program. To this end, the following inspections will be conducted.
  - As-needed inspection: Inspections to be conducted when AMED determines that is necessary.
  - Midterm inspection: Inspections are conducted on the results up to September of each fiscal year in principle.
  - Year-end inspection: Inspections to be conducted on the Subsidized Project Year-End Report.
  - Determination inspection : After the entire Subsidized Project period, conduct inspections on the Subsidized Project Accomplishments Reports and determine the Amount of the Expenses Covered by Subsidy.
- In order to determine the Expenses Covered by Subsidy for each fiscal year, we will inspect the execution status of the Subsidized Project and the accounting processing status by conducting an end-of-year inspection on the “Subsidized Project Year-End Report" that the Business Operator ~~you~~ submits each fiscal year.
- After the entire Subsidized Project period, we will determine the amount of Expenses Covered by Subsidy by conducting inspections after receiving the “Subsidized Project Accomplishments Report" that the Business Operator submits.

6-5 Project Progress Management

- PS, PO, etc. will manage the progress of all adopted projects.
- PS and PO will understand the progress status of projects overall and provide the necessary guidance and advice to ensure that projects run smoothly. Furthermore, Business Operator and Principal Investigator are obligated to cooperate with PS and PO. Based on the guidance and advice provided by PS and PO, Subsidized Project may be revised plans or terminated (including early completion of projects due to achievement of Subsidized Project goals) as deemed necessary.
- Based on the Innovative Research and Development Promotion Fund Subsidy (*kakushinteki kenkyukaihatsu suishin kikin hojokin*) Guidelines, in each fiscal year, AMED requests submission of “Subsidized Project Results Report” as an attachment to “Subsidized Project Year-End Report (Subsidized Project Accomplishments Report for the final year) ". In addition, AMED may request the submission of “Results Report " specific to this project every fiscal year and at the end of the Subsidized Project Period. In addition to the above, AMED may request Business Operator and Principal Investigator to submit the Progress Report as necessary.
- For the progress management, we hold debriefing sessions, conduct surveys (documents to record the progress of the Subsidized Project), hearing review (interviews and accounting confirmations for each individual project), and site visits (confirmation of actual development status at the Subsidized Project implementation site) and Stage Gate Evaluations, etc., to try to realize the exit strategy.

6-6 Return of Accomplishments, etc.

- The evaluation item I will examine whether the applicant plans to return the accomplishments of the project to Japan. In addition, it is the obligation of the applicant to make efforts to develop some kind of practical application in Japan in the future.

- For five years after the final fiscal year in which the Subsidized Project period ends, if it is recognized that the commercialization of the results of the implementation of the Subsidized Project (including assignment of intellectual property rights, the establishment of license or provide others with the results of implementation of the Subsidized Project) has generated revenue, a portion of the revenue will be required to be paid.

- Commercialization of the implementation results of the Subsidized Project means that the pipeline developed in the Subsidized Project is commercialized and sales profits are generated as pharmaceuticals, etc.

- In order to confirm whether or not there is revenue, a Subsidy Revenue Status Report (Form 19) must be submitted to AMED for five years after the final fiscal year in which the Subsidized Project period ends. If there is revenue, a Commercialization Performance Report must also be submitted.

- Please refer to Article 31 and 32 of the Innovative Research and Development Promotion Fund Subsidy (*kakushinteki kenkyukaihatsu suishin kikin hojokin*) Guidelines and Subsidy Revenue Status Report (Form 19) for details on the Commercialization Performance Report and the revenue payment.

(Reference) Amount of revenue payment

- The amount to be paid for each year will be determined based on the Subsidy Revenue Status Report (Form 19)
- The maximum amount of total payment for 5 years is the total amount granted as a Subsidy. The maximum amount of payment for each year is 1/5 of the total Subsidy amount.
- "Revenue" is the amount obtained by subtracting the necessary expenses from the income obtained from the product sales of the Subsidized Project results.

Amount of revenue for each year	Payment amount for each year
Less than 1/10 of total amount of Subsidy	None
More than 1/10 and 4/10 or less of total amount of Subsidy	2/3 of the amount obtained by deducting 1/10 of the total amount of Subsidy from the revenue
More than 4/10 of total amount of Subsidy	1/5 of total amount of Subsidy

For example, if the project is implemented with Expenses Covered by Subsidy of 3 billion yen (Subsidy of 2 billion yen).

Amount of revenue each year	Payment amount for each year
200 million yen or less	0
More than 200 million yen and less than 800 million yen	～400 million yen
Over 800 million yen	400 million yen

7. Contact for Inquiries

7 Contact Details

Inquiry content	Contact address
Subsidized Project, evaluation, how to fill in proposal documents, etc.	AMED Division of Technology Transfer Department of Intellectual Property and Technology Transfer E-mail: v-eco"AT"amed.go.jp ※Please make sure to send us your inquiry by e-mail. ※When making an inquiry, please make the subject of the e-mail "Inquiry about Strengthening Program for Pharmaceutical Startup Ecosystem /Call for proposals from Pharmaceutical Startups" and specify in the body of the e-mail the address (name of the corporation, name of the person in charge, telephone number, and e-mail address).
How to use e-Rad system	The Help desk on e-Rad portal site (Slide 34)

※Please change "AT" to "@" in the e-mail address. For other details, please refer to the Application Guideline.

- Please also refer to the "Frequently Asked Questions and Answers (FAQ)" posted on the Application Information page on the AMED website.
https://www.amed.go.jp/koubo/19/02/1902B_00047.html