

Cyclic Innovation for Clinical Empowerment (CiCLE)

**Japan Agency for Medical Research and Development (AMED),
National Research and Development Agency**



Cyclic Innovation for Clinical Empowerment (CiCLE)

Second supplementary budget
for FY2016:
55 billion yen

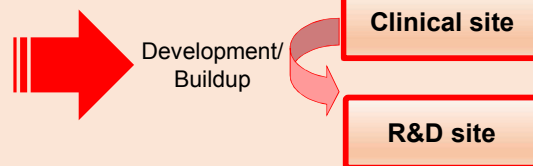
Aiming to

- Establish foundations for future-generation medical innovation
- Develop new drugs, medical devices, regenerative medicine products, medical technologies and others

CiCLE supports as follows;

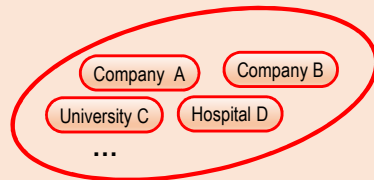
• Development and/or buildup of foundations for reverse translational research (rTR)

- Industry-academia-government collaboration (company demanded)
- Application of human clinical data
- Application of biobanks or advanced ICT
- Human resource development



• Development and/or buildup open innovated foundations in medical fields

- Collaboration of organization in non-competitive field
- Collaboration among companies (demanded), hospitals, universities and research institutes.
- Strategic development of drug discovery with the intellectual property consolidation.



• Practical implementation in medical fields

- Industry-academia-government collaboration (company demanded)
- Development of drugs, medical devices, regenerative medicine products, medical technologies and others

Merits

➤ Available to various projects as follows;

- For (1) **medical R&D** or (2) **improving the environment for medical R&D**.
- From the basic research to practical realization development. The intellectual property are attributed to the contracted founding company. (Japanese version of the US Bayh-Dole Act)
- For **clinical trials**.
- For company's in-house technology being conditional on industry-academia-government collaboration.

➤ Available to long-term and/or large-scale budget for fiscal years

- AMED and the representative organization make agreement for fiscal years contract.
- The project period extends **within 10 years** in principle.
- The total budget is **from 100 million to 10 billion yen** per project.
- The contracted funds for awarded projects **can be used freely a large injections or urgent requirements through each fiscal years**.

➤ AMED share a part of R&D risks.

- The representative organization bear the repayment fully when achieved, partially when not achieved.

➤ Interest-free and within 15 years repayment periods

- Repayment starts after the completion of project.
- **Interest-free** and **within 15 years**.
- Flexible repayment options.

Schemes Implemented

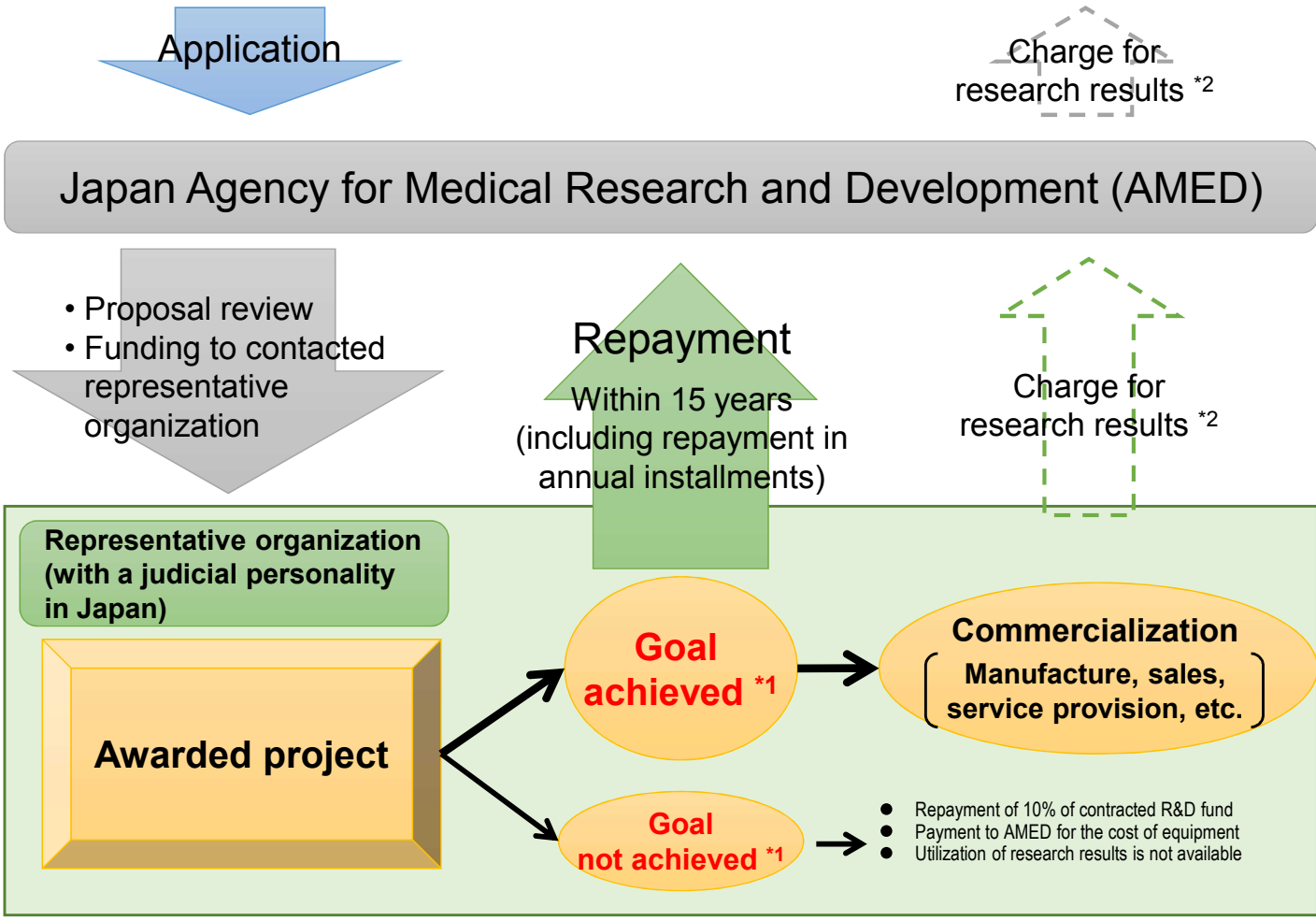


This program is classified into three types:

(A) Improving the environment for medical R&D type
 Improving the environment for development of collaborative foundation that contributes to R&D for the practical application of drugs, medical devices, regenerative medicine products, medical technologies and human resource training.

(B) R&D type
 R&D geared towards practical application of drugs, medical devices, regenerative medicine products, medical technologies with a mixed team of companies, universities and institutes based on industry-academia collaboration or industry-industry collaboration.

(C) Practical realization development type
 Practical realization development of drugs, medical devices, regenerative medicine products, medical technologies, implemented in industry-academia collaboration based on seeds (patents, etc.)



Within 10 years in principle
 100 million – 10 billion yen /project

(Includes general administrative expenses.
 100 million – 5 billion yen per project in principle for practical realization development programs)

***1 Whether the goal has been achieved or not is determined by the attainment degree of the minimum technical level/improvement level at the time of proposal submission.**

***2 The charge for research results is to be paid to AMED in accordance with sales (with some exceptions). If seed patents exist, AMED pay the charge for research results to patent holder.**

Contracted project of CiCLE

Improving the environment for medical R&D type

Project title	Representative company	Abstract
Establishment of a world-leading special peptide drug manufacturing CMO	PeptiDream Inc.	The primary goal of this project is to establish, by summer of 2019, facilities of a contract manufacturing organization (CMO) to enable the supply of non-standard/constrained peptides globally for both drug development and commercial sales purposes. PeptiDream, a biopharmaceutical company has a revolutionary next-generation hit finding platform, Shionogi Pharmaceutical Company, and Sekisui Chemical Company strategically founded a joint CMO company. The CMO widely incorporates innovative technologies found throughout Japan, and creates a stable and reliable supply chain by utilizing several patents held by PeptiDream. The ultimate mission is to contribute to mitigating the increasing burden of healthcare expense with the latest equipment, knowledge, and technology. The facility of approx. 6,000 m ² will be located in the city of Settsu in Osaka.

Contracted project of CiCLE

R&D type

Project title	Representative company	Abstract
Empirical research to platformize oral rice-based biopharmaceuticals	Astellas Pharma Inc.	MucoRice-CTB (CTB: cholera toxin B subunit) is a rice-based vaccine that can be stored at room temperature and orally administered, expressing CTB in rice as an antigen using transgenic techniques. In addition to not requiring strict temperature control and injection specific to biopharmaceuticals, if cultivation technology is established and efficient production becomes possible, the medical costs will be reduced and contribute to the international community by meet the needs of the developing countries. The purpose of this research is to demonstrate the possibility of practical application by implementing clinical trials, developing seed banks, and establishing a production system.
Industry-medico collaboration laboratory for dementia to create new promising drug targets	Eisai Co., Ltd.	Eisai-Keio Innovation laboratory for Dementia (EKID), an industry-academia collaboration site, established by Eisai. Co., Ltd. in collaboration with Keio University will maximize the benefits gained from comprehensive, collaborative basic and clinical research tied to technology/personnel exchanges and with the aim to discover new drug targets for the treatment of dementia. We can collect and analyze human samples with detailed clinical information while ethically maintaining patient rights and dignity, build hypotheses derived from multi-omics/multimodal analysis of this data by use of Artificial Intelligence (AI), then validate them with models reflecting dementia pathology.
Development of an innovative therapeutic drug for fibrodysplasia ossificans progressiva (FOP)	Daiichi Sankyo Co., Ltd.	The aim of this research and development program is to develop anti-ALK2 antibody as a therapeutic drug for FOP, a designated intractable disease in Japan, based on the findings in joint research between Daiichi Sankyo and Saitama Medical University. FOP is a progressive, serious disease in which bone tissue forms where it is not normally present, such as in muscles, tendons and other soft tissues. The estimated prevalence is 1case per 2 million population worldwide. The cause has been reported to be a mutation in the ALK2 gene, but an effective treatment has not been developed yet. In achieving the goal of this project, an innovative orphan drug is expected to be launched from Japan.

Contracted project of CiCLE

R&D type

Project title	Representative company	Abstract
Drug discovery research aiming at development of agents against infections with bacteria showing antimicrobial resistance (AMR)	Sumitomo Dainippon Pharma Co., Ltd.	This project's goal is to discover new drugs against antimicrobial resistant bacterial infections through a close cooperation between Sumitomo Dainippon and the Omura drug discovery group. Sumitomo Dainippon will dispatching several scientists to a new joint group which will conduct discovery research. Structural optimization of lead compounds, efficacy evaluation, pharmacokinetic, and safety studies in-vitro and in animals will be conducted to select clinical candidate compounds. Our objective is to successfully discover and develop a positive Phase III clinical candidate during the collaboration period.
Development of malaria vaccine and establishment of its commercial manufacturing process	Nobelpharma Co., Ltd.	The purpose of this project is to contribute to the global health by obtaining the regulatory approval of NPC-SE36 which is expected to prevent one of three major infectious diseases, a Plasmodium falciparum malaria vaccine in developing countries such as Africa. NPC-SE36, having protein antigen of SE36 and a recombinant of SERA 5 protein which rarely seen in the gene polymorphism, is a prophylactic vaccine for P. falciparum. We are aiming to obtain 2 indications, preventive vaccination for children in malarial areas, and travelers to the endemic areas from the developed countries. Safety of NPC-SE36 in human has already been confirmed, and the data showed a protective efficacy of over 70%.; therefore, planning and conducting the clinical studies and establishing the manufacturing for the commercial use.

Contracted project of CiCLE

Practical realization development type

Project title	Representative company	Abstract
Development of a novel vaccine technology based on nucleic acid encapsulated in nanoparticle for protection against viral disease	Daiichi Sankyo Co., Ltd.	Nucleic acid encapsulated in nanoparticle (NP-NA) is a novel modality discovered by Daiichi Sankyo, Co., Ltd. and the base technology as a platform applicable to innovative drugs for prophylactic and therapeutic vaccines. NP-NA efficiently delivers its own nucleic acids into the target cells such as antigen presenting cells, and strongly elicits antigen-specific immune responses through direct priming, by which intracellular de novo protein antigen presentation via major histocompatibility class I is facilitated. The induced antigen-specific cytotoxic T lymphocyte (CTL) responses then eliminate cancer cells and host cells latently, or through the process cells become chronically infected with intracellular pathogens. The goals of this project are to (1) further develop NP-NA technology, and to (2) explore safety and immunogenicity profiles of NP-NA vaccine in Ph-1 clinical trials through the collaboration with the National Institutes of Biomedical Innovation, Health and Nutrition.

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