Post-marketing database study version

MID-NET®
Medical Information Database Network

わかる! MID-NET®
(Introduction to MID-NET®)

MID-NET® is a database that is managed and operated by the Pharmaceuticals and Medical Devices Agency (PMDA) with the collaboration of cooperating hospitals (10 organizations) in order to contribute to the improvement of safety measure operations.

Participation by 10 organizations including over 20 hospitals across Japan

Tohoku University Hospital, The University of Tokyo Hospital, Chiba University Hospital, Kitasato Institute Group, NTT Hospital Group, Hamamatsu University Hospital, Tokushukai Group, Kagawa University Hospital, Kyushu University Hospital, Saga University Hospital

This document introduces the characteristics of MID-NET® and presents a clear and easy-to-understand explanation of how to assess the possibility of using MID-NET® to conduct a post-marketing DB study, starting from the stage before the application for utilization.

pmda 独立行政法人 医薬品医療機器総合機構
Pharmaceuticals and Medical Devices Agency

Access to PMDA (Tokyo)
Shin-kasumigaseki Bldg., 3-3-2 Kasumigaseki, Chiyoda-ku, Tokyo

MID-NET® onsite center (Shin-kasumigaseki Bldg. 20F)

The nearest exit of each station

● Subway Ginza Line	Toranomon Station	Exit No.11, Exit No.5
● Subway Hibiya Line / Chiyoda Line / Marunouchi Line	Kasumigaseki Station	Exit A13
● Subway Chiyoda Line / Marunouchi Line	Kokkai-gijidoumae Station	Exit No.3
● Subway Namboku Line / Ginza Line	Tameike-sanno Station	Exit No.8

Related websites
PMDA website: https://www.pmda.go.jp/
MID-NET® website: https://www.pmda.go.jp/safety/mid-net/0001.html

For inquiries, please contact
Office of Medical Informatics and Science, Pharmaceuticals and Medical Devices Agency
Shin-Kasumigaseki Building, 3-3-2 Kasumigaseki, Chiyoda-ku, Tokyo
Email : wakaru-midnet@pmda.go.jp
Phone: 03-3506-9473

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Pharmaceuticals and Medical Devices Agency

PMDA Website ▶

Process for assessing possibility of conducting a post-marketing database study

Possibility assessment is usually carried out starting before the application for utilization and during review

Internal possibility assessment

- Depending on the characteristics of the development product, consider the contents of additional safety specifications and the method of implementation
  - Drug use-results survey
  - Post-marketing database study
  - Post-marketing clinical study

Application for utilization

Application review by PMDA

Initial meeting → Preparation of review report (1) → Expert Discussion → Preparation of review report (2) → Committees/subcommittees → Approval

Possibility assessment

Study plan concretization

Good Point 1

What about the information I need to conduct a possibility assessment and concretize the study plan...
It's easy with MID-NET®!

- ☑ Reliable data!
- ☑ Multiple types of data are available, including results of lab tests!
- ☑ Abundant validated outcome definitions!
- ☑ Inquire or consult us at any time to check the number of surveyable datums!

Good Point 2

You can consult us before the application for utilization!!
Support for MID-NET® possibility assessment

- ☑ Get early support for multiple items by following the designated procedure for provision of detailed information!
- ☑ Feasibility and reliability consultations are also possible
- ☑ Plentiful support for companies with no experience of post-marketing DB study!

Please contact us early on!
We offer flexible support geared to your situation

Contact wakaru-midnet@pmda.go.jp

Flow of MID-NET® use

Confirm basic information about MID-NET® → Access/obtain detailed information about MID-NET® → Application for utilization → Conclude contract / Pay utilization fee → Create program (Data extraction) → Analysis → Report the end of the utilization

Before utilization | **At the time of utilization** | **At the end of utilization**
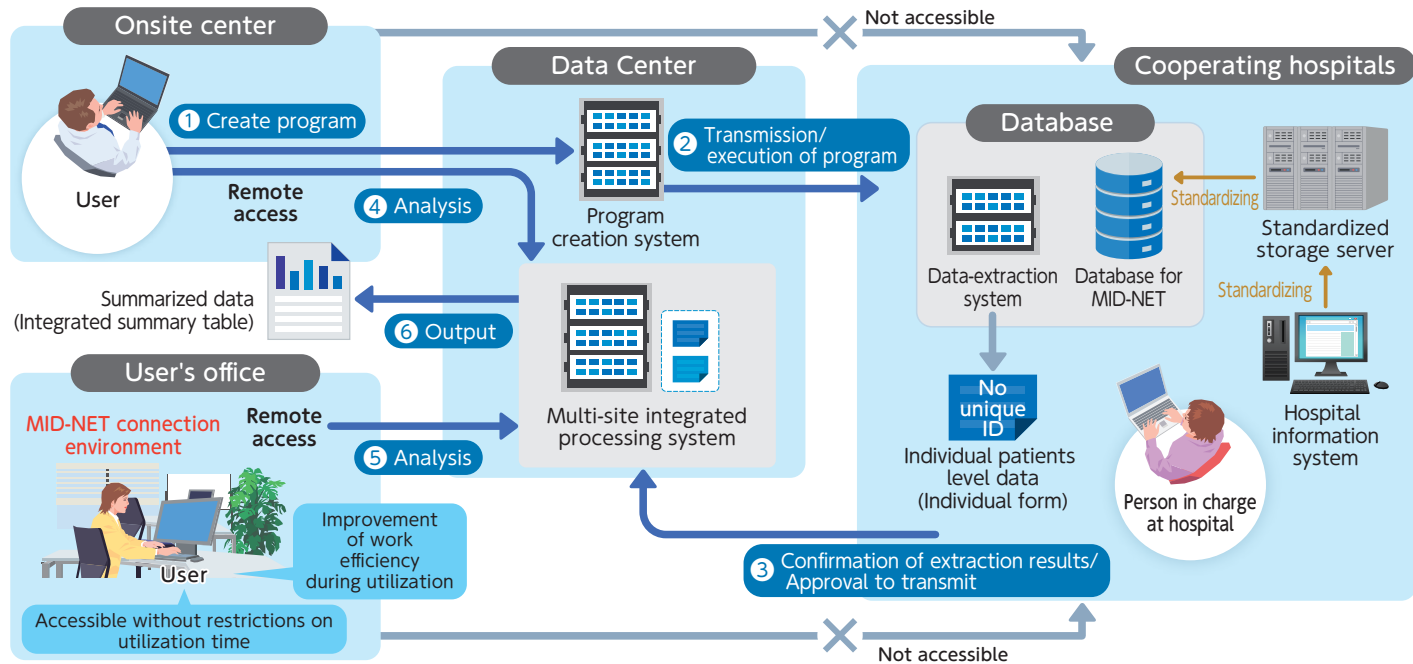
Good Point 3

User-friendly environment provided
Full customer service from before utilization to end of utilization!

- ☑ Easy access to the information you need!
- ☑ Simplification, shortening, and streamlining of various procedures!
- ☑ Enhanced predictability of data extraction timing!
- ☑ Remote access for analytic work!
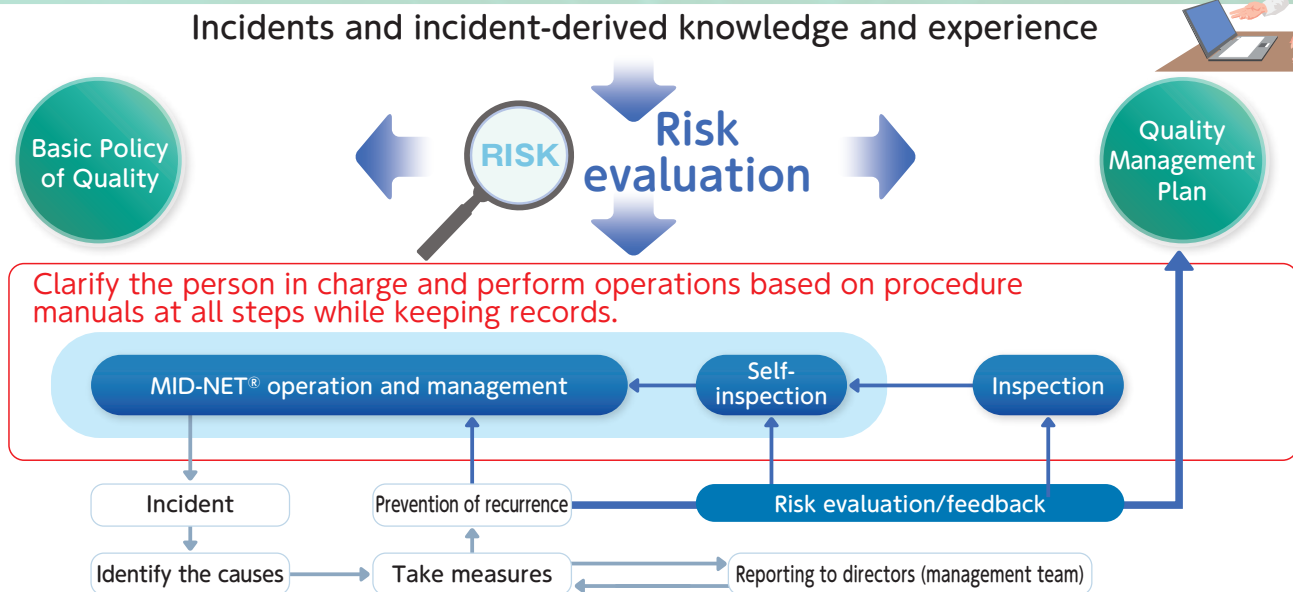- ☑ Clear action scheme for re-examination application!

Flow of analysis using MID-NET®

- Users can extract data meeting the intended purposes by (1) creating a program at the onsite center (specifying data extraction conditions that meet the intended purpose) and (2) sending it to the cooperating hospitals' data-extraction system (request for running program).
- The data extracted from cooperating hospitals (individual patients level data) is sent to the data center after (3) confirmation/approval by the person in charge at the hospital.
- Extracted data sent to the data center can be analyzed by users at (4) the onsite center or (5) from a remote access environment (MID-NET connection environment). (6)After confirmation by the administrator, the results of analysis can also be output.

Onsite center

User
❶ Create program
Remote access
❹ Analysis
Summarized data (Integrated summary table)
❻ Output

Data Center

❷ Transmission/execution of program
Program creation system
Multi-site integrated processing system

Cooperating hospitals

Database
Data-extraction system
Database for MID-NET
Standardizing
Standardized storage server
Standardizing
No unique ID
Individual patients level data (Individual form)
Person in charge at hospital
Hospital information system

Not accessible ✕

User's office

MID-NET connection environment
Remote access
❺ Analysis
User
Accessible without restrictions on utilization time
Improvement of work efficiency during utilization

❸ Confirmation of extraction results/Approval to transmit

Not accessible ✕

We manage and operate the database in compliance with the GPSP*
*Ministerial Ordinance on Good Post-marketing Study Practice for Drugs

Incidents and incident-derived knowledge and experience

Basic Policy of Quality
RISK
Risk evaluation
Quality Management Plan

Clarify the person in charge and perform operations based on procedure manuals at all steps while keeping records.

MID-NET® operation and management ← Self-inspection ← Inspection
Incident → Identify the causes → Take measures → Prevention of recurrence
Risk evaluation/feedback → Reporting to directors (management team)

To maintain the quality of data, we are continually implementing activities according to the quality management plan.
We provide high-quality data by confirming consistency with original data, etc.
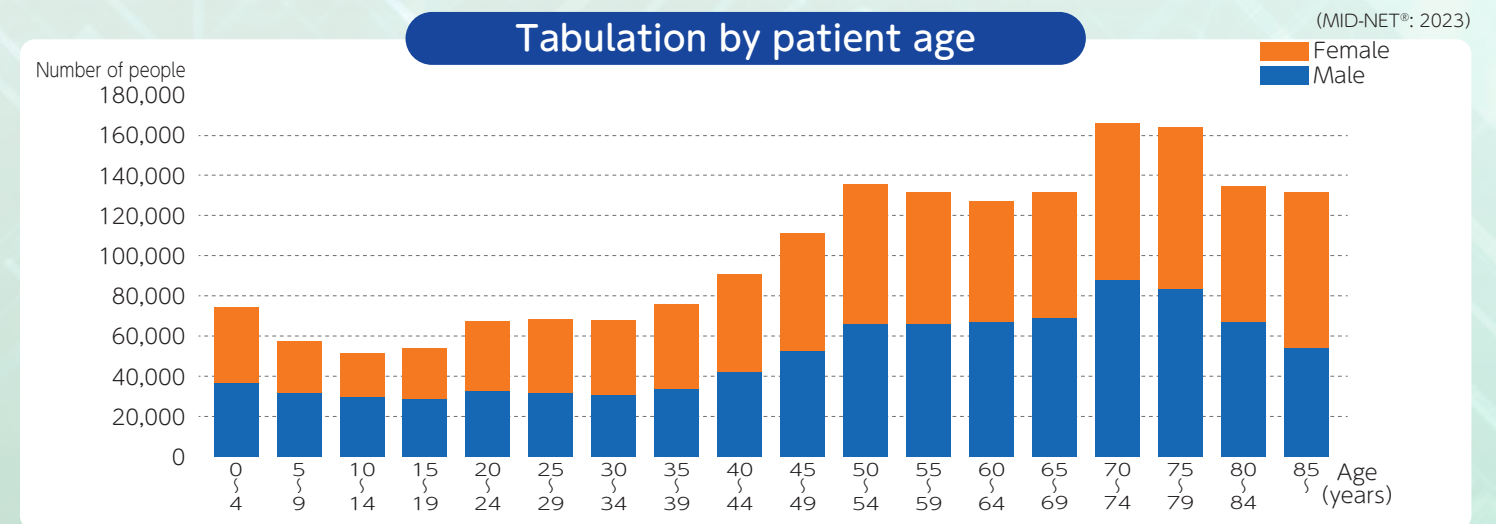
Reference articles, etc. to understand MID-NET®

- Yamaguchi, M. et al. Pharmacoepidemiol Drug Saf.2019 ;28 (10) :1395-1404. DOI: 10.1002/pds.4879
- Sawada, S. et al. Ther Innov Regul Sci. 2021 ;55(3):539-544. DOI: 10.1007/s43441-020-00247-8
- Kajiyama, K. et al. Clin Pharmacol Ther. 2021 ;110(2):473-479. DOI: 10.1002/cpt.2263
- Hasegawa, T. et al. Ther Innov Reg Sci. 2022; 56:625-31. DOI: 10.1007/s43441-022-00400-5
- Kinoshita, Y. et al. Clin Pharmacol Ther. 2023. online ahead of print. DOI: 10.1002/cpt.2850

For related literature, specific examples, etc., please visit the MID-NET® website.

Information that can be handled on MID-NET®

Possible to utilize multiple types of data

● MID-NET®: data on approximately 8 million patients (as of December 2023, including 10 additional hospitals in Tokushukai Group)

Tabulation by patient age

(MID-NET®: 2023)

■ Female
■ Male

Number of people

180,000
160,000
140,000
120,000
100,000
80,000
60,000
40,000
20,000
0

Age (years): 0~4, 5~9, 10~14, 15~19, 20~24, 25~29, 30~34, 35~39, 40~44, 45~49, 50~54, 55~59, 60~64, 65~69, 70~74, 75~79, 80~84, 85~

Feel free to ask us about the number of surveyable datums!

Additional assessments are possible if you consult us early on!

Database for MID-NET

Summarized electronic medical records/claims/DPC data

HIS (Hospital Information System) data
- Patient Information
- Information on hospital visits, etc. (outpatient, admission, discharge)
- Disease/injury information
- Prescription information
- Injection information
- Radiology information
- Bacteriological test information
- Lab test information
- Physiological test information

Claims data (medical claim files)
- Claims disease/injury information
- Claims surgery information
- Claims specific equipment information
- Claims medical management fee information
- Claims medical practice information
- Claims drug information

DPC data (Diagnosis Procedure Combination)
- DPC patient information
- DPC admission/discharge information
- DPC disease/injury information
- DPC medical practice information

Lab test items

Results of approximately 360* lab test items are available!

Examples of available results data
- Red blood cell count
- White blood cell count
- Hemoglobin
- Hematocrit
- Platelet count
- PT activity (%)
- INR value
- Albumin
- Creatine kinase
- GOT
- GPT
- LDH
- Alkaline phosphatase
- g-GTP
- Creatinine
- Urea nitrogen
- Glucose
- Glycosylated haemoglobin A1c
- Triglycerides
- Cholesterol
- HDL cholesterol
- LDL cholesterol
- Sodium
- Potassium
- Chloride
- Calcium
- Total bilirubin
- Direct bilirubin

*As of December 2023

A wealth of validated outcome definitions

- Malignancies
- Interstitial pneumonia
- Acute coronary syndrome
- Thromboembolism (acute pulmonary thromboembolism)
- Ketoacidosis
- Hypothyroidism
- Neutrophil count decreased/neutropenia
- Gastrointestinal perforation
- Stroke (cerebral infarction, erebral haemorrhage)
- Pancreatitis acute
- Intestinal obstruction
- Artery dissection
- Heart failure

NCDA data also available

● NCDA[※1] : Approximately 4.45 million patients (as of September 2023)

※1 Database summarizing medical information from NHO network hospitals operated by National Hospital Organization

Full customer service

Easy access to the information you need!

- **Information and documents required at each stage can be obtained from MID-NET® website**
- **Complete range of Materials for GPSP inspection that can be used from database selection to compliance review**
- ☑ Our website was completely updated in November 2023! Improved environment for easier access
- ☑ When you select the database to use, a detailed explanation of necessary information, tailored to DB study management tool, etc., can be provided via web conference system.

Simplification, shortening, and streamlining of various procedures!
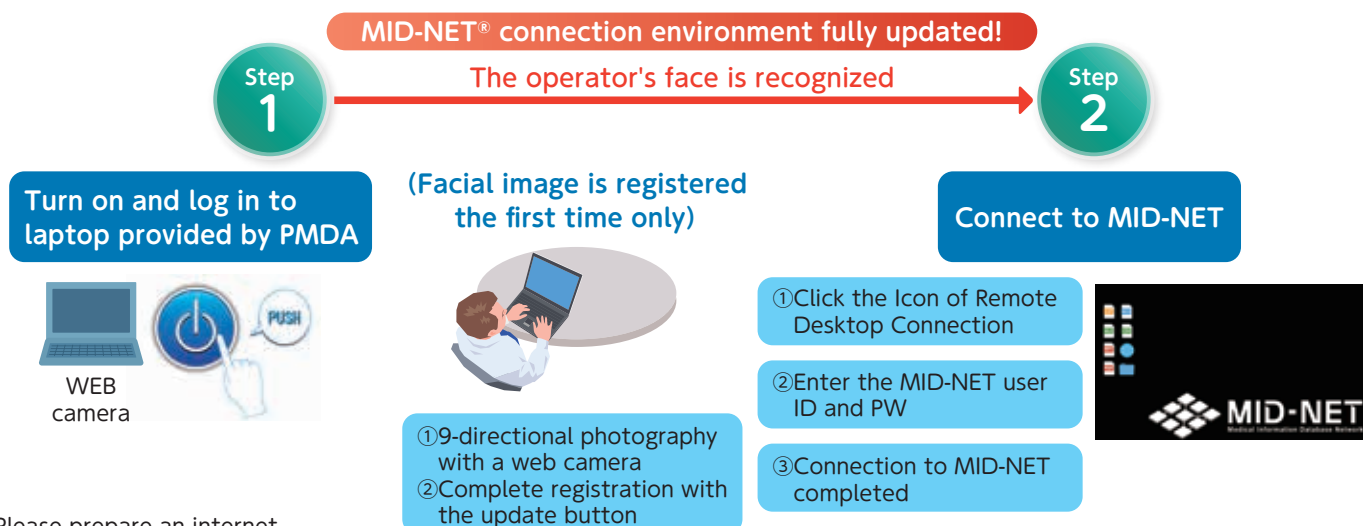
- **As-needed revision of notifications and guidelines to make them easier to understand**
- **Get training on MID-NET® utilization through e-learning**
  Please see MID-NET® website for how to implement MID-NET training, etc.
- **Planning to start accepting online appointments for onsite center** (around April 2024)

Enhanced predictability of data extraction timing!

- **Flexible adjustment to changing conditions**
- ☑ We coordinate with individual situations so that the various procedures can be carried out smoothly
- ☑ Even before you apply for utilization, we anticipate the timing of the start of utilization when coordinating your schedule to enhance predictability

Remote access for analytic work!

- **Easy access through MID-NET® connection environment at any time from your office**

MID-NET® connection environment fully updated!

Step 1 → The operator's face is recognized → Step 2

Connect to MID-NET

Turn on and log in to laptop provided by PMDA

WEB camera

(Facial image is registered the first time only)

①9-directional photography with a web camera
②Complete registration with the update button

①Click the Icon of Remote Desktop Connection
②Enter the MID-NET user ID and PW
③Connection to MID-NET completed

Please prepare an internet connection environment.

Safety management measures will change as the system evolves but cannot be fully implemented by system functions alone. We will continue to establish operating rules. Please check the current rules.
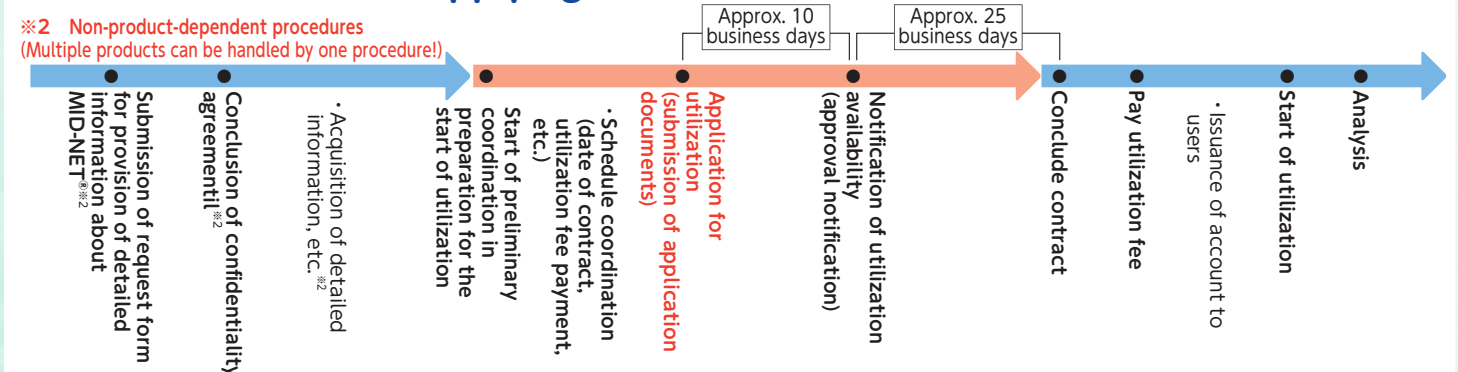
Clear action scheme for re-examination application!

- We also offer support for submission of necessary data at the time of application for re-examination by the prescribed procedure (no additional fee)
  Utilization history: Used by 9 companies for 12 products (**Re-examination completed for 2 companies of 2 products**) (as of December 2023)
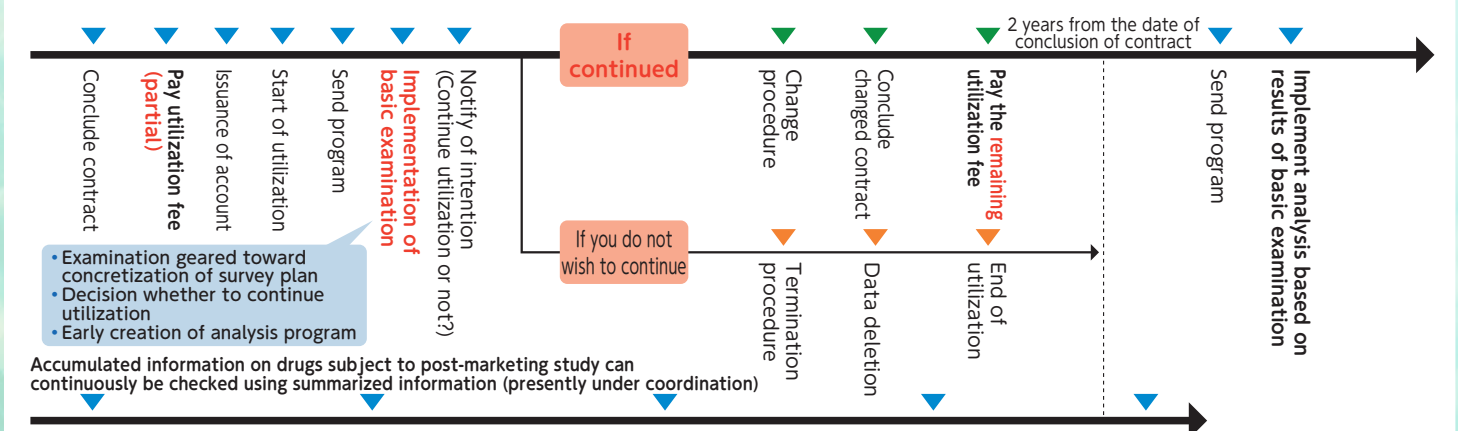
For efficient utilization

- **Please see below for minimum time requirements for procedures from application for utilization to conclusion of contract.**
- **Please apply for utilization about 35 business days before the date of utilization fee payment and conclusion of contract.**
- **If you take the start time for utilization into consideration when determining the desired contract conclusion date, it will be easier to coordinate the schedule leading up to utilization.**

Flow before and after applying for utilization

※2 Non-product-dependent procedures (Multiple products can be handled by one procedure!)

Approx. 10 business days | Approx. 25 business days

- Submission of request form for provision of detailed information about MID-NET※2
- Conclusion of confidentiality agreement※2
- Acquisition of detailed information, etc.※2
- Start of preliminary coordination in preparation for the start of utilization
- Schedule coordination (date of contract, utilization fee payment, etc.)
- Application for utilization (submission of application documents)
- Notification of utilization availability (approval notification)
- Conclude contract
- Pay utilization fee
- Issuance of account to users
- Start of utilization
- Analysis

Key points of the basic examination

- **At the initial stage of utilization, you can check whether the database contains sufficient information to enable you to develop a concrete survey plan. This check is called the basic examination.**
- **The basic examination is available if you make a partial payment of the utilization fee.**
- **You can decide whether or not to continue based on the results of the basic examination. If you decide to continue utilizing MID-NET®, you will then complete the necessary change procedures and pay the remaining utilization fee by the due date.**

2 years from the date of conclusion of contract

- Conclude contract
- **Pay utilization fee (partial)**
- Issuance of account
- Start of utilization
- Send program
- **Implementation of basic examination**
- Notify of intention (Continue utilization or not?)

If continued:
- Change procedure
- Conclude changed contract
- **Pay the remaining utilization fee**
- End of utilization
- Send program
- Implement analysis based on results of basic examination

If you do not wish to continue:
- Termination procedure
- Data deletion

- Examination geared toward concretization of survey plan
- Decision whether to continue utilization
- Early creation of analysis program

Accumulated information on drugs subject to post-marketing study can continuously be checked using summarized information (presently under coordination)

Utilization categories and utilization fees

	Amount of utilization fee (per utilization)※3		
	If no basic examination is performed (Full payment)	If basic examination is performed (Partial payment of utilization fee)	If utilization is continued after implementation of basic examination (Remaining amount)
Post-marketing study (assuming utilization of individual patients level data)	42,123,000 JPY	5,410,000 JPY	36,713,000 JPY
Investigations other than post-marketing studies (when individual patients level data is utilized※4)	21,061,500 JPY	5,410,000 JPY	15,651,500 JPY

※3 If NCDA data is utilized, a separate utilization fee will be added.
※4 There is also a category for no utilization of individual patients level data (utilization of summary table)

You pay the same total utilization fee whether you continue utilization after performing basic examination or utilize without performing basic examination!
If you are utilizing MID-NET® for the first time, performing a basic examination is definitely recommended!