PhUSE Single Day Event

Inter-organizational SEND Model in Japan: CRO-Sponsor collaboration for SEND

Shin-ichi Horikawa

Ina Research Inc.

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Agenda

1. Matters concerning SEND
2. PhUSE Inter-organizational SEND Model
3. Inter-organizational SEND Model in Japan
4. Summary

Matters concerning SEND

1. Who is responsible for SEND?

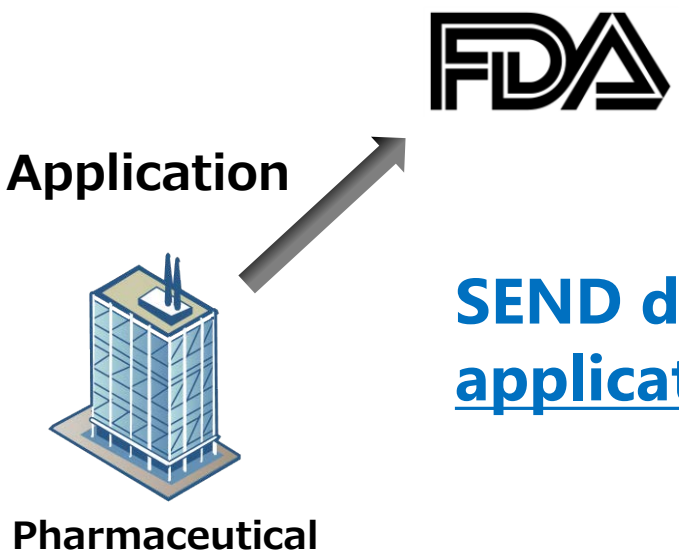
2. Purposes and expectations for SEND

3. Methods of SEND data preparation

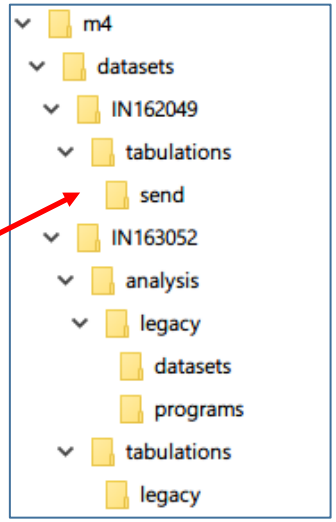
1. Who is responsible for SEND?

SEND is…

An Applicant (pharmaceutical)-Centered Project



SEND data is part of application materials



1. Who is responsible for SEND?

SEND is not just for pharmaceuticals.

From a CRO's perspective

Pharmaceutical

Provision of SEND data service

CRO

- Assistance to Sponsors in application preparation
  - ⇒ Providing SEND data for CRO studies
  - ⇒ Providing SEND data for non-CRO studies

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- Promotion of SEND by collaboration with CROs
  - ⇒ Providing more extensive SEND services
  - ⇒ Offering several patterns of SEND preparation based on best practices

1. Who is responsible for SEND?

SEND is not just for pharmaceuticals.

From an IT vendor's perspective

・Develop efficient SEND conversion environments

⇒ Provision of a SEND data conversion systems
System updates for the system users
Sales of SEND data conversion systems

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・Intense competition between IT vendors encourages the improvement of IT infrastructure

⇒ Achieve seamless operability between systems

⇒ Expansion of the automation processes (electronic formatted data)

1. Who is responsible for SEND?

SEND is not just for the pharmaceuticals.

From a solution provider's perspective

- Assistance for SEND data preparation (FDA submission) in all aspects

⇒ Consultation for SEND data conversion

⇒ Providing assistance for FDA submission as well as system selling

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Keep suggesting the essence of SEND as a SEND preacher

⇒ Assist SEND related persons to select an optimal approach

⇒ Assist establishment of SEND structure for overall optimization

2. Purposes and expectations for SEND

What's expected from applicants (pharmaceuticals)

- To generate high-quality SEND datasets that will not be refused by the FDA
- To obtain up-to-date information on FDA, CDISC, PhUSE
- To minimize the workload of applicants (pharmaceuticals)
- To generate flexible SEND data (adaptable to in-house specifications)

3. Methods of SEND data preparation

Applicant (pharmaceutical)-centered SEND data preparation

- **In-house studies**:

  Option A: Use own SEND converter
  Option B: Outsource to SEND conversion service providers or primary CROs

- **CRO studies**:

  Option A: Use SEND converter owned by the sponsor
  Option B: CRO generates SEND data
  Option C: Outsource to SEND conversion service providers or primary CROs

PhUSE Inter-organizational SEND Model

1. I-SEND for PhUSE
2. I-SEND Scenario 1, 2 and 3
3. PhUSE's perspective
4. Responses to SEND in non-US countries

1. I-SEND for PhUSE

I-SEND developed 3 use-case scenarios incorporating data and process flows identified through collaborative sessions among representatives from CROs, Sponsors and Informatics/Data Management Vendors.

Scenario 1:
CRO Study with SEND Dataset Fully Assembled by CRO

Scenario 2:
A CRO generating SEND datasets for a study with the Sponsor or its designee providing PK/TK data

Scenario 3:
CRO Study with SEND Dataset Fully Assembled by Sponsor

2. I-SEND Scenario 1

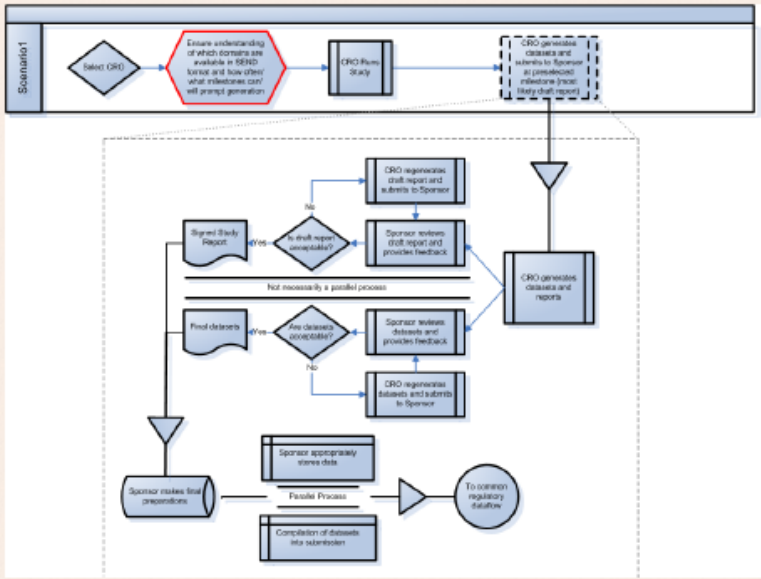
CRO Study with SEND Dataset Fully Assembled by CRO

Scenario 1: CRO Study with SEND Dataset Fully Assembled by CRO

➢A clear understanding of deliverables, limitations, milestones, and timing should be established before study initiation.

➢Important discoveries:

- Challenges with interim data files, with incomplete data or some domains missing
- Study setup information is important to define ahead of time (e.g., TS and DM)
- Previously, a step for generation of final data sets after review was included, which does not occur in reality, as the reviewed datasets will be used
- In reality, the draft report and SEND data set flows do not always happen in parallel

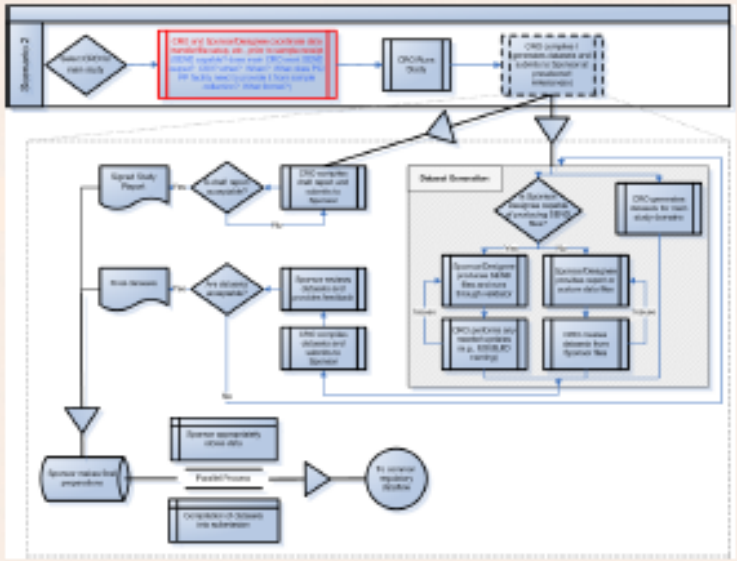


2. I-SEND Scenario 2

A CRO generating SEND datasets for a study with the Sponsor or its designee providing PK/TK data

Scenario 2: A CRO generating SEND datasets for a study with the Sponsor or its designee providing PK/TK data

- In addition to topics identified under Scenario 1, this scenario introduces further considerations, ideally discussed prior to study initiation.
- Important discoveries:
  - Third party often used for PK/TK, with files (non-SEND) passed to CRO for SEND PC/PP generation
  - *Significant* effort in generation of datasets from third party files

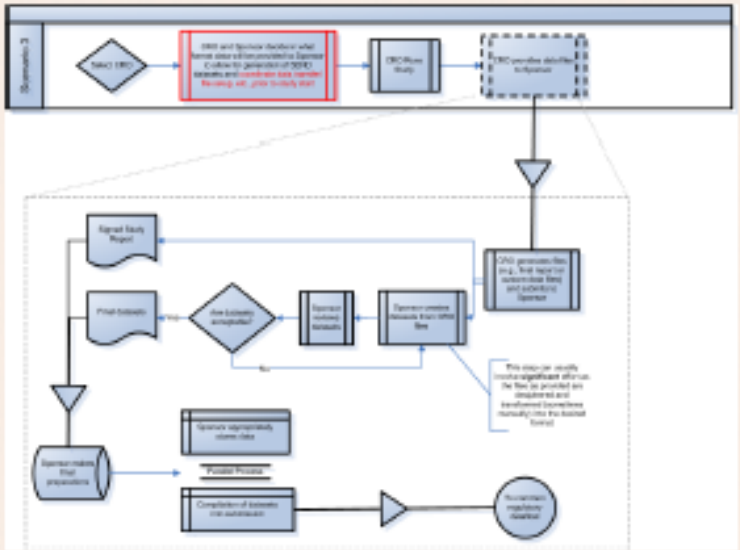


2. I-SEND Scenario 3

CRO Study with SEND Dataset Fully Assembled by Sponsor

Scenario 3: CRO Study with SEND Dataset Fully Assembled by Sponsor

- This scenario builds on topics identified under Scenario 1 with additional considerations that should be discussed prior to study initiation.
- Important discoveries:
  - Most common occurrence is for finalized studies that the Sponsor wants to warehouse
  - Involves *significant* effort and QC working with final PDF or OCR'd reports and legacy data capture systems
  - No review loops with CRO in that the final data files are used
  - Not generally for regulatory submission
  - Some domains and variables that support regulatory submissions may be omitted



3. PhUSE's perspective

- Approaches to SEND implementation vary across organizations.
- Adoption of the use of SEND varies across primary CROs.
- Early SEND file delivery is a challenge for CROs.
- SEND file delivery is less likely to occur in parallel with draft report authoring and delivery.
- Creating SEND files from legacy data (i.e. data from previously completed studies) presents a significant resource challenge.

4. Responses to SEND in non-US countries

"Responses to the Standard for Exchange of Nonclinical Data （SEND） in non-US countries"

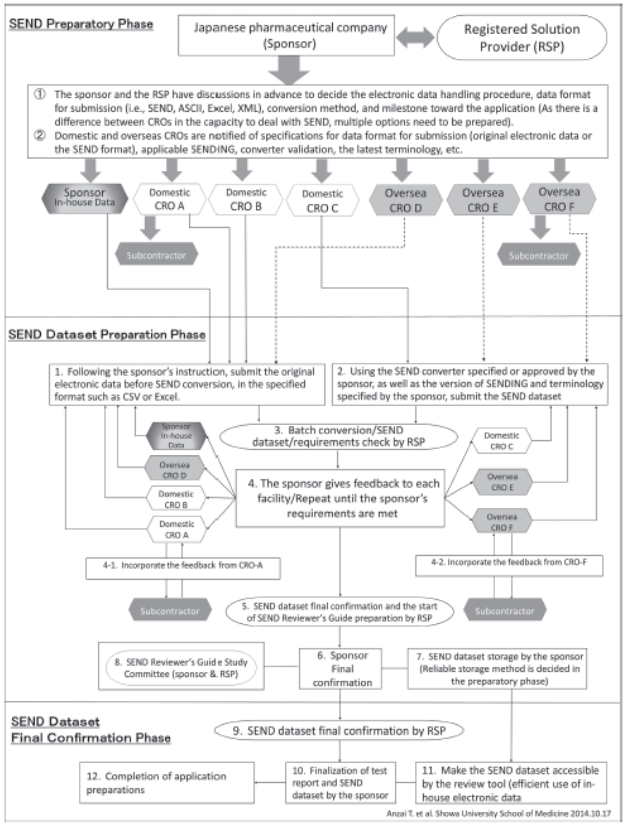
J Toxicol Pathol. 2015 Apr;28(2):57-64. doi: Anzai T[1], Kaminishi M[1], Sato K[1], Kaufman L[2], Iwata H[3], Nakae D[4].
1) Showa University School of Medicine, 2) PDS Life Sciences Ltd. 3) LunaPath LLC., 4) Faculty of Applied Biosciences, Tokyo University of Agriculture

Trend in US (PhUSE I-SEND):

- Region-based model in which US pharmaceuticals apply to the US authority using US CROs.

Trend in non-US countries:

- Use more than 1 Japan-based CRO as well as CROs in multiple countries



Inter-organizational SEND Model in Japan

1. Framework for SEND at Ina Research Inc.

2. Workflow for SEND at Ina Research Inc.

3. Future challenges for INA in each process

1. Framework for SEND at Ina Research Inc. (INA)

Collaboration with PDS

Pharmaceuticals

- Ina Research Inc.
  IT manager, data manager,
  toxicologist (Study Director), pathologists,
  study report writing team, translation team

- PDS
  IT manager, toxicologists, pathologists

SEND Partnership

Ina Research Inc.

pds Intuitive Software Insightful Solutions

1. Framework for SEND at INA

Points considered at INA for establishment of SEND framework

1. Using minimum resources required

⇒ Minimize investment in business activities other than entrusted study implementation
⇒ Minimize disruptions at introduction of SEND (IT-related matters)

2. Selection criteria for outsourcing companies

⇒ Ability to collect latest information (information management ability)
⇒ Extensive experience and practical accomplishment in SEND
⇒ GLP-conscious, highly-reliable processes

2. SEND workflow at INA

Distinct responsibilities for SEND implementation

1) Sponsor

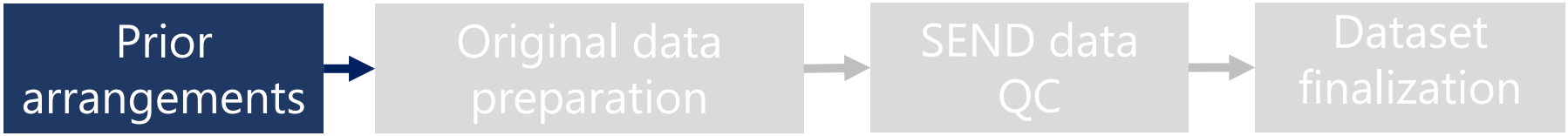
2) Ina Research Inc.

3) Test sites

4) PDS

2. SEND workflow at INA

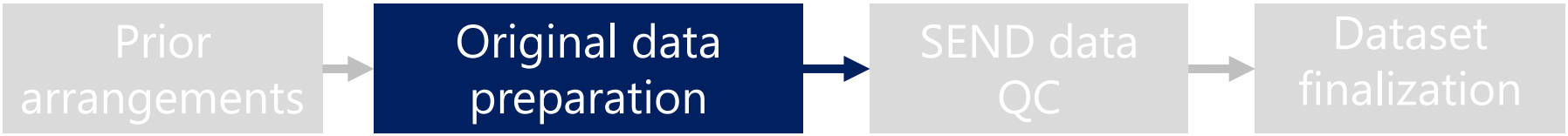
Specific work descriptions at INA



- Clarification of the contract terms and conditions, roles and deliverables
- Prior arrangements start at preparation of a study protocol
- For multi-site studies, prior discussions with the test site(s) to determine data handling procedures

2. SEND workflow at INA

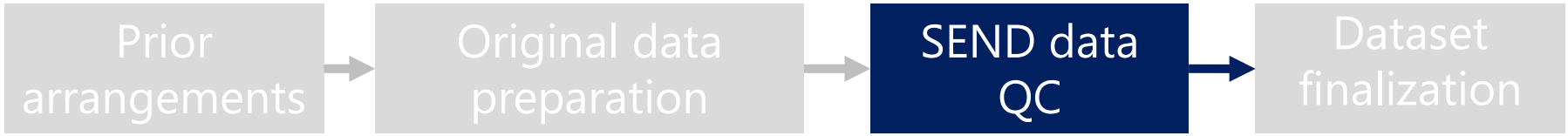
Specific work descriptions at INA



- Preparation of electronic data (before conversion) in standardized formats
  - ※ Utilize CSV export function for safety study data in LIMS
  - ※ Manually create electronic data files for study designs, etc. based on the study protocol/final report
- Obtain electronic data in a specified format from the test sites
- It is important to retain authenticity of the original data that will be the data source for SEND conversion

2. SEND workflow at INA

Specific work descriptions at INA

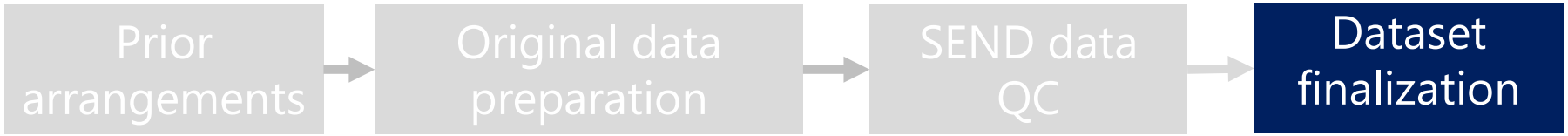


SEND data review (QC) at INA

- SEND datasets
- Define.xml files
- Study Data Reviewer's Guide

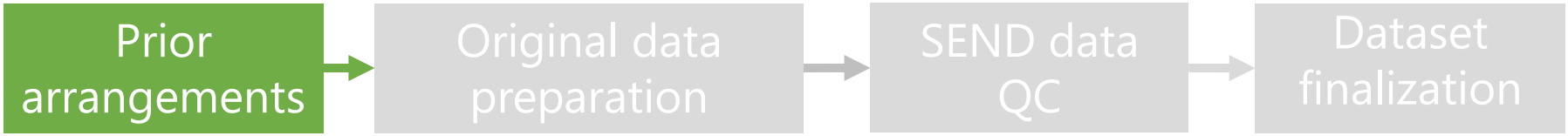
2. SEND workflow at INA

Specific work descriptions at INA



- Finalization of SEND data
- Preparation of the SEND report
- FDA trial submission following SEND data finalization

3. Future challenges for INA in each process



- To develop standard deliverables from INA
- To better understand a Sponsor's requests and adapt SEND data exactly to their needs
- To re-consider the data handling procedures between INA and test sites (currently, test site(s) provide the electronic data in a specified format)

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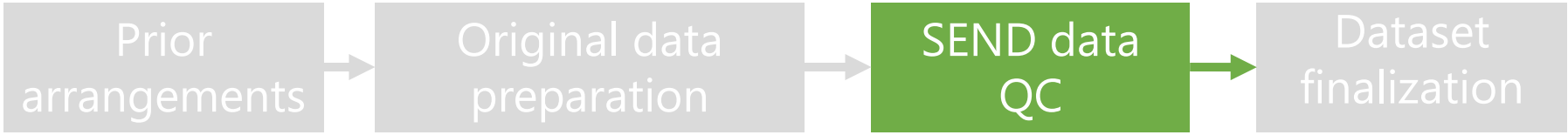
Receiving SEND dataset created by the test sites is under consideration

3. Future challenges for INA in each process

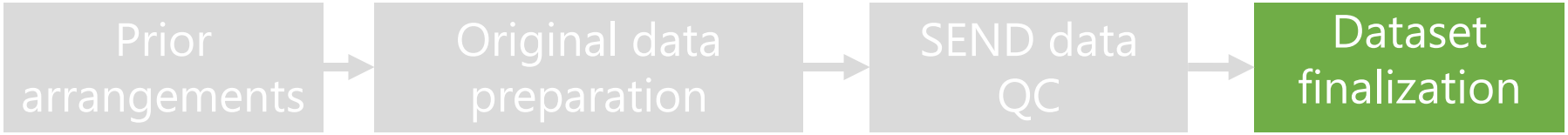
- To prepare original electronic data in standardized format for all studies
- To explorer the possibility of automatic generation of original electronic data
- To find more efficient QC procedures for original electronic data
- To establish standard procedures for the generation of original electronic data (improvement of check lists)

3. Future challenges for INA in each process



- Implementation of efficient review (QC) by using appropriate review tools.
- To establish standard procedures for data review (improvement of check lists)
- To have flexibility in response to Sponsor's requests for Study Data Reviewer's Guide
  → Learn practical know-how on preparation of SDRG to have ability to provide it from INA.

3. Future challenges for INA in each process



- To establish archiving strategies (area, procedures) for SEND data and related records/documents
- To standardize the finalization procedures (timing, conditions)
- Operational improvement toward prompt finalization

Summary

1. Key points for SEND implementation

2. Key points for I-SEND

3. Preparation for regulatory submission

1. Key points for SEND implementation

From INA's perspective:

- Information-gathering ability (information management ability)
- Selection of business partners (highly-reliable procedures)
- Simulation practice (SEND pilot trial)

From a CRO's perspective:

- Flexible responses for SEND
  (flexibility in the company, responses to clients' requests)
- To establish highly-reliable procedures

2. Key points for Inter-organizational SEND

- Prior distribution of roles
  (specific responsibility assignment)
- Presentation and management of more detailed SEND specification (rules for SEND conversion)
- Prior arrangement with test sites for multi-site studies
- Clarification of finalization timing and conditions

3. Preparation for regulatory submission

Preparation toward SEND implementation is ……

Proof of Concept

- There are limitations to desk-bound discussion.
- Outsource to an experienced SEND solution provider/CRO to gain not just a SEND dataset, but experience in the process itself
- Find solutions to a variety of challenges revealed through experience.

Thank you for your attention

Ina Research Inc.

Shin-ichi Horikawa

Phone: +81-265-72-6616

E-Mail：s-horikawa@ina-research.co.jp