Overview of SEND-Related Activities in Japan: Legacy Data / FDA Trial Submission

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contents

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1. INTRODUCTION

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The need of SEND in Japan

* Application to the FDA
* Data exchange with the licensee
* Data sharing with joint development
* Data exchange with CRO
* Data construction for in house

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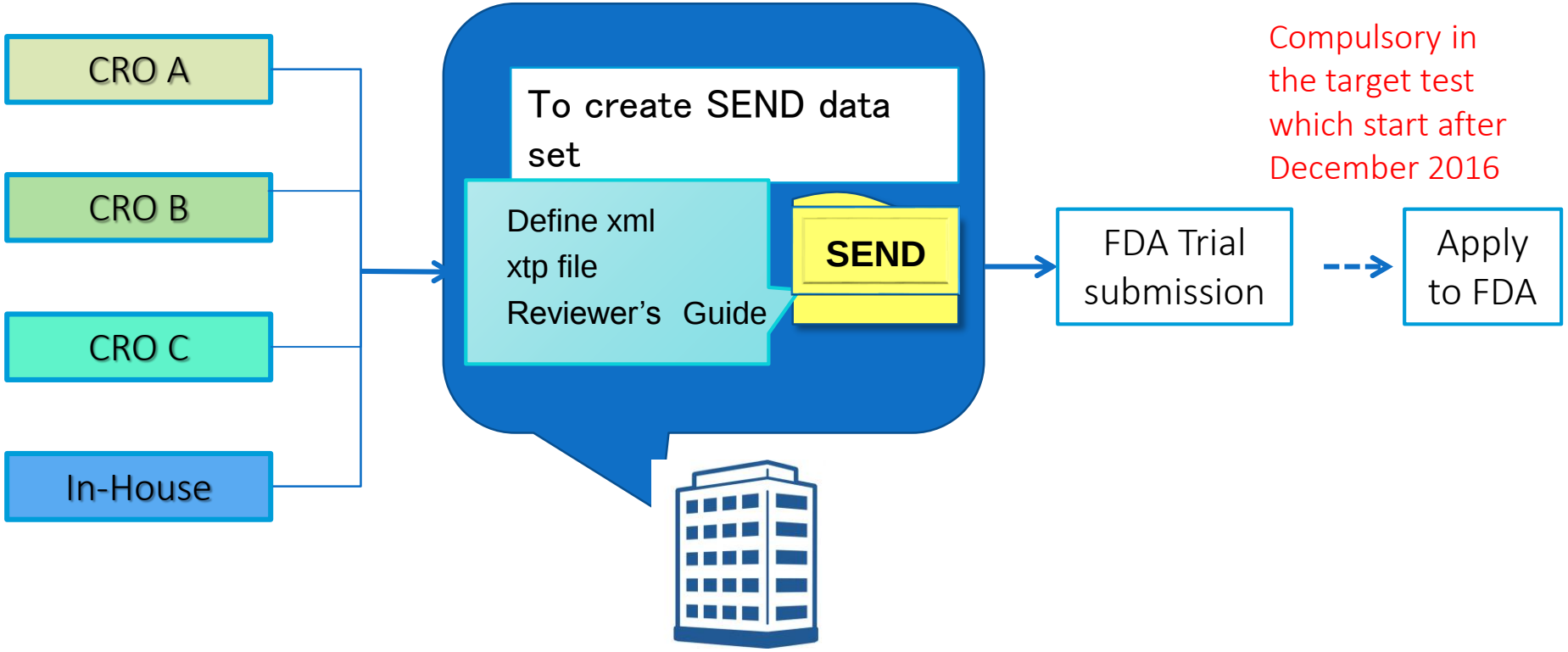
Flow of creating SEND data set



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2. SEND situation in Japan

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① SEND situation of pharmaceutical company

How to create SEND data set？

Pattern①

- Set up SEND system within a company

Pattern②

- Outsourcing to IT vendor /IT Solution Provider

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① SEND situation of pharmaceutical company

Pattern①

Set up SEND system within a company
to create SEND data set（Eg: Mitox、Provantis、PDS etc.）

Task of Pharmaceutical company

- QC check of data
- QC check of Reviewers guide, finalized
- Compilation of other CRO data, unified terminology
- Trial submission to FDA
- QC check for conversion data
- Control for System version （SEND IG/Control terminology）

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① SEND situation of pharmaceutical company

Pattern②

Outsourcing to IT vendor / IT Solution Provider

Task of Pharmaceutical company

- Data which can not be converted to the SEND data (manually input occurs)
- Confirmation of control terminology conversion validity of the SEND data that have been created
- Final confirmation of SEND data that have been created
- Selection of outsourcing contact person

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① SEND situation of pharmaceutical company

Which study data is going to create SEND data set ?

Pattern①

- To create SEND for only test which start since December 2016

Pattern②

- To create SEND for the test has been done(legacy data)even before December 2016

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① SEND situation of pharmaceutical company

Pattern①

To create SEND for only test which start since December 2016

- SEND of all the target test which start since 17th December 201
- SEND of only the target test which start since 17th December 2016 that is expected to FDA .

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① SEND situation of pharmaceutical company

Pattern②

To create SEND for the test has been done (legacy data)even before December 2016

- Apply at the strategically SEND data in anticipation of FDA application(Possibility of the examination period shortening)
- System construction of SEND data creation within a company
- For the effective use of internal data

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②SEND situation of CRO

How to create SEND data set ?

Pattern①

- Set up SEND system within a company

Pattern②

- Outsourcing to IT vendor / IT Solution Provider

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②SEND situation of CRO

Pattern①

- Set up SEND system within a company to create SEND
  （Eg: Mitox、Provantis、PDS etc.）

TASK

- Create Reviewers guide
- Trial submission to FDA
- QC check of conversion Data
- control of System version
- Responding to client-specified term

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②SEND situation of CRO

Pattern②

Outsourcing to IT vendor / IT Solution Provider

TASK

Whether the data can be provided in electronic format
If you can not provide an electronic data, manual input is generated.
（or if the manual input has occurred, create internally or outsource)

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3. To create SEND from legacy data

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① The need for SEND of legacy data

Apply at the strategically SEND data in anticipation of FDA application
(Possibility of the examination period shortening)

System construction of SEND data creation within a company

For the effective use of internal data

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② Important point for creating SEND from legacy data

1） Handling data which difficult to convert to SEND

2） Handling of Control Terminology

3） QC Check of data

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② Important point for creating SEND from legacy data

1） Handling data which difficult to convert to SEND

Support

Perform a manual input into a form that can be converted to SEND.

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1） Handling data which difficult to convert to SEND

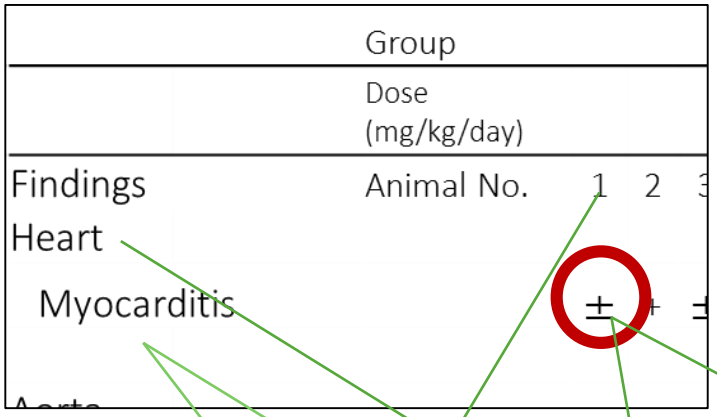
Example：Appendix format（Pathology data）

	Group	Control										3SJ001									
	Dose (mg/kg/day)											5									
Findings	Animal No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Heart																					
Myocarditis		±	+	±	-	-	±	-	-	-		-	-	-	-	-	-	+	-	-	-
Aorta																					-
		-	-	-	-	±	-	-	-	-	-	-	-	-	±	-	-	-	-	-	

Notes) - : No abnormal changes ± : Very slight + : Slight 2+: Moderate 3+: Marked
A: Non-graded change NE: Not examined NA: Not applicable

1） Handling data which difficult to convert to SEND

Example：Appendix format（Pathology data）



Raw data (containing the basic findings and any modifiers)

Basic findings without the modifier, such as distribution, frequency, grade

Observing organ / tissue

Grade

MI domain

STUDYID	DOMAIN	USUBJID	MITEST	MIORRES	MISTRESC	MISPEC	MIMETHOD	MISEV
3SJ001	MI	3SJ001-1	Microscopic findings	Myocarditis, very slight	Myocarditis	HEART	H&E	MINIMAL
3SJ001	MI	3SJ001-1	Microscopic findings	Normal	NORMAL	ARTERY, AORTA	H&E	

1） Handling data which difficult to convert to SEND

Things you need when creating SEND data set from legacy data

* The underlying data for creating data
* Final report
* SEND Implementation Guide
* SEND Control Terminology
* (If any) client provisions of the glossary

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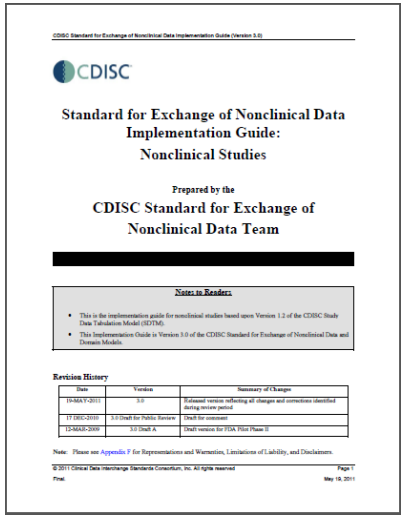
1） Handling data which difficult to convert to SEND

Appearance of the Manual input data

If there is no provision to create internally, to create along the SEND Implementation Guide.



CDISC Standard for Exchange of Nonclinical Data Implementation Guide (Version 3.0)

CDISC

Standard for Exchange of Nonclinical Data Implementation Guide: Nonclinical Studies

Prepared by the
CDISC Standard for Exchange of Nonclinical Data Team

Notes to Readers:

- This is the implementation guide for nonclinical studies based upon Version 1.2 of the CDISC Study Data Tabulation Model (SDTM).
- This Implementation Guide is Version 3.0 of the CDISC Standard for Exchange of Nonclinical Data and Domain Models.

Revision History

Date	Version	Summary of Changes
19-MAY-2011	3.0	Released version reflecting all changes and corrections identified during review period
17-DEC-2010	3.0 Draft for Public Review	Draft for comment
12-MAR-2009	3.0 Draft A	Draft version for FDA Pilot Phase II

Note: Please see Appendix F for Representations and Warranties, Limitations of Liability, and Disclaimers.

Final 19 May 2011

Glossary of Manual input data

The terms of the SEND Control Terminology and input along the default of the terms internally.

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2） Handling of Control terminology

- **Controlled Terminology（CT）:**
  Standard vocabulary and code collection that has been controlled for all of CDISC models and standard

- **Task for handling of Controlled Terminology（CT）**
  - Scientific verification (which term is selected or more appropriate)
  - Strategic build of internal data warehouse (for continue to use any data capture, or to search in the future)
  - Corresponding to the CT update of which is updated on a quarterly basis
- **The latest CT is stored in the following.**
  http://evs.nci.nih.gov/ftp1/CDISC/SEND/

2） Handling of Control terminology

Represents the raw data, including basic findings and any modifiers

Row	STUDYID	DOMAIN	USUBJ ID	MISEQ	MITESTCD	MITEST	MIORRES
1	123	MI	123-01	1	MIEXAM	Microscopic Examination	Brain, temporal cortex, necrosis, bilateral, focally extensive, slight
2	123	MI	123-02	2	MIEXAM	Microscopic Examination	Brain, temporal cortex, necrosis, bilateral, focally extensive, trace

Row	MISTRESC	MISPEC	MIANTREG	MILAT	MISEV
1 (cont)	Necrosis	BRAIN	TEMPORAL CORTEX	BILATERAL	MILD
2 (cont)	Inflammation	BRAIN	TEMPORAL CORTEX	BILATERAL	MINIMAL

"slight"and"trace" does not apply to SEND CT by CDISC terminology in both.

"slight" is mapped, USUBJID 123-01 MISEV section listed as "MILD".
Also mapped "MINIMAL" and "Trace" is displayed in the MISEV section of the USUBJID 123-02.

"Distribution presents a SEND 3.0 MI domain qualifier is not set to "focally extensive“ is stored in the SUPPMI (supplemental qualifiers domain for microscopic findings and histopathological findings add a modifier) domain.

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3）QC Check of data

The need for QC of SEND data set that was created from the legacy data

- Current situation at Three S Japan

When we create the date by manual input from legacy data, perform all QC check

Method: Print out the SEND data, check with red marks.

Reference materials：Original data、Final report

Task：The number of data is enormous, it takes time to check all.

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3）QC Check of data

The need for QC of SEND data set that was created from the legacy data

- Our future policy
  Set how to check for each domain, section.

  Example:
  -"STUDYID" and "DOMAIN" section are described the same data all within the domain, so that to confirm on the Viewer.
  -Manual input item is performed an exhaustive check on the paper.

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3）QC Check of data

Task

Pharmaceutical company, regardless of creating SEND outsource or internally, it is necessary to always check the data. How to check the data should be considered in-house.

Examination item

- Consider to install of the Viewer of the SEND data
- What Domain to check
- Whether perform 100% check or a random check
- The confirmation data on the Viewer or to check on the paper

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3）QC Check of Data

Consistent with the original data

- Contents of the SEND data based on ground data, or not properly reflect adequately all of the data.
- SEND data in numeric values and unit basis data content to reflect properly?
- SEND data in each domain that reflects appropriate original data?

Row	STUDYID	DOMAIN	USUBJID	BWSEQ	BWTESTCD	BWTEST	BWORRES	BWORRESU	BWSTRESC	BWSTRESN	BWSTRESU	BWSTAT
1	ABC	BW	ABC-001-001	1	BW	Body Weight	250	g	250	250	g	
2	ABC	BW	ABC-001-001	2	BW	Body Weight	240	g	240	240	g	
3	ABC	BW	ABC-001-001	3	BW	Body Weight	280	g	280	280	g	
4	ABC	BW	ABC-001-001	4	BW	Body Weight	190	g	190	190	g	
5	ABC	BW	ABC-001-001	5	BW	Body Weight	225	g	225	225	g	
6	ABC	BW	ABC-001-001	6	BW	Body Weight	245	g	245	245	g	
7	ABC	BW	ABC-001-001	7	BW	Body Weight	50	g	50	50	g	
8	ABC	BW	ABC-001-001	8	BW	Body Weight	260	g	260	260	g	
9	ABC	BW	ABC-001-001	9	BW	Body Weight						NOT DONE
10	ABC	BW	ABC-001-001	10	BW	Body Weight	229	g	229	229	g	
11	ABC	BW	ABC-001-001	11	BW	Body Weight	243	g	243	243	g	
12	ABC	BW	ABC-001-001	12	TERMBW	Terminal Body Weight	225	g	225	225	g	

Row	BWREASND	BWBLFL	BWFAST	BWEXCLFL	BWREASEX	VISITDY	DTC
1 (cont)		Y				1	-06-19
2 (cont)						7	6-26
3 (cont)						14	7-02
4 (cont)				Y	FASTING BY HUMAN ERROR	21	
5 (cont)						28	
6 (cont)						35	
7 (cont)				Y	FAULTY EQUIPMENT	42	
8 (cont)						49	
9 (cont)	TECHNICIAN OVERSIGHT					56	14
10 (cont)						63	1999-08-21
11 (cont)						70	1999-08-28
12 (cont)			Y			75	1999-09-03

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3）QC Check of Data

When the DataSet QC check list

The term

- Are those based it on the SEND Control Terminology listed?
- If you have internal rules on how to use such terms and acronyms based on it, is provided.
- To SEND appropriate terminology is used?
- Abbreviations and terms used throughout the domain?

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3）QC Check of Data

When the DataSet QC check list

Calculation result

- If the numbers based on the calculated original data to SEND in the results are listed correctly.

Example：

- BG: Body weight gain
- FW： Food Utilization Efficiency
- OM：Body weight ratio / Brain weight ratio

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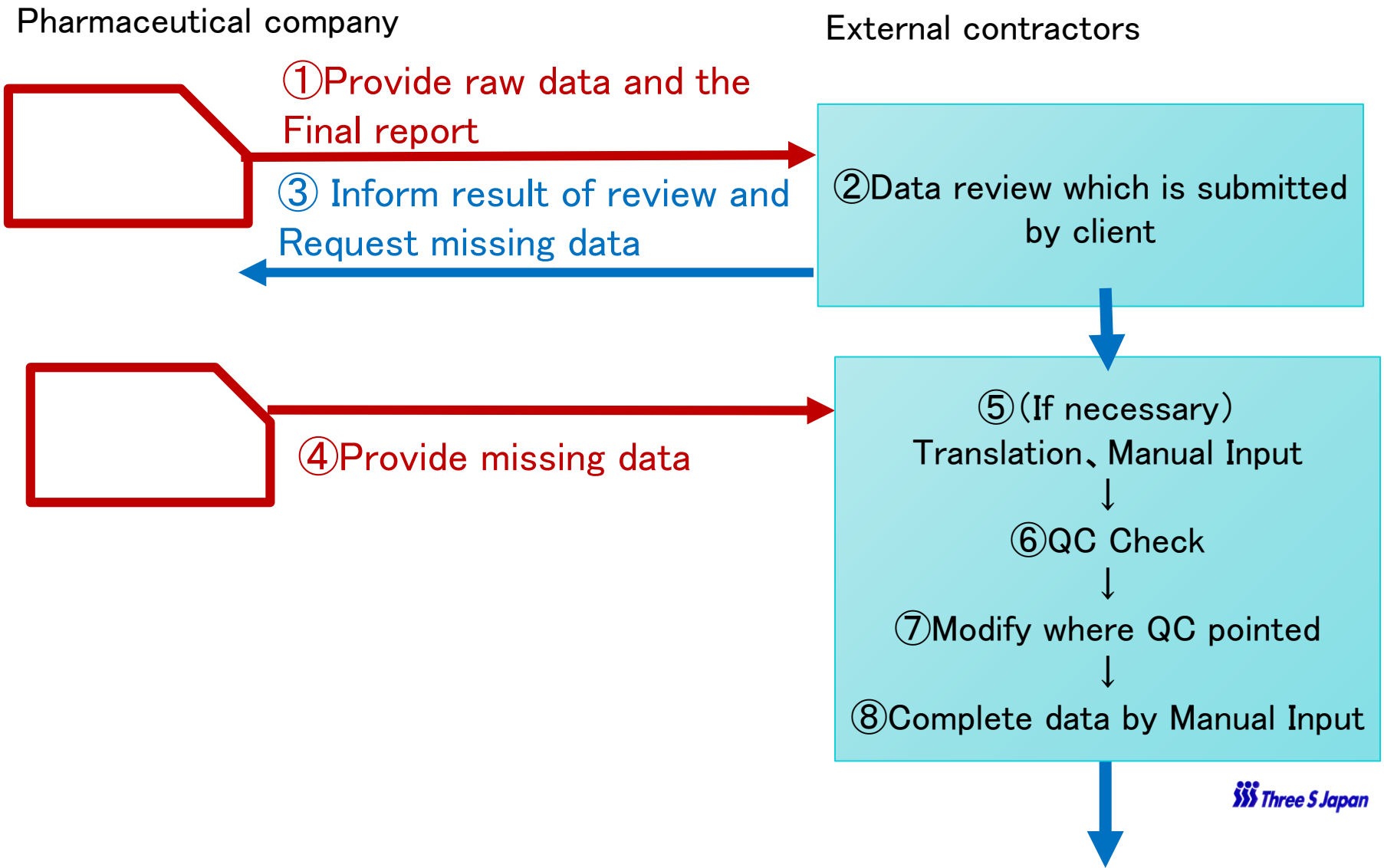
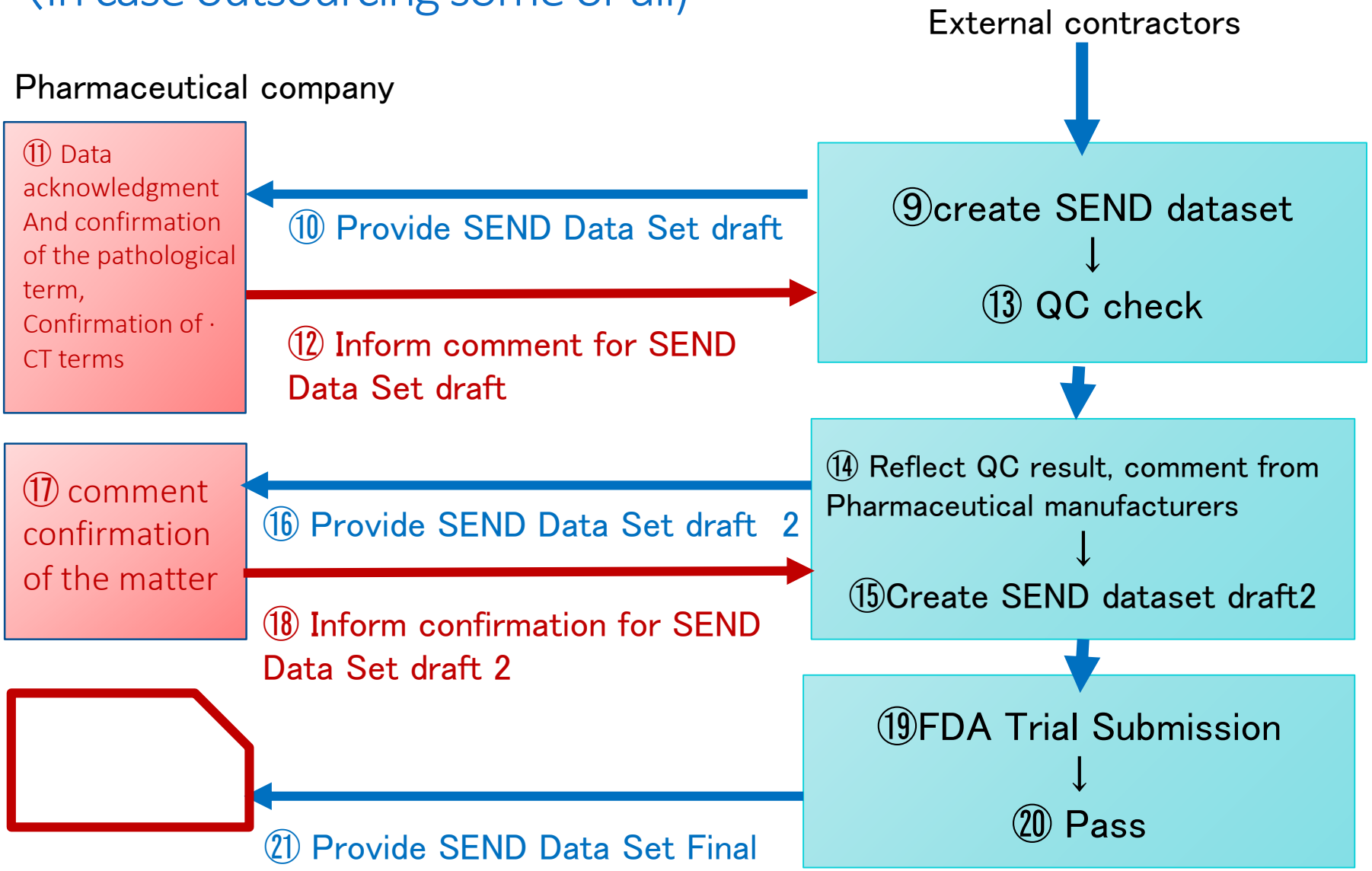
③ Flow for creating SEND data set from legacy data (In case outsourcing some or all)



③ Flow for creating SEND data set from legacy data (In case outsourcing some or all)



Create SEND Data set from legacy data

Task when you create all SEND data internally

①Data input on how to validate the data and company data from CRO verifiers, and other validation methods and verification done by anyone?
(Test Director? The IT Department?), And modification procedure when an error is found

(2) Final test report integrity verification, data QC, who will do and how to. Check the integrity of data
(3) Dealing with data (TS domain, etc.) cannot be converted automatically in the internal
(4) Create SEND and that is consistent with the Final Report

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4. Summary

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Summary

- SEND Data Set for pharmaceutical company have created by deploying internal systems or outsource.

-The testing policy of the company, started even before 12/2016 pharmaceutical company to create the SEND Data Set.

- Create SEND data set from legacy data, to consider how to respond to “how to handle with the manual input for data which difficult to convert to SEND", "handling with Control Terminology" "QC".

Thank you !

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