Relationship between Pharma and CRO in method development and transfer - based on the survey by JBF Discussion Group

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Disclaimer

- The views and opinions expressed herein represent those of the DG2016-23 and do not necessarily represent the views, opinions or practices of all Japanese Pharma/CRO or JBF.

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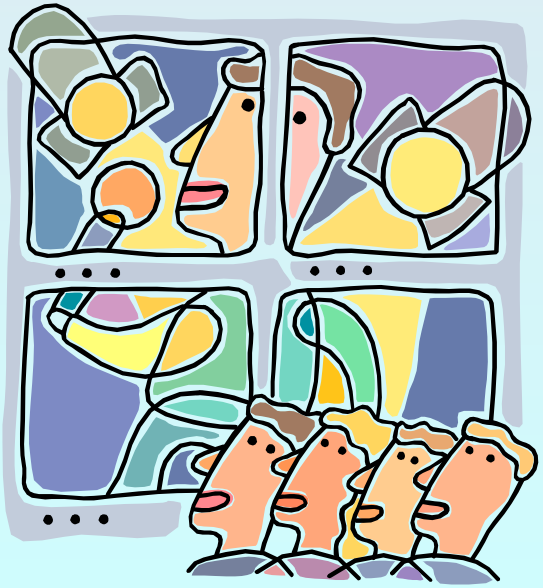


Background

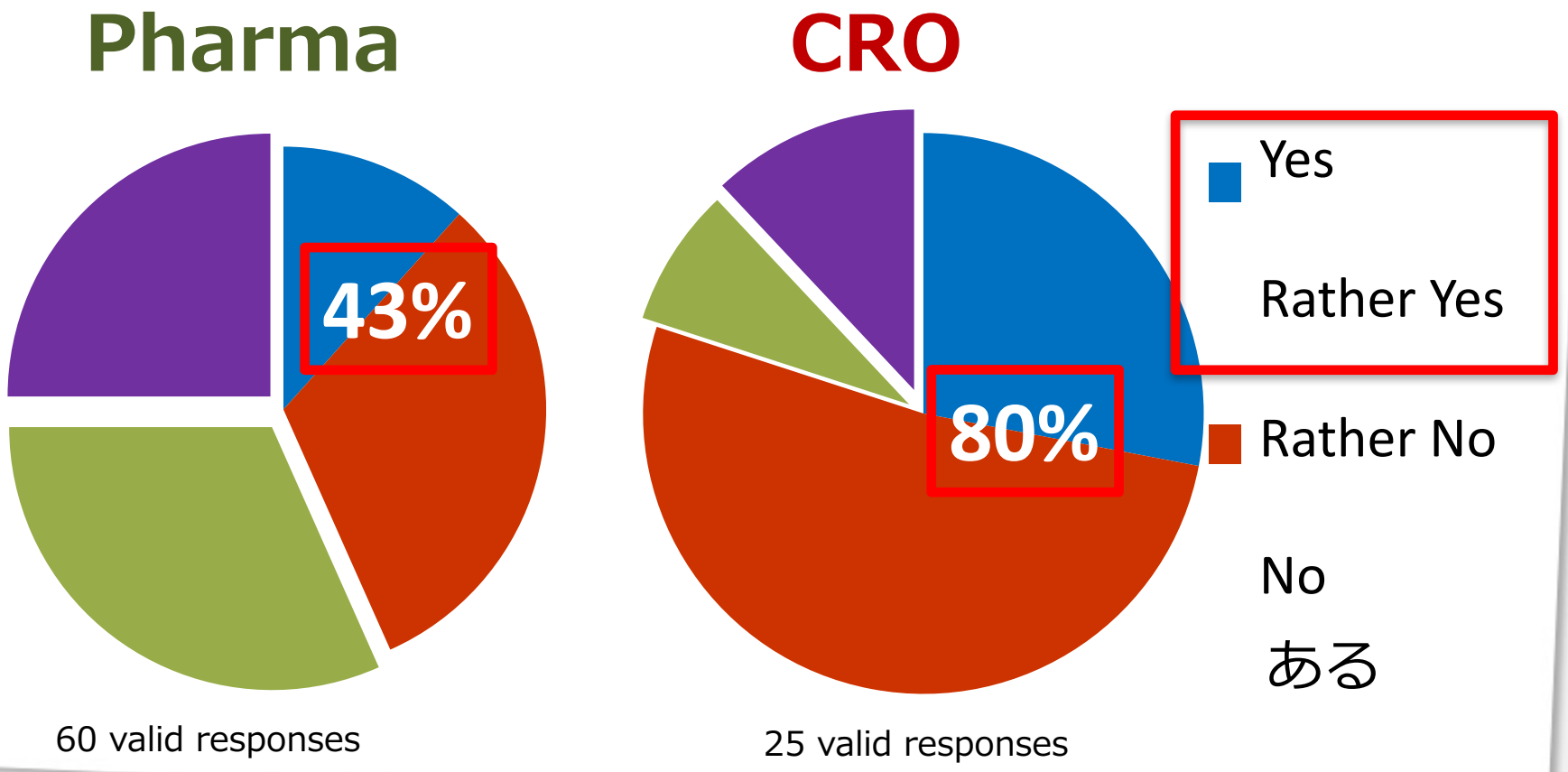
- We believe good collaboration between Pharma and CRO is important in successful bioanalytical studies.
- Sometimes we both have an unexpected problem to conduct the bioanalysis studies(Some of them may be avoidable).
- This presentation is based on the survey by JBF DG-2016-23, and picked-up some items.

Survey for contract studies

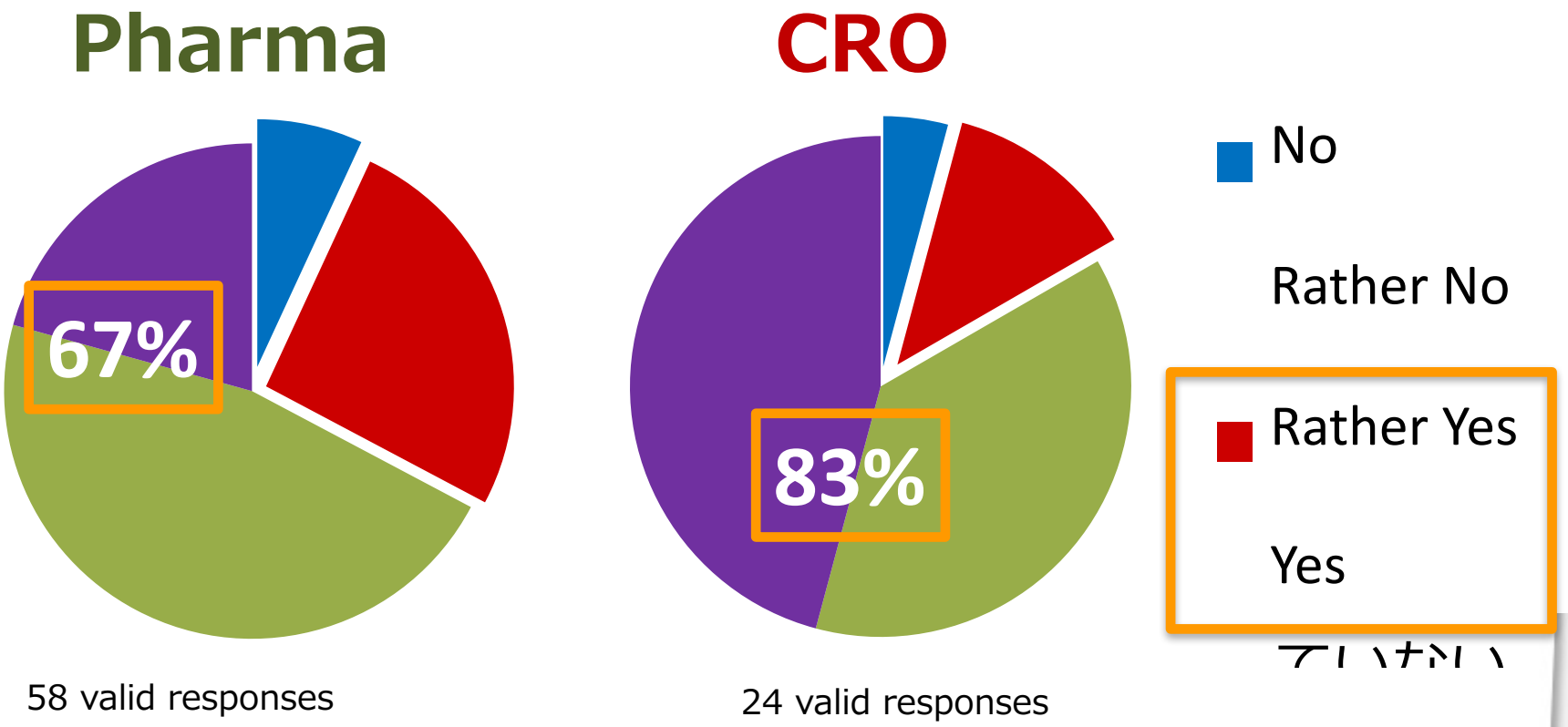
- JBF DG-2016-23 team have carried out the questionary survey to Pharma and CROs in Japan on September 2016
- Target: LC/MS/MS, method development, regulated bioanalysis
- Answer: Total 111(Pharma: 73, CRO: 38)

  Non-Clin-PK(71), TK(65), Clin-PK(88) overlapped
- Based on personal opinion(not company)

Q. Do you need improvements of your contracted study operations?
<in method development stage>



Q. Do you have enough scientific discussion?
<in method development stage>



Q: What are you working on for improvement of your contracted study operations?

Pharma

- Explain the core of method carefully
- Provide information together
- Use communication tools depend on the situation
- Apply TC/Web-meeting
- Hold F2F meeting if possible
- Train a contact person
- Establish a simple method for easy transfer

Summary by JBF-DG

- ✓ Share Information
- ✓ Face to Face Meeting
- ✓ Smooth Communication

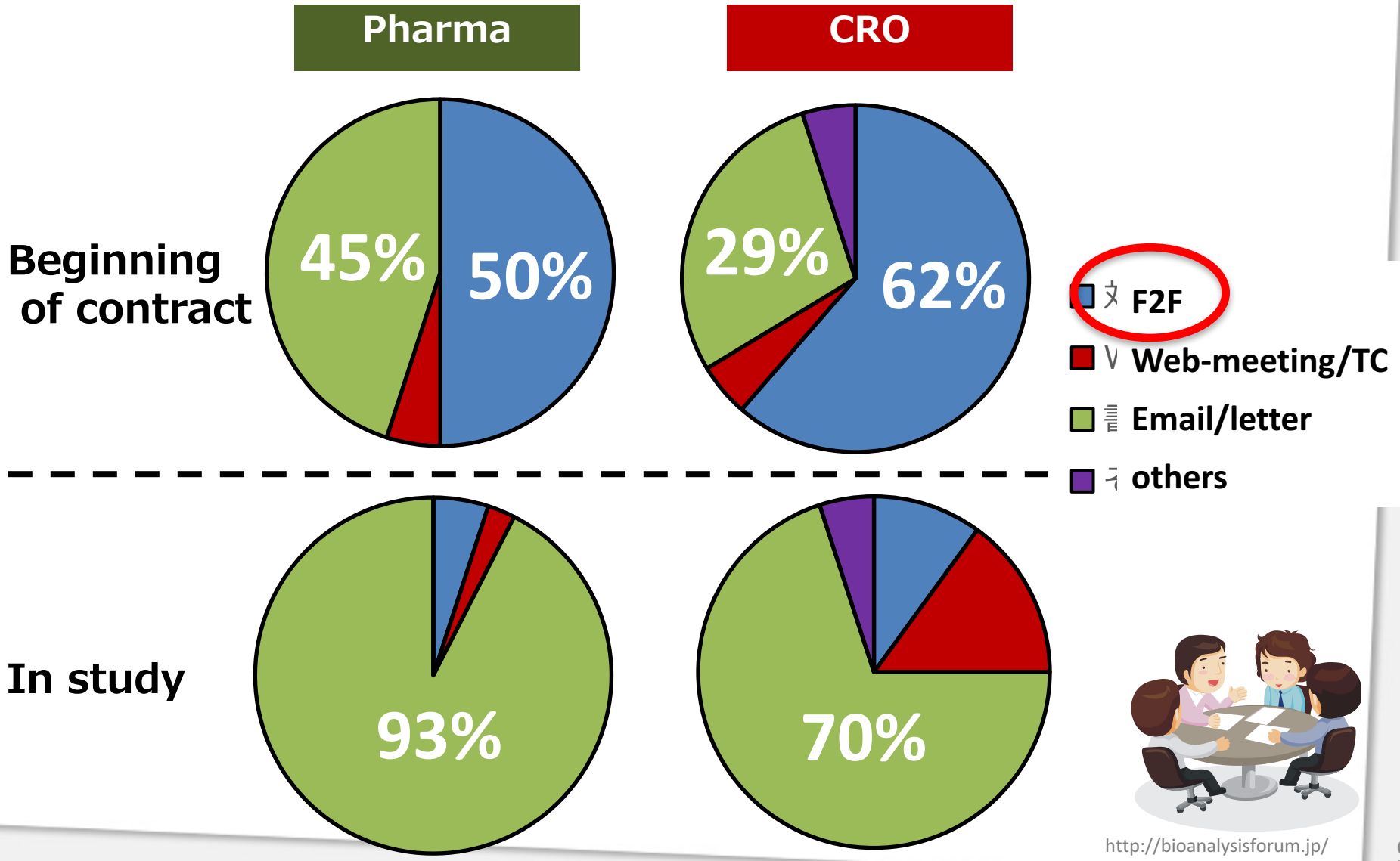
CRO

- Use not only email but also telephone/F2F meeting
- Share information with Sponsor
- Explain carefully, honestly and clearly
- Quick response at the time of a problem occurrence
- Propose based on scientific data
- Internal information sharing(in CRO, between SD)

Summary by JBF-DG

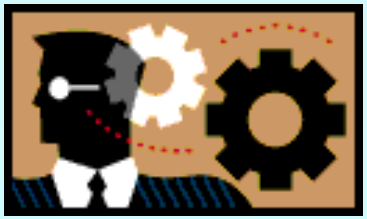
- ✓ Face to Face Meeting
- ✓ Smooth Communication
- ✓ How to share Information

Q. How to share information of method/compound?



Case Study

- **Picked-up case studies from answers of the survey by JBF DG-2016-23**



Case Study 1

Share Information

- Unspoken rule in sponsor's laboratory were cause of the failure of method transfer.
  Ex. frequency of Analytical column wash after analysis, Preparation of reagents, QC samples, mixing time, and etc.

< Action taken >

To keep consistency between Sponsor's standard rule and CRO's one, had a communication and shared the detailed description

< Lesson learnt >

- Share the detail instruction and the purpose of the process to avoid the change/switch lightly
- Recognize that our own approach/procedure is not always common sense.

Case Study 2

Communication

- Changed the method qualified by Pharma without authorization
- Re-investigate some items even though these have already investigated by Pharma

< Action taken >

To keep contact/report periodically and when problem occurrence

< Lesson learnt >

- **It is necessary to inform CRO that the proposed method is robust enough with adequate data, and Pharma also share what Pharma want CRO to investigate.**
- **It makes both easy to find the discussion points when problem occurrence.**

Case Study 3

Unsuitable Case

- **Failed validation study even though CRO completed method development and qualification.**

< Action taken >

Pharma gave up using the investigated method for PK sample analysis

< Lesson learnt >

- **It is necessary to make it clear any risks/ possible factors of validation study failure during method development stage.**
- **Method development and validation is conducted by separate teams, respectively, in some CRO.**

Case Study 4

Communication

- Lost on the intended opinion/direction by email
- Taking a lot of time due to the time difference

< Action taken >

To have TC with a Japanese liaison of CRO and to use a clear and simple sentence

< Lesson learnt >

- **Recognize Japanese procedure and interpretation of BMV Guidance/Guideline is not always common.**
- **It is necessary to discuss to a detail concern after having understood both differences**

Case Study 5 (Domestic incident)

- Less contact when problem occurrence
- Taking a long time to fix the problem or NO solution

< Action taken >

To confirm it by email and telephone, and have a meeting Web/VTC or in person

< Lesson learnt >

- **Watch-out and a diligent confirmation is necessary when less-contact with CRO**
- **The relationship to discuss the solution process is important and it is not enough to report after it is settled.**

From the open discussion@JBF 2017

- Picked-up individual opinions from open discussion beside the presentation poster at 8th JBF symposium 2017 in Tokyo

Link to:
http://bioanalysisforum.jp/images/2017_8thJBFS/P4_DG2016-23_HP.pdf
(sorry in Japanese)

Impression/ working with oversea CRO

Opinions from participants of 8th JBF symposium in 2017

Positive opinion

- ✓ **Understanding the regulation properly and proposing the alternative**
- ✓ **Conduct a variety validation parameters**
- ✓ **Recently CRO got no critical observation form authority**
- ✓ **There are the good points and bad points, but feels it in Positive.**

Negative opinion

- ✓ **SD and analyst is in the different building, so concern their communication**
- ✓ **SD suddenly left, and new SD did not understood the study.**
- ✓ **CRO went bankrupt after communication with CRO disappeared**
- ✓ **Less response in a vacation season**
- ✓ **Severe in contract and estimate contents**

Q. What is the advantage of Japanese/Oversea CROs?

Pros for Japanese CROs

Answers	Quantity
On schedule	14
Communication (Language/Time-zone)	14
Quality	15
Correspondence (careful/attentive)	8
Others: - Less mistake for preparing documents - Good relationship between Tox and TK analysis members - Listen Sponsor opinion etc.	

Valid responses: 33

Pros for Oversea CROs

Answers	Quantity
Cost	5
Speed	4
LIMS	3
Regulation	10
Alternative proposal	4
Others: - Systematic plan/process/price - IT facility - Resource coordination - High problem resolution and responsibility - Connection with authority etc.	

An Ideal CRO, Japanese Pharma expect

- Rapid turn around and cost performance like an oversea CRO with a careful work like a domestic CRO
- Providing an appropriate proposal and solution at the trouble of method development/ transfer/ validation/ sample analysis
- Recommendation with well-understanding of the local guidance/guideline and survive FDA/EMA/PMDA inspection
- Enough communication with person in the clinical study and work like as a study team member
- Providing the high quality data rapidly with high traceability by standardized systems like LIMS/eNote

Opinions to Pharma from CRO

Please tell us “Proposal, Appeal point or Difficulties in the collaboration with Pharma.

- **Please note we would work together for the drug development, NOT as a subcontractor**
- **The schedule moving up(sometimes monthly) after the contract is very hard.**
- **There may be too little disclosure of the information.**
- **It is helpful to inform at least what kind of functional group analyte has, if it is difficult to disclose chemical structure.**

Conclusion/Proposal

- Almost of all problems/troubles are caused by less-communication and less-information.
- **Culture differences** in communication may make it more difficult when Japanese Pharma works with oversea CRO.
- Pharma and CRO have the same goal, successful bioanalysis.
- So I hope we can see improvement if we (try to) have frequent and informative communication with global mindset.

Acknowledgement

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Thank you for your attention!
9th JBF symposium
6-8th Feb, 2018 @Tokyo