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 questionnaire 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>

**Pharma**

- Yes: 43% (60 valid responses)
- Rather Yes: 80% (25 valid responses)
- Rather No: 6%
- No: 3%

**CRO**

- Yes: 80% (25 valid responses)
- Rather Yes: 6%
- Rather No: 6%
- No: 3%
Q. Do you have enough **scientific discussion**?<br><i>&lt;in method development stage&gt;</i>

**Pharma**
- Yes: 67% (58 valid responses)
- Rather Yes: 83%

**CRO**
- No: Rather No
- Yes: 83% (24 valid responses)
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

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
✓ Share Information
✓ Face to Face Meeting
✓ Smooth Communication

Summary by JBF-DG
✓ Face to Face Meeting
✓ Smooth Communication
✓ How to share Information
Q. How to share information of method/compound?

Beginning of contract:
- Pharma: 45% F2F, 50% Web-meeting/TC, 29% Email/letter, 62% others
- CRO: 29% F2F, 62% Web-meeting/TC, 29% Email/letter, 93% others

In study:
- Pharma: 93% Email/letter
- CRO: 70% Email/letter
Case Study

- Picked-up case studies from answers of the survey by JBF DG-2016-23
Case Study 1

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

- 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

- 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

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

Impression/ working with overseas 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

<table>
<thead>
<tr>
<th>Answers</th>
<th>Quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td>On schedule</td>
<td>14</td>
</tr>
<tr>
<td>Communication (Language/Time-zone)</td>
<td>14</td>
</tr>
<tr>
<td>Quality</td>
<td>15</td>
</tr>
<tr>
<td>Correspondence (careful/attentive)</td>
<td>8</td>
</tr>
</tbody>
</table>

Others:
- Less mistake for preparing documents
- Good relationship between Tox and TK analysis members
- Listen Sponsor opinion etc.

### Pros for Oversea CROs

<table>
<thead>
<tr>
<th>Answers</th>
<th>Quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost</td>
<td>5</td>
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<tr>
<td>Speed</td>
<td>4</td>
</tr>
<tr>
<td>LIMS</td>
<td>3</td>
</tr>
<tr>
<td>Regulation</td>
<td>10</td>
</tr>
<tr>
<td>Alternative proposal</td>
<td>4</td>
</tr>
</tbody>
</table>

Others:
- Systematic plan/process/price
- IT facility
- Resource coordination
- High problem resolution and responsibility
- Connection with authority etc.

Valid responses: 33
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!

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