

Clinical trial consultation system  
(utility and successful cases from  
company's point of view)

**3<sup>rd</sup> China-Japan Symposium  
on Drug Development**

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**Japan Pharmaceutical Manufacturers Association (JPMA)  
New Drug Regulatory Affairs Department,  
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# 1. Introduction: A Questionnaire Survey in JPMA

- **Number of consultation meetings** in a year for each company

No. consultation	No. of companies (Oct. 2008 – Sept. 2009)	No. of companies (Oct. 2009 – Sept. 2010)
0	9	7
1	9	9
2	12	12
3	6	4
4	5	5
5	3	6
6 -10	9	9
11 - 20	4	6
21 -	1	0
Total	58	58

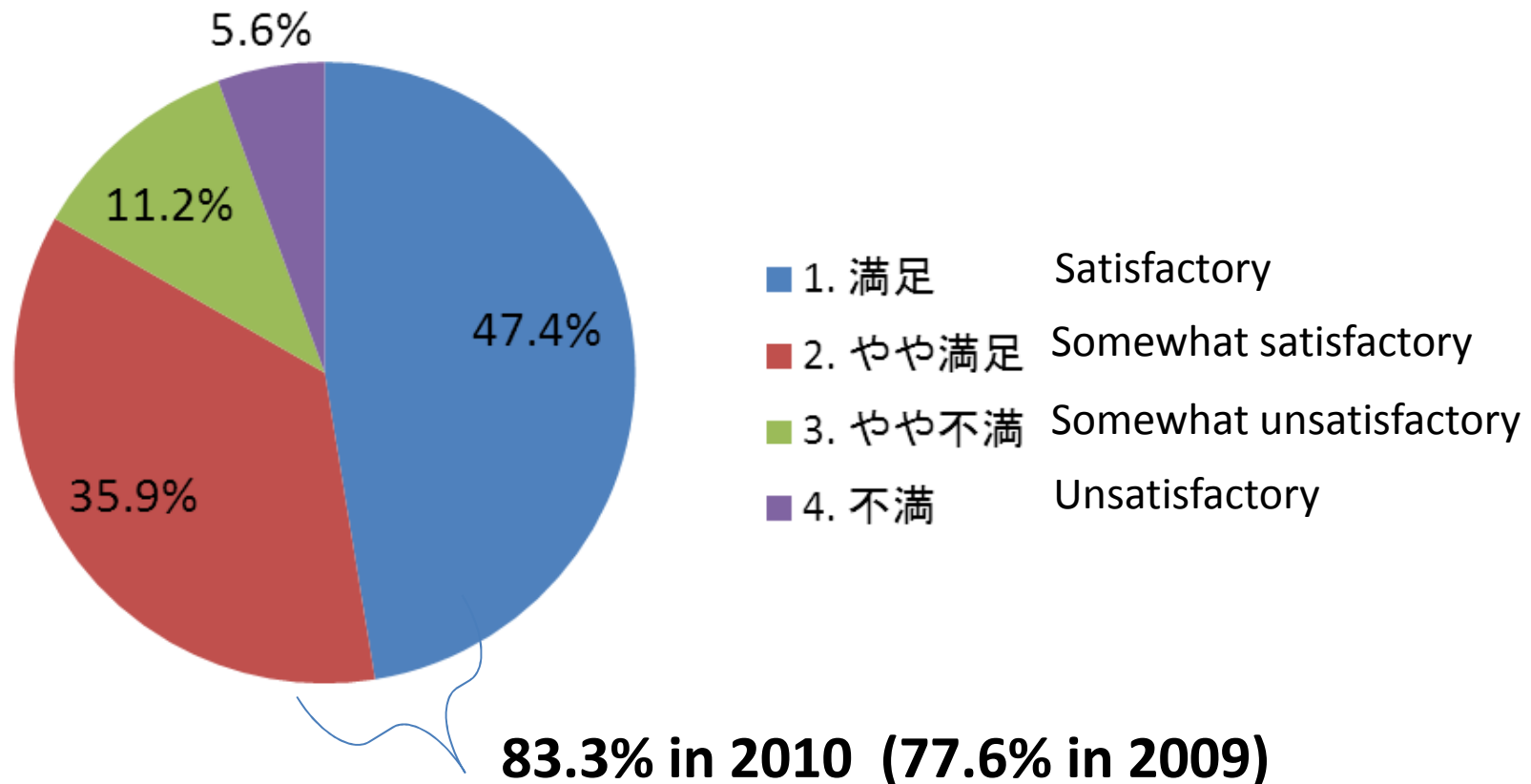
Based on answers from 58  
companies in JPMA

Oct.2008-Sept.2009  
Total 238 consultations

Oct.2009-Sept.2010  
Total 243 consultations

# 1. Introduction: A Questionnaire Survey in JPMA

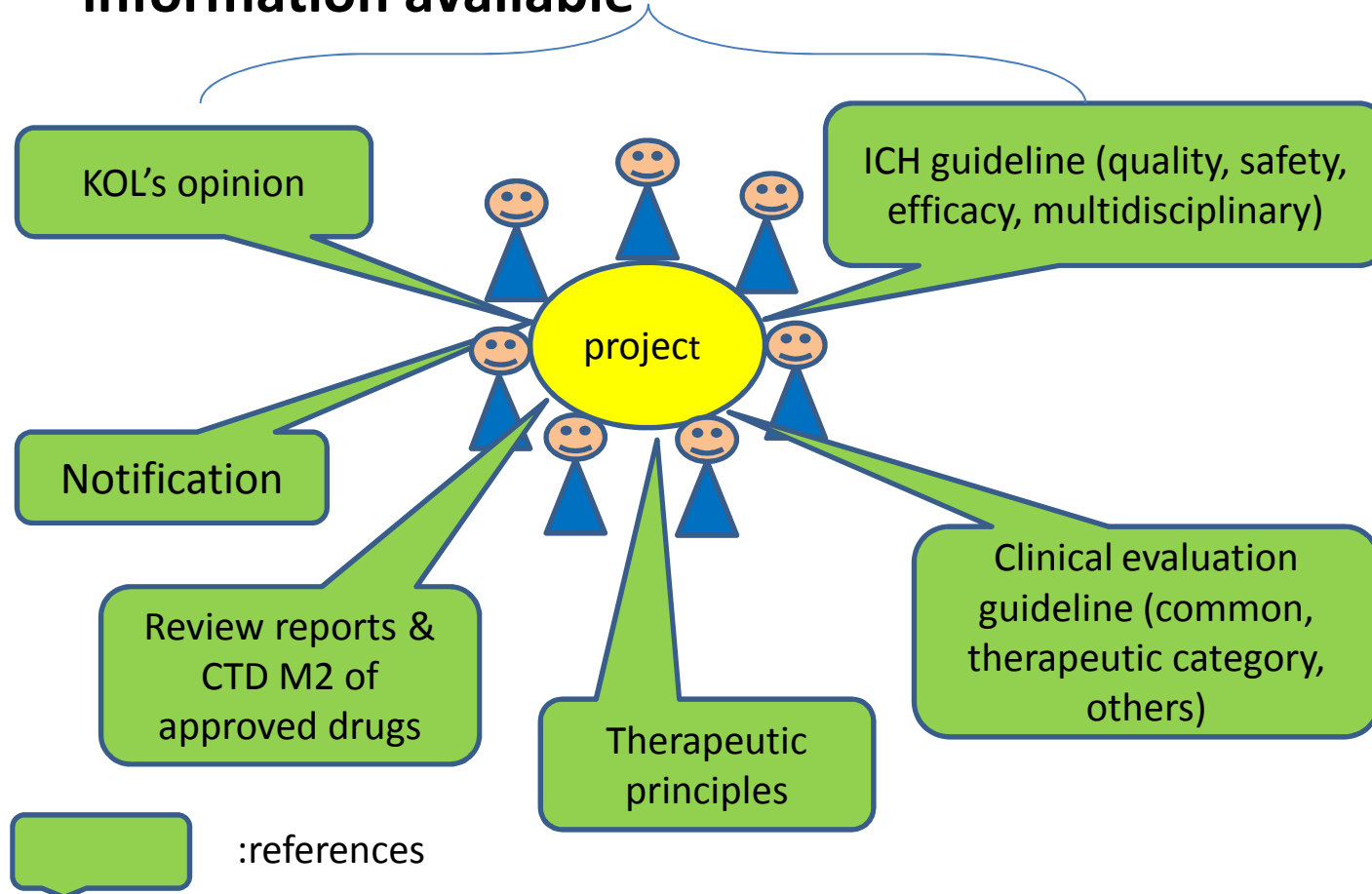
- Satisfaction level is high.



## 2. How to approach the meeting

### Discussion within a project team

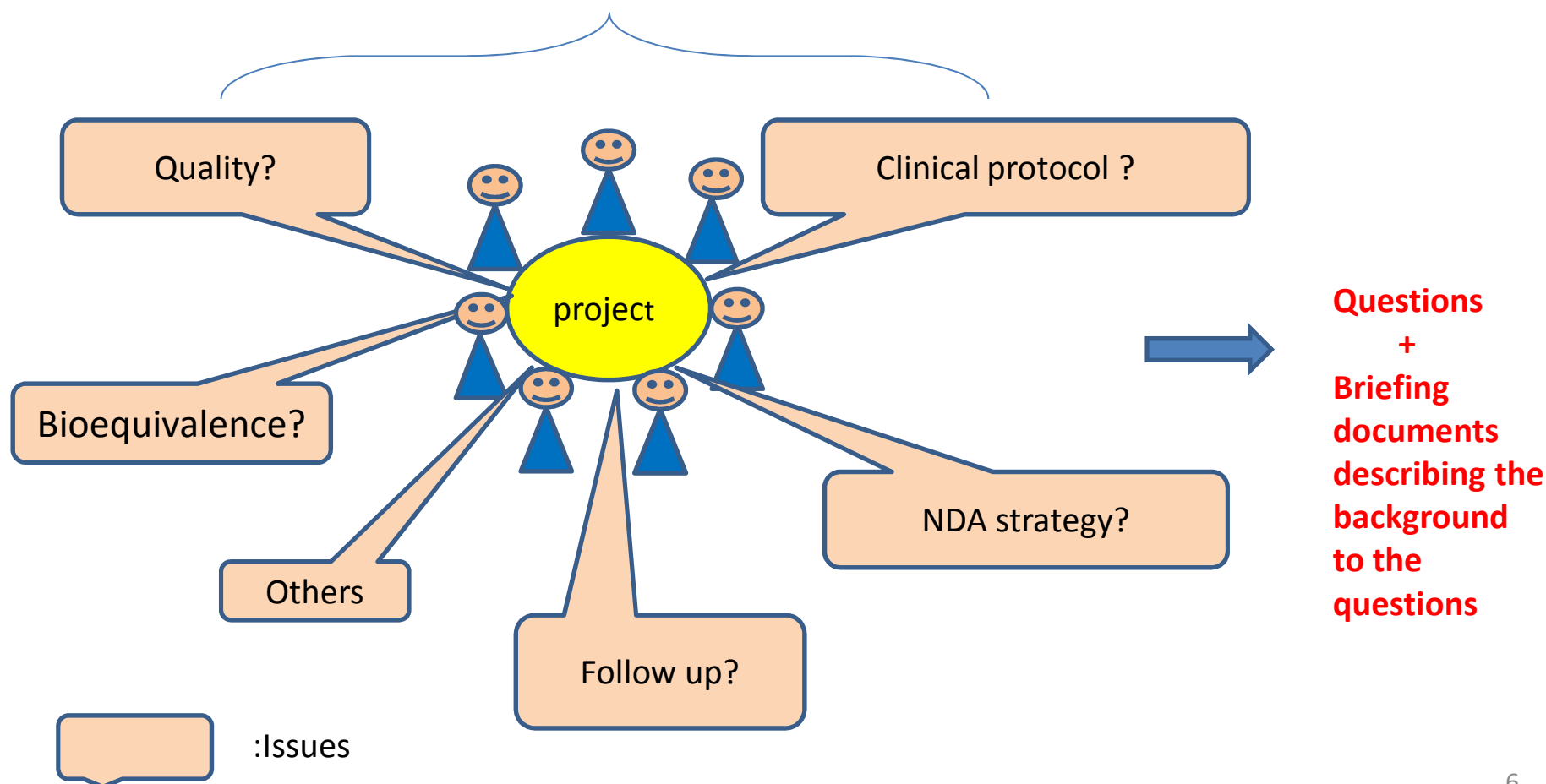
**Planning a new drug application strategy based on information available**



## 2. How to approach the meeting

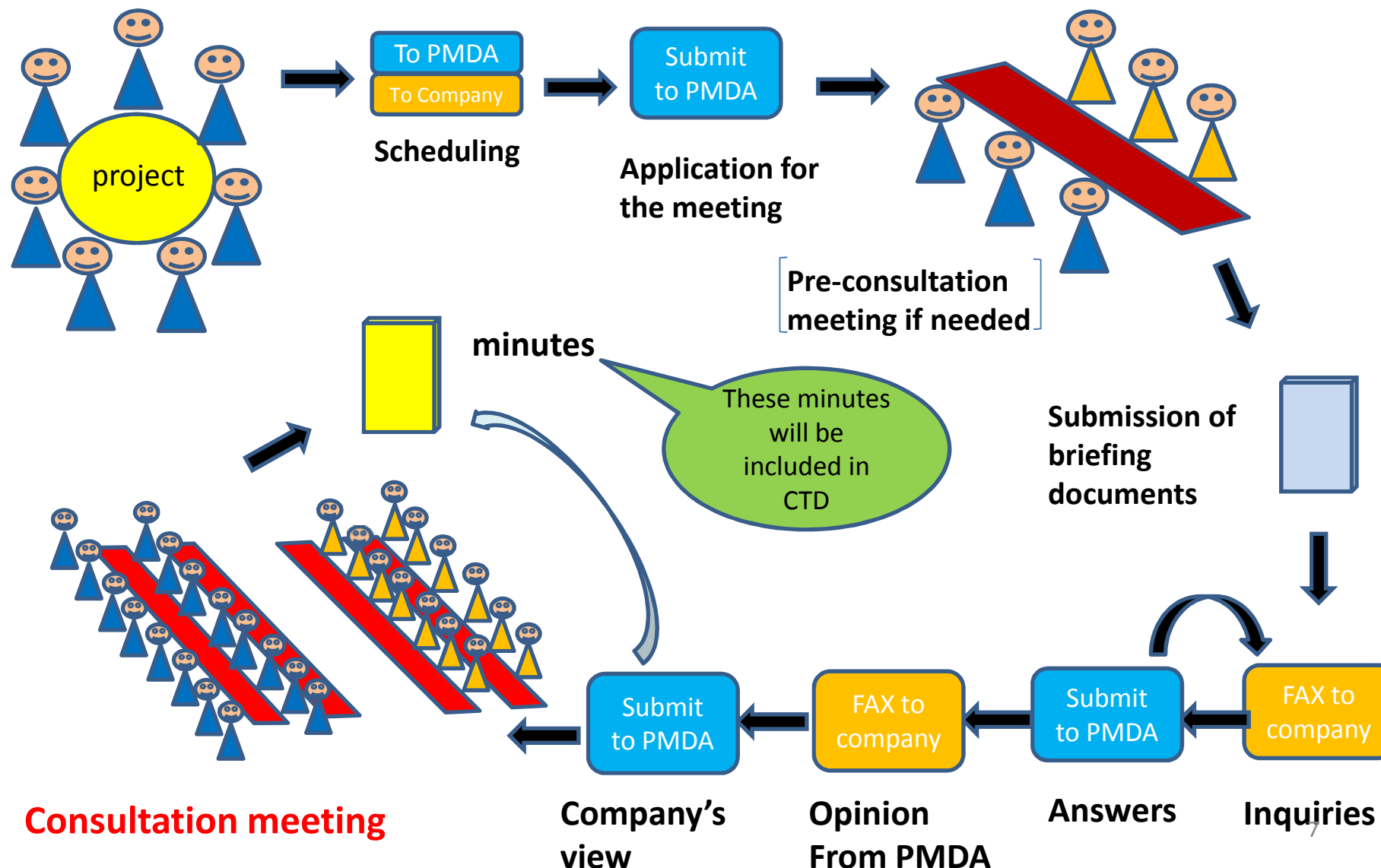
### Discussion within a project team

**Planning to have a consultation meeting to solve issues raised during the development period.**



## 2. How to approach the meeting

### Implementation of a consultation meeting



### 3. Utility and successful cases

- (1) A case of “INAVIR<sup>®</sup>,”
- (2) Cases of some projects in the following consultation meetings
  - 1) Consultation before start of phase I study for drugs  
Case 1 - 5
  - 2) Consultation before start of late phase II study for drugs  
Case 6 - 9
  - 3) Consultation after completion of phase II study for drugs  
Case 10 - 13
  - 4) Pre-application consultation for drugs  
Case 14 - 16



Minutes of consultation meetings are not open to the public.  
They are property of the companies.



### 3. Utility and successful cases

#### A case of “INAVIR<sup>®</sup>”

**Brand name:** INAVIR<sup>®</sup> DRY POWDER INHALER 20mg

**JAN:** Laninamivir octanoate hydrate

A long-acting neuraminidase inhibitor with therapeutic efficacy after a single dosage

**Indication:** Treatment of influenza A or B virus infection

**Dosage and administration :**

For adults :Single dose inhalation of LO 40mg

For pediatric patients:

<10-year old: Single dose inhalation of LO 20mg

≥10-year old: Single dose inhalation of LO 40mg



### 3. Utility and successful cases

A case of “INAVIR<sup>®</sup>”



Designated as a Priority product for consultation meetings

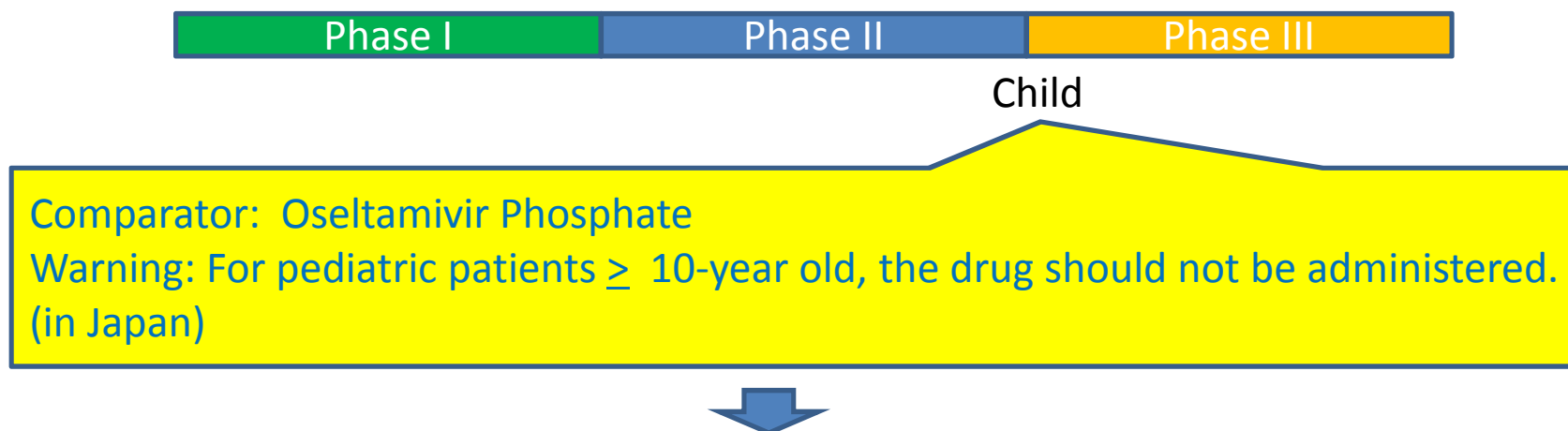
#### Number of clinical studies

Adult :	Japan	4	2	1
	Global			1
	Others		1	
Child	Japan		1	1
PK	Japan	3		

By utilizing the consultation meetings during Phase I –III, the clinical data package was confirmed.

### 3. Utility and successful cases

A case of “INAVIR<sup>®</sup>”



By utilizing the consultation meetings, the following clinical studies were confirmed.

- 1) Phase II/III DB study (For pediatric patients < 10-year old)  
20mg once, 40mg once, Oseltamivir Phosphate 75mg twice daily for 5 days
- 2) Phase III DB study (For patients 10-19 years old)  
20mg once, 40mg once
- 3) PK study (For pediatric patients  $\leq$  15-year old)

### 3. Utility and successful cases

# A case of “INAVIR<sup>®</sup>”



After the consultation meeting, the following clinical studies were conducted.

- 1) Phase III comparative study (Inhaler A vs Inhaler for marketing)
- 2) PK study using inhaler for marketing

### 3. Utility and successful cases

A case of “INAVIR<sup>®</sup>”

Prior assessment consultations were conducted as a pilot project in 2009.



NDA submission: Jan. 29, 2010

Second committee on New Drugs: Jul. 29, 2010

NDA approval: Sep. 10, 2010

### 3. Utility and successful cases

#### Examples of consultation meeting fees

Consultations	Fees (YEN)
Procedure consultations for drugs	139,800
Consultation on bioequivalence testing, etc. for drugs	556,000
<b>Consultation before start of phase I study for drugs</b>	<b>4,239,400</b>
Quality consultation for drugs	1,478,300
Safety consultation for drugs	1,782,800
Consultation before start of early phase II study for drugs	1,623,000
<b>Consultation before start of late phase II study for drugs</b>	<b>3,028,400</b>
<b>Consultation after completion of phase II study for drugs</b>	<b>6,011,500</b>
<b>Pre-application consultation for drugs</b>	<b>6,011,400</b>
Consultation on the protocol of clinical trials for reevaluation and reexamination of drugs	3,320,600
Consultation at completion of clinical trails for reevaluation and reexamination of drugs	3,319,400
Additional consultation for drugs	2,675,600

### 3. Utility and successful cases

## Consultation before start of phase I study for drugs

#### Case 1:

We clarified what studies should be done in Japan, in case foreign data in non-clinical and clinical studies were used for the NDA. After discussing clinical trial design, items under consideration were clarified, and we could conduct the clinical study based on company's plan with safeguards for the safety of the subjects.

#### Case 2:

The number of patients with the target disease is too limited to conduct Phase I study in Japan. We were advised to join a global study to facilitate evaluation of the efficacy in Japanese patients and to develop the product efficiently. We could share the information with PMDA about what data should be available for the complete package from the reviewer's point of view.

### 3. Utility and successful cases

## Consultation before start of phase I study for drugs

#### Case 3:

We could set up many appropriate items in our protocol. We could confirm the requirements in the global study we planned, and also get the view from PMDA about the long-term administration study.

#### Case 4:

We asked about primary clinical studies and data packages for the product, and got advice from PMDA that we could omit some major clinical studies by utilizing foreign clinical data and conducting an additional PK study.

#### Case 5:

We agreed with PMDA about joining a global phase I study. We could identify examination items to be added for monitoring safety.



### 3. Utility and successful cases

#### Consultation before start of late phase II study for drugs

##### Case 6:

We could set up a more appropriate primary endpoint in our protocol, and add necessary examination items. There were some items that could not be changed as PMDA recommended. However, we could get advice for the unchanged items.

##### Case 7:

For an Asian multinational study, the following items were discussed constructively, and we could get appropriate and concrete advice considering the possibility of success.

- Development plan for NDA and data package
- Study design and contents of investigation
- Number of patients (total and Japanese patients)

### 3. Utility and successful cases

#### Consultation before start of late phase II study for drugs

##### Case 8:

We could confirm whether to join the global study with children.  
And we could get good advice for the developing strategy  
(clinical data package).

##### Case 9:

As we found it difficult to show the dose-response relationship in the primary endpoint in a foreign confirmation study with an active comparator, we consulted about setting the primary endpoint in Japan. As a result, we could set up our own endpoint separately.

### 3. Utility and successful cases

#### Consultation after completion of phase II study for drugs

##### Case 10:

We could confirm our decision on appropriate doses from the results of a Ph II study. PMDA gave us advice considering practical usage in the market. Therefore we could put the factors into our protocol. Also, we could confirm the appropriateness for the clinical data package.

##### Case 11:

Regarding the number of Japanese patients in a global study, the proposal from our company was discussed positively, and we could get the advice about setting a practical number of patients, considering the PK data and the safety of the product.

### 3. Utility and successful cases

#### Consultation after completion of phase II study for drugs

##### Case 12:

**We could get consensus about joining a global study.** The data package and issues to be solved before NDA were also confirmed. We got advice about practical details for conducting the global study.

##### Case 13:

**For the bilateral study (China/Japan, II/III), we could get an answer about the number of Japanese patients needed.**

### 3. Utility and successful cases

#### Pre-application consultation for drugs

##### Case 14:

Although the results of Phase III study were not what we expected, **PMDA advised us they fulfilled the requirements for a data package**, considering their characteristics and the results of other studies. Therefore we could file an application without conducting additional studies, and get the approval. If there had been no consultation meeting in Japan, additional studies might have been conducted.

##### Case 15:

We felt the consistency of PMDA's advice, comparing this meeting with the former one for the same project. **We could get appropriate advice about adding information to the CTD.**

##### Case 16:

**We could confirm whether the bridging study was acceptable at the meeting.**

## 4. Summary

- Many companies are utilizing consultation meetings during development, and the satisfaction level is high.
- After discussion within a project team based on information available, issues for consultation are clarified, and a meeting application is made.
- There are many types of consultation meetings available including prior assessment meetings. At each meeting, the issues are discussed based on data submitted beforehand.
- The minutes will be made, and they will be attached to CTD in NDA
- The consultation system is well organized, and the utility is very high as many companies reported successful cases.

**Thank you for your attention**

