Provisional Translation (as of October 2014) *

Outline of Execution Plan of the Pilot Project in FY 2015 (draft)

October 1, 2014

○ Purpose

To confirm that the analysis of the submitted clinical study data for new drugs using introduced software enables the reviewers to obtain the necessary for the review;

To consider the utilization of the analysis results in the new drug review process in the actual review situation;

And to consider the utilization of the electronic clinical study data for conformity inspection.

○ Target studies

1) The pilot conducted under the actual situation of regulatory review using the electronic study data of new drug application submitted during the data receiving period

- CDISC compliant data

  The entire clinical studies package that will be required to be submitted after starting the electronic submissions as shown in the document "Basic Principles on Electronic Submission of Study Data for New Drug Applications" in new drug products (including follow-on biologics) that are submitted to be reviewed in Japan from January 1st to September 30th, 2015 (It would be of great help to receive all studies corresponding to those requirements).

- Data for population PK and/or PK/PD analysis

  Datasets for population PK and/or PK/PD analysis obtained from one or more clinical studies in the same new drug products provided as the clinical data in conformance to CDISC

2) The pilot conducted using the electronic study data except for the data corresponding to item 1

- CDISC compliant data

* This English version of the Japanese Notification is provided for reference purposes only. In the event of any inconsistency between the Japanese original and the English translation, the former shall prevail.

Clinical studies (phases II and III) of new drugs (including follow-on biologics) that include those of Japanese subjects and that are either approved, currently under regulatory review, or scheduled to be reviewed in Japan by December 31st, 2014 or from October 1st, 2015. More than one study per one application.

- Data for population PK and/or PK/PD analysis

  Datasets for population PK and/or PK/PD analysis that include those of Japanese subjects obtained from one or more clinical studies on new drugs (including follow-on biologics) and that are either approved, currently under regulatory review, or scheduled to be reviewed in Japan by December 31st, 2014 or from October 1st, 2015.

○ Period (tentative)

January 2015 – March 2016

Data collection: January – September 2015

Analysis: January 2015 – March 2016

○ Implementation Details

- CDISC compliant data

  - Confirm CDISC conformance of the submitted clinical study data.

  - Confirm that by using the data visualizing/exploratory analysis software, certain study results which are generally reported in application (distribution of background factors, results of primary and secondary efficacy endpoints, occurrence of adverse events, etc.) can be obtained.

  - Confirm that by using the statistical analysis software, the results of primary endpoints and other useful results for the review can be obtained. Confirm the details of the analysis program, if submitted, and conduct analysis based on those details to confirm the results.

  - Examine the extent of analysis feasible in the review process; estimated workload; and utilization of the analysis results in the actual review situation for future review process.

  - Examine exploratorily the utilization of the electronic clinical study data for conformity inspection by checking the electronic data in some clinical studies, which are submitted during this pilot project time, using the data

visualizing/exploratory analysis software. We do not intend to verify the conformity of the submitted data itself.

- Data for population PK and/or PK/PD analysis
  - Confirm by using NONMEM that the primary analysis regarding PK and/or PK/PD which was planned and performed in the clinical trial can be re-analyzed and the results can be obtained based on the information of analysis program.
  - Examine the extent of analysis feasible in the review process; estimated workload; and utilization of the analysis results in the actual review situation for future review process.

○ Persons in charge

Includes persons in charge of the project, reviewers from the reviewing office of each drug product whose clinical study data were submitted and inspectors from office of conformity audit.