Clinical Outcome Assessments (COA) Qualification Program
DDT COA #000018: Pneumonia Patient-Reported Outcome Measure (PNEUMO-PRO)
August 2, 2018 Update

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Attention:
Clinical Outcome Assessments Staff
Office of New Drugs Office of New Drugs
Center for Drug Evaluation and Research
CDER Central Document Room
5901-B Ammendale Road
Beltsville, MD 20705-1266

Subject: Response to FDA Comments on *DDT #000018 Revised psychometric protocol and SAP for the Pneumonia Patient Reported Outcome Measure (PNEUMO-PRO©) for the measurement of community-acquired bacterial pneumonia (CABP) symptoms*

Thank you for your letter of June 20 with feedback regarding the modification of the enrollment window for the PNEUMO-PRO and SKINFECT-PRO validation studies. Please see below for a summary of your comments and our response and request for next steps.

DDT team comments:
Please refer to your June 6, 2018 submission for PNEUMO-PRO© (DDT #000018). We offer comments after conducting a preliminary review of your responses and associated documents. Please note an additional response letter will be sent at a later date containing further comments and recommendations.
At this time, it is not appropriate to expand the enrollment criteria window from 24 to 48 hours. If patients do not begin completing the instrument until the second day of treatment, this may jeopardize the instrument's ability to detect symptom improvement change at day 3-5.
However, we offer the following suggestions for enhancing enrollment:

- *Modify your inclusion criteria from "at least 3 symptoms" to "at least 2 symptoms". This is consistent with FDA's draft guidance Community-Acquired Bacterial Pneumonia: Developing Drugs for Treatment.*
- *Include hospital-acquired bacterial pneumonia (HABP) patients (ex. From screening log-respiratory diagnosis attributed to other source (HAP).*

Additionally, it is acceptable to modify the inclusion criteria to reflect self-report of a fever.

ICONs Response:
Whilst the ICON/FNIH team respect and value the decision of the DDT, the ICON/FNIH team would like to request the opportunity to schedule a meeting with the DDT team to discuss this enrollment window issue further based on the following:

1. **Recommendations from the study funders (FDA-CDER) –** Following the DDT's response, the ICON team and study funders had a meeting on July 16 and follow-up communication on July 25th, 2018 to discuss the issue of the enrollment window. It was advised by Dr. John Farley to promptly request a meeting with the DDT team in order to review the data collected from the first 30 CABP patients and discuss any other potential protocol enhancements.

2. **Feedback from the clinical sites** – Several sites have reported to the ICON team that they are experiencing difficulty recruiting patients and successfully enrolling them into the study within the 24 hour window. Some patients are too sick to be approached within the first 24 hours of treatment and patients who are admitted to hospital during the weekends are not eligible as they do not meet the 24 hour enrollment criteria by the Monday, when site staff are able to engage with them.

3. **Interim data checks –** The ICON team have been conducting interim data checks starting as of June 20, and as of July 16, the clinical sites had enrolled 30 CABP patients in to the PNEUMO-PRO validation study.

As such, the ICON and FNIH team would like to formally request a meeting with the DDT qualification team, with the addition of Dr. Thushi Amini and Dr. John Farley. As part of this meeting, the ICON team would like to present the interim data check results based on the data collected from patients enrolled up to approximately 14 days before a scheduled meeting. This presentation will focus on the improvement of core symptoms over time for each item from baseline, and the association between symptom severity and time between the first dose of antibiotics and the first PNEUMO-PRO questionnaire completion.

The ICON team look forward to your response. Do not hesitate to contact the team should you have any questions.

Kind regards,
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