Clinical Outcome Assessments (COA) Qualification Program
DDT COA #000018: Pneumonia Patient-Reported Outcome Measure (PNEUMO-PRO)
February 3, 2017 Update

I. Introduction

The Foundation for the National Institutes of Health Biomarkers Consortium (FNIH BC) is interested in developing reliable, well-defined and clinically relevant endpoints that measure tangible benefits for patients in clinical trials of antibacterial drugs. FNIH BC identified Community- acquired Bacterial Pneumonia (CABP) as a priority indication, and subsequently developed a candidate list of endpoints for use in clinical trials. As part of this effort, the FNIH BC seeks to develop a patient-reported outcome (PRO) symptom instrument in accordance with the Food and Drug Administration (FDA) PRO guidance used to support labeling claims (FDA PRO guidance, 2009) for use in clinical trials of antibacterial interventions. The intention is that the PRO instrument will be used to identify and assess symptoms related to clinically relevant endpoints for CABP.

The ICON Commercialisation & Outcomes (ICON) Clinical Outcomes Assessments (COA) group is collaborating with the FNIH BC to develop three reliable, well-defined, and clinically relevant PRO symptom instruments, that measure tangible patient benefits of treatment interventions in antibacterial drug clinical trials, one in CABP, one in hospital-acquired bacterial pneumonia (HABP), and one in acute bacterial skin and skin structure infection (ABSSSI). Through a consortium-based approach, the FNIH BC Project Teams, together with ICON COA, have applied symptom related evidence generated from the published literature and results from qualitative, post-treatment interviews to create the current CABP and ABSSSI disease models and conceptual frameworks. This work informed the development of the proposed CABP-specific PRO and ABSSSI-specific PRO instruments for use in future clinical trials of antimicrobial drugs. Using the same approach, work is currently underway to develop a PRO instrument for hospital-acquired bacterial pneumonia.

The FNIH BC has requested the new CABP PRO, ABSSSI PRO, and future HABP PRO instruments be developed according to the FDA qualification process outlined in the FDA Qualification Process for Drug Development Tools Guidance (Qualification Process DDT Guidance, 2014). This protocol details the objectives, methods, and analysis required for ICON to demonstrate the psychometric properties of the CABP PRO in accordance with the FDA PRO guidance, and satisfy the communication and scoping document requirements for the qualification process. A separate protocol has been prepared for ABSSSI and will be developed for HABP in the near future.

II. Project Objectives

The objective of this study is to evaluate the psychometric properties of the new CABP PRO instrument. The psychometric properties of the CABP PRO will be measured in a patient population characterized by a diagnosis of CABP. This project is part of a broader effort between ICON and FNIH BC to support an FDA label claim submission used in clinical trials for anti- bacterial interventions and other studies as appropriate. The psychometric

properties that the study will assess include:

- Item level properties (item variability, item-total correlations, Rasch analyses)
- Domain Structure (Exploratory Factor Analysis (EFA))
- Reliability (internal consistency, test-retest)
- Construct validity (known groups/discriminant, convergent/divergent)
- Ability to detect change
- Responder definition (distribution-based, anchor-based)