Attachment to

Guidance on Qualification Process for Drug Development Tools

Qualification of Exacerbations of Chronic Pulmonary Disease Tool for Measurement of Symptoms of Acute Bacterial Exacerbation of Chronic Bronchitis in Patients With Chronic Obstructive Pulmonary Disease

DRAFT GUIDANCE

This guidance attachment is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 90 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document contact Dr. Elektra Papadopoulos at 301-796-0900.

This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

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Clinical/Medical

Guidance for Industry[1]
Qualification of Exacerbations of Chronic Pulmonary Disease Tool for Measurement of Symptoms of Acute Bacterial Exacerbation of Chronic Bronchitis in Patients With Chronic Obstructive Pulmonary Disease

DDT Type: Clinical outcome assessment (COA)

DDT Tracking Number: DDTCOA-000003

Referenced COA: Exacerbations of Chronic Pulmonary Disease Tool (EXACT)

Type of COA: Patient-reported outcome (PRO)

The Center for Drug Evaluation and Research (CDER) has determined that the EXACT, an electronically administered PRO measure, is qualified as a measure of symptoms of acute bacterial exacerbation of chronic bronchitis in patients with chronic obstructive pulmonary disease (ABECB-COPD) in the context of use described below.

The contact information for public access to the EXACT and its user manual also appears below.

Section I: Concept of Interest

The EXACT total score measures symptoms of ABECB-COPD.

Section II: Context of Use

The EXACT is qualified as a well-defined and reliable measure of symptoms of ABECB-COPD, for use in phase 2 studies. Additional development work is needed to further assess measurement properties over the course of an exacerbation, including ability to detect meaningful change in response to an acute intervention.

At the present time, a responder definition has not been determined to aid interpretation of the clinical meaningfulness of changes observed in clinical study results. When designing confirmatory clinical trials, sponsors should discuss the interpretation of clinically meaningful change with the appropriate CDER review division.

We encourage exploratory analyses to evaluate the EXACT's longitudinal measurement properties and the amount of change in an individual patient that can be considered meaningful for use in the interpretation of effectiveness. We expect that as further experience with the instrument is gained, the qualification statement will be expanded to

[1] This guidance has been prepared by the Office of New Drugs in the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration.

include recommendations for a responder definition or other additional information to aid in interpretation of clinically meaningful change.

A. Study population

Outpatients with acute bacterial exacerbations of chronic bronchitis in patients with COPD who meet the clinical trial entry criteria as described in the guidance for industry *Acute Bacterial Exacerbations of Chronic Bronchitis in Patients With Chronic Obstructive Pulmonary Disease: Developing Antimicrobial Drugs for Treatment*[2]

B. Clinical trial design

Superiority trial

C. Endpoint positioning

The EXACT is currently qualified as an endpoint in phase 2 studies. It is intended for ultimate use as a primary or secondary endpoint in confirmatory clinical trials.

D. Labeling or promotional claim(s) based on the COA

The EXACT is intended to ultimately support labeling claims related to change in ABECB-COPD symptoms.

Section III: COA Interpretation

A responder definition for the targeted patient population is not yet available. FDA recommends that a responder definition be evaluated and identified. When designing confirmatory clinical trials, sponsors should discuss with the appropriate CDER review division how EXACT may be used.

Section IV: Contact Information for Access to the Qualified COA

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Instructions for Use in a Regulatory Submission: Please reference DDT # [DDTCOA-000003] and this guidance in your application.

[2] We update guidances periodically. To make sure you have the most recent version of a guidance, check the FDA Drugs guidance Web page at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.