
Chronic Obstructive Pulmonary Disease: Use of the St. George's Respiratory Questionnaire as a PRO Assessment Tool Guidance for Industry

**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**

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TABLE OF CONTENTS

I.	INTRODUCTION AND BACKGROUND.....	1
II.	CONSIDERATIONS FOR THE SGRQ.....	2
A.	Administration	2
B.	Scoring	2
C.	Method of Analysis	3
D.	Use of the SGRQ	3
	REFERENCES.....	5

Chronic Obstructive Pulmonary Disease: Use of the St. George's Respiratory Questionnaire as a PRO Assessment Tool Guidance for Industry¹

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I. INTRODUCTION AND BACKGROUND

- The purpose of this guidance is to provide information to sponsors developing drugs for the treatment of chronic obstructive pulmonary disease (COPD).² This guidance addresses the use of the St. George's Respiratory Questionnaire (SGRQ), a patient-reported outcome measure (PRO) assessment tool used in interventional clinical trials in patients with COPD.
- The information on SGRQ presented in this guidance was previously provided in an appendix to the draft guidance for industry *Chronic Obstructive Pulmonary Disease: Developing Drugs for Treatment*, which published in May 2016 and was subsequently withdrawn for reasons unrelated to the subject of this guidance.
- In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.
- COPD is a chronic progressive disease caused by chronic inflammation and destruction of the airways and lung parenchyma and is usually associated with tobacco smoking or prolonged exposure to other noxious particles and gases. The term COPD encompasses a

¹ This guidance has been prepared by the Division of Pulmonary, Allergy, and Rheumatology Products in the Center for Drug Evaluation and Research at the Food and Drug Administration. You may submit comments on this guidance at any time. Submit comments to Docket No. FDA-2017-D-6821 (available at <https://www.regulations.gov/docket?D=FDA-2017-D-6821>) (see the instructions for submitting comments in the docket).

² For the purposes of this guidance, all references to *drugs* include both human drugs and therapeutic biological products, including small and large molecule drugs, unless otherwise specified.

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spectrum of pulmonary processes, with chronic bronchitis and emphysema as two clearly defined entities within that spectrum.

- For sponsors conducting clinical trials of drugs to treat COPD, FDA recognizes several categories of outcome measures that may be appropriate to assess efficacy, including PRO measures such as the SGRQ.
- The SGRQ measures health status in patients with obstructive airway diseases such as COPD.

II. CONSIDERATIONS FOR THE SGRQ

- The SGRQ is available in several versions. Up-to-date information, versions, translations, and manuals for each version can be found on the developer's instrument website.³ This up-to-date information refers specifically to the version available as of 2018 at the time of publication of this document. The original SGRQ is a 50-item instrument (questionnaire) with weighted responses. There are several versions of the 50-item instrument, each with a different recall period: 1 year, 3 months, or 4 weeks.
- As of March 2016, only the 3-month and 4-week recall versions were available from the developer.⁴ The shorter 40-item COPD-specific version, SGRQ-C, does not have a defined recall period. Not all versions have equivalent validation information.⁵

A. Administration

- The SGRQ is self-administered by the patient and the investigator should score the SGRQ in accordance with current manuals, as appropriate.
- Versions in languages other than English should undergo linguistic and cultural validation for all languages and cultures in which the sponsor conducts the studies.
- The SGRQ can be administered using a paper or electronic platform, provided the latter development has followed accepted procedures (Coons et al. 2009).

B. Scoring

- The SGRQ total score is made up of three components: (1) symptoms — frequency and severity of symptoms; (2) activity — effect of disease on common daily physical

³ See the St. George's University of London Health Status Research website at <http://www.healthstatus.sgu.ac.uk/>.

⁴ Ibid.

⁵ Throughout this guidance, the term *SGRQ* refers to the 50-item, 3-month or 4-week recall version or the 40-item SGRQ-C version, unless otherwise specified.

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activities; and (3) impacts — psychosocial effects of the disease. In the context of this guidance, sponsors should only use the total score.

- When using one or more individual domains as a measure in clinical trials, a sponsor should discuss this with the review division.
- The minimum clinically important difference for the total score between patients and within-patient has been determined to be at least 4 units on the SGRQ scale (Jones 2002; Jones 2005). For the FDA, no evidence exists to support the use of other values.

C. Method of Analysis

- Responder analysis is the FDA's preferred primary method for reporting results from SGRQ data. This analysis compares patients who improve with patients who deteriorate or do not change. A sponsor can present responder analyses as the responder rate for each arm and the difference in the responder rates, or the odds ratio. Other analyses may be appropriate, and the sponsor should discuss these with the review division.
- Because the time course of SGRQ responses can provide useful information, frequent measurements (e.g., once a month)⁶ during a clinical trial are appropriate. Because treatment effect may be slow in onset, in shorter trials (such as those of 6 months or less), an average estimate over the trial period may underestimate the benefit with chronic therapy; end-of-treatment measurements may provide a more accurate estimate of the benefit from chronic therapies. In longer trials, taking an average over the latter part of the trial period, such as over the last 3 months, may be appropriate.
- At the study design phase, a sponsor should consider missing data and their plan to adequately address the missing data in the analysis. A sponsor should consider that an absent SGRQ score caused by patient withdrawal may not be missing at random. During the protocol development phase, a sponsor should discuss with the review division methods of addressing missing data.

D. Use of the SGRQ

- A sponsor can obtain scores from the SGRQ either using the SGRQ or the shorter SGRQ-C. For the FDA, both versions are acceptable in COPD trials. However, within the same drug development program, or at least within the same trial, the sponsor should use only one version (i.e., the SGRQ or the SGRQ-C).
- A sponsor can use the SGRQ as a PRO assessment of efficacy in submissions to investigational new drug applications, new drug applications, and biologics license applications. A sponsor should discuss with the review division the use of the SGRQ for stratification or enrichment purposes early in the protocol development phase.

⁶ This is applicable to SGRQ-C, which does not have a specific recall period, and the version of the SGRQ with a 4-week recall period, but this is not applicable to the version of the SGRQ that has a 3-month recall period.

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- A sponsor can use the SGRQ as a coprimary endpoint⁷ or as a secondary endpoint providing supporting evidence of efficacy in a clinical trial. For example, a sponsor can consider the use of SGRQ as a coprimary endpoint, along with another measure of efficacy (such as measure of lung function), in a trial with a drug that has a relatively small effect on a single outcome measure (such as lung function), which may become more clinically convincing through corroboration by SGRQ data.
- In general, FDA considers SGRQ information to be clinically important, and a sponsor should report the data obtained in clinical trials irrespective of the direction of the results.

⁷ Multiple primary endpoints become coprimary endpoints when it is necessary to demonstrate an effect on each of the endpoints to conclude that a drug is effective.

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