Guidance document for the Use of Patient Reported Outcomes in Advertising

January 2013

Patient Reported Outcomes Checklist

Item No	Checklist Item (clients can use this tool to help make decisions regarding use of PRO data in advertising claims)	√
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Definition:
A patient reported outcome (PRO) is defined as a measurement based on a report that comes directly from the patient (i.e. the study subject in a clinical trial). A PRO can be measured by self-report or by interview. Examples of PROs include health-related quality of life and functional impairment measures. Similarly, there exist proxy-reported outcomes, which are derived from information from parents, providers or caregivers about their perceptions of how a patient is feeling.

1. Key Benefits:
PROs can provide additional information that may be helpful and of interest to the clinician (i.e. the patient perspective). Clinical outcomes don’t always relate to how the patient feels.

2. Key Pitfalls:
Reporting of PROs from clinical trials tend to be poor and prone to bias.

3. Managing pitfalls:
The following checklist provides 9 helpful principles to guide industry and the PAAB staff in determining whether a PRO presentation may appear within advertising/promotional systems (APS). The checklist relates only to factors specific to PRO endpoints. Refer to the PAAB code for general factors relating to acceptability of a study.

□ 3.1 Consistency with Terms of Market Authorization

Principles:
Drug advertising should be consistent with the Health Canada approved Terms of Market Authorization (TMA).

Rationale:
Advertising content which is inconsistent with the TMA would contravene section 9.1 of the Food and Drugs Act.

Application:
The observation must not contradict anything in the TMA (with respect to magnitude, direction, or duration). Claims relating to PRO endpoints must appear clearly within the context of the Health Canada approved indication.

□ 3.2 Requirement for blinding

Principles:
PRO measurements must be based on high-level, well-designed and well-controlled evidence.

Rationale:
PROs are subjective measurements; therefore the study must be blinded in order to minimize bias.

Application:
PRO measurements should be conducted in a blinded study design.

□ 3.3 Reliable and valid endpoint

Principle:
Where an endpoint which is not in the TMA relates to a scale, a questionnaire or some other similar instrument, that instrument must be reliable and valid and available to competitors to use in their trials.

Rationale:
The outcome is only as valid/reliable as the instrument used to derive it.
The degree to which an outcome is affected by a drug versus other factors is important for decision making.

Application:
The PRO endpoint should be widely accepted as a measurement of drug outcomes in that specific patient group or condition. This may be supported by showing that the endpoint is discussed in at least one of the following:

- a TMA within the therapeutic area (not required to be the sponsor's TMA)
- consensus guidelines
- an authoritative medical text
- multiple peer-reviewed trials including at least one competitor's trial.

For example, instruments designed by the manufacturer will not be considered unless this principle can be adhered to.

□ 3.4 Pre-defined Endpoints

Principle:
Claims should be based on assessments which were designed to measure the observed outcomes.

Rationale:
To minimize measurement biases.

Application:
The PRO endpoint must be pre-defined in the study protocol.

□ 3.5 In cases where PRO is not the primary outcome: Consistency with the primary endpoint

Principle:
A PRO endpoint cannot salvage a failed study.

Rationale:
The study is powered to assess the primary endpoint.

Application:
Within the study itself, the PRO endpoint must be directionally consistent with the primary endpoint. Note however that the PAAB may require disclosure of other failed secondary endpoints to balance claims based on primary endpoints in order to avoid overly selective presentations (see 3.8 below).

□ 3.6 Requirements for highlighting specific domains/items comprising the PRO instrument

Principle:
Claims may not highlight specific domains/items comprising the PRO instrument unless there is pre-defined statistical analysis for the specific domains/items.

Rationale:
To be considered evidence for claims, results must achieve statistical significance.

Application:
If the PRO instrument is a composite endpoint or is comprised of individual domains/items, claims for the individual domains/items must have statistical significance. Note that all of the items can be presented with statistical analysis for each item. The domains/items presentation should not be overly selective (see also 3.8 below).

In cases where there is no statistical analysis for the individual domains/items, a non-promotional description of the PRO instrument may be considered, similar to the context of a study design parameter. The presentation must be complete and there should be no emphasis on a particular domain/item.

□ 3.7 Considerations for claims relating to “clinically meaningful”

Principle:
Thresholds for claims similar to “clinically meaningful” must be established a priori within the published paper or based on consensus guidelines and/or authoritative textbooks.

Rationale:
Such claims attribute further meaning or importance to the result which must be pre-defined and/or validated.

Application:
- The specific terminology (e.g. “clinically meaningful”, “clinically relevant”, etc.) must appear within the body copy and the definition should be disclosed (this may appear in the study parameters or footnote).

□ 3.8 No cherry-picking in PROs

Principle:
Presentations should not be overly selective.

Rationale:
Emphasizing only positive findings does not promote an element of trust.

Application:
The sponsor cannot only present positive aspects of PROs and ignore negative or non-significant findings.
Claims for PRO domains/items must be directionally consistent with the overall PRO total/composite score to be considered. Additionally, the domain or subscale must be identified as a component of the overall measurement tool within the claim.

For example, if a select domain/item of a PRO was statistically significant but the total or composite score was not, a claim for the PRO would not be acceptable.

Note that a claim for the total PRO score does not require discussion of the individual domains/items.

□ 3.9 The presentation should identify that the PRO endpoint is not an approved indication

Principle:
The presentation must not mislead.

Rationale:
The reader may mistakenly interpret that this is an approved indication.

Application:
The PRO endpoint must appear clearly within the context of the Health Canada approved indication.