



Guidance Document for
The Use of Secondary Endpoints
In Advertising

February 2013

Secondary Endpoints Checklist

Item No	Checklist Item (clients can use this tool to help make decisions regarding use of secondary endpoint data in advertising claims)	√
Considerations		
3.1	Consistency with Terms of Market Authorization	
3.2	Reliable and valid endpoint	
3.3	Predefined Endpoints	
3.4	Consistency with the primary endpoint	
3.5	No cherry-picking	
3.6	The claim should identify that the presentation relates to a secondary endpoint	

1. **Key Benefits:**

Information in addition to the primary endpoint may be of interest to the clinician.

2. **Key Pitfalls:**

Although these additional endpoints may be of interest, they may be more prone to bias because the study is not specifically powered to assess them.

3. **Managing pitfalls:**

The following checklist provides 6 helpful principles to guide industry and the PAAB staff in determining whether a secondary endpoint presentation may appear within advertising/promotional systems (APS). The checklist relates only to factors specific to secondary 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 secondary endpoints must appear downstream from prominent presentation of the relevant Health Canada approved indication (i.e. disclosure of the indicated outcome).

□ 3.2 Reliable and valid endpoint

Principle:

Where the endpoint is not in the TMA, the instrument must be reliable, valid and available to competitors to use in their trials. For surrogate outcomes, there must be evidence demonstrating that changes in a surrogate outcome are predictive of similar changes in final outcomes.

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:

A secondary outcome should be widely accepted as a measurement of drug outcomes in that specific patient group and 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.

□ 3.3 Predefined Endpoints

Principle:

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

Rationale:

To minimize measurement biases.

Application:

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

□ 3.4 Consistency with the primary endpoint

Principle:

A secondary endpoint cannot salvage a failed study.

Rationale:

The study is powered to assess the primary endpoint.

Application:

Within the study itself, the secondary endpoint must be directionally consistent with the primary endpoint in order to be used as support for claims of benefit. Note however that the PAAB may require disclosure of failed secondary endpoints to balance claims based on primary endpoints in order to avoid overly selective presentations (see 3.5 below).

□ 3.5 No cherry-picking

Principle:

Presentations should not be overly selective.

Rationale:

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

Application:

The sponsor cannot selectively present positive secondary endpoints and ignore negative secondary endpoints.

There is no need to disclaim failed secondary endpoints when only the primary endpoint is promoted (except for particularly related secondary endpoints).

Examples of scenarios where a secondary endpoint would be considered to be particularly related to the primary endpoint include:

- *Primary endpoint = diastolic blood pressure, Secondary endpoint = systolic blood pressure*
- *Primary endpoint = composite of incidence of either death or stroke, Secondary endpoints = incidence of death along with and a separate endpoint for incidence of stroke*

□ 3.6 The claim should identify that the presentation relates to a secondary endpoint

Principle:

The claim must not mislead.

Rationale:

The reader may mistakenly interpret that this is a primary endpoint.

Application:

The APS must clearly identify that this is a secondary endpoint (i.e. within the claim, not a footnote).