# Acceptability of the active comparator used in global development when used in HTA submissions across seven jurisdictions

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## Introduction

- Requirements for clinical evidence for the safety and efficacy of a new medicine versus a placebo are being supplanted by a growing interest from regulatory agencies in requesting or undertaking a relative efficacy evaluation.
- HTA agencies assess the relative effectiveness of new medicines to ascertain the added therapeutic value of a new product compared with existing treatments or standard of care.
- Therefore, it is important for companies to choose the right active comparators in the development phase to ensure the scientific validity of trial designs and to be able to provide the evidence for the value proposition of a new product.
- However, while a company may have only one global development plan with one consolidated data package, there are multiple HTA agencies considering the submission package for pricing and reimbursement decisions, each with diverging evidentiary needs and local standards of care.
- What must be determined is whether companies' global development comparator choices meet these divergent local jurisdiction evidentiary requirements.

## Objectives

- Investigate the inclusion of active comparators in the global development of new medicines and the acceptance of comparator choice by HTA agencies across seven diverse jurisdictions

## Methods

- Data for 54 compounds collected directly from eight major pharmaceutical companies were studied to determine if active comparators were included in global development and the acceptance of the comparator by HTA agencies in Australia, Canada, England, France, Germany, Spain and Italy.
- The time of the first regulatory approval of the products ranged from October 2007 to July 2015.
- A comparative analysis was conducted to assess the extent of acceptance (fully, partially, not accepted) of the global comparator by HTA agencies as well as whether additional comparators were required by the HTA agencies for assessment and the rationale for those additional requirements.

## Results

- Fifty four percent of the 54 compounds studied were assessed against an active comparator during global development
- The full acceptance of the comparator used in global trials varied at the jurisdictional level from 31% for Australia to 71% for Italy and Canada (Figure 1).
- All HTA agencies in the study required additional comparators to be included for review for one or more submissions (Figure 2).
- Linkages between the acceptance of the global comparator and local requirements were explored (Figure 3). Australia and England had the highest percentage (50% and 33% respectively) of product reviews that included partial acceptance of a global comparator and requirements for an additional comparator for local assessment.
- Germany rejected the highest proportion of submissions (17%), based on the global comparator choice with requests for a local relevant comparator.

## Conclusions

- Good acceptance ( e.g. full acceptance >60% of submissions in four of seven jurisdictions) of the comparator used in the global clinical trials at the jurisdictional level was identified.
- The key reason for additional comparators was the jurisdictions' need for a local relevant comparator, which does emphasise that divergence in standard of care across jurisdictions needs to be considered for local submissions (Figure 4).
- Early dialogue with HTA agencies during development and prior to HTA submission can help identify the most relevant comparators to meet both global regulatory and local HTA needs.

**Figure 1: Percentage of submissions for which the global comparator choice was fully accepted by HTA agencies**

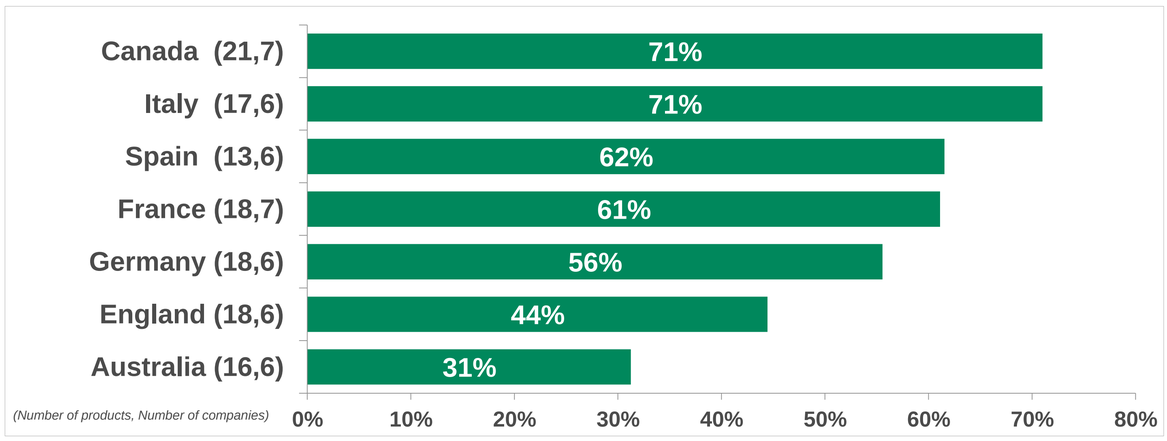


**Figure 2: Percentage of submissions that included requests for additional comparators for review by HTA agencies**

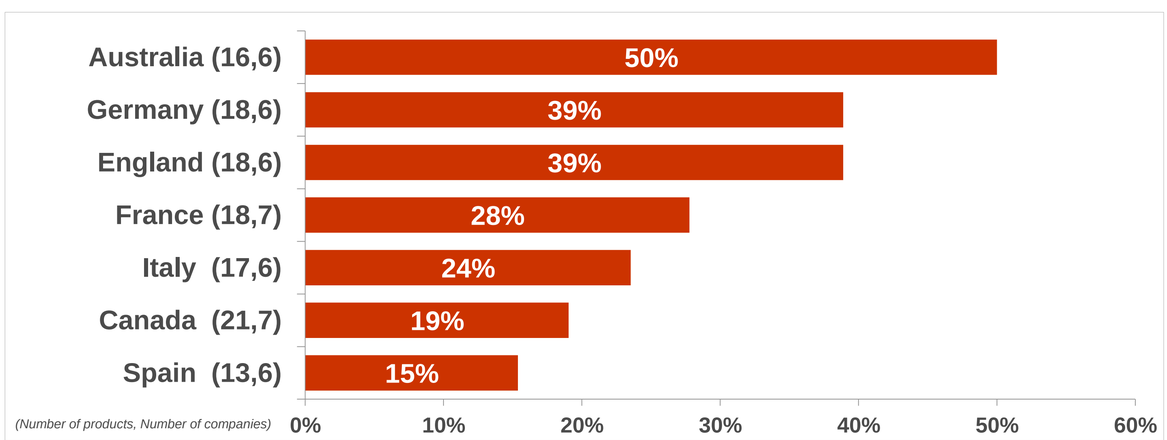


**Figure 3: Link between global comparator acceptance and requirement for additional comparator (percentage of total submissions)**

| Acceptance | Fully | Partially | Partially | Not accepted | Not accepted | No comparator included in global trial | No comparator included in global trial |
|---|---|---|---|---|---|---|---|
| **Additional comparator required** | No | No | Yes | No | Yes | No | Yes |
| **Australia** | 31% | 13% | 50% | | | 6% | |
| **Canada** | 71% | | 14% | | | 10% | 5% |
| **England** | 44% | 11% | 33% | | | 6% | 6% |
| **France** | 61% | 6% | 11% | | 11% | 6% | 6% |
| **Germany** | 56% | | 11% | | 17% | 6% | 11% |
| **Italy** | 71% | | 12% | 6% | 6% | | 6% |
| **Spain** | 62% | 15% | 8% | 8% | | | 8% |

**Figure 4: Rationale for requesting additional comparators**


## Bibliography

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