

INTRODUCTION

- In France, the Economic and Public Health Assessment Committee (CEESP) issues an initial opinion on the cost-effectiveness of a drug or medical technology.
- During the **contradictory phase (CP)**, manufacturers may challenge conclusions of the draft opinion through written observations or a hearing with the CEESP, before the final version of the economic opinion is sent to the Economic Committee for Health Products (CEPS).
- While manufacturers cannot present further evidence, they may challenge methodological reservations, or a conclusion of major global uncertainty, as well as request revisions of statements and data based on available data and results.

OBJECTIVES

- Our aim was to review and analyse the outcomes of recent contradictory phases in the context of CEESP economic appraisals in order to understand when manufacturers requested changes, and in which cases the CEESP changed the level of methodological reservation or conclusion of major global uncertainty in the final opinion.

METHODS

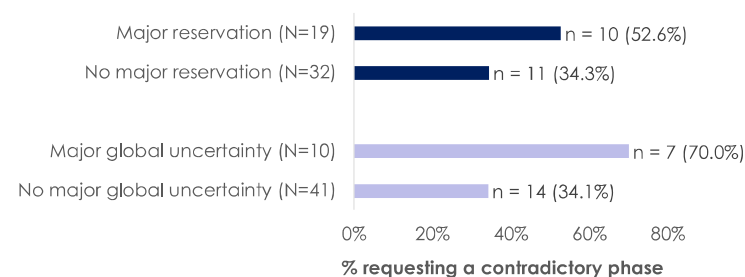
- We conducted a **comprehensive review** of all economic opinions published by the CEESP over the last two years, since January 2022.
- This involved a detailed **examination of each opinion and transcript of CEESP hearings** to identify cases when manufacturers challenged levels of reservations or labels of global major uncertainty.
- The goal was to identify common patterns, determine the frequency of important change requests, and whether changes to opinions were granted.
- Specifically, we sought to determine whether these led to the addition or removal of important reservations and the reasons associated to these decisions. Changes to wording only of reservations or conclusions were not extracted.

RESULTS

Overview of appraisals in which a contradictory phase was requested

- 51 economic opinions were reviewed over the study period. Among these, 21 (41.2%) included contradictory phases.
- Appraisals including at least one major methodological reservation or a label of major global uncertainty more frequently requested changes leading to contradictory phases (Figure 1).

Figure 1. Characteristics of opinions requesting contradictory phases



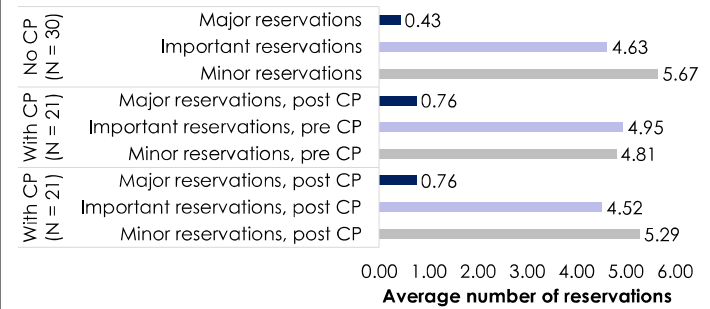
Reassessment of reservations or global major uncertainty

- Throughout the studied period, no contradictory phase led to the requalification of any major reservation or the removal of major global uncertainty.

RESULTS

- **Seven exchanges (29%)** resulted in the **removal of 10 important methodological reservations**, and one (5%) led to the addition of an important reservation due to the inclusion of an additional analysis requested by the manufacturer.
- Opinions that included a requalification had, on average, a higher number of important reservations in the initial draft opinion compared to other opinions.

Figure 2. Impact of contradictory phase on average number of methodological reservations



- Within the 7 contradictory phases that led to requalification of important reservations to minor reservations:
 - One manufacturer was present during the audition while the others provided written observations only
 - 3 requalifications were related to the budget impact analysis,^{2,3} while the 7 others were related to the cost-effectiveness analysis^{4,5,6,7}
 - 3 were for COVID-19, 3 for cancer-type diseases and one for a rare genetic disease
- In cases of requalification, manufacturers frequently highlighted the minimal impact of the methodological choice or parameter uncertainty on results, using previously presented sensitivity analyses to argue for the requalification:
 - Two demonstrated choices were in fact conservative
 - In four cases, manufacturers demonstrated that the analyses presented were indeed in line with guidelines and what had initially been requested, in particular regarding sensitivity analyses
 - In three cases, the manufacturer argued that the methodological choice had little impact on results based on results of sensitivity analyses

CONCLUSIONS

- Although contradictory phases are often driven by major methodological reservations or characterized major uncertainty, **manufacturer arguments did not lead to the requalification of these aspects.**
- The CEESP reconsidered the level of some important reservations, indicating a **selective impact of contradictory phases.**

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