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HPR132

A Factual Check That Cannot Reach the Reasoning: The Factual-Accuracy Paradox

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BACKGROUND

Tovorafenib, an orphan medicine with conditional European marketing authorisation for BRAF-altered paediatric low-grade glioma (pLGG) after at least one prior systemic therapy, was the subject of the first published JCA (JCA-MP-2024-06; endorsed 30 April 2026).[1] Its pivotal evidence was a single-arm phase 2 study (FIREFLY-1 trial).[2]

Before adoption, the developer may "signal any purely technical or factual inaccuracies" in the draft reports but "shall not provide any comments on the results of the draft assessment" (Art. 11(5) HTAR),[3] within 7 days, or 5 days in specified cases such as accelerated assessment (Art. 14(4) IR 2024/1381).[4]

Where a disputed point is both factual and methodological, it is unclear what this review right can reach.

OBJECTIVE

To examine where the factual-accuracy stage of the tovorafenib JCA drew the line between correcting facts and contesting the assessors' methodological reasoning.

METHODS

Procedural case analysis of the published JCA report (v1.0)[1] and its official factual-accuracy annex (9 June 2026),[5] read against the HTAR, IR 2024/1381 and HTACG procedural guidance.[4,6]

1	**Extract rules** HTAR, IR and HTACG rules on the factual-accuracy check
2	**Code** Each of the 31 annex comments tallied by the assessors' published response code (Figure 1)
3	**Trace** PV/EM items traced to the final report to check whether its wording changed
4	**Classify** Factual vs methodological content of the disputed items

Figure 1. The legal limit on developer comments and the assessors' three response codes[3,5]

Legal limit (Art. 11(5) HTAR)
"The health technology developer shall not provide any comments on the results of the draft assessment."

Code 1	Code 2	Code 3
"1. Corrected"	"2. Outside the scope of the factual accuracy check"	"3. Information in the dossier that the HTD classified as incorrect during the factual accuracy check. No changes made"

Abbreviations: Art., Article; **HTAR,** Health Technology Assessment Regulation; **HTD,** health technology developer.

RESULTS

Rules: HTACG guidance limits comments to "fact-related typos/mistakes (e.g., numbers)".[6]

Distribution: the annex lists 31 comments with 32 coded replies (one row carries two codes): 5 corrected, 23 outside the scope of the check and 4 dossier errors with no changes made (Figure 2). Replies are codes only, without reasons.[5]

Corrections included one PV/EM-related item on missing baseline covariate data (draft p. 62). The check could correct this PV/EM fact, but not the judgement built on it.

Dossier errors flagged by the developer, e.g., prior-radiotherapy adjustment of PFS, were not acted on; the report states they have "no effect on the estimates of relative effectiveness and safety" (p. 14).

Key dispute (Figure 3): the report found it "not possible to establish whether the identification process was comprehensive" (p. 56) and linked residual confounding to "shortcomings in the HTD's confounder identification process" (p. 77). The developer replied that the process followed HTACG guidance and that only two further comparator variables were available, neither identified as a PV/EM by clinical experts. The reply was coded outside scope; the sentence is unchanged in the published report. The disputed PV/EM finding is carried into the summary report as a stated source of residual confounding for all MAIC estimates (summary report p. 13), alongside small effective sample size.[7]

A defence of the choice of MAIC over STC (draft p. 53) was likewise coded outside scope.

Figure 2. Distribution of response codes (32 coded replies to 31 comments)[5]

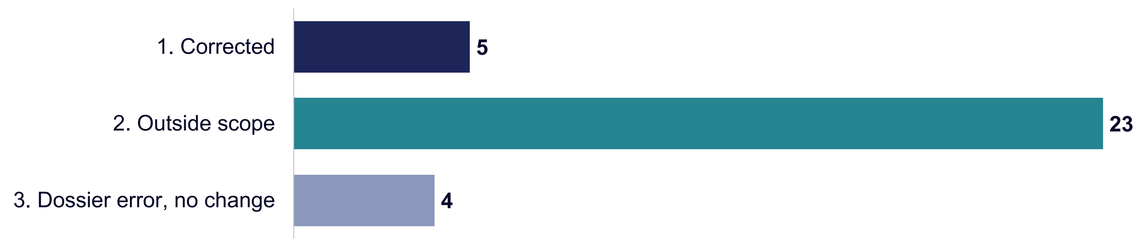
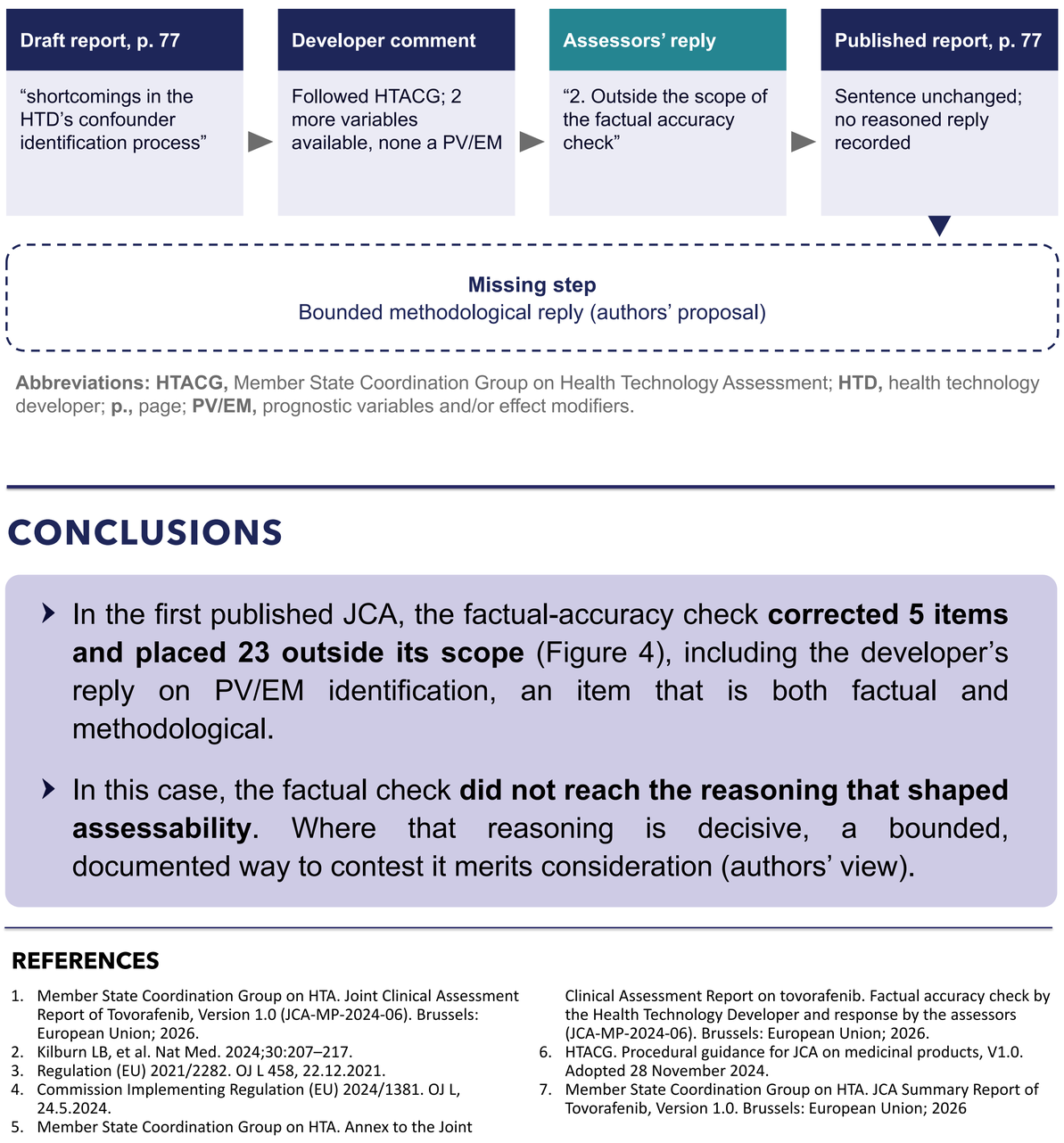


Figure 3. The PV/EM dispute: from draft statement to unchanged published text[1,5]



Abbreviations: HTACG, Member State Coordination Group on Health Technology Assessment; **HTD,** health technology developer; **p.,** page; **PV/EM,** prognostic variables and/or effect modifiers.

Figure 4. Key numbers: 23 of 32 coded replies fell outside the scope of the factual-accuracy check

23 of 32	5 of 32	4 of 32
coded replies: outside the scope of the check	coded replies: corrected in the report	coded replies: dossier errors, no change made

IMPLICATIONS

Mixed items fall outside the check: the PV/EM item combines a fact with a judgement, and its factual part received a code, not a reasoned answer.

Developers: document the PV/EM identification process fully in the dossier; within this stage there is no documented route to test the assessors' methodological reasoning. Commission review (HTAR Art. 28(d)[3]) checks procedure only; errata cover factual errors only.

HTA bodies and policymakers: introduce a bounded, documented reply to methodological points that rest on facts, without reopening the assessment.

Limitation: *this is a single case (one JCA and its published annex). We saw the developer's position only through its written comments and could not test whether a reasoned reply would have changed the report.*

CONCLUSIONS

- In the first published JCA, the factual-accuracy check **corrected 5 items and placed 23 outside its scope** (Figure 4), including the developer's reply on PV/EM identification, an item that is both factual and methodological.
- In this case, the factual check **did not reach the reasoning that shaped assessability**. Where that reasoning is decisive, a bounded, documented way to contest it merits consideration (authors' view).

REFERENCES

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3. Regulation (EU) 2021/2282. OJ L 458, 22.12.2021.
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5. Member State Coordination Group on HTA. Annex to the Joint Clinical Assessment Report on tovorafenib. Factual accuracy check by the Health Technology Developer and response by the assessors (JCA-MP-2024-06). Brussels: European Union; 2026.
6. HTACG. Procedural guidance for JCA on medicinal products, V1.0. Adopted 28 November 2024.
7. Member State Coordination Group on HTA. JCA Summary Report of Tovorafenib, Version 1.0. Brussels: European Union; 2026

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