EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Executive Director

Letter of Support for an Acceptability Score Test in relative acceptability testing for oral medicines in children under 12 years of age

On 10/03/2022, the Applicant Clinsearch requested a follow up qualification advice for their Acceptability Score Test pursuant to Article 57(1)(n) of Regulation (EC) 726/2004 of the European Parliament and of the Council. On 12/01/2023, the SAWP agreed on the advice to be given to the Applicant. On 26/01/2023, the CHMP adopted the advice to be given to the Applicant.

The Letter of Support is issued on the basis of this qualification advice.

The ClinSearch Acceptability Score Test (CAST) is intended to be used to score the acceptability of oral medicines in children under 12 years of age.

The CAST is a data driven approach based on a large set of real-life observer-reported outcomes collected for many medicine intakes in paediatric subjects. Each evaluation combined several observed behaviours (e.g. required dose intake, time needed, patient reaction, use of food/drink to mask a bitter taste, crushing a tablet which cannot be swallowed) to reflect the ability and willingness of patients and caregivers to use (preparing and administering) medicines as intended. Subsequently, multivariate data analysis—mapping and clustering processes—mined the large set of data in order to summarise the key information into an intelligible model: a three-dimensional map (3D-map) juxtaposing two distinct acceptability profiles, "Positively accepted" and "Negatively accepted". This acceptability reference framework aims to permit standardised acceptability evaluation with any medicine assessed using the standardised questionnaire, then positioned on the map and assigned an acceptability profile.

The attempt to concretise and quantify the “catch-all” concept acceptability is highly appreciated. The reference framework potentially permits a standardised and *relative* evaluation of acceptability of oral medicines in children under 12 years of age, as supportive information. A medicine can be assessed by the standardised questionnaire, positioned on the map and assigned an acceptability profile that can be compared to reference medicines likewise positioned on the map.

CAST has been applied to a dataset independent from the original dataset used for development, while at the same time being further developed. Nevertheless, prospective replication of findings in an independent and representative data set is needed. For regulatory purposes this is required to ensure

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that the end result is reproducible (over time, settings and users), and reliable at the level of final scoring. Further, the broad 'setting-less' context of use needs more substantiation.

From a clinical perspective, the CAST score per se does not allow a direct interpretation of what drives the multi-faceted concept of acceptability. Therefore, the different components of the score should be provided with the summary score. For an anticipated claim of better acceptability of one product over the other this should be clear.

In this context, further experience of the CAST score in clinical development plans, including replication of findings, and more insights into the difference in CAST scores between products, to address outstanding issues will be welcomed.

Yours sincerely,

Emer Cooke

Executive Director