

**DRUG DEVELOPMENT TOOL
LETTER OF INTENT DETERMINATION
DDT COA #000116**

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Dear Drs Paller and Lai:

We have completed our review of the Letter of Intent (LOI) for Drug Development Tool (DDT) COA #000116 received on November 20, 2020 by the CDER Clinical Outcome Assessments (COA) Qualification Program, submitted under section 507 of the Federal Food, Drug, and Cosmetic Act.

The LOI is for the PROMIS Itch Questionnaire – Children Impact (PIQ-C-Impact) which includes both patient-reported outcome (PRO) and observer-reported outcome (ObsRO) instruments, proposed for the assessment of the impacts upon itch on children’s daily living. The proposed context of use is to derive a secondary endpoint measure(s) for use in clinical trials for therapeutics for itch.

FDA has completed review of your LOI and has determined that we are unable to accept your LOI at this time. We do not see a drug development need for a secondary endpoint in clinical trials assessing itch-related impacts in the pediatric population. At this time, there is a need to first identify a pediatric measure (for children less than 12 years of age) for evaluating itch severity for primary endpoint evaluation, as opposed to impact of itch.

In reviewing the PIQ-C-Impact, we have the following comments regarding items included in the item bank:

- a. Some of the concepts being measured appear to be too broad (e.g. PIQC01 “could not do some activities”) and/or might be influenced by factors beyond the treatment (PIQC29 “felt depressed”, PIQC49 “felt frustrated”), and consequently not sensitive to treatment effect.

- b. Some of the items may not be understood (e.g. PIQC29 “felt depressed”, PIQC49 “felt frustrated”, PIQC43 “sleep was restless”) or considered relevant by all children (e.g., PIQC04 “hard to read a book”, PIQC39 “hard to do sports”).
- c. Some of the items appear to lack clinical relevance (e.g., PIQC02 “hard to run”, PIQC45 “hard to wear shorts”).
- d. Some of the concepts being measured in the ObsRO version appear to be proxy-reported outcomes (e.g., PIQC48 “my child was angry”, PIQC29 “my child was depressed”). Proxy-reported outcome instruments are discouraged when measuring concepts that are only known by the patient because they do not necessarily reflect how patients feel and function in daily life. We recommend including items that are observable by a parent or caregiver.
- e. A 7-day recall period may not be well understood in children less than 12 years of age.

We do not agree with a broad context of use for “cutaneous disorders such as atopic dermatitis, ichthyosis, epidermolysis bullosa, and other skin disorders.” We still have concerns that the presentation of itch may differ across these diseases. Therefore, we recommend narrowing the context of use to a specific dermatological condition, preferably atopic dermatitis.

Please contact the CDER COA Qualification Program at COADDTQualification@fda.hhs.gov should you have any questions (refer to DDT COA #000116). We would welcome a teleconference to further discuss this response letter and ways to address gaps related to pediatric itch measurement for drug development.

Sincerely,

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