DRUG DEVELOPMENT TOOL
LETTER OF INTENT DETERMINATION
DDT COA #000120

Steve Xu, MD
1900 Greenwood St., Unit 8
Evanston IL 60201

Dear Dr. Xu:

We have completed our review of the Letter of Intent (LOI) for Drug Development Tool (DDT) COA #000120 received on August 19, 2019 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 Scratch Sensor, a Digital Health Technology (DHT) COA, proposed for the assessment of itch related behavior in patients ≥ 2 years of age or older with mild, moderate, or severe atopic dermatitis.

FDA has agreed to accept your LOI into the CDER COA Qualification Program. Please refer to our general comments below for advice on the Scratch Sensor as you continue to develop this drug development tool.

General Comments

In preparing to submit a Qualification Plan (QP), please ensure that the QP submission addresses the scientific issues and the recommendations outlined below.

Comments regarding the concept of interest:

1. Obtain input from atopic dermatitis patients and/or caregivers to determine what is the most meaningful measure of scratch (e.g., scratch time, scratch events, and scratch intensity) from the sensor device. Consider also working with patient advocacy groups to gather meaningful patient data. You may use other sources of patient experience data such as the Voice of the Patient report from the Patient Focused Drug Development (PFDD) for Atopic Dermatitis meeting, when available.

2. Explore the difference between nighttime vs. daytime scratching as scratching behavior may be affected by certain factors during sleep.

3. Plan to examine the relationship between scratching behavior and itch. There is concern that some patients may have a higher tolerability to itch (e.g., some

patients may have more self-control than others which may result in less scratching, but the itch intensity is unaltered).

4. Provide evidence to support that the proposed scratch outputs (i.e., scratch time, scratch events, scratch intensity) measure the intended concept. Additionally, provide more details on how you are defining scratch intensity (e.g., the scratch rate, the depth of scratch). It is unclear how sensor displacement correlates with scratch intensity.

Comments regarding the device:

5. It appears that your algorithm was trained and validated using only 8 subjects. It is unclear how this small sample size will provide assurance that the algorithm is adequately trained and validated. Provide scientific rationale for your training and validation sample size.

6. You state that "the scratch detection algorithm uses two separate convolutional neural network long short-term memory (CNN-LSTM) models, one for the 205 Hz x, y, z-axis accelerometer data, and one for the 1600 Hz z-axis accelerometer data."
    a. Provide a description of how the scratch detection algorithm operates (e.g., process flow diagram).
    b. It appears that sampling will be done only at two specific frequencies. However, elsewhere in your submission, you state that the accelerometer output is sampled from 0-1600 Hz. In your future submission, explain why 205 Hz and 1600 Hz were selected for your algorithm.

7. You state that "patients will be surveyed for device usability and software ease of use via the Systems Usability Index®, a well-established tool to assess the complexity of technology." However, it is not clear how the patient is intended to interact with the app (i.e., what tasks the patient is expected to perform). In your future submission, clarify the critical tasks that patients are expected to perform with respect to the app. In addition, address the usability considerations outlined in our human factors guidance: https://www.fda.gov/media/80481/download. Plan to also assess feasibility of the use of this device in infants and younger children (e.g., will the device stay in position/place without intentional/unintentional removal from the patient?).

8. The ADAM device is battery-operated and rechargeable. In your future submission, provide information to demonstrate electrical safety per IEC 60601-1 and electromagnetic compatibility per IEC 60601-1-2:2014. Additionally, the battery life of 24 hours for the ADAM device may be too short to capture important continuous data as data cannot be collected while charging. This may also lead to lower compliance of device usage for patients due to the daily burden of charging the device. Explore increasing the battery life to at least 1 week of continuous use, or potentially utilizing a separate device for daytime and another for nighttime.

9. You propose to evaluate the ADAM device in a clinical study with 20 patients. We recommend increasing the sample size of your study to increase the power and reliability of the data.

10. The ADAM device appears to be embedded within a flexible rubber-like material and coated on one side with an adhesive polymer called STRATAGEL. In your future submission, provide the following information:
    c. Identify the flexible rubber-like material.
    d. Clarify if STRATAGEL has been cleared or approved in any premarket submission.
    e. Provide information to demonstrate biocompatibility of all patient-contacting device components in accordance with the following guidance: https://www.fda.gov/media/85865/download. This information is important to ensure that the device does not elicit adverse tissue response.
    f. Explain how mechanical stresses from bending, stretching, and compression during device use may affect the sensor (i.e., accelerometer) response characteristics (e.g., sensitivity, range, linearity, etc.) and how you will mitigate these effects. Further explain how these mechanical stresses may affect the displacement of the device.

11. You state that there will be both local and remote storage of data as well as wireless data transfer. Data storage and transfer should include measures for ensuring secure communications and protection of patient information from unauthorized access. In your future submission, address the following:
    g. Indicate the logic flow of how the data collected from the patient is processed by the ADAM device, transmitted to smart phone and ultimately to a remote server in the cloud.
    h. Clarify who will have access to the information on the cloud server.
    i. Address the following regarding the mobile phone application:
        i. If applicable, discuss the Operating System (OS) version requirements or limitations to run the app.
        ii. Discuss functionality and compatibility of app with regards to various smart phone manufactures.
        iii. Provide minimum smart phone hardware/memory requirements to host the app.
        iv. Describe measures taken to prevent the app from unauthorized access, data gathering or data sharing of unrelated private information (e.g., contact names, passwords, URL's history, etc.) from patients' smart phone.
        v. Discuss if the app for a given patient can reside on multiple smart phones (parent, sibling, etc.).
        vi. The process in which a newer version of app is installed on the same smart phone.
    j. Describe the security measures you have implemented to prevent compromising patient data when information arrives at the cloud server.

12. For additional information, we recommend that you refer to the following guidance documents:
    - Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices (https://www.fda.gov/media/73065/download). The following modules are recommended to be included within Software Development Life Cycle in your future submission:
        - Level of Concern
        - Software Description
        - Device Hazard Analysis
        - Software Requirements Specification (SRS)
        - Architecture Design Chart
        - Software Design Specification (SDS)
        - Traceability Analysis
        - Software Development Environment Description
        - Verification and Validation Documentation
        - Revision Level History
        - Unresolved Anomalies (Bugs or Defects)
        - Content of Premarket Submissions for Management of Cybersecurity in Medical Devices (https://www.fda.gov/media/86174/download).
        - Software as a Medical Device (SAMD): Clinical Evaluation (https://www.fda.gov/media/100714/download).

Please contact the CDER COA Qualification Program at COADDTQualification@fda.hhs.gov should you have any questions (refer to DDT COA #000120).

Sincerely,

Elektra J. Papadopoulos -S

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