October 20, 2022

I. Panel Questions

FDA is seeking input on the benefit-risk assessment for the AvertD Test when indicated as follows:

AvertD is a prescription, qualitative genotyping test used to detect and identify 15 clinically relevant genetic polymorphisms in genomic DNA isolated from buccal samples collected from adults. The 15 detected genetic polymorphisms are involved in the brain reward pathways that are associated with opioid use disorder (OUD) and identify patients who may be at increased genetic risk for OUD. Information from AvertD provides patients 18 years of age or older and healthcare providers with objective information to be used for informed decision-making prior to the first prescription of oral opioids for acute pain. The information from AvertD is intended to be used in combination with a clinical evaluation and assessment of the patient.

In particular, we are seeking input from the Advisory Panel to determine how the data from the clinical study and clinical performance of the AvertD Test should be interpreted.

Our over-arching question for the Advisory Panel is whether the clinical study population adequately represents the intended use population such that the performance data derived from the clinical study are representative of the expected performance of the test when it is marketed and used in the intended use population. We have the following discussion questions for the panel to address during the Advisory Committee Meeting:

1. As described in the FDA and Sponsor Executive Summaries and panel presentations, there are several factors that contribute to the uncertainty in whether the observed clinical study results accurately represent the device's performance in the intended use population for the test. For each of the following factors, please discuss its impact on: a) clinical study subject enrollment and the resulting clinical study population; b) clinical study test performance interpretation; c) applicability of the study results to the intended use population.
    a. Use of different CRF versions during the study to collect the data including completion of an additional CRF after study completion to support that subjects met the inclusion/exclusion criteria specified in the protocol;
    b. Confidence with which the study excluded subjects whose index oral opioid exposure was illicit and/or for treatment of chronic pain;
    c. Recruitment of subjects both from treatment sites and from non-treatment sites;
    d. Determination of index oral opioid exposure based on subject recollection and the additional information available in the medical records/histories at enrollment sites;
    e. Assignment to a risk pool based on SUD and OUD status, absence of OUD-positive subjects in the low-risk pool, and subsequent use of risk pools to select study participants;
    f. Demographic make-up of the study population with regard to race, ethnicity, age, and sex

2. Given the device design, in which 15 SNPs that are associated with OUD as well as other mental health and SUDs are evaluated, and the clinical study design, please discuss the following:
    - Does the clinical study provide sufficient information to understand whether the device is detecting risk of OUD specifically or risk of OUD in addition to other comorbidities?
    - Does the information collected following initial study completion (i.e., Form 3) clarify whether the device may be detecting comorbidities in the clinical study population?

3. The reported sensitivity and specificity of the AvertD test, when tested in the clinical study population, is 82.76% and 79.23%, respectively. The negative likelihood ratio is 0.22 and the positive likelihood ratio is 3.98.
    - Does the reported device performance in the clinical study population represent the probable performance of the device in the intended use population?
    - Please discuss the clinical significance of the study results, including sensitivity, specificity, positive and negative likelihood ratios.
    - With the consideration that genetics is only one contributor to the overall risk of developing OUD, please discuss the level of sensitivity and specificity that would be clinically acceptable for a genetic risk test for helping to identify individuals at increased risk of developing OUD.

4. Please discuss the benefits and risks of genetic testing as an aid in assessing the risk of developing OUD following exposure to prescription oral opioids for acute pain.

5. Taking into consideration the current methods for assessing the risk of developing OUD after exposure to prescription oral opioids for acute pain, please discuss the clinical validity of AvertD.

6. If you believe that additional information in the labeling (e.g., warnings, limitations) would be appropriate to mitigate some risks for this test, please describe the specific risks and the labeling mitigations that should be included to minimize those risks associated with use of the device. Are there other mitigations to consider to minimize risk associated with use of the device?

Voting Question

1. Do the probable benefits to health from use of the AvertD device outweigh the probable risks for the proposed indications, taking into account the probable risks and benefits of currently available alternative forms of detecting risk of developing OUD?