

## **FDA Questions for Panel Members:**

The reclassification process for down-classifying a device from Class III to Class II depends on being able to mitigate the risks associated with use of the diagnostic device such that there is reasonable assurance of safe and effective use. Similar considerations exist for deciding whether a new device is appropriate for the de novo regulatory pathway, i.e., whether Class II designation is appropriate at the time an application is filed for a device with a new intended use. As described earlier, in both instances FDA is mandated to publish a Special Controls Guidance that outlines the steps that a sponsor should follow for developing a new diagnostic device for the specified intended use. In this context, please discuss the following:

### **1) For nucleic acid amplification assays that detect *M. tuberculosis* complex directly from respiratory samples:**

- a) Please discuss the risks associated with inaccurate test results for *M. tuberculosis* complex detection (i.e., false-positive and false-negative results).
- b) Please discuss the minimum device performance standards (e.g., sensitivity and specificity) that should be recommended for these tests. In your discussion, please comment on the appropriate reference method for clinical studies and the role of both prospective and archived/banked patient samples in demonstrating device performance.
- c) Based on the above considerations and the earlier presentations, please discuss if sufficient risk mitigation is possible for FDA to initiate the reclassification process from Class III to Class II devices for this use through drafting of a Special Controls Guidance. In your discussion, please note if there are any specific special controls in addition to those previously mentioned that should be considered for these devices.

### **2) For nucleic acid amplification assays that detect genetic mutations associated with antibiotic resistance to *M. tuberculosis* complex directly from respiratory specimens:<sup>1</sup>**

- a) Please discuss the risks associated with inaccurate results for the detection of genetic mutations associated with antibiotic resistance to *M. tuberculosis* complex.
- b) Considering the relative infrequency of antibiotic resistance mutations in different populations, please discuss the appropriate role of prospectively collected samples, archived/banked samples, and

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<sup>1</sup> Please note that diagnostic assays for *M. tuberculosis* mutations associated with drug resistance can only be approved or cleared for antibiotics that are FDA-approved for the treatment of tuberculosis.

spiked samples in determining device performance; in addition, please comment on the minimum device performance standards that should be recommended for these assays.

- c) Based on the above considerations and the earlier presentations, please discuss if sufficient risk mitigation is possible for FDA to consider classifying these devices as Class II by drafting a Special Controls Guidance through the *de novo* regulatory pathway. In your discussion, please note if there are any specific special controls in addition to those previously mentioned that should be considered for these devices.

**3) For immunologically-based tests such as IGRAs that are intended for the detection of tuberculosis infection by indirect means:**

- a) Please discuss the risks associated with inaccurate test results for the detection of tuberculosis infection (i.e., false-positive and false-negative results).
- b) Please discuss possible special controls to mitigate each of these risks, including the following:
  - i) Clinical studies that would be appropriate for documenting device performance.
  - ii) Minimum device performance standards (e.g., sensitivity and specificity) that should be recommended in guidance.
- c) Based on the above considerations and the earlier presentations, please discuss if sufficient risk mitigation is possible for FDA to initiate the reclassification process from Class III to Class II devices for this use through drafting a Special Controls Guidance.