

**Draft discussion questions for Lung CAD devices**

- L1. Establishing ground truth (i.e., whether disease is present, and if so, its location and extent) is crucial for the evaluation of the performance of any CAD device. Please provide your recommendations for defining ground truth for lung CAD devices. (*Section II.C.4, page 20; Section IV.D.1, page 69*)
- L2. Please discuss the role of standalone performance testing in the clinical evaluation of lung CAD devices.
- a. If you believe standalone testing should be requested in the evaluation of these devices, please provide your recommendations or comments on whether certain substrata (e.g., nodule size, shape, pathology or location; co-morbidities; CT dose or imaging protocol; or others) should be considered in device testing and labeling. (*Section IV.D.2, page 70*)
  - b. If you believe that there are specific situations where standalone performance testing may not be important, please comment on what those might be.
- L3. Please discuss the role of reader performance testing in the clinical evaluation of lung CAD devices.
- a. If you believe reader performance testing should be considered in the evaluation of these devices, please provide your comments or recommendations on:
    - i. The appropriate primary endpoint(s) and corresponding clinically significant effect size(s). Please specifically comment on the use of ROC analyses (*Section II.D, page 28; Section IV.D.3, page 72*);
    - ii. The merits of per lesion, per region, and/or per patient endpoints in the assessment of the endpoints (*Section II.E.4, page 36; Section IV.D.3, page 72*);
    - iii. Whether reading time should be assessed, and if so, how (*Section II.A.1, page 12*).
  - b. If you believe that there are specific situations where reader performance testing may not be necessary, please comment on what those might be.
- L4. Please discuss whether there are other types of performance testing you believe should be considered in the clinical evaluation of lung CAD devices.

L5. The prevalence of lung cancer cases in the population having chest x-rays and chest CT is relatively low. Please provide comments on the practice of using an enriched dataset for the clinical evaluation testing discussed in questions L2-L4. (*Section IV.D.3, page 71*)

- a. If you believe that an enriched dataset may be used for these evaluations, please discuss what you believe to be the appropriate clinical, imaging, and pathological characteristics (or range of characteristics) for that database. Please consider such items as:
  - i. Numbers of patients with no nodules, single nodules, or multiple nodules;
  - ii. Range of nodule sizes.
- b. If you believe that enrichment is inappropriate, please provide your reasons and whether there would be an alternative method of assessing these devices in light of the low prevalence of disease.

L6. FDA does not specify indications for use, but reviews indications for use that are requested by companies. What are the Panel's views regarding second reader versus concurrent reading using a CAD device? Specifically, (*Section IV.D.3, page 73*)

- a. How are lung CADs used clinically?
- b. Are second reader and concurrent reading modes both clinically relevant options for use in practice? If not, which paradigm(s) are appropriate for lung CAD devices?
- c. Do you believe users understand that if a device is labeled as a second reader, they (i.e. the physician) should always read the radiological image completely before turning on the CAD?

L7. Chest x-ray and chest CT are done for many important reasons other than looking for lung nodules. Can the use of CAD affect the diagnosis for these other conditions? Can the presence of other conditions alter the effectiveness of the CAD function or the risk-benefit profile of a lung CAD device? If the answer to either of these questions is "yes," then are their specific conditions that should be represented by patients in the test database? (*Section IV.A, page 61*)

**Draft discussion questions for other topics**

**General Methodologies** (Section II of briefing document)

- G1. To what extent should Sponsors provide algorithm descriptions, training dataset descriptions, standalone performance of the device on the training database, and/or stability analysis of the algorithm to training as part of original CAD submissions or as part of subsequent algorithm updates? (*Section II.B, page 13*)
- G2. What may be appropriate constraints on the reuse of test data in order to balance data integrity and data collection for CAD assessment? (*Section II.C.3, page 18*)
- G3. In a paired design, when each reader reads images with and without CAD, should there be a washout period between readings? Do you have any suggestions for improving paired designs for reader-CAD studies? (*Section II.C.6, page 26*)
- G4. What are appropriate control groups for reader performance testing? (*Section II.E.1, page 34*)
- G5. Please comment on the appropriateness of using a standardized weighted analysis as a primary or secondary analysis of a CAD study. A standardized analysis weights observations according to a standard distribution for important clinical variables thought to be representative of the target population. (*Section II.E.3, page 35*)

**Other CAD Devices** (Section VI of briefing document)

1. We have focused thus far on devices that are used primarily for Computer Aided Detection. Do you have comments on the types of testing needed for Computer Aided Diagnostic (CADx) devices, compared to the types of testing you have discussed in this meeting?
2. What emerging CAD areas should FDA be aware of? Do you have comments on the types of testing needed for other possible CAD devices—present and future—compared to the types of testing you have discussed in this meeting? (*Section VI.A, page 87*)
3. Do you have comments on the levels of testing for the different types of computer-based technologies compared to the testing you have discussed in this meeting? (*Section VI.B, page 87*)