

Draft discussion questions for Mammography CAD devices

- M1. Please discuss the role of standalone performance testing in the clinical evaluation of mammography CAD devices.
- a. If you believe standalone testing should be requested in the evaluation of these devices, please provide your recommendations or comments on:
 - i. The merits of per lesion, per view, per breast and/or per patient endpoints (*Section II.E.4, page 36; Section III.D.2, page 57*);
 - ii. Whether certain substrata (e.g., mammographic finding type, finding size, breast composition, or others) should be considered in device testing and labeling (*Section III.D.2, page 56*); and
 - iii. What marking or scoring methodology should be used for reporting findings (*Sections II.C.5, page 21; Section III.D.2, page 57*).
 - b. If you believe that there are specific situations where standalone performance testing may not be important, please comment on what those might be.
- M2. Please discuss the role of reader performance testing in the clinical evaluation of mammography 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*);
 - ii. The merits of per lesion, per view, per breast, and/or per patient endpoints in the assessment of the endpoints (*Sections II.E.4, page 36*);
 - iii. Whether effectiveness analyses should be conducted separately or not for cancers manifesting as masses versus microcalcifications;
 - iv. 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.
- M3. Please discuss whether there are other types of performance testing you believe should be considered in the clinical evaluation of mammography CAD devices.
- M4. The prevalence of breast cancer cases in a screening population is relatively low. Please provide comments on the practice of using an enriched dataset for the clinical evaluation testing discussed in questions M1-M3. (*Section III.A.2, page 42; Section III.D.3, page 58*)
- a. If you believe that an enriched dataset may be used for these evaluations, please discuss what you believe to be the appropriate clinical and mammographic characteristics (or range of characteristics) for that database. Please consider

whether the following characteristics of the screening population should be considered when designing an enriched database or stress test:

- i. Breast density: 40-50% of patients with heterogeneously dense or extremely dense breasts;
- ii. Proportion and types of masses and microcalcifications: approximately evenly distributed with a sufficient number of additional patients with architectural distortion alone;
- iii. Size and palpability for cancers: non-palpable and a majority with size < 1.0 cm;
- iv. Distributions of microcalcifications: small clusters of up to five microcalcifications for a third of the cases, and;
- v. Type of microcalcification clusters: representation of types of microcalcifications according to the American College of Radiology (ACR) BI-RADS descriptors, e.g., punctuate, fine linear, round, etc

In addition, please comment on whether the expected effect size should be adjusted if an enriched dataset is used. If so, how and why?

- 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.
- M5. Mammograms obtained on FFDM devices have characteristics that are strongly dependent on engineering design and specific device hardware and software. If a mammography CAD has been approved to operate with screen-film or specific FFDM device(s), what data should be used to assess its performance with a different FFDM device? Are both device standalone performance and reader performance testing necessary? Would one or the other suffice? Are there other types of studies that should be provided instead or additionally? (*Section III.D.4, page 60*)
- M6. 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,
- a. How are mammography 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 mammography 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?
- M7. FDA has provided you with a bibliography of the published literature for mammography CAD devices. Please discuss whether these publications provide us with any additional information as to how such devices should be evaluated in the future. (*Section III.C, page 52*)

Draft discussion questions for Colon CAD devices

- C1. Please discuss the potential clinical utility of CTC Colon CAD. Possibilities to consider include: (*Section V.A.5, page 78*)
- improved sensitivity to detect polyps of different sizes
 - reduced reading times
 - guiding optical colonoscopy
- C2. 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 colon CAD devices. (*Section II.C.4, page 20; Section V.D.1, page 81*)
- C3. Please discuss the role of standalone performance testing in the clinical evaluation of colon 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 V.D.2, page 83*)
 - b. If you believe that there are specific situations where standalone performance testing may not be important, please comment on what those might be.
- C4. Please discuss the role of reader performance testing in the clinical evaluation of colon 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 V.D.3, page 85*);
 - ii. The merits of per lesion, per segment, and/or per patient endpoints in the assessment of the endpoints (*Section II.E.4, page 36; Section V.D.3, page 84*);
 - 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.

C5. Please discuss whether there are other types of performance testing you believe should be considered in the clinical evaluation of colon CAD devices.

C6. Please provide comments on the practice of using an enriched dataset for the clinical evaluation testing discussed in questions C3-C5. (*Section V.D.3, page 83*)

a. If you believe that an enriched dataset may be used for these evaluations, please discuss what you believe to be the appropriate clinical and mammographic characteristics (or range of characteristics) for that database. Please consider such items as:

- i. Proportion of patients having polyps;
- ii. Proportion of patients having multiple polyps;
- iii. Polyp size.

b. If you believe that enrichment is inappropriate, please provide your reasons and whether there would be an alternative method of assessing these devices.

C7. 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 V.D.3, page 85*)

- a. How are colon 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 colon 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?