Position on
Skin Lesion Analyzers (SLAs)

Support:

- Maintain the current regulatory regime, continue to mandate a Class III approval process for SLA devices.

Oppose:

- The approval of SLAs, including mobile applications, for use by laypersons for screening for skin cancer and other lesions

Skin Lesion Analyzers (SLAs)

SLAs are intended for adjunctive use in a clinical setting, their use should be restricted to physicians who are dermatologists, and their approval should require a randomized clinical trial that shows that the diagnostic accuracy of dermatologists skilled in the diagnosis of similar skin lesions is improved with concurrent use of the SLA.

SLA devices are early in their developmental trajectory, with only 2 such devices ever having been approved by FDA, and only one currently being marketed. Since uptake of these devices has been slow, and there are very few current users, our understanding of how they are best used is similarly limited. SLA devices are potentially a highly heterogenous group of devices. Specifically, they are founded on a wide range of technologies (e.g., only one of the currently approved devices is based on visual image analysis) and may provide outputs of varying types. SLA devices should be developed for different applications, including detection of malignant lesions in some cases, and benign lesions in others. Among malignant lesions, they may be designed to detect melanoma, or common nonmelanoma skin cancers (i.e., keratinocyte carcinomas) such as basal cell carcinoma or squamous cell carcinoma, or any of the many rare nonmelanoma skin cancers or other cancers presenting on the skin (e.g., dermatofibrosarcoma protuberans, microcystic adnexal carcinoma, sebaceous carcinoma, atypical fibroxanthoma, pleomorphic dermal sarcoma, primary cutaneous mucinous carcinoma, Merkel cell carcinoma, extramammary Paget's disease, eccrine carcinoma, cutaneous leiomyosarcoma, etc.).

Disclaimers should come with use by laypersons and warn the patient about the need to also see a dermatologist, and the limitations of screening in low-risk cases as well as the limitations of screening only selected lesions. SLAs for lay use should have extremely high sensitivities so that their performance in real world settings is not lower than that of dermatologists in clinical settings; specificities should also be high. As with other SLAs, SLAs for lay use should also not be approved until a randomized clinical trial shows their safety and effectiveness.

SLA devices are inherently different from imaging and analysis devices using various technologies that *only provide raw data to the user without interpreting this data*. In contradistinction, SLA devices include those that use AI-based or other algorithms to interpret the data obtained, and to classify it in a clinically relevant manner. It is this latter functionality that distinguishes class III SLA devices from current class II devices that use similar technologies without delivering qualitative interpretation of results. It is this difference which we believe makes it imperative that SLA devices remain class III.

To the extent that algorithms inherent to the operation of SLA devices are proprietary and diverse, it is difficult to create simple benchmarks to validate their safety and effectiveness. These algorithms remain black boxes, with potentially unknown and unpredictable points of failure. The extreme dependence of SLAs on these algorithms is qualitatively different from the dependence of non-SLA electronic and mechanical devices for skin assessment on their internal workings.

Additionally, depending on the training sets and testing sets used, SLA devices may appear to be more robust and accurate than they would be in a real-world setting. For instance, a test set of melanoma cases for visual image analysis could contain cases that are all either clearly melanoma or clearly nonmelanoma, thereby deviating from the real-world environment, in which there is an abundance of challenging cases that contain many features of melanoma but are benign, while others have visual features consistent with benign behavior but are in fact melanomas.

Indeed, histopathological analysis remains the only accepted gold standard for determining whether a skin lesion is benign or malignant, and if malignant, what type of tumor it is. As such, it is imperative that the FDA continue to require histopathology, and histopathology alone as ground truth. While this may be inconvenient for device developers and those conducting clinical trials, any lower standard, such a hybrid standard, is unethical and potentially dangerous for patients.

SLAs should be at least as accurate as a trained dermatologist, with real-world sensitivity of 95% or greater in detecting skin cancers. While dermatologists may have sensitivities of 90-92% when reviewing challenging cases, most real-world cases evaluated by laypersons will be obvious rather than challenging in terms of their diagnosis. and so, these lay-use SLA devices will need much higher test sensitivities to have levels of detection and performance comparable to that of a dermatologist. Specificities of SLA devices aimed at laypersons should also be high to avoid extremely high levels of overdiagnosis. Disclaimers should advise the lay user that these devices cannot substitute for live, in-person evaluation by a dermatologist, and that any outputs suggesting a concerning lesion should necessitate an immediate visit to a dermatologist for definitive evaluation.

A further concern regarding SLA devices intended as skin cancer screening tools for lay users is that lay users are not trained in appropriate lesion selection and may mistakenly screen the wrong lesion. As such, a lay user may choose to assess a lesion that they perceive as concerning but that would not be viewed as concerning by a board-certified dermatologist; the same lay user may neglect to assess a different lesion than they do not perceive as concerning but that would have been classified as concerning for cancer by a dermatologist. It is impractical for a lay user to screen every square centimeter of their skin surface area with an SLA device, selection failure of the type described will dramatically

decrease the utility of even a properly functioning SLA device for lay use. A false sense of security associated with screening the wrong lesion may further endanger the lay user.

We are concerned about effectiveness of SLAs on patients with darker Fitzpatrick skin types, IV-VI, as well as more generally in patients with skin of color and patients of mixed racial backgrounds. A robust mechanism must be implemented to ensure that adequate numbers of cases from darker skin types are included in training sets for SLAs such that these SLAs are able to detect skin cancers and dermatoses in clinical and real-world settings. SLAs should not be approved for only lighter skin types.