

SUMMARY MINUTES

OF THE

GASTROENTEROLOGY AND UROLOGY DEVICES

ADVISORY PANEL

OPEN SESSION

November 19, 1999

**Room 020
9200 Corporate Blvd.
Rockville, Maryland**

**Gastroenterology and Urology Devices
Advisory Panel**

November 19, 1999

Panel Participants

Craig F. Donatucci, M.D.
Acting Panel Chair

Robert H. Hawes, M.D.
Voting Member

Joseph H. Steinbach, Ph.D.
Voting Member

Michael S. Epstein, M.D.
Temporary Voting Member

LTCDR Fathia Gibril
Temporary Voting Member

Mark A. Talamini, M.D.
Temporary Voting Member

Lawrence W. Way, M.D.
Temporary Voting Member

Karen L. Woods, M.D.
Temporary Voting Member

Diane K. Newman, RNC, MSN, DRNP, FAAN
Consumer Representative

Alan H. Bennett, M.D.
Industry Representative

FDA Participants

Mary J. Cornelius
Executive Secretary, Gastroenterology and Urology Devices Panel

Daniel Schultz, M.D.

Elias Mallis
Gastroenterology/Renal Devices Branch

William Sacks, Ph.D., M.D.

OPEN SESSION

Acting Panel Chair Craig F. Donatucci, M.D., called the session to order at 8:40 a.m., noting that the voting members present constituted a quorum and asking the panel members to introduce themselves and give their areas of expertise.

Panel Executive Secretary Mary Cornelius read appointments to temporary voting status for Drs. Epstein, Gibril, Talamini, Way, and Woods. Ms. Cornelius also read the conflict of interest statement, noting that no conflicts had been found. Ms. Cornelius listed tentative future panel meeting dates as January 27-28, April 13-14, August 31-September 1, and November 30-December 1, 2000.

OPEN PUBLIC HEARING

There were no requests to address the panel from the audience.

Dr. Kimber Richter, deputy director of the Office of Device Evaluation, introduced **Dr. Feigal, Director of the FDA's Center for Devices and Radiological Health**. He acknowledged the important role advisory committees play in the evaluation process and thanked the panel members for their efforts.

Dr. Richter presented a certificate of recognition to Dr. Alan Bennett for his seven years of service to the panel and to Dr. Leonard Vertuno for his eight years of service, noting that Dr. Vertuno was unable to attend the session because of illness.

PREMARKET APPROVAL APPLICATION P990050: SPECTRASCIENCE'S

OPTICAL BIOPSY SYSTEM

Sponsor Presentation

Mr. John Yager introduced the Optical Biopsy System, a laser-induced autofluorescence spectrophotometry system for use as an aid during endoscopic examination of the colon. He described the clinical trials and hypothesis and read the proposed intended use.

Mr. Ron Zimmerman described the device and its characteristics, noting that the system uses laser-induced autofluorescence of tissue to differentiate between tissues of different morphologies. He listed the device components and explained the computer subsystem and software application. System testing included electrical, laser safety, biocompatibility, and verification and validation testing

Dr. Stephan Norsted outlined the study hypothesis and design, which was a paired observation-experiment using a screening program paradigm employing blinding. He listed the criteria for patient selection and inclusion and exclusion criteria and outlined the patient and pathologist procedures. Dr. Norsted described the methods of analysis, classification of results, and reproducibility of results, as well as sample size calculations.

Dr. Kenneth Wang presented the clinical study results. After describing the objectives and endpoints, he listed the investigators at the five participating sites and gave statistics on patient population and demographics. Dr. Wang also explained findings on inter and intra-observer variation on tissue classification reproducibility. He concluded that clinical trial results support the hypothesis that the sensitivity of optical biopsy-assisted endoscopy is greater than unassisted endoscopy for the classification of adenomatous polyps.

Dr. John Bond discussed current practices and guidelines related to endoscopy of the colon, such as those from the American College of Gastroenterology. He saw the primary value of adjunctive screening tools as assisting the endoscopist who is performing flexible

sigmoidoscopy or colonoscopy in distinguishing between small adenomatous polyps that have relevance to colorectal cancer and hyperplastic polyps, which do not. He presented statistics on the epidemiology of colorectal cancer and the adenoma-carcinoma sequence. He reviewed the recommendations and guidelines on colorectal screening for patients with small adenomas and discussed potential benefits of an adjunctive screening tool.

Mr. Chet Sievert concluded the presentation with a restatement of the device's clinical utility in providing adjunctive information to distinguish between small hyperplastic and adenomatous polyps before making treatment decisions.

FDA Presentation

Mr. Elias Mallis began the FDA presentation by reading the indications for device use and introducing the FDA review team. He described the device's components and principle of operation and discussed preclinical tests on laser safety, which found no risk of mutagenicity, carcinogenicity, or tissue trauma. Software documentation provided by the sponsor was also acceptable. There were no biocompatibility, sterilization, electrical safety, or mechanical integrity issues of concern to the FDA.

Dr. William Sacks gave the FDA clinical review. He described the device's intended use, but noted that not all endoscopists base their decision on whether to biopsy a polyp on their visual assessment of the polyp type. He looked at the sensitivity and specificity and positive predictive value data presented in the PMA. Dr. Sacks concluded that despite the company's intended purpose for the device—an improvement in sensitivity—one can still evaluate the utility of an improvement in specificity for those who biopsy every polyp, although it must be evaluated in light of the necessary loss in sensitivity. In his view, one consideration for the panel was

whether the practice of biopsying all polyps is changing toward biopsying only polyps that visual assessment suggests are adenomatous.

Dr. Sacks also discussed whether departures from study protocol in failing to apply the device to every polyp encountered resulted in inadvertent bias. He noted a center-to-center variation in measured device sensitivity, which may have been caused by case mix and may raise a question on data generalizability. He asked whether the trial data are adequate for evaluating the device performance in a screening population as opposed to one at higher risk. Dr. Sacks concluded by asking whether endoscopists in those centers with low combined sensitivity for visual assessment should rely on visual assessment along with the device, or simply biopsy all polyps, or recommend colonoscopy for any polyp found on sigmoidoscopy. He also read the FDA questions for panel review.

Panel Clinical Review

Dr. Robert H. Hawes focused his review on the question of when an optical biopsy system would be used, noting that it is impossible to separate the clinical implications from the technological issues. He observed that the environments in which the device could be used differed: colonoscopy is done by physicians and gastroenterologists and is approved for screening but only reimbursed for high-risk situations. Flexible sigmoidoscopy can be done by non-physicians and is done to detect polyps. He noted that this technology does not improve polyp detection but rather the differentiation between adenomatous and nonadenomatous polyps. The device would not influence physician treatment choices for large polyps, which would be referred for colonoscopy, or for adenomas, which would be removed, but the device might change treatment choices on hyperplastic polyps. In particular, he thought an important

question concerned polyps smaller than five millimeters and the false negative rate of hyperplastic polyps. He raised three questions for the panel to consider: when would the technology be applied, does it have a place in polyp management, and who should use the device. Dr. Hawes thought this device would be applied during flexible sigmoidoscopy; that it could have a place in polyp management, but he stated that his practice is to remove all polyps, regardless of type.

Panel Questions

In discussing current clinical practice with regard to the management of colonic polyps, the panel agreed that such management takes place in two different environments: colonoscopy and flexible sigmoidoscopy. The panel thought the policy during colonoscopy is to remove all visible polyps except for multiple small polyps in the rectum and distal sigmoid, in which case one or two are removed. During flexible sigmoidoscopy, the practitioner should sample one or two polyps; if these prove hyperplastic, the patient would not be referred on for further treatment. The panel agreed that there was some confusion in the material presented about current practice during colonoscopy rather than flexible sigmoidoscopy, in that colonoscopists do remove all visible polyps. In flexible sigmoidoscopy, if the practice is not to remove all polyps then the device would have a place. The panel stressed that the important issue is the difference between the approach to polyps taken during flexible sigmoidoscopy versus colonoscopy.

The panel was not in complete consensus on whether the data supported the safety and effectiveness of the device for use in a screening population of average risk. The majority felt the data were applicable to a screening population but had concerns that this study did not

specifically discuss a screening population and that the procedure was a colonoscopy, not a flexible sigmoidoscopy.

The panel was also split on whether the protocol deviations had introduced bias, with half of the panel thinking a bias was unlikely and the other half concerned that there might be some technical reason why certain polyps cannot be sampled with this technique.

The panel had a mixed opinion on the effect of the variability of the devices used in the trial. Some saw the discrepancy as significant, some attributed it to the small number of polyps overall, and some thought the sponsors' explanation was adequate to allay concern.

On labeling, the panel did not feel compelled to limit usage to either colonoscopy or flexible sigmoidoscopy. The panel excluded device use with patients at high hereditary risk for colorectal cancer. There was a consensus that some training should be required for all those wanting to use this device, but there was a strong recommendation that the FDA not mandate specific biopsy correlation with the results. A mandated training requiring certification would be difficult, but a statement urging that the first x number of results be correlated with pathology or biopsy results to ensure correct use would be acceptable.

The panel was split about a mandated postapproval study, with half stating that no study was required if the device was approved for physician use only and half wanting a mandated postmarket study in a setting of flexible sigmoidoscopy screening and using a greater number of patients with a greater number of polyps of different sizes.

OPEN PUBLIC HEARING

There were no requests from the audience to address the panel.

Panel Executive Secretary Mary Cornelius read the voting rules and options.

A motion was made and seconded to recommend the PMA as approvable with the condition that a postmarket study be performed in which the company would collect data on device use for screening in the flexible sigmoidoscopy setting of 10 patients per machine for two years, at the end of which a report would be submitted to the FDA. This was amended to allow the FDA to design a study to include screening by colonoscopy as statistically acceptable. After discussion, this motion failed by a vote of five to two.

A motion was made and seconded to recommend the device as approvable for use by physicians on the condition that it not be used in cases of familial polyposis and that there be no mandated postmarket study. An amendment was proposed that labeling should include a number of cases specified by the FDA in which a certain number of biopsies should be performed to correlate physician diagnosis with pathology results. The amendment failed by a vote of four to three.

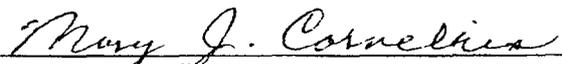
That motion was restated that the device be recommended as approvable for use by physicians but not applied to patients with familial polyposis and with no mandated postmarket study. The motion failed by a vote of five to two.

A motion was made and seconded to recommend the PMA as not approvable. This motion failed by a vote of four to three.

A motion was made and seconded to recommend the PMA as approvable with the condition that a postmarket study be mandated to study this technology in screening by flexible sigmoidoscopy with an appropriate number of cases and polyps as determined by statistical analysis to distinguish adenomatous and hyperplastic polyps. After discussion, this motion passed by a vote of four to three.

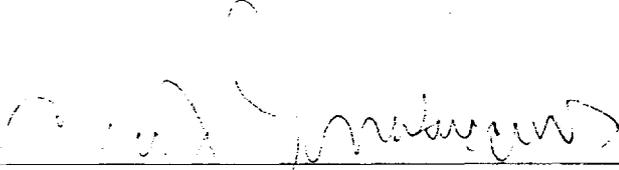
Panel Chair Dr. Donatucci thanked the panel, FDA, and sponsors, and adjourned the meeting at 3:35 p.m.

I certify that I attended the Open Session of the Gastroenterology and Urology Devices Advisory Panel Meeting on November 19, 1999, and that this summary accurately reflects what transpired.



Mary J. Cornelius
Panel Executive Secretary

I approve the minutes of this meeting as recorded in this summary.



Craig F. Donatucci, M.D.
Acting Panel Chair

Summary minutes prepared by
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