



January 27, 2003

Mark B. McClellan, M.D.
Commissioner of Food and Drugs
5600 Fishers Lane Room 1471
Rockville, Md. 20857

Subject: Computerized Thermal Imaging

Dear Dr. McClellan:

I must bring to your attention a number of issues regarding the Center for Devices and Radiological Health's Office of Device Evaluation's mismanagement of Computerized Thermal Imaging's PMA submission. Over the past few months, there have been a number of very disturbing occurrences, culminating last week in a letter rejecting our PMA.

Computerized Thermal Imaging is a small Utah - and Oregon - based public start-up company which had, until recently, 64 employees. We invested more than \$60 million and 5 years in the development of a unique adjunctive breast-imaging device, which is non-invasive and painless. And now all is about to be lost due to ODE's mishandling of the review, very apparent bias and failure to follow review procedures. I am writing to you now because we have reached an impasse with ODE. Without your personal involvement to help move this product towards approval, this product will have to be abandoned.

The PMA submission seeks review and approval of a breast imaging device that uses new infrared technology designed to distinguish between benign and malignant breast masses, preventing painful, disfiguring and needless benign breast biopsies. Four out of every five breast biopsies are negative. Breast healthcare is a major women's healthcare issue, and we believe that reducing the number of benign biopsies will significantly improve quality of life and reduce healthcare costs for women with identified breast masses. Clinical results, obtained in a four year clinical trial, demonstrated 99.3% sensitivity. There was a 19.2% specificity improvement over current clinical practice, meaning that tens of thousands of women could potentially avoid biopsies each year. We are confident these sensitivity and specificity figures will improve with actual use and product maturation.

I have a number of concerns with the review process, best expressed by way of example. The following list is by no means exhaustive, but I believe illustrates my point that the process was significantly flawed:

- (1) The company and ODE agreed to use the new PMA "fast track" 5 module submission approach. This process started during 1999. Three years later, the company was informed during July 2002 that its clinical trial results showed efficacy and that the company would be invited to the FDA's Advisory Panel on October 16, 2002. On October 1, 2002 and October 3, 2002, the company was told there were now major statistical concerns and that the panel meeting needed to be postponed. ODE officials stated -- in a manner that CTI perceived as threatening - that if the company didn't agree to postpone the October 16, 2002 Advisory Panel meeting and was successful at the Panel meeting, the FDA might not approve our PMA. It is inexplicable that these ODE concerns relating to the panel meeting were not expressed to CTI until two weeks before the panel meeting. This concern is further magnified because we had repeatedly asked to meet with ODE throughout the summer, only to be rebuffed.
- (2) In a subsequent meeting on October 8, 2002 with the ODE Director, he stated there was a breakdown of the internal FDA processes. A new Advisory Panel date of December 10, 2002, was established. During the remainder of October 2002 the company was asked to respond to 15 new multi-part questions totaling more than 40 sub-questions. However, most of these October 2002 questions were comprised of previously asked and answered questions. It is astonishing that ODE would ask these 40 questions weeks after the scheduled date of the panel meeting. The company was forced to expend substantial resources to answer these questions.
- (3) The postponement of the October 16, 2002 Advisory Panel date was "leaked" by ODE via e-mail and an automated voicemail hotline immediately after our meeting on October 8, 2002. The e-mail was sent to a CTI investor by an ODE staffer. The leak occurred even though it was agreed at that meeting that all communications about the postponement would be coordinated with the company. This improper disclosure cost the company's shareholders over \$25 million in market capitalization in a single day.
- (4) In early October 2002, the ODE review group forwarded an extremely negative 3 page memorandum to the Advisory Panel members. When we saw the document, we strongly objected because its content was factually incorrect and biased; ODE has since admitted that this memorandum contained inaccuracies. In response to our protest, the memo was withdrawn. However, the adverse effect on the Advisory Panel members who read it could not be undone.
- (5) Because of the errors in this memorandum and other mistakes the FDA staff reviewer made, we asked that the author of the memorandum be removed from the review team. This request was denied. The reviewer played a pivotal role in attacking the PMA at the panel meeting that was held on December 10, 2002.
- (6) At the December 10, 2002 Advisory Panel meeting, two members of the FDA ODE review staff disregarded all previous and documented understandings from the April/ May 2002 timeframe. They resurrected old issues and statistical disputes that the company and FDA had previously regarded as inapplicable or resolved. They proceeded to vigorously criticize our product, with no attempt at balance, resulting in a 4-3 decision not to approve. It is also worth noting that the two non-voting panel members stated they would have voted for approval. Notwithstanding the staff's position that they are "free to reconsider statistical evidence at any time," this last-minute repudiation of prior agreements is inexplicable given our personal availability, previous discussions, documented

understandings and conclusions reached during the course of the PMA review process.

- (7) At the December 10, 2002 Advisory Panel meeting, there was a motion made by the panel statistician to "approve the product with conditions." CDRH has written procedures directing that there be discussion of the conditions for approval before voting on approval with conditions. These procedures were not followed. Instead, the panel was forced to vote yes or no on approval, without first hearing what the recommended conditions were. The company has made several inquiries as to why Cry's procedures were not followed, but never received an answer.
- (8) At the December 10, 2002 Advisory meeting, the company learned that 3 of the 7 voting panel members had financial interests with competitors. However, waivers were granted by ODE. These conflicts were a complete surprise to the company.
- (9) After the December 10, 2002 Advisory panel meeting the company was assured by the ODE Director, that we would receive comments quickly and that our PMA would not languish. We were also promised the opportunity to work with ODE in addressing the panel's concerns. Nevertheless, the company was prevented from having substantive discussions with ODE. The first follow up meeting was scheduled for January 13, 2003, but was rescheduled to January 24, 2003, due to "a need for additional review time." Thus, ODE's promises for prompt discussions notwithstanding, six weeks went by before any discussion and meeting.
- 10) Less than 24 hours before the meeting on January 24, 2003, I personally received a faxed letter to the hotel stating the PMA was not approvable. This abrogated promises to have substantive discussions with ODE after the panel. This utter lack of notice also gave us virtually no opportunity to prepare a response to the letter or formulate a strategy for addressing it.
- 11) On January 24, we met with ODE officials. In view of the letter sent to us the day before, the meeting was a futile, empty exercise.

It has always been my understanding that the mission of CDRH was to work with companies to screen and bring new product technology to market. It surprises me that after nearly 4 years of PMA module submissions and extensive two-way dialog that the ODE would act as they have. There is no dispute that ODE made multiple mistakes during the product review. We firmly believe that these were not just harmless procedural errors, as ODE apparently contends. Instead these errors undermined the process and led to substantive mistakes and erroneous conclusions. This behavior affects not only us; it also discourages small business innovation and investment.

During your confirmation hearing, you expressed your commitment to promoting the introduction of new technologies. Unfortunately, ODE has apparently not shared that perspective.

We are not alone in believing the panel meeting was flawed. Since the December 10, 2002 Advisory Panel meeting, the company has received numerous positive communications from the many individuals that attended and read the transcripts expressing dismay over the process.

We believe that the data demonstrates the device should be made available. CTI remains prepared to conduct an extensive post-approval study, as the panel's statistician tried to recommend at the panel meeting. However, CTI cannot conduct another pre-approval

study, as ODE now insists we do. Four years after submitting the PMA, we have run out of resources. Without the assistance of you and your staff, we believe that this important technology will never be available to American women and the health professionals that make breast cancer detection and treatment a priority in the United States.

As always, CTI is willing to work closely with ODE to resolve any open issues. We look forward to discussing this important issue with you.

Sincerely,

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