

APPROVABLE!

A Giant Step Forward for OraSure Western Blot

By John Fitchen, *EPT Newswire*

It all began over two years ago with the planning and execution of the clinical trial. Then came the expenditure of thousands of man and woman hours that went into optimizing and producing the product; to gathering, processing and analyzing the data; to organizing, writing and assembling the OraSure Western Blot PMA that was submitted on June 12, 1995.

But the latest chapter began on Monday, December 18th. We had been hoping for a letter from the FDA since December 11th, the 180-day PMA review deadline, and had been assured by Ron Maynor (the chair of the review committee) that its arrival was imminent. After a week of being patient, we couldn't wait any longer. (It's always a close call on whether to badger FDA about something you really want to know: you really want to know, but you run the risk of annoying the very person in whose hands rests the fate of the product.) We huddled and decided that the best action was for Richard to call Ron Maynor on an informal basis to ask whether the FDA was affected by the budget battle: "Are you guys open for business?" and "By the way, anything new on our letter?"

Richard came down to my office to report on the call. "It's good news," he said. "Ron told me the letter is finalized; it's going through the signature process. He said we should have it today or tomorrow morning at the latest." "Did he give you any idea of what the letter says?" I asked. "He told me we wouldn't be unhappy with what the letter says, but he didn't give any specifics."

As I processed the double negative that seemed to add up to a positive, we went to talk to Al. Since we had not yet been inspected, the very best we could hope for was an "approvable" letter. This is a mechanism (actually a more common mechanism than outright approval) by which the FDA lets companies

know that a new product, and the clinical trials supporting it, are acceptable; that the product will be approved pending completion of additional tasks, sometimes minor, often more involved, but usually not major since that would likely beget a so-called "deficiency" letter. We cautiously allowed ourselves to think that Ron Maynor's double negative sounded more like an "approvable" letter than a "deficiency" letter.

Monday came and went, and Tuesday morning, and Tuesday afternoon. Nothing came. We began to ruminate about the meaning of the delay. Had one of Maynor's superiors raised questions or expressed doubts? Had the Agency focused on some problem with the clinical trial? Had Sharon Geyer (the *bête noire* of the OraSure PMA) somehow managed to inject her poison into the process at the eleventh hour?

Wednesday morning Richard called Ron Maynor again. He was out. Then later, Richard got a voice mail message that the letter was being "firmed up" and that we should have it in the next day or two. Now the gastrointestinal churning began in earnest. "Firmed up"—what the hell did that mean? Was the whole thing back to square one? Were they redrafting the letter from scratch? Would delivery of the letter be postponed until after the holidays? We realized, of course, that no matter how much we worried, it would not affect the outcome.

We worried anyway.

By Friday, when Ron Maynor had called to say the letter should be coming "any minute", Al and Richard and I began to move in a fretful pack, checking each of the three fax machines every 5 to 10 minutes. (We wondered if our movements would give people a clue that something important was up. Duh! As Nancy Lime said to me later, "You guys shouldn't walk around in groups. It makes us nervous.") Al finally asked me if I wanted to take a long walk outside, reasoning on the watched pot theory that unless we left the premises the letter wouldn't come.

We walked for 10 minutes. The wind was cold. Screw it; let's go back. We came in the front door and asked the question with our eyes. Sitting behind the reception desk, Paige shook her head—nothing. We trudged upstairs. Mary Hagen commented that Al was acting like an expectant father. Al told her it looked like the “birth” would come after the first of the year.

Half an hour later Paige called my office. “I think I've got what you need,” she said calmly. I reached the front desk in seconds. I ran upstairs to make copies, trying to read as I went. It took only two sentences to get the gist:

“The Center for Biologics Evaluation and Research (CBER) has completed its review of your premarket approval application (PMA) for OraSure® HIV-1 Western Blot Kit. Based upon the information provided in support of your request, your PMA has been found approvable subject to your submission of the following.”

I tried to read “the following” as the pages flipped through the copier. “Doesn't look like much,” I thought, but I knew the letter had to be read carefully.

I found Al in Andy's office (Richard had gone to lunch). I closed the door and handed them copies, pointing as I did to the fax cover sheet upon which was handwritten: “Approvable Letter: BP950004”. We started reading, then Al said, “We've got to get out of here. We've got to be able to read this letter thoroughly and thoughtfully without interruption. We've got to know what it says and how we will respond before we start talking about it.”

We filed out of Andy's office trying to conceal our excitement. According to SEC rules, until the news was given out in an official press release, we had to keep it secret. Mary was talking to Jan Misley and turned to look right at me. I couldn't help it, I grinned from ear to ear.

We drove to the Marriott Courtyard and pulled up chairs around a table in the lobby. Each of us read through the stipulations line by line. Almost in unison we said, “This is nothing. What they're asking us to submit is just paperwork.” (We put names by each of the points. Most of them were in Micki's arena. We made a mental note that we needed her assessment of the stipulations before we could confidently consider them minor.) We read on: approval, as we already knew, was also dependent on passing inspection and negotiation of final labeling. No surprises there. The rest was boilerplate: standard references to CFR this and CFR that.

As he had almost a year to the day earlier, Al looked me straight in the eye. “Here we go, Dr. Fitchen”, he said, “Here we go.” We all knew that this was big. It meant that we were close to having a complete and compelling product. A non-invasive

way to carry out screening *and* confirmatory testing for HIV antibodies. A full algorithm.

We joked about developing a Yuletide tradition with the FDA—two years in a row receiving a key letter on the Friday before Christmas. We said a quiet prayer of thanks to Ron Maynor for his reasonableness and his wisdom in moving our product forward, working it through the review process. We headed back to the office.

When we got there, we tried to enter calmly—business as usual. Mary took one look at us and said, “It's lucky you guys don't work for the CIA.” We huddled with Gil who began working on a press release. I called Donna Sturgess and Ted Kyle at SB and tried to reach Micki at home. She had taken Albert to a movie but would call as soon as she got home, Chris assured me.

Richard returned from lunch and we handed him the letter. His take was the same as ours: “Looks good to me”. We gathered in Al's office to work on the announcement and organize the mechanics of the release on Tuesday. “I wish I could be here next week,” said Richard. “Maybe I should cancel my vacation so I can help spread the good news on Tuesday.” We convinced him that he should go home to Atlanta for Christmas with his family.

A while later, Andy and I got talking about stability testing of the OraSure Western blot. He told me that on January 3, 1996 Product Development would complete 25 months of stability testing on the product. “You mean we've actually got real-time stability data for over two years?” I asked. “What a company!”

A while later, Al came in with Micki in tow. “I've heard what I need to know”, he said. He turned to Micki and nodded for her to give her assessment. “Hey, piece of cake. We can get this out in a day!” she said.

It had all been moving pretty fast. In a two-hour period we had got the letter, reviewed and nailed down all the particulars, tried repeatedly to contact our partners, and drafted a release announcing the news. There was finally a quiet moment. In that quiet moment, Andy told us about his Chinese dinner Wednesday night and the message inside his fortune cookie. We'd all been so worried by the delay that he hadn't shared it until now. Amazingly, prophetically, it read:

***'A letter soon will make you glad;
'Twill be the nicest one you've had.'***

Good job, fortune cookie; great job, Epitope. We are a persistent band of men and women determined to make a difference. With the approvability of OraSure Western blot we are poised on the threshold of success. As Al said, “*Here we go!*”

— Christmas 1995