

# Telcon held with Fibrocell Science Inc October 30, 2009 - Laviv

Our STN: BL 125348/0

## Fibrocell Representatives:

Jeanne Novak, Ph.D., Sponsor's Authorized Representative  
Declan Daly, CEO, Fibrocell Technologies  
John Maslowski, VP Operations, Fibrocell Technologies  
Karen Donhauser, VP Quality, Fibrocell Technologies  
Dana Weinberger, Ph.D., Alternate Regulatory Contact  
Michael Strauss, Ph.D., CMC Lead  
Kevin Hennegan, Ph.D., Program Lead  
Lee Buttrill, Director of Operations

## FDA Representatives:

Terrig Thomas, PhD  
Gang Wang PhD  
Don Fink, PhD  
Kim Benton, PhD  
Keith Wonnacott, PhD  
Lori Tull, RAC

A telecon was arranged to update the Agency on the progress being made regarding Fibrocell's September 17, 2009 written responses to the Pre-License Inspection form 483 issues.

Our overall concern was that, based on the current committed timelines proposed by Fibrocell, CBER will not have sufficient time to review and verify the results of the proposed studies and commitments within the current BLA review cycle. The timeframes proposed by sponsor to correct almost all of the nine observations cited on the 483 will not start or be completed by November or December 2009.

Whereas all the observations cited on the 483 are considered important, it was stressed that responses to the corrective actions for Items #1 and #2 should be prioritized.

In response to 483 Item #1 regarding inadequate Quality Systems to investigate and close out deviations, Fibrocell stated that they intend to close all 370 open reports by the end of December 2009. They intend to provide a report to the FDA by the end of 2009 regarding the progress and documentation of the closure all open investigation and deviation events.

Dr.Wang emphasized that the deficiencies identified for the Quality System are critical and the proposed timeframe is not acceptable in that we will not be able to evaluate if the Quality System has been improved upon before the end of the BLA review cycle. We requested that the sponsor close all open investigation and deviation events in November and submit a summary report no later than the end of November 2009. The summary report should also include information such as trend analysis, root causes, and preventive and corrective actions to ensure that such deviations can be minimized in the future.

In responding to 483 Item #2 regarding inadequate media fill studies, Fibrocell stated that they intend to conduct media fill studies in December 2009, but did not specify the timeframe for submitting the results to the Agency. Dr. Wang pointed out that the proposed timeframe is not acceptable for the current BLA review cycle as it will be difficult to approve the product without reviewing the media fill results. The sponsor had been requested to conduct media fill studies simulating all critical aseptic manipulations -----(b)(4)----- provide additional assurance that the product can be manufactured aseptically without contamination.

It was reiterated that the media fill studies need not cover the entire length of manufacturing processes, but key aseptic operations and worst-case scenarios, such as maximum capacity, maximum occupancy, and planned and unplanned interventions should be considered. Sterility testing of growth media and personal and environmental monitoring should also be included in the media fill studies. Dr. Wang indicated that given the limited review time remaining, an interim summary report followed by an amendment with a full report may be acceptable. The sponsor replied that they will start the media fill studies in November and provide an interim summary report in the first week of December 2009. A full study report will be submitted as an amendment once it becomes available.

Fibrocell is proposing to use -(b)(4)- instead of ---(b)(4)--- as the contract laboratory for performing mycoplasma testing on the commercial product. Dr. Fink told the sponsor that -(b)(4)-- has provided a -----(b)(4)----- protocol and test result obtained using the Fibrocell product, but has not provided the protocol for the mycoplasma test. A copy of the SOP describing the mycoplasma testing protocol performed by --(b)(4)- was requested for review by the Agency.