Ombudsman's Summary of the Scientific Issues in Dispute for the Medical Devices Dispute Resolution Panel Meeting on Acorn Cardiovascular, Inc.'s CorCap CSD

The CorCap Cardiac Support Device (CorCap CSD), manufactured by Acorn Cardiovascular, Inc. (Acorn), is a non-resorbable polyester mesh implanted around the heart to provide ventricular support and reduce ventricular wall stress. It is indicated for patients with dilated cardiomyopathy who are worsening despite optimal medical management.

On August 12, 2005 FDA issued Acorn a not approvable letter regarding its Premarket Approval Application (PMA) P040049 for the CorCap CSD. Specifically, FDA's letter stated:

> "FDA believes that there is a lack of a reasonable assurance of safety as described in 21 CFR 860.7(d). In particular, FDA is concerned about the risk of peri-operative death, safety of re-operation due to adhesions, and whether or not pericardial constriction will be observed in the long term in patients treated with the CorCap device."
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> "FDA believes that there is a lack of a reasonable assurance of effectiveness as described in 21 CFR 860.7(e). In particular, FDA is concerned about the amount of missing data for the primary endpoint, the lack of statistical significance in any secondary endpoints, and the absence of a specific patient population in which this device appears to be effective."

In response to this decision, Acorn amended the PMA with a *post hoc* reanalysis of the original data set with the objective of identifying a sub-population in which the CorCap CSD was safe and effective, referred to as the focused cohort. FDA issued a second not-approvable determination on February 2, 2006 for the amended PMA. This letter stated:

> "FDA believes the results of your focused cohort analysis have generated an interesting and promising hypothesis regarding a patient population in which your device may be safe and effective. (…) In order to demonstrate the safety and effectiveness of your device, we believe that the least burdensome approach is a prospective study that clinically validates the risk-benefit profile of your device in the patient population identified by the focused cohort analysis. This study may be able to leverage the data from your earlier clinical studies."

Acorn disagrees with FDA's decision to issue the August 2005 not-approvable letter, as well as the subsequent February 2006 not-approvable letter, and the reasons for issuing them. It is Acorn's opinion that the data submitted in the PMA as amended provides

reasonable assurance of safety and effectiveness for the proposed intended use. Specifically, Acorn believes the 300 patient clinical trial provides valid scientific evidence of safety and effectiveness, and that this result is not undermined by the concerns listed by FDA in the August 12, 2005 not-approvable letter.
Thus, the Dispute Resolution Panel, to whom Acorn has appealed the not-approvable decision, will be charged with reviewing and making a recommendation to the CDRH Center Director as to the approvability of the PMA, i.e.:

> Does the PMA as amended provide valid scientific evidence that demonstrates a reasonable assurance of the safety and effectiveness of the CorCap CSD for its intended use in the original patient population and/or the focused cohort?

In consideration of that recommendation, the panel is asked to determine the following:

1. Whether the overall trial results for the primary effectiveness endpoint are interpretable and clinically meaningful.

2. Whether the secondary endpoint results are supportive of the safety and effectiveness of the device.

3. Whether FDA's safety concerns have been addressed by the data provided.

4. Whether the data submitted by Acorn adequately address FDA's safety and effectiveness concerns for the original patient population and/or the focused cohort.

This Summary of Scientific Issues in Dispute is an overview. It is not intended to be a full and detailed statement of all such issues and arguments that will be presented at the panel meeting by FDA and the sponsor. Specifically, FDA is to present data and analyses to support its not-approvable determinations, and Acorn is to present its reasons for disputing the not-approvable determinations.

Les Weinstein
CDRH Ombudsman
October 3, 2006

Panel's Charge (From the Ombudsman's Summary of the Scientific Issues in Dispute)

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4. Whether the data submitted by Acorn adequately address FDA's safety and effectiveness concerns for the original patient population and/or the focused cohort.