

The purpose is to request that FDA permit an expanded indication for the Novacor LVAS. This request is made in the context of two significant realities: (1) there is an indisputable and ongoing shortage of donor hearts that severely limits the number of cardiac transplants available to end-stage heart-failure patients. (2) After almost twenty years of clinical experience and more than 1500 implants, the safety and effectiveness profile of the Novacor LVAS is well established.

The clinical focus of this submission is a group of heart-failure patients not listed for transplant, but with relative contraindications that have potential to resolve during LVAS support. If these conditions resolve, the patient would move on to transplant listing. If not, the LVAS recipient would be supported long term – the same as listed patients who receive a ventricular assist device explicitly as a bridge to transplant, but who then develop contraindications to transplant.

The clinical data supporting this request is available from the U.S. Bridge-to-Transplant (BTT) Study that led to the original PMA approval for the Novacor LVAS. These data are applicable to the proposed expanded indication due to the presence of a group of BTT subjects (both LVAS recipients and controls) that clinically represent patients who may not be listed for transplant due to relative contraindication conditions. A summary of the clinical data supporting this request is provided in Attachment 5.A, *Expanded Indication for Use of the Novacor[®] LVAS*,

. The subject data are a summary of the data provided in which is provided in Attachment 5.B.

Since there is no national standard for listing criteria, transplant acceptance criteria is not uniform from center to center or across time. As transplant experience has evolved, so too has clinical evaluation of the suitability of any

individual patient for receipt of a scarce donor heart. Also, a patient's heart-failure symptoms and clinical status often deteriorates between the time of transplant listing and receipt of a ventricular assist device as a "bridge". Thus, while Novacor LVAS recipients in the BTT Study were on a transplant list at Study enrollment, their clinical condition at implant is representative of other patients who are not placed on constrained transplant lists.

This clinical data clearly demonstrate (1) a significant survival benefit outweighing potential risks and (2) an adverse-event rate that is highest in the early LVAS support period and that declines over at least a two-year period. Of equal, critical, importance is the uniquely high reliability and durability of the Novacor LVAS – consistently demonstrated both *in vitro* and clinically, and across all worldwide experience.

There have been no recipient deaths attributed to device failure in more than 1500 implants to date.

[Note: 1444 implants, with 1077 of current configuration, as of 4/15/03 data cutoff date.] The single known wearout mode (main bearing wear) is progressive, noncatastrophic and has detectable symptoms before wearout: all of which permit elective pump replacement.

In summary, the almost two-decade clinical history of the Novacor LVAS demonstrates a significant survival benefit, well-characterized efficacy, and unmatched multiyear reliability and durability. Therefore, we believe that there is a compelling basis for indication expansion. The public health is served by making this established technology available to a group of end-stage heart-failure patients who would otherwise likely die.