

Seventieth Meeting of the
Obstetrics and Gynecology Devices Panel

Thursday, June 23, 2005
Holiday Inn, Gaithersburg, MD

Neovanta STAN[®] S31 Fetal Heart Monitoring System (P020001)
DRAFT Discussion Questions June 16, 2005

Safety and Effectiveness

The PMA for the STAN Fetal Heart Monitoring System (STAN system) was initially reviewed in 2002. The pivotal study supporting its safety and effectiveness was a multi-center randomized controlled study conducted in Sweden. The panel considered the PMA in April 2002 and expressed concerns about differences between Sweden and the U.S. for labor management practices and underlying medical terminology. When FDA found the PMA “not approvable,” Neovanta was asked to conduct bridging studies in the U.S. to show that clinicians here could learn the STAN system technology and apply it clinically in an appropriate way. Neovanta designed two U.S. bridging studies and discussed them in a closed session panel meeting (June 9, 2003). After addressing panel comments, Neovanta conducted the two studies and submitted their results in this follow-up submission: (1) the Education Study (Tab 5, Volume 1 in Panel Package) and (2) the Clinical Use Study (CUS) (Tab 6, Volume 1 in Panel Package).

1. In the Education Study, U.S. clinical investigators underwent the STAN training program, which included the following:
 - Self study (textbook and interactive CD)
 - Material covers basic physiology related to fetal hypoxia and fetal surveillance during labor including EFM interpretation, fetal ECG physiology, and fetal ECG interpretation
 - Interactive CD include FHR+ST interpretation exercises and a quiz
 - Interactive on-site tutorial (including case discussions)
 - Written certification test consisting of 18 multiple choice questions

Investigators were then asked to evaluate 51 separate cases with the STAN tracing and identify if intervention was indicated. Their responses were compared to those of a panel of experts trained in the use of STAN technology. In addition to agreement between US investigators and the STAN experts on the decision to intervene, the timing of intervention was also evaluated, i.e. whether the timing of the intervention was within 20 minutes of the STAN experts.

A summary of the results from the Education Study follows:

Percent Agreement with True Intervention Status (as defined by cord arterial pH Level < 7.15)

Reader (N)	Exam 1 FHR-Only Reading, Before Training		Exam 2 FHR-Only Reading, After Training		Exam 3 FHR+ST Reading, After Training		Proportion of Readers that Improved from Exam 2 to 3
	Mean	Range	Mean	Range	Mean	Range	
US Clinicians (13)	47	37-63	53	41-67	69	43-88	92
EU Experts (7)	--	--	59	51-63	85	75-90	100

Intervention Rate (%) stratified by cord arterial pH Level

Reader (N)	pH < 7.05		pH 7.05-7.14		pH >=7.15	
	Mean	Range	Mean	Range	Mean	Range
US Clinicians (13)	90	67-100	75	40-100	39	3-88
EU Experts (7)	91	78-100	64	50-80	9	6-19

Question:

Given the results of the Education Study, does the Panel believe that this shows U.S. clinicians, in a classroom setting, can learn and successfully use the STAN system? Is variation among readers in the effectiveness of the training a concern?

2. In the Clinical Use Study (CUS), the STAN system was used for the management of 530 women in labor at six U.S. sites. These same cases were evaluated by a panel of STAN experts. Management decisions made by U.S. investigators were compared to recommendations of the expert panel. Three endpoints were compared:

- negative predictive value (NPV) – i.e. the probability that non-intervention results in a normal outcome in the cohort of infants with non-reassuring FHR tracings for whom the STAN system allows continued labor
- positive percent agreement (PPA) – i.e. the rate of agreement between US investigators and STAN experts on intervention in cases requiring intervention
- negative percent agreement (NPA) – i.e. the rate of agreement between US investigators and STAN experts on non-intervention in cases of NRFHR that do not require intervention

The study hypothesis given in the protocol specified targets for each of these three endpoints. The sponsor’s analysis of these comparisons are given in the table below:

	NPV μ (95%CI)	PPA μ (95%CI)	NPA μ (95%CI)
Analysis per protocol	95.2% (180/189) (91.2%, 97.8%)	83.8% (31/37) (68.0%, 94.7%)	90.4% (444/491) (87.8%, 97.0%)

Question:

The *a priori* targets for NPV and NPA were met, but the lower bound on the 95%CI for PPA was 68% (verses the 75% target). Considering the various analysis strategies, please discuss the clinical implications of these findings. Does the CUS Study demonstrate that US clinicians can learn and successfully use the STAN technology in the clinical setting?

3. Do the results from these two bridging studies conducted in the U.S. (Education and CUS) when considered along with the previously reviewed studies (e.g., the Swedish RCT) collectively demonstrate the safety and effectiveness of the STAN S31 Fetal Heart Monitoring System for its stated indication for use?

Labeling and Training

4. Does the panel have any comments on the labeling and instructions for use provided by the sponsor?
5. The STAN Educational Program has evolved since the early clinical trials of this device. The elements of this program since the start of the Swedish RCT are presented in the following table:

STAN Clinical Development Program – Sweden to US

Components of STAN Educational Program	Clinical Setting			
	Swedish RCT	US Education Study	US Clinical Use Study	Available Resources*
Textbook and CD ROM	X	X	X	X
Certification Test	X	X	X	X
Credentialing			X	X
Continuing Education				X

*These resources will be provided to physicians in the event of PMA Approval (Tab 1, Volume 9 in PMA).

Question:

Does the panel believe that the STAN Educational Program used for the US Clinical Use Study together with the existing Continuing Education opportunity available on the Internet should be basic requirements of STAN training for US clinicians if the PMA is approved? Does the Panel feel that Continuing Education requirements should include annual re-certification?

Post-approval Study

6. Does the panel have input regarding any issues that should be addressed in a post-approval study?

Note: Post-approval studies may provide additional information about an approved device; however, the safety and effectiveness must be demonstrated before approval. The results of a post-approval study should not be expected to change the “approval” status of a device.