

Seventy-Third Meeting of the  
**Obstetrics and Gynecology Devices Panel**

Thursday, December 13, 2007  
Hilton Washington DC North, Gaithersburg, MD

**Cytoc Surgical Products - Adiana Transcervical Sterilization System  
(P070022)**

**Draft Panel Discussion Questions**

Safety

1. The rates of adverse events reported on the day of the Adiana procedure are provided in Table 1. These are reported as the percentage of patients who experienced each type of adverse event.

**Table 1: Adverse Events reported on day of placement procedure (N=645 subjects)**

<b>Event</b>	<b>Number</b>	<b>Percentage</b>
Cramping	165	26%
Vaginal Spotting	79	12%
Post-procedural Bleeding	65	10%
Pelvic Pain	58	9%
Back Pain	52	8%
Nausea	30	5%
Headache	28	4%
Vomiting	16	2%
Post-procedural Pain	15	2%
Other	22	3.4%

- Only moderate – severe side effects reported. Some subjects may have reported more than one side effect.
- Eight of the 645 subjects had two procedures.
- “Other” includes events that occurred at a rate  $>0.5\%$  and  $\leq 1\%$ : arthralgia (7), dysuria (6), abdominal distension (4), post-procedural discharge (1), vaginal discharge (2) and vasovagal reaction (2).

Note: There was one reported case of hyponatremia that occurred during hysteroscopic placement, not listed in the table above.

Table 2 summarizes all adverse events in the clinical trial reported to be at least “possibly” related to the matrices or placement procedure during the first year of reliance on the Adiana System.

**Table 2: Adverse Events by Body Systems, First Year of Reliance<sup>1,2</sup>**  
(N=625 patients implanted with a least one device)

Adverse Events by Body System	Number	Percentage
<b>Abdominal:</b>		
Abdominal pain	2	<1
Nausea	4	1
Vomiting	3	<1
<b>Musculoskeletal:</b>		
Back pain	21	3
<b>Nervous System:</b>		
Headache	4	1
<b>Genitourinary:</b>		
Amenorrhea	2	<1
Cramping – unrelated to menses	35	6
Dysmenorrhea	32	5
Dyspareunia	5	1
Menorrhagia	9	1
Pelvic pain	19	3
Vaginal spotting	6	1
Vaginal bleeding	27	4
Vaginal discharge	3	<1
<b>Pain/discomfort – uncharacterized:</b>		
Discomfort	2	<1
Pain	2	<1

<sup>1</sup> Only severe events occurring at a frequency  $\geq 0.5\%$  are reported

<sup>2</sup> Percentages are presented by subject frequency

In addition to the adverse events listed in the above two tables, there were two reported cases of ectopic pregnancies that occurred while relying on the device.

*Is the safety profile of this device clinically acceptable?*

### Effectiveness

#### 2. Device Placement, Tubal Occlusion and Contraceptive Efficacy

- a. The bilateral placement success rate at first attempt is 94% (604 of 645 subjects). The bilateral occlusion rate, as determined by HSG performed three months after device placement, is 94% (570 of 604 subjects).
- b. To date, ten (10) women in the pivotal study became pregnant while relying on the Adiana device after successful placement with the Adiana Transcervical Sterilization System. The pregnancies occurred as follows:

<i>Contraceptive Efficacy of Adiana Transcervical Sterilization System</i>				
	# of subjects <sup>1</sup>	# of pregnancies while relying	estimated pregnancy rate <sup>2</sup>	
			point-estimate	95% confidence interval
Year 1	553	6	1.08%	0.22-1.93
Year 2	321	3	1.82%	0.63-3.02
Year 3	133	0	---	---
Year 4	0 <sup>3</sup>	1 <sup>3</sup>	---	---

<sup>1</sup> number of subjects having completed evaluation as of the database freeze on March 1, 2007

<sup>2</sup> estimate based on life table methods

<sup>3</sup>As of the date of the database freeze on March 1, 2007, no subject had completed 4 years of reliance. One pregnancy was reported in a subject who had begun but not completed her 4<sup>th</sup> year of reliance.

Notes on efficacy table above:

- There were too few subjects who completed years 3 and 4 to accurately determine the estimated pregnancy rates and corresponding confidence intervals.
- Of the six relying subjects who became pregnant during year 1, three pregnancies were attributed by the sponsor to clinical mis-reads of HSG.

*Are the study effectiveness rates (bilateral placement, bilateral occlusion, and pregnancy) clinically acceptable?*

### Risk-Benefit

3. *Does the panel believe that the long-term benefits of contraceptive effectiveness, as evidenced by the 1- and 2-year pregnancy rates, outweigh the device risks? The panel may also consider other possible clinical benefits, e.g., hysteroscopic placement instead of laparoscopic placement.*

### Labeling & Training

4. Cytoc plans to market devices exclusively to physicians who have successfully completed the Physician Training Program. Physicians must be experienced in the use of operative hysteroscopy or will need to obtain training. Since performing and accurately interpreting HSGs is important to the success of the Adiana Transcervical Sterilization procedure, a separate training program for interpreting HSGs has been developed.

*Does the panel have any comments on the training plan proposed by the sponsor?*

5. The sponsor provided labeling for the Adiana Delivery Catheter and the Adiana RF Generator. This included draft versions of the Instructions for Use, RF Generator Specification and Installation Manual, HSG Protocol, and Patient Manual.

*Does the panel have any comments on the labeling provided by the sponsor?*

### Post Approval Study (PAS)

6. To assess long-term safety and effectiveness of the device, the sponsor proposed to continue follow-up of the premarket cohort for up to five years. The primary objective will be to determine the device failure/effectiveness rates at 3, 4, and 5 years of use.

*Please comment on whether the proposed PAS plan is appropriate to address device long-term safety and effectiveness postmarket.*