Center for Devices and Radiological Health
Condition of Approval Studies
As a Postmarket Tool for
PMA Approved Cohort 1998 - 2000

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EXECUTIVE SUMMARY

From the beginning of 1998 through the end of 2000, CDRH approved 127 PMAs and required Condition of Approval Studies for 45 (35%) of these. The purpose of this study was to characterize the use of these studies by systematically collecting and evaluating descriptive information on them. This study only considers clinical Condition of Approval studies required under 21 CFR 814.82.

The authors were not able to find information on these studies in the manufacturers' Annual Reports for 26 (58%) of the 45 Condition of Approval Studies. We then conducted a survey of lead reviewers to obtain additional information. This survey indicated that for 11 PMAs where the final study results were known to be due, final results had not been received by ODE in 6 (54%) cases. Reviewers reported 10 (22%) cases in which there were no results yet. There were 2 studies (4.4%) that had not been started by the sponsor, and 1 study that the sponsor indicated it could not (or would not) perform. There were 4 PMAs for which the responding reviewer was uncertain as to the status of the study. Based on both the review of the annual reports and the lead reviewer survey, we were unable to find any information on 8(18%) of the 45 PMAs.

Our study suggests that performance of Condition of Approval Studies is suboptimal, with no available study results for many PMAs years after they have been approved, failure of the manufacturer to start or perform the study, potentially fraudulent data from one (1) study, and status of 'study unknown' to the reviewer (4). Overall, based on the reviewer survey, fewer than half of the PMA Condition of Approval studies (42%) were completed (5) or in progress but not yet due (14). Another 2 Condition of Approval Studies were not completed because the device was withdrawn from the U.S. market.
The study also revealed that due to a lack of Center systems for tracking Condition of Approval Studies, it is very difficult for anyone to obtain information on the studies or their status, unless that person has extensive knowledge of the individual products under study.

Recommendations are provided for improving the tracking of Condition of Approval Studies and for improving manufacturer compliance with the terms of performance of studies agreed upon at the time of PMA approval.

The preliminary summary results were presented to the Center's senior management staff in April 2003. Shortly following the presentation, the Center initiated several actions to address the study's findings. Many of these activities are on-going. The study report was finalized on March 18, 2005. The final report includes information on the actions the Center has taken to ensure that both the Center and manufacturers do a better job complying with PMA Condition of Approval studies.

Introduction

Premarket Approval (PMA) Applications are required of manufacturers seeking FDA approval from the Center for Devices and Radiological Health (CDRH) for class III medical devices. Generally, a class III device is a novel high risk medical device for which there is a requirement to demonstrate reasonable assurance of safety and effectiveness. The desire to make important health care technologies rapidly available to the public is an incentive for CDRH to evaluate PMAs in a prompt and expeditious manner. At the time of PMA approval, there may be remaining concerns about the safety and/or effectiveness of the medical device. In such instances, CDRH may require the manufacturer to conduct a "Condition of Approval" study. These studies are meant to address additional issues of safety and effectiveness that may not have been fully addressed in premarket studies. Manufacturers agree to perform these studies as a condition of approval. This allows the manufacturer to market the device while collecting further information on its performance. As a result, the performance of Condition of Approval Studies as a postmarket tool is of significant importance to the evaluation of medical devices throughout the Total Product Life Cycle.

The purpose of the present study was to characterize the use of Condition of Approval (CoA) Studies by systematically collecting and evaluating descriptive information on the performance of CoA studies. We also examined regulatory actions that were taken based on results from these CoA Studies.

Methods

We generated a list of PMAs approved between January 1, 1998, and December 31, 2000, by assessing monthly listings of PMA approvals on the CDRH website.[1] We then checked this list against a list of PMAs for that time period provided by the Office of Device Evaluation (ODE) Program Operations Staff, Premarket Approval Section (POS/PAS). Every PMA approval order was reviewed for requirements for a CoA study. We narrowed our consideration to CoA studies that required further clinical data. This would include continued follow-up of the clinical cohort from a manufacturer's pivotal clinical study or the requirement for a new study to address a safety or efficacy issue that had not been anticipated in the manufacturer's approval study. It would not include a requirement for further materials or mechanical testing or for required registries for the purpose of user notifications. We also identified the lead reviewer for each of the PMAs that had a CoA Study. We attempted to retrieve documents with information on CoA studies (including protocols; evidence that the study was underway; or preliminary, interim, or final results) from IMAGE, a CDRH database that has scanned images of PMA documents.

Next, we informally interviewed POS/PAS staff about various aspects of tracking the results of CoA studies, including:

1. how to ascertain if CDRH received results from a specific CoA study ;

2. how to ascertain if the lead reviewer for the PMA received and reviewed results from a CoA study;

3. whether any memos or other communications about the progress or results of a CoA study could be retrieved;

4. if any regulatory actions were taken because of the results of a CoA study; and

5. what procedures are in place to follow-up on a manufacturer's progress on a CoA study.

Because of their greater familiarity with filing and finding documents, we enlisted the ODE/POS staff to retrieve (hard copies of) reports from manufacturers that included results from CoA studies. We provided staff with a list of PMAs that had CoA studies with the instructions to retrieve any document that had bearing on the study, but particularly any document(s) with results or indications of the current status of the CoA study.

Finally, we designed a survey for ODE lead reviewers of PMAs for which a CoA study was required. The purpose of the survey was to solicit information about the status of the CoA studies and whether any regulatory action was taken as a response to deficiencies in the performance of these studies or in response to results from the CoA study bearing on the safety or effectiveness of the device. We used Zoomerang, an on-line survey service to conduct the lead reviewer survey.[2] The survey and follow-up surveys were sent out on or around October 31, 2002, November 20, 2002, and December 17, 2002. Final cutoff date for reviewer response was January 2, 2003.

Results

Condition of Approval Studies Ordered

There were 127 PMAs approved for the three year period under study January 1, 1998 through December 31, 2000. This did not include PMA supplements. Of these PMAs, 45 (35%) required a CoA study (Table 1). A complete listing of PMAs for this period is available in Appendix 1. The CoA studies fell into several broad categories: 1) continued follow-up for some specified period of time of the clinical cohort from the pivotal study or IDE, 2) new protocol with defined endpoints, sample size, and duration of follow-up, and 3) unspecified study with the manufacturer instructed to submit a protocol within a specified period of time after device approval.

Table 1. PMAs approved with Condition of Approval Studies from 1998 – 2000.

Year PMA Approved	PMAs Approved	PMAs with COAS (%)
1998	43	15 (34.9)
1999	35	15 (42.8)
2000	49	15 (32.6)
Total	127	45 (35.4)

Interviews with POS/PAS Staff on Tracking Condition of Approval Studies

Interviews with POS/PAS indicated that there was no formal mechanism to track progress of CoA studies. Nor was there any formal mechanism for ascertaining whether the lead reviewer had received, reviewed, or acted on any results from a CoA study. The staff reported that there are no standard mechanisms for tracking or monitoring the CoA studies. Results from CoA studies may be submitted in the manufacturer's Annual Report.

Locating Documents with IMAGE and through POS/PAS Staff

We attempted to find documents related to the performance of Condition of Approval Studies in IMAGE. However, because of the lack of an indexing feature in IMAGE, reviewing the documents was not reliable. Also, because of the lag in scanning documents, we were uncertain if our inability to find documents related to CoA studies was because there weren't any, or because there were documents that had not yet been scanned. Since information on a CoA study is most likely to be found in the Annual Reports from manufacturers, we provided a list of PMAs with CoA studies for POS/PAS staff to retrieve any postmarket reports or annual reports.

Table 2 summarizes the results of this endeavor. We requested information on 45 PMAs for the three year period. Overall, we received files for 19/45 (42%) PMAs from POS/PAS staff. A complete listing of the PMAs and their status as of August 2002, based on these records, is available in Appendix 2. Staff was unable to retrieve any information for the majority of PMAs (58%). Based on the information found in the annual reports, staff located interim or final study results for 15/45 (33%) of PMAs. In addition, staff forwarded some evidence that a study was underway, but no data was yet available (a study protocol or mention in the annual report that the study was underway), for an additional 3/45(6.7%) of PMAs.

Table 2. Condition of Approval Study Status based on retrieval of manufacturer's Annual Report by POS/PAS staff as of August 2002. All available reports reviewed and categorized.

COAS Status	1998	1999	2000	Total
Evidence study in progress (no results available)	1 (6.7)	0 (0.0)	2 (13.3)	3 (6.7)
Interim results	2 (13.3)	4 (26.7)	3 (20.0)	9 (20.0)
Final results	5 (33.3)	1 (6.7)	0 (0.0)	6 (13.3)
Unknown[a]	7 (46.7)	9 (60.0)	10 (66.7)	26 (57.8)
Manufacturer will not perform	0 (0.0)	1 (6.7)	0 (0.0)	1 (2.2)
Total[b]	15 (100.0)	15 (100.1)	15 (100.0)	45 (100.0)

a. No file received
b. Total percents may exceed 100% due to rounding

Lead Reviewer Survey

We compiled a list of lead reviewers from the approval letters. We looked up the lead reviewer in the CDRH or FDA global directory and found that about 40% of lead reviewers had left the agency or were no longer in the Branch or Division in which the PMA had been reviewed.

The survey was sent by e-mail from POS/PAS to each identified lead reviewer or the branch chief. Overall, there were 47 responses for 42 PMAs. Three of these responses were to surveys that were incorrectly sent for PMAs for which there was no required CoA study with clinical data. These responses were not included in the data tables . There were responses from both the first and subsequent lead reviewer for 5 PMAs. There was no response for 6 of the PMAs even after three attempts. The response rate for the PMAs was 86.6% (39/45). Table 3 shows the responses to the lead reviewer survey (in which only the current lead reviewer response was used).

Table 3. Response to Reviewer's Survey for 45 PMAs with Condition of Approval Study ordered. When a second reviewer is identified and responds, that response is used (not the original lead reviewer's response).

Question	PMA Approval Year			
	1998	1999	2000	Total (%)
Are you still the lead reviewer for this PMA?				
Yes	9 (60.0)	7 (46.7)	11 (73.3)	27 (60.0)
No	5 (33.3)	5 (33.3)	2 (13.3)	12 (26.7)
No response	1 (6.7)	3 (20.0)	2 (13.3)	6 (13.3)

Has the manufacturer started the condition of approval study yet?				
Yes	9 (60.0)	12 (80.0)	9 (60.0)	30 (66.7)
No	2 (13.3)	0 (0.0)	1 (6.7)	3 (6.67)
Don't know	3 (20.0)	0 (0.0)	3 (20.0)	6 (13.3)
No response	1 (6.7)	3 (20.0)	2 (13.3)	6 (13.3)
Are the final study results due yet?				
Yes	4 (26.7)	4 (26.7)	3 (20.0)	11 (24.4)
No	8 (53.3)	8 (53.3)	10 (66.7)	26 (57.8)
No response	3 (20.0)	3 (20.0)	2 (13.3)	8 (17.9)
What is the current submission status for the condition of approval study?				
Complete all results received	1 (6.7)	3 (20.0)	1 (6.7)	5 (11.1)
Interim (ongoing) results received	5 (33.3)	5 (33.3)	4 (26.7)	14 (31.1)
No results received	1 (6.7)	1 (6.7)	4 (26.7)	6 (13.3)
Incomplete results (manufacturer intends submission to be last)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other status[a]	6 (40.0)	2 (13.3)	4 (26.7)	12 (26.7)
No response	2 (13.3)	4 (26.7)	2 (13.3)	8 (17.8)
Did you write a memo or conduct a formal study on the study results?				
Yes	7 (46.7)	7 (46.7)	6 (40.0)	20 (44.4)
No	6 (40.0)	5 (33.3)	7 (46.7)	18 (40.0)
No response	2 (13.3)	3 (20.0)	2 (13.3)	7 (15.6)
Was any regulatory action taken based on the results of the study?[b]				
No	10 (66.7)	9 (60.0)	8 (53.3)	27 (60.0)
Yes	1 (6.7)	2 (13.3)	3 (20.0)	6 (13.3)
Don't know	1 (6.7)	1 (6.7)	0 (0.0)	2 (4.4)
No response	3 (20.0)	3 (20.0)	4 (26.7)	10 (22.2)

a. The other status that reviewers identified were sometimes overlapping with the choices in the survey:
- 3 cases of don't know;
- 2 cases of device not marketed (therefore study not finished);
- 2 cases of study not started;
- 1 cases of ongoing but not sure if results received;
- 1 case of study ongoing;
- 1 case of study potentially fraudulent and under review;
- 1 case of all results not available, inability to do study;
- 1 case of through annual report .

b. Regulatory actions mentioned include
- 4 labeling ,
- 1 medical alert/advisory, and
- 1 application integrity policy (AIP) applied and lifted .

Based on the results of the lead reviewer survey, in many cases (40.0%) the current lead reviewer was not the initial lead reviewer. In most cases, the lead reviewer reported that the manufacturer (sponsor) had started the CoA study (66.7%). In 6 cases (13.3%), the lead reviewer reported that s/he did not know whether or not the study was started. In 4 of these cases, the original reviewer was no longer the lead reviewer for that PMA.

Lead reviewers were also asked whether the final study results were due and, if so, the due date. Reviewers responded that 11/45 (24.4%) studies were due but were unable to

give a due date. For instance, due date was given as "six months after starting trial," "no date in approval order," and "approximately 2002." For the 11 studies that were reported by lead reviewer to be due, the study status for 8 of these studies (45.4%) was complete with all results received.

Lead reviewers reported that regulatory actions were taken based on the results of the CoA study in six cases (Table 3). In 4 cases, the regulatory action was a required revision of labeling. In one case, a medical advisory issued, and in one case, the agency applied the Application Integrity Policy to the sponsor's submissions.

Discussion

Our study characterized the use of CoA studies at the CDRH. Based on information from Approval Letters, we identified 45 of 127 PMAs approved between January 1998, and December 31, 2000, that had a CoA study required to collect clinical data. The study period (1998-2000) was selected because of the complete availability of PMA approvals for those years on the internet and because, when this study was undertaken, we assumed that sponsors would have a minimum of two years to begin CoA studies and submit interim results.

Lead reviewers expressed ambivalent feelings about the use of CoA studies. While 40% said that the current method of implementing, gathering, and assessing CoA studies is effective, 28% indicated that there were features of the current method that they did not find effective (the remaining 32% did not respond to this question or the response was ambiguous). Reviewers' concerns included: inadequate compliance by manufacturers with CoA studies; lack of FDA authority to obtain compliance; lack of continuity between reviewers including turnover and shifting responsibilities due to changes in branch and division make-up; lack of agency action for poor performance, undermining incentive for manufacturers to perform studies appropriately or in a timely manner.

Our findings indicate that CDRH has limited procedures for monitoring manufacturer's progress and results from Condition of Approval studies. These studies are not adequately tracked for completion, even though they are considered a "Condition of Approval." The Approval Order Letter to the manufacturer explicitly states that failure to comply with the Conditions of Approval invalidates the approval. However, this circumstance has not been used to revoke a PMA.

In our research on medical device postmarket studies, lead reviewers reported that final study results were due for 11 manufacturers but complete study results had only been received from 5 manufacturers at the time they were surveyed. Comments from lead reviewers indicated that in some cases the due date for a study was ambiguous (e.g. "six months after the study starts"). This increases the difficulty of tracking studies if there is no firm, unambiguous due date. Reviewers also said that no results had been received for 10 of the PMAs approved between 1998 and 2000. There were an additional two studies that lead reviewers asserted were not started. The survey was completed at the end of 2002, so that each PMA had been approved a minimum of two years earlier. Our research did not address the quality of the CoA studies ordered or performed.

Tracking study progress and assuring that CoA studies are performed appropriately are very important. We therefore recommend the following:

- Responsibility for tracking and monitoring CoA Studies should be transferred to the Office of Surveillance and Biometrics, which has the responsibility for postmarket patient safety studies.
- Formal standards and procedures for tracking all Condition of Approval Studies should be introduced. Tracking should include dates due, annual or other reports

- from manufacturers that include study results or evidence that study is underway, and any regulatory actions that are taken because of results from Condition of Approval studies (or lack of results).
- Annual Reports or other reports with evidence of progress or results from Condition of Approval Studies should be indexed in IMAGE to make them easy to retrieve.
- Due dates for Condition of Approval Studies should be concrete and enforced by closely tracking the status of the reports and reviewing the Center's enforcement options.
- Manufacturers should be queried and reminded when Condition of Approval study results are not provided on schedule.
- Since Condition of Approval studies are often proposed by the FDA's advisory panels when reviewing PMA applications, feedback should be given to the responsible panel on a routine basis regarding the progress and results of these studies.
- Study requirements and periodic status reports for Condition of Approval Studies should be posted on the Agency's website along with similar status reports from CDER and CBER.
- Establish a procedure for taking action when commitments to perform Condition of Approval Studies are not met. Consideration should be given to applying/adopting the provisions we promulgated to enforce §522 (Postmarket surveillance studies) to CoA studies when sponsors fail to fulfill the conditions in the PMA letter.

Bibliography

[1] Monthly PMA Listings. http://www.fda.gov/cdrh/pmapage.html#monthly Accessed 12/31/02

[2] Zoomerang. http://www.zoomerang.com/Login/index.zgi

Appendix 1. Devices approved between 1998 and 2000.
(List retrieved May 2002 Condition of Approval Study 0 = no,1 = yes)

Approval Date	PMA Number	Condition of Approval	Device Name
1/29/98	P960030	0	Passive plus DX endocardial steroid eluting pacing leads
1/30/98	P970012	0	Medtronic kappa 400 series pacemakers
2/20/98	P970052	0	FACT, ARC, LYNX and Guardian Baloon coronary dilatation catheters
3/10/98	P970038	0	Tandem-R free PSA assay and Tandem MP free PSA assay
3/12/98	P970017	0	Hologic sahara clinical bone sonometer
3/31/98	P970037	0	AutoDELFIA hAFP Test Kit
4/3/98	P950031	0	Lobob cleaner
4/28/98	P940026	0	Lobob C/D/S Cleaning, disinfecting, and storage solution
4/29/98	P970032	0	Saltest System
4/30/98	P940025	0	Lobob W/RW Drop
5/27/98	P960057	1	Adcon-L adhesion barrier gel
5/29/98	P970044	1	Urowave microwave thermotherapy system
5/29/98	P970026	0	Soundscan 2000 and SoundScan Compact
6/24/98	P970062	1	Genestone 190 Lithotripter
6/25/98	P970051	1	Nucleus 24 cochlear implant system
6/26/98	P970058	1	M1000 ImageChecker
6/26/98	P970046	0	Achilles Bone Sonometer
7/16/98	P970061	1	Scimed radius coronary stent with delivery system
7/16/98	P960011	0	BioLon 1% Sodium hyaluronate viscoelastic surgical aid fluid
7/16/98	P960018	0	Needlyzer the needle destroyer model ND2
7/30/98	P970005	0	Kremer excimer laser system for laser in situ keratomileusis (LASIK) for the correction of primary myopia with and without astigmatism
8/6/98	P980015	0	Sharpx needle destruction unit
8/11/98	P980001	1	NIR ON Ranger w/SOX and NIR ON Ranger premounted stent
8/12/98	P960034	0	CeeOn Heparin surface modified ultraviolet absorbing polymethylmethacrylate posterior chamber intraocular lens
8/19/98	P970024	1	Angeion sentinel implantable cardioverter defibrillator
8/20/98	P950015	1	The heart laser CO2 TMR system
8/26/98	P960052	0	DermaBond
9/25/98	P980018	1	DAKO Hercep test
9/25/98	P980017	0	Possis perma-seal dialysis access graft
9/25/98	P980025	0	Logicon caries detector
9/29/98	P980009	1	Magic Wallstent endoprosthesis
9/29/98	P970034	0	Ultraviolet absorbing polymethylmethacrylate posterior chamber intraocular lens
9/29/98	P980012	0	Novacor LVAS
10/2/98	P960006	0	Sweet tip RX modes steroid eluting positive fixation porous tip, pacing leads
10/5/98	P960014	0	Magellan C PTCA catheter
10/9/98	P980016	1	Medtronic model GEM DR dual chamber implantable cardiverter defibrillator system
10/27/98	P980023	1	Phylax implantable cardioveter defibrillator system
11/2/98	D970012	1	AMS series inflatable prosthesis product
11/2/98	P970043	0	LADAR vision excimer laser system
11/10/98	P950032	0	Apligraft
12/11/98	P980024	0	Pathvysion Her2 DNA probe kit
12/17/98	P970053	0	Nidek EC-5000 excimer laser system
12/23/98	P970010	1	Norian SRS Cement

Appendix 1 continued

Approval Date	PMA Number	COA	Device Name
1/29/99	P980035	0	Medtronic Kappa 700/600 Series pacemaker
2/2/99	P960025	1	Lumbar I/F Cage with VSP Spine System
2/2/99	P980003	1	Chilli Cooled Ablation System
2/5/99	P980006	0	PureVision visibility tinted contact lens for extended wear
2/8/99	P980041	0	Access AFP Reagents on the Access Immunoassay Analyzer
2/11/99	P970029	1	Eclipse TMR Holmium Laser System
3/12/99	P980037	0	Angiojet Rheolytic thrombectomy system
4/9/99	P980031	1	KeraVision Intacs
4/16/99	P970033	1	TransScan T-scan
4/27/99	P970025	0	Pro-Trac II tacrolimus ELISA kit
4/28/99	P980046	0	Home Access Hepatitis C Check and Hepatitis C Check Express
5/4/99	P960016	0	Daig Livewire TC Steerable Electrophysiology Catheter
5/14/99	P970015	1	InterFix threaded fusion device
6/3/99	D970003	1	Guidant Pulsar Models Pulse Generators
7/2/99	P980052	1	TMJ concepts patient fittet TMJ reconstruction prosthesis system
7/2/99	P960033	0	Staarvisc sodium hyaluronate viscoelastic
8/6/99	P970054	0	Biotrin parvovirus B19 IgG enzyme immunoassay
8/6/99	P970055	0	Biotrin parvovirus B19 IgMenzyme immunoassay
9/13/99	P980053	1	Durasphere injectable bulking agent
9/15/99	P980049	1	Defender II Model 9201 Implantable cardioverter defibrillator
9/25/99	P990033	0	PepGen P-15
9/27/99	P990001	0	Diva platform implantable pulse generators and provit III application software
9/27/99	P990008	0	Cook MBC PTCA balloon dilatation catheter
9/28/99	P990017	1	Ancure tube system, Ancure bifurcated system, Ancure iliac balloon catheter
9/28/99	P990020	1	AneuRx stent graft system
9/28/99	P970056	0	Keracor 116 opthalmic excimer laser system
9/28/99	P980043	0	Medtronic Hancock II Bioprosthetic Heart Valve
9/30/99	P990002	1	FemSoft insert
9/30/99	P990004	0	Surgifoam absorbable gelatin sponge
11/12/99	P990014	1	Hydroview composite hydrogel foldable ultraviolet absorbing posterior chamber intraocular lens, model H60M
11/12/99	P980008	0	LaserScan LSX Excimer laser system for photorefractive keratectomy for myopia
11/19/99	P990010	0	VISX, Inc Excimer laser system model c (star s2) for laser in situ keratomileusis (LASIK) for the correction of myopia with or without astigmatism
12/3/99	P990019	0	BLU-U
12/8/99	P990009	1	FloSeal Matrix, FloSeal matrix hemostatic sealant
12/16/99	P970049	0	Dishler excimer laser system for laser in situ keratomileusis (Lasik) correction of myopia with or without astigmatism
1/6/00	P990016	0	Ultrasonic bone ultrasound
1/20/00	P990035	0	Omnisense ultrasound bone sonometer
1/28/00	P990066	0	Senographe 2000 D Full Field Digital Mammography System
2/3/00	P980040	0	Sensar soft acrylic uv light absorbing posterior chamber intraocular lens
2/23/00	P990027	0	Technolas 217A Excimer laser system for lase in-situ keratomileusis (LASIK) correction
2/24/00	P990023	0	Cellugel Opthalmic Viscosurgical Device
4/2/00	P990013	0	Collamer ultraviolet absorbing posterior chamber intraocular lens models

Appendix 1 continued

Approval Date	PMA Number	COA[1]	Device Name
4/12/00	P990048	0	Zeiss visualas 690 laser and visulink pdt adapter
4/12/00	P990049	0	Coherent Opal Photoactivator Laser Console and Laser Link Adapter
4/18/00	P950020	0	Cutting Balloon
4/18/00	P990054	0	Chilli Cooled Ablation System
5/1/00	P990074	1	McGhan Medical RTV Saline-Filled Breast Implant
5/10/00	P990075	1	Mentor Corporation Saline-Filled and Spectrum Mammary Prostheses
5/12/00	P990053	1	Oxifirst Fetal oxygen saturation monitoring system
5/21/00	P990071	0	Sockert 70 RF Generator for Cardiac Ablation
5/26/00	P990028	1	FocalSeal-L Synthetic Absorbable Sealant
6/13/00	P990030	0	CoStasis Surgical hemostat and DynaStat Surgical Hemostat
6/14/00	P980050	1	Medtronic Jewel AF 7250 Dual Chamber Implantable Cardioverter Defibrillator
6/15/00	P990025	0	Navi-Star diagnostic/ablation deflectable tip catheter
6/22/00	P990037	1	Vascular Solutions Duett Sealing Device
6/30/00	P990021	0	Diomed 630 PDT Laser
6/30/00	P990078	0	Sunrise Hyperion LTK System
7/11/00	P990018	0	Menicon Z (tisilfocon A) Rigid Gas Permeable Lens
7/14/00	P000006	1	Mentor Alpha I Inflatable Penile Prosthesis
7/21/00	P990034	0	Medtroni IsoMed Constant Flow Infusion System
7/25/00	P990064	1	Mosaic Porcine Bioprssthesis
8/1/00	P990039	0	QUS-2 Calcaneal Ultrasonometer
8/22/00	P990072	0	Horizon 55 EW Soft Hydrophilic Contact Lenses for extended Wear
8/31/00	P990052	1	Vibrant P Soundbridge System (Vibrating Ossicular Prosthesis)
9/5/00	P970042	1	Medstone STS Lithotripter for the treatment of symptomatic, solitary, radiolucent, non-calcified gallstones
9/8/00	P990055	0	Bayer Immuno1 complexed PSA Assay
9/19/00	P980010	0	DTU-one Ultrasound Scanner
9/25/00	P990040	0	Trufill n-butyl cyanoacrylate liquid embolic system
9/29/00	P000009	0	Phylax AV implantable cardioverter defibrillator with program software
9/29/00	P000011	0	Biodivysic AS PC (Phyosphorylcholine) coated stent and delivery system
9/29/00	P000014	0	Vitros immunodiagnostic products anti-HBs reagent pack and callibrators
10/12/00	P990086	1	HealthTronics OssaTron
10/13/00	P990046	1	ATS open pivot bileaflet heart valve
10/16/00	P000022	1	Medtronic AVE BeStent 2 ith discrete Technology over the wire coronary stent delivery system
10/20/00	P000015	0	Nucleus 24 auditory brainstem implant system
11/3/00	P000018	1	Novoste Beta-Cath system
11/3/00	P990036	1	Cordis checkmate system
11/14/00	P990050	0	Optical biopsy system
11/22/00	P990056	0	Elecsys total PSA immunoassay and Elecsys total PSA Calset
11/28/00	P990081	0	Ventan Medical Systems Pathway HER2 (Clone CB11)
11/29/00	P000020	0	Stinger ablation catheter and templin extension cable
12/12/00	P000027	0	Elecsys Free PSA immunoassay for Elecsys 1010 and 2010 immunoassay and analyzers
12/21/00	P970013	0	Microny SR+ Model
12/21/00	P980020	0	Q-103 Needle management system

Appendix 2. Status of CoA studies (1998 – 2000) based on record retrieval as of August 2002. *

CoA Studies 0 = no; 1=yes

PMA File 0 = no; 1 = yes (annual report file, or other file with status of study available)

Study status (F = Final Results, P = Evidence study in progress; I = Interim results found; U = Unknown, no file available. N= Manufacturer will not do study)

Approval Year	PMA Number	COAS	PMA File Located	Study Status	Device Name
1998	P960057	1	1	F	Adcon-L adhesion barrier gel
1998	P970010	1	1	F	Norian SRS Cement
1998	P970044	1	1	P	Urowave microwave thermotherapy system
1998	P970051	1	1	I	Nucleus 24 cochlear implant system
1998	P970058	1	1	F	M1000 ImageChecker
1998	P970061	1	1	I	Scimed radius coronary stent with delivery system
1998	P980016	1	1	F	Medtronic model GEM DR dual chamber implantable cardiverter defibr system
1998	P980023	1	1	F	Phylax implantable cardioveter defibrillator system
1998	D970012	1	0	U	AMS series inflatable prosthesis product
1998	P950015	1	0	U	The heart laser CO2 TMR system
1998	P970024	1	0	U	Angeion sentinel implantable cardioverter defibrillator
1998	P970062	1	0	U	Genestone 190 Lithotripter
1998	P980001	1	0	U	NIR ON Ranger w/SOX and NIR ON Ranger premounted stent
1998	P980009	1	0	U	Magic Wallstent endoprosthesis
1998	P980018	1	0	U	DAKO Hercep test
1999	P960025	1	1	I	Lumbar I/F Cage with VSP Spine System
1999	P970029	1	1	N	Eclipse TMR Holmium Laser System
1999	P980003	1	1	I	Chilli Cooled Ablation System
1999	P980053	1	1	F	Durasphere injectable bulking agent
1999	P990002	1	1	I	FemSoft insert
1999	P990014	1	1	I	Hydroview composite hydrogel foldable ultraviolet absorbing posterior intraocular lens, model H60M
1999	P970015	1	0	U	InterFix threaded fusion device
1999	P970033	1	0	U	TransScan T-scan
1999	P980031	1	0	U	KeraVision Intacs
1999	P980049	1	0	U	Defender II Model 9201 Implantable cardioverter defibrillator
1999	P980052	1	0	U	TMJ concepts patient fittet TMJ reconstruction prosthesis system
1999	P990009	1	0	U	FloSeal Matrix, FloSeal matrix hemostatic sealant
1999	P990017	1	0	U	Ancure tube system, Ancure bifurcated system, Ancure iliac balloon ca
1999	P990020	1	0	U	AneuRx stent graft system
1999	D970003	1	0	U	Guidant Pulsar Models Pulse Generators
2000	P000006	1	1	I	Mentor Alpha I Inflatable Penile Prosthesis
2000	P970042	1	1	P	Medstone STS Lithotripter for the treatment of symptomatic, solitary, radiolucent, non-calcified gallstones
2000	P990052	1	1	I	Vibrant P Soundbridge System (Vibrating Ossicular Prosthesis)
2000	P990053	1	1	P	Oxifirst Fetal oxygen saturation monitoring system
2000	P990075	1	1	I	Mentor Corporation Saline-Filled and Spectrum Mammary Prostheses
2000	P000018	1	0	U	Novoste Beta-Cath system
2000	P000022	1	0	U	Medtronic AVE BeStent 2 ith discrete Technology over the wire coronary stent delivery system
2000	P980050	1	0	U	Medtronic Jewel AF 7250 Dual Chamber Implantable Cardioverter Def
2000	P990028	1	0	U	FocalSeal-L Synthetic Absorbable Sealant

Appendix 2 continued

Approval	PMA	COAS	PMA	Study	Device Name

Year	Number		File Located	Status	
2000	P990036	1	0	U	Cordis checkmate system
2000	P990037	1	0	U	Vascular Solutions Duett Sealing Device
2000	P990046	1	0	U	ATS open pivot bileaflet heart valve
2000	P990064	1	0	U	Mosaic Porcine Bioprssthesis
2000	P990074	1	0	U	McGhan Medical RTV Saline-Filled Breast Implant
2000	P990086	1	0	U	HealthTronics OssaTron

*For additional information on status of these studies, see Appendix 3.

Appendix 3. Response to reviewer survey and recodes for study status in Table 4 as of January 6, 2003.

PMA#	Study Started (q4)		Study Status from Survey (table 3) (q6)	Status Recode (table 4)
1 P980009	-		-	No response
2 P970033	-		-	No response
3 P990014	-		-	No response
4 D970003	-		-	No response
5 P990046	-		-	No response
6 P990064	-		-	No response
7 P970062	U		-	Unknown (U)
8 P990036	U		No results received	Unknown (U)
9 P970058	Yes	Δ	Complete, all results received	Final results
10 P980031	Yes	Δ	Complete, all results received	Final results
11 P980049	Yes	Δ	Complete, all results received	Final results
12 P990009	Yes	Δ	Complete, all results received	Final results
13 P990052	Yes	Δ	Complete, all results received	Final results
14 D970012	Yes		Interim (ongoing) results received	Interim results
15 P970010	Yes		Interim (ongoing) results received	Interim results
16 P970051	Yes		Interim (ongoing) results received	Interim results
17 P980001	Yes	Δ	Interim (ongoing) results received	Interim results
18 P980016	Yes		Interim (ongoing) results received	Interim results
19 P970015	Yes		Interim (ongoing) results received	Interim results
20 P980052	Yes		Interim (ongoing) results received	Interim results
21 P990002	Yes		Interim (ongoing) results received	Interim results
22 P990017	Yes		Interim (ongoing) results received	Interim results
23 P990020	Yes		Interim (ongoing) results received	Interim results
24 P000006	DK		Interim (ongoing) results received	Interim results
25 P990028	Yes		Interim (ongoing) results received	Interim results
26 P990074	Yes		Interim (ongoing) results received	Interim results
27 P990075	Yes		Interim (ongoing) results received	Interim results
28 P980018	Yes		No results received	In progress
29 P960025	Yes		-	In progress
30 P980003	Yes		No results received	In progress
31 P000018	Yes		No results received	In progress
32 P990053	Yes		No results received	In progress
33 P990086	Yes		No results received	In progress
34 P980050	Yes	Δ	Other:All results not available, inability to do study	Study will not be performed (other)
35 P970044	No		Other: Never marketed in US, company withdrew	Study will not be performed (other)
36 P990037	U	Δ	Other:Not sure since no longer lead reviewer	Unknown (U)
37 P000022	Yes		Other: Ongoing, not sure if results received	In progress

38	P950015	No	Other:Study not initiated	Not started
39	P970042	No	Other:Study not yet initiated by sponsor	Not started
40	P980053	Yes	Other: Study ongoing	In progress
41	P960057	Yes Δ	Other: The data were fraudulent and will be re-reviewed	Other
42	P970024	U	The devices were no longer being marketed	Study will not be performed*
43	P970029	Yes Δ	Other: Don't know	In progress
44	P970061	U	Other:Not the current reviewer, don't know status	Unknown (U)
45	P980023	Yes Δ	Other:Through annual report	In progress

Δ = Lead reviewer said study is due

Appendix 4: Actions the Center for Devices and Radiological Health has taken to address the problems identified in the study:

In 2002, because of a growing concern that CoA studies were not being performed or completed by some manufacturers as required, CDRH undertook an internal review of the status of CoA studies ordered by the agency from January 1, 1998 to December 31, 2000. CDRH evaluated the status of the studies through early 2002. The review was intended to provide a snapshot in time.

The following highlights the major actions the Center has taken to address the problems identified in the study:

- Responsibility for tracking, designing, and evaluating CoA studies has been transferred from the Office of Device Evaluation (ODE), where limited resources are focused primarily on the pre-market evaluation of new products, to the Office of Surveillance and Biometrics, which has primary responsibility for monitoring the safety and effectiveness of products after they reach the market.

- Three additional epidemiologists have been hired to work with companies and ODE early in the PMA review process on the design of their CoA studies. They also will help track and evaluate study results.

- CDRH plans to publish a draft guidance for industry and FDA reviewers to provide clear guidelines for the content, format, and due dates of CoA study reports. Uniformity in reporting will help the agency track the status of studies.

- A new electronic tracking system has been put in place that will enable CDRH to formally track the status of CoA studies. Firms will be notified immediately if reports are overdue.

- CDRH will periodically report the results of CoA studies to the Center's Advisory Panels.

- CDRH is considering posting periodic status reports on CoA studies on the agency's website.

[1] Monthly PMA Listings. http://www.fda.gov/cdrh/pmapage.html#monthly Accessed 12/31/02

[2] Zoomerang. http://www.zoomerang.com/Login/index.zgi