PALMAZ® Balloon-Expandable Stent for Renal Arteries - P890017/S010

Issued July 10, 2002

- Part 1 - Approval Order
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Updated August 8, 2002

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

Ms. Karen Wilk
Manager, Endovascular Regulatory Affairs
Cordis Corporation
P.O. Box 4917
Warren, N.J. 07059

JUL 10 2002

Re: P890017/S10
Cordis PALMAZ® Balloon Expandable Stent (Models P104R, P154R, P204R)
Filed: December 6, 2001
Amended: February 19, April 16, May 7 and17, June 4 and 27, 2002

Dear Ms. Wilk:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) supplement for the Cordis PALMAZ® Balloon Expandable Stent (Models P104R, P154R, P204R). This device is indicated for use in patients with atherosclerotic disease of the renal arteries following suboptimal percutaneous renal angioplasty (PTRA) of a de novo or restenotic lesion ($\leq$ 22 mm in length) located within 10 mm of the aortorenal artery border and with a reference vessel diameter of $\geq$ 4 mm and $\leq$ 8 mm. Suboptimal PTRA results are defined by one or more of the following unfavorable results: $\geq$ 50 % residual stenosis by visual estimate, $\geq$ 20 mmHg peak translesional pressure gradient , $\geq$ 10 mm Hg mean translesional pressure gradient, and/or Grade D dissection (a spiral shaped filling defect within the lumen of the vessel) or any dissection with significant compromise in lumen flow. The PMA supplement is approved. You may begin commercial distribution of the device as modified in accordance with the conditions described below and in the "Conditions of Approval" (enclosed).

The sale, distribution, and use of this device are restricted to prescription use in accordance with 21 CFR 801.109 within the meaning of section 520(e) of the Federal Food, Drug, and Cosmetic Act (the act) under the authority of section 515(d)(1)(B)(ii) of the act. FDA has also determined that, to ensure the safe and effective use of the device, the device is further restricted within the meaning of section 520(e) under the authority of section 515(d)(1)(B)(ii), (1) insofar as the labeling specify the requirements that apply to the training of practitioners who may use the device as approved in this order and (2) insofar as the sale, distribution, and use must not violate sections 502(q) and (r) of the act.

In addition to the postapproval requirements outlined in the enclosure, you have agreed to provide the following data in a postapproval report: three-year clinical follow-up of the patients enrolled in the ASPIRE2 Trial. The clinical follow-up should report the blood pressure, current

number of antihypertensive medications, and serum creatinine of these patients. In addition, major adverse events (death, Q-wave myocardial infarction, target lesion revascularization or significant embolic events) that occurred since the two-year follow-up should be included in the post-approval report.

Expiration dating for this device has been established and approved at five years.

CDRH does not evaluate information related to contract liability warranties, however you should be aware that any such warranty statements must be truthful, accurate, and not misleading, and must be consistent with applicable Federal and State laws.

CDRH will notify the public of its decision to approve your PMA by making available a summary of the safety and effectiveness data upon which the approval is based. The information can be found on the FDA CDRH Internet HomePage located at http://www.fda.gov/cdrh/pmapage.html. Written requests for this information can also be made to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. The written request should include the PMA number or docket number. Within 30 days from the date that this information is placed on the Internet, any interested person may seek review of this decision by requesting an opportunity for administrative review, either through a hearing or review by an independent advisory committee, under section 515(g) of the act.

Failure to comply with the conditions of approval invalidates this approval order. Commercial distribution of a device that is not in compliance with these conditions is a violation of the act.

You are reminded that, as soon as possible and before commercial distribution of your device, you must submit an amendment to this PMA submission with copies of all approved labeling affected by this supplement in final printed form. The labeling will not routinely be reviewed by FDA staff when PMA supplement applicants include with their submission of the final printed labeling a cover letter stating that the final printed labeling is identical to the labeling approved in draft form. If the final printed labeling is not identical, any changes from the final draft labeling should be highlighted and explained in the amendment.

All required documents should be submitted in triplicate, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

PMA Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Blvd.
Rockville, Maryland 20850

If you have any questions concerning this approval order, please contact Judy Danielson at (301) 443-8243.

Sincerely yours,

Donna-Bea Tillman, Ph.D.
Acting Director
Division of Cardiovascular and
Respiratory Devices
Office of Device Evaluation
Center for Devices and
Radiological Devices

Enclosure

Last Modified: 1-31-02

CONDITIONS OF APPROVAL

PREMARKET APPROVAL APPLICATION (PMA) SUPPLEMENT. Before making any change affecting the safety or effectiveness of the device, submit a PMA supplement for review and approval by FDA unless the change is of a type for which a "Special PMA Supplement-Changes Being Effected" is permitted under 21 CFR 814.39(d) or an alternate submission is permitted in accordance with 21 CFR 814.39(e) or (f). A PMA supplement or alternate submission shall comply with applicable requirements under 21 CFR 814.39 of the final rule for Premarket Approval of Medical Devices.

All situations that require a PMA supplement cannot be briefly summarized; therefore, please consult the PMA regulation for further guidance. The guidance provided below is only for several key instances.

A PMA supplement must be submitted when unanticipated adverse effects, increases in the incidence of anticipated adverse effects, or device failures necessitate a labeling, manufacturing, or device modification.

A PMA supplement must be submitted if the device is to be modified and the modified device should be subjected to animal or laboratory or clinical testing designed to determine if the modified device remains safe and effective.

A "Special PMA Supplement - Changes Being Effected" is limited to the labeling, quality control and manufacturing process changes specified under 21 CFR 814.39(d)(2). It allows for the addition of, but not the replacement of previously approved, quality control specifications and test methods. These changes may be implemented before FDA approval upon acknowledgment by FDA that the submission is being processed as a "Special PMA Supplement - Changes Being Effected." This procedure is not applicable to changes in device design, composition, specifications, circuitry, software or energy source.

Alternate submissions permitted under 21 CFR 814.39(e) apply to changes that otherwise require approval of a PMA supplement before implementation of the change and include the use of a 30-day PMA supplement or annual postapproval report (see below). FDA must have previously indicated in an advisory opinion to the affected industry or in correspondence with the applicant that the alternate submission is permitted for the change. Before such can occur, FDA and the PMA applicant(s) involved must agree upon any needed testing protocol, test results, reporting format, information to be reported, and the alternate submission to be used.

Alternate submissions permitted under 21 CFR 814.39(f) for manufacturing process changes include the use of a 30-day Notice. The manufacturer may distribute the device 30 days after the date on which the FDA receives the 30-day Notice, unless the FDA notifies the applicant within 30 days from receipt of the notice that the notice is not adequate.

POSTAPPROVAL REPORTS. Continued approval of this PMA is contingent upon the submission of postapproval reports required under 21 CFR 814.84 at intervals of 1 year from the date of approval of the original PMA. Postapproval reports for supplements approved under the original PMA, if applicable, are to be included in the next and subsequent annual reports for the original PMA unless specified otherwise in the approval order for the PMA supplement. Two copies identified as "Annual Report" and bearing the applicable PMA reference number are to be submitted to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Blvd., Rockville, Maryland 20850. The postapproval report shall indicate the beginning and ending date of the period covered by the report and shall include the following information required by 21 CFR 814.84:

1. Identification of changes described in 21 CFR 814.39(a) and changes required to be reported to FDA under 21 CFR 814.39(b).

2. Bibliography and summary of the following information not previously submitted as part of the PMA and that is known to or reasonably should be known to the applicant:

   a. unpublished reports of data from any clinical investigations or nonclinical laboratory studies involving the device or related devices ("related" devices include devices which are the same or substantially similar to the applicant's device); and

   b. reports in the scientific literature concerning the device.

If, after reviewing the bibliography and summary, FDA concludes that agency review of one or more of the above reports is required, the applicant shall submit two copies of each identified report when so notified by FDA.

ADVERSE REACTION AND DEVICE DEFECT REPORTING. As provided by 21 CFR 814.82(a)(9), FDA has determined that in order to provide continued reasonable assurance of the safety and effectiveness of the device, the applicant shall submit 3 copies of a written report identified, as applicable, as an "Adverse Reaction Report" or "Device Defect Report" to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Blvd., Rockville, Maryland 20850 within 10 days after the applicant receives or has knowledge of information concerning:

1. A mix-up of the device or its labeling with another article.

2. Any adverse reaction, side effect, injury, toxicity, or sensitivity reaction that is attributable to the device and:

   a. has not been addressed by the device's labeling; or

   b. has been addressed by the device's labeling but is occurring with unexpected severity or frequency.

3. Any significant chemical, physical or other change or deterioration in the device, or any failure of the device to meet the specifications established in the approved PMA that could not cause or contribute to death or serious injury but are not correctable by adjustments or other maintenance procedures described in the approved labeling. The report shall include a discussion of the applicant's assessment of the change, deterioration or failure and any proposed or implemented corrective action by the applicant. When such events are correctable by adjustments or other maintenance procedures described in the approved labeling, all such events known to the applicant shall be included in the Annual Report described under "Postapproval Reports" above unless specified otherwise in the conditions of approval to this PMA. This postapproval report shall appropriately categorize these events and include the number of reported and otherwise known instances of each category during the reporting period. Additional information regarding the events discussed above shall be submitted by the applicant when determined by FDA to be necessary to provide continued reasonable assurance of the safety and effectiveness of the device for its intended use.

REPORTING UNDER THE MEDICAL DEVICE REPORTING (MDR) REGULATION.
The Medical Device Reporting (MDR) Regulation became effective on December 13, 1984. This regulation was replaced by the reporting requirements of the Safe Medical Devices Act of 1990 which became effective July 31, 1996 and requires that all manufacturers and importers of medical devices, including in vitro diagnostic devices, report to the FDA whenever they receive or otherwise become aware of information, from any source, that reasonably suggests that a device marketed by the manufacturer or importer:

1. May have caused or contributed to a death or serious injury; or

2. Has malfunctioned and such device or similar device marketed by the manufacturer or importer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

The same events subject to reporting under the MDR Regulation may also be subject to the above "Adverse Reaction and Device Defect Reporting" requirements in the "Conditions of Approval" for this PMA. FDA has determined that such duplicative reporting is unnecessary. Whenever an event involving a device is subject to reporting under both the MDR Regulation and the "Conditions of Approval" for a PMA, the manufacturer shall submit the appropriate reports required by the MDR Regulation within the time frames as identified in 21 CFR 803.10(c) using FDA Form 3500A, i.e., 30 days after becoming aware of a reportable death, serious injury, or malfunction as described in 21 CFR 803.50 and 21 CFR 803.52 and 5 days after becoming aware that a reportable MDR event requires remedial action to prevent an unreasonable risk of substantial harm to the public health. The manufacturer is responsible for submitting a baseline report on FDA Form 3417 for a device when the device model is first reported under 21 CFR 803.50. This baseline report is to include the PMA reference number. Any written report and its envelope is to be specifically identified, e.g., "Manufacturer Report," "5-Day Report," "Baseline Report," etc.

Any written report is to be submitted to:

Food and Drug Administration
Center for Devices and Radiological Health
Medical Device Reporting
PO Box 3002
Rockville, Maryland 20847-3002

Copies of the MDR Regulation (FOD # 336&1336)and FDA publications entitled "An Overview of the Medical Device Reporting Regulation" (FOD # 509) and "Medical Device Reporting for Manufacturers" (FOD #987) are available on the CDRH WWW Home Page. They are also available through CDRH's Fact-On-Demand (F-O-D) at 800-899-0381. Written requests for information can be made by sending a facsimile to CDRH's Division of Small Manufacturers International and Consumer Assistance (DSMICA) at 301-443-8818.

SUMMARY OF SAFETY AND EFFECTIVENESS DATA

1. General Information

Device Generic Name: Renal Stent

Device Trade Name: PALMAZ® Balloon Expandable Stent for the Renal Arteries

Applicant's Name and Address: Cordis Corporation
P.O. Box 4917
Warren, NJ 07059

Premarket Approval Application (PMA) Number: P890017/S10

Date(s) of Panel Recommendation: None

Date of Notice of Approval to Applicant: July 10, 2002

The PALMAZ® Balloon Expandable Stent, Model P308, was approved on September 29, 19991 (P890017) for use following a suboptimal angioplasty procedure of the common or external iliac arteries. The sponsor submitted this supplement for the PALMAZ® Balloon Expandable Stent, Models P104R, P154R and P204R, to expand the indication for use in the renal arteries. The updated pre-clinical and clinical data to support this indication are provided in this summary. Some of the pre-clinical tests were presented in the original PMA application. For more information on the data that supported approval of the indication or use in the iliac arteries, the summary of safety and effectiveness data (SSED) for P890017 should be referenced. Written requests for copies of the SSED can be obtained from the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20857. The SSED can also be found on the FDA CDRH Internet Home Page located at http://www.fda.gov/cdrh/pmapage.html.

2. Indications for Use

The PALMAZ® Balloon-Expandable Stent is indicated for use in patients with atherosclerotic disease of the renal arteries following suboptimal percutaneous renal angioplasty (PTRA) of a de novo or restenotic lesion (≤ 22 mm in length) located within 10 mm of the aortorenal artery border and with a reference vessel diameter of ≥ 4 mm and ≤ 8 mm. Suboptimal PTRA results are defined by one or more of the following unfavorable results.

1) ≥50% residual stenosis by visual estimate
2) ≥20mmHg peak translesional pressure gradient
3) ≥10mmHg mean translesional pressure gradient

4) Grade D dissection (a spiral shaped filling defect within the lumen of the vessel) or any dissection with significant compromise in lumen flow

3. Device Description

The PALMAZ Balloon-Expandable Stent is a 316L stainless steel, slotted tube which is expanded with the use of the recommended delivery systems (refer to Table 1).

The delivery system, the POWERFLEX® Plus PTA Catheter, consists of a dual lumen shaft design with a distal inflatable balloon. Two radiopaque marker bands indicate the dilating section of the balloon.

Table 1. Device Models

Stent Description		Stent Lengths		POWERFLEX PLUS	Recommended Cordis Catheter Sheath Introducer (CSI) and Guiding Catheter	
Product Code	Nominal Dia (mm)	Unexpanded (mm)	Expanded (mm)	Catalog Number[1]	CSI Size French	Guiding Catheter Size French
P104R	4	10.0	9.9	412-4010	6F	8F
	5	10.0	9.7	412-5010	6F	8F
	6	10.0	9.4	412-6010	6F	8F
	7	10.0	9.0	412.7010	7F	9F
	8	10.0	8.5	412-8010	7F	9F
P154R	4	15.0	14.8	412-4015	6F	8F
	5	15.0	14.5	412-5015	6F	8F
	6	15.0	14.0	412-6015	6F	8F
	7	15.0	13.4	412-7015	7F	9F
	8	15.0	12.6	412-8015	7F	9F
P204R	4	20.0	19.7	412-4020	6F	8F
	5	20.0	19.3	412-5020	6F	8F
	6	20.0	18.7	412-6020	6F	8F
	7	20.0	17.8	412-7020	7F	9F
	8	20.0	16.8	412-8020	7F	9F

Use Cordis Crimping Tool CRT20 and Introducer Tube INTR4 for all product codes and lengths.
French size conversions: 6F (2.0mm), 7F (2.3mm), 8F (2.7mm), 9F (3.0mm)
[1]Catheter suffices for the POWERFLEX PLUS refers to the usable catheter length. Any of the following catheter length suffixes may be used: T (40cm), V (65cm), S (80cm), L (110cm) and X (135cm). NOTE: Not all balloon sizes are sold in all catheter lengths.

4. Contraindications

The PALMAZ Balloon-Expandable Stent is contraindicated for use in patients who have a lesion that cannot be crossed with a wire and/or balloon catheter.

5. WARNINGS and PRECAUTIONS

See WARNINGS and PRECAUTIONS in the final labeling (Instructions for Use).

6. Adverse Events

6.1 Observed Adverse Events

A total of 51 patients with proximal renal artery disease were evaluated in the ASPIRE (Analysis of Stents versus PTA In Renal Arteries) clinical feasibility study. There were no major in-hospital complications reported during the study. There were eight major adverse events in 51 patients out to 720 days, which included four deaths and four cases of target lesion revascularization.

Note: The remaining adverse event information and the information in the subsequent section (Clinical Studies) is based upon the ASPIRE2 Pivotal study.

A total of 208 patients were evaluated as part of the multi-center, prospective, non-randomized study to evaluate the safety and effectiveness of the PALMAZ Balloon-Expandable Stent in patients with atherosclerotic proximal renal artery stenosis that was suboptimally treated with percutaneous transluminal renal angioplasty (PTRA).

As shown in Table 2, there were twenty major device or procedure-related adverse events reported in 208 patients out to 270 days. One patient experienced a significant embolic event postoperatively and died at 80 days of cardiac arrest due to renal failure.

There were eleven deaths (5.2%) that were non-device and procedure related. Five of the deaths were cardiac-related and six were non-cardiac. Two patients died due to myocardial infarction, one patient at 145 days and the other at 253 days. Three patients died due to cardiac arrest: one patient at 90 days, one patient at 127 days and one patient at 243 days. One patient died at 48 days subsequent to an embolic event from the aorta and superior mesenteric artery. One patient died at 81 days following aortic valve replacement surgery. One patient died at 87 days subsequent to viral pneumonia with acute inflammatory pneumonitis and respiratory distress. One patient died at 140 days subsequent to hyperkalemia due to renal failure and severe cardiomyopathy. One patient experienced a device or procedure related significant embolic event at day 7. This patient subsequently died at day 164 due to sepsis. One patient died at day 208 due to a cerebral vascular accident.

Table 2. Device or Procedure Related Observed Adverse Events to 270 Days for the PALMAZ Balloon-Expandable Stent ASPIRE 2 Clinical Study

Parameter	Percent (N=208 Patients)	95% CI
In-hospital Event		
Major Adverse Event (Death, QMI, TLR, Embolic)	3 (1.4%)	[0.3%, 4.2%]
Death (device or procedure related)	0 (0.0%)	[0.0%, 1.8%]
Q-wave MI	0 (0.0%)	[0.0%, 1.8%]
Target lesion revascularization	0 (0.0%)	[0.0%, 1.8%]
Significant embolic event[1]	3 (1.4%)	[0.3%, 4.2%]
Stent Thrombosis	1 (0.5%)	[0.0%, 2.7%]

CVA	0 (0.0%)	[0.0%, 1.8%]
Major bleeding	2 (1.0%)	[0.1%, 3.4%]
Major Vascular	5 (2.4%)	[0.8%, 5.5%]

Parameter	Percent (N=208 Patients)	95% CI
Out-of-hospital Event		
Major Adverse Event (Death, QMI, TLR, Emboli)	17 (8.2%)	[4.8%, 12.8%]
Death (device or procedure related)	1 (0.5%)	[0.0%, 2.7%]
Q-wave MI	0 (0.0%)	[0.0%, 1.8%]
Target lesion revascularization	10 (4.8%)	[2.3%, 8.7%]
Significant embolic event[1]	8 (3.8%)	[1.7%, 7.4%]
Stent Thrombosis	1 (0.5%)	[0.0%, 2.7%]
CVA	0 (0.0%)	[0.0%, 1.8%]
Major bleeding	1 (0.5%)	[0.0%, 2.7%]
Major Vascular	5 (2.4%)	[0.8%, 5.5%]
Combined (In-and-Out-of-hospital)		
Major Adverse Event (Death, QMI, TLR, Emboli)	20 (9.6%)	[6.0%, 14.5%]
Death	1 (0.5%)	[0.0%, 2.7%]
Q-wave MI	0 (0.0%)	[0.0%, 1.8%]
Target lesion revascularization	10 (4.8%)	[2.3%, 9.3%]
Significant embolic event[1]	11 (5.3%)	[2.7%, 9.3%]
Stent Thrombosis	2 (1.0%)	[0.1%, 3.4%]
CVA	0 (0.0%)	[0.0%, 1.8%]
Major bleeding	3 (1.4%)	[0.3%, 4.2%]
Major Vascular	10 (4.8%)	[2.3%, 8.7%]

Note: (1) Significant embolic event (SEE) is defined as causing end-organ damage, (e.g., unanticipated kidney/bowel infarct, lower extremity ulceration or gangrene) or loss of kidney function. Five patients were categorized as SEE due to a true embolic event. Three patients were categorized as SEE due to contrast reaction, secondary to acute tubular necrosis (ATN).

6.2 POTENTIAL ADVERSE EVENTS

Adverse events (in alphabetical order) that may be associated with implantation of a stent in renal arteries (in addition to those listed in Table 2) include:

- Allergic reaction to stainless steel or its components
- Aneurysm
- Death
- Dissection
- Embolization of plaque or cholesterol
- Failure to deliver the stent to the intended site
- Fistulization
- Hematoma requiring treatment
- Hemorrhage
- Infection/fever
- Myocardial ischemia/infarction
- Nephrectomy/renal transplantation
- Peripheral neuropathy
- Persistent abdominal pain
- Persistent vessel spasm
- Pseudoaneurysm
- Reaction to contrast media

- Renal failure/dialysis
- Restenosis of vessel (greater than 50% obstruction)

- Rupture or perforation of vessel
- Stent migration or embolization
- Stroke
- Thrombosis/vessel occlusion

6.3 Stent Delivery Failures

Stent treatment of 252 lesions was attempted in the ASPIRE2 Pivotal Study. There were five stent delivery failures. The circumstances of the delivery failures are as follows: stent was deployed distal to the intended location with a second stent successfully delivered (n=3); unable to deploy stent, stent was retrieved and a subsequent stent successfully delivered (n=1); unable to deploy stent, stent was retrieved (n=1).

7. Alternative Procedures

Alternative procedures to treat renal artery stenosis include percutaneous transluminal renal angioplasty (PTRA) and surgical procedures (e.g., aorto-renal bypass, extra-anatomic bypass, combined aortic graft and aorto-renal bypass, adjunctive transaortic renal endarterectomy).

8. Marketing History

The PALMAZ Balloon-Expandable Medium Stents were first sold commercially in 1991 by Johnson & Johnson Interventional System Company. Since that time, more than 225,000 of these devices have been distributed throughout the world, including the European Union, Eastern Europe, Canada, Latin America, and Australia. The device has been available in the United States since 2000 for use in the treatment of atherosclerotic lesions of the common or external iliac artery following suboptimal angioplasty procedure and since 1991 for the palliation of malignant neoplasms in the biliary tree.

The device has not been withdrawn from marketing in any of these countries for any reason related to safety and effectiveness.

9. Summary of Pre-clinical Studies

9.1 Biocompatibility

The material and manufacturing methods used to construct the PALMAZ Balloon-Expandable Medium Stents (Models P104R, P154R and P204R) are identical to the materials and manufacturing methods used to construct the approved PALMAZ Balloon-Expandable Stents Model P308 approved under P890017. Therefore the biocompatibility testing provided in the original premarket approval application P890017 is also applicable to the current application for the PALMAZ Balloon-Expandable Medium Stents.

Biocompatibility of the materials used in the construction of the POWERFLEX Plus delivery catheter was determined by the results of previous testing conducted on these materials or combination of materials, as well as testing conducted on the finished POWERFLEX Plus catheter. The testing, including those recommended in the FDA modified matrix of

International Standard ISO-10093, "Biological Evaluation of Medical Devices Part 1: Evaluation and Testing," were: cytotoxicity, sensitization, irritation, systemic toxicity, implantation, hemolysis, hemocompatibility, pyrogenicity, and physio-chemical testing. The results of all biocompatibility tests were acceptable.

9.2 Bench Testing

Previous Preclinical Studies

The PALMAZ Balloon-Expandable Stent Model P308 was commercially approved for marketing under the original premarket approval application P890017. The PALMAZ Balloon-Expandable Medium Stent Models P104R, P154R and P204R differ from the PALMAZ Balloon-Expandable Stent Model P308 only in length and the specified expansion diameter. Therefore, the preclinical testing of the stent wire material (material specification, mechanical properties and corrosion resistance), and compatibility with magnetic resonance imaging provided in P890017 is applicable to the PALMAZ Stent Models P104R, P154R and P204R. Please refer to the SSED of the original PMA P890017 for a summary of this testing.

Additional Pre-Clinical Studies

The PALMAZ Balloon-Expandable Stent Models P104R, P154R and P204R have undergone additional pre-clinical testing as follows:

Stent Testing

Stent Free Area and Dimensional Change
The stent free area, i.e., the open area of the stent and the change in stent length was calculated for all diameters that the Palmaz stent could theoretically be expanded to. The percent free area for all stent lengths ranged from 80.65% for the smallest diameter (4 mm) to 88.87% for the largest diameter (8 mm). The calculated stent length decreased a maximum of 15% for the 10 mm nominal length and 16% for the 15 mm and 20 mm nominal stent lengths with the stent expanded to largest diameter (8 mm). The percentage of free area with the PALMAZ Stent is similar to the percentage of free area with stents approved for the vascular system.

Stent Recoil
Stent recoil is calculated as a function of the pressurized stent diameter while on the balloon, and the stent diameter after the balloon is deflated and removed. The acceptance criterion is < 10% recoil for any length - diameter combination. The worst case situation is the smallest expansion diameter (4mm) since the stent would need to recoil the smallest absolute distance to reach the 10% threshold. In addition to the 4mm diameter, 5 and 8mm diameters were also tested. Five (5) stents of each length were tested. All stents satisfactorily met the recoil criteria.

Stent Uniformity
Stent Uniformity data is captured as part of Stent Recoil testing. Since all stents were within 10% of their stated diameter, they have also opened uniformly. Stent Uniformity data is based on the relaxed stent diameters.

Radial Strength
To determine the radial strength of the stent, five samples of each stent length were expanded to the maximum diameter (8mm) within a latex tube. The latex tube with expanded stent was placed in a pressure vessel and circumferential pressure was applied until the stent collapsed (irreversible stent deformation). All stents exceeded the acceptance criteria with the average radial pressure to collapse of the stent 5.3 psi for the 10 mm length, 4.4 psi for the 15 mm length and 7.8 psi for the 20 mm length.

Stress and Fatigue Testing
Stress and Fatigue Testing was conducted on P394 Palmaz Stents, which are identical in design to the Palmaz Stent models P104R, P154R with the exception of a longer stent length. A total of 10 stents expanded to 9 mm (1 mm greater than the maximum labeled diameter) were subjected to fatigue testing with a pulsed pressure of 100 mm Hg pressure for a maximum of 614 million cycles. The stents were examined under scanning electron microscopy (SEM) after 100, 400, 500 and 614 million cycles. The SEM examination did not show any metallurgical defects that could cause failure of the stent.

To further assess the fatigue strength of the Palmaz Stent in the renal artery, a finite elements analysis (FEA) was conducted on the 20 mm long (P204) Palmaz Stent expanded to 9 mm and a 300 mm Hg pressure differential. The results of the FEA indicated a satisfactory safety factor was present and fatigue failure of the stent was unlikely.

Stent and Delivery System Testing

Maximum Balloon Pressure
To determine the burst strength of the PowerFlex Plus delivery catheter with the mounted Palmaz Stent, a total of 50 samples (10 each of the extreme balloon diameters and lengths and a medium-sized stent diameter) were tested to burst. The test results showed with a 95% confidence that 99.9% of the stented balloons would not burst at or below the labeled rated burst pressure of 15 atm.

Stent Diameter versus Balloon Inflation Pressure
To assess the change in stent diameter with inflation of the delivery catheter balloon, 45 stent/catheter systems representing each balloon length and diameter were inflated in 1 atmosphere increments up to the rated burst pressure. The test results showed that all of the stent diameters were within 10% of the labeled stent diameter when expanded with inflation pressures from the nominal 10 atm up to the rated burst pressure of 15 atm.

Balloon Deflatibility and Deflation Time
To evaluate the ability to deflate and withdraw the balloon and determine the time to deflate 90% of the balloon, 19 stent/catheter systems representing the smallest and largest balloon diameter and length and the longest catheter shaft length were tested. All the test samples met the acceptance criteria for the smallest and largest balloon diameter, ≤ 9.5 seconds and ≤ 21 seconds, respectively.

Bond Strength

To determine the strength of the bonds used in the construction of the delivery catheter, tensile testing was conducted on five samples each of the following bonds: proximal and distal balloon to catheter bond, marker band to inner catheter, and y-connector to catheter bond. The test results found that the strength of the bonds exceeded the acceptance criteria of ≥ 8 Newtons for the balloon to catheter and marker band to inner catheter bonds. The tensile test results of the y-connector to catheter bond also exceeded the acceptance criterion of ≥ 15 Newtons.

Stent Crimping (Stent Retention)
To determine the minimum tensile force required to dislodge the Palmaz Stent from the delivery catheter balloon, ten samples of the shortest stent/balloon combination (4mm stent diameter by 10mm long balloon) were tensile tested. All of the stent/balloon catheter samples met the acceptance criteria of ≥ 0.7 Newtons.

Crossing Profile
To determine the crossing profile of the stent/catheter system, the outer diameter measurement were taken of 45 Palmaz Stent samples mounted on 45 delivery catheters representing each balloon length and diameter were measured. The crossing profile measurements found that the 4 mm, 5mm and 6 mm diameter stent/catheter systems are compatible with 6 Fr.catheter sheath introducers and the 7 mm and 8 mm diameter stent/catheter systems are compatible with 7 Fr.catheter sheath introducers.

Catheter Body Maximum Pressure
To determine the maximum pressure limits of the delivery catheter's balloon inflation lumen and guidewire lumen, 10 samples were tested to failure. The test results found that both lumens exceeded their respective acceptance criteria; ≥ 15 atm for the balloon inflation lumen and ≥ 33 atm for the guidewire lumen.

Contrast Medium Flow
To evaluate the use of the catheter for injection of contrast medium at pressures ranging from 10 atm to 30 atm, 5 samples of the shortest catheter length (40 cm) and 5 samples of a worst case longest catheter length (150 cm) were tested. The test results showed that the average flow rate per minute for the 40 cm length ranged from 4.9 cc with 10 atm to 13.2 cc with 30 atm. The average flow rate per minute for the 150 cm length ranged from 1.7 cc with 10 atm to 5.1 cc with 30 atm. All test samples met the acceptance criteria of no leaking, bulging or burst catheter failures.

9.3 Sterility Packaging and Shelf Life Testing

Sterility
The packaging materials and sterilization process for the PALMAZ Balloon-Expandable Medium Stents (Models P104R, P154R and P204R) are identical to the packaging materials and sterilization process used for the PALMAZ Balloon-Expandable Stents Model P308 approved under P890017. Therefore the sterility testing provided in the original premarket approval application P890017 is also applicable to the current application for the PALMAZ Balloon-Expandable Medium Stents.

The POWERFLEX Plus delivery catheter is sterilized using an ethylene oxide sterilization process. Validation of the sterilization process for the POWERFLEX Plus delivery catheter is based on the ANSI/AAMI/ISO 1135-1994 "Medical Devices – Validation and Routine Control of Ethylene Oxide Sterilization." The validation results demonstrated that the sterilization process can achieve a sterility assurance level of 10^{-6}.

Packaging and Shelf-life Tests