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December 20, 1999

DOCKET NUMBER
PROPOSED RULE PR 20, 32 435
(63FR43516)

OFFICE OF THE SECRETARY
ADJUDICATIONS

'99 DEC 27 A10:46

DOCKETED
USNRC

The Honorable Richard A. Meserve, Chairman
United States Nuclear Regulatory Commission
One White Flint North
11555 Rockville Pike
Rockville, MD 20852-2738

Dear Chairman Meserve:

The American College of Cardiology (ACC), a medical society that represents 25,000 cardiovascular specialists, has been an active participant in the revision process of 10 CFR Part 35,"Medical Use of Byproduct Material." We believe that the proposed changes will maintain safety, decrease the regulatory burden and increase public confidence in the regulation of radiation.

The cardiology community has a special interest in the process not only with respect to the use of diagnostic applications such as myocardial perfusion imaging, but also in the evolving field of intravascular radiation for restenosis prevention (intravascular brachytherapy). We believe that this modality has the potential to overcome the biggest problem associated with interventional cardiology procedures: tissue proliferation. As the attached table (Clinical Trials Using Intravascular Brachytherapy for the Inhibition of Restenosis) demonstrates, intravascular radiation for restenosis prevention can be performed in many different ways. We appreciate the fact that the Nuclear Regulatory Commission (NRC) and Part 35 Writing Group have recognized the emerging nature of intravascular radiation for restenosis prevention and acknowledged these changing circumstances in the draft final rule version of 10 CFR, Part 35.1000. Following adoption of a standard protocol, the NRC will address regulatory treatment of intravascular radiation for restenosis prevention.

Over the years, the ACC has been pleased to nominate cardiologists to serve on the Advisory Committee on the Medical Uses of Isotopes (ACMUI). That representation has allowed the cardiology community to provide input into issues related to nuclear cardiology. The ACMUI has a broad composition that represents all the stakeholders in the medical use of byproduct materials. Dr. Manuel Cerqueira, the cardiology community's representative to the ACMUI, has been named to chair that panel. He is a recognized expert in nuclear cardiology and board certified in nuclear medicine. As chair, he will see that all viewpoints are represented fairly.

Dr. Cerqueira does not practice interventional cardiology or have expertise in the emerging technology of intravascular radiation for restenosis prevention. No one presently serving on the ACMUI has either the clinical and technical knowledge or experience sufficient to provide expertise on intravascular radiation. Given the significance of this emerging modality, the ACC believes it is appropriate for an interventional cardiologist to sit on the ACMUI.

An interventional cardiologist with expertise in intravascular radiation for restenois prevention will provide the committee with the unique perspective required to understand the complicated issues involved in the clinical management of patients in the cardiac catheterization

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laboratory where the studies will be performed. The addition of a representative from the interventional cardiology community would assure that the committee receive expert information from practitioners in the field. The cardiology community believes that the addition of an interventional cardiologist is critical to guaranteeing the safety of patients and users.

The cardiology community looks forward to a continuing dialogue with the NRC and the ACMUI on issues related to the medical uses of byproduct material in cardiology procedures. Addition of an interventional cardiologist to the ACMUI would assure that the advisory panel could provide the commissioners the most relevant information on new developments related to intravascular radiation for restenosis prevention.

Thank you for considering the views of the more than 25,000 ACC members.

Sincerely,

Arthur Garson, Jr., M.D., M.P.H., F.A.C.C.
President

Attachment

cc: Commissioner Nils J. Diaz
Commissioner Greta Joy Dicus
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Commissioner Jeffrey S. Merrifield
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CLINICAL TRIALS USING INTRAVASCULAR BRACHYTHERAPY FOR THE INHIBITION OF RESTENOSIS

Study Name	Principle Investigator	Type of Trial	Trial Design	No. of Patients	Vascular Bed	Lesion Type	Treatment	Isotope	Type of Radiation	Dose or Activity	Delivery Platform	Delivery Method	Centered Source	Results and Status
Venezuela	Condado, et al	Feasibility	Open Label	21	Coronary	De novo	PTCA	^{192}Ir	Gamma	20-25 Gy to arterial dose 19-55 Gy	Catheter	Hand	Non-Centered	Completed Clinical and angiographic follow up to 24 months demonstrated safety and less late loss; [illegible] noted in two
SCRIPPS	Teirstein, et al	Feasibility Efficacy	Randomized Controlled	55	Coronary	Restenosis	PTCA and Stent	^{192}Ir	Gamma	8-30 Gy to media by IVUS	Catheter	Hand	Non-Centered	Completed Significant reduction of restenosis 54% vs [illegible] in the irradiated group
Swiss I	Verin, et al	Phase I	Open Label	15	Coronary	De novo	PTCA	^{90}Sr	Beta	18 Gy to lumen surface	Catheter	Afterloader	Centered	Completed [illegible] and safety but not efficacy [illegible] 4 pts
HERT	Long, et al	Phase I	Open Label	23	Coronary	De novo	PTCA	^{90}Sr/Y	Beta	12, 14, 16 Gy to 2 mm from source	Catheter	Hydraulic device	Non-Centered	Completed Demonstrated feasibility and safety Restenosis 13%, Late loss index of 4%
BERT Canada	Roman, et al	Phase I	Open Label	30	Coronary	De novo	PTCA	^{90}Sr/Y	Beta	12,14,16 Gy to 2 mm from source	Catheter	Hydraulic device	Non-Centered	Completed Demonstrated feasibility and safety Restenosis rate 10%. Negative late loss
BERT European	Serruys, et al	Phase I	Open Label	30	Coronary	De novo	PTCA	^{90}Sr/Y	Beta	12, 14, 16 Gy to 2 mm from source	Catheter	Hydraulic device	Non-Centered	Enrollment completed. Data expected Summer, 1998
PREVENT	Raizner, et al	Phase I	Randomized, Controlled	84	Coronary	De novo or Restenosis	PTCA, Stent	^{32}P	Beta	0, 16, 20, 24 Gy to 1.0 mm into artery wall	Catheter	Afterloader	Centered	Enrollment completed. Data expected Fall 1998
ARIST	Waksman, et al	Phase II	Randomized, Controlled	100	Coronary	In-stent restenosis	PTCA, Stent	^{192}Ir	Gamma	15 Gy to 2.3 mm from source	Catheter	Hand	Non-Centered	Enrollment completed
ARIST SVG	Waksman, et al	Phase II	Randomized, Controlled	120	Coronary	In-stent restenosis in saphenous vein grafts	PTCA, Stent	^{192}Ir	Gamma	15 Gy to 2.4 mm from source	Catheter	Hand	Non-Centered	Enrollment started December 1997

CLINICAL TRIALS USING INTRAVASCULAR BRACHYTHERAPY FOR THE INHIBITION OF RESTENOSIS

Study Name	Principle Investigator	Type of Trial	Trial Design	No. of Patients	Vascular Bed	Lesion Type	Treatment	Isotope	Type of Radiation	Dose or Activity	Delivery Platform	Delivery Method	Centered Source	Results and Status
WRIST LONG	Waksman, et al	Phase II	Randomized Controlled	120	Coronary	In-stent restenosis in long (36-88 mm) lesions	PTCA, Stent	^{192}Ir	Gamma	15 Gy to 2.0 mm	Catheter	Hand	Non-Centered	Enrollment started January 1998
BETACATH	Kantz, et al	Phase II	Randomized Control	1100	Coronary	De novo	PTCA, Provisional Stent	^{90}Sr/Y	Beta	14-18 Gy to 2 mm from source	Catheter	Hydraulic device	Non-Centered	Enrollment started Jan. 1998
Swiss II	Verin, et al	Phase I	Open Label	100	Coronary	De novo	PTCA	^{90}Y	Beta	9-18-32 Gy to Surface	Catheter	Afterloader	Centered	Enrollment started September 1997
GAMMA I	Leon, et al	Phase II	Randomized, Controlled	250	Coronary	In-stent restenosis	PTCA, Stent	^{192}Ir	Gamma	8 - 32 to media by IVUS	Catheter	Hand	Non-Centered	Enrollment started December 1997
CURE	Weinberger, et al	Feasibility and Safety	Open Label	60	Coronary	De novo or restenosis	PTCA, Stent	^{188}Re	Beta	20 to balloon surface	Catheter	Liquid filled balloon	Centered	Enrollment started October 1997
ARREST	Waksman, et al	Phase II	Randomized, Controlled	700	Coronary	De novo	PTCA and provisional stenting	^{192}Ir	Gamma	8 - 32 to media by IVUS	Catheter	Afterloader	Centered	Enrollment started spring 1998
INHIBIT	Waksman, et al	Phase II	Randomized, Controlled	200	Coronary	In-stent restenosis	PTCA, Stent	^{32}P	Beta	20 to 1.5 mm into wall	Catheter	Afterloader	Centered	Enrollment anticipated June 1998
IRIS IA	Fischell, et al	Phase I	Open label	32	Coronary	De novo, restenosis	Radioactive stent (Palmaz-Schatz stent)	^{32}P	Beta	Low activity 0.5 to 1.0 uCi	Stent	Catheter	Centered	Completed. Excellent feasibility and safety. Angiographic restenosis 31%
IRIS IB	Moses, et al	Phase I	Open label	25	Coronary	De novo restenosis	Radioactive stent (Palmaz-Schatz stent)	^{32}P	Beta	Activity 1.7 to 3.5 uCi	Stent	Catheter	Centered	Completed. Excellent feasibility and safety. Restenosis data available Summer 1998
Heidelberg	Henriksen, et al	Phase I	Open label	15	Coronary	Restenosis	Radioactive stent (Palmaz-Schatz stent)	^{32}P	Beta	Activity 3.0 uCi	Stent	Catheter	Centered	Enrollment completed. No major adverse events at four months
Milan	Colombo	Phase I	Open label	[illegible]	Coronary	De novo restenosis	Radioactive stent (Palmaz-Schatz stent)	^{32}P	Beta	Activity 5.0 and 8.0 uCi	Stent	Catheter	Centered	Enrollment started January 1998

CLINICAL TRIALS USING INTRAVASCULAR BRACHYTHERAPY FOR THE INHIBITION OF RESTENOSIS

Study Name	Principle Investigator	Type of Trial	Trial Design	No. of Patients	Vascular Bed	Lesion Type	Treatment	Isotope	Type of Radiation	Dose or Activity	Delivery Platform	Delivery Method	Centered Source	Results and Status
Isostent	Fischell et al	Phase I	Open label	30	Coronary	De novo, restenosis	Radioactive stent (BX stent)	^{32}P	Beta	Activity 0.5 to 1.5 uCi	Stent	Catheter	Centered	Enrollment started March 1998
German	Liermann, et al	Feasibility and efficacy	Open label	25	Superficial femoral artery	De novo	PTA and stent	^{192}Ir	Gamma	12 Gy	Catheter	Afterloader	Not centered	Completed. Five year follow-up shows 80% patency. No adverse radiation effects
PARIS	Waksman et al	Phase I	Open label	30	Superficial femoral artery	De novo	PTA	^{192}Ir	Gamma	14 Gy	Catheter	Afterloader	Centered	Completed. Demonstrated feasibility and safety
PARIS II	Waksman et al	Phase II	Randomized controlled	300	Superficial femoral artery	De novo	PTA	^{192}Ir	Gamma	[illegible]	Catheter	Afterloader	Centered	[illegible]
Washington Hospital Center	Waksman, et al	Phase I	Open label	11	AV dialysis shunt	De novo restenosis	PTA	^{192}Ir	Gamma	14 Gy	Catheter	Afterloader	Not Centered	18 lesions treated. 6-12 weeks
New York Hospital Center	[illegible]	Phase I	Open label	19	AV dialysis shunt	De novo or restenosis	PTA	Orthovoltage	[illegible]	[illegible] Gy	External	External beam	Not centered	10 patients [illegible] months