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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 restenosis 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

PDR PR 20 63FR 43516

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Richard Meserve, NRC Chairman, December 20, 1999 page 2

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
Commissioner Edward McGaffigan, Jr.
Commissioner Jeffrey S. Merrifield
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CLINICAL TRIALS USING INTRAVASCULAR BRACHYTHERAPY FOR THE INHIBITION OF RESTENOSIS

Study Name	Principal 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
Venereda	Condado et al	Feasibility	Open Label	21	Coronary	De novo	PTCA	¹⁹² Ir	Gamma	20-25 Gy, actual dose 10-45 Gy	Catheter	Hand	Non-centered	Completed Clinical and angiographic follow-up in 24 months demonstrated safety and low late loss. Enrollment halted in 1998.
STRIPPY	Simonson et al	Feasibility Efficacy	Randomized Controlled	55	Coronary	Restenosis	PTCA and Stent	¹⁹² Ir	Gamma	3-10 Gy to media and IVUS	Catheter	Hand	Non-centered	Completed Significant reduction of re-angiosclerosis in the irradiated group.
SWAN I	Verma et al	Phase I	Open Label	15	Coronary	De novo	PTCA	¹⁹² Ir	Beta	18 Gy to segment surface	Catheter	Afterloader	Centered	Completed Completed in 1998. Enrollment halted in 1998. Late loss index of 10%.
HERI	Hong et al	Phase I	Open Label	23	Coronary	De novo	PTCA	¹⁹² Ir	Beta	12, 14, 16 Gy to 2 mm from source	Catheter	Hydraulic Drive	Non-centered	Completed Demonstrated feasibility and safety. Restenosis rate 15%. Late loss index of 10%.
HERI Canada	Hogan et al	Phase I	Open Label	30	Coronary	De novo	PTCA	¹⁹² Ir	Beta	12, 14, 16 Gy to 2 mm from source	Catheter	Hydraulic Drive	Non-centered	Completed Demonstrated feasibility and safety. Restenosis rate 16%. Negative late loss.
HERI European	Narula et al	Phase I	Open Label	30	Coronary	De novo	PTCA	¹⁹² Ir	Beta	12, 14, 16 Gy to 2 mm from source	Catheter	Hydraulic Drive	Non-centered	Completed Enrollment completed. Data expected Summer 1998.
PREVENT	Pachter et al	Phase I	Randomized Controlled	84	Coronary	De novo or Restenosis	PTCA, Stent	¹⁹² Ir	Beta	0, 16, 26, 34 Gy to 1.0 mm into artery wall	Catheter	Afterloader	Centered	Enrollment completed. Data expected Fall 1998.
ARIST	Wakeman et al	Phase II	Randomized Controlled	100	Coronary	In-stent restenosis	PTCA, Stent	¹⁹² Ir	Gamma	15 Gy to 2.0 mm from source	Catheter	Hand	Non-centered	Enrollment completed.
ARIST S-61	Wakeman 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	Kantrowitz, et al	Phase II	Randomized Control	1100	Coronary	De novo	PTCA, Provisional Stent	⁹⁰ Sr	Beta	14-18 Gy to 2 mm from source	Catheter	Hydraulic device	Non-Centered	Enrollment started July 1998
Swiss II	Verzin, et al	Phase I	Open Label	160	Coronary	De novo	PTCA	¹³⁷ Cs	Beta	9-18 Gy to surface	Catheter	Aftersloader	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
CLARE	Weinberger, et al	Feasibility and Safety	Open Label	60	Coronary	De novo or restenosis	PTCA, Stent	¹⁸⁶ Re	Beta	20 to balloon surface	Catheter	Liquid filled balloon	Centered	Enrollment started October 1997
ARREST	Wassman, et al	Phase II	Randomized, Controlled	700	Coronary	De novo	PTCA and provisional stenting	¹⁹² Ir	Gamma	8-32 to media by IVUS	Catheter	Aftersloader	Centered	Enrollment started Spring 1998
INHIBIT	Waksman, et al	Phase II	Randomized, Controlled	200	Coronary	In-stent restenosis	PTCA, Stent	¹²⁵ I	Beta	20 to 1.0 mm into wall	Catheter	Aftersloader	Centered	Enrollment anticipated June 1998
IRIS IA	Fischell, et al	Phase I	Open label	32	Coronary	De novo, restenosis	Radioactive stent (Palmaz-Schatz stent)	¹²⁵ I	Beta	Low activity: 10.5 to 1.0 uCi	Stent	Catheter	Centered	Completed. Excellent feasibility and safety. Angiographic restenosis: 43%
IRIS IB	Moses, et al	Phase I	Open label	25	Coronary	De novo, restenosis	Radioactive stent (Palmaz-Schatz stent)	¹²⁵ I	Beta	Activity: 7.7 to 1.5 uCi	Stent	Catheter	Centered	Completed. Excellent feasibility and safety. Restenosis data available Summer 1998
Herdelberg	Henriksen, et al	Phase I	Open label	15	Coronary	Restenosis	Radioactive stent (Palmaz-Schatz stent)	¹²⁵ I	Beta	Activity: 3.0 uCi	Stent	Catheter	Centered	Enrollment completed. No major adverse events at four months
Milan	Colombo	Phase I	Open label		Coronary	De novo restenosis	Radioactive stent (Palmaz-Schatz stent)	¹²⁵ I	Beta	Activity: 6.0 and 8.0 uCi	Stent	Catheter	Centered	Enrollment started January 1998

CLINICAL TRIALS USING INTRAVASCULAR BRACHYTHERAPY FOR THE INHIBITION OF RESTENOSIS

Study Name	Principal Investigator	Type of Trial	End Point	No. of Patients	Interv. Type	Isotope	Dose of Activity	Delivery Platform	Delivery Method	Center	Restenosis and Stent
Boehm	Fischell et al	Phase I	Open label	30	Coronary	De novo	Radioactive stent (BX stent)	Stent	Catheter	Centered	Intervention started March 1998
Levin	Levin et al	Phase I	Open label	25	Superficial	De novo	PTA and stent	Catheter	Arterial	Non-centered	Completed 1 year follow-up shows 30% restenosis
Waksman et al	Waksman et al	Phase I	Open label	30	Superficial	De novo	PTA	Catheter	Arterial	Centered	Completed 12 months follow-up and safety
PARRIS II	Waksman et al	Phase II	Randomized controlled	300	Superficial	De novo	PTA	Catheter	Arterial	Centered	12 months follow-up
Waksman et al	Waksman et al	Phase I	Open label	11	Arterial	De novo	PTA	Catheter	Arterial	Non-centered	12 months follow-up
New York Hospital Center	New York Hospital Center	Phase I	Open label	10	Arterial	De novo or restenosis	PTA	Catheter	Arterial	Non-centered	12 months follow-up