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RADIOISOTOPE POWERED CARDIAC PACEMAKER PROGRAM

TECHNICAL MEMORANDUM

REPORT XXX

ON THE STATUS OF THE CLINICAL STUDIES OF THE

NUCLEAR PACEMAKER MODEL NU-5

FROM THE

ARCO MEDICAL PRODUCTS COMPANY,

A SUBSIDIARY OF ATLANTIC RICHFIELD

31 January 1996

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TABLE OF CONTENTS

I. PROGRAM HISTORY

Arco Nuclear Model NU-5 pacemakers were implanted in humans from 1973 to 1978 as part of a clinical study to investigate their performance. The pacemaker power source is a sintered PU-238 oxide fuel pellet from which its decay flows through thermoelectric wires and eventually converted to a DC voltage by normal thermocouple action. Extensive testing such as dog implantations, impact tests, crush tests, temperature and cremation tests, and capsule pressure considerations were completed to ensure pacemaker integrity in the unlikely event of an accident.

During the clinical study phase, reports were sent to the Nuclear Regulatory Commission with information as specified in both the "Research Protocol for Clinical Investigation of the Arco Nuclear NU-5 Pacemaker" and attached "Contents of Sponsor's Periodic Report on Clinical Performance of Pacemaker" (Attachment A). The last full report during this study phase was submitted on October 15, 1980. After that, certain reporting requirements changed and semi-annual inventories were submitted to conform with the license. A copy of the latest inventory submittal is included as Attachment B.

In order to more fully update the Nuclear Regulatory Commission, per their verbal request, a report was submitted on January 15, 1988. This report, and all subsequent reports, will be submitted per Condition 12 of our material license and presents in addition to the above:

- Implanted and explanted pacemaker tables with relevant information as specified in Attachment A, "Contents of Sponsors Periodic Report on Clinical Performance of Pacemakers" (Tables I and II)
- Calculation of nuclear pacemaker failure rate and mode as required in Attachment A, Section II.D (Attachment C)
- A list of the pacemaker failure related explants since the last reporting period (Attachment D)

II. PURPOSE OF THE TECHNICAL MEMORANDUM

The purpose of this technical memorandum is to report upon and update the progress of the clinical study of the Arco Medical Products NU5 model radioisotope powered cardiac pacemakers from February 1, 1995 to January 31, 1996 as specified in the "Contents of Sponsor's Periodic Report on Clinical Performance of Pacemakers." This is the thirtieth technical memorandum summarizing the clinical data to be submitted to the Materials Branch of the United States Nuclear Regulatory Commission, in compliance with license SNM-1993 which replaced #37-14916-01.

III. CLINICAL IMPLANT STATUS OF THE NUCLEAR PACEMAKERS

Tables I and II list nuclear pacemakers implanted and explanted, respectively. The pacemakers are listed in numerical order with the fixed rate units first, followed by the demand units.

Information listed on Tables I and II are the pacemaker identification and any follow-up information required in the "Contents of Sponsor's Periodic Report on Clinical Performance of Pacemakers." Specifically, the follow-up information listed is in items A.1.J, and A.1.M through A.1.O. Items A.1.K and A.1.L are covered in the explanted pacemaker table. The information requested from items A.1.A to A.1.I is static and can easily be referenced from previous reports.

Information shown in Table II is also represented in the same format. Along with pacemaker identification are the implant service days and reason for explantation corresponding to items B.1.J and B.1.K, respectively. Item B.1.K is depicted as a number which must be referenced to Attachment to Table II. Items B.1.A to B.1.I are also static and can be easily referenced in Attachment B. Attachment D describes pacemakers explanted due to pacemaker failure.

IV. NUCLEAR PACEMAKER ACCOUNTABILITY AND FOLLOW-UP

Data from all investigators have been accounted for except where patients have elected not to attend their semi-annual physician follow-up. The right hand column of Table I is entitled "Contact." A "yes" indicates current physician/patient contact, "LTF" indicates patient is lost-to-follow after numerous physician attempts to contact the patient, and "N/A" indicates patient has left the United States permanently. A" - " in the bracelet & ID present column indicates no information was retrieved from physician follow-up correspondence indicating the patients had the bracelets and wallet cards on their possession.

V. CLINICAL PERFORMANCE ANALYSIS

Five goals were outlined in Attachment A, Section II for program performance analysis, and listed as subsections "A" through "E." Subsection goals "A," "B", and "E" were completed by Arco Biostatisticians on former reports. Thus, this and all subsequent reports, will contain relevant information only on goals "C" and "D."

The pacemaker failure rate, as shown on Attachment C, has been calculated for the period from 10/15/80 to 1/31/96 and from program inception to date; columns "A" and "B" respectively. All calculations were based on data from 79 and 125 implants, due to one patient who left the United States resulting in no pacemaker service data. As can be seen in Attachment C the pacemaker percent failure is 16.80% for the total program and 21.52%

from 10/15/80 to 1/31/96. This yields an average monthly failure rate of 0.14 and 0.18 for those same respective time periods.

Based on the data found in Attachments C and D, there is no evidence reported of any long term adverse side affects or other unknown factors associated with the nuclear pacemakers. Additionally, there is no statistical evidence suggesting any deleterious failure rates or modes associated with the program.

TABLE I
IMPLANTED PACEMAKERS
AS OF 1/31/96

PACEMAKER ID		PACEMAKER SERVICE INFORMATION			SUPPLEMENTAL	
MODEL #	PACER#	IMPLANT DATE	FOLLOW-UP DATE	IMPLANT DAYS	BRACELET & ID PRESENT	CONTACT
NU-5F	90	04/10/73	11/30/95	8269	–	YES
NU-5F	94	06/05/73	12/11/95	8224	–	YES
NU-5F	103	04/09/73	12/26/95	8296	–	YES
NU-5F	120	07/24/73	10/01/76	1165	–	N/A
NU-5F	126	06/12/73	01/09/96	8246	–	YES
NU-5F	149	08/07/73	11/21/95	8141	–	YES
NU-5D	459	11/18/75	10/09/95	7265	–	YES
NU-5F	481	10/01/76	08/24/95	6901	–	YES
NU-5F	483	03/04/75	12/07/95	7583	–	YES
NU-5D	490	03/05/75	08/21/95	7474	–	YES
NU-5D	498	04/15/75	12/13/95	7547	–	YES
NU-5D	499	09/13/76	11/02/95	6989	–	YES
NU-5D	504	04/20/77	12/07/95	6805	–	YES
NU-5D	506	05/19/75	12/28/95	7528	–	YES
NU-5D	509	04/04/75	11/14/95	7529	–	YES
NU-5D	513	03/18/75	10/31/95	7532	–	YES
NU-5D	523	11/13/76	01/02/96	6989	–	YES
NU-5D	527	05/14/75	10/02/95	7446	–	YES
NU-5D	529	03/13/76	11/28/95	7199	–	YES
NU-5D	537	08/04/76	10/31/95	7027	–	YES
NU-5D	539	10/24/75	01/15/96	7388	–	YES
NU-5D	544	12/09/75	12/19/95	7315	–	YES
NU-5D	562	11/19/76	10/31/95	6920	–	YES
NU-5D	586	01/23/76	08/01/86	3843	–	L.T.F.
NU-5D	611	07/07/76	12/15/95	7101	–	YES

L.T.F. – LOST TO FOLLOW

N/A – LEFT THE USA PERMANENTLY

TABLE II
EXPLANTED PACEMAKERS
10/15/90 TO 01/31/96

PACEMAKER ID		PACEMAKER SERVICE INFORMATION		EXPLANT DATA	
MODEL #	PACER#	IMPLANT DATE	EXPLANT DATE	IMPLANT DAYS	EXPLANT CODE
NU-5F	70	04/10/73	07/09/90	6299	13
NU-5F	74	05/12/73	04/01/89	5803	36
NU-5F	80	02/19/74	01/05/91	6480	03
NU-5F	83	04/10/73	08/01/86	4861	03
NU-5F	85	04/09/73	10/29/91	6777	02
NU-5F	86	04/10/73	09/19/91	6736	11
NU-5F	97	06/05/73	09/01/88	5504	21
NU-5F	100	04/09/73	02/12/87	5057	19
NU-5F	107	04/10/73	01/15/87	5028	03
NU-5F	115	07/06/73	08/01/89	5870	03
NU-5F	128	06/12/73	02/09/88	5355	03
NU-5F	131	06/13/73	09/19/93	7403	03
NU-5F	138	12/10/73	12/17/82*	3294	36
NU-5F	140	06/13/73	10/15/81	3046	36
NU-5F	144	07/27/73	10/02/87	5180	06
NU-5F	145	09/14/73	09/24/81*	2932	22**
NU-5F	155	12/03/73	10/24/94	7630	14
NU-5F	157	11/23/73	05/22/87	4928	06
NU-5F	175	05/14/74	08/01/89	5558	13
NU-5F	318	05/22/74	06/28/88	5145	25
NU-5F	341	09/09/74	03/17/95	7494	25
NU-5F	342	10/08/74	09/16/87	4726	22**
NU-5F	361	10/29/74	12/21/81*	2610	36
NU-5F	362	10/25/74	12/03/91	6979	02
NU-5F	363	10/10/75	08/01/89	5044	21
NU-5D	408	07/05/74	01/15/82	2751	25
NU-5D	460	03/06/75	04/13/90	5517	13
NU-5D	462	03/03/75	01/25/91	5807	13
NU-5D	465	03/24/75	07/28/92	6336	02
NU-5D	467	06/04/75	03/21/80*	1752	36
NU-5D	474	11/23/73	09/30/88	5425	25
NU-5D	476	01/27/75	11/29/89	5420	13
NU-5D	477	05/16/75	11/19/81	2379	36
NU-5D	492	01/17/75	05/15/87	4501	19
NU-5D	496	02/07/75	12/15/81*	2503	36
NU-5D	501	04/17/78	04/14/87	3284	36
NU-5D	508	03/14/75	03/09/81	2187	25
NU-5D	515	07/16/75	10/08/88	4833	06
NU-5D	519	05/22/75	09/20/88	4870	06
NU-5D	524	02/12/76	11/20/94	6856	03
NU-5D	525	05/30/75	09/19/95	7417	02,03
NU-5D	528	06/17/76	12/14/81	2006	36
NU-5D	532	03/08/76	08/31/93	6385	02
NU-5D	535	08/29/75	01/31/84	3077	22**
NU-5D	542	12/02/75	04/20/95	7079	01
NU-5D	545	02/05/75	10/02/82*	2796	36
NU-5D	549	11/15/75	06/12/87	4227	21
NU-5D	571	08/29/75	01/15/82*	2331	36
NU-5D	572	10/08/75	01/07/92	5935	03
NU-5D	581	02/17/76	12/05/94	6866	36
NU-5D	583	03/04/76	12/01/85	3559	22**
NU-5D	587	06/03/76	11/16/88	4549	39
NU-5D	592	08/04/76	12/28/88	4529	21
NU-5D	623	07/28/76	01/06/82*	1988	36
NU-5D	624	05/26/76	12/16/81*	2030	36

* EXPLANT DATA UNAVAILABLE. DATE SHOWS LAST PATIENT CONTACT REPORT RECIEVED.

** DETAILS REPORTED AS NON--PACEMAKER RELATED, PACER NOT RETURNED.

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ATTACHMENT TO TABLE II

CODES USED FOR EXPLANTING DATA

01	Battery Depletion	23	Lead Could Not Be Removed From Pacer
02	Impending Pacemaker Wearout	24	Muscle Stimulation
03	Patient Death	25	Elective Replacement, Not Pacer Related, Pacer Normal
04	Wound Dehiscence (Opening)	26	Lead Could Not Be Inserted Into Pacer, or Set Screw Could Not Be Tightened
05	Infected Pocket (Pacemaker Bursa Infection)	27	Pacer Rate Increase/ Decrease Reported, Pacer Normal Upon Return
06	Loss of Sensing Function, Pacer Not in Design Specifications	28	Pacer Rate Change, Pacer in Specification
07	Competition	29	Loss of Capture, Non-Pacer Related (Plug Missing, Fluid in Terminal)
08	Electronics Failure	30	Pacer Returned Because of Cracked Epoxy
09	Lithium Battery Failure	31	Automatic Rate Equals Magnetic Rate, Physiological Reasons
10	Nuclear Battery Failure	32	Non-Pacer Related Oversensing
11	Random Failure	33	Set Screw Head Stripped
12	Delaminated Capacitor	34	Pacer in Spec., Explanted Due to Apparent Pacer Inhibition

Attachment To Table II - Continued

13	Lead Changed, Pacer Removed	35	Automatic Rate Equals Magnetic Rate, Electronic Failure
14	Patient Requires Faster Rate Pacer	36	Pacer Returned Without Details; Pacer in Specification
15	Loss of Sensing, Patient or Lead Related, Pacer Normal on Return or Reimplanted	37	Pulse Width Variation due to Psuedofusion; Pacer in Specification
16	Electronics Damaged During Defibrillation	38	Advisory Return, Pacer in Electrical Spec. Upon Request
17	Pacemaker Erosion Reported	39	Loss of Capture, Pacer Related
18	Pacer Reported Not in Spec. at Implant, or After Implant, Unit Normal on Return	40	Advisory Unit Not in Specification Upon Return, Non-Feedthrough Related; Pacemaker Still Functioning
19	Loss of Capture, Non-Pacer Related	41	Connection Problem
20	Feedthrough Failure (Advisory Group)	42	EMI Filter Capacitor Shunt; Results in Low Output Amplitude
21	Pacemaker Rate Change, Pacer Out of Specification		
22	Pacer Explanted, Problem Reported Without Details, Pacer Not Returned		

ATTACHMENT A

RESEARCH PROTOCOL FOR CLINICAL INVESTIGATION OF THE ARCO NUCLEAR NU-5 PACEMAKER*

MARCH 25, 1974

*As of May 17, 1975, ARCO Nuclear Company became ARCO Medical Products Company.

ARCO Nuclear Company
Subsidiary of Atlantic Richfield Company
P. O. BOX 540 / LEECHBURG, PENNSYLVANIA 15656, U.S.A. / PHONE (412) 845-8111

I. Title of Study

Clinical Investigation of The ARCO Nuclear NU-5 Pacemaker.

II. Purpose

The purpose of this study is to clinically investigate the performance of the ARCO Nuclear NU-5 Radioisotope Powered Cardiac Pacemaker. This clinical investigation is based on sound biostatistical methods[1] and has five major goals which are:

A. Determine the random failure rate of the nuclear pacemaker and compare it to the conventional battery powered pacemaker. This determination will also include a characterization of "infant mortality" failure rates and modes.

B. Determine the failure rate distributions and which distributions apply in the statistical treatment of the reliability data. This will include a determination of the accuracy of the Poisson assumptions.

C. Confirmation that there are no long term adverse side effects or other unknown factors associated with nuclear pacemakers.

D. Determine nuclear pacemaker longevity by characterizing the "wear out" failure rate and mode.

E. Characterize the practicable aspects of the follow up, traceability and recovery of nuclear pacemakers.

III. Description of Pacemaker

The nuclear pacemaker to be implanted during the course of this study is the ARCO Nuclear Model NU-5. Complete technical data on the pacemaker including radiation levels, reliability tests and safety tests under conditions of normal use and conditions of credible accidents are on file with the U. S. Atomic Energy Commission. Due to the extensive amount of previous testing, the participating medical institutions are not required to perform radiation testing. Under this protocol, the Model NU-5 pacemaker contains a maximum of 0.45 grams of plutonium-238 (less than 8 curies). The resulting dose rate at the maximum point on the pacemaker surface is 5.64 millirads per hour and 0.37 millirads per hour at 5 centimeters from the surface along the maximum dose rate line. The Model NU-5 pacemaker is available in two types -- fixed rate or demand (R-wave inhibited). Use of the magnet in this protocol applies only to the Model NU-5 demand type pacemaker.

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[1] The ARCO Nuclear Statistical Basis For Clinical Investigation of Radioisotopic Pacemakers - August 10, 1973

IV. Patient Selection

Patients may be of either sex with a maximum age of 65 or minimum age equal to the age of majority for the state of residence (special cases, however, may be considered on an individual basis by the appropriate licensing authority for older or younger patients) who:

A. Warrant replacement of their existing pacemaker or the insertion of a new pacemaker due to chronic heart block or other cardiac rhythm disturbances and

B. Have demonstrated emotional maturity, stability, that they are reliable patients who have a record of stable residence in the community such that they are willing to cooperate in, and are likely to remain available for the long term follow-up required and

C. Have no medical condition which in the physician's best judgement would limit life expectancy to less than 10 years.

Exclusions are the presence of a coexisting disease which may potentially limit life - e.g., potentially progressive heart disease, cerebrovascular disease, diabetes with any end organ manifestation or of greater than 10 years' known duration, renal disease, and neoplastic disease. Probability of lack of full cooperation, high mobility in the population, emotional disturbance, alcoholism, or other factors may also contra-indicate participation.

V. Duration of Study

It is anticipated that implantations of nuclear pacemakers under this study will continue for about two years and that the minimum time to achieve goals A, B and E under Section II is two-three years. Longevity studies and long term side effects studies may require much more time, perhaps in excess of ten years, due to the potentially long life capability of the nuclear pacemaker and its design characteristics.

Informed consent shall be obtained from all patients for participation in the program and for the ultimate removal of the pacemaker after its expected useful life is exceeded, its failure or the death of the patient, whichever occurs first. The study will continue throughout this period with follow-up by the clinics and reporting to ARCO Nuclear on implanted pacemakers.

VI. Control Group

In order to accurately compare the nuclear pacemaker with conventional pacemakers sound biostatistical practices require use of control groups. Therefore, a series of comparable control patients with conventional pacemakers of the same type (i.e., demand or fixed rate, bipolar or unipolar) will be followed. The control patients will be treated and followed using the same procedure for patient selection, medical procedures, follow-up, and reporting. The control group will be at least as large as the nuclear pacemaker study group.

VII. Implantation Procedures and Lead Systems

Fundamentally, conventional techniques of pacemaker insertion are to be utilized, but with particular attention to insuring that the electrodes and leads utilized have an expected life comparable to that of the pacemaker (in excess of 10 years) and that they have appropriate pacing thresholds. Because of the 10 or more year goal, it is vital that extreme care be taken to use the best available leads and to insure the best possible lead placement and configuration within the body. Since this is an investigational program, and not routine clinical use, it is preferable that a limited number of lead systems be used in order to limit the number of variables in the total pacing system and thus develop more meaningful data on longevity and reliability. Table 1 specifies the preferred leads to be used. It should be noted that the NU-5 pacemaker is of the monopolar type.

In patients with an existing lead, the following shall be done as a minimum, prior to implantation.

A. Appropriate chest films must be taken to assess the possibility of unduly sharp curves in leads.

B. The type of existing electrode must be ascertained and if it is not listed in Table I its use must be approved in advance by ARCO Nuclear. If doubt exists in the judgment of the responsible physician as to the reliability and/or compatibility of an existing lead, it should be replaced by a new one listed in Table 1. For existing leads, appropriate adapters may be used to fit the pacemaker; these should be of the type listed in Table 1 or approved in advance by ARCO Nuclear.

The threshold for pacing shall be tested for all electrodes whether old or new at the time of nuclear pacemaker implant prior to connecting the lead to the pacemaker. Only those leads may be utilized in which acceptable thresholds are demonstrated by these tests. Acceptable thresholds and test procedures are discussed elsewhere in this protocol.

It is important to note that certain information be obtained and recorded prior to and at the time of implantation. It is, therefore, necessary that the Accountability and Implant Data Form (a copy of which is Figure 1) be fully studied and understood prior to participating in this clinical study.

The NU-5 nuclear pacemaker is supplied sealed in gas permeable plastic double bags. Sterilization procedures prior to shipping are

TABLE I

Preferred Leads

Mfg.	Model	Type	System	Adapter
CORDIS	323-451	Myocardial	Monopolar	None
	322-256	Endocardial	Monopolar	None
	322-620	Endocardial	Monopolar	None
	322-251	Endocardial	Monopolar	None
	322-261	Endocardial	Monopolar	None
	322-281	Endocardial	Monopolar	None
MEDTRONIC	5814	Myocardial	Bipolar	Cordis 331-521
	5819	Endocardial	Bipolar	Cordis 331-521
	6901	Endocardial	Bipolar	Cordis 331-521
	6907	Endocardial	Monopolar	Cordis 331-521
	6909	Endocardial	Monopolar	Cordis 331-521

NOTES:

1. To use a lead or adapter not listed, ARCO Nuclear approval is required.

2. For bipolar leads, use electrodes with lowest measured stimulation threshold of pair.

3. For the Cordis 322 series, leads 256 or 620 are preferred due to lower stimulation thresholds in general than leads 251, 261 or 281.

NUCLEAR POWERED CARDIAC PACEMAKER

[illegible] DATA · [illegible]

PATIENT IDENTIFICATION

Patient Name ____________________
Last ____ First ____ Initial

Social Security No. ____________________

Hospital Record No. ____________________

Home Address ____________________

City ____________ State ____________ Zip ____________

Area Code and Telephone No. ____________________

Business Address ____________________

City ____________ State ____________ Zip ____________

Area Code and Telephone No. ____________________

Name, address, and telephone of 1st person to be contacted if patient cannot be located
____
____

City ____________ State ____________ Zip ____________

Area Code and Telephone No. ____________________

Relationship to Patient ____________________

Name, address, and telephone of 2nd person to be contacted if patient cannot be located
____
____

City ____________ State ____________ Zip ____________

Area Code and Telephone No. ____________________

Relationship to Patient ____________________

Physician(s) and Hospital:

Name ____________________

Office Address ____________________

City ____________ State ____________ Zip ____________

Area Code and Telephone No. ____________________

PACEMAKER

Model No. ____________________

Serial No. ____________________

Date of Implant ____________________

Placement: [illegible]
[illegible]
[illegible]

Stimulation Rate at Implant: with Magnet ____________ w/o Magnet ____________

Stimulation Rate 24 hrs. After Implant: with Magnet ____________ w/o Magnet ____________

Threshold Measurements:

Current ____________ ma. Pulse Width ____________ msec

Voltage ____________ volts, Pulse Width ____________ msec

Equipment used to take threshold ____________________
____

Previous Implant: Yes ______ No ______ If Yes

Manufacturer ____________________

Model ____________________

Date of Implant ____________________

Why Removed ____________________

Total Number of Previous Implants ____________________

HEART LEAD

Manufacturer ____________________

Model No. ____________________

Serial No. ____________________

Date of Implant ____________________

Placement: Epicardial: [illegible]
[illegible]
Endocardial: [illegible] ____________________

Previous Leads: Epicardial
Number, Models, and Implant Dates? ____________________
How Many Removed? ____________________
Endocardial:
Number, Models, and Implant Dates? ____________________
How Many Removed? ____________________

CLINICAL DATA

Patient's Birth Date ____________________ Sex ____________

Race ____________ Height ____________ Weight ____________

Right handed / Left handed ____________________

Etiology of Arrhythmia ____________________

Kind of Arrhythmia ____________________

Previous Drug Therapy for Arrhythmia ____________________

Associated Diseases ____________________

Temporary Pacing [illegible] Yes ______ No ______

Anesthesia used during surgery ____________________

Antibiotics: [illegible]

Cortisone or other anti-inflammatory drugs
[illegible]

[illegible] Yes ______ No ______ If Yes, how long? ____________________

Did complications or [illegible]

If yes, [illegible] ____________________

Comments ____________________
____

Title ____________________

Date ____________________

Signature ____________________

This form should be completed and returned [illegible]

For urgent questions and/or assistance concerning this pacemaker, please call [illegible]

[illegible]

[illegible]

[illegible]

performed in gaseous ethylene oxide. If the bag is found to be opened or accidentally ruptured, the nuclear pacemaker may be re-sterilized in ethylene oxide gas at temperatures not to exceed 50°C. Following sterilization at least 72 hours should elapse prior to implantation to allow complete aeration. If a pacemaker is dropped, it should not be implanted but, instead, returned to AMCO Nuclear.

VIII. Threshold Specifications and Measurements

In order to determine if a particular lead can be used with the nuclear pacemaker, its stimulation threshold must be measured and found to be acceptable in addition to meeting all of the previously discussed requirements. The stimulation threshold must be measured at the time of nuclear pacemaker insertion but prior to connection to the pacemaker. It is important that both current and voltage stimulation thresholds be measured. It is also important that battery powered instruments be used in threshold measurements since the exposed lead represents a direct current path to the heart and even a minute amount of leakage current from power lines represents a potential fibrillation risk if entering the heart directly.

The stimulation threshold will be measured utilizing a battery operated pulse generator with adjustable amplitude and width. The calibrated accuracy should be at least ± 10% and the pulse duration should be adjusted to be in the range of 0.70 to 1.00 milliseconds. The pulse generator rate should be in the range of 65 - 80 ppm. The negative terminal of the pulse generator is connected to the lead whose threshold is being measured and the positive terminal of the pulse generator is connected to the indifferent lead which is placed in contact with subcutaneous tissue. With the output amplitude of the pulse generator initially set at approximately zero, the amplitude is gradually increased until consistant capture occurs. The amplitude at which consistant capture occurs is recorded as the stimulation threshold. Both current threshold and voltage threshold values shall be measured and recorded. It is suggested that an EKG recorder be used to observe consistent capture and that the output of the pulse generator set at threshold values be observed on an oscilloscope and recorded with a scope camera.

Only those electrodes may be utilized in which the measured threshold is no greater than 1.25 ma and 0.90 volts if newly implanted or 2.50 ma and 1.8 volts if chronically implanted (whether endocardial or myocardial).

IX. Accountability and Implant Data Form

In order to insure adequate data for this study it is vital that the Accountability and Implant Data Form (Figure 1) be completed promptly after each implantation and distributed within seven days after implantation as follows:

Orange	-	Operating Room Copy
Green	-	Surgeon's Copy
Blue	-	Patient's Medical Record
White	-	ARCO Nuclear Copy (Pre-addressed and Stamped)

It should be noted that among other things the pulsing rate of the pacemaker shall be measured and recorded on the Accountability and Implant Data Form immediately upon implantation and 12 — 24 hours after implantation. The rates should be checked by a pulse interval measuring device accurate to ± 1 millisecond or ± 0.1 pulses per minute. It is recommended that the Accountability and Implant Data Form be reviewed in detail prior to participation in this clinical study to insure that all data requested is obtained and reported.

Examples of the type of information required are:

A. Pacemaker model, type and serial number

B. Date of implantation, surgical procedure and site of implantation

C. Lead identification by type, model and serial numbers, newly implanted or pre-existing, date of implantation, vein used and location of electrode

D. Threshold measurements and equipment used

E. Stimulation rate of the pacemaker both with and without magnet (if applicable)

F. History of previous implants, removals of pacemakers or leads, and reasons for such removals.

X. Follow-Up Data

At intervals of every three months during the first year and six months thereafter following nuclear pacemaker implantation each patient shall receive a follow-up examination and the resulting data shall be reported to ARCO Nuclear on the Follow-Up Data Form (a copy of which is Figure 2). Typical follow-up data includes:

A. Identification of patient, pacemaker, hospital, physician

B. Date of implantation and follow-up examination

C. Performance of pacemaker including stimulation rate (with and without magnet, if applicable)

D. Indication of any malfunction, modifications or replacements of pacemaker or lead system

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P.O. BOX 342 / LEECHBURG, PENNSYLVANIA 15656 / U.S.A. TELEPHONE (412) 845-8111

FOLLOW-UP DATA FORM

(To be used each time patient is contacted and/or examined including telephone transmission of ECG.)

PATIENT IDENTIFICATION SHEET

Patient Name _____
Last First Initial

Patient Hospital Record No. _____

Pacemaker Serial No. _____

Date of Implantation _____

Date of Follow-Up _____

Name of Physician _____

Address _____

City _____ State _____ Zip _____

Area Code and Telephone No. _____

Patient has I.D. Card: Yes _____ No _____

Patient is wearing Bracelet or its Equivalent: Yes _____ No _____

Contact maintained with patient: Yes _____ No _____

PACEMAKER FUNCTION

Satisfactory _____

Unsatisfactory _____

Stimulation Rate: with Magnet _____ w/o Magnet _____

Change from previous rate _____

Change from initial rate _____

MEDICAL EXAMINATION

Summary: _____

_____

Reposition: Pacemaker/lead/both

Reason _____

_____

Explantation: Pacemaker/lead/both

Reason _____

_____

Autopsy Results (if applicable) _____

_____

Cause of Death (if applicable) _____

Title _____

Date _____

Signature _____

This form should be completed and returned to the manufacturer within 10 days of taking follow-up data.

For urgent questions and for assistance concerning this pacemaker, please call 412-845-8111.

(MANUFACTURER'S COPY)

Seal Here After Folding

FIGURE 2

E. Physician's opinion and comments on pacemaker and lead system

F. Summary of medical examination

G. Indicate whether patient is carrying ID card and wearing bracelet and whether contact with patient has been maintained since last follow-up

The follow-up data shall include pulse interval measurements (using a device with a ± 1 millisecond or 0.1 ppm accuracy) and a recording of the electrocardiogram (with and without the magnet, if applicable). The Follow-Up Data form shall be completed and returned to ARCO Nuclear within 10 days of each examination. In addition, the Follow-Up Data form shall be used everytime the patient is examined even if such examinations take place more often than the specified frequency including telephone transmissions of ECGs.

The impulse rate of the pacemaker will vary in a predictable manner due to radioactive decay of the fuel and consequent decrease in voltage from the energy source to the electronic circuit or due to slight improvement in the nuclear battery efficiency brought about by gettering action and slight redistribution of thermal heat flow within the battery caused by vigorous patient physical activity which causes pulse rate to slightly increase after implant and then stabilize. If the measured pacemaker rate (either with or without the magnet) deviates from the initial rate recorded after implantation by more than 5 pulses per minute, ARCO Nuclear shall be notified immediately. If the pulse fails to capture (during non-refractory phases of the cardiac cycle), ARCO Nuclear shall be notified immediately, and the investigators shall seek to pursue the etiology, looking both to potential failures external to the pacemaker and to the pacemaker.

XI. Explanation

Pacemakers will be removed if clinically indicated due to failure, malfunction, development of "excessive" competition between the pacemaker and normal conducted beats, the death of the patient, the anticipated exhaustion of the unit or if the pacemaker rate changes by more than 10 pulses per minute. Whenever possible - i.e., whenever the patient's welfare is not compromised - ARCO Nuclear will be consulted prior to the removal of a pacemaker. Any pacemaker or lead which is explanted or repositioned for any reason shall be reported in writing within 1 week to ARCO Nuclear. The report shall include reasons for action taken, date of action, and associated tests performed. The pacemaker and, if possible, the intact lead system shall be removed upon death and returned to ARCO Nuclear for evaluation. If no autopsy is performed, the most probable cause of death shall be stated. Autopsy findings (if applicable) related to the pacemaker shall be reported and, if possible, the function of the pacemaker and lead system will be determined at autopsy.

All nuclear pacemakers that are explanted for any reason shall be returned to ARCO Nuclear as soon as possible in a shipping package

supplied by ARCO Nuclear and in accordance with labeling and shipping instructions also supplied by ARCO Nuclear. At explantation the nuclear pacemaker rate shall be recorded (with and without the magnet, if applicable) and ARCO Nuclear shall be consulted, if possible, for additional tests to be performed.

XII. Notifications

ARCO Nuclear and the licensing agency shall be notified within 24 hours of the death of any nuclear pacemaker bearer, and any adverse reaction and/or malfunction involving a pacemaker system, including the leads. ARCO Nuclear shall be notified within 10 days of loss of contact with a nuclear pacemaker bearer.

XIII. Records

Data and vital statistics pertaining to the nuclear pacemaker patients shall be maintained as individual files separately from routine hospital records. These records shall include:

A. The blue copy of the Accountability and Implant Data Form

B. Copies of all Follow-Up Data Form

C. A fully executed copy of the document "Informed Consent For Surgical Implantation Of Radioisotope Powered Cardiac Pacemaker" (a copy of which is attached)

D. Any additional information deemed important by the medical staff

XIV. Informed Consent

All patients shall sign the informed consent statement entitled "Informed Consent For Surgical Implantation Of Radioisotope Powered Cardiac Pacemaker" (a copy of which is attached). Using this document the patient, or his representative shall be informed and shall agree in writing to the following:

A. That nuclear pacemakers are under investigation, there are alternative treatments and the patient is willing to participate in the investigation

B. That after the patient's death, or if the useful life of the pacemaker is exceeded, or if it ceases to function effectively for the patient's medical needs, or if the patient requests to have the pacemaker removed, the nuclear pacemaker must be returned to ARCO Nuclear

C. The patient will always carry the ID card and bracelet on his person, and to notify the hospital of any change in his address or telephone number.

D. The patient will notify, through the hospital, and ARCO Nuclear, the appropriate licensing authority prior to any travel outside the United States.

E. Acknowledgment that the patient has had the opportunity to ask questions pertaining to the surgical procedures, nuclear pacemaker, follow-up procedures, and possible alternate methods of treatment.

Copies of the signed consent form shall be given to the patient, to ARCO Nuclear and placed in the patient's medical file.

XV. Patient Identification

All nuclear pacemaker patients shall carry credentials identifying them as nuclear pacemaker patients. These credentials will include an identification bracelet of the Medical-Alert type and a wallet size identification card. On the bracelet will be engraved the patient's name, the words "Radioactive Pacemaker", the trefoil radiation symbol, the word "Plutonium", and the words "In emergency hospitalization or death call collect (phone number of hospital)". A facsimile of the identification card is Figure 3 which contains the patient's name, the trefoil radiation symbol, the work "Radionuclide", a statement that the patient is the implantee of a Radioisotope Powered Cardiac Pacemaker, manufacturer's name and phone number, pacemaker model number, amount and type of contained radionuclide, the words "In case of death from any cause or emergency or trauma involving pacemakers telephone collect (name and phone number of participating institution and doctor (s) in charge)", the words "Instruct phone operator call concerns Nuclear Pacemaker - Urgent!", and the words "Regulations require removal of pacer upon death."

Both the bracelet and identification card will be supplied to the participating institution by ARCO Nuclear following receipt of the Accountability and Implant Data Form. The institution will then give the bracelet and identification card to the patient and remind the patient to always carry them on his person. If the permanent bracelet and ID card are not available when the patient is discharged from the hospital, a temporary bracelet and ID card containing the same information shall be given to the patient until the permanent ones are supplied.

For each participating institution the telephone operators will be issued the following instructions:

A. Any collect calls concerning nuclear pacemakers will be accepted.

B. The operator should obtain as much information from the caller as possible including:

1. Caller's name and where to reach him

2. Patient's name, condition and where to reach him

URGENT

Medical Alert!

_____

is the implantee of a
Radioisotope Powered
Cardiac Pacemaker

Radionuclide is
Plutonium-238 < 8 Curies

Made by
ARCO Nuclear Company
Model Number is NU-5

SEE OTHER SIDE
FOR EMERGENCY
INSTRUCTIONS

Regulations require removal of pacemaker upon death.

URGENT

Medical Alert!

(Continued from reverse side)

In case of death from any cause or emergency or trauma involving pacemakers telephone, collect, the:

_____
(HOSPITAL)

_____
(PHONE NUMBER)

_____
(DOCTOR)

_____
(DOCTOR)

OR telephone, collect, the
ARCO NuclearCompany
(412) 845-8111
(Location, Pa. 15656)

Instruct phone operator call concerns
Nuclear Pacemaker – Urgent!
Regulations require removal of
pacemaker upon death.

FIGURE 3

3. If any physician is present, and if so, his name and where he can be reached.

4. Condition of pacemaker, if known (i.e., expelled or still implanted).

5. Information on patient's ID card, if available.

C. Such calls represent potentially severe emergencies and the operator should immediately contact the institution's Radiation Safety Officer and responsible doctor while keeping the caller on the line and standing by.

D. If the Radiation Safety Officer or the responsible physician or designated alternate cannot be reached, contact Cardiac Care Unit physician on duty and advise of the situation and what information is available.

XVI. Participating Institution Requirements

During the investigational phase of nuclear pacemaker use, licenses are being issued only to medical institutions that can assure continuity of follow-up of patients with implanted pacemakers rather than to individual physicians. A license issued to a medical institution authorizes a specified implantation limit in terms of number of plutonium fueled pacemakers and requires the licensed institution to be responsible for the follow-up and recovery of the nuclear pacemakers implanted in patients under the license. The physicians designated as the responsible investigators by the medical institution should have substantial experience with pacemakers in the specialities of cardiology and thoracic surgery. The medical institution is expected to have an established program and appropriate facilities for the implantation and follow-up of cardiac pacemakers.

Each application from a medical institution should include:

A. Identification of the institution as the applicant.

B. Incorporation of this research protocol by reference with a commitment to follow it.

C. For each physician on the study team, his name, specialty board certification, previous experience in the implantation and follow-up of implantable pacemakers including specific information on the duration and number of pacemakers implanted and/or followed, a breakdown of how many of the implants used myocardial leads and endocardial leads, and position of the physician with the applicant.

D. A description of the applicant's present pacemaker implantation and follow-up program including size, duration and types of implantations.

E. Description of the physical facilities and equipment available for implantation and follow-up. This should include specific test equipment required to carry out the tests discussed in this protocol.

F. A description of the applicant's procedures for accountability and security against loss or theft of pacemakers before implantation and after removal from patients.

G. A description of the applicant's procedures to assure notification of appropriate individuals within the licensed medical institution upon receipt of a report or inquiry concerning a pacemaker bearer. Include written instruction given to telephone operators (as outlined in Section XV of this protocol).

H. A procedure for periodically reviewing all implantation and follow-up records on nuclear pacemaker patients and follow-up as necessary to verify that loss of contact with the patient has not occurred.

I. An acknowledgment from the institution administration of their long-term commitment and responsibility for the follow-up and recovery of nuclear pacemakers.

A standardized application form will be provided by ARCO Nuclear to qualified institutions that wish to apply to participate in this study. This form will facilitate rapid processing of such applications placing the above required information in a compact stardard format.

INFORMED CONSENT FOR SURGICAL IMPLANTATION OF RADIOISOTOPE POWERED CARDIAC PACEMAKER

I understand that for the treatment of my cardiac condition - a disturbance of normal cardiac conduction - a cardiac pacemaker is to be implanted in me. I also understand that the surgical procedure (may/will) require the placement of a new electrode and lead into or onto the surface of my heart and the implantation of a new cardiac pacemaker, and I understand that while the surgical procedure is not of unreasonable risk, the possibility of complications or even death exists. The procedure has been explained to me, in a manner that I could understand, and I have had the opportunity to ask any questions which I would like.

It is my understanding that a radioisotope powered cardiac pacemaker, which is now undergoing its initial clinical use in approximately 480 persons, will be utilized for the implantation. I have been told that the pacemaker design has been extensively tested over a period of several years. I have been told that on the basis of these experiments in animals and in the laboratory, units of this type are predicted to have a reliable life expectancy comparable to (and hopefully considerably in excess of) that of current standard cardiac pacemakers. However, I understand that it is impossible to be certain of the pacemaker's actual reliability, and no guarantee has been given to me concerning the results which may follow. I understand that the pacemaker does produce radiation, but I have been told by my attending physician that it is the medical judgment that this radiation presents a negligible hazard to me and the members of my household.

I understand that in consenting to the implantation of this pacemaker, I am authorizing, as well, all standard operating procedures, including the administration of anesthetics which may be incident to the operation. For the purpose of advancing medical and scientific knowledge, I consent to the admittance of observers to the operating room.

Ultimately - after my death or earlier, if the useful life of the pacemaker is exceeded, if it ceases to function effectively for my medical needs, or if I request to have it removed - the pacemaker must be removed and returned to ARCO Nuclear Company or to its designee, _____ _____(Clinic). Accordingly, I agree to contact _____ _____(Clinic) at regular intervals of no less than three months during the first year and every six months thereafter and whenever I change my residence. I will always carry the appropriate identification card on my person and will at all times wear the standard identification bracelet.

Notwithstanding my contacting the implanting clinic following the insertion of a cardiac pacemaker of any sort, I agree to remain in periodic contact with my personal physician. I will also instruct all members of my household and inform those who have extended contact with me that I have received a radioisotope powered cardiac pacer implant.

I understand that the radioisotope powered cardiac pacemaker is an experimental unit. In order to assess the effectiveness of the device, and to monitor my personal well-being, _____(Clinic) is interested in collecting data upon the device. Accordingly, I agree to visit _____(Clinic) in person or to transmit by telephone (with the aid of a device supplied to me and applied to the surface of my skin) my electrocardiogram and an indication of the functioning of the pacemaker. I agree to permit this monitoring to be performed at least once every three months for the first year and every six months thereafter. I further agree to provide information on my clinical condition as it pertains to the pacemaker at no less than six month intervals. Furthermore, I consent to disclosure by the clinic of any information acquired by the clinic in regard to the implantation of the radioisotope powered cardiac pacemakers; provided, however, in no event shall such disclosures include my identification without my specific written approval.

I understand and agree that I must notify _____(Clinic) prior to any travel outside of the United States.

I have had the opportunity to ask any questions pertaining to the surgical procedure, the radioisotope powered cardiac pacemaker, and the mandatory follow-up procedure, and these questions have been answered to my satisfaction. The possible alternate methods of treatment, including the use of conventional chemical battery powered pacemakers, have been called to my attention, and I have been given an opportunity to ask any questions about these alternative methods.

With these facts in mind and with the intent of being legally bound, I release any right to claim that the implantation of a radioisotope powered cardiac pacemaker was not properly authorized, and I agree to the follow-up procedures and the ultimate return of the unit as detailed above. I agree to assume the risk of the implantation of a radioisotope powered pacer and release and discharge ARCO Nuclear, the implanting clinic and my physician from failures not caused by their fault or negligence.

_____	_____	_____
Witness (preferably a relative)		Date
_____	_____	_____
Date	Patient's signature or two persons authorized to consent for the patient.	Date
	_____	
	_____	
	Relationships to the patient signing if other than the patient.	

I certify that I have explained the above procedure.

CONTENTS OF SPONSOR'S PERIODIC REPORT ON CLINICAL PERFORMANCE OF PACEMAKERS (FOR NUCLEAR PACEMAKERS AND CONVENTIONAL PACEMAKER CONTROLS)

A. For pacemakers in satisfactory service:

1. Tabulate each implanted nuclear and control pacemaker identified by serial or other assigned number. For each pacemaker include the following:

   a. Date of manufacture
   b. Date of implant.
   c. Indicate whether fixed rate or demand.
   d. Age of patient (at implant)
   e. Implanting institution (can be coded).
   f. Type of leads (make and model).
   g. Indicate bi-polar or unipolar.
   h. Indicate myocardial or endocardial.
   i. Date of lead implant.
   j. Duration (in days at time of report) of pacemaker service.
   k. Indicate the nature and date of any additional related surgery relocations, or post implantation complications.
   l. Indicate whether any lead was replaced, repaired, or relocated and data(s) thereof.
   m. Date of mose recent follow-up examination.
   *n. Indicate whether patient was carrying I.D. card and wearing I.D. bracelet.
   o. Indicate whether effective contact was being maintained with patient.

B. For pacemakers no longer satisfactorily pacing the patient:

1. Tabulate each nuclear and control pacemaker identified by serial or other assigned number and include the following:

   a. Date of manufacture
   b. Date of implant.
   c. Indicate whether fixed rate or demand.
   d. Age of patient (at implant).
   e. Implanting institution (can be coded).
   f. Type the leads (make and model).
   g. Indicate bi-polar or unipolar.
   h. Indicate myocardial or endocardial.
   i. Date of lead implant.
   j. Duration (in days) of satisfactory pacemaker service before removal or replacement.
   k. For each removed or replaced pacemaker or lead system, explain in detail the reasons therefore and date thereof.

*not applicable for control patients with conventional pacemakers.

k. In case of death of the patient give: date and cause of death, autopsy findings related to the pacemaker, determination at autopsy (if possible) of whether pacemaker and lead system were still operable, post-removal evaluation by sponsor of pacemaker and lead operability, and final disposition of pacemaker.

C. Accountability

1. Have all implanted nuclear pacemakers been accounted for during reporting period? If not, explain in detail.

2. Has adequate follow-up contact with any patient been lost during the reporting period? If yes, explain in detail.

ATTACHMENT B

ARCO

444 South Flower Street
Los Angeles, California 90071
Telephone 213 486 1724
Fax 213 486 1740

Environmental Remediation

February 8, 1996

Jolene Bisseger
U. S. Department of Energy
Chicago Operations Office
Safeguard and Security Division
9800 South Cass Avenue
Argonne, IL 60439

Re: Semi-Annual Inventory--Nuclear Pacemakers

Dear Ms. Bisseger:

As of February 8, 1996, we have in temporary storage at Roy F. Weston, Inc., One Weston Way, West Chester, PA 19380, fifty-three (53) nuclear pacemakers:

Model Number	Pacer Number	Fuel Cell Number
NU5F	138	A-078
NU5F	140	A-026
"Fixed Rate"	337	*
NU5F	361	B-044
NU5D	408	B-069
NU5D	467	B-121
NU5D	477	B-138
NU5D	486	*
NU5D	496	B-161
NU5D	508	B-062
NU5D	522	*
NU5D	528	B-213
NU5D	545	B-196
NU5D	571	B-170
NU5D	623	B-290
NU5D	492	B-159
NU5D	624	B-271
NU5F	083	A-086
NU5D	484	**
NU5F	107	A-102
NU5F	100	A-095

Model Number	Pacer Number	Fuel Cell Number
NU5F	157	A-039
NU5D	501	B-169
NU5D	543	***
NU5F	128	A-060
NU5D	549	B-200
NU5F	318	B-004
NU5F	097	A-064
NU5D	474	B-124
NU5F	074	A-042
NU5D	515	B-154
NU5D	519	B-156
NU5D	175	A-067
NU5D	592	B-251
NU5F	363	B-048
NU5D	587	B-246
NU5F	070	A-027
NU5D	476	B-060
NU5D	460	B-117
NU5F	080	A-084
NU5D	462	AN-1-55
NU5F	086	A-088
NU5F	085	A-087
NU5F	362	B-046
NU5D	572	B-201
NU5D	465	B-065
NU5F	131	A-100
NU5D	532	B-083
NU5F	155	A-031
NU5D	581	B-237
NU5F	341	B-002
NU5D	542	B-189
NU5D	525	B-190

* Pacers never implanted. Returned to Weston by John Fuqua of the Texas Heart Institute.

** Pacer never implanted. Returned to Weston by Radiation Protection, Alleghany General Hospital, 320 E. North Avenue, Pittsburgh, PA. 15212; (412) 359-4174.

*** Pacer never implanted. Returned to Weston by William Rottenburg, Intermedics, Inc., of Freeport, Texas.

Thank you for your continued assistance in our efforts to comply with our monitoring and storage requirements. If you have any questions regarding this inventory, please call me at (213) 486-3641.

Sincerely,

Michael C. Mc Anulty

Michael C. Mc Anulty
Project Administrator

ATTACHMENT C

REMOVAL AND FAILURE RATES FOR NUCLEAR PACEMAKERS

	A 10/15/80 - 1/31/96	B PROGRAM TOTAL
# Of Implants	80	126
# Of Removals	55	101
# Of Failures	17	21
Average Months of Service/Patient	116.5	119.0
Percent Removals	69.62	80.80
Percent Failures	21.52	16.80
Average Monthly Removal Rate (x100)	0.60	0.68
Average Monthly Failure Rate (x100)	0.18	0.14

ATTACHMENT D

PACEMAKER FAILURE RELATED EXPLANTS

Pacemaker failures between 1 February 1995 and 31 January 1996 were as follows:

NU-5 #525 Surgeon reported that the pacemaker was failing and there was a infection in the area of the pacemaker.

NU-5 #542 Surgeon reported that the pacemaker battery was depleted and the lead was fractured.