HUMAN CLINICAL PROTOCOL

for

THE CORATOMIC C-101
RADIOISOTOPE POWERED CARDIAC PACER

November 1, 1975

Coratomic®
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CORATOMIC C-101 (Attachment 4)
RADIOISOTOPE CARDIAC PACER PROTOCOL

November 1, 1975

1. Investigational Program

The purpose of the Coratomic C-101 Investigational Program is to obtain statistical data under controlled conditions to determine the reliability, efficacy and longevity of the C-101 Pacer. Its objective is also to provide greater increased longevity compared to standard pacers and prolonged relief from consequences of symptomatic bradycardia for those patients receiving the C-101 Pacer.

2. Description of the Pacer and Radionuclide Power Source

The totally implanted, battery powered cardiac pacer has been in clinical use since 1960, and is now the selected method of treatment for heart block and other forms of symptomatic bradycardia. It is also used in selected cases of symptomatic tachyarrhythmias. An extensive literature has arisen in connection with cardiac pacing, and selected references are listed in Exhibit 1. The physician responsible for this study is cognizant of these and other relevant references, and has had extensive experience in the use of cardiac pacers.

The C-101 Pacer is an R-wave inhibited demand pacer with a projected life of greater than 20 years. It is electronically similar to demand pacers which have been in use for many years. The Pacer provides a nominal 72 beat per minute pulse rate when the patient's R-wave is not sensed, and is inhibited when the R-wave is sensed. The unit is hermetically sealed and shielded against electromagnetic interference. It has an asynchronous "magnet rate" of 90 beats per minute, used to ascertain cardiac capture and for operational verification, and will switch to the same fixed rate rather than becoming inhibited if high energy electromagnetic fields are present.

The fuel used for the C-101 Pacer is plutonium-238 in its oxide form, pressed and sintered into a hard, ceramic pellet. The isotopic battery has been so designed that excess electrical power is available at the end of a 20 year life. The pacers have undergone extensive testing for efficacy, including excessive mechanical shock, impact, and vibration testing, and the nuclear fuel is contained in such a manner to prevent fuel release under any credible accident, including building or auto accident, fire, fall from an airplane, crushing, corrosion in sea water, or accidental cremation.

Data concerning radiation level, safety, and efficacy testing is on file with the United States Nuclear Regulatory Commission, as a Master Protocol.

The Coratomic Pacer has been used in dogs since September 1973, and animal testing to assure higher reliability is continuing as part of Coratomic's data gathering and licensing program.

3. Patient Selection

The patients to be selected for this clinical study will be those who have heart block or other forms of symptomatic bradycardia requiring an implanted pacer. The physician will select patients who have a life expectancy of at least ten* and preferably twenty years, in order to obtain a maximum amount of data concerning longevity and reliability of the unit. An influential factor, however, other than longevity is that the small size and weight of the Coratomic unit may enhance the longevity of the patient compared to other pacemakers, and data on all age groups will, therefore, be of value since additional variables other than life expectancy are important in the C-101 test. For example, the smaller size and weight of the unit may be statistically significant in reducing pressure necrosis, lead failure or other volume and shape induced failures unknown at this time. For this reason, life expectancy alone, although still significant, is not as dominant a factor as in the use of other nuclear pacemakers heretofore licensed for clinical applications, and patients with a life expectancy less than 20 years should form part of the statistical sample. In certain cases, also, the physician may judge the use

*The 1971 Life Insurance Fact Book Institute of Life Insurance, New York, N.Y., Page 107, indicates that in the U.S. total population the life expectancy of a 72 year old is 10.27 years.

of the C-101 to be paramount in prolonging life in an older patient who has had many previous operations, or is resistant to frequent operations, or is not mentally capable of handling a rechargeable unit. In these cases, expected to be a small percentage, the physician may use his discretion in implanting the C-101.

From a statistical point of view only, it would be ideal if the distribution of patients with C-101 Pacers were weighted in the same manner as the general pacer population, thus providing the most accurate statistical data where the greater number of patients with pacers exist. An attempt will be made to skew the total pacer population in this manner by continued feedback and communication between individual physicians, and the statistical correlation center at Coratomic.

Patients whose life expectancies are limited to less than 10 years by reason of co-existing diseases will, except for conditions of extreme need, be excluded from this study. Cooperative and reliable patients, who are stable and non-mobile members of the community will be selected to assure accurate long-term follow-up reporting and study.

4. Implantation Time Period

The clinical implantation period discussed in this protocol will continue for two years, at which time this study will have completed its implantation period. All patients will be monitored until the death of the patient or removal of the pacer.

5. Follow-Up and Reporting

A careful follow-up and reporting procedure will be followed during the life of the patient or until the pacer is removed. At each examination period an electrocardiogram will be obtained, with and without the application of a magnet to induce fixed rate operation of the pacer. The following examination in time after implant will be followed as closely as possible: 24 hours, 1 week, 1 month, 3 month and 6 month intervals, thereafter, until removal. Telephone transmission and testing of pulse intervals can be used to supplement the regular in-office examination schedule. It is recognized that general medical care may be more frequent than this, but this is the minimal time between tests of pacer function by the study clinic, or responsible physician.

6. Patient Control Group

A reference control group, identified as closely as possible in age, sex, stability and diagnosis will be used. An attempt should be made to include in this group pacer systems using lithium or rechargeable nickel cadmium batteries to provide comparative data on other potentially long lived systems. The number of patients in this group should be equal to the C-101 group. All data and information collected from this group will be identical to that obtained with the C-101 Pacer. All patients in the control group will have unipolar electrodes and have R-wave inhibited electronics powered by conventional sources currently available.

7. Implantation Procedures and Leads

Conventional methods of pacemaker insertion are to be used, ensuring as far as possible that the electrodes and leads used have an expected life comparable to the pacemaker and that they have appropriate pacing thresholds. In patients with an existing lead, the type of existing electrode must be compatible. If not, standard adaptors may be used. Spliced leads may not be used. Ideally, Coratomic leads should be utilized to assure long-term compatibility with the pacer materials. Myocardial or endocardial leads may be used with any of the standard surgical approaches for lead implantation in either the left or the right ventricle. The C-101 pulse generator may be implanted in the subcutaneous tissue of the abdomen, chest wall, the subpectoral muscular tissue of the chest wall, or any other area deemed suitable by the responsible physician.

8. Stimulation Threshold Measurements

The pacing threshold will be tested for all electrodes, old or new, utilizing a battery operated, calibrated (±5% accuracy) pulse generator with an adjustable amplitude and of a pulse duration of .8 to 1.2 milliseconds.

Only those electrodes may be utilized in which a threshold is demonstrated no greater than 1.5 ma if newly implanted or 4.0 ma if chronically implanted, whether transvenous or epicardial, measured at a pulse width of 1.0 milliseconds.

9. Sensing Measurements

If possible, the amplitude and width of the patients QRS wave should be measured. Measurement should be between a ground plate in the pacer subcutaneous pocket and the lead terminal distal to the heart.

10. Registration and Implant Reports

Immediately upon implantation of the C-101, the physician or hospital will complete a Registration and Implant Data Form, and forward it, within 10 days, to the Coratomic Data Center. The form includes identification of the pacemaker, the patient, the physician, the hospital, and heart lead, and adapter (if used), stimulated rate, and clinical data concerning the patient and his or her cardiac disease. The data form is shown as Exhibit II, attached,

11. Follow-up Data

The follow-up data, reported at intervals as discussed in 5 above, "Follow-up and Reporting", will be prepared by the investigator and submitted to the Coratomic Data Center on the Follow-up Data Form. This form is attached, (Exhibit III) and provides information on the patient, C-101 Pacer function and a brief clinical history of the patient including laboratory data, adverse reactions to the implanted device, if any, a description of the reactions and opinions as to the nature and major cause of the reactions, and an evaluation of the efficacy of the device and procedure.

12. Data and Reports of Removal and Replacement

Removal and Replacement constitutes particularly significant data, and therefore, a special form, "Pacer Failure and Removal or Patient Death", is provided, Exhibit IV. This form has all pertinent required data concerning the patient, investigator, hospital, and reasons for removal and replacement including whether the failure was of battery, electronic, or lead origin. Corrective procedures and results of patient examinations are also required.

13. Notification of Deaths, Adverse Reactions or Malfunctions

Notification of death is included in the form, "Pacer Failure and Removal or Patient Death", shown in Exhibit IV. The cause of death and autopsy findings are included.

14. Notification of Loss of Patient Contact

This notification is included in the Follow-up Data Form, Exhibit III. The reasons for loss of contact and steps taken to reestablish contact are included. If loss of contact is reported on this form, Coratomic, with data provided in the initial implant form, Exhibit II, will attempt to pursue the patient until a satisfactory explanation or terminus of the lost pacer case is provided.

15. Information To and Consent From the Patient

a. All patients will be completely informed about the nature of the clinical trial by the investigator, and to confirm this communication, will sign the informed consent form (Exhibit V). They will be informed of alternative procedures.

b. All patients accepting the pacemaker must agree to the follow-up scheme summarized above and to the removal and return to the physician (and from them to Coratomic) of the unit upon the completion of its expected useful life (20 years), its failure, or upon the patients death, whichever occurs first. A legally binding document (Exhibit V) will be signed by the patient, a witness, his spouse, and/or a relative of the patient.

c. The patient will be required to carry an identification card as stated in the form shown in Exhibit V. This card is shown in Exhibit VI. The card will identify the carrier as a radioisotope powered cardiac pacer patient, will specify the manufacturer and model number of the subjects pacemaker, specify the radionuclides contained in the pacer, and present explicit instructions for notification of responsible parties in the event of accident or difficulty. The patient will also be required to carry a uniform anatomical Gift Act Card, as shown in Exhibit VII. If the patient has not attained majority age, the agreement card shown in Exhibit VIII should be executed by the patient where possible and his or her legal guardian.

d. The patient will also be required to carry an identification bracelet of the medical-alert type which will carry the same patient's name and a statement to call the proper emergency telephone and physician in emergency. This bracelet is mentioned in Exhibits III and IV.

e. The patient will participate in follow-up examinations as discussed in 5 above, and he will be required to agree to do so on the informed consent form of Exhibit V.

f. The patient will notify the hospital of any change in address or contact and will be required to agree to do so on the informed consent form of Exhibit V.

g. The patient will be required to notify the hospital of his intention to travel in foreign countries. The hospital will, in turn, notify Coratomic, who will notify the Nuclear Regulatory Commission. The patient agrees to provide this information on the informed consent form (Exhibit V).

16. Record Retention

All pacer records will be maintained separately from the routine hospital records, either by a centralized authority so designated, health physics personnel, or the pacemaker clinic within the hospital's jurisdiction, or the physician responsible for the study.

EXHIBIT I

(Attachment 4)

REFERENCES

1. Smyth, Nicholas P. D.: Cardiac Pacemaking. *Surgical Diseases of the Chest*, Second Edition in Press, Editor Brian Blades., C. V. Mosby Co., St. Louis, Mo., 1974.

2. Chardack, William M.: Cardiac Pacemakers and Heart Block. *In Surgery of the Chest* (Chapter 38), Second Edition, Editors John H. Gibson, Jr., David C. Sabiston and Frank C. Spencer. W. B. Saunders Co., Philadelphia, Pa., 1969.

3. Furman, Seymour, and Escher, Doris J. W. : *Principles and Techniques of Cardiac Pacing*. Harper and Row, New York, N.Y., 1970.

4. Thalen, Hilbert J.: *The Artificial Cardiac Pacemaker:* Its History, Development and Clinical Application. C. C. Thomas, Springfield, Ill., 1969.

5. Hurzeler, Philip; Decaprio, Vincent; and Furman, Seymour, Montefiore Hospital and Medical Center, New York, N.Y.: *Endocardial Electrograms and Pacer Sensing;* paper presented at AAMI 10th Annual meeting March 17–18, 1975.

REGISTRATION AND IMPLANTATION DATA FORM

CORATOMIC C-100 SERIES ISOTOPIC PULSE GENERATOR

Please complete this form. Retain one copy for your records and return (within 10 days) one copy to:

CORATOMIC INCORPORATED
DATA CENTER
P. O. Box 434
Indiana, Pennsylvania 15701

(please print or type)

1. Patient Name _____
Last First Initial

Social Security No. _____ Hospital Record No. _____

Home Address _____

City _____ State _____ Zip _____ A/C & Phone _____

Business Address _____

City _____ State _____ Zip _____ A/C & Phone _____

Name, address, and telephone of person(s) to be contacted if patient cannot be located: _____

City _____ State _____ Zip _____ A/C & Phone _____

Relationship to Patient _____

Name, address, and telephone of alternate person(s) to be contacted if patient cannot be located: _____

City _____ State _____ Zip _____ A/C & Phone _____

Relationship to Patient _____

2. Physician(s) and Hospital:

Name _____

Office Address _____

City _____ State _____ Zip _____ A/C & Phone _____

3. Radioisotope Powered Pacer Information:

Serial No. _____ Date of Implant _____

Placement: subcutaneous/submuscular/intramuscular/other
right/left pectoral/abdominal/other
existing/new pocket

Stimulation rate: with Magnet _____ without _____

Threshold measurements: voltage _____ current _____

Pulse width _____ other method (describe): _____

Equipment used to measure threshold _____

4. Previous Implant Information: ☐ Yes ☐ No If yes:

Manufacturer _____

Model _____ Date of implant _____

Why removed _____

Total number of previous implants _____

5. Lead:
Manufacturer _____

Model No. _____ Serial No. (for new leads only) _____ Date of implant _____

Placement: Myocardial: ☐ right/left ventricle ☐ transthoracic/ ☐ anterior mediastinal

Endocardial: vein used _____

Previous leads (if applicable and available):
Myocardial: Number, models, and implant dates; how many removed?

Endocardial: Number, models, and implant dates; how many removed?

6. Clinical data:
Patient's age _____ Sex _____ Race _____ Height _____

Weight _____ ☐ Right handed ☐ Left handed

Etiology of arrhythmia _____

Kind of arrhythmia _____

Previous drug therapy for arrhythmia _____

Associated diseases _____

Temporary pacing (for initial implants only) ☐ Yes ☐ No

Anesthetics used during surgery _____

Antibiotics: locally/systemically/none

Cortisones or other anti-inflamatory drugs: locally/systemically/none

Was pocket drained: ☐ Yes ☐ No If yes, how long? _____

Did complications or adverse reaction occur in: pacemaker/lead surgery

If yes, treatment _____

Comments _____

EXHIBIT III

FOLLOW-UP DATA FORM

CORATOMIC C-100 SERIES ISOTOPIC PULSE GENERATOR

Please complete this form. Retain one copy for your records and return one copy to:

CORATOMIC, INCORPORATED
DATA CENTER
P. O. Box 434
Indiana, Pennsylvania 15701

1. Patient Name _____ _____ _____
Last First Initial

Social Security No. _____ Patient Hospital Record No. _____

Pulse Generator Serial No. _____ Date of Implantation _____ Date of Follow-up _____

Name of Physician _____

Name of Hospital _____ Telephone No. _____

Address _____

City _____ State _____ Zip _____

Patient has I.D. Card: Yes _____ No _____ Patient is wearing Bracelet or its Equivalent: Yes _____ No _____

C-100 Series Pacer Information

_____ Satisfactory _____ Unsatisfactory Stimulation Rate – with Magnet _____

without Magnet _____

Description of adverse reactions _____

Nature and cause of adverse reaction _____

Description of side effects _____

Toxicity _____

Contraindications _____

Ineffectiveness _____

Pacer malfunction _____

Pacer degradation _____

Has any repair, relocation or replacement of leads been necessary? Yes _____ No _____

3. Has satisfactory contact been maintained with the patient for follow-up and accountability purposes? Yes _____ No _____

If no, why was contact lost? _____

What steps have been taken to re-establish contact? _____

. Summary of medical examination, including laboratory data (at yearly intervals) _____

PACER FAILURE AND REMOVAL OR PATIENT DEATH FORM

CORATOMIC C-100 SERIES ISOTOPIC PULSE GENERATOR

Please complete this form. Retain one copy for your records and return one copy to:

CORATOMIC, INCORPORATED
DATA CENTER
P. O. Box 434
Indiana, Pennsylvania 15701

1. Patient Name _____
Last First Initial

Social Security No. _____ Patient Hospital Record No. _____

Pulse Generator Serial No. _____ Date of Implantation _____

Date of Follow-up _____

Name of Physician _____

Name of Hospital _____ Telephone No. _____

Address _____

City _____ State _____ Zip _____

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

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

2. Pacer Failure

Battery Failure _____ Lead Failure _____ Electronics Failure _____

Description of Failure _____

_____

Corrective Procedure Due to Failure

Replaced Pacer _____

Model and Serial Number of Replacement _____

Replaced Lead _____

Model and Serial Number of Replacement Lead _____

3. Patient Death

Causes of Death _____

_____

_____

Autopsy Findings _____

_____

_____

_____

Was Pacer functioning at time of death? Yes _____ No _____ Was Lead functioning at time of death? Yes _____ No _____

4. Summary of Medical Examinations (if other than death) _____

_____

_____

_____

_____

_____

EXHIBIT V

INFORMED CONSENT FOR SURGICAL IMPLANTATION OF RADIOISOTOPE POWERED CARDIAC PACER

CORATOMIC C-100 SERIES ISOTOPIC PULSE GENERATOR

I understand that for the treatment of my cardiac condition – a disturbance of normal cardiac conduction – a cardiac pacer is to be implanted in me. I understand that the surgical procedure may/will require the implantation of a new electrode or lead into or onto the surface of my heart. While the surgical procedure is not of unreasonable risk, the possibility of complications or even death exist. The procedure has been explained to me, and I have had the opportunity to ask any questions concerning it.

I understand that the pacer to be used for the implantation is a radioisotope powered cardiac pacer manufactured by Coratomic. The pacer is now undergoing its initial clinical use. Although the pacer has been extensively tested, it is of relatively new design, and there is no assurance that its components will last the full design life. On the basis of experiments in animals and in the laboratory, units of this type are expected to have a reliable life expectancy in excess of that of current standard cardiac pacers. I understand that the cardiac pacer does produce radiation, but I have been told by my attending physician that it is his medical judgment that this radiation presents a negligible hazard.

I understand that in consenting to the implantation of this pacer, 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.

Since the device contains radioisotope material (Plutonium-238), ultimately, after my death or earlier, if the useful life of the pacer is exceeded, if it ceases to function effectively for my medical needs, or if I request to have it removed, the pacer must be returned to Coratomic via _____ (licensed institution). Accordingly, I agree to contact _____ (institution) at regular intervals of no less than six months, and whenever I change my residence. I will always carry the appropriate indentification card on my person, and will at all times wear the standard identification bracelet.

Notwithstanding my contacting the implanting institution following the insertion of a cardiac pacer of any sort, I am advised to remain in contact with my personal physician.

I agree to notify the hospital, who will, in turn, notify Coratomic of my intention to travel in foreign countries. Coratomic will, in turn, notify the Nuclear Regulatory Commission.

I understand that the radioisotope powered cardiac pacer is a highly technical prosthetic device and in order to assess the effectiveness of its use _____ (institution) and Coratomic are interested in collecting data upon the device. Accordingly, I agree to examination by my physician at no less than the following intervals: at 1 month, 3 months and 6 month intervals, thereafter, following the insertion of the pacer. I further agree to provide information on my clinical condition as it pertains to the pacer at no less than 6-month intervals. Furthermore, I consent to disclosure by the clinic or Coratomic of any information acquired by the clinic in regard to the implantation of the radioisotope powered cardiac pacer, provided, however, in no event shall disclosure other than to Coratomic include my identification without my specific written approval.

I have had the opportunity to ask questions pertaining to the surgical procedure, the radioisotope powered cardiac pacer, and the follow-up procedure. The possible alternate methods of treatment, including the use of conventional chemical battery powered pacers and rechargeable pacers have been called to my attention.

With these facts in mind and intending to be legally bound, I hereby authorize the surgical procedure whereby the Coratomic radioisotope powered pacer will be implanted in me waiving the right to claim that such procedure was not properly authorized, and I agree to the follow-up procedures and to the ultimate return of the unit as detailed above.

_____
Witness (Date)

_____
Patient's signature or person authorized to consent for the patient. (Date)

_____
Relationship to the patient signing if other than the patient.

Please sign 3 copies:

1 copy to patient
1 copy to hospital
1 copy to Coratomic

I certify that I have explained the above procedure.

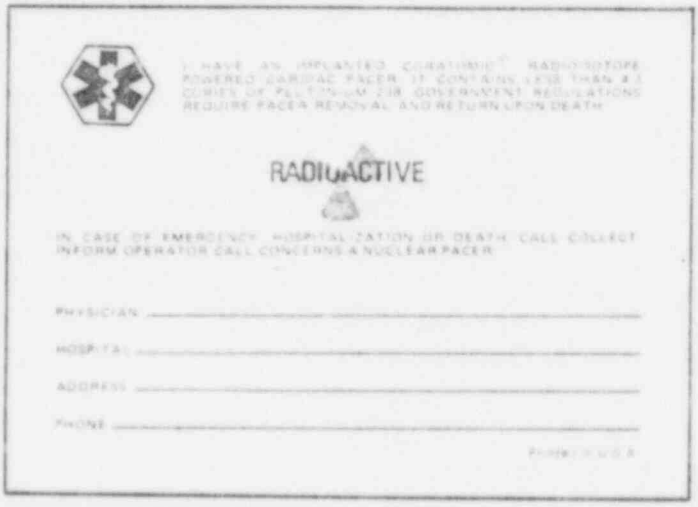
_____
Dr. (Date)

EXHIBIT VI

PATIENT IDENTIFICATION CARDS

CORATOMIC C-100 SERIES ISOTOPIC PULSE GENERATORS

(Front)



(Back)

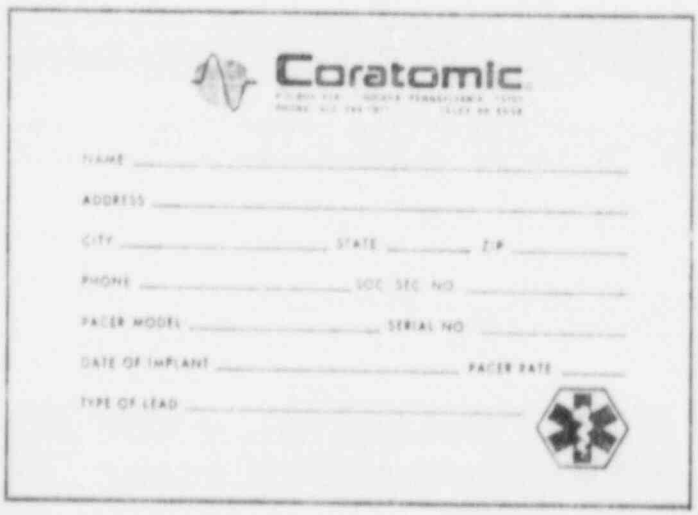
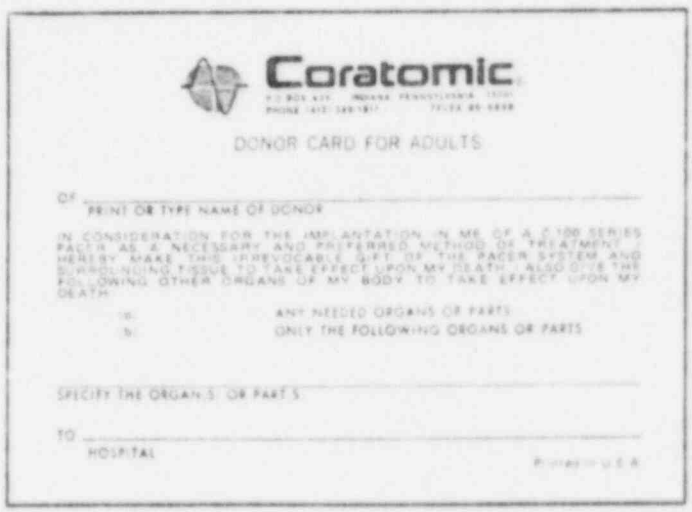


EXHIBIT VII

DONOR CARDS FOR ADULTS

CORATOMIC C-100 SERIES ISOTOPIC PULSE GENERATOR

(Front)



Coratomic

DONOR CARD FOR ADULTS

OF _____
PRINT OR TYPE NAME OF DONOR

IN CONSIDERATION FOR THE IMPLANTATION IN ME OF A C-100 SERIES PACER, AS A NECESSARY AND PREFERRED METHOD OF TREATMENT, I HEREBY MAKE THIS IRREVOCABLE GIFT OF THE PACER SYSTEM AND SURROUNDING TISSUE TO TAKE EFFECT UPON MY DEATH. I ALSO GIVE THE FOLLOWING OTHER ORGANS OF MY BODY TO TAKE EFFECT UPON MY DEATH:

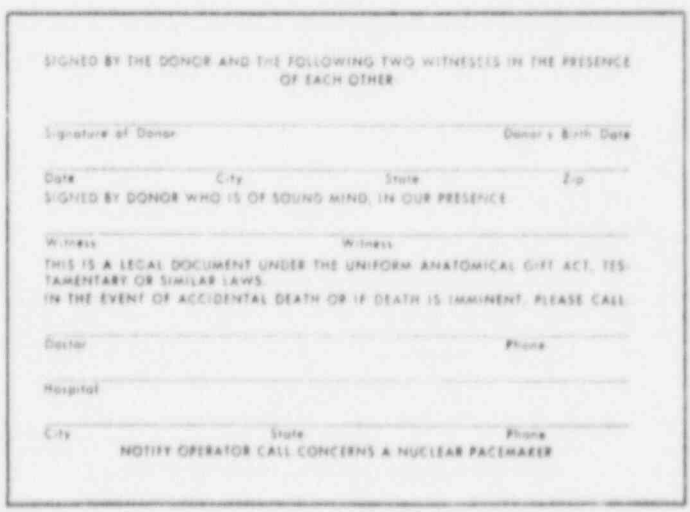
a) ANY NEEDED ORGANS OR PARTS
b) ONLY THE FOLLOWING ORGANS OR PARTS

SPECIFY THE ORGAN S OR PART S

TO _____
HOSPITAL

Printed in U.S.A.

(Back)



SIGNED BY THE DONOR AND THE FOLLOWING TWO WITNESSES IN THE PRESENCE OF EACH OTHER

Signature of Donor — Donor's Birth Date

Date — City — State — Zip

SIGNED BY DONOR WHO IS OF SOUND MIND, IN OUR PRESENCE

Witness — Witness

THIS IS A LEGAL DOCUMENT UNDER THE UNIFORM ANATOMICAL GIFT ACT, TESTAMENTARY OR SIMILAR LAWS.
IN THE EVENT OF ACCIDENTAL DEATH OR IF DEATH IS IMMINENT, PLEASE CALL

Doctor — Phone

Hospital

City — State — Phone

NOTIFY OPERATOR CALL CONCERNS A NUCLEAR PACEMAKER

DONOR CARDS FOR MINORS

CORATOMIC C-100 SERIES ISOTOPIC PULSE GENERATOR

(Front)

Coratomic

DONOR CARD FOR MINORS

OF _____
PRINT OR TYPE NAME OF DONOR

IN CONSIDERATION FOR THE IMPLANTATION IN ME OF A C-100 SERIES PACER AS A NECESSARY AND PREFERRED METHOD OF TREATMENT, I HEREBY MAKE THIS IRREVOCABLE GIFT OF THE PACER SYSTEM AND SURROUNDING TISSUE TO TAKE EFFECT UPON MY DEATH. I ALSO GIVE THE FOLLOWING OTHER ORGANS OF MY BODY TO TAKE EFFECT UPON MY DEATH:

(a) ANY NEEDED ORGANS OR PARTS
(b) ONLY THE FOLLOWING ORGANS OR PARTS

_____
SPECIFY THE ORGAN S OR PART S

TO _____
HOSPITAL

Printed in U.S.A.

(Back)

SIGNED BY THE DONOR AND OR HIS OR HER LEGAL GUARDIAN AND THE FOLLOWING TWO WITNESSES IN THE PRESENCE OF EACH OTHER

_____
Signature of Donor — Donor's Birth Date

_____
Signature of Legal Guardian of Donor Indicate relationship of guardian Parent etc

_____
Date — City — State — Zip

DONOR and or GUARDIAN ARE OF SOUND MIND

_____
Witness — Witness

THIS IS A LEGAL DOCUMENT UNDER THE UNIFORM ANATOMICAL GIFT ACT, TESTAMENTARY OR SIMILAR LAWS
IN THE EVENT OF ACCIDENTAL DEATH OR IF DEATH IS IMMINENT, PLEASE CALL

_____
Doctor — Phone

_____
Hospital

_____
City — State — Phone

NOTIFY OPERATOR CALL CONCERNS A NUCLEAR PACEMAKER

EXHIBIT IX

INSTRUCTIONS FOR HOSPITAL OR CLINIC TELEPHONE OPERATORS

CORATOMIC C-100 SERIES ISOTOPIC PULSE GENERATOR

Project Nuclear Pacemaker

Instructions to Operator:

1. Accept any collect call with reference to "Project Nuclear Pacemaker".
2. Any call concerning "Project Nuclear Pacemaker" involves a patient with a nuclear pacer and requires immediate action to insure that there is no danger of radiation exposure and recovery of the nuclear pacer.
3. Obtain as much information from the caller as is possible including:

   Caller's Name and Where he may be Reached.

   Patient's Name, Status, and Where he may be Reached.

   Attending Physician (if any) and Where he may be Reached.

   Information from Patient I.D. Card

   Patient's Social Security No. _____

   Date of Implant _____

   Pacer Serial Number _____

4. Notify immediately: _____

   _____

   (Name, address, telephone number of physician responsible for study)

   If he cannot be reached, notify: _____

   _____

   Name, address, telephone number of alternative physician.

If neither can be reached, contact physician on duty for the Cardiac Care Unit; inform him that this involves a nuclear pacer; and advise him of the information you have and the urgency of the matter.

EXHIBIT X

SUGGESTED APPLICATION FORMAT FOR NUCLEAR POWERED PACEMAKERS

CORATOMIC C-101 ISOTOPIC PULSE GENERATOR

Chief, Materials Branch Division of Fuel
Cycle and Materials Safety
U. S. Nuclear Regulatory Commission
Washington, D. C. 20555

Re: Application for license to participate in the research study involving the implantation of Coratomic C-101 nuclear powered pacemakers. Each containing 250 milligrams of Pu-238 (< 4.3 curies)

Gentlemen:

The following information is submitted in application for a license to participate in the investigational program utilizing the Coratomic C-101 nuclear powered pacer.

1. Applicant: _____
(Hospital or Medical Institution)
_____
(Address)
_____
(State and Zip Code)

2. Physicians responsible for study: (Provide this information for EACH physician on the study team.)

Name:
Office Address:
Telephone Number:
State Licensed in Which to Practice:
Specialty Board Certification:

Position with the Applicant:

Previous experience in the clinical implantation and follow-up of pacemakers by physicians: (include duration of pacemaker experience, total number of implant physician has done, and the total number he has done at the applicant's facilities.)

3. Protocol to be followed:
HUMAN CLINICAL PROTOCOL FOR THE CORATOMIC C-101 RADIOISOTOPE POWERED CARDIAC PACERS DATED NOVEMBER 1, 1975.

4. A maximum of ____ Coratomic C-101 pacemakers is requested to be implanted annually during the study.

5. Description of physical facilities and equipment at the applicant institution or hospital:

(Include description of cardiac care unit and operating facilities and list specific equipment needed and available to carry out the study; include equipment for measuring stimulation thresholds, threshold parameters, and overall pacemaker function).

6. Description of applicant's present pacemaker implantation and follow-up program: (Include size, i.e., number of patients, and duration.)

7. Describe methods applicant will establish to maintain records of implantation and follow-up of patients separate from routine hospital records. (Include procedures for assuring continuity of follow-up and determining any possible loss of follow-up with a patient).

8. Confirm that the applicant institution or hospital will establish appropriate control procedures to insure the physical security of the pacemaker while in the possession of the applicant. These procedures will include keeping track, by serial number, of the location of each pacemaker and requiring that they be kept under lock and key when not being used to guard against loss or theft. Confirm that all activities will be conducted in accordance with the regulations under Title 10, Code of Federal Regulations, Part 70.

9. Describe the applicants procedures to assure notification of appropriate individuals upon receipt of an emergency report of inquiry concerning a pacemaker bearer. Include written instructions to be given to telephone operators.

10. Confirm that the physicians responsible for and participating in the study represent that they are familiar with Coratomic C-101 Protocol and the Coratomic C-101 Pacer and understand that the issuance of a license is conditional upon the following of this protocol.

11. Confirm that the applicant institution agrees to continue the follow-up reporting and recovery procedures during the life of the patient and until the pacemaker is recovered and returned to Coratomic, Inc., P.O. Box 434, Indiana, Pa. 15701, even in the event the physicians named in the application to participate in the study are no longer associated with the applicant.

12. Confirm that packaging, labeling, and shipping instructions to be furnished by Coratomic, Inc. will be followed upon the return of the pacemaker for approved disposal.

13. The applicant hospital or medical institution hereby requests a license to receive, possess, store, and implant the Coratomic C-101 nuclear powered pacemaker in accordance with this application.

Signed: Applicant: _____ By: _____
(Hospital or Medical Institution) (Name and title of individual signing on behalf of the applicant)

Physicians responsible for study: _____
(Letter should be signed by each of the physicians listed as responsible for study.)

HUMAN IMPLANTATION PROTOCOL

FOR

THE CORATOMIC C-101-P

RADIOISOTOPE POWERED CARDIAC PACER

March 2, 1983

Coratomic
P. O. BOX 434, INDIANA, PENNSYLVANIA 15701
PHONE (412) 349-1811 · TELEX 86-6658

24pp.

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CORATOMIC C-101-P

RADIOISOTOPE CARDIAC PACER PROTOCOL

March 2, 1983

1. Description of the Pacer and Radionuclide Power Source

An extensive literature has arisen in connection with cardiac pacing, and selected references are listed in Exhibit 1. The physician responsible for pacer implantation is cognizant of these and other relevant references and has had extensive experience in the use of cardiac pacers.

The C-101-P pacer utilizes a programmable hybrid circuit, the pacing modes and operating parameters of which can be noninvasively changed using a Coratomic hand-held programmer. It is electronically similar to programmable pacers which have been in use for many years. While the unit is normally used as an R-wave inhibited (VVI) pacemaker, the implanting physician may elect to use the pacer for asynchronous (VOO) pacing when appropriate indications are present.

The pacing rate is programmable at 13 settings ranging from 38 to 120 PPM. Pulse current can be set to either 4 or 10 mA. Sensitivity is programmable to 1.5, 2.5, 4, or 5 mV. The pacer can be changed from its normal R-wave inhibited (VVI) mode to asynchronous (VOO) pacing by placing the sensitivity selector to its FR (Fixed Rate) setting.

The unit is hermetically sealed and shielded against electromagnetic interference. It has an asynchronous "magnet rate", identical to the programmed pacing rate, used to ascertain cardiac capture and for operational verification. If high energy electromagnetic fields are present, the pacer will switch to a fixed rate rather than becoming inhibited.

The fuel used for the C-101-P is plutonium-238 in its oxide form, pressed and sintered into a hard, ceramic pellet. The isotopic battery has been so designed that excess electrical power is available at the end of a 40 year life. The pacers have undergone extensive testing for efficacy, including excessive mechanical shock, impact, and vibration testing, and the nuclear fuel is contained in such a manner to prevent fuel release under any credible accident, including building or auto accident, fire, fall from an airplane, crushing, corrosion in sea water, or accidental cremation.

Data concerning radiation level, safety, and efficacy testing is on file with the United States Nuclear Regulatory Commission, as a Master Protocol.

2. Patient Selection

Cooperative and reliable patients, who are stable, and non-mobile members of the community, will be selected to assure accurate long-term follow-up reporting.

3. Follow-Up and Reporting

The physician or hospital will be required to contact the patient at least every six months, and report the contact to Coratomic. This contact will be maintained during the life of the patient or until the pacer is removed. "In-person" follow-up visits are preferable; however, telephone contacts are acceptable. At the time of follow-up, patients should be reminded of the importance of carrying their I. D. card and wearing their I. D. jewelry. Any complications or adverse reactions must be reported to Coratomic by the physician or hospital. Coratomic will consolidate the reporting of patients and notify the Nuclear Regulatory Commission of the results of its accountability program twice per year. If the patient's whereabouts are unknown, Coratomic will, through its contacts with the hospitals and physicians, locate the patient and forward this information to the hospitals to provide complete accountability.

4. Implantation Procedures and Leads

Conventional methods of pacemaker insertion are to be used, ensuring as far as possible that the electrodes and leads used have an expected life comparable to the pacemaker and that they have appropriate pacing thresholds. In patients with an existing lead, the type of existing electrode must be compatible. If not, standard adapters may be used. Spliced leads may not be used. Ideally, Coratomic leads should be utilized to assure long-term compatibility with the pacer materials. Myocardial or endocardial leads may be used with any of th standard surgical approaches for lead implantation in either the left or the right ventricle. The C-101-P pulse generator may be implanted in the subcutaneous tissue of the abdomen, chest wall, the subpectoral muscle tissue of the chest wall, or any other area deemed suitable by the responsible physician.

5. Stimulation Threshold Measurements

The pacing threshold will be tested for all electrodes, old or new, utilizing a battery-operated, calibrated ($\pm$5% accuracy) pulse generator with an adjustable amplitude and of a pulse duration of .8 to 1.2 milliseconds.

Only those electrodes may be utilized in which a threshold is demonstrated no greater than 1.5 mA if newly implanted or 4.0 mA if chronically implanted, whether transvenous or epicardial, measured at a pulse width of

1.0 milliseconds.

6. Sensing Measurements

If possible, the amplitude and width of the patient's QRS wave should be measured. Measurement should be between a ground plate in the pacer subcutaneous pocket and the lead terminal distal to the heart.

7. Registration and Implant Reports

Immediately upon implantation of the C-101-P, the physician or hospital will complete a Registration and Implant Data Form, and forward it within 10 days to the Coratomic Data Center. The form includes identification of the pacemaker, the patient, the physician, the hospital, the heart lead and adapter (if used), stimulated rate, and clinical data concerning the patient and his or her cardiac disease. The data form is shown as Exhibit II, attached.

8. Follow-up Data

The follow-up data, reported at six-month intervals, will be prepared by the physician or hospital and submitted to the Coratomic Data Center on the Follow-up Data Form (see Exhibit III, attached). This form summarizes information on the patient and lists any complications, adverse reactions or pacer malfunction. "In-person" follow-up visits are preferable; however, telephone contacts are acceptable. At the time of follow-up, patients should be reminded of the importance of carrying their I. D. card and wearing their I. D. jewelry.

9. Reports of Removal and Replacement

A special form, "Pacer Failure and Removal or Patient Death," (Exhibit IV) is provided. This form records all pertinent required data concerning the patient, physician, hospital and reasons for pacer removal and replacement, including whether the failure was of battery, electronic, or lead origin. Corrective procedures and results of patient examinations are also required.

In the event of pacer removal, the pacer must be recovered and returned to Coratomic. The hospital and/or the physician shall notify Coratomic, and the licensing agency, of the pacer removal, and Coratomic will send the proper shipping container and instructions to the explanting institution for the pacemaker's return.

10. Notification of Deaths, Adverse Reactions or Malfunctions

Notification of death is included in the form "Pacer Failure and Removal or Patient Death" (Exhibit IV). The cause of death and autopsy findings are included.

In the event of patient death, the pacer must be recovered and returned to Coratomic. The hospital and/or the physician shall notify Coratomic, and the licensing agency, of the patient death and pacer removal within 24 hours of such occurrence, and Coratomic will send the proper shipping container and instructions to the explanting institution for the pacemaker's return. Coratomic will immediately notify the Nuclear Regulatory Commission of the patient death.

11. Notification of Loss of Patient Contact

The hospital must notify Coratomic, and the licensing agency, within ten days of the loss of contact with a nuclear powered pacemaker patient. This notification can be made on the Follow-up Data Form, Exhibit III, which outlines the reasons for loss of contact and steps taken to reestablish contact. When loss of contact is reported, Coratomic will immediately notify the Nuclear Regulatory Commission and will pursue the patient using data from the initial implant form (Exhibit II) until a satisfactory explanation is obtained. Coratomic will advise the hospital of their findings.

12. Information To and Consent From the Patient

a. All patients accepting the pacemaker must agree to maintain contact with the physician or hospital as summarized above and to the removal and return to the physician (and from them to Coratomic) of the unit upon completion of its expected useful life (40 years), its failure, or upon the patient's death, whichever occurs first. A legally binding document (Exhibit V) will be signed by the patient, a witness, the patient's spouse, and/or a relative of the patient.

b. The patient will be required to carry an identification card as stated in the form shown in Exhibit V. This card is shown in Exhibit VI. The card will identify the carrier as a radioisotope powered cardiac pacer patient, will specify the manufacturer and model number of the patient's pacemaker, specify the radionuclides contained in the pacer, and present explicit instructions for notification of responsible parties in the event of accident or difficulty. At the time of follow-up, patients should be reminded of the importance of carrying their I. D. card. The patient will also be required to carry a uniform anatomical Gift Act Card, as shown in Exhibit VII. If the patient has not attained majority age, the agreement card shown in Exhibit VIII should be executed by the patient where possible and his or her legal guardian.

c. The patient will also be required to carry an identification bracelet or other equivalent jewelry of the medical-alert type which will carry the same patient's name and a statement to call the proper emergency

telephone number. At the time of follow-up, patients should be reminded of the importance of wearing their I. D. jewelry. This medical alert jewelry is mentioned in Exhibits III and IV.

d. The patient will maintain contact with the physician or hospital as discussed in 2 above, and he will be required to agree to do so on the informed consent form of Exhibit V.

e. The patient will notify the hospital of any change either in his/her address or in the names and addresses of two persons to be contacted if the patient cannot be located. The patient will be required to agree to do so on the informed consent form (Exhibit V).

f. The patient will be required to notify the hospital of his intention to travel in foreign countries. The hospital will in turn notify Coratomic, who will notify the Nuclear Regulatory Commission. The patient agrees to provide this information on the Informed Consent Form (Exhibit V).

13. Record Retention

All pacer records will be maintained separately from the routine hospital records, either by a centralized authority so designated, health physics personnel, or the pacemaker clinic within the hospital's jurisdiction, or the physician responsible for the implantation program.

The hospital or the implanting physician will notify Coratomic of any change in the patient's address or condition so that Coratomic may maintain current records on the patient.

The patient's chart, both at the hospital and in the physician's office, must prominently indicate that the pacemaker must be returned to Coratomic upon its removal from the patient for any reason.

14. Accountability and Recovery

Under a special nuclear material license issued for implanting radioisotopic pacemakers, the patient's hospital assumes the responsibility for the control, accountability and recovery of the special nuclear materials (plutonium) in the pacemaker. Conditions for accountability and recovery include the following:

a. The hospital shall not receive or transfer in any single transaction one gram or more of plutonium contained in the nuclear-powered pacemakers without notifying the Division of Safeguards, U. S. Nuclear Regulatory Commission, Washington, DC 20555, and, in addition, completing and distributing Form NRC-741 as required by Section 70.54 of 10 CFR Part 70.

b. The hospital shall report to Coratomic, Inc. (the manufacturer of the pacemaker), and to the licensing agency,within 24 hours of occurrence, the death of any nuclear-powered pacemaker patient. Coratomic will immediately advise the Nuclear Regulatory Commission.

c. The hospital shall report to Coratomic, Inc., and to the licensing agency, within 10 days, the loss of contact with a nuclear-powered pacemaker patient. Coratomic will immediately advise the Nuclear Regulatory Commission.

d. The implanting hospital should normally be able to follow a patient for life, considering that non-mobile patients are selected and that telephone contacts may be used for follow-up. In unusual cases where follow-up difficulties are experienced, Coratomic should be contacted to try to arrange transfer of responsibility to another hospital. Responsibility could be transferred to another hospital if:

(1) The new hospital is properly licensed and agrees in writing to accept full responsibility in accordance with the protocol;

(2) The old hospital transfers responsibility in writing;

(3) The patient signs revised consent forms and receives revised I. D. card and I. D. jewelry;

(4) The appropriate licensing agencies are notified of the transfer and provided copies of the documentation.

Following a proper transfer, the old hospital may of course amend or terminate its license as appropriate.

REFERENCES

1. Smyth, Nicholas P. D.: Cardiac Pacemaking. *Surgical Diseases of the Chest,* Second Edition in Press, Editor Brian Blades., C. V. Mosby Co., St. Louis, Mo., 1974.

2. Chardack, William M.: Cardiac Pacemakers and Heart Block. *In Surgery of the Chest* (Chapter 38), Second Edition, Editors John H. Gibson, Jr., David C. Sabiston and Frank C. Spencer. W. B. Saunders Co., Philadelphia, Pa., 1969.

3. Furman, Seymour, and Escher, Doris J. W. : *Principles and Techniques of Cardiac Pacing.* Harper and Row, New York, N.Y., 1970.

4. Thalen, Hilbert J.: *The Artificial Cardiac Pacemaker:* Its History, Development and Clinical Application. C. C. Thomas, Springfield, Ill., 1969.

5. Hurzeler, Philip; Decaprio, Vincent; and Furman, Seymour, Montefiore Hospital and Medical Center, New York, N.Y.: *Endocardial Electrograms and Pacer Sensing;* paper presented at AAMI 10th Annual meeting March 17–18, 1975.

EXHIBIT II
REGISTRATION AND IMPLANTATION DATA FORM
CORATOMIC C-100 SERIES ISOTOPIC PULSE GENERATOR

Please complete this form. Retain one copy for your records and return(within 10 days) one copy to:

CORATOMIC, INC.
DATA CENTER
P. O. Box 434
Indiana, PA 15701

IMPORTANT: The isotopic pacemaker must be recovered and returned to Coratomic in the event of patient death or pacemaker removal. Please contact Coratomic for proper shipping container.

(please print or type)

1. Patient Name _____
Last First Initial
Social Security No. _____ Hospital Record No. _____
Home Address _____
A/C & Phone _____
Business Address _____
A/C & Phone _____
Name, address, and telephone of person(s) to be contacted if patient cannot be located _____
A/C & Phone _____
Relationship to Patient _____
Name, address, and telephone of alternate person(s) to be contacted if patient cannot be located _____
A/C & Phone _____
Relationship to Patient _____
2. Physician(s) and Hospital:
Name _____
Office Address _____
A/C & Phone _____
3. Radioisotope Powered Pacer Information:
Serial No. _____ Date of implant _____
Placement: subcutaneous/submuscular/intramuscular/other
right/left pectoral/abdominal/other
existing/new pocket
Stimulation rate: with Magnet _____ without _____
Threshold measurements: voltage _____ current _____ pulse width _____
other method (describe): _____
Equipment used to measure threshold _____
4. Previous Implant Information: Yes No If yes:
Manufacturer _____ Model _____ Date of implant _____
Why removed _____
Total number of previous implants _____
5. Lead: Manufacturer _____ Model No. _____
Serial No. (for new leads only) _____ Date of implant _____
Placement: Myocardial: right/left ventricle
transthoracic/transmediastinal
Endocardial: vein used _____
Previous leads (if applicable and available):
Myocardial: Number, models, and implant dates; how many removed?
_____
Endocardial: Number, models, and implant dates; how many removed?

(continued next page)

EXHIBIT II
(continued)

6. Clinical data:
Patient's age _____ Sex _____ Race _____ Height _____
Weight _____ Right handed/Left handed
Etiology of arrhythmia _____
Kind of arrhythmia _____
Previous drug therapy for arrhythmia _____
Associated diseases _____
Temporary pacing (for initial implants only) Yes No
Anesthetics used during surgery _____
Antibiotics: locally/systemically/none
Cortisones or other anti-inflamatory drugs: locally/systemically/none
Was pocket drained: Yes No If yes, how long? _____
Did complications or adverse reactions occur in pacemaker/lead surgery? ___
If yes, treatment _____
Comments _____
_____

EXHIBIT III
FOLLOW-UP DATA FORM
CORATOMIC C-100 SERIES ISOTOPIC PULSE GENERATOR

IMPORTANT: The isotopic pacemaker must be recovered and returned to Coratomic in the event of patient death or pacemaker removal. Please contact Coratomic for proper shipping container.

Please complete this form. Retain one copy for your records and return (within 10 days) one copy to:

CORATOMIC, INC.
DATA CENTER
P. O. Box 434
Indiana, PA 15701

1. Patient Name _____
Last First Initial
Social Security No. _____ Hospital Record No. _____
Home Address _____
_____ A/C & Phone _____
Business Address _____
_____ A/C & Phone _____
Name, address, and telephone of person(s) to be contacted if patient cannot be located _____
_____ A/C & Phone _____
Relationship to Patient _____
Name, address, and telephone of alternate person(s) to be contacted if patient cannot be located _____
_____ A/C & Phone _____
Relationship to Patient _____
2. Physician(s) and Hospital:
Name _____
Office Address _____
_____ A/C & Phone _____
3. Radioisotope Powered Pacer Information:
Serial No. _____ Date of Implant _____
Date of Follow-Up _____
Was follow-up an "in-person" visit or telephone contact? _____
Was patient reminded of the importance of carrying I. D. card and wearing I. D. jewelry? Yes No
Patient has I. D. card Yes ___ No ___
Patient is wearing Bracelet or its Equivalent: Yes ___ No ___
C-100 Series Pacer Information: Satisfactory ___ Unsatisfactory ___
Stimulation Rate: with Magnet _____
without Magnet _____
List any complications, adverse reactions, or pacer malfunction:

_____

_____

_____
Has any repair, relocation or replacement of leads been necessary? yes/no
Has satisfactory contact been maintained with the patient for follow-up and accountability purposes? Yes ___ No ___
If no, why was contact lost? _____
What steps have been taken to re-establish contact? _____

_____

EXHIBIT IV
PACER FAILURE AND REMOVAL
OR PATIENT DEATH FORM
CORATOMIC C-100 SERIES ISOTOPIC PULSE GENERATOR

IMPORTANT: The isotopic pacemaker must be recovered and returned to Coratomic in the event of patient death or pacemaker removal. Please contact Coratomic for proper shipping container.

Please complete this form. Retain one copy for your records and return one copy to:

CORATOMIC, INC.
DATA CENTER
P. O. Box 434
Indiana, PA 15701

1. Patient Name _____
Last First Initial
Social Security No. _____ Patient Hospital Record No. _____
Pulse Generator Serial No. _____ Date of Implantation _____
Date of Follow-up _____
Name of Physician _____
Name of Hospital _____ Telephone No. _____
Address _____
City _____ State _____ Zip _____
Patient has I. D. card: Yes ___ No ___
Patient is wearing Bracelet or its Equivalent: Yes ___ No ___
How was pacemaker disposed of? _____
2. Pacer Failure
Battery Failure ___ Lead Failure ___ Electronics Failure ___
Description of Failure _____
_____
Corrective Procedure Due to Failure
Replaced Pacer ___
Model and Serial Number of Replacement _____
Replaced Lead ___
Model and Serial Number of Replacement Lead _____
3. Patient Death
Causes of Death _____
_____
_____
Autopsy Findings _____
_____
_____
_____
Was Pacer functioning at time of death? Yes ___ No ___
Was Lead functioning at time of death? Yes ___ No ___
4. Summary of Medical Examinations (if other than death) _____
_____
_____
_____
_____
_____

(Attachment 5)

EXHIBIT V
INFORMED CONSENT FOR SURGICAL IMPLANTATION
OF RADIOISOTOPE POWERED CARDIAC PACER
CORATOMIC C-100 SERIES ISOTOPIC PULSE GENERATOR

I understand that for the treatment of my cardiac condition - a disturbance of normal cardiac conduction - a cardiac pacer is to be implanted in me. I understand that the surgical procedure may/will require the implantation of a new electrode or lead into or onto the surface of my heart. While the surgical procedure is not of unreasonable risk, the possibility of complications or even death exist. The procedure has been explained to me, and I have had the opportunity to ask any questions concerning it.

I understand that the pacer to be used for the implantation is a radioisotope powered cardiac pacer manufactured by Coratomic. Although the pacer has been extensively tested, there is no assurance that its components will last the full design life. On the basis of past experience, units of this type are expected to have a reliable life expectancy in excess of 40 years. I understand that the cardiac pacer does produce radiation, but that this radiation is negligible.

Since the device contains radioisotope material (Plutonium-238), ultimately, after my death or earlier, if the useful life of the pacer is exceeded, if it ceases to function effectively for my medical needs, or if I request to have it removed, the pacer must be returned to Coratomic via _____ (licensed institution). Accordingly, I agree to contact _____ (institution) at least every six months, and whenever I change my residence. I will always carry the appropriate identification card on my person, and will at all times carry the Uniform Anatomical Gift Act donor card and wear either a medical alert bracelet or its equivalent.

Notwithstanding my contacting the implanting institution following the insertion of a cardiac pacer of any sort, I am advised to remain in contact with my personal physician.

I agree to notify the hospital, who will, in turn, notify Coratomic of my intention to travel in foreign countries. Coratomic will, in turn, notify the Nuclear Regulatory Commission.

I agree to provide the hospital with the names, addresses, and telephone numbers of two persons to be contacted if I cannot be located. I also agree to notify the hospital of any changes in the names, addresses, or telephone numbers of the two persons to be contacted.

I agree to maintain contact with my physician at least every six months following the insertion of the pacer. Furthermore, I consent to disclosure by the clinic or Coratomic of any information acquired by the clinic in regard to the implantation of the radioisotope powered cardiac pacer, provided, however, in no event shall disclosure other than to Coratomic include my identification without my specific written approval.

I have had the opportunity to ask questions pertaining to the surgical procedure, the radioisotope powered cardiac pacer, and the follow-up procedure. The possible alternate methods of treatment, including the use of conventional chemical battery powered pacers have been called to my attention.

With these facts in mind and intending to be legally bound, I hereby authorize the surgical procedure whereby the Coratomic radioisotope powered pacer will be implanted in me waiving the right to claim that such procedure was not properly authorized, and I agree to the follow-up procedures and to the ultimate return of the unit as detailed above.

(continued next page)

EXHIBIT V (Attachment 5)
(continued)

Witness (Date)

Patient's signature or person authorized to consent for the patient (Date)

Relationship to the patient signing if other than the patient

Please sign 3 copies.

1 copy to patient
1 copy to hospital
1 copy to Coratomic

I certify that I have explained the above procedure

Dr. (Date)

EXHIBIT VI
PATIENT IDENTIFICATION CARDS
CORATOMIC C-100 SERIES ISOTOPIC PULSE GENERATORS

(Front)

Coratomic.

NAME _____

ADDRESS _____

CITY _____ STATE _____ ZIP _____

PHONE _____ SOC SEC NO _____

PACER MODEL _____ SERIAL NO _____

DATE OF IMPLANT _____ PACER RATE _____

TYPE OF LEAD _____

(Back)

I HAVE AN IMPLANTED CORATOMIC® RADIOISOTOPE POWERED CARDIAC PACER. IT CONTAINS LESS THAN 4.3 CURIES OF PLUTONIUM 238. GOVERNMENT REGULATIONS REQUIRE PACER REMOVAL AND RETURN UPON DEATH.

RADIOACTIVE

IN CASE OF EMERGENCY, HOSPITALIZATION OR DEATH, CALL COLLECT. INFORM OPERATOR CALL CONCERNS A NUCLEAR PACER.

PHYSICIAN _____

HOSPITAL _____

ADDRESS _____

PHONE _____

Printed in U.S.A.

(Attachment 5)

EXHIBIT VII
DONOR CARDS FOR ADULTS
CORATOMIC C-100 SERIES PULSE GENERATOR

(Front)

Coratomic

DONOR CARD FOR ADULTS

OF _____
PRINT OR TYPE NAME OF DONOR

IN CONSIDERATION FOR THE IMPLANTATION IN ME OF A C-100 SERIES PACER, AS A NECESSARY AND PREFERRED METHOD OF TREATMENT, I HEREBY MAKE THIS IRREVOCABLE GIFT OF THE PACER SYSTEM AND SURROUNDING TISSUE TO TAKE EFFECT UPON MY DEATH. I ALSO GIVE THE FOLLOWING OTHER ORGANS OF MY BODY TO TAKE EFFECT UPON MY DEATH:

(a) ANY NEEDED ORGANS OR PARTS
(b) ONLY THE FOLLOWING ORGANS OR PARTS

SPECIFY THE ORGANS OR PARTS _____

TO _____
HOSPITAL

Printed in U.S.A.

(Back)

SIGNED BY THE DONOR AND THE FOLLOWING TWO WITNESSES IN THE PRESENCE OF EACH OTHER

Signature of Donor _____ Donor's Birth Date

Date _____ City _____ State _____ Zip

SIGNED BY DONOR WHO IS OF SOUND MIND, IN OUR PRESENCE

Witness _____ Witness

THIS IS A LEGAL DOCUMENT UNDER THE UNIFORM ANATOMICAL GIFT ACT, TESTAMENTARY OR SIMILAR LAWS.

IN THE EVENT OF ACCIDENTAL DEATH OR IF DEATH IS IMMINENT, PLEASE CALL

Doctor _____ Phone

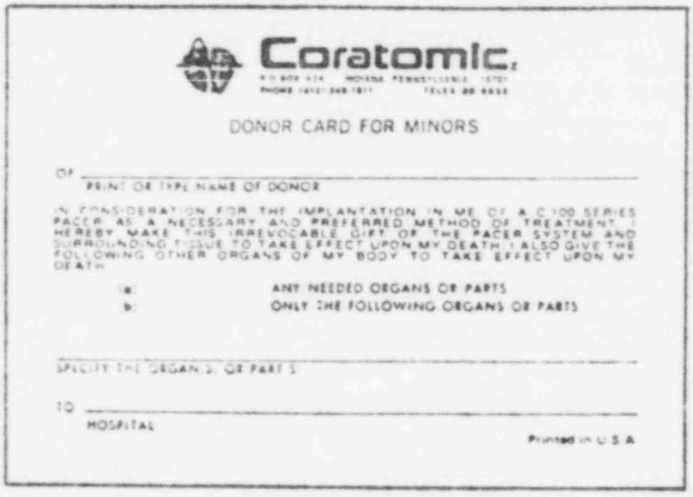
Hospital

City _____ State _____ Phone

NOTIFY OPERATOR CALL CONCERNS A NUCLEAR PACEMAKER

EXHIBIT VIII
DONOR CARD FOR MINORS
CORATOMIC C-100 SERIES ISOTOPIC PULSE GENERATOR

(Front)



Coratomic

DONOR CARD FOR MINORS

OF _____
PRINT OR TYPE NAME OF DONOR

IN CONSIDERATION FOR THE IMPLANTATION IN ME OF A C-100 SERIES PACER AS A NECESSARY AND PREFERRED METHOD OF TREATMENT, I HEREBY MAKE THIS IRREVOCABLE GIFT OF THE PACER SYSTEM AND SURROUNDING TISSUE TO TAKE EFFECT UPON MY DEATH. I ALSO GIVE THE FOLLOWING OTHER ORGANS OF MY BODY TO TAKE EFFECT UPON MY DEATH:

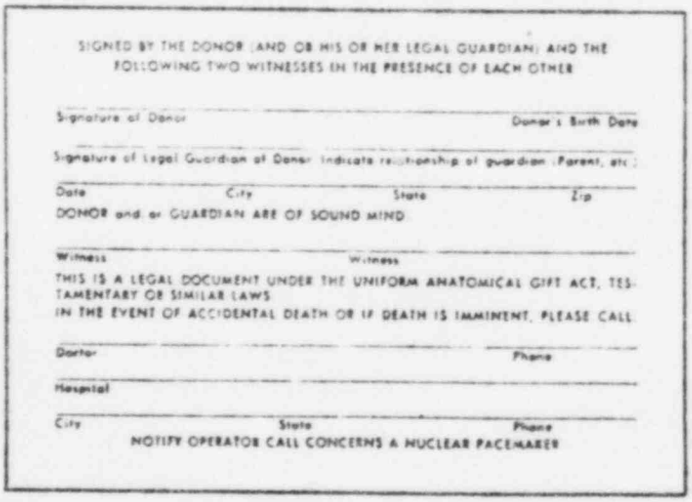
a. ANY NEEDED ORGANS OR PARTS
b. ONLY THE FOLLOWING ORGANS OR PARTS

_____
SPECIFY THE ORGAN(S) OR PART S

TO _____
HOSPITAL

Printed in U.S.A.

(Back)



SIGNED BY THE DONOR (AND OR HIS OR HER LEGAL GUARDIAN) AND THE FOLLOWING TWO WITNESSES IN THE PRESENCE OF EACH OTHER

_____ _____
Signature of Donor Donor's Birth Date

_____
Signature of Legal Guardian of Donor Indicate relationship of guardian (Parent, etc.)

_____
Date City State Zip

DONOR and or GUARDIAN ARE OF SOUND MIND

_____ _____
Witness Witness

THIS IS A LEGAL DOCUMENT UNDER THE UNIFORM ANATOMICAL GIFT ACT, TESTAMENTARY OR SIMILAR LAWS

IN THE EVENT OF ACCIDENTAL DEATH OR IF DEATH IS IMMINENT, PLEASE CALL

_____ _____
Doctor Phone

_____
Hospital

_____
City State Phone

NOTIFY OPERATOR CALL CONCERNS A NUCLEAR PACEMAKER

EXHIBIT IX
SUGGESTED APPLICATION FORMAT FOR NUCLEAR POWERED PACEMAKERS
CORATOMIC C-101-P ISOTOPIC PULSE GENERATOR

Send to:

Material Licensing Branch
U. S. Nuclear Regulatory Commission
Washington, DC 20555

Or - Agreement State Licensing Agency
(if appropriate)

Re: Application for license to participate in the implantation of Coratomic C-101-P nuclear powered pacemakers, each containing 250 milligrams of Pu-238(≈4.3 curies).

Gentlemen:

The following information is submitted in application for a license to participate in the implantation of Coratomic C-101-P nuclear powered pacers.

1. Applicant: _____
(Hospital or Medical Institution)

_____
(Address)

_____
(State and Zip Code)

2. Physicians responsible for implantation program: (Provide this information for EACH physician involved)

Name:
Office Address:
Telephone Number:
State Licensed in Which to Practice:
Specialty Board Certification:
Position with the Applicant:
Previous experience in the implantation and follow-up of pacemakers by physician:
(include duration of pacemaker experience, total number of implants physician has done, and the total number he has done at the applicant's facilities.)

3. Protocol to be followed:
HUMAN IMPLANTATION PROTOCOL FOR THE CORATOMIC C-101-P RADIOISOTOPE POWERED CARDIAC PACER, DATED MARCH 2, 1983.

4. A maximum of ___ Coratomic C-101-P pacemakers is requested to be implanted annually.

5. Description of physical facilities and equipment at the applicant institution or hospital:
(Include description of cardiac care unit and operating facilities and list specific equipment needed and available for the implantation program; include equipment for measuring stimulation thresholds, threshold parameters, and overall pacemaker function.)

6. Description of applicant's present pacemaker implantation and follow-up program: (Include size, i. e., number of patients, and duration.)

EXHIBIT IX
(continued)

7. Describe methods applicant will establish to maintain records of implantation and follow-up of patients separate from routine hospital records. (Include procedures for assuring continuity of follow-up and determining any possible loss of follow-up with a patient.)

8. Confirm that the applicant institution or hospital will establish appropriate control procedures to insure the physical security of the pacemakers while in the possession of the applicant. These procedures will include keeping track, by serial number, of the location of each pacemaker and requiring that they be kept under lock and key when not being used to guard against loss or theft. Confirm that all activities will be conducted in accordance with the regulations under Title 10, Code of Federal Regulations, Part 70.

(continued next page)

EXHIBIT IX
(continued)

9. Describe the applicant's procedures to assure notification of appropriate individuals upon receipt of an emergency report of inquiry concerning a pacemaker bearer. Include written instructions to be given to telephone operators.

10. Confirm that the physicians responsible for and participating in the implantation program represent that they are familiar with the Coratomic C-101-P Protocol and the Coratomic C-101-P Pacer and understand that the issuance of a license is conditional upon the following of this protocol.

11. Confirm that the applicant institution agrees to continue the follow-up reporting and recovery procedures during the life of the patient and until the pacemaker is recovered and returned to Coratomic, Inc., P. O. Box 434, Indiana, PA 15701, even in the event the physicians named in the application are no longer associated with the applicant.

12. Confirm that packaging, labeling, and shipping instructions to be furnished by Coratomic, Inc. will be followed upon the return of the pacemaker for approved disposal.

13. The applicant hospital or medical institution hereby requests a license to receive, possess, store, and implant the Coratomic C-101-P nuclear powered pacemaker in accordance with this application.

Signed: Applicant: _____
(Hospital or Medical Institution)

By: _____
(name and title of individual signing on behalf of the applicant)

Physicians responsible for implantation program:

_____

(Letter should be signed by both an officer of the applicant and the physicians responsible for the implantation program. Type or print names under signatures.)

EXHIBIT X
INSTRUCTIONS FOR HOSPITAL OR CLINIC TELEPHONE OPERATORS
CORATOMIC C-100 SERIES ISOTOPIC PULSE GENERATOR

Nuclear Pacemaker

Instructions to Operator:

1. Accept any collect call with reference to a Nuclear Pacemaker.

2. Any call concerning a Nuclear Pacemaker involves a patient with a nuclear pacemaker and requires immediate action to insure that there is no danger of radiation exposure and recovery of the nuclear pacer.

3. Obtain as much information from the caller as is possible including:

   Caller's Name and Where he may be Reached.

   Patient's Name, Status, and Where he may be Reached.

   Attending Physician (if any) and Where he may be Reached.

   Information from Patient I. D. Card

      Patient's Social Security No. _____

      Date of Implant _____

      Pacer Serial Number _____

4. Notify immediately: _____

_____
Name, address, telephone number of physician responsible

If he cannot be reached, notify: _____

_____
Name, address, telephone number of alternative physician.

If neither can be reached, contact physician on duty for the Cardiac Care Unit; inform him that this involves a nuclear pacer; and advise him of the information you have and the urgency of the matter.

(Attachment 6)

QUALITY ASSURANCE INCOMING INSPECTION OF FUEL CAPSULES

Capsules are loaded by a qualified fabrication according to Coratomic Specification #1141. Loaded capsules are delivered to Coratomic with a data sheet for each capsule that includes wipe test results, helium leak test results, quantity of fuel loaded, gamma and neutron dose measurement, capsule material certification numbers and welding parameters.

The following procedure will be used in the order listed:

1. Upon receipt the capsules will be logged into the incoming capsule inspection log Doc. #7115-11 and also into the Isotopic Sources log.

2. Capsules will then be wipe tested.

   A. Wipe the entire exterior surface of the fuel capsule (especially the weld seams) with Whitmans 41 filter paper or equivalent. Use a 1" square piece.

   B. Measure the activity on the wipe paper using an Alpha sensitive meter that has been calibrated with a .001 microcurie Pu-239 Alpha Standard. Standard will give a reading with tolerances.

   C. Record the removable activity in microcuries in the incoming capsule inspection log Doc. #7115-11.

   D. Any capsule that shows more than .005 microcuries of removable contamination shall be removed from service. The capsule must be repaired or disposed of in accordancewith the NRC and a report must be filed with the NRC within five days in accordance with the leak check condition of the special Nuclear Material License. (Check with Manager, Q.A. and Radiation Safety Officer for decontamination and disposition.)

3. Capsules will then have a neutron count performed.

   A. The Alpha sensing meter and the 488A Victoreen Geiger Counter will be used for this. Insure that the Alpha sensitive meter has been calibrated with the Pu-239 Alpha Standard. Check the battery in the 488A Victoreen Geiger Counter.

   B. Wrap the capsule in tissue and place in the paraffin drum.

   C. Place the 488A on X1 scale and fast response. Place the external-internal switch on the Alpha sensing meter on the external position and start count.

   D. Record information in the incoming inspection log Doc. #7115-11. Turn 488A OFF after use.

4. Identifiying Capsules

   A. The following information is scribed on each capsule.

QUALITY ASSURANCE INCOMING INSPECTION OF FUEL CAPSULES (Cont'd)

B. The  is scribed first. Set the New Hermes Scriber on #3 position. Center capsule and scribe - DO NOT SCRIBE ON WELD SEAM.

C. The X000 is scribed second. Set scriber on position #4. Center capsule and scribe - DO NOT SCRIBE ON WELD SEAM.

D. Make sure information is readable on capsule.

5. Leak checking capsules

A. Pressurize capsules for two hours at 100 PSI.

B. Place in methanol and observe any bubbles coming from capsules.

C. Record information in incoming inspection log Doc. #7115-11.

6. Storing Capsules

A. All nuclear fuel capsules are stored in the safe in vials marked with I.D. number and radioactive tape around the vial.

B. Capsules are released from the safe by Q.A. and a record is kept of the disposition of each capsule (Doc. #7115-11 and Isotopic Sources log).

SPECIAL NOTE

Capsules stored in the safe for longer than six months must be wipe tested and information recorded in Isotopic Sources log before they can be released.

Capsules that are in completed batteries or pacers and kept by Coratomic must be checked for emissions every six months by wiping the outside of the battery or pacer or package it is contained in and by checking the battery or pacer output.

REVISIONS												
1	CR#	323	CR#		CR#		CR#		CR#		CR#	
	Date	2/16/78	Date		Date		Date		Date		Date	
2	CR#	572	CR#		CR#		CR#		CR#		CR#	
	Date	7/18/79	Date		Date		Date		Date		Date	
	CR#		CR#		CR#		CR#		CR#		CR#	
	Date		Date		Date		Date		Date		Date	
	CR#		CR#		CR#		CR#		CR#		CR#	