Biocontrol Technology, Inc.

070-01342

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October 4, 1988

Dr. John Glenn
U. S. Nuclear Regulatory Commission
Region I
Nuclear Material Section B
475 Allendale Road
King of Prussia, PA 19406

RE: License No. SNM-1319
Docket No. 070-01342
Control No. 107573

Dear Dr. Glenn:

Biocontrol Technology, Inc. (formerly Coratomic, Inc.) recently received approval from the Food and Drug Administration to market the Coratomic model Pulsar-N1 nuclear-powered pacemaker. Enclosed is a copy of our approval letter from the FDA dated September 26, 1988.

The Coratomic model Pulsar-N1 nuclear-powered cardiac pacemaker uses the same type and amount of nuclear fuel, the same battery, and the same fuel capsule as the Coratomic models C-100, C-101, and C-101-P. We are hereby requesting an amendment to our U. S. Nuclear Regulatory Commission Materials License No. SNM-1319 to allow us to manufacture and distribute the Coratomic model Pulsar-N1 nuclear-powered pacemaker, in addition to our other authorized uses. Enclosed is a copy of the protocol entitled "Human Implantation Protocol for the Coratomic Pulsar-N1 Radioisotope Powered Cardiac Pacer", dated October 25, 1985. We are also enclosing a check in the amount of $120.00 payable to the U. S. Nuclear Regulatory Commission.

Sincerely,

John R. Klingensmith

John R. Klingensmith
Patient Records Specialist

Enclosures

cc: Mr. William C. Nealon
Victor Parsonnet, M.D.

Log Oct 20
Remitter
Check No. 5065
Amount $120
Fee Category 1K
Type of Fee AMD
Date Check Rcvd. 10/21/88
Date Completed 10/27/88
By L. Klingensmith

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Biocontrol Technology, Inc.

P.O. Box 434 • Indiana, Pennsylvania 15701

License Fee Branch
Accounting and Finance
Office of the Controller
U.S. Nuclear Regulatory Commission
Washington, DC 20555

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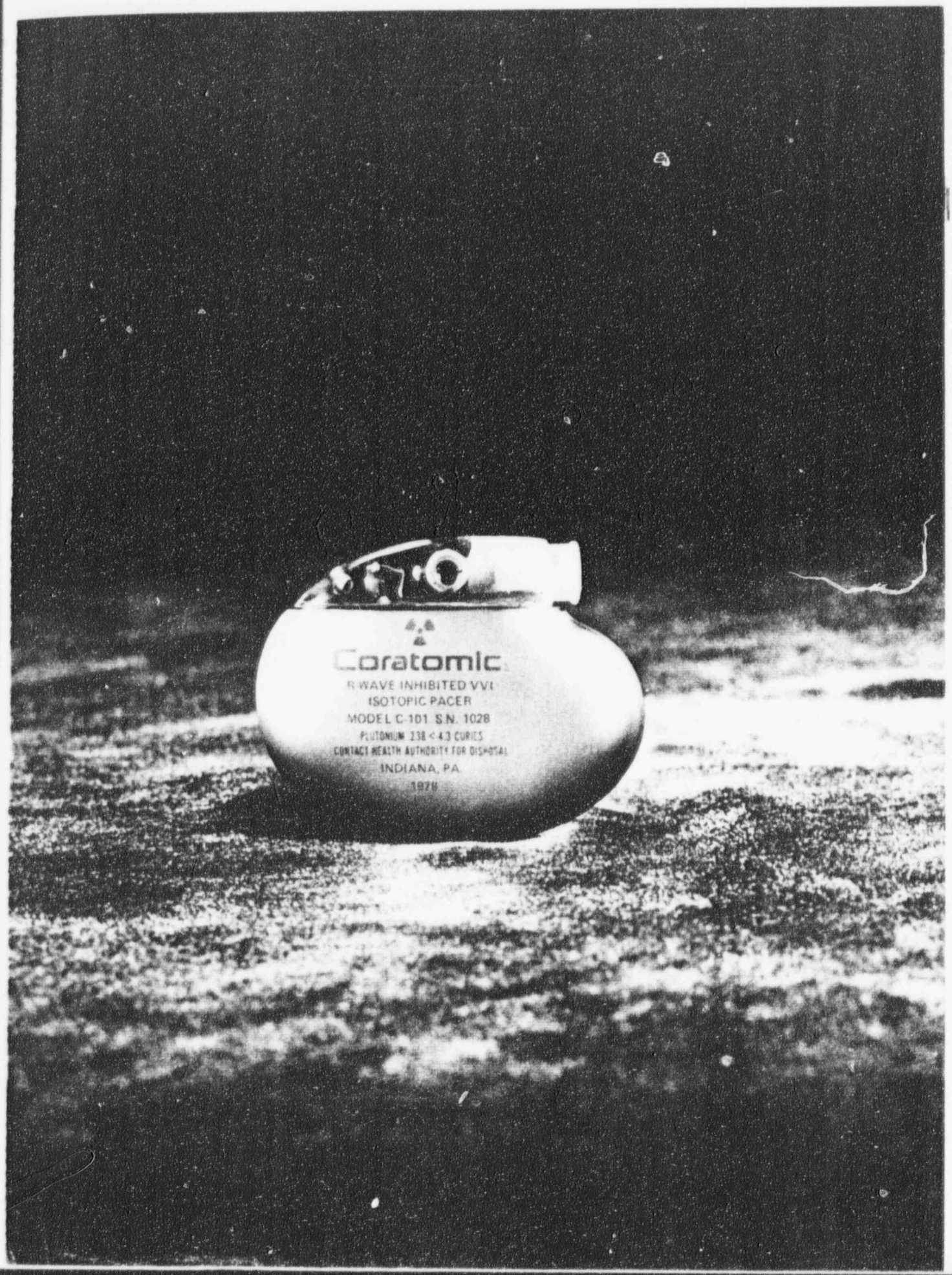
RECEIVED


Coratomic
R-WAVE INHIBITED VVI
ISOTOPIC PACER
MODEL C-101 S.N. 1028
PLUTONIUM 238 < 4.3 CURIES
CONTACT HEALTH AUTHORITY FOR DISPOSAL
INDIANA, PA.
1978


Coratomic
R-WAVE INHIBITED VVI
ISOTOPIC PACER
MODEL C-101 S.N. 1026
PLUTONIUM 238 < 4.3 CURIES
CONTACT HEALTH AUTHORITY FOR DISPOSAL
INDIANA, PA.

CIRCUITS

The critical circuitry in the C-101-P is contained in two hybrid packages. The use of the hybrids and a Kapton flex-circuit greatly reduces size requirements and, due to the minimum number of hand-wired interconnections, improves reliability.

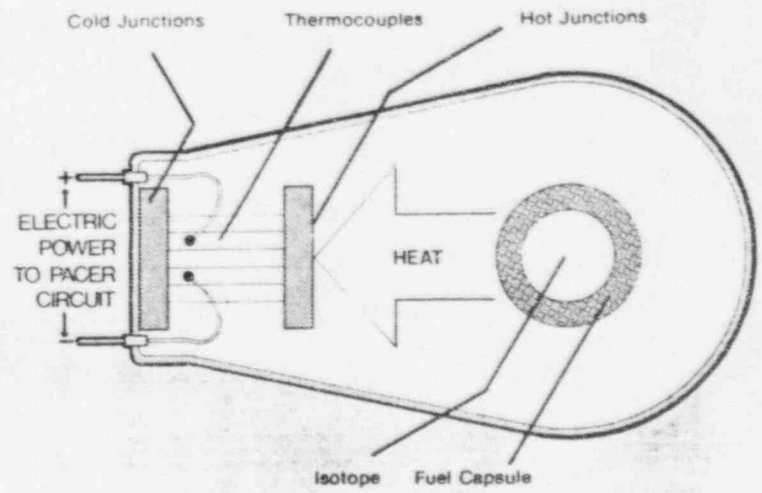
An extra measure of circuit reliability is achieved through a rigorous testing program which uses a quality assurance specification evolved from MIL-STD-883, method 2017. This and other aspects of the reliability program are more fully detailed in the section entitled, "Reliability."

ISOTOPIC BATTERY

The most striking feature of the C-101-P is its longevity, and the key to this longevity is the enormous energy stored in plutonium, the fuel in its isotopic battery. After 80 years of use, this fuel retains more than half of its original energy. To insure that the isotope is safely contained in the battery, Coratomic shields the fuel in a set of extremely durable leak-tight containers. This system has proved its ruggedness in a variety of simulated accidents ranging from an accidental cremation to a midair collision of two jet planes.

RELIABILITY

To match the potential for lifetime pacing offered by the isotopic battery, Coratomic uses high-reliability production and quality control procedures originally developed in the aerospace industry. A comprehensive test program is then used to evaluate the pacer design and finally to test every production pacer.



OPERATION

Plutonium fuel emits high energy helium nuclei called alpha particles. These high energy particles are stopped by the inner wall of the metal fuel capsule. Some of their energy is transferred to the capsule when they collide with it, and this heats the capsule wall. Heat is conducted to one junction of a semiconductor thermocouple while the opposite junction is kept at body temperature. As a result of this temperature difference, the thermocouple produces electrical energy.

The amount of heat produced is quite small: approximately 140 milliwatts. This does not appreciably heat the pacer case when the pacer is implanted. In fact, the case temperature remains at body temperature.

Each thermocouple produces only a low voltage — too low to operate transistor circuitry. Multiple thermocouples are connected in series in the battery to raise the voltage to a level

where it can operate a transistorized dc-dc converter. The converter increases the battery output to approximately 6 volts, which powers the pacer. A stabilizing diode maintains constant voltage input to the circuit, calculated to keep pacing rate and output current constant during the first 94% of the pacer's life. After this time, the rate decreases by 10% and then levels off at the lower pacing rate.

ENERGY DENSITY

The key to the C-101-P's long calculated life is energy density of plutonium. This battery makes use of the energy which binds the nucleus of an atom together. This force is hundreds of times stronger than the intermolecular bond which joins chemical compounds in conventional batteries. High energy density enables Coratomic to pack decades of pacing life into a small biocompatible package.

SAFETY

Coratomic performed a series of environmental safety tests to insure that the isotopic fuel in the C-101-P will never be released even in the most serious imaginable accident.

The cremation test insures that no isotopic fuel would escape from the fuel capsule even if a pacer was accidentally cremated. Coratomic has cremated a fueled pacemaker at 1,300°C for 90 minutes and the fuel capsule came through undamaged.

The impact tests simulate a grim accident where two jets collide in midair. The pacer falls to the ground, striking solid rock at over 100 mph. In Coratomic's testing an unprotected fuel capsule survived impact onto granite at 50 meters per second with no fuel leakage.

A pacer patient could also be caught in an industrial fire. To insure that his pacer would survive without releasing its fuel, Coratomic heated a pacer to 800°C, quickly quenched it in cold water, and then crushed it with more than a ton of force. In this test the C-101-P fuel capsule survived with no leakage.

Even if a C-101-P was lost at sea, four special corrosion-resista encapsulations would shield the fuel. In four years of salt water corrosion testing, no measurable corrosion of even the outermost encapsulation could be determined with sophisticated analytical techniques. This indicates that the fuel will be safe even after prolonged immersion for more than a thousand years.

RADIATION

Each pacer contains approximately 270 milligrams of medical-grade plutonium-dioxide fuel which emits ionizing radiation in three forms: alpha particles, photons or gamma rays, and neutrons. Virtually all the alpha particles and about 20% of the photons are contained within the metal pacer case. The rest of the radiation is of the low linear energy transfer (low LET) type, which can travel for some distance through tissue without interacting.

In fact, the Nuclear Regulatory Commission (NRC) has determined that all tissue not directly touching the pacer receives radiation in lower doses than the safety limits set by the National Council on Radiation Protection for radiation workers. The muscle and connective tissue, in intimate contact with the pacer case, are considered by the NRC to be especially radiation resistant. This is based on a large volume of experience relating to the irradiation of normal tissues in beams directed at malignancies. These doses are invariably

delivered at far higher rates than the pacer produces, yet they result in an extremely low incidence of neoplasms. It is uncertain that the few such neoplasms on record are radiation related. In sum, the NRC has recommended routine use of isotopic pacers, having determined that the levels of radiation emitted are medically acceptable for adult implantees.

ISOTOPIC BATTERY RELIABILITY

Coratomic's isotopic battery is one of the most severely tested pacemaker power sources ever developed. It is the only second-generation isotopic pacer battery, the product of three years research by many of the scientists who designed the Atomic Energy Commission pacer.

Three factors determine isotopic battery longevity: component reliability, the integrity of the thermoelectric module, and isotopic fuel decay. Battery components with measurable failure rates include interconnections and a hermetic container. The total failure rate of these components is calculated to be 0.15% per year. Thermoelectric modules have been on test for 4 years with no degradation. Only half of the battery's plutonium fuel is consumed in 90 years. The pacer is designed to operate close to this halfway point for a calculated 45 years average pacing life at constant rate.

Sound engineering design, careful component selection, and rigorous testing combine to make the C-101-P a safe and reliable pacer for your patients.

QUALIFICATION TESTING

In order to qualify for production and distribution each new pacer design must pass the same severe battery of tests originally used to qualify the C-101 isotopic pacer. This test series is designed to simulate a lifetime of normal use and is based on guidelines established by the Nuclear Regulatory Commission. Some of the specific mechanical tests to which the C-101-P design was subjected include:

4 g vibration for 30 minutes	simulates normal use
3,000 axial shocks at 50 g	simulates normal use
96 axial shocks at 545 g	simulates falling accidents
5 foot drop to concrete	simulates severe accidents
-40°C to +60°C cycling	simulates extreme shipping conditions
pressurization to 4 atmospheres	simulates a diver in 128 feet of water

All incoming components are individually tested as they are received, while all in-process components are tested at each critical assembly and/or fabrication stage.

Reliability and Testing

CIRCUIT TESTING

Before each circuit is hermetically sealed, it is subjected to a thorough visual examination under magnification. Once sealed, every circuit is baked for 24 hours at 125° C., subjected to 10 temperature cycles from -55° C. to 125° C., accelerated to 5,000 g, leak tested on a mass spectrometer, and then burned-in under load for 168 hours at 125° C.

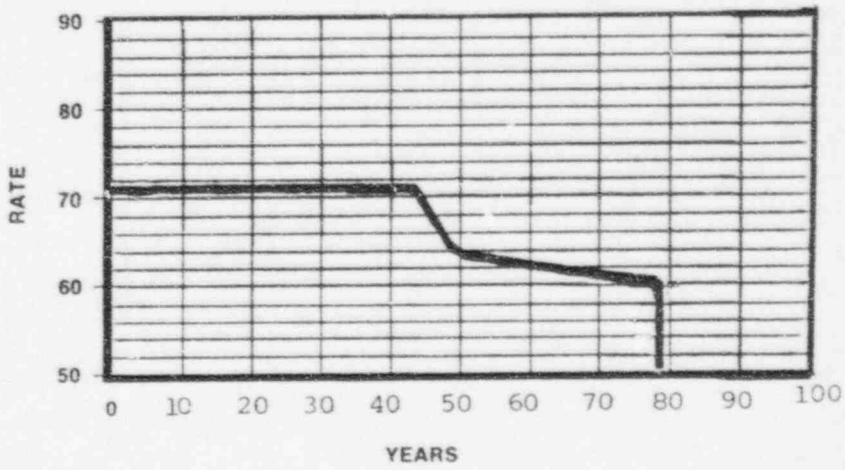
ACCEPTANCE TESTING

Every Coratomic pacer is subjected to Acceptance Testing before the unit is released for shipment. Every test sequence is designed to stress different pacer parts and detect premature failures.

- Vibration tested in each axis (x, y, z) for 10 minutes at a nominal 4g at frequencies from 20-500-20 Hz.
- Hermetically tested to insure seal for $< 1 \times 10^{-8}$ cc-atm/sec.
- All pacers are burned in under intermediate intensive observation for 360 hours, or more.

Pacer Function

The graph shown below illustrates the calculated Rate vs. Longevity curve for the Coratomic Model C-101-P Isotopic Programmable Pacemaker.



At 40-45 years, a rate drop of approximately 10% will begin. The transition to the 10% decrease will take approximately 3 years. After the 3 year period, the rate will remain relatively constant for an additional 30 years.

DIMENSIONS

Weight	61gm
Maximum Thickness	1.9cm
Height	5.1cm
Length	6.4cm
Volume	39cc
Specific Gravity	1.56gm/cc

NOTE: Where applicable, all electrical characteristics noted at right are measured into a 510 ohm load at 37°C.

MODES

- Normally used as an R-wave inhibited (VVI) pacemaker.
- Asynchronous (VOO) pacing can be obtained by placing the SENSITIVITY selector to its FR (Fixed Rate) setting.

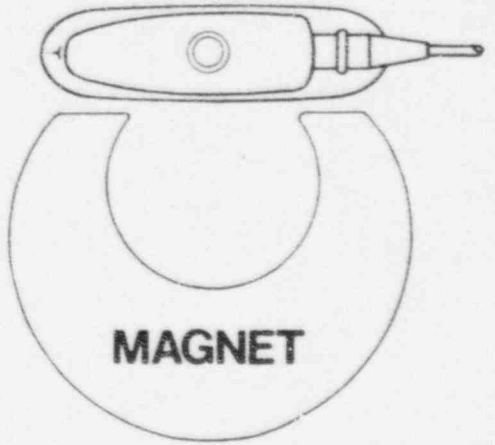
ELECTRICAL CHARACTERISTICS

Pacing Rate	Programmable @ 38 to 120 PPM
Pulse Current	Programmable @ 4 and 10 ma[1]
Sensitivity	Programmable @ 1.5, 2.5, 4, 5 mv
Pulse Width	1.0 ± 0.1 msec @ BOL[2]
Pulse Voltage	5.4v,nominal @ 10.6ma
Escape Rate	Same as programmed pacing rate
Magnetic Rate	Same as programmed pacing rate
Noise Rate	Same as programmed pacing rate
Noise Rate Threshold[3]	< 25 hz[4]
Refractory Period	Programmed Period X .375

[1]Measured at leading edge of pulse, Beginning-of-Life (BOL).
[2]Increases to 1.4 msec at End-of-Life (EOL).
[3]Measured with 10 mv rms sine wave.
[4]The Ovalith-P will switch to an asynchronous mode at the programmed rate when continuous electromagnetic interference is encountered at or above its noise threshold.

MAGNETIC RATE

Since the patient's intrinsic rhythm may inhibit the pacer occasionally, it is recommended the rate be checked with an external magnet. This temporarily turns off the amplifier and places the unit into an asynchronous mode equal to the programmed rate setting.



CAUTION: The use of the magnet to place the pacer into a fixed rate mode may result in the development of competitive rhythms.

OUTPUT CURRENT AND CURRENT LIMITING

The output current can be limited to either 10 ma or 4 ma by using the Coratomic programmer. With this feature, battery life can be maximized to the extent the lower setting maintains effective capture. At either setting, the current limiting feature prevents battery depletion in those instances when the pacer is operating into a low impedance lead system.