P7-83

Dr. Augusto Alonso Olea

STRONTIUM-89 STUDY
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Strontium-89 Chloride Injection

Caution-Radioactive Material
FOR RESEARCH USE ONLY

Activity at Calibration: 4-Millicuries
Calibration Date and Time: 28 May 1996, 12:00 Noon EST
Lot No. 5001
Production Point: Miami, Florida

Description: Strontium-89 Chloride is a sterile, non-pyrogenic, aqueous solution containing no preservative.

Each Milliliter contains:
Strontium Chloride 1-3 mg
Water q.s. to 1 mL

The radioactive concentration is 37 MBq/mL, 1 mCi/mL. and the specific activity is 2.96-6.17 Mbq/mg, 80-167 uCi/mg at time of labeling. The pH of the solution is 4-7.5.

Physical Characteristics: Strontium-89 decays by beta emission with a physical half-life of 50.5 days. The maximum beta energy is 1.491 MeV.

Precautions: This product should only be used by persons qualified by training and experience in the safe use of radionuclides and who have been approved by the appropriate government agency or authorities in the use of radioisotopes at a duly licensed facility. Strontium-89, like other radioactive materials, must be handled with care and appropriate safety measures taken to minimize radiation to personnel. The radiation dose hazard in handling Strontium-89 Chloride is similar to that from Phosphorus-32. The beta emission has a range in water of about 8 mm and in glass of about 3 mm, but the bremsstrahlung radiation may augment the contact dose. Measured values of the dose on the surface of the unshielded vial containing 4 mCi of Strontium-89 is calculated to be on the order of 28 Rads per hour. It is recommended that the vial be kept inside the transportation shield wherever possible.

How Supplied: Strontium-89 is supplied in a 7 mL vial containing up to 148 Mbq, 4 mCi. The vial is shipped in a Regulatory agency-approved transportation shield and contains a package insert.

Storage: The vial and its contents should be stored inside its transportation container at room temperature, (15-25^0 C, 59-77^0 F).

Calibration: The calibration date (for radioactivity content) is shown above. The expiration date will be 28 days after the calibration date.

Availability: Bi-weekly on Fridays pre-calibrated to the following Tuesday.

Radioactive Decay Factors: Radioactive decay factors to be applied to the stated value for radioactive concentration at calibration are as follows:

DECAY OF STRONTIUM-89

Day	Factor	Day	Factor	Day	Factor	Day	Factor	Day	Factor	Day	Factor	Day	Factor
-24	1.39	-16	1.25	-8	1.12	+2	0.98	+10	0.87	+18	0.78	+26	0.70
-22	1.35	-14	1.21	-6	1.09	+4	0.96	+12	0.85	+20	0.76	+28	0.68
-20	1.32	-12	1.18	-4	1.06	+6	0.92	+14	0.83	+22	0.74		
-18	1.28	-10	1.15	-2	1.03	+8	0.90	+16	0.80	+24	0.72		
				0=Calibration	1.00								

***Days before (-) or after (+) the calibration date stated on the vial.**

Radioisotopes for Health Science Applications
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Radioactive Materials License No. 2605-1

Product Information Bulletin issued May, 1996

Society Of Nuclear Medicine Procedure Guideline For Bone Pain Treatment

I. Purpose

The purpose of this guideline is to assist nuclear medicine practitioners in evaluating patients who might be candidates for Strontium-89 treatment of bone pain due to osteoblastic metastases; to provide information for performing this treatment; and to assist in understanding the sequelae of therapy.

II. Background Information and Definitions

A. Definitions

1. Strontium-89 therapy means the intravenous injection of the radionuclide Strontium-89 as the soluble salt strontium chloride. Strontium 89 emits a beta particle with maximum energy 1.463 MeV, mean energy 0.58 MeV, average soft tissue range 2.4 mm and a 0.01% abundant gamma emission with a photopeak of 0.910 MeV. It has a 50.5 day physical half life.

2. "Osteoblastic" or "osteoblastic metastases" mean foci of increased activity on bone scintigraphy caused by osseous reaction to tumor in bone.

B. Background

Intravenous injection of Strontium 89 (Strontium-89) chloride has been approved by the U.S. Food and Drug Administration (FDA) for the treatment of bone pain due to osteoblastic metastasis. Physicians involved in treating such patients should have an understanding of the natural history of the disease process and should be able to

collaborate closely with the physician or group of physicians handling the overall management of the patient's disease.

The administration of this agent falls under the guidelines of the Nuclear Regulatory Commission (N.R.C.), Title 10 CFR Part 35.300 or Agreement State Institutional License. Institutional licenses must specifically list individuals licensed to use Section 35.300 materials.

As other radiopharmaceuticals are approved by the FDA for the treatment of bone pain due to osteoblastic metastases, they will be added to the guideline.

III. Common Indications

Strontium 89 chloride (and the other unsealed beta- or conversion electron emitting radiopharmaceuticals under development or available commercially, i.e. P-32 orthophosphate) is indicated for the treatment of bone pain due to a metastatic malignancy that has involved multiple skeletal sites and has evoked an osteoblastic response on bone scintigraphy. (Where there is danger of either spinal cord compression from vertebral metastases or pathologic fracture in the extremities, Strontium-89 therapy should only be used in conjunction with other forms of management directed at these complications.)

IV. Procedure

A. Facility/Personnel

1. Strontium-89 may only be administered in a facility with a valid radioactive materials license incorporating Section 35.300 or comparable Agreement State License.

2. All administering physicians (the physician writing the prescription and injecting the dose) must be listed on the NRC or Agreement State license or specifically designated under a broad license.

3. Patients should be seen in consultation by the administering/treating physician in collaboration with the physician assuming overall patient management.

4. The administering physician should be Board Certified in Nuclear Medicine, Radiology, Radiation Oncology or be able to document equivalent training, competency and experience in the safe use and administration of unsealed radiotherapeutic sources.

5. The administering physician should participate in the ongoing and follow- up care of the patient as part of the patient management team.

6. The facility in which the treatment is carried out must have proper radiation safety procedures, including waste disposal, handling of contamination of personal belongings, etc.

B. Patient Preparation

1. Prior to administration of Strontium-89 the patient should have had recent bone scintigraphy (4-8 weeks) documenting increased osteoblastic activity in the painful sites.

Radiographs taken within 4-8 weeks demonstrating osteosclerotic lesions are not adequate, since there are rare cases where the increased bone density has occurred slowly and bone scintigraphy shows little increased activity. In such cases Strontium-89 uptake will be inadequate.

2. Bone scintigraphic abnormalities should be correlated with appropriate physical examination and imaging studies to ascertain that osseous or soft tissue abnormalities which might cause cord compression or pathologic fracture in an extremity are not present. Strontium-89 would be indicated in these circumstances only in conjunction with local radiation therapy or surgical intervention and only if there are other painful osteoblastic sites.

3. In general, patients should not have received long acting myelosuppressive chemotherapy (e.g. nitrosoureas) for 6-8 weeks, and full doses of other forms of myelosuppressive chemotherapy or systemic radiotherapy for approximately 4 weeks prior to administration of Strontium-89 and for 6 12 weeks after Strontium-89 administration, because of the potential for severe leukopenia or thrombocytopenia. Caution should be employed if Strontium-89 is used in conjunction with myelosuppressive chemotherapy.

4. The patient should not have received external beam hemi-body radiation within 2-3 months prior to administration of Strontium-89 to reduce the probability of combined myelotoxicity from the external and internal radiation sources during this period.

5. Complete blood counts should usually be obtained within 7 days prior to administration of Strontium-89. The patient's platelet count should probably exceed 60,000 and preferably 100,000/μl; the leukocyte count should

probably exceed 2,400 - 3,000 and preferably 5,000/μl; and the absolute granulocyte count should exceed 2,000/μl to receive Strontium-89. Results below these blood count levels are not absolute contraindications to treatment but raise the chance of infection or bleeding.

6. The presence or absence of hormone therapy is irrelevant to administration of Strontium-89. Bone pain could be worsening while hormone therapy is controlling other sites of tumor, so hormone therapy need not be discontinued. Strontium-89 can be of value after failure of hormone therapy to control the pain of osseous metastases.

7. Before using Strontium-89, the pain usually should be severe enough to limit activity and/or require narcotic analgesia for control of symptoms.

8. Active disseminated intravascular coagulation (D.I.C.) may be a risk factor for severe thrombocytopenia post-therapy. Deaths have been reported in patients with D.I.C. following therapy with beta-emitting radiopharmaceuticals and this potential risk must be carefully considered before administering Strontium-89 in the presence of D.I.C.

9. Hypercalcemia should not deter Strontium-89 treatment unless accompanied by renal failure.

10. The patient need not fast before administration of the radiopharmaceutical.

11. The radiopharmaceutical should be administered slowly through an intravenous catheter or a running intravenous line to avoid infiltration, to reduce the hand dose to the injecting physician and to permit flushing of the

syringe so that all of the Strontium-89 is injected. A plastic syringe shield or equivalent is suggested for administration of the radiopharmaceutical. Flush the syringe and intravenous line from the syringe to the patient with saline from the running intravenous line or a saline filled syringe attached to a 3-way stopcock.

12. Hospitalization is not required for the administration of Strontium-89.

13. A patient who has a life expectancy of less than 2 - 3 weeks is unlikely to benefit from Strontium-89 and, at his/her death, the pathologist will require certain precautions (goggles, double gloving) if an autopsy is performed less than one week post administration. There is no problem with cremation if the crematorium handles annually bodies containing less than 2 Ci of all radionuclides except I-131 where there is a 200 mCi limit per year.

14. The usual administered activity of Strontium-89 ranges from 1.5-2.2 MBq/kg (40-60 uCi/kg). Some physicians calculate the activity based on lean body mass, reduce the activity given in patients with azotemia, or slightly increase the administered activity with diffuse widespread metastases. There are no unequivocal data on these adjustments.

15. The procedure may be repeated 12 or more weeks after the first injection if blood counts are at the suggested levels. The response rate following the second treatment is about 50%.

C. Information Pertinent to Performing the Procedure

1. Patient demographics (age, sex, weight, height, diagnosis)

2. Indications for therapy

3. Current medications, especially those affecting coagulation and bisphosphonates.

4. Extent of disease on bone scan obtained 4-8 weeks prior to therapy

5. CBC, prothrombin time and serum creatinine within a week before therapy.

6. Relevant radiographs and/or MRI of painful sites to exclude severe lytic lesions or cord compression.

7. Life expectancy estimate.

8. Negative pregnancy test in women of childbearing age. No breast feeding. These are absolute contraindications to therapy.

D. Instructions For Patients

1. The patient should be told that Strontium-89 has a 60-80% probability of reducing the bone pain due to cancer spread in bone, but that the chance of relieving pain completely is low.

2. The patient should be told that this is not a curative treatment for cancer, but a palliating treatment for pain, even though some cancer cells will be killed.

3. The patient should be told that the two major side effects are:

a. a possible significant increase in bone pain ("flare") occurring within 21 days after injection, and lasting 2-5 days. ("Flare" is unusual after the second week).

b. a possibility that the leukocyte and platelet counts may decrease by 30-70% of baseline values or possibly even to lower levels which could lead to infection if leukocytes are too low or bleeding if the platelets are too low. Bleeding or the risk of bleeding could require platelet transfusion. Marrow replacement by tumor, Strontium-89 therapy, chemotherapy and external beam radiotherapy have additive effects on myelosuppression, and the presence of two or more of these risk factors increases the possibility of clinically significant marrow suppression.

4. A written consent form is suggested including indications, success rate and the risks of severe infection, bleeding and death. Local hospital policies and state regulations should be followed. The patient should be told that pain reduction is unlikely before the first week, more probable in the second week, and could occur as late as 25 days or longer after injection.

5. The patient should be told that he/she may continue with a normal diet, that he/she should be careful to avoid soiling underclothing or areas around toilet bowls for a week following injection, and that if any underclothing is significantly soiled with urine, it should be washed separately. Sitting down to urinate will reduce the possibility of contamination. A double toilet flush should be adequate after urination. Urinary excretion is greatest (80-90%) for the first 48 hours following injection. Wash hands after urination.

6. If the patient is being cared for in a hospital, then his/her attendants should wear gloves and gowns if contact with urine, feces, saliva or blood is anticipated. Catheter bags should be quickly transferred to the toilet for emptying with the attendant wearing gloves. Gloves should also be worn at home if soiled garments are to be handled. (There is no significant salivary secretion of Strontium-89 so no other precautions are required).

7. In incontinent patients, a plastic mattress cover and adult urine absorbing undergarments are recommended; condom drainage or bladder catheterization should also be considered for several days to a week.

E. Precautions

1. The degree of leukopenia and thrombocytopenia present should not be severe, as noted in IV.B.5.

2. Previous, especially recent, chemotherapy or wide-field radiation can worsen Strontium-89 induced leukopenia or thrombocytopenia.

3. Renal failure may require reducing the activity injected.

4. Exclude spinal cord compression.

5. Do not use Strontium-89 alone with ≥50% destruction of an involved bone, especially of an arm or leg, or for pain due to pathologic fracture.

6. Injection technique must be used to avoid infiltration. No specific therapy is available if infiltration occurs, but local heat may increase the rate of reabsorption and therefore decrease the local radiation dose.

7. Exclude active disseminated intravascular coagulation.

8. In women of childbearing age, the pregnancy test must be negative.

9. See IV.D.5, D.6, D.7.

F. Radiopharmaceutical: Strontium-89

1. Usual therapeutic administered activity is 1.5-2.2 MBq/kg (40-60 uCi/kg)

2. Radiation Dosimetry *

Organ	mGy/MBq	rad/mCi	rad/3.5 mCi
Bone Surface	17.0	63.0	220.5
Red Bone Marrow	11.0	40.7	142.5
Lower Bowel Wall	4.7	17.4	60.9
Bladder Wall	1.3	4.8	16.8
Testes	0.8	2.9	10.2
Ovaries	0.8	2.9	10.2
Uterine Wall	0.8	2.9	10.2
Kidneys	0.8	2.9	10.2
Effective Dose	2.9	10.7	37.4

* *ICRP 53, page 171*

may be mentioned on the report, usually beginning 2 weeks post injection and then every 1-3 weeks for a total of 12-16 weeks. The physician performing the therapy is urged to follow the blood counts if possible.

2. The referring physician may be reminded that pain reduction does not occur until 1-3 weeks have passed.

3. The physician should not assume the patient has failed Strontium-89 therapy until a full four weeks after injection.

4. A few patients who have failed to respond to the first Strontium-89 injection have had pain reduction with a second injection 12 weeks later.

K. Quality Control

1. The institutional Quality Management Program mandated by the Nuclear Regulatory Commission should be followed.

2. There should be close coordination in all aspects of patient workup and follow up with the referring physician.

3. The relevant patient information (IV.C.) should be reviewed before Strontium-89 injection.

L. Sources of Error

1. Improper use of dosage calibrator. The use of the P-32 setting on the modern dosage calibrator approximates that of the Strontium-89 setting.

The radioactivity must be measured in geometry and in containers consistent with previous calibration of the dosage calibrator.

2. The radiopharmaceutical should be injected through a running intravenous line or intravenous catheter to avoid infiltration of the material injected, reduce hand dose, and permit flushing of all Strontium-89 activity out of the syringe and into the patient.

V. Disclaimer

The Society of Nuclear Medicine has developed guidelines to promote the cost-effective use of nuclear medicine procedures. These generic recommendations cannot be applied to all patients in all practice settings. The guidelines should not be deemed inclusive of all proper procedures or exclusive of other procedures reasonably directed to obtaining the same results. The spectrum of patients seen in a specialized practice setting may be quite different than the spectrum of patients seen in a more general practice setting. The appropriateness of a procedure will depend in part on the prevalence of disease in the patient population. In addition, the resources available to care for patients may vary greatly from one medical facility to another. For these reasons, guidelines cannot be rigidly applied.

Advances in medicine occur at a rapid rate. The date of a guideline should always be considered in determining its current applicability.

VI. Issues Requiring Further Clarification

Relative response rates of osteoblastic metastasis from different primary cancers. Preliminary data are available on this topic (Taylor, 1994).

VII. Concise Bibliography

1. Edwards GK, Santoro J, Taylor AT, et al. Use of bone scintigraphy to select patients with multiple myeloma for treatment with Strontium-89. *J Nucl Med* 1994;35:1992-1994.

2. Herold TJ, Gross GP, Hung JC. A technique for measurement of Strontium-89 in a dose calibrator. *J Nucl Med Technol* 1995;23:26-28.

3. McEwan AJ, Amyotte GA, McGowan DG, et al. A retrospective analysis of the cost effectiveness of treatment with Metastron (^{89}Strontium-Cl) in patients with prostate cancer metastatic to bone. *Nuclear Medicine Communications* 1994;15:499-504.

4. McEwan AJ, Porter AT, Venner PM, et al. An evaluation of the safety and efficacy of treatment with Strontium-89 in patients who have previously received wide field radiotherapy. *Antibody Immunoconjugates Radiopharm* 1990;3:91-98.

5. Porter AT, McEwan AJ, Powe JE, et al. Results of a randomized phase-III trial to evaluate the efficacy of Strontium-89 adjuvant to local field external beam irradiation in the management of endocrine resistant metastatic prostate cancer. *Int J Radiat Oncol Bio. Phys* 1993;25:805-813.

6. Quilty PM, Kirk D, Bolger JJ, et al. A comparison of the palliative effects of Strontium-89 and external beam radiotherapy in metastatic prostate cancer. *Radiother Oncol* 1994;31:33-40.

7. Robinson RG, Blake GM, Preston DF, et al. Strontium-89: treatment results and kinetics in patients with painful metastatic prostate and breast cancer in bone. *Radiographics* 1989;9:271-281.

8. Silberstein EB, Williams C. Strontium-89 therapy for the pain of osseous metastases. *J Nucl Med* 1985;26:345-348.

9. Taylor AJ Jr. Strontium-89 for the palliation of bone pain due to metastatic disease. *J Nucl Med* 1994;35:2054.

VIII. Last Board of Trustees Approval Date: 2/12/95

IX. Next Anticipated Approval Date: 1997

X. Appendix: Description of Guideline Development Process

A. Guideline Development Subcommittee

Howard Dworkin, MD; James Fletcher, MD; Robert Hattner, MD; and J. Anthony Parker, MD, PhD.

B. Task Force Members

This guideline was reviewed by members of the Therapy Council. Members included Robert Carretta, MD; R. Edward Coleman, MD; B. David Collier, MD; Edward Eikman, MD; John Freitas, MD; Patrick Hastings, CNMT; Robert Henkin, MD; Richard Holmes, MD; Homer Hupf, PhD; Harry Lessig, MD; Alexander McEwan, MB; Darrell McIndoe, MD; August Miale Jr., MD; Conrad

Nagle, MD; Donald Podoloff, MD; Myron Pollycove, MD; David Price, MD; James Seabold, MD; Carl Seidel; Aldo Serafini, MD; George Sfakianakis, MD, PhD; Edward Silberstein, MD; Suresh Srivastava, PhD; Andrew Taylor Jr., MD; Italo Zanzi, MD.

C. History of Board of Trustees Approval Dates

Version 1.0 - February 12, 1995

D. Revision History

1. Draft 0.0 - Initial Author: Written by Edward B. Silberstein, MD and Andrew T. Taylor Jr., MD

a. Names of each detailed reviewer:

This guideline was reviewed by members of the Therapy Council. Members included Robert Carretta, MD; R. Edward Coleman, MD; B. David Collier, MD; Edward Eikman, MD; John Freitas, MD; Patrick Hastings, CNMT; Robert Henkin, MD; Richard Holmes, MD; Homer Hupf, PhD; Harry Lessig, MD; Alexander McEwan, MB; Darrell McIndoe, MD; August Miale Jr., MD; Conrad Nagle, MD; Donald Podoloff, MD; Myron Pollycove, MD; David Price, MD; James Seabold, MD; Carl Seidel; Aldo Serafini, MD; George Sfakianakis, MD, PhD; Edward Silberstein, MD; Suresh Srivastava, PhD; Andrew Taylor Jr., MD; Italo Zanzi, MD.

b. Names of other reviewers:

None

c. Line by line listing of all comments and the action taken on each comment (No action; Partial implementation; Done).

No report on file

d. Date completed:

8/94

2. Draft 0.1

a. Names of each detailed reviewer:

This guideline was reviewed by members of the Therapy Council. Members included Robert Carretta, MD; R. Edward Coleman, MD; B. David Collier, MD; Edward Eikman, MD; John Freitas, MD; Patrick Hastings, CNMT; Robert Henkin, MD; Richard Holmes, MD; Homer Hupf, PhD; Harry Lessig, MD; Alexander McEwan, MB; Darrell McIndoe, MD; August Miale Jr., MD; Conrad Nagle, MD; Donald Podoloff, MD; Myron Pollycove, MD; David Price, MD; James Seabold, MD; Carl Seidel; Aldo Serafini, MD; George Sfakianakis, MD, PhD; Edward Silberstein, MD; Suresh Srivastava, PhD; Andrew Taylor Jr., MD; Italo Zanzi, MD.

b. Names of other reviewers:

None

c. Line by line listing of all comments and the action taken on each comment (No action; Partial implementation; Done).

No report on file

d. Date completed:

10/13/94

3. Draft 0.2

a. Names of each detailed reviewer and the percentage of lines with which the reviewer agreed:

Howard Dworkin, MD (97%); James Fletcher, MD (87%); Robert Hattner, MD (99%); J. Anthony Parker, MD (99%); Henry Royal, MD (87%).

Total Percent Agreement (average): 94%

b. Names of other reviewers:

Members of the Guideline Development Subcommittee during the St. Louis meeting in November 1994.

c. Line by line listing of all comments and the action taken on each comment (No action; Partial implementation; Done).

See attachment titled Comment Report - *Procedure Guideline for Bone Pain Treatment (version 0.2)*

d. Date completed:

12/19/94

4. Draft 0.3

a. Names of each detailed reviewer and the percentage of lines with which the reviewer agreed:

David Brill, MD (97%); Manuel Brown, MD (96%); Duncan Burdick, MD (99%); R. Edward Coleman, MD (83%); Jeffrey Dobkin, MD (92%); Kevin Donohoe, MD (73%); James Fletcher, MD (100%); John Freitas, MD (96%); Robert Hattner, MD (100%); Shiv Gupta, MD (95%); Robert Henkin, MD (76%); Richard Holmes, MD (99%);Gerald Mandell, MD (98%); Alexander McEwan, MB (96%); Darrell McIndoe, MD (100%); J. Anthony Parker, MD (100%); Richard Pierson Jr., MD (89%); Aldo Serafini, MD (99%); Carl Seidel (99%); Suresh Srivastava, PhD (91%).

Total Percent Agreement (average): 94%

b. Names of other reviewers:

None

c. Line by line listing of all comments and the action taken on each comment (No action; Partial implementation; Done).

See attachment titled Comment Report - *Procedure Guideline for Bone Pain Treatment (version 0.3)*

d. Date completed:

1/23/95

5. Draft 0.4

a. Names of each detailed reviewer and the percentage of lines with which the reviewer agreed:

Not applicable

b. Names of other reviewers:

Members of the Commission on Health Care Policy Network. The Commission on Health Care Policy Reference Committee on 2/11/1995.

c. Line by line listing of all comments and the action taken on each comment (No action; Partial implementation; Done).

No report on file

d. Date completed:

2/11/95

6. Draft 0.5 - Approved by the Board of Trustees on 2/12/95.

a. Names of each detailed reviewer and the percentage of lines with which the reviewer agreed:

Not applicable

b. Names of other reviewers:

None

c. Line by line listing of all comments and the action taken on each comment (No action; Partial implementation; Done).

No report on file

d. Date completed:

570 2/12/95 (with minor modifications from Henry Royal, MD, Edward
571 Silberstein, MD and members of the Guideline Development
572 Subcommittee)
573
574

Radioisotopes for Health Science Applications

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STRONTIUM-89 STUDY PRETREATMENT EVALUATION

NAME: _____ AGE: _____ DATE: ___ ___ ___

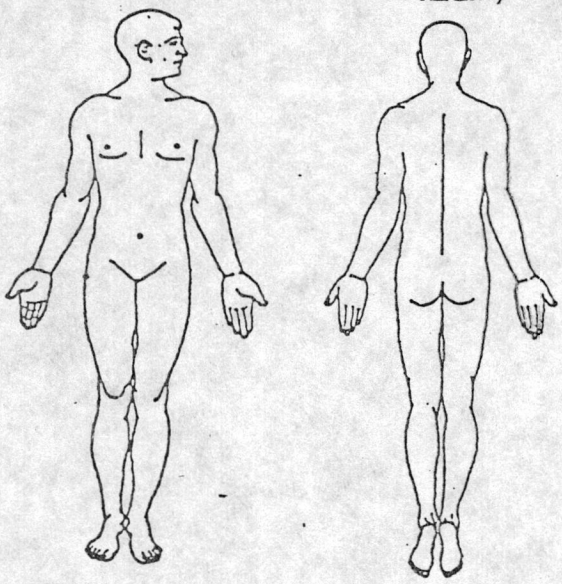
NATURE OF PAIN _____

DATE & TIME OF INJURY/ OR ONSET OF PAIN _____

MOST PROMINENT SYMPTOMS:

- ☐ PAIN
- ☐ WEAKNESS
- ☐ NUMBNESS
- ☐ DIFFICULTY WALKING
- ☐ BENDING/LIFTING
- ☐ OTHER: _____

REGION & DISTRIBUTION OF PAIN:
(SHADE APPROPRIATE AREA)



MY TREATMENT HAS INCLUDED:

- ☐ PAIN MEDICATIONS.
- ☐ ANTI-INFLAMMATORY MEDS.
- ☐ EPIDURAL STEROID
- ☐ CHIROPRACTOR
- ☐ COLD PACKS
- ☐ HOT PACKS
- ☐ MASSAGE
- ☐ STRETCHING/FLEX
- ☐ OTHER: _____
- ☐ PHYSICAL THERAPY/ TYPE: ☐ ULTRASOUND ☐ ELECTRICAL STIM.
- ☐ OTHER: _____ ☐ NO TREATMENT TO DATE

LIST DRUGS CURRENTLY ON (IF ANY): _____

HAVE YOU USED ANY PAIN MEDICATION IN THE PAST 8 HOURS? ☐YES ☐NO

DO YOU UNDERSTAND THE CONCEPT OF STRONTIUM-89 TREATMENT YES ☐ NO

HAVE YOU EVER USED Sr-89, P-32, Sm-153, MORPHINE OR OTHER OPIATE?

IF YES, FOR WHAT CONDITION? _____

WAS IT BENEFICIAL? ☐GREATLY ☐MODERATELY ☐SLIGHTLY ☐NOT AT ALL

DO YOU HAVE ANY OTHER SYMPTOMS?

FROM COSMETICS _____, ANTIPERSPIRANTS _____, DEODORANTS _____

CURRENT PAIN INTENSITY: RATE YOUR PRESENT PAIN LEVEL ON A 0-10 SCALE

WITH 0 = NO PAIN 10 = WORST PAIN YOU HAVE EXPERIENCED.

0	1	2	3	4	5	6	7	8	9	10
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

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PROJECT: STRONTIUM-89 STUDY

4. INITIAL POST-APPLICATION ASSESSMENT FORM

TO BE COMPLETED BY MONITOR AND/OR PATIENT IMMEDIATELY AND AFTER TREATMENT

PATIENT: _____ DATE: _____

TREATMENT SITE: _____

IMMEDIATELY POST-TREATMENT: RATE YOUR PAIN LEVEL ON A 0-10 SCALE

WITH 0 = NO PAIN, 10 = WORST PAIN YOU HAVE EXPERIENCED.

0	1	2	3	4	5	6	7	8	9	10
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

DESCRIBE THE SENSATION OR RELIEF THAT YOU FEEL AT THIS TIME.

___ NOTHING, ___ TINGLING, ___ SHARP PAIN, ___ MUSCLE CONTRACTION
___ RELAXATION, ___, ___ TENSION, COLD, ___ HEAT, ___ NUMBNESS
OTHER: _____
AT: _____ AT _____ AT _____

15 DAYS POST-TREATMENT: (RATE YOUR PAIN LEVEL) 0 _____ 10

ARE THERE NOTICEABLE CHANGES SINCE STIMULATION? _____

IF SO, PLEASE DESCRIBE _____

30 DAYS POST-TREATMENT: (RATE YOUR PAIN LEVEL) 0 _____ 10

ARE THERE NOTICEABLE CHANGES SINCE STIMULATION? _____

IF SO, PLEASE DESCRIBE _____

45 DAYS POST-TREATMENT: (RATE YOUR PAIN LEVEL) 0 _____ 10

ARE THERE NOTICEABLE CHANGES SINCE STIMULATION? _____

IF SO, PLEASE DESCRIBE _____

FACILITY: _____

TEST MONITOR: _____

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STRONTIUM-89 STUDY

5. INTENTIONALLY LEFT BLANK

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STRONTIUM-89 STUDY

6. FINAL PATIENT QUESTIONNAIRE - POST-TREATMENT

THE PURPOSE OF THIS EVALUATION FORM IS TO COMPILE INFORMATION

EFFECTIVENESS OF STRONTIUM-89

Please answer the following questions, check the appropriate box and add your comments:

1. DID THE TEST MONITOR PROVIDE APPROPRIATE INSTRUCTIONS PRIOR TO USE O; STRONTIUM-89 ☐ YES ☐ NO
   AND, WERE THEY: CLEAR ___ AMBIGUOUS ___ CON FUSING ___
   COMMENTS: _____

2. WAS THE DRUG EASY TO APPLY TO YOUR AREA OF PAIN? ☐YES ☐NO
   COMMENTS: _____

3. PLEASE COMMENT ON THE PERCEPTION OF THE DRUG
   COMFORTABLE_____ ANNOYING_____ IRRITATING_____
   OTHER _____

4. WAS THE STRONTIUM-89 EFFECTIVE IN REDUCING YOUR PAIN? _____
   COMPLETELY (100%) ___ GOOD (75%) ___ FAIR (50%) ___ POOR (25%) ___
   COMMENTS: _____

_____

_____

Radioisotopes for Health Science Applications
BIO-NUCLEONICS, INC.
Radioactive License No. 2605-1 U.S. EIN NO. 65-0462896
1910 N.E. Miami Court Miami, Florida 33312
TEL.: 305 576-0996 FAX: 305 573-2293

DOCUMENTATION: DATA COLLECTION FORMS OVERVIEW

STRONTIUM-89 STUDY

6. FINAL PATIENT QUESTIONNAIRE - POST-TREATMENT (CONTINUED)

7. WERE YOU ABLE TO PROGRESSIVELY FEEL PAIN REDUCTION?

☐ YES ☐ NO COMMENTS: _____

8. WERE THERE ANY ADVERSE EFFECTS OR REACTIONS? ☐ YES ☐ NO

COMMENTS: _____

9. DO YOU FEEL THAT THIS DEVICE PROVIDES AN EASY AND EFFECTIVE MEANS OF PAIN CONTROL? ☐ YES ☐ NO

COMMENTS: _____

10. IF RELIEF WAS PROVIDED, DID THE DRUG IMPROVE PERFORMANCE OF ANY ACTIVITIES AT HOME OR AT WORK? ☐ YES ☐ NO

PLEASE SPECIFY: _____

_____

11. WOULD YOU CHOOSE TO USE THIS DRUG FOR PAIN CONTROL AGAIN?

☐ YES ☐ NO COMMENTS: _____

_____

12. WOULD YOU RECOMMEND THE USE OF THIS DRUG FOR PAIN CONTROL TO OTHERS? ☐ YES ☐ NO COMMENTS: _____

_____

FACILITY: _____

TEST MONITOR: _____

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E-Mail: bionucmed@aol.com

STRONTIUM-89 STUDY

7. POST-TREATMENT ASSESSMENT FORM

TO BE COMPLETED AT END OF STUDY BY CLINICAL MONITOR

PILOT TEST STUDY: Number:_____ Date:_____

PATIENT: _____ PHONE #: _____

ADDRESS: _____

DIAGNOSIS: _____

LOCATION OF PAIN: _____

METHOD OF TREATMENT _____

_____

INITIAL PRE-TREATMENT PAIN ASSESSMENT (SUBJECTIVE):

0 _____ 10 (SUBJECTIVE - SINGLE ASSESSMENT)

POST TREATMENT PAIN ASSESSMENT (SUBJECTIVE):

0	10	IMMEDIATE	0	10	2 WEEKS
0	10	8 HOURS	0	10	1 MONTH
0	10	12 HOURS	0	10	45 DAYS
0	10	1 DAY	0	10	2 MONTHS
0	10	3 DAYS	0	10	3 MONTHS
0	10	1 WEEK	0	10	6 MONTHS

AVERAGE LENGTH OF RELIEF AFTER Sr-89 ADMINISTERED:_____

COMMENTS: _____

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PROJECT: STRONTIUM-89 STUDY

7. POST-TREATMENT ASSESSMENT FORM (CONTINUED)

THERAPIST ASSESSMENT

PRE-TREATMENT		POST TREATMENT
_____	PAIN DISTRIBUTION	_____
_____	QUALITY	_____
_____	EDEMA	_____
_____	RANGE OF MOTION	_____
_____	SKIN IRRITATION	_____
_____	ERYTHEMA	_____
_____	OTHER	_____

FACILITY: _____

TEST MONITOR: _____

SIGNATURE: _____

CLINICAL DIRECTOR: _____

SIGNATURE: _____

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STRONTIUM-89 STUDY

DOCUMENTATION: DATA COLLECTION FORMS OVERVIEW

POST-TREATMENT ASSESSMENT FORM

TO BE COMPLETED AT END OF APPLICATION

PILOT TEST STUDY: Number:_____ Date:_____

PATIENT: _____ PHONE #: _____

ADDRESS: _____

PATIENT'S SEX, AGE, WEIGHT

DIAGNOSIS: _____

LOCATION OF PAIN: _____

TREATMENT MODE (S) _____

TREATMENT PROTOCOL: _____

DOSIS ADMINISTERED IN MILLICURIES/DATE: _____

PARAMETERS: _____

_____

INITIAL PRE-TREATMENT PAIN ASSESSMENT (SUBJECTIVE):

0 _____ 10 (SUBJECTIVE - SINGLE ASSESSMENT)

POST TREATMENT PAIN ASSESSMENT (SUBJECTIVE):

0 _____ 10 0 _____ 10

0 _____ 10 0 _____ 10

LENGTH OF RELIEF

INVESTIGATIONAL REVIEW BOARD

APPROVAL REQUIRED FOR CLINICAL STUDIES BY:

DEPARTMENT OF HEALTH & HUMAN SERVICES REGULATIONS
OFFICE FOR PROTECTION FROM RESEARCH RISKS
NATIONAL INSTITUTES OF HEALTH .

THE CRITERIA, GUIDELINES, PROTOCOL DOCUMENTS AND DATA COLLECTION FORMS CONTAINED WITHIN THIS INFORMATION PACKET HAVE BEEN APPROVED BY THE INVESTIGATIONAL REVIEW BOARD (IRB) AS APPROVED BY AND IN COMPLIANCE WITH THE RULES AND REGULATIONS ESTABLISHED BY THE DEPARTMENT OF HEALTH & HUMAN SERVICES (DHHS).

THE ATTACHED DOCUMENTS SERVE AS SATISFACTION THAT EACH CLINICAL CENTER INVOLVED IN RESEARCH PROJECT WILL FOLLOW THE PATIENT PROTECTION PROCEDURES COVERED IN THE BELMONT REPORT, A MANDATORY GOVERNMENT RESEARCH DIRECTIVE THAT IS DESCRIBED BY THE OFFICE FOR PROTECTION FROM RESEARCH RISK AS:

" THE ETHICAL PRINCIPLES AND GUIDELINES FOR THE PROTECTION OF HUMAN SUBJECTS OF RESEARCH, REPORT OF THE NATIONAL COMMISSION FOR THE PROTECTION OF HUMAN SUBJECTS OF BIOMEDICAL AND BEHAVIORAL RESEARCH (BASIC ETHICAL PRINCIPLES: RESPECT FOR PERSONS, BENEFICIENCE, JUSTICE) . "

Single Project Assurance

Certification of IRB Approval and Institutional Endorsement

Project title_____

DHHS Project number_____

Project Investigator or Director_____

Date of IRB Approval _____Date of Next Scheduled IRB Review_____

The officials signing below assure that the project referenced above was approved by the IRB on the date indicated and that the project will be nducted in accordance with the requirements of Part 46, Title 45 of the Code of Federal Regulations and this Assurance document. A dated roster listing the current membership of the designated IRB is attached.

I. Authorized Official of the Institution Providing This Assurance

Signature_____Date:_____

Please type the following items.

Name and Title:

Address:

FAX:

Telephone:

II. Authorized Official of the Institution with the IRB
(Include only if different from the institution above)

This institution authorizes the designation of its IRB for review of the project referenced in this Assurance.

Signature_____Date:_____

Please type the following items.

Name and Title: Principal Investigator

Address:

FAX:

Telephone:

III. IRB Chairperson
(Must be completed in all cases [see IRB membership list])

Signature_____Date:_____

Please type the following items.

Name and Title: , IRB Chairperson

Address:

FAX:

Telephone:

MPA number if applicable Not Applicable

EXAMPLE

SINGLE PROJECT ASSURANCE

(PLEASE RESUBMIT AS CHANGES OCCUR)

INSTITUTIONAL REVIEW BOARD (IRB) MEMBERSHIP

DATE: _____

NAME OF INSTITUTION PROVIDING THIS ASSURANCE _____ ASSURANCE NO: _____

NAME OF INSTITUTION WITH THE IRB (if different from above) SAME ASSURANCE NO: _____

MEMBER NAME FIRST	M.I.	LAST	HIGHEST DEGREES EARNED	PRIMARY SCIENTIFIC OR NONSCIENTIFIC SPECIALITY	AFFILIATION WITH INSTITUTION(S) ABOVE (YES/NO; IF YES, WHICH ONE)
				Spa Mgmt/ Safety	NO
				Admin/Pers Mgmt	NO
				Technology Dir.	NO
				Gen. Surgeon	NO
				Food Safety/USDA	NO
				Minister	NO
				Home Health Care	NO
				[illegible]	NO
**					
NV					

ADDRESS AND PHONE NUMBER FOR CHAIRPERSON ONLY

IRB CHAIR SIGNATURE: _____

Note: Each IRB shall include at least one member w primary concerns are in nonscientific areas, as well one member who is not otherwise affiliated with this institution. Please review 45 CFR 46.107 for other membership requirements.

* DENOTES CHAIRPERSON
** DENOTES ALTERNATES (IF ANY, DENOTE MEMBER FOR WHOM ALTERNATE WILL SERVE
NV DENOTES NON-VOTING MEMBERS

EXAMPLE

Assurance Coordinator, Assurance Branch
Division of Human Subject Protections
Office for Protection from Research Risks

Investigational Review Board (IRB) Members

Project Number:
Project Title: **STRONTIUM-89 STUDY**

Dr. Richard H. Kaufman - IRB Chairman, Cyclotec Medical Industries, Inc.
Director, Quayside Health Spa - 2,000 members + personnel. Focus on safety.

William A. Zimmerman, Distribution/ Operations Manager
Malone & Hyde/ dba: Fleming Foods - Responsible for all personnel/ equipment/ safety.

Jeanie L. McGuire, Director of Technology Transfer - University of Miami
Co-founder, Greater Miami Chamber of Commerce Biomedical Exchange.

Felix H. Pow-Sang, Physician Assistant, Parkway General Hospital, Miami, FL, USA
M.D./ Surgery, Peru - 2 years experience in Community Health Care programs, Peru.

Richard S. Welch, Chief Inspector, South Florida - USDA Dept. of Agriculture (ret.)
Focus on Inspector Management, Community Health & Food Safety.

Wyburn K. Osborn, Minister, Miami Shores Christian Church, Miami Shores, FL
Ministrations to all ethnicities. Directs Red Cross distributions to 2,000 people monthly.

Deanna M. Osborn, Register Nurse - Current focus: Home Health Care Management
Experienced and expert in Emergency Care as well as all other nursing specialties.

William R. Christianson, General Manager, Towers of Quayside Homeowners Assoc.
Responsible for all facilities, personnel & residents. Focus on safety.

SPECIAL NOTE:

This list includes members from all walks of life; and represents a variety of genders, ethnicities and cultures. They have been carefully selected as people who are responsible for, constantly involved with, and concerned about the safety and welfare of different types of people in their industries and in their communities.

PART 2

IRB, Institution, and Investigator Compliance with 45 CFR 46

I. Applicability

Part 2 of this Assurance applies to the following research project which is conducted or sponsored by this institution and supported by the Department of Health and Human Services (DHHS).

Project title _____

DHHS Project number _____

Project Investigator or Director _____

II. Institutional Responsibilities

A. This institution has complied and will continue to comply with the requirements of 45 CFR 46 as specified below.

B. In accordance with the compositional and quorum requirements of 45 CFR 46.107 and 46.108, the Institutional Review Board (IRB) designated in Part 3 and in the attached roster is responsible for the initial and continuing review of this project.

C. This institution has provided and will continue to provide both meeting space for the IRB and sufficient staff to support the IRB's review and record keeping duties.

D. In addition to the review and approval of the IRB, this institution has reviewed and sponsors the project referenced above.

III. IRB Review

A. The IRB shall review, and have the authority to approve, require modification in, or disapprove this research activity or proposed changes in it before human subjects may be involved.

B. The convened IRB reviewed and approved the above project.

C. The IRB determined, in accordance with the criteria found at 45 CFR 46.111, and where applicable, 45 CFR 46 Subparts B, C, and D, that protections for human research subjects are adequate.

D. The IRB has the authority to suspend or terminate approval of the above referenced research in accordance with 45 CFR 46.113 for (1) non-compliance with 45 CFR 46, and this Assurance document or the IRB's requirements, and (2) for elimination of unexpected serious harm to subjects.

E. The IRB has determined that legally effective informed consent [copy of document must be attached unless specified otherwise by OPRR] will be obtained in a manner and method which meets the requirements of 45 CFR 46.116 and 46.117

F. Certification of IRB approval, at least annually shall be submitted to the DHHS awards unit that issued the award, as a condition for receipt of funds for a non-competing continuation and/or additional involvement of human subjects.

G. Continuing reviews by the IRB shall be conducted at intervals appropriate to the degree of risk, but not less than once per year (45 CFR 46.109[e]). The IRB may be called into an interim review session by the Chairperson at the request of any IRB member or Institutional Official to consider any matter concerned with the rights and welfare of any subject.

H. The IRB shall prepare and maintain adequate documentation of its activities in accordance with 45 CFR 46.115.

I. The IRB shall report promptly to institutional officials and the Office for Protection from Research Risks (OPRR):

(1) any serious or continuing noncompliance by investigators with the requirements of the IRB,
(2) any suspension or termination of IRB approval,
(3) any unanticipated problems or injuries involving risks to subjects or others, and
(4) any changes in this research activity which are reviewed and approved by the IRB.

J. Where appropriate, the IRB will determine that adequate additional protections are ensured for fetuses, pregnant women, prisoners, and children as required under Subparts B, C, and D of 45 CFR 46. The IRB will notify OPRR promptly when IRB membership is modified to satisfy the requirements at 45 CFR 46.304 and when the IRB fulfills its duties under 45 CFR 46.305(c).

K. The IRB will comply fully with the requirements of all applicable Federal policies and guidelines, including those concerning notification of sero-positivity, counseling, and confidentiality of subjects.

IV. Research Investigator Reporting Responsibilities

A. Investigators acknowledge and accept their responsibility for protecting the rights and welfare of human research subjects and for complying with all applicable provisions of this Assurance and 45 CFR 46.

B. Research investigators shall report promptly to the IRB proposed changes in this research activity and the changes shall not be initiated without IRB review and approval except where necessary to eliminate apparent immediate hazards to the subjects.

C. Research investigators shall report promptly to the IRB any unanticipated problems involving risks to subjects and others.

TO:
IRB Chairman

FROM:

RE: Assurance of Emergency Medical Care.
Project Number:
Project Title: Strontium-89 Clinical Trial

The policies and procedures relative to patient care at

requires all professional staff to be CPR certified and to follow specific guidelines when and if a medical emergency occurs. Our facility in which the clinical testing will be performed is located within a building that is 90% medical.

Therefore during normal working hours, when clinical testing will be performed, there are at least five - ten physicians present in the building of which two or more are either in the suite opposite ours or directly adjacent that can easily be contacted immediately if an unanticipated medical emergency occurs.

Every reasonable precaution to minimize risk is utilized and our approval as a Medicare Certified Facility plus yearly inspection by peers to assure continued participation in a preferred provider organization requires such.

Respectfully submitted,

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E-Mail: bionucmed@aol.com

Single Project Assurance

Assurance of Compliance with DHHS Regulations for Protection of Human Research Subjects

BIO-NUCLEONICS, INC. (BNI) hereinafter known as the "institution", hereby gives assurance that it will comply with the Department of Health and Human Services (DHHS) regulations for the protection of human research subjects (45 CFR 46) as specified below.

Part 1

Ethical Principles and Institutional Policies Governing Research Involving Human Subjects

I. Applicability

Except for research exempted or waived under the DHHS regulations 45 CFR 46.101, Part 1 of this Assurance applies to all research involving human subjects, and all other activities which even in part involve such research, regardless of whether the research is otherwise subject to federal regulation, if:

a. the research is sponsored by this institution, or
b. the research is conducted by or under the direction of any employee or agent of this institution in connection with institutional responsiblilities, or
c. the research is conducted by or under the direction of any employee or agent of this institution using any property or facility of this institution, or
d. the research involves the use of this institution's nonpublic information to identify or contact human research subjects or prospective subjects.

To: Dr.
IRB Chairperson

From:

Principal Investigator

Regarding:
Project Title: Strontium-89 Clinical Trial

Subject: Assurance of Emergency Medical Care

Regarding Facilities at:

This facility is not a "testing of human subjects" facility. We have qualified this facility for OPRR approval as per requisitional guidelines Bio-Nucleonics the research company qualifying for approvals.

All **BNI** testing of human subjects will be conducted at:

As such, **BNI** does not have medical staff on premise - but - as BIO-NUCLEONICS is performing this study in collaboration with and in cooperation with local major medical institutions. namely:

Any emergency situations that might arise are more than manageable at either of these emergency room centers.

Respectfully submitted,

Principal Investigator

(Example of a Model Patient Consent Form)

Revised (INSERT DATE HERE)

(INSERT INSTITUTION OR HOSPITAL NAME HERE)

CLINICAL RESEARCH CONSENT FORM

STUDY NO. SRBNI-0596

STRONTIUM-89 AS A PALLIATIVE AGENT FOR PATIENTS WITH BONE METASTASES

PURPOSE

You have been told by your physician that you have a cancerous tumor which has spread to your bones and is the cause of your pain.

You are being asked to participate in a research study involving the use of a radioactive substance, Strontium-89 solution, to treat the pain from cancer which has spread to bones.

The purpose of this study is to find out how well a radioactive agent, Strontium-89, can decrease bone pain from metastases.

ALTERNATIVES

The alternatives to participation in this research study is to have the standard treatments for pain, including chemotherapy or external radiation therapy as determined by your physician.

PROCEDURES

If you decide to participate in this study you may first receive a complete set of tests including history and physical examination, blood tests, urine tests, chest x-ray, x-rays of painful bones, a bone scan and an EKG. If you are a women who has not reached menopause, you will also have to have a pregnancy test. These tests can be done as an outpatient and will take five to seven days. About 10 days before treatment, you will also be asked to keep a daily and weekly journal of when and how severe your pain is and how much pain medication you have used.

You will then be admitted to the hospital and will be given about a quart of liquids (by mouth or through a vein). You will be given an injection study drug through a vein. The drug will be either Strontium-89 which is a radioactive substance that goes to your bones or a placebo without the radioactive substance and which is not expected to help your pain. You will not be told which type of study drug you will receive. You will be given up to a liter of liquids to make sure your kidneys eliminate any drug which isn't taken up by your bones.

All urine from the first 6 hours after you receive the drug must be collected. If you have a blockage of your urinary system or if you have a problem with urine leakage, you will have to have a catheter placed in your bladder during this 6 hour period. Radiation

measurements may be made of your body by the radiation safety officer (whether or not you received a radioactive drug) and you will be allowed to leave the hospital when the radioactivity in your body is below a certain level. This should take a few hours after dosing.

After you are discharged, you will continue to keep your pain diary and will have blood tests done twice a week for a month, then once a week for a month, then every two weeks for 2 more months. You will be seen in clinic every other time you have your blood drawn. At the end of 4 months you will have another bone scan and bone X-rays and a complete set of blood tests (about 3 tablespoons).

If your pain has begun diminishing by 4 weeks after your treatment, you will be told whether you received the active drug or the control (no active radiation) drug and will be given the option of receiving an injection of the radioactive drug. If you wish to do so, you will then be followed for an additional 4 months.

If you fail to complete your pain diary or to keep your appointments for laboratory tests or clinic visits (unless rescheduled within an acceptable time), you will be dropped from the study. If you have chemotherapy, hormone therapy, or external radiation therapy within the first month of the study, you will also be dropped from the study.

BENEFITS

No benefit can be promised from your participation in this study. It is hoped that you may experience partial or complete relief from bone pain associated with you metastatic cancer for a period of time (if you receive the active radiation treatment).

RISKS

The treatments used in this program may cause some of the side effects listed, however, is unlikely to cause all of the side effects listed.

The Strontium-89 used in this study is a radioactive substance and exposes you to a dose of radiation, which is how it works to treat the cancer in your bones. The radiation may be enough to cause some damage to your bone marrow which would result in a decrease in your white blood cells and platelets. This may make you more susceptible to infection and bleeding. Your bone marrow should recover by itself within 4-6 weeks.

You may have an allergic reaction to the carrier portion of the drug, or you may have a problem with a drop in the calcium level in your blood. Both of these problems are very rare.

This therapy is <u>not</u> expected to control your tumor and being off anti-cancer therapy during this time may put you at risk of developing progressive disease at a more rapid rate than someone being on some form of therapy.

As with any drug, there may be unexpected side effects, including death.

The risks associated with intravenous (into a vein) infusion are commonly discomfort and/or bruise at the site of puncture, and less commonly formation of blood clots, infection, bleeding from the puncture site, and possibly fainting.

If you are pregnant or planning to get pregnant you may not participate in this study. This therapy may affect the fetus and cause birth defects. The investigators advise the use of effective birth control methods in situations where there is a risk of conceiving a child. In the event of a related research injury, you should contact the Principal Investigator immediately.

FINANCIAL OBLIGATIONS

You or your insurance carrier will be responsible for routine medications, laboratory work, x-rays and bone scans, hospitalization and other associate costs of this treatment. The study drug will be provided without charge. You should be aware that some insurance carriers will not pay for the costs of care associated with the use of investigational therapy.

OTHER PERTINENT FACTS:

a) The Principal Investigator and your physicians will be more than happy to answer any additional questions, either at the beginning of your treatment or at any later time.

b) Your participation in this study is voluntary. You may refuse or withdraw from this study at any time without affecting your medical care and treatment or without loss of any benefits. If you choose to stop your participation in the study, please notify the investigator. The investigator and/or Bio-Nucleonics, who is sponsoring this research can also discontinue your participation in this study without your consent if he/she feels that it is in your best interest or if there are administrative reasons.

c) Your consent to participate in this study includes consent for the investigator and his assistants to review all your medical records as may be necessary for the purposes of this study. Your records and results will not be identified as pertaining to you in any publication without your expressed permission. The investigator and his assistants will consider your records confidential to the extent permitted by law. However, in some circumstances, the local Ministry of Health or other Government authority, U.S. Food and Drug Administration (FDA) Bio-Nucleonics or their designees may request copies of your records. If this happens, the above requests will be honored.

d) You will receive a copy of this informed consent sheet for your own information. You may use this document for consultation with family members, other physicians and friends before you consider signing. If you do not know of any other physicians, your doctors would be happy to recommend some for additional opinions.

e) Please ask your Physicians prior to taking other medications, even aspirin, since there may be significant drug incompatibilities.

f) On request, you will be informed of the outcomes of the study, upon its termination.

g) If you participate in this study, you will be exposed to certain risks of physical injury similar to those connected with standard treatment. In addition, it is possible in the course of the study that new adverse effects of treatment may be discovered that result in physical injury. If you experience an injury due as a direct consequence of this study, medical treatment will be offered to you. The sponsor will provide compensation of such treatment only for care not cover by your medical insurance and which, in mutual opinion of the investigator and sponsor, was cause by the drug used in this study.

If you have any questions about rights as a patient on this research study, you should feel free to call _____ at Telephone _____ or the University/Medical Center by telephone at _____, during the hours of ____AM and _____PM weekdays. If you have any questions about the research study, you may call the Principal Investigator at the telephone number shown below.

I have received a copy of this informed consent which I have read and understand. I hereby consent to be a participant in this study.

Date_____ Patient_____

Witness_____

Principal Investigator:

Name Here
Telephone No. _____ or _____ (days)
Telephone No. _____ (Evenings)

Revised (Date Here)

NAME OF INSTITUTION HERE
ADDRESS
CITY