

U.S. NUCLEAR REGULATORY COMMISSION  
REGION III

Report No. 030-01391/90001(DRSS)

Docket No. 030-01391

License No. 12-01087-07

Category G 1

Priority 1

Licensee: V.A. Edward Hines, Jr., Medical Center (Hines)  
Hines, IL 60141

Special Inspection Conducted On: February 7, 1990

Inspector: W. P. Reichhold  
W. P. Reichhold

1 MARCH 1990  
Date

Approved By: George W. Sreniawski for  
D. J. Sreniawski, Chief  
Nuclear Materials Safety  
Section 1

MARCH 3, 1990  
Date

Inspection Summary

Inspection on February 7, 1990 (Report No. 030-01391/90001(DRSS))

Areas Inspected: This special, announced inspection was performed in response to a diagnostic misadministration of iodine-131 hippuran. The inspection included a review of the circumstances surrounding the misadministration, and a review of the corrective actions Hines is taking to prevent a similar misadministration.

Results: No violations were found.

## DETAILS

### 1. Persons Contacted

- \*John R. Fears, Chief Executive Officer
- \*Lawrence Case, Radiation Safety Officer
- Gary Eastman, Chief Nuclear Medicine Technologist
- Lisa Urano, Staff Nuclear Medicine Technologist

\*Indicates the individuals present at the exit meeting on February 7, 1990.

### 2. Purpose of Inspection

This was a special inspection performed to review the circumstances surrounding a diagnostic misadministration of iodine-131 hippuran. Hines reported the misadministration to the NRC Region III office on February 1, 1990. The inspection included a review of the circumstances surrounding the misadministration and the corrective actions Hines is taking to prevent a similar misadministration.

### 3. Incident: On February 1, 1990, a nuclear medicine technologist was preparing a dose of thallium-201 for a patient's heart scan.

Hines receives their thallium-201 in multi-dose vials in a white shielded container. Hines receives their iodine-131 hippuran in a multi-dose vial that also has a white shielded container. On the day of the incident, thallium-201 and iodine-131 hippuran, both in their containers, were in the dose preparation area. Both containers were labeled correctly. The technologist needed a volume of 2.5 milliliters of thallium-201 to obtain the prescribed dose (3.5 millicuries) needed to do a heart scan.

The technologist was not able to withdraw the total volume of thallium-201 due to insufficient quantity. The technologist assumed that the second white container was also thallium-201, but it contained iodine-131 hippuran. The technologist withdrew the remaining volume from the iodine-131 hippuran container by mistake. The patient was given a mixture of thallium-201 and iodine-131 hippuran. The technologist found the error because the image of the patient's heart was not clear. Iodine-131 hippuran can contain 3% free iodine. The patient was given potassium iodide to reduce the radioactive iodine uptake by the thyroid. Hines estimated that the patient's thyroid dose was 14 rads. This dose is about the same thyroid dose a patient would receive from a diagnostic renal function scan using iodine-131 hippuran (see attached product data). The patient's heart scan was successfully completed later that day.

Conclusion: No NRC requirements were violated. Hines reported the misadministration to Region III by telephone on February 1, 1990. Hines submitted a written report on the misadministration within 15 days as required by NRC regulations (see attached). Hines' actions to prevent a similar misadministration is outlined in their letter dated February 7, 1990 (copy attached).

Attachment: Ltr dtd 2/7/90,  
VA Hines to NRC



Veterans  
Administration

February 7, 1990

Chief, Material Safety and Safeguards Section  
U.S. N.R.C.  
799 Roosevelt Road  
Building 4  
Glen Ellyn, IL 60137

Dear Sir:

Subject: Compliance with 10 CFR Part 35.33.(C)

On February 1, 1990, a misadministration occurred at this facility in which a patient received an estimated dose to the thyroid gland of approximately 14 rads. This exceeds your regulation which states: "... an organ dose greater than 2 rem ..."

The circumstances involving the details which caused the occurrence are described in the following attachments. Your required form NRC 473 is also attached. We refer you also to conversations between members of our staff which transpired on February 7, 1990 with your Mr. Bill Reichhold.

If you require information other than the enclosed, please contact our Hospital Radiation Safety Officer, Mr. Lawrence Case at (708) 343-7200 Ext. 1955.

Sincerely yours,

A handwritten signature in dark ink, appearing to read "Joan R. Fears".

Joan R. Fears  
Director

Attachments

cc: DM&S Regional Director's Safety Staff (138S17)

FEB 13 1990

### DIAGNOSTIC MISADMINISTRATION REPORT

IN1: LICENSE NAME: EDWARD HINES JR. HOSPITAL  
 IN7: LICENSE NUMBER: 1121-101108171-1017

IN3: CITY: HINES  
 IN4: STATE: IL  
 IN5: EVENT DATE: 10/21/01  
 IN6: REPORT DATE: 10/16/01

IN7: TYPE OF MISADMINISTRATION:  
 801: WRONG RADIOPHARMACEUTICAL  
 802: WRONG PATIENT  
 803: DOSAGE DIFFERING FROM PRESCRIBED BY 50%  
 804: WRONG ROUTE?  
 IN8: DID THE MISADMINISTRATION INVOLVE AN ISOTOPE OF IODINE:  
 899: YES  
 1111: NO  
 IN9: NUMBER OF PATIENTS WHO RECEIVED A MISADMINISTRATION UNDER THIS REPORT: 1

IN10: INTENDED		IN10A: INTENDED				IN11: GIVEN			
ISOTOPE	MILLICURIES	ISOTOPE	CHEMICAL FORM	STUDY	MILLICURIES	ISOTOPE	CHEMICAL FORM	STUDY	
3.5		TL201	CHLORIDE	CARDIAC THALLIUM	3.0	TL201	CHLORIDE	CARDIAC THALLIUM	
					776	I131	HYPURAN		

IN12: PRECIPITATOR

<input type="checkbox"/> 171: REFERRING PHYSICIAN	<input type="checkbox"/> 176: NOT LAB TECHNOLOGIST
<input type="checkbox"/> 172: WARD NURSE	<input checked="" type="checkbox"/> 177: IMAGING TECHNOLOGIST
<input type="checkbox"/> 173: WARD CLERK	<input type="checkbox"/> 178: CLINIC RECEPTIONIST
<input type="checkbox"/> 174: NUCLEAR PHARMACY	<input type="checkbox"/> 179: SCHEDULING TECHNOLOGIST
NAME OF NUCLEAR PHARMACY: _____ CITY: _____ STATE: _____	<input type="checkbox"/> 180: PATIENT
	<input type="checkbox"/> 181: OTHER

IN13: ERROR

NOT LAB	REFERRAL	ADMINISTRATION	OTHER
<input checked="" type="checkbox"/> 111: MISLABELED A SYRINGE	<input type="checkbox"/> 120: MISUNDERSTOOD REFERRING PHYSICIAN'S REQUEST	<input type="checkbox"/> 130: SELECTED WRONG PATIENT	<input type="checkbox"/> 140: OTHER
<input type="checkbox"/> 112: MISLABELED A VIAL OR VIAL SHIELD	<input type="checkbox"/> 121: REQUESTED WRONG STUDY	<input type="checkbox"/> 131: ANSWERED WAITING ROOM PAGE INTENDED FOR OTHER PATIENT	
<input type="checkbox"/> 113: RECONSTITUTED WRONG REAGENT KIT	<input type="checkbox"/> 122: REQUESTED STUDY FOR WRONG PATIENT	<input type="checkbox"/> 132: BROUGHT WRONG PATIENT TO CLINIC	
<input type="checkbox"/> 114: PLACED RECONSTITUTED VIAL IN WRONG SHIELD		<input type="checkbox"/> 133: SELECTED WRONG SYRINGE FROM DOSAGE CART	
<input checked="" type="checkbox"/> 115: SELECTED WRONG VIAL WHEN DRAWING DOSAGE			
<input type="checkbox"/> 116: SET DOSE CALIBRATOR IMPROPERLY			
<input type="checkbox"/> 117: MISLEAD DOSE CALIBRATOR			
<input type="checkbox"/> 118: MISUNDERSTOOD RADIOPHARMACEUTICAL OR DOSAGE ORDER			

IN14: CONTRIBUTING FACTORS

<input type="checkbox"/> 161: STUDENT TECHNOLOGIST	<input type="checkbox"/> 185: REQUISITION NOT CHECKED	IN15: ACTION TAKEN TO PREVENT RECURRENCE
<input type="checkbox"/> 162: NEW EMPLOYEE	<input type="checkbox"/> 186: PATIENT CHART NOT CHECKED	
<input type="checkbox"/> 163: FOREIGN LANGUAGE	<input type="checkbox"/> 187: NEW PROCEDURE	<input type="checkbox"/> 101: IMPROVE SUPERVISION OF PERSONNEL
<input type="checkbox"/> 164: PATIENT INCOHERENT OR UNCOOPERATIVE	<input type="checkbox"/> 188: HEAVY WORKLOAD	<input type="checkbox"/> 102: IN ACTION
<input type="checkbox"/> 165: ISOTOPE NOT CHECKED	<input type="checkbox"/> 189: OTHER _____	<input type="checkbox"/> 103: OTHER _____
		<input checked="" type="checkbox"/> 104: REINSTRUCT PERSONNEL
		<input checked="" type="checkbox"/> 105: REPRIMAND PERSONNEL (VERBAL COUNSEL BY SERVICE CHIEF)

IN16: EFFECT ON PATIENTS:  NONE APPARENT  
 IN17: ABSTRACT (SEE ABSTRACT)

(SEE ATTACHED REPORTS)

NUCLEAR REGULATORY COMMISSION USE

IN18: YES	IN19: AS	IN20: REGIONAL LDC NUMBER	IN21: ACCESSION NUMBER	IN22: INITIALS
NO				

Misadministration (Diagnostic/Therapeutic)

Report of the Chief of Service:

Name of patient: [REDACTED]  
Social Security No: [REDACTED]  
Prescribed Dose: 3.5 mCi TL201  
Administered Dose: 3.0 mCi TL201 + 0.716 mCi of I131 hippuran.  
Date of Misadministration: Feb. 1, 1990

1. Please see the chief technologist's report detailing the circumstances of misadministration to this patient.
2. Mr. [REDACTED] was examined by one of our resident physician, who in consultation with an attending physician determined that the patient would not experience any ill effect from the misadministration.
3. It was estimated by our health physicist and chief technologist that the patient received 716 uCi of I-131 hippuran. The method by which this dose was determined is described in the chief technologists report. Based on this information, exposure was estimated using the package insert for hippuran with the following results:

Kidney: .06 Rads  
Gonads: .08 Rads  
Total Body: .08 Rads  
Thyroid: .08-28 Rads

The large thyroid dose range is the result of the possible range of free I-131 in a hippuran preparation (0-3% free I-131). After reviewing this dosimetry data, the only intervention which was considered appropriate was administration of KI (SSKI) to block the thyroid uptake of free I-131. Accordingly, the exposure to this patient's thyroid was reduced by approximately 50% (Medical Management of Radiation Accidents, FA Metler Jr. (Ed) CRC Press) such that the upper limit for dose to thyroid in this individual was in fact 14 Rads.

4. The question of misadministration was discussed with the chief technologist and other technologists and steps were taken to minimize the likelihood of misadministrations in the future.
5. The referring physician was notified of the misadministration by phone at approximately 2:00 p.m. and explained that we did not anticipate any clinical ill effect from the relatively low dose of I131.

## Report of Incident

### Chief technologist's report:

On February 1, 1990, Mr. [REDACTED], SS [REDACTED], was referred from 10E for a persantine thallium study. The prescription written by the resident physician and countersigned by an authorized user, read 3.5 mCi TL201. The technologist, Lisa Urano, drew up a thallium dose from a partially used vial. Not being able to get the full ordered dose of TL201 from that vial, she picked up another vial of what she thought was TL201; but it was however I131 hippuran. To complete the dose, a certain volume of I131 was withdrawn from the vial. The total dose measured in the dose calibrator was 3.58 mCi. Upon noticing the error and because the heart was not visualized clearly, a second dose of TL201 (3.6 mCi) was administered as ordered by an authorized user. Upon investigation into the amount of each isotope given, it was determined that the total dose of TL201 was approximately 3.0 mCi and the maximum dose of I131 hippuran was approximately 716 uCi. The latter was estimated in the following way: Upon receiving the vial on the morning of 1/29/90, the activity was assayed at 1.60 mCi, (inventory # 4339). On the morning of 2/1/90 this activity physically decayed to approximately 1240 uCi. Prior to this incident, a I131 hippuran dose was drawn from this vial for a renal scan for another patient. This dose was assayed at 329 uCi. 195 uCi remained in the vial after Mr. [REDACTED] injection leaving a difference of 716 uCi in the vial which was withdrawn for Mr. [REDACTED].

The dose slip read 3.58 mCi of Tl-201; since 716 uCi of I-131 would give a reading of approximately 0.6 mCi with the dose calibrator on the Tl-201 scale we estimate that the injected activity of Tl-201 was 3.0 mCi.

In order to prevent reoccurrence of this type of incident, the thallium 201 and iodine 131 hippuran vials will be clearly marked in indelible ink. In addition, we will consider purchasing the I131 hippuran from a different source in order to not have on hand, like vial shields with different isotopes.

The technical staff discussed these proposals with the service chief and agreed to implement them. Additional safeguards such as only removing from storage the vial required and replacing it to storage immediately after use as also discussed. This episode does not, we feel, represent a pattern, but rather an unfortunate reality of human error. We will strive to reach 100% accuracy and do everything within our power to prevent a reoccurrence.

The patient's primary physician was contacted regarding this error by Dr. Bushnell.





**Physical Characteristics**

Iodine-131 decays by beta and associated gamma emissions with a physical half-life of 8.04 days.<sup>1</sup> The principal beta emissions and gamma photons are listed in Table 1.

**Table 1. Principal Radiation Emission Data<sup>1</sup>**

Radiation	Mean Percent Per Disintegration	Energy (keV)
Beta-1	2.12	69.4 Avg.
Beta-3	7.36	96.6 Avg.
Beta-4	89.3	191.6 Avg.
Gamma-7	6.05	284.3
Gamma-14	81.2	364.5
Gamma-17	7.26	637.0

**External Radiation**

The specific gamma ray constant for iodine-131 is 2.27 R/hr-mCi at 1 cm. The first half-value thickness of lead (Pb) for iodine-131 is 0.24 cm. A range of values for the relative attenuation of the radiation emitted by this radionuclide that results from interposition of various thicknesses of Pb is shown in Table 2. For example, the use of 4.6 cm of Pb will decrease the external radiation exposure by a factor of about 1,000.

**Table 2. Radiation Attenuation by Lead Shielding<sup>2</sup>**

Shield Thickness (Pb), cm	Coefficient of Attenuation
0.24	0.5
0.95	10 <sup>-1</sup>
2.6	10 <sup>-2</sup>
4.6	10 <sup>-3</sup>
6.5	10 <sup>-4</sup>

To correct for physical decay of this radionuclide, the fractions that remain at selected time intervals before and after the date of calibration are shown in Table 3.

<sup>1</sup>Kocher, David C., "Radioactive Decay Data Tables", DOE/TIC 11026, page 133 (1981).

<sup>2</sup>Data supplied by Oak Ridge Associated Universities, Radiopharmaceutical Internal Dose Information Center, Oak Ridge, TN, 1987.

**Table 3. Physical Decay Chart; Iodine-131, Half-Life 8.04 Days**

Days	Fraction Remaining	Days	Fraction Remaining	Days	Fraction Remaining
0*	1.000	11	0.387	21	0.164
1	0.917	12	0.355	22	0.150
2	0.842	13	0.326	23	0.138
3	0.772	14	0.299	24	0.126
4	0.708	15	0.274	25	0.116
5	0.650	16	0.252	26	0.106
6	0.596	17	0.231	27	0.098
7	0.547	18	0.212	28	0.089
8	0.502	19	0.194	29	0.082
9	0.460	20	0.178	30	0.075
10	0.422				

\*Calibration Day.

**CLINICAL PHARMACOLOGY**

Following intravenous injection of Hippuran I 131 the appearance, concentration and excretion of the tracer in the kidney can be monitored. Tubular cell secretion is primarily displayed. An index of renal vascular competence and renal evacuation may also be estimated.

**INDICATIONS AND USAGE**

Hippuran I 131 Injection is a diagnostic aid in determining renal function, renal blood flow, and urinary tract obstruction, and a renal imaging agent.

**CONTRAINDICATIONS**

None known.

**WARNINGS**

This drug may contain up to 3% free iodine-131. A saturated solution of potassium iodide or a dose of 10 to 20 drops of Lugol's solution should be administered prior to and following the examination to decrease thyroid accumulation of iodine-131.

## PRECAUTIONS

### General

As in the use of other radioactive material, care should be taken to insure minimum radiation exposure to the patient, consistent with the proper patient management, and to insure minimum radiation exposure to occupational workers.

The vial contents are sterile. It is essential that the user follow the directions carefully and adhere to strict aseptic procedures.

### Carcinogenesis, Mutagenesis, Impairment of Fertility

No long-term animal studies have been performed to evaluate the carcinogenic or mutagenic potential, or whether this drug affects fertility in males or females.

### Pregnancy Category C

Animal reproduction studies have not been conducted with iodohippurate sodium I 131. It is also not known whether iodohippurate sodium I 131 can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Iodohippurate sodium I 131 should be given to a pregnant woman only if clearly needed.

Ideally, examinations using radiopharmaceuticals, especially those elective in nature, of a woman of childbearing capability should be performed during the first few (approximately 10) days following the onset of menses.

### Nursing Mothers

Iodine-131 is excreted in human milk during lactation, therefore, formula feedings should be substituted for breast feedings.

### Pediatric Use

Safety and effectiveness in children have not been established.

Radiopharmaceuticals should be used only by physicians who are qualified by specific training in the safe use and handling of radionuclides produced by nuclear reactor or particle accelerator and whose experience and training have been approved by the appropriate government agency authorized to license the use of radionuclides.

## ADVERSE REACTIONS

As with all organic iodine-containing compounds, the possibility of allergic type reactions must be kept in mind. Nausea, vomiting and fainting have been reported in conjunction with the administration of Hippuran I 131 Injection.

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## DOSAGE AND ADMINISTRATION

The suggested dose range employed in the average patient for renal function studies (70 kg) is up to 1.295 megabecquerels (35 microcuries) administered intravenously [18.5 kilobecquerels (0.5 microcurie) per kilogram body weight].

When renal imaging is required, the dose for the average patient (70 kg) is up to 12.95 megabecquerels (350 microcuries) [111 to 185 kilobecquerels (3 to 5 microcuries) per kilogram body weight].

The patient dose should be measured by a suitable radioactivity calibration system immediately prior to administration.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

### Instructions for the handling of Iodohippurate Sodium I 131:

1. Waterproof gloves should be used during the entire handling and administration procedure.
2. Using proper shielding, the vial containing the Iodohippurate Sodium I 131 should be visually inspected to insure that it is free of particulate matter and discoloration prior to use.
3. Maintain adequate shielding during the life of the product and use a sterile, shielded syringe for withdrawing and injecting the preparation.

### Radiation Dosimetry

The estimated radiation doses<sup>3</sup> to an average patient (70 kg) from an intravenous dose of 12.95 megabecquerels (350 microcuries) of Iodohippurate Sodium I 131 are shown on Table 4. The values are based on a completely blocked thyroid and a biphasic excretion curve. After administration of the drug about 62% of the activity has an effective half-life of 7.4 minutes, and 38% has an effective half-life of 37 minutes.

<sup>3</sup>Method of calculation: A Schema for Absorbed-Dose Calculation for Biologically Distributed Radionuclides, Supplement No. 1, MIRD Pamphlet No. 1, *J. Nucl. Med.*, p. 7, 1968.

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Table 4. Absorbed Radiation Doses

Tissue	Absorbed radiation doses for 12.95 megabecquerels (350 microcuries)	
	mGy	rads
Thyroid	0.39*	0.039*
Kidneys	0.28	0.028
Bladder Wall	20.0	2.000
Testes	0.39	0.039
Ovaries	0.46	0.046
Total Body	0.39	0.039

\*This product may contain up to 3% free iodine-131. If the thyroid is not blocked with saturated potassium iodide or Lugol's solution, and the thyroid uptake is 25%, the absorbed radiation dose for the thyroid would be 1.4 rads. This value will decrease proportionately if less than 3% free iodine-131 is present, or if the uptake is less than 25%. Conversely, it will increase if the uptake is greater than 25%.

**HOW SUPPLIED**

**Catalog Number**

115 Hippuran I 131 Injection (Iodohippurate Sodium I 131 Injection). A sterile, non-pyrogenic solution containing 37.5% propylene glycol, 0.1% methylparaben, and 0.03% propylparaben as preservatives; 0.015% sodium citrate and 0.005% edetate disodium as stabilizers. May contain sodium hydroxide or hydrochloric acid for pH adjustment and trace quantities of sodium acetate. Hippuran I 131 Injection is available in vials containing 37 megabecquerels (1 millicurie) with a concentration of 9.25 megabecquerels (0.25 millicurie) per milliliter and specific activity of 11.1 megabecquerels (0.3 millicurie) per milligram as of time of calibration.

In conformance with recommendations in the U.S.P., Hippuran I 131 Injection should not be used after six weeks from the date of manufacture. The expiration date for the product is stated on the label.

**Storage and Handling**

Store at room temperature (Below 86°F/30°C).

Storage and disposal of Hippuran I 131 Injection should be controlled in a manner that is in compliance with the appropriate regulations of the government agency authorized to license the use of this radionuclide.

**PERFORMING THE RENOGRAM**

**Patient Preparation**

The state of hydration of the patient will influence the excretion of the tracer and the shape of the renogram curve. In dehydrated patients, the time required to reach the peak radioactivity level in the kidney is prolonged, and the second and third phases of the renogram are flatter. False differences in rates of tracer excretion may occur due to increased pooling of highly concentrated urine in slight non-pathologic variations of the ureteral outlets. In the hydrated patient, good second phase comparisons are obtained, but differences in rates of excretion may be obscured.

**Positioning**

The patient is generally placed in a sitting position. The prone or supine position may also be employed if the patient is unable to maintain a steady sitting position. A gamma camera interfaced with a computer is placed directly over the kidneys at right angles to the back.

**Interpretation of Results**

The renogram provides diagnostic information relating to two basic problems: those affecting kidney function or blood supply and those obstructing urinary tract flow.

Figure 1 is a schematic representation of a normal renogram. The three segments of the curve were originally called the vascular, tubular and excretion phases. Dore et al.<sup>4</sup> renamed these segments as: 1) tracer appearance, 2) blood flow, and 3) drainage.

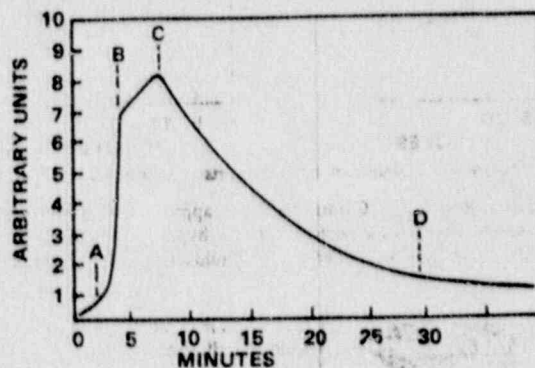


Figure 1. Normal Renogram

<sup>4</sup> Dore, E.K., Taplin, G.V. and Johnson, D.E., Current Interpretation of the Sodium Iodohippurate I 131 Renocystogram, J.A.M.A. 185:925, September 21, 1963.

**HIPPURAN® I 131 INJECTION**  
Iodohippurate Sodium I 131 Injection

The first phase, segment AB, represents the initial appearance of the radioactivity under the detector. This appearance is noted a few seconds following the injection and lasts about 30 seconds. The second phase, segment BC, is the uptake of the tracer by the kidney. The shape of this portion of the curve is affected by changes in the renal blood flow and the cellular function of the kidney. This slowly rising second phase of the renogram usually lasts for about 2 to 5 minutes. Segment CD, or the third phase, represents the removal of the tracer from the kidney pelvis. The state of hydration, capacity of the renal pelvis, anatomic relations between the pelvis and the ureter, and any existing pathologic abnormalities influence the shape of this curve. The tracing is normally continued for about 30 minutes, although sufficient information may be obtained after about 15 minutes.

Illustrated in Figures 2 and 3 are examples of abnormal renograms. Figure 2 is a renogram showing a moderate decrease in function or blood supply in the right kidney; Figure 3 shows an acute unilateral (right) urinary tract obstruction.

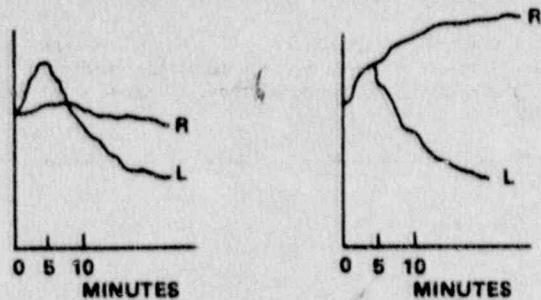
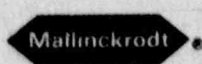


Figure 2. Abnormal Renograms Figure 3.

The U.S. Nuclear Regulatory Commission has approved distribution of this radiopharmaceutical to persons licensed to use byproduct material listed in Sections 35.100 and 35.200, and to persons who hold an equivalent license issued by an Agreement State.



Diagnostic Products Division  
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