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EPIDEMIOLOGY OF PLUTONIUM EFFECTS IN WORKERS

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Los Alamos National Laboratory
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DEPARTMENT OF ENERGY
Office of Health and Environmental Research**

PURPOSE OF LOS ALAMOS EPIDEMIOLOGY STUDIES FOR DOE

- To Study Effect of Plutonium on Humans by Evaluating:
 - Death Rates for Specific Causes
 - Disease (Cancer) Rates for Specific Causes
 - Dose/Effect Relationships (Risk)
 - Confounding Factors
(e.g., External Radiation, Chemicals, Smoking)
- To Measure Overall Health of Workers at Facilities with Major Plutonium Processes

SOURCES OF RELEVANT DATA FOR ASSESSING PLUTONIUM HAZARDS

Experimental Animal Data for Plutonium

Rodents

Dogs (Battelle NW, Lovelace, Utah)

Alpha-Particle Induced Cancer in Humans

Uranium Miners (Radon-222)

Thoratrast Patients (Thoron-232)

Dial Painters (Radium-226)

German Patients (Radium-224)

Pu Measurements in Human Autopsy Tissues

BIOLOGY OF PLUTONIUM EXPOSURES

Intake

Inhalation of Particles
Contaminated Wounds

Deposition

Lung and Associated Lymph Nodes	(Insoluble)
Bone and Liver	(Soluble)
Lesser Quantities in Other Organs	(Soluble)

DOSIMETRY OF PLUTONIUM DEPOSITED IN THE BODY

Body Depositions (Activity)

Urine Excretion - Systemic Deposition

Direct Chest Counts - Lung Deposition

Alpha Radiation Doses from Plutonium

Calculate Organ Doses

using metabolic (ICRP) model

COHORTS INCLUDED IN THE STUDY OF HEALTH EFFECTS FROM PLUTONIUM

<u>Facility</u>	<u>Work Period</u>	<u>No. of Workers</u>	<u>Vital Status Data End</u>
Rocky Flats	1951-79	9500	1983 *
Mound	1943-79	6900	1983 *
Los Alamos Lab	1943-78	23200	1981 ** 1983 *
Los Alamos Zia	1946-78	14700	1984
Pantex	1951-78	5400	1978 *

* Valid for White Males

** Valid for White Females

RADIATION EXPOSED WHITE MALES IN COHORTS TO STUDY EFFECTS FROM PLUTONIUM

<u>Facility</u>	<u>Number</u>	<u>External > 1 Rem</u>	<u>Internal Pu > 2 nCi</u>
Rocky Flats	7162	3354	1471
Mound	4847	1364	194
Los Alamos Lab	16317	2301	320
Los Alamos Zia	9842	431	173
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Total	38168	7450	2158

TECHNIQUES USED TO STUDY HUMAN HEALTH EFFECTS FROM PLUTONIUM

<u>Type</u>	<u>Examples</u>
Clinical Follow-up	1944-45 Pu Workers
Cohort Mortality	Rocky Flats, Mound
Case-Control	Brain Tumors, Melanoma
Cancer Incidence	Los Alamos Males
Special Studies	Smoking, SSA
County Mortality	Los Alamos

ANALYTIC METHODS USED IN LOS ALAMOS COHORT MORTALITY STUDIES

Stratified Analyses

Standardized (Internal) Rate Ratio Analyses

Cox Regression Models (MOX software)

Standardized Mortality Analyses

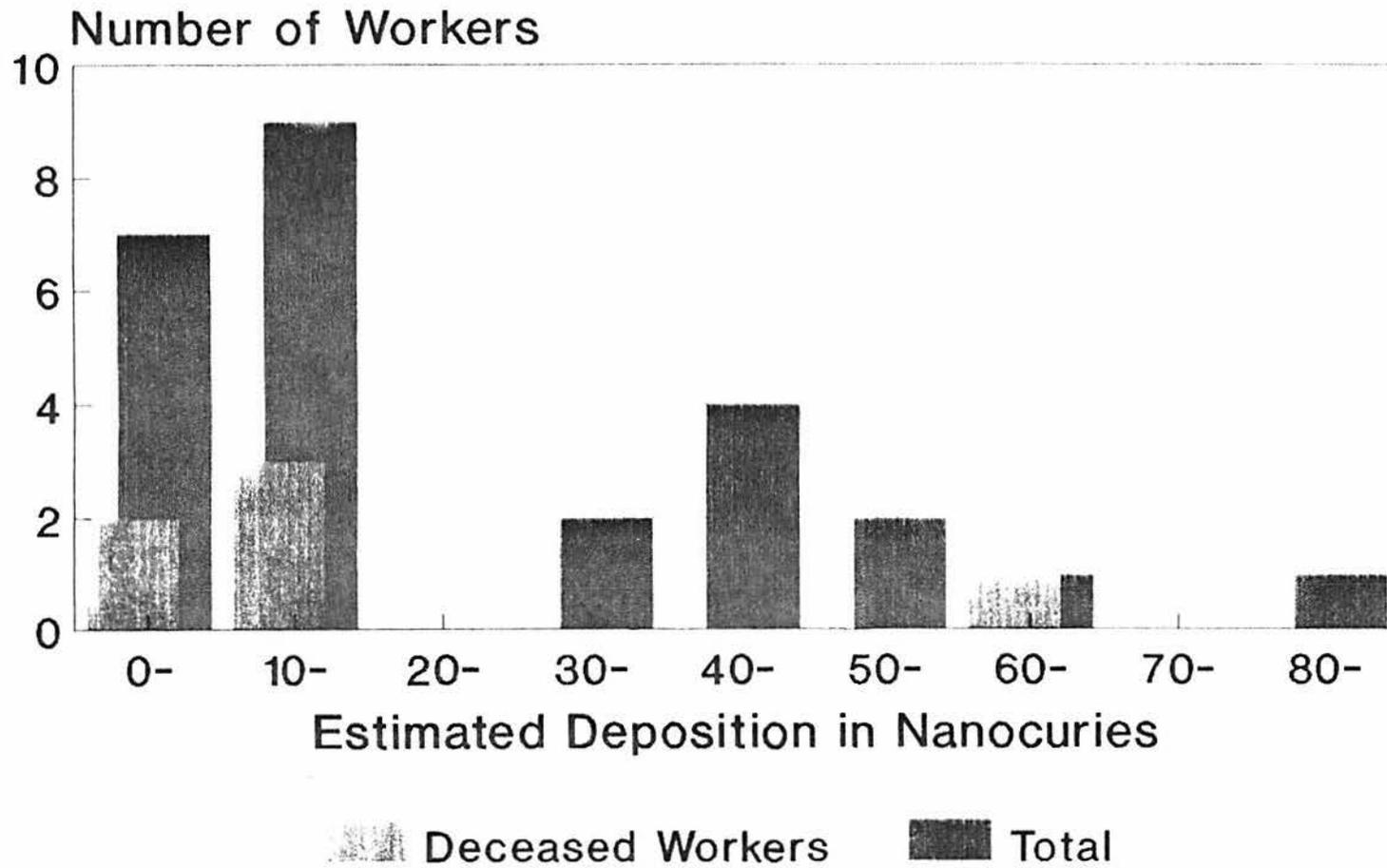
Dose-Response Analyses by Induction Times

- **Directly Adjusted Mortality Rates**
- **Standardized Rate Ratios**

PUBLISHED ARTICLES AND REPORTS

<u>Subject</u>	<u>Number</u>
Los Alamos	
Manhattan District Workers	5
Other Worker Studies	8
County Mortality	2
Mound	
(Submitted Papers)	2
Rocky Flats	6
Pantex	3
Multiple Study Summaries	5
Special Topics	5
Social Security Follow-up, Data Quality Control	
Lost-to-Follow-up Bias, Gastric Ca in NM	

PU DEPOSITION FOR 26 MANHATTAN PROJECT WORKERS AS OF 1989



RISK RATIO OF MORTALITY FROM ALL CAUSES THRU 1987

26 MANHATTAN Pu WORKERS -- 876 LOS ALAMOS WORKERS

Risk Ratio	=	0.68
Maximum Likelihood Estimate		

Approximate 95% CI	=	0.25 - 1.87
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LA Male Workers Matched by 1943-45 Hire Period,
Range of Birthdates, and No Pu Deposition.

DEATHS IN MANHATTAN PROJECT WORKERS EXPOSED TO PLUTONIUM IN 1944-45

<u>ID No.</u>	<u>Age at Death</u>	<u>Year of Death</u>	<u>Cause of Death</u>	<u>Pu (nCi) End</u>	<u>[Max]</u>
15	36	1959	Myocardial infarction	10	[22]
16	52	1975	Trauma from auto/ pedestrian accident	19*	[18]
27	62	1982	Respiratory failure from pneumonia and congestive heart failure	7*	[--]
10	71	1985	Lung cancer	14	[31]
25	70	1988	Lung cancer	4*	[11]
3	66	1989	Lung cancer	69	[163]

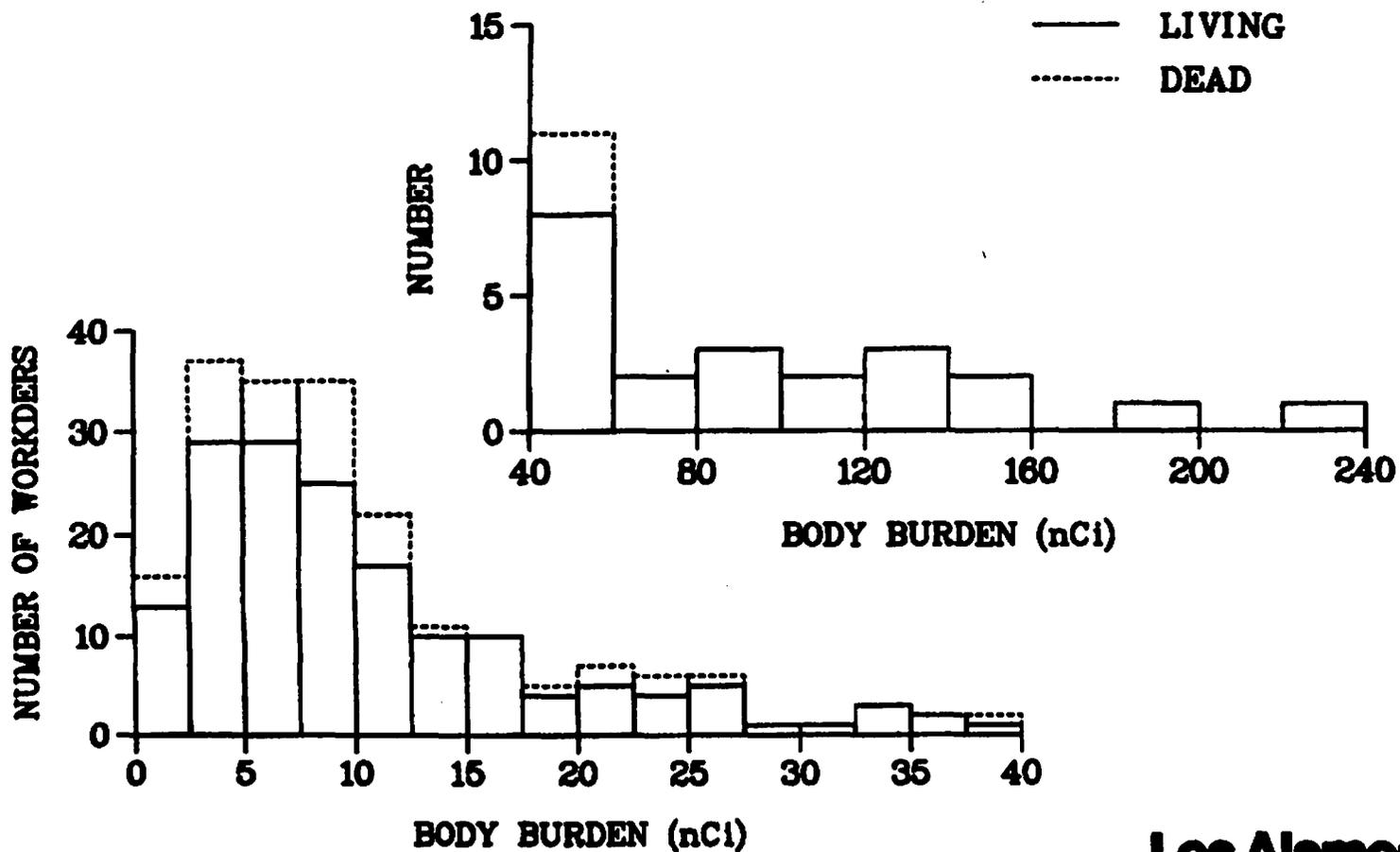
* Estimated by Pu tissue measurements

Mortality in Highest Plutonium-Exposed Workers at Los Alamos Through 1980

Number: 224 White Males
Average Year of Entry: 1947 at Age 31
Comparison Group: U.S. White Males
Follow-up Completeness: 100%

Deaths	Expected	Observed	
All Causes	77	43	56%
All Cancers	15	8	54%
Heart Disease	40	18	45%

DISTRIBUTION OF PLUTONIUM DEPOSITION IN 224 LOS ALAMOS WORKERS



Los Alamos

Potential Excess Lung Cancers Predicted By Gofman Theory in 82 Smokers With Plutonium Depositions

Average age at Exposure	38 yrs
Average Length of Exposure	26 yrs
Lung Cancer Dose at Age 38	7.7 nCi
Average Total Pu Deposition	18 nCi
Lifetime Excess Lung Cancers (excess limited to 1 per person)	48-65
Expected Cases by 1980	9-13
Observed Cases by 1980	0

INCIDENT CANCERS OF LOS ALAMOS LAB

MALE* EMPLOYEES VS NM TUMOR REGISTRY: 1969-1978

<u>Cancers</u>	<u>Observed</u>	<u>Expected</u>	<u>SIR</u>	<u>Exact 95% C.I.</u>
All Cancers	61	100.9	0.60	0.46-0.78
Prostate	10	8.9	1.13	0.54-2.08
Colon	8	7.8	1.03	0.44-2.02
Lung	6	24.2	0.25	0.09-0.54
Lymphosarcoma	5	2.0	2.49	0.81-5.81
Leukemia	4	3.4	1.18	0.32-3.02

* White Males without Hispanics

SMOKING STUDY OF LOS ALAMOS LAB EMPLOYEES FROM 1978 TO 1983

	<u>Males</u>	<u>Females</u>
U. S. Workers*	39.9%	33.2%
New Mexico	31.7%	27.5%
Lab Employees	25.1%	21.6%

*U.S. Health and Human Services Report 85-50207 (1985)

**STANDARDIZED MORTALITY RATIOS* AMONG WHITE MALES
WORKERS AT MOUND FACILITY: 1944-1972**

<u>Cause</u>	<u>Observed</u>	<u>Expected</u>	<u>SMR</u>	<u>90% C.I.</u>
All Causes	987	1056.6	93	89- 99
All Cancers	213	212.2	100	89-113
Lung	82	68.9	119	98-143
Lung, WWII	26	13.7	190	133-264
Post WWII	56	55.3	101	80-126

* Compared with U.S. mortality adjusted for age and year

RELATIVE RISKS* BY POLONIUM-210 DOSE CATEGORIES FOR MOUND WORKERS: 1944-1972

<u>Cause</u>	<u>Doses (mSv)</u>			<u>Trend</u>
	<u>10-99.9</u>	<u>100-999</u>	<u>>1000</u>	
All Causes	1.09	0.79	0.86	- 0.03
All Cancers	1.18	0.86	0.66	- 0.49
Digestive	1.31	1.37	1.00	- 0.04
Lung	1.23	0.54	0.34	- 0.32
Prostate	0.90	0.69	0.00	- 0.55
Blood Cells	0.86	0.20	0.51	- 0.23

* With 10 year Latency Period

STANDARDIZED MORTALITY RATIOS FOR 5,413 WHITE MALES AT ROCKY FLATS: 1952-1979

<u>Cause</u>	<u>Observed</u>	<u>Expected</u>	<u>SMR</u>	90% <u>C.I.</u>
All Causes	409	656.2	62	57-68
All Cancers	95	134.2	71	59-84
Lung	30	46.6	64	46-87
Brain	6	5.0	119	52-236
Unspecified (Brain)	7	1.9	376	177-707
Blood Cells	9	14.1	64	33-111
Circulatory System	193	315.0	61	54-69

Case-Control Study of Brain Cancers in Rocky Flats Employees

Brain Cancer Cases vs 4 Control Persons

3 Control Groups Used

Factors Compared:

1. Plutonium Exposures
2. External Radiation
3. Non-Radiation Hazards

Result: No Occupational Factors Identified

INTERNAL RATE RATIOS* OF EXPOSED VS. NONEXPOSED ROCKY FLATS WHITE MALES

<u>Causes of Death</u>	<u>External</u> <u>(> 10 mSv)</u>		<u>Plutonium</u> <u>(> 2 nCi)</u>	
	<u>I.R.R.</u>	<u>90% C.I.</u>	<u>I.R.R.</u>	<u>90% C.I.</u>
All Causes	1.00	0.84- 1.20	1.33	1.05- 1.68
All Cancers	0.80	0.55- 1.16	1.24	0.75- 2.07
Digestive	1.02	0.52- 2.01	1.68	0.58- 4.71
Lung	0.69	0.36- 1.36	0.61	0.15- 1.91
Brain	0.70	0.19- 2.27	0.35	0.03- 2.10
Unspecified (Brain)	1.73	0.27- 11.69	0.71	0.06- 5.63
Blood Cells	1.18	0.28- 5.00	9.86	1.26- 94.03

* With 5 year Latency Period

**RATE RATIOS FOR LYMPHOPOIETIC/HEMATOPOIETIC CA
FOR ROCKY FLATS BY PU EXPOSURE AND INDUCTION TIME**

<u>Induction Time</u>	<u>Pu Exposed</u> (≥ 2 nCi)	<u>Pu Unexposed</u> (< 2 nCi)	<u>RR</u>	<u>90% C.I.</u>
2 Years	4	1	7.69	0.99-72.93
5 Years	4	1	9.86	1.26-94.03
10 Years	2	3	5.22	0.57-38.80

TENTATIVE CONCLUSIONS FROM EPIDEMIOLOGY STUDIES OF HUMAN HEALTH EFFECTS FROM PLUTONIUM

(Slide 1)

1. Persons Exposed to Pu from 1944-1970 Are Key to these Studies.
2. Pu - Induced Cancers Will Occur Mostly after Long Latent Periods (30 + yrs)
3. Most Likely Pu - Induced Cancers Are Bone, Lymphopoietic, Hematopoietic, and Lung.

TENTATIVE CONCLUSIONS FROM EPIDEMIOLOGY STUDIES OF HUMAN HEALTH EFFECTS FROM PLUTONIUM

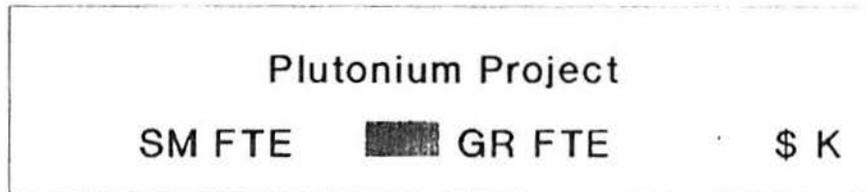
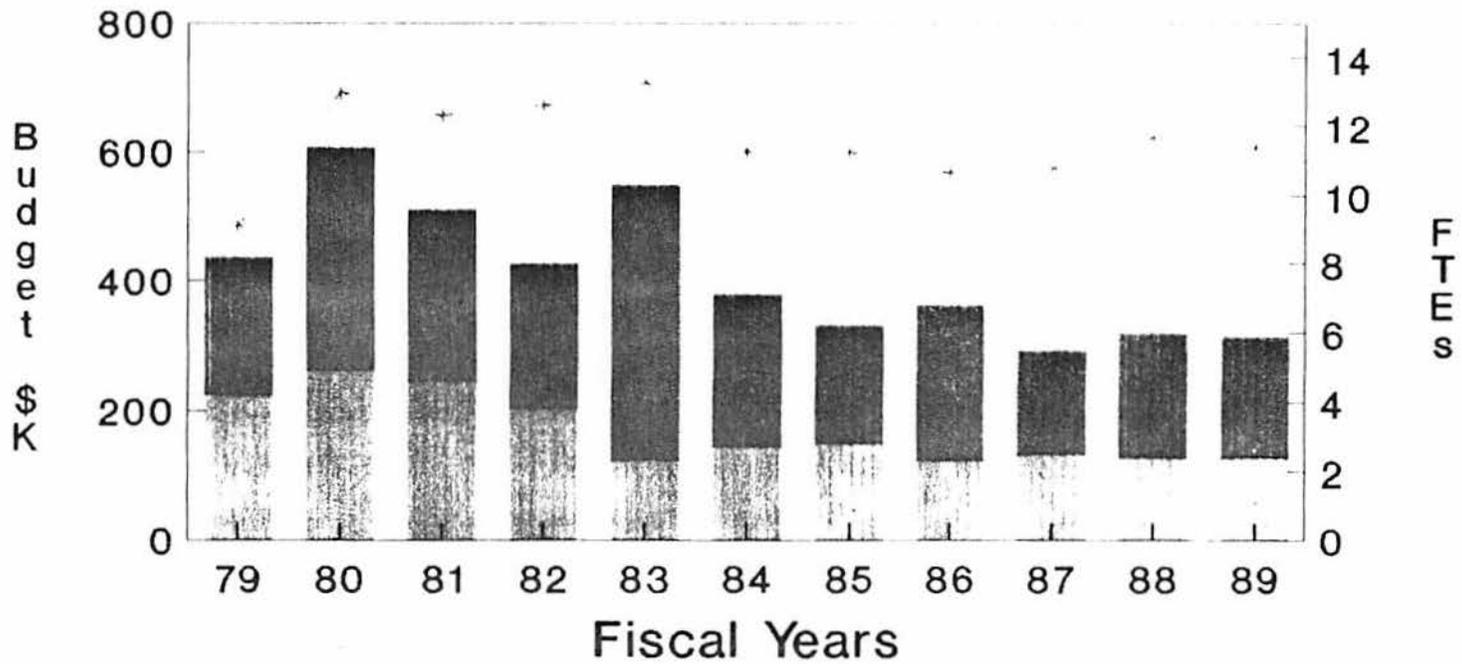
(Slide 2)

4. Confounding May Be Serious from Smoking, Chemicals, and External Radiation (Neutrons).
5. Mortality Rate Ratios Appear Different for Workers Exposed to Pu vs. External Radiation.
6. Risk Estimate of Lung Cancer Induced by Pu Developed by Dr. Gofman is Excessive.

ONGOING AND FUTURE WORK NEEDED

1. Complete Mortality Studies for Mound (Pu), Los Alamos Lab and Zia White Male Cohorts.
2. Reanalyze Updated Rocky Flats Mortality Data.
3. Perform Analysis of Combined Mortality Data on Rocky Flats, Mound, and Los Alamos Cohorts.
4. Conduct Cohort Study of Disease (Morbidity) for Workers with Pu Depositions > 2 nCi.
5. Conduct Case-Control Studies of Specific Findings from Above Studies.
6. Investigate Confounding from Chemical Exposures (e.g., Brain Tumors at Rocky Flats).

STAFFING AND BUDGET FOR PLUTONIUM WORKERS PROJECT



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Los Alamos National Laboratory

November 1989

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