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<b>Submitting Organization</b>	CABOT CORPORATION		
<b>Contractor</b>	HILL TOP RESEARCH LTD		
<b>Document Title</b>	LETTER FROM CABOT CORP TO USEPA REGARDING ACUTE ORAL TOXICITY IN RATS - MEDIAN LETHAL DOSAGE DETERMINATION: CESIUM ACETATE AND CESIUM FORMATE, W/ATTCHMTS (2 RPTS) & DATEL 5/28/99		
<b>Chemical Category</b>	CESIUM ACETATE; CESIUM FORMATE		

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**FYI-99-001358**

MR 23047

May 28, 1999

Via Federal Express

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Attn: FYI Coordinator  
U.S. Environmental Protection Agency  
401 M Street, S.W.  
Washington, D.C. 20460



**8499000019**

Re: TSCA Section 8(e) For Your Information Submission for Cesium Acetate and Cesium Formate

Dear Sir or Madam:

The enclosed acute oral toxicity studies for cesium acetate (CAS No. 3396-11-0) and cesium formate (CAS No. 3495-36-1) are being submitted by Cabot Corporation pursuant to current guidance issued by the Environmental Protection Agency (EPA) indicating EPA's interpretation of section 8(e) of the Toxic Substances Control Act (TSCA). Cabot has made a determination that a significant risk of injury to health or the environment is not presented by the findings in this submission. However, in the interest of sharing information with the EPA, Cabot is voluntarily providing this information as a For Your Information (FYI) submission. We have evaluated our submission of this information carefully because we fully understand that a FYI submission does not satisfy a company's obligation to immediately inform EPA under section 8(e) of TSCA.

**Cesium Acetate**

As detailed in the enclosed submission, cesium acetate was tested in an acute oral toxicity study in rabbits in accordance with EPA Pesticide Assessment Guidelines, Subdivision F (81-1) EPA

Cabot Corporation  
Billerica Technical Center  
157 Concord Road  
P. O. Box 7001  
Billerica, Massachusetts 01821-7001  
(978) 663-3455

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FYI Coordinator

May 28, 1999

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Health Effects Testing Guidelines (TSCA Guideline no. 798.1175) and the OECD Guidelines for Testing of Chemicals No. 401. Groups of 5 female and 5 male rats were treated orally with 1.25, 1.58, 2.0, or 5.0 g/kg undiluted cesium acetate. There were no deaths, no significant clinical signs, and no gross pathological changes noted upon necropsy in the 1.25 g/kg group. Eight of 10 animals in the 1.58 g/kg group and all animals in the 2.0 and 5.0 g/kg groups died. These observations as well as significant clinical signs are summarized in the table below.

Treatment Group (g/kg)	Male Mortality	Female Mortality	Significant Clinical Signs
1.25	0/5	0/5	none
1.58	3/5	3/5	convulsions (also seen in 1 surviving animal), gasping, depression, labored breathing, piloerection, hunched posture
2.0	5/5	5/5	labored breathing, depression, convulsions, piloerection, eyes squinting
5.0	5/5	5/5	gasping, convulsions, labored breathing, depression, excess salivation, coma

Potential signs of neurotoxicity (e.g., convulsions, excess salivation, depression, eyes squinting, and coma) were observed but were generally associated with moribund animals or were transient. For example, for one of the animals in the 1.58 g/kg group that survived the 14-day post-exposure period, convulsions were observed at 0.5 hours post-dosing, and depression was observed through the day 1 observation. During necropsy, findings in animals in the 3 highest treatment groups included hemorrhagic intestines, darkened or mottled lungs/liver/spleen and congested kidneys; however, no pathological changes were noted in the 2 males and 2 females from the 1.58 g/kg group that survived throughout the 14-day observation period.

**Cesium Formate**

As detailed in the enclosed submission, cesium acetate was tested in an acute oral toxicity study in rabbits in accordance with EPA Pesticide Assessment Guidelines, Subdivision F (81-1) EPA Health Effects Testing Guidelines (TSCA Guideline no. 798.1175) and the OECD Guidelines for Testing of Chemicals No. 401. Groups of 5 female and 5 male rats were treated orally with 1.25, 1.58, 2.0, or 5.0 g/kg undiluted cesium formate. There were no deaths and no gross pathological changes noted upon necropsy in the 1.25 and 1.58 g/kg group; however, clinical signs were observed in the 1.58 g/kg group. Nine of 10 animals in the 2.0 g/kg group and all of the animals in the 5.0 g/kg group died. These observations as well as significant clinical signs are summarized in the table below.

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Dose (g/kg)	Male Mortality	Female Mortality	Significant Clinical Signs
1.25	0/5	0/5	none
1.58	0/5	0/5	depression, labored breathing, convulsions (2 animals), piloerection, hunched posture
2.0	5/5	4/5	labored breathing, convulsions, eye squinting, piloerection, masticatory movements, ataxia, depression
5.0	5/5	5/5	depression, labored breathing, convulsions, gasping, piloerection, masticatory movements, excess salivation

Potential signs of neurotoxicity (e.g., convulsions, excess salivation, depression, eyes squinting, masticatory movements, and ataxia) were observed but were generally associated with moribund animals or were transient. For example, in 2 of the animals in the 1.58 g/kg group that survived the 14-day post-exposure period, convulsions were observed up to 1 hour post-dosing, and depression was observed through the day 1 observation. During necropsy, findings in animals in the 2 highest treatment groups included hemorrhagic lungs and intestines, darkened or mottled lungs/liver/spleen and congested kidneys; however, no pathological changes were noted in animals in the 2 lowest treatment groups.

In summary, the potential signs of neurotoxicity are either associated with moribund animals or are transient and are generally not considered reportable under section 8(e). However, because these observations as well as the necropsy findings (e.g., evidence of severe intestinal irritation) were relatively consistent between the cesium acetate and the cesium formate studies, Cabot has chosen to submit these studies for your information.

If you have any questions regarding this submission, please do not hesitate to contact me at 978-670-6965.

Sincerely,

*D. Cooper Rees*

D. Cooper Rees, Ph.D., DABT  
 Director of Toxicology and Corporate Toxicologist

Enclosures (2)

cc: Rosina Toscano, U.S. EPA - Region I  
 John Dubeck, Esq., Keller and Heckman, LLP

**A-06**

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## REPORT FOR

# Acute Oral Toxicity In Rats - Median Lethal Dosage Determination: Cesium Acetate

PROJECT NO. 96-8308-21

FOR

Cabot Corporation  
157 Concord Road  
Billerica, MA 01821-7001

February 4, 1997

BY  
HILL TOP RESEARCH, Ltd.  
(formerly Hill Top Research, Inc.)  
Main and Mill Streets  
Miamiville, OH 45147

**A 07**

**Cabot Corporation**  
**Ref: 96-8308-21**

February 4, 1997

**TITLE:** Acute Oral Toxicity in Rats - Median Lethal Dosage Determination

**TEST MATERIAL:** Cesium Acetate

**AUTHOR:** Kenneth J. Harrod, B.A.

**COMPLETION DATE:** May 30, 1997

**PERFORMING LABORATORY:** Hill Top Research, Ltd. (formerly Hill Top Research, Inc.)  
Main and Mill Streets  
Miamiville, OH 45147

**HILL TOP PROJECT NO.:** 96-8308-21

**SPONSORED BY:** Cabot Corporation  
157 Concord Road  
Billerica, MA 01821-7001

**SUBMITTED BY:**

**DATE SUBMITTED:**

**EPA DATA REQUIREMENT:**

**Cabot Corporation**

**Ref.: 96-8308-21**

**February 4, 1997**

**CONFIDENTIALITY STATEMENT**

**Hill Top Research, Ltd. (formerly Hill Top Research, Inc.) shall not disclose information contained in this report or any other information related to the study which is the subject of this report to third parties without prior written consent of the Study Sponsor.**

A 09

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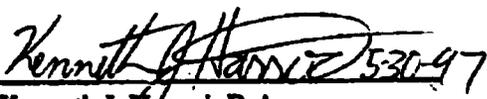
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**COMPLIANCE STATEMENT**

All aspects of this study, as defined in the Protocol, were conducted in accordance with Good Laboratory Practice Standards (40 CFR).

HILL TOP RESEARCH, Ltd.  
(formerly Hill Top Research, Inc.)

 530-97

Kenneth J. Harrod, B.A.  
Study Director  
Acute Toxicology

SPONSOR

---

Howard Marks, Ph.D.  
Consulting Toxicologist  
Cabot Corporation

SUBMITTER

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Howard Marks, Ph.D.  
Consulting Toxicologist  
Cabot Corporation

**Cabot Corporation**

**Ref.: 96-8308-21**

**February 4, 1997**

**HILL TOP RESEARCH, Ltd.**  
**(formerly Hill Top Research, Inc.)**

**IMPORTANT NOTICE**

Hill Top Research, Ltd. (formerly Hill Top Research, Inc.), submits this report with the understanding that no portion of it will be used for advertising or promotion without obtaining our prior written consent to the specific proposed use. When such use is desired we will be glad to assist in the preparation of mutually acceptable excerpts or summaries.

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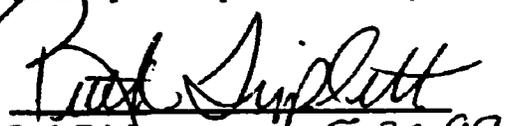
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February 4, 1997

**REPORT APPROVAL**

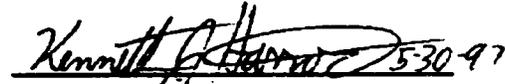
Report Prepared by:

HILL TOP RESEARCH, Ltd.  
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Ruth Triplitt 5-30-97  
Department Secretary  
Acute Toxicology

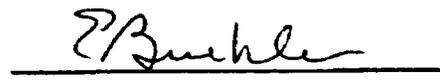
Report Approved by:

HILL TOP RESEARCH, Ltd.  
(formerly Hill Top Research, Inc.)

  
Kenneth J. Harrod, B.A. 5-30-97  
Study Director  
Acute Toxicology

Report Issued by:

HILL TOP RESEARCH, Ltd.  
(formerly Hill Top Research, Inc.)

  
Edwin V. Buehler, Ph.D.  
Vice President, Scientific Affairs  
Acute Toxicology 5.30.97

**CONTRIBUTORS**

The following members of Hill Top Research, Ltd. (formerly Hill Top Research, Inc.) contributed to the conduct and reporting of Project No. 96-8308-21:

<b><u>Name</u></b>	<b><u>Title</u></b>	<b><u>Function</u></b>
E. Buehler, Ph.D.	Vice President, Scientific Affairs Director of Toxicology	Director of Toxicology
J. Kreuzmann, B.A.	Branch Manager II	Manager, Toxicology
T. Morris, B.S.	Department Manager	Manager, Toxicology
L. Goble	Office Manager	Report Supervisor Office Management
E. Darks, B.S.	Study Manager	Conduct of Study
K. Harrod, B.A.	Study Coordinator	Study Director Conduct of Study
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V. Banks	Technician I	Conduct of Study
M. Marshall	Technician I	Conduct of Study
R. Triplett	Department Secretary	Report Preparation

Cabot Corporation

Ref.: 96-8308-2i

February 4, 1997

**SUMMARY/CONCLUSIONS**

The acute oral toxicity of undiluted Cesium Acetate was evaluated in compliance with the conditions specified in the regulation for the enforcement of the Federal Insecticide, Fungicide, and Rodenticide Act (40 CFR), the Toxic Substances Control Act (40 CFR), and the OECD Guidelines.

The test material was administered undiluted to groups of five male and five female Sprague Dawley rats at dose levels of 5.0 g/kg, 2.0 g/kg, 1.58 g/kg, 1.25 g/kg. Following a single oral administration, the animals were observed for 14 days or until death.

Based on the mortality observed, the acute oral LD<sub>50</sub> value was calculated to be 1.55 g/kg with the 95% Confidence Limits of 1.45 g/kg and 1.66 g/kg. Clinical signs noted during the observation period included varying degrees of depression, convulsions, respiratory distress, excess salivation, gross signs of distress, diarrhea, and external staining. Clinical signs were noted at all dose levels investigated. However, the only clinical sign noted at the 1.25 g/kg dose level was fecal stains. All surviving animals exhibited body weight gain at day 14. Gross necropsy findings for animals that died during the observation period included those generally seen in agonal animals indications of gastro-intestinal irritation, and external staining. There were no gross pathological changes observed in animals which survived the 14 day observation period. The test material is classified in FIFRA Toxicity Category III (40 CFR 156, Proposed) based on the response observed following oral administration.

Cabot Corporation  
Ref.: 96-8308-21

February 4, 1997

**METHODS** (See Appendix 1 for Protocol)

**Study Identification**

Hill Top Project Number: 96-8308-21

**Reference Code**

96-8308-21/CABC 2-1-2/06-10-96/ORIGINAL

**Testing Facility**

Hill Top Research, Ltd. (formerly Hill Top Research, Inc.)  
Main and Mill Streets  
Miamiville, OH 45147  
Phone: (513) 831-3114  
Fax: (513) 831-1217

**Sponsor**

Cabot Corporation  
157 Concord Road  
Billerica, MA 01821-7001

**Data Retention**

All records that would be required to reconstruct the study and demonstrate adherence to the Protocol will be maintained. Following completion of the study, the original raw data and the original of the final report will be maintained indefinitely in Hill Top's commercial off-site records storage facility in the form of hard copy to comply with EPA record keeping regulations. The testing facility will retain a copy of these study records in the form of microfilm.

Cabot Corporation

Ref.: 96-8308-21

February 4, 1997

**Study Dates**

Project Initiation Date:	December 26, 1996
Experimental Start Date:	January 7, 1997
Experimental Termination Date:	January 30, 1997
Project Completion Date:	May 30, 1997

**Purpose**

This study was designed to establish an estimated oral median lethal dose ( $LD_{50}$ ) of a test material in rats.

**Applicable Regulations**

This study was conducted according to the Good Laboratory Practice Standards of the EPA's Federal Insecticide, Fungicide, and Rodenticide Act (40 CFR, Part 160). The study was designed to satisfy EPA Pesticide Assessment Guidelines, Subdivision F (81-1) EPA Health Effects Testing Guidelines (TSCA Guideline No. 798.1175) and the OECD Guidelines for Testing of Chemicals (401). This study was placed on the master schedule of EPA regulated studies.

**Quality Assurance**

The Protocol, study conduct, and the final report were audited by the Quality Assurance Unit in accordance with applicable Standard Operating Procedures (SOPs).

**Test Material**

Identification:	Cesium Acetate
Sample Number:	2378-221
Physical Description:	A cloudy liquid.
Storage Conditions:	Room temperature

**Test Material Purity and Stability**

The Sponsor assumes responsibility for purity and stability determinations (including under test conditions). Information on composition and method of synthesis was held by the Sponsor. Analyses of test material for concentration, solubility, homogeneity, and stability were not done by Hill Top Research, Ltd. (formerly Hill Top Research, Inc.).

**Test Material Disposition**

The test material container was weighed when received at the testing facility, and a record of all test material use was maintained. Test material was stored in the original container:

Unused test material was returned at the termination of the study to the Sponsor. The test material was packed in a suitable container to maintain the temperature conditions specified by Sponsor during transit plus an adequate margin of safety for any transit delays.

**Test System Justification**

The rat is the animal model of choice. The test system is designated by federal regulations since it has been used historically for this type of study and allows the data to be compared to that of other compounds.

**Test Animals**

Naive, young adult male and female Sprague-Dawley derived albino rats weighing 198-303 grams were used. The animals were purchased from a vendor who equals or exceeds U.S.D.A. standards even though rats are not regulated animals.

**Animal Supplier**

Harlan Sprague Dawley, Inc.  
P.O. Box 29176  
Indianapolis, IN 46229

**Number of Animals**

Forty animals (five/sex/dose level).

**Housing and Animal Care**

All animals were acclimated to the laboratory for at least five days before being used. Animals were housed in groups of five in wire mesh suspension cages and were supplied Teklad 4% Mouse/Rat Diet and tap water *ad libitum* during both acclimation and test periods except for withholding food overnight prior to dosing. The animal room was maintained on a 12-hour light/12-hour dark cycle and at a temperature of 64-79°F and a relative humidity of 30-70%. There were no contaminants in either the feed or the water that were expected to affect the outcome of this study.

**Animal Selection**

The animals were randomly caged according to Standard Operating Procedures.

**Animal Identification**

Cage cards, individually numbered ear tags, and tail marks with permanent ink were used to identify each rat.

**Test Material Administration**

Overnight prior to dosing, food (but not water) was withheld from the rats. The time of fasting and dosing was documented. Groups of five male and five female rats received the test material by gavage at varying dose levels so that a median lethal dose could be calculated. Four groups were used for the study. The test material was administered undiluted using the bulk density to determine the dose volume. Individual doses were calculated using post-fast body weights. The test material was administered at a dose levels of 5.0 g/kg, 2.0 g/kg, 1.58 g/kg, and 1.25 g/kg.

**Observations**

All surviving animals were observed frequently for gross signs of systemic toxicity and mortality on the day of test material administration and at least twice daily thereafter for a total of fourteen days.

A gross necropsy was performed on all animals which died. In the event of any death, the Sponsor was promptly informed.

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**Interpretation**

The test material was categorized in accordance with 40 CFR 156, Proposed as described below:

1. Category I - Up to and including 50 mg/kg
2. Category II - Greater than 50 mg/kg thru 500 mg/kg
3. Category III - Greater than 500 mg/kg thru 5000 mg/kg
4. Category IV - Greater than 5000 mg/kg

**Body Weights**

Body weights were measured for each animal on the day of dosing, on Day 7 of the observation period, and at the time of necropsy either at the end of the 14 day observation period or following the death of any animal which did not survive this period.

**Termination**

At the end of the 14 day observation period, each surviving rat was euthanized by carbon dioxide inhalation and weighed. A gross necropsy was performed on each animal.

**RESULTS****A. Mortality**

Mortality data for each dose level are presented in Table 1. Based on the cumulative mortality observed during the 14 day observation period following a single oral dose of undiluted Cesium Acetate the acute oral LD<sub>50</sub> value was calculated to be 1.55 g/kg with 95% Confidence Intervals of 1.45 g/kg and 1.66 g/kg.

**B. Clinical Observations**

Clinical observations are summarized in Tables 2-9. Clinical signs noted during the observation period included varying degrees of depression, convulsions, respiratory distress, excess salivation, gross signs of distress, diarrhea, and external staining. Clinical signs were noted at all dose levels investigated. However, the only clinical sign noted at the 1.25 g/kg dose level was fecal stains.

**C. Body Weight**

Body weight data are summarized in Tables 10-13. All animals exhibiting body weight gain at Day 14.

**D. Gross Necropsy**

Gross necropsy findings are summarized in Tables 14-17. Gross necropsy findings for animals that died during the observation period included those generally seen in agonal animals indications of gastro-intestinal irritation, and external staining. There were no gross pathological changes observed in animals which survived the 14 day observation period.

**E. Conclusion**

The test material, Cesium Acetate, is classified in Toxicity Category III based on the response observed following oral administration.

**PROTOCOL DEVIATIONS**

The Protocol was followed without deviation.

**REFERENCE**

Litchfield, J.T. Jr., and Wilcoxon, F. (1949). J. Pharmacol. Exp. Ther., 96, 99-113.

**Table 1**  
**Cumulative Mortality Data for Male and Female Rats**  
**Treated Orally with Undiluted Cesium Acetate**

Dosage (Undiluted)	Cumulative Number of Deaths									
	Number of Animals	First Several Hours Following Treatment (Day 0)	Day After Treatment							
			1	2	3	4	5	7	13	14
<b>Males</b>										
5.0 g/kg	5	5	ND	ND	ND	ND	ND	ND	ND	ND
2.0 g/kg	5	5	ND	ND	ND	ND	ND	ND	ND	ND
1.58 g/kg	5	2	3	3	3	3	3	3	3	3
1.25 g/kg	5	0	0	0	0	0	0	0	0	0
<b>Females</b>										
5.0 g/kg	5	5	ND	ND	ND	ND	ND	ND	ND	ND
2.0 g/kg	5	1	3	5	ND	ND	ND	ND	ND	ND
1.58 g/kg	5	1	3	3	3	3	3	3	3	3
1.25 g/kg	5	0	0	0	0	0	0	0	0	0

ND = No Data. All animals had died by this point.





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February 4, 1997

Table 3 (Cont.)

Clinical Observations for Female Rats Treated Orally with Undiluted Cesium Acetate at a Dose Level of 5.0 g/kg

		Animal Number 6-451, 7-452, 8-453, 9-454, 10-455 (9)																		
Clinical Sign	Post dose	Post-dose Timing (-Hours)			Time	Study Day														
		0.25	0.50	0.50		1	2	3	4	5	6	7	8	9	10	11	12	13	14	
Diarrhea			10		A															
					P															
Death			6-9	10	A															
					P															

Post Dose = Day of Dosing.

A = First Observation.

P = Second Observation.

B



Cabot Corporation  
 Ref: 96-8308-21

February 4, 1997

**Table 4 (Cont.)**  
**Clinical Observations for Male Rats Treated Orally with Undiluted Cesium Acetate at a Dose Level of 2.0 g/kg**

Animal Number 1-486, 2-487, 3-488, 4-489, 5-490 (♂)																			
Clinical Sign	Post dose	Post-dose Timing (~Hours)		Time	Study Day														
		0.25	0.50		2.25	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Severely depressed			4	A															
Piloerection			4	P															
Comatose			5	A															
Death				P															

Post Dose = Day of Dosing.      A = first Observation.      P = Second Observation.



Table 5 (Cont.)

Clinical Observations for Female Rats Treated Orally with Undiluted Cesium Acetate at a Dose Level of 2.0 g/kg

Animal Number 6-491, 7-*, 8-493, 9-494, 10-495 (♀)																						
Clinical Sign	Post dose	Post-dose Timing (~Hours)			Time	Study Day																
		0.25	0.50	2.0		1	2	3	4	5	6	7	8	9	10	11	12	13	14			
Urine stains				7,8	A	6,8																
					P	6,8																
Piloerection				6,10	A																	
					P																	
Eye squinting					A	6,8																
					P	6,8																
Death				9	A	7,10 6,8																
					P																	

Post Dose = Day of Dosing. A = First Observation. P = Second Observation. \* = Ear tag lost prior to dosing.

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Cabot Corporation  
 Ref.: 96-8308-21

**Table 6**  
**Clinical Observations for Male Rats Treated Orally with Undiluted Cesium Acetate at a Dose Level of 1.58 g/kg**

Clinical Sign	Post dose	Post-dose Timing (-Hours)				Time	Animal Number 1-506, 2-507, 3-538, 4-569, 5-510 (♂)																				
		0.50	0.75	2.75	5.0		Study Day																				
							1	2	3	4	5	6	7	8	9	10	11	12	13	14							
Normal behavior	1-5					A		1,3	1,3	1,3	1,3	1,3	1,3	1,3	1,3	1,3	1,3	1,3	1,3	1,3	1,3	1,3	1,3	1,3	1,3	1,3	1,3
Convulsions		1				A		1,3	1,3	1,3	1,3	1,3	1,3	1,3	1,3	1,3	1,3	1,3	1,3	1,3	1,3	1,3	1,3	1,3	1,3	1,3	1,3
Grasping		1,5	5		4	A																					
Moderately depressed		1,5	2,5	1,4	1,3, 4	P																					
Fecal stains		1,5	1,2, 4,5	1,3,4	1,3, 4	A																					
Slightly depressed		2-4	3	3		P																					







**Table 9**  
**Clinical Observations for Female Rats Treated Orally with Undiluted Cesium Acetate at a Dose Level of 1.25 g/kg**

Animal Number 6-471, 7-*, 8-473, 9-474, 10-475 (9)																				
Clinical Sign	Post dose	Post-dose Timing (-Hours)		Time	Study Day															
		2.0	3.75		6.0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
Normal behavior	6-10	6-10	6-10	6-10	A	6-10	6-10	6-10	6-10	6-10	6-10	6-10	6-10	6-10	6-10	6-10	6-10	6-10	6-10	
		6	6	9	P	6-10	6-10	6-10	6-10	6-10	6-10	6-10	6-10	6-10	6-10	6-10	6-10	6-10	6-10	6-10
Fecal stains					A															
					P															
Death					A															
					P															

Post Dose = Day of Dosing.    A = First Observation.    P = Second Observation.    \* = Ear tag lost prior to dosing.

Table 10

**Body Weight Data in Male and Female Rats Treated Orally  
with Undiluted Cesium Acetate at a Dose Level of 5.0 g/kg**

Animal Number	Sex	Body Weight (grams)			Body Weight Change (grams) Day 0 - 14
		Day 0	Day 7	Day 14	
1 - 446	M	258	253 <sup>a</sup>	ND	NA
2 - 447	M	238	234 <sup>a</sup>	ND	NA
3 - 448	M	255	250 <sup>a</sup>	ND	NA
4 - *	M	243	239 <sup>a</sup>	ND	NA
5 - *	M	256	252 <sup>a</sup>	ND	NA
<b>Mean</b>		250	NA	ND	NA
<b>Standard Deviation</b>		9	NA	ND	NA
6 - 451	F	212	210 <sup>a</sup>	ND	NA
7 - 452	F	198	195 <sup>a</sup>	ND	NA
8 - 453	F	213	209 <sup>a</sup>	ND	NA
9 - 454	F	210	206 <sup>a</sup>	ND	NA
10 - 455	F	215	210 <sup>a</sup>	ND	NA
<b>Mean</b>		210	NA	ND	NA
<b>Standard Deviation</b>		7	NA	ND	NA

<sup>a</sup>Body weight taken at death and was not used in the calculation of mean body weight or standard deviation.

ND = No data.

NA = Not applicable.

\* = Eartag lost prior to dosing.

Table 11

**Body Weight Data in Male and Female Rats Treated Orally  
with Undiluted Cesium Acetate at a Dose Level of 2.0 g/kg**

Animal Number	Sex	Body Weight (grams)			Body Weight Change (grams) Day 0 - 14
		Day 0	Day 7	Day 14	
1 - 486	M	297	290 <sup>a</sup>	ND	NA
2 - 487	M	283	265 <sup>a</sup>	ND	NA
3 - 488	M	287	273 <sup>a</sup>	ND	NA
4 - 489	M	280	272 <sup>a</sup>	ND	NA
5 - 490	M	293	284 <sup>a</sup>	ND	NA
<b>Mean</b>		288	NA	ND	NA
<b>Standard Deviation</b>		7	NA	ND	NA
6 - 491	F	231	205 <sup>a</sup>	ND	NA
7 - *	F	236	219 <sup>a</sup>	ND	NA
8 - 493	F	230	204 <sup>a</sup>	ND	NA
9 - 494	F	222	218 <sup>a</sup>	ND	NA
10 - 495	F	210	191 <sup>a</sup>	ND	NA
<b>Mean</b>		226	NA	ND	NA
<b>Standard Deviation</b>		10	NA	ND	NA

<sup>a</sup>Body weight taken at death and was not used in the calculation of mean body weight or standard deviation.

ND = No data.

NA = Not applicable.

\* = Eartag lost prior to dosing.

Table 12

**Body Weight Data in Male and Female Rats Treated Orally  
with Undiluted Cesium Acetate at a Dose Level of 1.58 g/kg**

Animal Number	Sex	Body Weight (grams)			Body Weight Change (grams) Day 0 - 14
		Day 0	Day 7	Day 14	
1 - 506	M	292	309	325	33
2 - 507	M	288	270 <sup>a</sup>	ND	NA
3 - 538	M	303	338	359	56
4 - 509	M	300	270 <sup>a</sup>	ND	NA
5 - 510	M	293	285 <sup>a</sup>	ND	NA
<b>Mean</b>		295	324	342	45
<b>Standard Deviation</b>		6	21	24	16
6 - 511	F	224	202 <sup>a</sup>	ND	NA
7 - 512	F	228	249	253	25
8 - 513	F	222	231	229	7
9 - 514	F	203	183 <sup>a</sup>	ND	NA
10 - 515	F	228	213 <sup>a</sup>	ND	NA
<b>Mean</b>		221	240	241	16
<b>Standard Deviation</b>		10	13	17	13

<sup>a</sup> Body weight taken at death and was not used in the calculation of mean body weight or standard deviation.

ND = No data.

NA = Not applicable.

Table 13

**Body Weight Data in Male and Female Rats Treated Orally  
with Undiluted Cesium Acetate at a Dose Level of 1.25 g/kg**

Animal Number	Sex	Body Weight (grams)			Body Weight Change (grams) Day 0 - 14
		Day 0	Day 7	Day 14	
1 - 466	M	264	314	344	80
2 - 467	M	263	332	329	66
3 - 468	M	275	334	356	22
4 - 469	M	265	308	332	67
5 - 470	M	266	328	354	88
<b>Mean</b>		267	323	343	65
<b>Standard Deviation</b>		5	12	12	26
6 - 471	F	222	235	238	16
7 - *	F	219	252	263	44
8 - 473	F	227	255	268	41
9 - 474	F	211	234	238	27
10 - 475	F	214	240	249	35
<b>Mean</b>		219	243	251	33
<b>Standard Deviation</b>		6	10	14	11

\* = Eartag lost prior to dosing.

Table 14

**Gross Necropsy Findings for Male and Female Rats Treated Orally with Undiluted Cesium Acetate at a Dose Level of 5.0 g/kg**

Animal Number	Study Day	Necropsy Findings	
		External	Internal
<b>Males</b>			
1 - 446	0	Saliva and fecal stains.	Stomach and intestines contain a large amount of clear yellow fluid; kidneys congested. No other gross pathological changes noted.
2 - 447	0	Saliva stains.	Stomach and intestines contain a large amount of clear yellow fluid; intestines hemorrhagic; kidneys congested. No other gross pathological changes noted.
3 - 448	0	None.	Stomach and intestines contain a large amount of clear yellow fluid; kidneys congested. No other gross pathological changes noted.
4 - *	0	Saliva and urine stains.	Stomach and intestines contain a large amount of yellow fluid; lungs mottled; intestines reddened; kidneys congested. No other gross pathological changes noted.
5 - *	0	Urine stains.	Lungs pale; stomach and intestines contain a large amount of clear yellow fluid. No other gross pathological changes noted.
<b>Females</b>			
6 - 451	0	Saliva and urine stains.	Lungs, liver, spleen mottled; stomach and intestines contain a large amount of clear yellow fluid. No other gross pathological changes noted.
7 - 452	0	Saliva stains.	Stomach and intestines contain a large amount of clear yellow fluid. No other gross pathological changes noted.
8 - 453	0	Saliva stains.	Lungs and liver mottled; kidneys congested; stomach and intestines contain a large amount of clear yellow fluid. No other gross pathological changes noted.
9 - 454	0	None.	Lungs mottled; kidneys congested; stomach and intestines contain a large amount of clear yellow fluid; intestines reddened. No other gross pathological changes noted.
10 - 455	0	Saliva and fecal stains.	Kidneys congested; stomach and intestines contain a large amount of clear yellow fluid. No other gross pathological changes noted.

\* = Eartag lost prior to dosing.

Table 15

**Gross Necropsy Findings for Male and Female Rats Treated Orally  
with Undiluted Cesium Acetate at a Dose Level of 2.0 g/kg**

Animal Number	Study Day	Necropsy Findings	
		External	Internal
<b>Males</b>			
1 - 486	0	Fecal stains; dried red material around eyes.	Stomach and intestines contain a large amount of clear yellow fluid. No other gross pathological changes noted.
2 - 487	0	Fecal stains.	Kidneys pale and congested; stomach and intestines contain a large amount of clear yellow fluid. No other gross pathological changes noted.
3 - 488	0	Fecal stains; dried red material around eyes.	Stomach and intestines contain a large amount of clear yellow fluid. No other gross pathological changes noted.
4 - 489	0	Fecal stains.	Stomach and intestines contain a large amount of clear yellow fluid. No other gross pathological changes noted.
5 - 490	0	Fecal stains.	Spleen darkened; stomach and intestines contain a large amount of clear yellow fluid. No other gross pathological changes noted.
<b>Females</b>			
6 - 491	2	Saliva stains on muzzle; severe fecal and urine stains.	Lungs reddened; liver, spleen and heart darkened; kidneys darkened and congested; stomach full with a blood like material; intestines full with a viscous blood like material. No other gross pathological changes noted.
7 - *	1	Saliva, fecal, and urine stains.	Spleen darkened; kidneys pale and congested; red fluid in stomach and intestines; moderate amount of postmortem autolysis. No other gross pathological changes noted.
8 - 493	2	Saliva stains on muzzle; severe fecal and urine stains.	Lungs, liver, and spleen darkened; stomach distended with gas, containing a small amount of brown-red fluid; intestines distended with gas in areas and areas contain a brown-red fluid; kidneys darkened and congested. No other gross pathological changes noted.
9 - 494	0	None.	Kidneys congested; stomach and intestines contain a large amount of clear red fluid. No other gross pathological changes noted.
10 - 495	1	Urine stains.	Spleen darkened; stomach and intestines contain clear yellow fluid. No other gross pathological changes noted.

\* = Eartag lost prior to dosing.

Table 16

**Gross Necropsy Findings for Male and Female Rats Treated Orally  
with Undiluted Cesium Acetate at a Dose Level of 1.58 g/kg**

Animal Number	Study Day	Necropsy Findings	
		External	Internal
<b>Males</b>			
1 - 506	14	None.	No gross pathological changes noted.
2 - 507	0	Fecal and urine stains; saliva stains on muzzle.	Liver and lungs darkened; stomach full with a red-yellow fluid; intestines full with a clear yellow fluid; left kidney pale and congested. No other gross pathological changes noted.
3 - 538	14	None.	No gross pathological changes noted.
4 - 509	1	Red stains around eyes and on muzzle; urine and fecal stains.	Lungs pale; liver mottled; spleen darkened; kidneys pale and congested; stomach and intestines slightly distended with gas; stomach contains a small amount of dark red fluid; intestines contain a large amount of cloudy brown-red fluid. No other gross pathological changes noted.
5 - 510	0	Fecal stains.	Lungs reddened; kidneys pale and congested; stomach contains a large amount of clear brown-red fluid; intestines greatly distended with a large amount of cloudy brown-red fluid. No other gross pathological changes noted.
<b>Females</b>			
6 - 511	1	Urine and saliva stains.	Lungs reddened; liver, spleen, and kidneys mottled; intestines and stomach contain a moderate amount of red-brown fluid; kidneys congested. No other gross pathological changes noted.
7 - 512	14	None.	No gross pathological changes noted.
8 - 513	14	None.	No gross pathological changes noted.
9 - 514	1	Urine stains	Lungs reddened; stomach full with a red-brown fluid; intestines contain a small amount of brown-red paste like material. No other gross pathological changes noted.
10 - 515	0	Urine and fecal stains; reddish fluid around urogenital area; saliva stains on muzzle.	Lungs pale; liver darkened; stomach greatly distended with a dark red-brown fluid; intestines distended in areas with red-brown fluid. No other gross pathological changes noted.

**Table 17**

**Gross Necropsy Findings for Male and Female Rats Treated Orally  
with Undiluted Cesium Acetate a Dose Level of 1.25 g/kg**

Animal Number	Study Day	Necropsy Findings	
		External	Internal
<b>Males</b>			
1 - 466	14	None.	No gross pathological changes noted.
2 - 467	14	None.	No gross pathological changes noted.
3 - 468	14	None.	No gross pathological changes noted.
4 - 469	14	None.	No gross pathological changes noted.
5 - 470	14	None.	No gross pathological changes noted.
<b>Females</b>			
6 - 471	14	None.	No gross pathological changes noted.
7 - *	14	None.	No gross pathological changes noted.
8 - 473	14	None.	No gross pathological changes noted.
9 - 474	14	None.	No gross pathological changes noted.
10 - 475	14	None.	No gross pathological changes noted.

\* = Eartag lost prior to dosing.

Cabot Corporation

Ref.: 96-8308-21

February 4, 1997

**QUALITY ASSURANCE STATEMENT**

This study was inspected in accordance with the SOP's of Hill Top Research, Ltd. (formerly Hill Top Research, Inc.). QA findings derived from the inspection(s) during the conduct of the study and from the inspection of the final report are documented and have been reported to the appropriate personnel.

Date of Inspection	Date Findings Reported to Study Director	Date Findings Reported to Management
January 7, 1997	January 10, 1997	January 13, 1997

Protocol	Date Reviewed
Final	December 27, 1996

Report	Date Reviewed
Draft	February 6, 1997
Final	May 27, 1997

Reviewed by:

  
\_\_\_\_\_  
Quality Assurance Auditor

5/21/97  
Date

  
\_\_\_\_\_  
Ralph Anderson, B.S.  
Director of Quality Assurance

5/27/97  
Date

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**D 05**

**Cabot Corporation**  
**Ref.: 96-8308-21**

**February 4, 1997**

**Appendix 1**

**Copy of Protocol**

**(Total Number of Pages - 6)**

96-8308-21  
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PROTOCOL

**ACUTE ORAL TOXICITY IN RATS - MEDIAN LETHAL DOSAGE DETERMINATION**

**Study Identification**

Hill Top Project Number: 96-8308-21

**Reference Code**

96-8308-21/CABC 2-1-2/06-10-96/ORIGINAL

**Testing Facility**

Hill Top Research, Inc.  
Main and Mill Streets  
Miamiville, OH 45147  
Phone: (513) 831-3114  
Fax: (513) 831-1217

**Sponsor**

Cabot Corporation  
157 Concord Road  
Billerica, MA 01821-7001

**Sponsor's Representative**

Mr. Howard Marks  
Phone: (508) 670-6978  
Fax: (508) 670-6955

**Study Director**

Kenneth J. Harrod, B.A.

**Acute Oral Toxicity in Rats - Median Lethal Dosage Determination**

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**Data Retention**

All records that would be required to reconstruct the study and demonstrate adherence to the Protocol will be maintained. Following completion of the study, the original raw data and the original of the final report will be maintained indefinitely in Hill Top's commercial off-site records storage facility in the form of hard copy to comply with EPA record keeping regulations. The testing facility will retain a copy of these study records in the form of microfilm.

**Proposed Study Dates**

Proposed Experimental Start Date: January 7, 1997  
Proposed Experimental Termination Date: January 30, 1997  
Proposed Draft Report Date: February 14, 1997

**Purpose**

This study is designed to establish an estimated oral median lethal dose (LD<sub>50</sub>) of a test material in rats.

**Institutional Animal Care and Use Committee**

Any subsequent modification of this method which is believed will significantly increase the stress to the animals involved will be presented to the Chairman of Hill Top's Institutional Animal Care and Use Committee or a designate for deliberation.

No analgesics may be given to the animals participating on this study without the express approval of the Study Director and the Sponsor. If approved, administration would be as defined by SOP'S 21-ANIC-14-0560F and 21-ANIC-14-0570A. A decision to euthanize animals prior to the completion of the standard observation period can be determined by the Study Director and the Sponsor.

The Sponsor, to the best of their knowledge, assures that this project is not an unnecessary duplication of previous experiments and that no feasible alternative test methodology is available. The Director of Toxicology at Hill Top Research, Inc., after an extensive and continuing literature review, also has determined that there are no validated alternatives to this method and concurs with the Society of Toxicology Position Paper (Fund. Appl. Toxicol. [1989] 13, 621-623).

**Applicable Regulations**

This study will be conducted according to the Good Laboratory Practice Standards of the EPA's Federal Insecticide, Fungicide, and Rodenticide Act (40 CFR, Part 160). The study is designed to satisfy EPA Pesticide Assessment Guidelines, Subdivision F (81-1) EPA Health Effects Testing Guidelines (TSCA Guideline No. 798.1175) and the OECD Guidelines for Testing of Chemicals (401). This study will be placed on the master schedule of regulated studies.

**Acute Oral Toxicity in Rats - Median Lethal Dosage Determination**

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**Quality Assurance**

The Protocol, study conduct, and the final report will be audited by the Quality Assurance Unit in accordance with applicable Standard Operating Procedures (SOPs).

**Test Material**

Identification: Cesium Acetate  
Lot Number: 2378-221  
Physical Description: A cloudy liquid  
Storage Conditions: Room Temperature

**Test Material Purity and Stability**

The Sponsor assumes responsibility for purity and stability determinations (including under test conditions). Information on composition and method of synthesis will be held by the Sponsor. Analyses of test material/vehicle for concentration, solubility, homogeneity, and stability will not be done by Hill Top Research, Inc.

**Test Material Disposition**

The test material container(s) will be weighed when received at the testing facility, and a record of all test material use will be maintained. Test material will be stored in the original container(s).

Unused test material will be returned at the termination of the study to the Sponsor. The test material(s) shall be packed in a suitable container to maintain the temperature conditions specified by Sponsor during transit plus an adequate margin of safety for any transit delays.

General safety precautions as required by the laboratory's policies and procedures will be followed. The Sponsor will supply basic toxicity data on the test materials to be used in this study. However, the toxicity of test materials is often not well characterized, and the contractor should be conservative in setting safety procedures.

**Test System Justification**

The rat is the animal model of choice. The test system is designated by federal regulations since it has been used historically for this type of study and will allow the data to be compared to that of other compounds.

**Test Animals**

Naive young adult male and female Sprague-Dawley derived albino rats weighing 200-300 grams will be used. Animals which fall outside of this range may be used at the discretion of the Study Director. The animals will be purchased from a vendor who equals or exceeds U.S.D.A. standards even though rats are not regulated animals.

**Acute Oral Toxicity in Rats - Median Lethal Dosage Determination**

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**Animal Supplier**

Harian Sprague Dawley, Inc.  
P.O. Box 29176  
Indianapolis, IN 46229

**Number of Animals**

Forty animals (five/sex/dose level) with additional animals used as necessary.

**Housing and Animal Care**

All animals will be acclimated to the laboratory for at least five days before being used. Animals will be housed in groups of five in wire mesh suspension cages and will be supplied Teklad 4% Mouse/Rat Diet and tap water ad libitum during both acclimation and test periods except for withholding food overnight prior to dosing. The animal room will be maintained on a 12-hour light/12-hour dark cycle and at a temperature of 64-79°F and a relative humidity of 30-70%. Slight variations from these ranges will not result in a Protocol deviation. There are no contaminants in either the feed or the water that would be expected to affect the outcome of this study.

**Animal Selection**

The animals will be randomly caged according to Standard Operating Procedures.

**Animal Identification**

Cage cards, individually numbered ear tags, and tail marks with permanent ink will be used to identify each rat.

**Test Material Administration**

Overnight prior to dosing, food (but not water) will be withheld from the rats. The time of fasting and dosing will be documented. Groups of five male and five female rats will receive the test material by gavage at varying dose levels so that a median lethal dose may be calculated. Generally four groups will be used for the study. The test material will be administered undiluted using the bulk density to determine the dose volume. Individual doses will be calculated using post-fast body weights. The dose levels utilized will be documented in the raw data.

**Observations**

All animals will be observed frequently for gross signs of systemic toxicity and mortality on the day of test material administration, and at least twice daily thereafter for a total of fourteen days.

A gross necropsy will be performed on any animal which dies. In the event of any death, the Sponsor will be promptly informed.

**Acute Oral Toxicity in Rats - Median Lethal Dosage Determination**

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**Interpretation**

The test material will be categorized in accordance with 40 CFR 156, Proposed as described below:

1. Category I - Up to and including 50 mg/kg
2. Category II - Greater than 50 mg/kg thru 500 mg/kg
3. Category III - Greater than 500 mg/kg thru 5000 mg/kg
4. Category IV - Greater than 5000 mg/kg

**Body Weights**

Body weights will be measured for each animal on the day of dosing, on Day 7 of the observation period, and at the time of necropsy either at the end of the fourteen day observation period or following the death of any animal which does not survive this period.

**Termination**

At the end of the fourteen day observation period, each surviving rat will be euthanized by carbon dioxide inhalation and weighed. A gross necropsy will be performed on each animal.

**Report**

A draft report will be issued and will include but not necessarily be limited to the following:

The study objectives and procedures;

Identification of the test system;

Identification of the test material, its descriptions, and appropriate characteristics;

Concentration of the test material and, if appropriate, the diluent used;

The dose level(s) incorporated in the study;

Initial, interim, and final body weights;

Critical observations directly related to the interpretation of the test;

The estimated LD<sub>50</sub> value, calculated by the method of Litchfield and Wilcoxon, and the 95% confidence limits;

Justifiable conclusions drawn from the study;

Appropriate classification of the test material.

**Notice**

This study will be run according to good laboratory practices. If it becomes necessary to make changes in the approved Protocol, the revisions and reasons for change will be documented, reported to the Sponsor, and will become part of the permanent file for that study. Similarly, the Sponsor will be notified as soon as is practical whenever an event occurs that is unexpected and could have an effect on the validity of the study.

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Hill Top Project Number: 96-8308-21 <sup>2.8</sup>

Acute Oral Toxicity in Rats - Median Lethal Dosage Determination

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**PROTOCOL APPROVAL FORM**

Toxicology Division  
Hill Top Research, Inc.

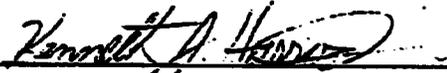
Protocol Title

Acute Oral Toxicity in Rats - Median  
Lethal Dosage Determination

Reference Code

96-8308-21/CABC 2-1-2/  
06-10-96/ORIGINAL

Protocol Approved By (Hill Top Research, Inc.):



Kenneth J. Harold, B.A.  
Study Director

12-26-96

Date

Protocol Approved By (Sponsor):



Mr. Howard Marks  
Sponsor's Representative

HOWARD MARKS, Ph.D.  
CONSULTING TOXICOLOGIST  
FOR CABOT CORPORATION

2 JAN 97

Date

Cabot Corporation

Sponsor's Name

157 Concord Road  
Billerica, MA 01821-7001

Sponsor's Address

D. 12

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RECEIVED  
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1999 JUN -4 AM 10:54

**REPORT FOR**

**Acute Oral Toxicity In Rats -  
Median Lethal Dosage Determination: Cesium Formate**

**PROJECT NO. 96-8305-21**

**FOR**

**Cabot Corporation  
157 Concord Road  
Billerica, MA 01821-7001**

**February 3, 1997**

**BY  
HILL TOP RESEARCH, Ltd.  
(formerly Hill Top Research, Inc.)  
Main and Mill Streets  
Miamiville, OH 45147**

**D: 13,****Cabot Corporation****Ref: 96-8305-21****February 3, 1997****TITLE: Acute Oral Toxicity in Rats - Median Lethal Dosage Determination****TEST MATERIAL: Cesium Formate****AUTHOR: Kenneth J. Harrod, B.A.****COMPLETION DATE: May 27, 1997****PERFORMING LABORATORY: Hill Top Research, Ltd. (formerly Hill Top Research, Inc.)  
Main and Mill Streets  
Miamiville, OH 45147****HILL TOP PROJECT NO.: 96-8305-21****SPONSORED BY: Cabot Corporation  
157 Concord Road  
Billerica, MA 01821-7001****SUBMITTED BY:****DATE SUBMITTED:****EPA DATA REQUIREMENT:**

**D:14**

Cabot Corporation

Ref.: 96-8305-21

February 3, 1997

**CONFIDENTIALITY STATEMENT**

Hill Top Research, Ltd. (formerly Hill Top Research, Inc.) shall not disclose information contained in this report or any other information related to the study which is the subject of this report to third parties without prior written consent of the Study Sponsor.

**E.01**

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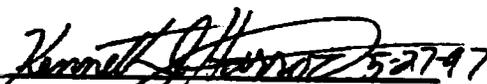
**Ref.: 96-8305-21**

**February 3, 1997**

**COMPLIANCE STATEMENT**

**All aspects of this study, as defined in the Protocol, were conducted in accordance with Good Laboratory Practice Standards (40 CFR).**

**HILL TOP RESEARCH, Ltd.  
(formerly Hill Top Research, Inc.)**

  
**Kenneth J. Harrod, B.A.  
Study Director  
Acute Toxicology**

**SPONSOR**

---

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for Cabot Corporation**

**SUBMITTER**

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**Howard Marks, Ph.D.  
Consulting Toxicologist  
for Cabot Corporation**

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**HILL TOP RESEARCH, Ltd.**  
(formerly Hill Top Research, Inc.)

**IMPORTANT NOTICE**

Hill Top Research, Ltd. (formerly Hill Top Research, Inc.), submits this report with the understanding that no portion of it will be used for advertising or promotion without obtaining our prior written consent to the specific proposed use. When such use is desired we will be glad to assist in the preparation of mutually acceptable excerpts or summaries.

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**REPORT APPROVAL**

Report Prepared by:

HILL TOP RESEARCH, Ltd.  
(formerly Hill Top Research, Inc.)

  
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Department Secretary  
Acute Toxicology

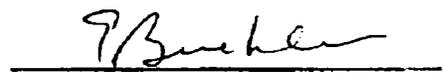
Report Approved by:

HILL TOP RESEARCH, Ltd.  
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Kenneth J. Harrod, B.A.  
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**E 07**

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**CONTRIBUTORS**

The following members of Hill Top Research, Ltd. (formerly Hill Top Research, Inc.) contributed to the conduct and reporting of Project No. 96-8305-21:

<b><u>Name</u></b>	<b><u>Title</u></b>	<b><u>Function</u></b>
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E 08

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### SUMMARY/CONCLUSIONS

The acute oral toxicity of undiluted Cesium Formate was evaluated in compliance with the conditions specified in the regulation for the enforcement of the Federal Insecticide, Fungicide, and Rodenticide Act (40 CFR), the EPA Pesticide Assessment Guidelines, Subdivision F (81-1), the Health Effects Testing Guidelines (TSCA Guideline No. 798.1175), and the OECD Guidelines for Testing of Chemicals (401).

The test material was administered undiluted to groups of five male and five female Sprague Dawley rats at a dose levels of 5.0 g/kg, 2.0 g/kg, 1.58 g/kg, 1.25 g/kg. Following a single oral administration, the animals were observed for 14 days or until death.

Based on the mortality observed, the acute oral LD<sub>50</sub> value was calculated to be 1.78 g/kg with the 95% Confidence Limits of 0.20 g/kg and 15.61 g/kg. Clinical signs noted during the observation period included varying degrees of depression, convulsions, respiratory distress, ataxia, excessive salivation, masticatory movements, gross signs of distress, and external staining. Clinical signs were noted at all dose levels investigated. However, the only clinical sign noted at the 1.25 g/kg dose level was fecal stains. All surviving animals exhibited body weight gain at day 14. Gross necropsy findings for animals that died during the observation period included those generally seen in agonal animals, indications of gastro-intestinal irritation, and external staining. There were no gross pathological changes observed in animals which survived the 14 day observation period. The test material is classified in FIFRA Toxicity Category III (40 CFR 156, Proposed) based on the response observed following oral administration.

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**METHODS** (See Appendix 1 for Protocol)

**Study Identification**

Hill Top Project Number: 96-8305-21

**Reference Code**

96-8305-21/CABC 2-1-2/06-10-96/ORIGINAL

**Testing Facility**

Hill Top Research, Ltd. (formerly Hill Top Research, Inc.)

Main and Mill Streets

Miamiville, OH 45147

Phone: (513) 831-3114

Fax: (513) 831-1217

**Sponsor**

Cabot Corporation

157 Concord Road

Billerica, MA 01821-7001

**Data Retention**

All records that would be required to reconstruct the study and demonstrate adherence to the Protocol will be maintained. Following completion of the study, the original raw data and the original of the final report will be maintained indefinitely in Hill Top's commercial off-site records storage facility in the form of hard copy to comply with EPA record keeping regulations. The testing facility will retain a copy of these study records in the form of microfilm.

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**Study Dates**

Project Initiation Date:	December 26, 1996
Experimental Start Date:	January 7, 1997
Experimental Termination Date:	January 30, 1997
Project Completion Date:	May 27, 1997

**Purpose**

This study was designed to establish an estimated oral median lethal dose (LD<sub>50</sub>) of a test material in rats.

**Applicable Regulations**

This study was conducted according to the Good Laboratory Practice Standards of the EPA's Federal Insecticide, Fungicide, and Rodenticide Act (40 CFR, Part 160). The study was designed to satisfy EPA Pesticide Assessment Guidelines, Subdivision F (81-1) EPA Health Effects Testing Guidelines (TSCA Guideline No. 798.1175) and the OECD Guidelines for Testing of Chemicals (401). This study was placed on the master schedule of EPA regulated studies.

**Quality Assurance**

The Protocol, study conduct, and the final report were audited by the Quality Assurance Unit in accordance with applicable Standard Operating Procedures (SOPs).

**Test Material**

Identification:	Cesium Formate
Sample Number:	2380-211
Physical Description:	A clear, colorless liquid.
Storage Conditions:	Room temperature

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### **Test Material Purity and Stability**

**The Sponsor assumes responsibility for purity and stability determinations (including under test conditions). Information on composition and method of synthesis was held by the Sponsor. Analyses of test material for concentration, solubility, homogeneity, and stability were not done by Hill Top Research, Ltd. (formerly Hill Top Research, Inc.).**

### **Test Material Disposition.**

**The test material container was weighed when received at the testing facility, and a record of all test material use was maintained. Test material was stored in the original container.**

**Unused test material was returned at the termination of the study to the Sponsor. The test material was packed in a suitable container to maintain the temperature conditions specified by Sponsor during transit plus an adequate margin of safety for any transit delays.**

### **Test System Justification**

**The rat is the animal model of choice. The test system is designated by federal regulations since it has been used historically for this type of study and allows the data to be compared to that of other compounds.**

### **Test Animals**

**Naive, young adult male and female Sprague-Dawley derived albino rats weighing 205-302 grams were used. The animals were purchased from a vendor who equals or exceeds U.S.D.A. standards even though rats are not regulated animals.**

### **Animal Supplier**

**Harlan Sprague Dawley, Inc.  
P.O. Box 29176  
Indianapolis, IN 46229**

### **Number of Animals**

**Forty animals (five/sex/dose level).**

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### **Housing and Animal Care**

All animals were acclimated to the laboratory for at least five days before being used. Animals were housed in groups of five in wire mesh suspension cages and were supplied Teklad 4% Mouse/Rat Diet and tap water ad libitum during both acclimation and test periods except for withholding food overnight prior to dosing. The animal room was maintained on a 12-hour light/12-hour dark cycle and at a temperature of 64-79°F and a relative humidity of 30-70%. There were no contaminants in either the feed or the water that were expected to affect the outcome of this study.

### **Animal Selection**

The animals were randomly caged according to Standard Operating Procedures.

### **Animal Identification**

Cage cards, individually numbered ear tags, and tail marks with permanent ink were used to identify each rat.

### **Test Material Administration**

Overnight prior to dosing, food (but not water) was withheld from the rats. The time of fasting and dosing was documented. Groups of five male and five female rats received the test material by gavage at varying dose levels so that a median lethal dose could be calculated. Four groups were used for the study. The test material was administered undiluted using the bulk density to determine the dose volume. Individual doses were calculated using post-fast body weights. The test material was administered at a dose levels of 5.0 g/kg, 2.0 g/kg, 1.58 g/kg, and 1.25 g/kg.

### **Observations**

All surviving animals were observed frequently for gross signs of systemic toxicity and mortality on the day of test material administration and at least twice daily thereafter for a total of fourteen days.

A gross necropsy was performed on all animals which died. In the event of any death, the Sponsor was promptly informed.

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**Interpretation**

The test material was categorized in accordance with 40 CFR 156, Proposed as described below:

1. Category I - Up to and including 50 mg/kg
2. Category II - Greater than 50 mg/kg thru 500 mg/kg
3. Category III - Greater than 500 mg/kg thru 5000 mg/kg
4. Category IV - Greater than 5000 mg/kg

**Body Weights**

Body weights were measured for each animal on the day of dosing, on Day 7 of the observation period, and at the time of necropsy either at the end of the fourteen day observation period or following the death of any animal which did not survive this period.

**Termination**

At the end of the fourteen day observation period, each surviving rat was euthanized by carbon dioxide inhalation and weighed. A gross necropsy was performed on each animal.

**RESULTS****A. Mortality**

Mortality data for each dose level are presented in Table 1. Based on the cumulative mortality observed during the 14 day observation period following a single oral dose of undiluted Cesium Formate the acute oral LD<sub>50</sub> value was calculated to be 1.78 g/kg with 95% Confidence Intervals of 0.20 g/kg and 15.61 g/kg.

**B. Clinical Observations**

Clinical observations are summarized in Tables 2-9. Clinical signs noted during the observation period included varying degrees of depression, convulsions, respiratory distress, ataxia, excessive salivation, masticatory movements, gross signs of distress, and external staining. Clinical signs were noted at all dose levels investigated. However, the only clinical sign noted at the 1.25 g/kg dose level was fecal stains.

**C. Body Weight**

Body weight data are summarized in Tables 10-13. All surviving animals exhibited body weight gain at Day 14.

**D. Gross Necropsy**

Gross necropsy findings are summarized in Tables 14-17. Gross necropsy findings for animals that died during the observation period included those generally seen in agonal animals, indications of gastro-intestinal irritation, and external staining. There were no gross pathological changes observed in animals which survived the 14 day observation period.

**E. Conclusion**

The test material, Cesium Formate, is classified in Toxicity Category III based on the response observed following oral administration.

**PROTOCOL DEVIATIONS**

The Protocol was followed without deviation.

**REFERENCE**

Litchfield, J.T. Jr., and Wilcoxon, F. (1949). J. Pharmacol. Exp. Ther., 96, 99-113.

**Table 1**  
**Cumulative Mortality Data for Male and Female Rats**  
**Treated Orally with Undiluted Cesium Formate**

Dosage (Undiluted)	Cumulative Number of Deaths									
	Number of Animals	First Several Hours Following Treatment (Day 0)	Day After Treatment							
			1	2	3	4	5	7	13	14
<b>Males</b>										
5.0 g/kg	5	4	5	ND						
2.0 g/kg	5	5	ND	ND	ND	ND	ND	ND	ND	ND
1.58 g/kg	5	0	0	0	0	0	0	0	0	0
1.25 g/kg	5	0	0	0	0	0	0	0	0	0
<b>Females</b>										
5.0 g/kg	5	4	5	ND						
2.0 g/kg	5	2	4	4	4	4	4	4	4	4
1.58 g/kg	5	0	0	0	0	0	0	0	0	0
1.25 g/kg	5	0	0	0	0	0	0	0	0	0

ND = No Data. All animals had died by this point.



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**Table 3**  
**Clinical Observations for Female Rats Treated Orally with**  
**Undiluted Cesium Formate at a Dose Level of 5.0 g/kg**

Clinical Sign	Post dose	Post-dose Timing (-Hours)		Time	Study Day													
		0.25	0.50		1	2	3	4	5	6	7	8	9	10	11	12	13	14
		7	7															
Slightly depressed	6-10			A														
Moderately depressed		7	7	A														
Labored breathing	6-10	6-10	7	A														
Gasping	6	7-10		A														
Severely depressed		6,8-10	8,10	A														
Convulsions		6,7,9		A														
Masticatory movements		8		A														

Post Dose = Day of Dosing.      A = First Observation.      P = Second Observation.  
 \* = Ear tag lost prior to dosing.



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**Table 4**  
**Clinical Observations for Male Rats Treated Orally with Undiluted Cesium Formate at a Dose Level of 2.0 g/kg**

Clinical Sign	Post dose	Post-dose Timing (~Hours)			Time	Study Day													
		0.25	1.25	3.0		1	2	3	4	5	6	7	8	9	10	11	12	13	14
Normal behavior	1-5				A														
Labored breathing		1-5	3,4		P														
Convulsions		1,2,5			A														
Eye Squinting		1,4,5			P														
Piloerection		1,4,5			A														
Masticatory movements		1,5			P														

**Table 4 (Cont.)**  
**Clinical Observations for Male Rats Treated Orally with Undiluted Cesium Formate at a Dose Level of 2.0 g/kg**

Animal Number 1-476, 2-477, 3-478, 4-479, 5-480 (♂)																			
Clinical Sign	Post dose	Post-dose Timing (~Hours)			Time	Study Day													
		0.25	1.25	3.0		1	2	3	4	5	6	7	8	9	10	11	12	13	14
Ataxia		5			A														
Slightly depressed		2,3			P														
Moderately depressed		1,4,5	3,4		A														
Fecal Stains			4		P														
Death	0	0	1,2,5	3,4	A														
					P														

Post Dose = Day of Dosing. A = First Observation. P = Second Observation.

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**Table 5**  
**Clinical Observations for Female Rats Treated Orally with Undiluted Cesium Formate at a Dose Level of 2.0 g/kg**

Clinical Sign	Post dose	Post-dose Timing (-Hours)			Time	Study Day													
		0.25	0.75	3.0		1	2	3	4	5	6	7	8	9	10	11	12	13	14
Normal behavior	6-10				A	7	7	7	7	7	7	7	7	7	7	7	7	7	7
Eye Squinting		6,8		6,9	A														
Labored breathing		6,8-10	6,8-10	8,9	A														
Slightly depressed		7-10	7	7	A														
Moderately depressed		6	8,10	8,9	P														
Masticatory movements		10			P														



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**Table 6**  
**Clinical Observations for Male Rats Treated Orally with**  
**Undiluted Cesium Formate at a Dose Level of 1.58 g/kg**

Animal Number 1-096, 2-097, 3-098, 4-099, 5-0*																							
Clinical Sign	Post dose	Post-dose Timing (-Hours)					Time	Study Day															
		0.75	1.0	3.0	5.0			1	2	3	4	5	6	7	8	9	10	11	12	13	14		
		1.5	1.5						1-5	1-5	1-5	1-5	1-5	1-5	1-5	1-5	1-5	1-5	1-5	1-5	1-5	1-5	
Normal behavior	1-5					A																	
Slightly depressed		2,4	2	1,2, 4,5	1,2, 4,5	A																	
Fecal Stains		2-4	2-4	2-5	1-5	A																	
Moderately depressed						P																	
Labored breathing		3	3,4	3	3	A																	
Convulsions		3	3,4			A																	

\* = Ear tag lost prior to dosing.



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**Table 7**  
**Clinical Observations for Female Rats Treated Orally with**  
**Undiluted Cesium Formate at a Dose Level of 1.58 g/kg**

Clinical Sign	Post dose	Post-dose Timing (-Hours)				Time	Study Day													
		0.50	0.75	3.0	5.0		1	2	3	4	5	6	7	8	9	10	11	12	13	14
Normal behavior	6-10	6-10				A	6-10	6-10	6-10	6-10	6-10	6-10	6-10	6-10	6-10	6-10	6-10	6-10	6-10	6-10
Slightly depressed			6-10	7-10	7-10	A	6-10													
Fecal stains				6-10	6-10	P	6-10													
Urine Stains				6-10	6-10	P	7													
Moderately depressed					6	A	6-10	7	7	6,7										
Piloerection					6-8, 10	P	6-10	7	7	6,7										
Labored breathing				6-10	6-10	A														
						P														

Animal Number 6-501, 7-502, 8-503, 9-504, 10-505 (9)

Post Dose = Day of Dosing. A = First Observation. P = Second Observation.





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**Table 9**  
**Clinical Observations for Female Rats Treated Orally with**  
**Undiluted Cesium Formate at a Dose Level of 1.25 g/kg**

Animal Number 6-461, 7-462, 8-463, 9-464, 10-465 (9)																					
Clinical Sign	Post dose	Post-dose Timing (~Hours)			Time	Study Day															
		2.0	3.75	6.0		1	2	3	4	5	6	7	8	9	10	11	12	13	14		
Normal behavior	6-10	6-10	6-10	6-10	A	6-10	6-10	6-10	6-10	6-10	6-10	6-10	6-10	6-10	6-10	6-10	6-10	6-10	6-10	6-10	
					P	6-10	6-10	6-10	6-10	6-10	6-10	6-10	6-10	6-10	6-10	6-10	6-10	6-10	6-10	6-10	6-10
Death					A																
					P																

Post Dose = Day of Dosing.      A = First Observation.      P = Second Observation.

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Table 10

**Body Weight Data in Male and Female Rats Treated Orally  
with Undiluted Cesium Formate at a Dose Level of 5.0 g/kg**

Animal Number	Sex	Body Weight (grams)			Body Weight Change (grams) Day 0 - 14
		Day 0	Day 7	Day 14	
1 - 436	M	265	249 <sup>a</sup>	ND	NA
2 - 437	M	261	256 <sup>a</sup>	ND	NA
3 - 438	M	257	252 <sup>a</sup>	ND	NA
4 - 439	M	251	246 <sup>a</sup>	ND	NA
5 - 440	M	255	251 <sup>a</sup>	ND	NA
Mean		258	NA	ND	NA
Standard Deviation		5	NA	ND	NA
6 - 441	F	225	221 <sup>a</sup>	ND	NA
7 - 442	F	209	198 <sup>a</sup>	ND	NA
8 - 443	F	209	203 <sup>a</sup>	ND	NA
9 - *	F	222	218 <sup>a</sup>	ND	NA
10 - 445	F	212	204 <sup>a</sup>	ND	NA
Mean		215	NA	ND	NA
Standard Deviation		8	NA	ND	NA

<sup>a</sup>Body weight taken at death and was not used in the calculation of mean body weight or standard deviation.

ND = No data.

NA = Not applicable.

\* = Ear tag lost prior to dosing.

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Table 11

**Body Weight Data in Male and Female Rats Treated Orally  
with Undiluted Cesium Formate at a Dose Level of 2.0 g/kg**

Animal Number	Sex	Body Weight (grams)			Body Weight Change (grams) Day 0 - 14
		Day 0	Day 7	Day 14	
1 - 476	M	289	283 <sup>a</sup>	ND	NA
2 - 477	M	284	277 <sup>a</sup>	ND	NA
3 - 478	M	276	269 <sup>a</sup>	ND	NA
4 - 479	M	285	270 <sup>a</sup>	ND	NA
5 - 480	M	288	283 <sup>a</sup>	ND	NA
<b>Mean</b>		284	NA	ND	NA
<b>Standard Deviation</b>		5	NA	ND	NA
6 - 481	F	212	196 <sup>a</sup>	ND	NA
7 - 482	F	213	232	228	NA
8 - 483	F	221	201 <sup>a</sup>	ND	NA
9 - 484	F	205	191 <sup>a</sup>	ND	NA
10 - 485	F	215	202 <sup>a</sup>	ND	NA
<b>Mean</b>		213	232	228	NA
<b>Standard Deviation</b>		6	NA <sup>b</sup>	NA <sup>b</sup>	NA

<sup>a</sup>Body weight taken at death and was not used in the calculation of mean body weight or standard deviation.

<sup>b</sup>Not calculated due to only one body weight.

ND = No data.

NA = Not applicable.

Table 12

**Body Weight Data in Male and Female Rats Treated Orally  
with Undiluted Cesium Formate at a Dose Level of 1.58 g/kg**

Animal Number	Sex	Body Weight (grams)			Body Weight Change (grams) Day 0 - 14
		Day 0	Day 7	Day 14	
1 - 496	M	295	328	347	52
2 - 497	M	287	312	322	35
3 - 498	M	284	302	334	50
4 - 499	M	302	333	351	49
5 - *	M	292	305	337	45
<b>Mean</b>		292	316	338	46
<b>Standard Deviation</b>		7	14	11	7
6 - 501	F	218	234	240	22
7 - 502	F	221	236	243	22
8 - 503	F	228	258	260	32
9 - 504	F	232	265	258	26
10 - 505	F	223	245	244	21
<b>Mean</b>		224	248	249	25
<b>Standard Deviation</b>		6	14	9	6

\* = Eartag lost prior to dosing.

Table 13

**Body Weight Data in Male and Female Rats Treated Orally  
with Undiluted Cesium Formate at a Dose Level of 1.25 g/kg**

Animal Number	Sex	Body Weight (grams)			Body Weight Change (grams) Day 0 - 14
		Day 0	Day 7	Day 14	
1 - 456	M	261	293	310	49
2 - 457	M	255	298	320	65
3 - 458	M	265	316	340	75
4 - 459	M	261	308	329	68
5 - 460	M	276	333	364	88
<b>Mean</b>		264	310	333	69
<b>Standard Deviation</b>		8	16	21	14
6 - 461	F	212	228	232	20
7 - 462	F	215	249	252	37
8 - 463	F	216	233	254	38
9 - 464	F	219	259	261	42
10 - 465	F	233	243	249	16
<b>Mean</b>		219	242	250	31
<b>Standard Deviation</b>		8	12	11	12

Table 14

**Gross Necropsy Findings for Male and Female Rats Treated Orally with  
Undiluted Cesium Formate at a Dose Level of 5.0 g/kg**

Animal Number	Study Day	Necropsy Findings	
		External	Internal
<b>Males</b>			
1 - 436	1	Urine stains.	Kidneys congested; stomach contains large amount of clear red fluid; intestines contain large amount of clear yellow fluid. Slight post mortem autolysis present. No other gross pathological changes noted.
2 - 437	0	None.	Lungs reddened; stomach and intestines contain large amount of clear yellow fluid; intestines hemorrhagic. No other gross pathological changes noted.
3 - 438	0	None.	Lungs hemorrhagic; stomach and intestines contain large amount of clear yellow fluid; intestines reddened. No other gross pathological changes noted.
4 - 439	0	None.	Lungs reddened; stomach and intestines contain large amount of clear yellow fluid. No other gross pathological changes noted.
5 - 440	0	None.	Stomach and intestines contain large amount of clear yellow fluid. No other gross pathological changes noted.
<b>Females</b>			
6 - 441	0	Saliva stains.	Liver mottled; kidneys congested; stomach and intestines contain large amount of clear yellow fluid; intestines reddened. No other gross pathological changes noted.
7 - 442	1	Saliva stains; urine stains.	Liver mottled; spleen darkened; kidneys congested; stomach contains large amount of clear red fluid; intestines contain large amount of tan fluid. Slight post mortem autolysis present. No other gross pathological changes noted.
8 - 443	0	Saliva stains; urine stains.	Lungs reddened; kidneys congested; stomach and intestines contain large amount of clear yellow fluid. No other gross pathological changes noted.
9 - *	0	None.	Stomach and intestines contain large amount of clear yellow fluid; intestines reddened. No other gross pathological changes noted.
10 - 445	0	Urine stains.	Stomach and intestines contain tan fluid. No other gross pathological changes noted.

\* = Eartag lost prior to dosing.

Table 15

**Gross Necropsy Findings for Male and Female Rats Treated Orally  
with Undiluted Cesium Formate at a Dose Level of 2.0 g/kg**

Animal Number	Study Day	Necropsy Findings	
		External	Internal
<b>Males</b>			
1 - 476	0	Fecal stains.	Spleen darkened; stomach contains large amount of clear yellow fluid; intestines contain large amount of reddish brown fluid. No other gross pathological changes noted.
2 - 477	0	Fecal stains.	Spleen darkened; stomach contains large amount of a clear yellow fluid; intestines contain a small amount of a clear red fluid. No other gross pathological changes noted.
3 - 478	0	Fecal stains.	Top of spleen darkened; left kidney congested; stomach contains large amount of clear yellow fluid; intestines contain small amount of clear red fluid. No other gross pathological changes noted.
4 - 479	0	Fecal stains.	Spleen darkened; kidneys congested; stomach and intestines contain a large amount of clear red fluid. No other gross pathological changes noted.
5 - 480	0	Fecal stains.	Top of spleen darkened; kidneys congested; stomach and intestines contain large amount of clear red fluid. No other gross pathological changes noted.
<b>Females</b>			
6 - 481	0	Urine and fecal stains.	Kidneys congested; stomach contains large amount of clear red fluid; intestines contain a small amount of clear red fluid. No other gross pathological changes noted.
7 - 482	14	None.	No gross pathological changes noted.
8 - 483	1	Urine and fecal stains.	Liver darkened; spleen darkened; kidneys congested; stomach and intestines contain red fluid. Slight post mortem autolysis present. No other gross pathological changes noted.
9 - 484	1	Urine stains.	Spleen darkened; kidneys congested; stomach contains large amount of red fluid; intestines contain red fluid. Slight post mortem autolysis present. No other gross pathological changes noted.
10 - 485	0	Urine and fecal stains.	Kidneys pale and congested; stomach contains a large amount of clear red fluid; intestines contain a small amount of clear red fluid. No other gross pathological changes noted.

Table 16

**Gross Necropsy Findings for Male and Female Rats Treated Orally  
with Undiluted Cesium Formate at a Dose Level of 1.58 g/kg**

Animal Number	Study Day	Necropsy Findings	
		External	Internal
<b>Males</b>			
1 - 496	14	None.	No gross pathological changes noted.
2 - 497	14	None.	No gross pathological changes noted.
3 - 498	14	None.	No gross pathological changes noted.
4 - 499	14	None.	No gross pathological changes noted.
5 - *	14	None.	No gross pathological changes noted.
<b>Females</b>			
6 - 501	14	None.	No gross pathological changes noted.
7 - 502	14	None.	No gross pathological changes noted.
8 - 503	14	None.	No gross pathological changes noted.
9 - 504	14	None.	No gross pathological changes noted.
10 - 505	14	None.	No gross pathological changes noted.

\* = Eartag lost prior to dosing.

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February 3, 1997

Table 17

**Gross Necropsy Findings for Male and Female Rats Treated Orally  
with Undiluted Cesium Formate a Dose Level of 1.25 g/kg**

Animal Number	Study Day	Necropsy Findings	
		External	Internal
<b>Males</b>			
1 - 456	14	None.	No gross pathological changes noted.
2 - 457	14	None.	No gross pathological changes noted.
3 - 458	14	None.	No gross pathological changes noted.
4 - 459	14	None.	No gross pathological changes noted.
5 - 460	14	None.	No gross pathological changes noted.
<b>Females</b>			
6 - 461	14	None.	No gross pathological changes noted.
7 - 462	14	None.	No gross pathological changes noted.
8 - 463	14	None.	No gross pathological changes noted.
9 - 464	14	None.	No gross pathological changes noted.
10 - 465	14	None.	No gross pathological changes noted.

Cabot Corporation

Ref.: 96-8305-21

February 3, 1997

**QUALITY ASSURANCE STATEMENT**

This study was inspected in accordance with the SOP's of Hill Top Research, Ltd. (formerly Hill Top Research, Inc.). QA findings derived from the inspection(s) during the conduct of the study and from the inspection of the final report are documented and have been reported to the appropriate personnel.

Date of Inspection	Date Findings Reported to Study Director	Date Findings Reported to Management
January 7, 1997	January 10, 1997	January 13, 1997

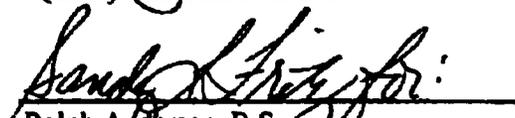
Protocol	Date Reviewed
Final	December 27, 1996

Report	Date Reviewed
Draft	February 6, 1997
Final	May 27, 1997

Reviewed by:

  
 Quality Assurance Auditor

5/27/97  
 Date

  
 Ralph Anderson, B.S.  
 Director of Quality Assurance

5/27/97  
 Date

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**Cabot Corporation**  
**Ref.: 96-8305-21**

**February 3, 1997**

**Appendix 1**

**Copy of Protocol**

**(Total Number of Pages - 7)**

96-8305-21  
p.3



PROTOCOL

**ACUTE ORAL TOXICITY IN RATS - MEDIAN LETHAL DOSAGE DETERMINATION**

**Study Identification**

Hill Top Project Number: 96-8305-21

**Reference Code**

96-8305-21/CABC 2-1-2/06-10-96/ORIGINAL

**Testing Facility**

Hill Top Research, Inc.  
Main and Mill Streets  
Miamiville, OH 45147  
Phone: (513) 831-3114  
Fax: (513) 831-1217

**Sponsor**

Cabot Corporation  
157 Concord Road  
Billerica, MA 01821-7001

**Sponsor's Representative**

Mr. Howard Marks  
Phone: (508) 670-6978  
Fax: (508) 670-6955

**Study Director**

Kenneth J. Harrod, B.A.

**Acute Oral Toxicity in Rats - Median Lethal Dosage Determination**

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**Data Retention**

All records that would be required to reconstruct the study and demonstrate adherence to the Protocol will be maintained. Following completion of the study, the original raw data and the original of the final report will be maintained indefinitely in Hill Top's commercial off-site records storage facility in the form of hard copy to comply with EPA record keeping regulations. The testing facility will retain a copy of these study records in the form of microfilm.

**Proposed Study Dates**

Proposed Experimental Start Date: January 7, 1997  
Proposed Experimental Termination Date: January 30, 1997  
Proposed Draft Report Date: February 14, 1997

**Purpose**

This study is designed to establish an estimated oral median lethal dose (LD<sub>50</sub>) of a test material in rats.

**Institutional Animal Care and Use Committee**

Any subsequent modification of this method which is believed will significantly increase the stress to the animals involved will be presented to the Chairman of Hill Top's Institutional Animal Care and Use Committee or a designate for deliberation.

No analgesics may be given to the animals participating on this study without the express approval of the Study Director and the Sponsor. If approved, administration would be as defined by SOP'S 21-ANIC-14-0560F and 21-ANIC-14-0570A. A decision to euthanize animals prior to the completion of the standard observation period can be determined by the Study Director and the Sponsor.

The Sponsor, to the best of their knowledge, assures that this project is not an unnecessary duplication of previous experiments and that no feasible alternative test methodology is available. The Director of Toxicology at Hill Top Research, Inc., after an extensive and continuing literature review, also has determined that there are no validated alternatives to this method and concurs with the Society of Toxicology Position Paper (Fund. Appl. Toxicol. [1989] 13, 621-623).

**Applicable Regulations**

This study will be conducted according to the Good Laboratory Practice Standards of the EPA's Federal Insecticide, Fungicide, and Rodenticide Act (40 CFR, Part 160). The study is designed to satisfy EPA Pesticide Assessment Guidelines, Subdivision F (81-1) EPA Health Effects Testing Guidelines (TSCA Guideline No. 798.1175) and the OECD Guidelines for Testing of Chemicals (401). This study will be placed on the master schedule of regulated studies.

**CONT:**

**Acute Oral Toxicity in Rats - Median Lethal Dosage Determination**

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**Quality Assurance**

The Protocol, study conduct, and the final report will be audited by the Quality Assurance Unit in accordance with applicable Standard Operating Procedures (SOPs).

**Test Material**

Identification: Cesium Formate  
Lot Number: 2380-211  
Physical Description: A clear, colorless liquid.  
Storage Conditions: Room Temperature

**Test Material Purity and Stability**

The Sponsor assumes responsibility for purity and stability determinations (including under test conditions). Information on composition and method of synthesis will be held by the Sponsor. Analyses of test material/vehicle for concentration, solubility, homogeneity, and stability will not be done by Hill Top Research, Inc.

**Test Material Disposition**

The test material container(s) will be weighed when received at the testing facility, and a record of all test material use will be maintained. Test material will be stored in the original container(s).

Unused test material will be returned at the termination of the study to the Sponsor. The test material(s) shall be packed in a suitable container to maintain the temperature conditions specified by Sponsor during transit plus an adequate margin of safety for any transit delays.

General safety precautions as required by the laboratory's policies and procedures will be followed. The Sponsor will supply basic toxicity data on the test materials to be used in this study. However, the toxicity of test materials is often not well characterized, and the contractor should be conservative in setting safety procedures.

**Test System Justification**

The rat is the animal model of choice. The test system is designated by federal regulations since it has been used historically for this type of study and will allow the data to be compared to that of other compounds.

**Test Animals**

Naive young adult male and female Sprague-Dawley derived albino rats weighing 200-300 grams will be used. Animals which fall outside of this range may be used at the discretion of the Study Director. The animals will be purchased from a vendor who equals or exceeds U.S.D.A. standards even though rats are not regulated animals.

**Acute Oral Toxicity in Rats - Median Lethal Dosage Determination**

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**Animal Supplier**

Harlan Sprague Dawley, Inc.  
P.O. Box 29176  
Indianapolis, IN 46229

**Number of Animals**

Forty animals (five/sex/dose level) with additional animals used as necessary.

**Housing and Animal Care**

All animals will be acclimated to the laboratory for at least five days before being used. Animals will be housed in groups of five in wire mesh suspension cages and will be supplied Teklad 4% Mouse/Rat Diet and tap water ad libitum during both acclimation and test periods except for withholding food overnight prior to dosing. The animal room will be maintained on a 12-hour light/12-hour dark cycle and at a temperature of 64-79°F and a relative humidity of 30-70%. Slight variations from these ranges will not result in a Protocol deviation. There are no contaminants in either the feed or the water that would be expected to affect the outcome of this study.

**Animal Selection**

The animals will be randomly caged according to Standard Operating Procedures.

**Animal Identification**

Cage cards, individually numbered ear tags, and tail marks with permanent ink will be used to identify each rat.

**Test Material Administration**

Overnight prior to dosing, food (but not water) will be withheld from the rats. The time of fasting and dosing will be documented. Groups of five male and five female rats will receive the test material by gavage at varying dose levels so that a median lethal dose may be calculated. Generally four groups will be used for the study. The test material will be administered undiluted using the bulk density to determine the dose volume. Individual doses will be calculated using post-fast body weights. The dose levels utilized will be documented in the raw data.

**Acute Oral Toxicity in Rats - Median Lethal Dosage Determination**

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**Observations**

All animals will be observed frequently for gross signs of systemic toxicity and mortality on the day of test material administration, and at least twice daily thereafter for a total of fourteen days.

A gross necropsy will be performed on any animal which dies. In the event of any death, the Sponsor will be promptly informed.

**Interpretation**

The test material will be categorized in accordance with 40 CFR 156, Proposed as described below:

1. Category I - Up to and including 50 mg/kg
2. Category II - Greater than 50 mg/kg thru 500 mg/kg
3. Category III - Greater than 500 mg/kg thru 5000 mg/kg
4. Category IV - Greater than 5000 mg/kg

**Body Weights**

Body weights will be measured for each animal on the day of dosing, on Day 7 of the observation period, and at the time of necropsy either at the end of the fourteen day observation period or following the death of any animal which does not survive this period.

**Termination**

At the end of the fourteen day observation period, each surviving rat will be euthanized by carbon dioxide inhalation and weighed. A gross necropsy will be performed on each animal.

**Report**

A draft report will be issued and will include but not necessarily be limited to the following:

The study objectives and procedures;

Identification of the test system;

Identification of the test material, its descriptions, and appropriate characteristics;

Concentration of the test material and, if appropriate, the diluent used;

The dose level(s) incorporated in the study;

Initial, interim, and final body weights;

Critical observations directly related to the interpretation of the test;

The estimated LD<sub>50</sub> value, calculated by the method of Litchfield and Wilcoxon, and the 95% confidence limits;

Justifiable conclusions drawn from the study;

Appropriate classification of the test material.

**Acute Oral Toxicity in Rats - Median Lethal Dosage Determination**

**Notice**

This study will be run according to good laboratory practices. If it becomes necessary to make changes in the approved Protocol, the revisions and reasons for change will be documented, reported to the Sponsor, and will become part of the permanent file for that study. Similarly, the Sponsor will be notified as soon as is practical whenever an event occurs that is unexpected and could have an effect on the validity of the study.

Acute Oral Toxicity in Rats - Median Lethal Dosage Determination

**PROTOCOL APPROVAL FORM**

Toxicology Division  
Hill Top Research, Inc.

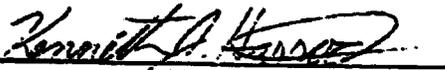
Protocol Title

Acute Oral Toxicity in Rats - Median  
Lethal Dosage Determination

Reference Code

96-8305-21/CABC 2-1-2/  
06-10-96/ORIGINAL

Protocol Approved By (Hill Top Research, Inc.):

  
Kenneth J. Harró, B.A.  
Study Director

12-26-96  
Date

Protocol Approved By (Sponsor):

  
Mr. Howard Marks  
Sponsor's Representative

HOWARD MARKS, Ph.D.  
CONSULTING TOXICOLOGIST  
FOR CABOT CORPORATION

2 JAN 97  
Date

Cabot Corporation  
Sponsor's Name

157 Concord Road  
Billerica, MA 01821-7001  
Sponsor's Address

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