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MRL (DDE) REPORT NO. 3

A STUDY OF SHORT INTERVAL EXPOSURES OF  
GOATS TO CG, CK, AND AC.

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MRL (DPG) REPORT NO. 3  
Project A 10.2

Medical Division, OC-CWS Project Specification 86

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AD-B 950565 -L

A STUDY OF SHORT INTERVAL EXPOSURES OF GOATS TO CG, CK, AND AC

by

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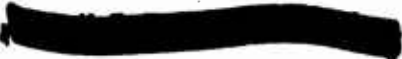
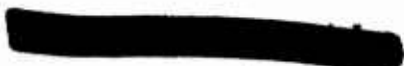
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A STUDY OF SHORT INTERVAL EXPOSURES OF GOATS TO CG, CK, AND AC

Project A 10.2 MRL (DPG) Report No. 3

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PLATES AND FIGURES

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ABSTRACT

MRL (DPG) REPORT NO. 3

OBJECT.

To determine the toxicity of CG, CK, and AC to goats and the respiratory behavior of goats when exposed for short periods, in order to calibrate this animal for use in field studies of surprise effects.

RESULTS.

1. Exposures of "masked" goats to CG concentrations of 1.3 to 50 mg./l. caused breath holding for 15 to 139 seconds while concentrations as low as 0.6 mg./l. caused respiratory depression.

2. Thirty second total exposures of goats to CG resulted in greater than 50% mortality only in the range of 10,000 to 12,000 mg.min./m<sup>3</sup>. Above this range the mortality probit showed a reverse trend. This phenomenon is accounted for by breath holding at very high concentrations.

3. Exposures of "masked" goats to CK in concentrations of 2 to 50 mg./l. resulted in marked respiratory depression followed by stimulation, and, in the case of casualty doses, another period of depressed breathing.

4. The respiratory response of "masked" goats to AC was characterized by a progressive onset of stimulated breathing followed by a marked depression of breathing. Very high concentrations (20 to 45 mg./l.) caused an initial respiratory depression.

5. The L(Ct)50's for the total exposures of unmasked goats were determined as follow:

CG (30 seconds) Indeterminate (See 2. above)  
CG (2 minutes) 6500  $\pm$  750 mg.min./m<sup>3</sup>  
CK (2 minutes) 7000  $\pm$  750 mg.min./m<sup>3</sup>  
AC (30 seconds) 1300 mg.min./m<sup>3</sup>

6. The approximate L(Ct)50's for exposures of goats wearing special masks\* were estimated as follow:

CG (t variable; average 100 seconds) 17,000 mg.min./m<sup>3</sup>  
CK (2 minutes) 14,000 mg.min./m<sup>3</sup>  
AC (15 seconds) 6,000 mg.min./m<sup>3</sup>  
AC (30 seconds) 3,000 mg.min./m<sup>3</sup>  
AC (2 minutes) 4,000 mg.min./m<sup>3</sup>

Thirty second exposures to CG and CK showed no correlation between the concentration and mortality.

\* without canister

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CONCLUSIONS.

1. The toxicity of nonpersistent agents during short exposures is largely dependent on the respiratory response of the subject during exposure.

2. Exposures to high concentrations of the irritant gases, CG and CK, result in reflex respiratory depression. This respiratory depression reduces the effectiveness of crash concentrations of these agents for surprise effects.

3. On the basis of physiological response, AC is the most desirable standard nonpersistent agent for surprise effects.

4. Short interval exposures of "masked" goats to a nonpersistent gas should be subject to the following limitations:

a. The effectiveness of the agent is reduced approximately one-half by the presence of the mask under the conditions tested.

b. The deadspace of the mask dilutes the agent, unless measures are taken to circulate the atmosphere through the mask.

c. Exposures to irritant gases of two minute duration or less result in marked variation in response.

d. Exposures to irritant gases of 30 second duration or less show no correlation between the concentration of agent and mortality.

RECOMMENDATIONS.

1. Field requirements for nonpersistent agents should be re-examined in the light of these results to establish new criteria for lethal surprise effects.

2. New methods for controlled short exposures of goats in the field to nonpersistent agents should be investigated.

3. Field data obtained with unmasked and "masked" goats should be re-evaluated.

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## GLOSSARY

1. Breath holding: Total cessation of respiration for a finite interval.
  2. Dead space: The space in the goat mask between the nose of the goat and the inlet and outlet valves.
  3. Masked goat: A goat wearing a special goat mask facepiece without a canister.
  4. Probit: A statistical unit such that "0 of the usual statistical table of deviates has been equated to the digit 5 and the deviate of the normal curve in terms of ' $\sigma$ ' added algebraically to secure the probit corresponding to each percentage kill" (C.I. Bliss, Ann Applied Biol. 22 134 (35)).
  5. Respiratory depression: Diminution of the amplitude of the respiratory excursion and/or the rate of respiration.
  6. Respiratory minute volume: Volume of air respired over an interval of one minute.
  7. Respiratory stimulation: Acceleration of the rate and/or increase in the amplitude of the respiratory excursion.
  8. Surprise effect: Effective exposure during the period before a soldier adjusts his mask.
  9. Short interval exposures: Exposures of two minutes duration or less.
  10. Agents: CG - Phosgene  
CK - Cyanogen Chloride  
AC - Hydrocyanic Acid
  11. Reference abbreviations:
    - D.P.G. - Dugway Proving Ground
    - E.A.M.R.D. - Edgewood Arsenal Medical Research Division
    - E.A.T.R. - Edgewood Arsenal Technical Report
    - M.R.L. (E.A.) - Medical Research Laboratory (Edgewood Arsenal)
    - N.D.R.C. - National Defense Research Committee
    - O.S.R.D. - Office for Scientific Research and Development
    - P.C.S. - Project Coordination Staff, Edgewood Arsenal
    - P.R. - Porton Report
    - T.C. - Training Circular
    - T.D.M.R. - Technical Division (Edgewood Arsenal) Memorandum Report
    - T.R.L.R. - Toxicological Research Laboratory (Edgewood Arsenal) Report
    - U.C.T.L. - University of Chicago Toxicity Laboratory
    - U.S.C.W. - U.S. Chemical Warfare Service
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MEDICAL RESEARCH LABORATORY  
MEDICAL DIVISION, OFFICE OF THE CHIEF, CWS  
Dugway Proving Ground, Tooele, Utah

A STUDY OF SHORT INTERVAL EXPOSURES OF GOATS TO CG, CK, AND AC

MRL (DPG) REPORT NO. 3

I. INTRODUCTION.

A. Object.

To determine the toxicity of CG, CK, and AC to goats and the respiratory behavior of goats when exposed for short periods, in order to calibrate this animal for use in field studies of surprise effects.

B. Authority.

1. CWS Project Program A 10.2 "Toxicity Determinations".
2. Medical Division Project Specification No. 86, "Bio-assay of Surprise Effects of Clouds Released from Munitions Charged with Non-persistent Agents".

II. HISTORICAL.

A. General.

In the tactical use of nonpersistent agents emphasis has been placed on the use of crash concentrations to attain surprise effects within two minutes. (U.S.C.W. Conference 102, OC-CWS; PCS Report No. 9, 17 May 1945; D.P.G. M.R. No. 21). Toward this end chemical warfare tactics have been developed for the use of such weapons as the 7.2" chemical rocket, the 4.2" mortar, and large capacity aircraft bombs. Estimates of munition requirements have emphasized 30 second to 2 minute exposures (P.C.S. Report No. 9), (T.C. 20, 26 April 1945).

In field trials of these weapons at Dugway Proving Ground, the assessment of surprise effects has been carried out by means of short interval chemical sampling and by corresponding short interval exposures of specially "masked" goats. Thirty second and two minute exposures were controlled by a remotely operated canister-bypass solenoid valve which was designed to permit an exposure of the goat to the gas cloud during the desired interval. (D.P.G. Weekly Report Series 2 - Report 83 - Part B). This apparatus was termed the "surprise" mask because of its application to the study of surprise effects. The results of the bio-assay obtained in the 7.2" chemical rocket trials of CG were erratic, particularly for 30 second exposures, and showed poor correlation with chemical data. (D.P.G. Weekly Report, Series 2 - Report 85, 86, Part B). In view of these results, and since published data on toxicity of the nonpersistent agents for goats was limited by the small numbers of animals used, a careful study of the

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physiological effects of short interval exposures to these agents was undertaken. During these studies it became apparent that a study of the respiratory response of the goats was also necessary to explain completely the toxicity for short exposures.

B. Toxicity of the Agents to Goats.

The available data on the toxicity of short exposures of CG, CK, and AC for goats are given in Table I.

TABLE I

<u>Agent</u>	<u>Time of Exposure</u>	<u>Degree of Toxicity</u>	<u>Ct</u> mg.min./m <sup>3</sup>	<u>No. Goats Used</u>	<u>Source of Data</u>
CG	1-10 Min.	L(Ct)40-80*	>4,400(2)	14	E.I.M.R.D. 5
CG	2 Min.	L(Ct)50	4,600	14	T.R.L.R. 20
CG	2 Min.	L(Ct)50*	>7,000	6	P.R. 976
CG	3 Min.	L(Ct)100*	6,600	8	Marshall(1)
CK	1 Min.	L(Ct)50*	4,500	4	P.R. 2603
CK	2 Min.	L(Ct)100*	5,000(2)	6	Suffield Report No. 71
CK	2 Min.	L(Ct)50	3,600	30	T.R.L.R. 26
CK	3 Min.	L(Ct)50*	6,000	6	P.R. 2603
AC	30 Sec.	L(Ct)100*	2,900	10	O.S.R.D. 1432
AC	30 Sec.	2/4 Mortality	4,850	4	P.R. 2298
AC	2 Min.	L(Ct)50	2,200	14	T.R.L.R. 23
AC	2 Min.	L(Ct)50*	5,000	5	P.R. 2298
AC	3 Min.	L(Ct)50	3,000	32	T.R.L.R. 23 (Summary of previous data)

- Notes (1) From Winternitz, M.C., "Pathology of War Gas Poisoning", Yale University Press, New Haven, Conn. 1920  
 (2) Estimated from field exposures  
 \* Estimated value

C. Physiological Effects of the Agents.

1. CG.

A recent paper (O.S.R.D. 4637) reviews the literature and presents original experimental data. Included are the L(Ct)50 values for various laboratory animals (but not including the goat), physiological effects of the agent on the lungs, the effect of temperature and other variables. Studies of the reactions of dogs exposed to CG (N.D.R.C. Monthly Progress Report 9-4-1-14, 10 March 1944) have shown that respiratory inhibition of 10 to 30 seconds duration occurred in anesthetized dogs when

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exposed to CG concentrations of 1.0 to 10.2 mg./l. Respiration returned to normal during the remainder of the one minute exposure. It was also found that during a one minute exposure dogs may be expected to breath 50 per cent of the calculated Ct, and 83 to 90 per cent during a 3 to 5 minute exposure. Rabbits and sheep, (Porton Report 2555) showed apnea on exposure to the agent, and horses reduced their breathing for one to two minutes when exposed to concentrations of 0.35 mg./l. of the agent.

Respiratory studies on anesthetized dogs exposed through a tracheal cannula for one minute to CG concentrations greater than 7.0 mg./l. showed the average reduction of the minute lung output was 62 per cent (O.S.R.D. 4637). In all except one test the first inhalation caused complete cessation of breathing with the lungs in the deflated stage. Apnea continued for 14 to 52 seconds and averaged 26 seconds. It was also shown that, following vagotomy, respiratory inhibition did not occur even though the dogs were exposed to 23.8 mg./l. Atropine, however, did not abolish the reflex. A concentration of 1.0 mg./l. caused 22 per cent respiratory reduction in anesthetized dogs during the first minute of exposure, and respiration was somewhat stimulated during the fifth minute of exposure.

## 2. CK.

Previous work on the toxicity of CK to various laboratory animals, exclusive of the goat, has been summarized (O.S.R.D. 5001). Data was presented on the  $L(Ct)_{50}$  values, pathology, and symptomatology. Original studies were made on the residual effects of CK on dogs and monkeys, the effect of repeated exposures on mice and dogs, and the toxicity of AC-CK mixtures.

The pathology of CK (Medical Division Report No. 34) and studies of its specific toxic activity have been presented (U.C.T.L. Informal Monthly Report N.S. 1, 15 April 1945). Detoxication by man was estimated to proceed at such a rate that 0.315 mg./l. could be inhaled indefinitely (E.A.T.R. 360). Detoxication by goats was estimated to be approximately 0.15 mg./l. (T.D.M.R. 638).

Respiratory depression during exposure to CK was demonstrated by Short and Watt (P.R. 2603), Coon (O.S.R.D. 5001), and Silver (E.A.T.R. 360). Respiratory stimulation was shown to follow respiratory depression (P.R. 2661). In field tests with rabbits at Dugway Proving Ground erratic results were obtained on the toxicity of the agent. These results have been attributed to reflex respiratory inhibition (DPG Weekly Report 54, Series 2, 3 May 1944).

Eight dogs, totally exposed to CK for 15 seconds, in concentrations of 46.7 to 50.3 mg./l. (nominal) survived. Six of these showed no symptoms at any time. Two of seven dogs exposed to CK for 30 seconds in concentrations of 41.4 to 47.9 mg./l. (nominal) survived. Five dogs exposed to CK for one minute to concentrations of 41.6 to 55.3 mg./l. (nominal) died. (Medical Division Informal Monthly Report, May 1945).

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### 3. AC.

Experimental studies on the toxicity of AC to various laboratory animals including the goat have been fully summarized by Coon et al (O.S.R.D. 1432, 13 April 1943). The stimulation of respiration by injection of AC and NaCN has long been known; a similar reaction following inhalation has been described in the literature (M.R.L. (EA) 15, T.D.M.R. 471, and T.D.M.R. 430). Respiratory depression following stimulation was described in T.P.L.R. 15. The time for the occurrence of convulsions was shown in T.R.L.R. 23, and that this reaction was related to concentration in T.D.M.R. 698. It has been reported that goats were able to detoxify the agent continuously when the concentration was 0.05 (O.S.R.D. 1432) and 0.10 mg./l. (T.R.L.R. 23).

### 4. Summary.

CG and CK in the concentrations required for lethal surprise effects have been observed to produce depression of respiration. With phosgene this depression was abolished by vagotomy and may be therefore presumed to be reflex in nature. AC and CK after the depression period, were found to produce respiratory stimulation within the surprise period. The data further demonstrated that for exposures of 2 minutes or less detoxication of AC and CK could be safely neglected. The reported data, for the most part, did not include an evaluation of the goat, and the studies, involving only small numbers of animals, did not warrant an extrapolation to field requirements. It was clear, with regard to AC, CK, and CG, that 1) the "Ct" requirement for surprise lethal effects differed in each case to an important degree from the requirement for prolonged exposures, and 2) that this difference could not be predicted from the reported data.

## III. EXPERIMENTAL.

### A. Materials and Equipment.

1. Dynamic flow gassing chamber (1150 liter volume)
2. Atomizers
3. Modified experimental goat mask
4. CG, CK, and AC
5. Recording tambour
6. Sampling and analytical equipment
7. Motoair vacuum pump (capacity 35 liters per minute at one-half atmosphere).

a. The dynamic flow gassing chamber (Plate 3) has a roller equipped carrier on which three goats may be placed and introduced into

[REDACTED]

the chamber for given exposure periods. The time of exposure can be controlled accurately within plus or minus one second. The chamber pumps have a maximum capacity of 3100 liters per minute (ca. 3 chamber volumes per minute). The inner walls of the chamber are porcelain coated and all metal parts are of stainless steel. Ports are available on the sides for introduction of agent and sampling. Glass windows permit observation during the exposures. The chamber is installed in a room equipped for rapid removal of toxic vapors from its atmosphere.

b. The agents, CG, CK, and AC were dispersed from atomizers of various sizes employing a stream of nitrogen over a capillary tip (Plate 2). The atomizer was fitted into a glass flask containing a weighed quantity of liquid agent. An ice-water bath was used to cool the agent during the dispersion of CG and CK, but with AC this measure was unnecessary. The concentration of agent in the chamber was controlled by: 1) the rate of nitrogen flow through the atomizer, 2) the size of the atomizer, and 3) the chamber flow rate.

c. A goat mask developed in this laboratory for controlled field exposures was modified for the respiratory studies (Plates 1, 4). The mask consists of a metal nose piece held in position by straps around the goat's head. Two rubber diaphragms within the nose piece insure a tight fit and still permit free nasal breathing. The goat, however, cannot open his mouth while wearing the mask. A vacuum pump drawing 30 to 34 liters of air per minute was connected to the mask. An outlet valve, a tube (1 inch in diameter and 12 inches in length) fitted with an inlet valve, and pressure tubing leading to a tambour for recording breathing were all attached to the nose piece.

d. The CG and AC used were standard CW fillings obtained from the Toxic Gas Yard, Dugway Proving Ground. CK was obtained from lots of CK under surveillance at Dugway Proving Ground and known to be of high purity.

## B. Animals.

380 Angora goats - These animals weighed between 55 and 110 pounds with an average of 80 pounds. They were obtained from southern Utah and normally lived at altitudes from 8,000 to 10,000 feet. Hemoglobin values for the herd averaged about 9.0 gm. per 100 cc blood with a range of 7.0 to 11.0 grams.

## C. Methods.

### 1. L(Ct)50 Determinations for Short Exposures.

Total exposures of unmasked goats were made in the dynamic flow gassing chamber in order to determine the L(Ct)50 for 30 second and 2 minute exposures to CG, 2 minute exposures to CK, and 30 second exposures to AC. Goats were exposed in groups of either two or three for the desired period. The chamber was operated at 1 to 3 chamber volumes per minute and

[REDACTED]

at least 5 minutes were allowed before exposures to permit the chamber to reach equilibrium. Samples of the chamber atmosphere were collected during the exact period of exposure either by two bubblers fastened to the carrier or by two bubblers sampling from the chamber ports. Animals exposed to CG were kept under observation 10 days; those exposed to AC and CK, until death or complete recovery. Goats exposed to AC were weighed.

## 2. Determination of Respiratory Behavior.

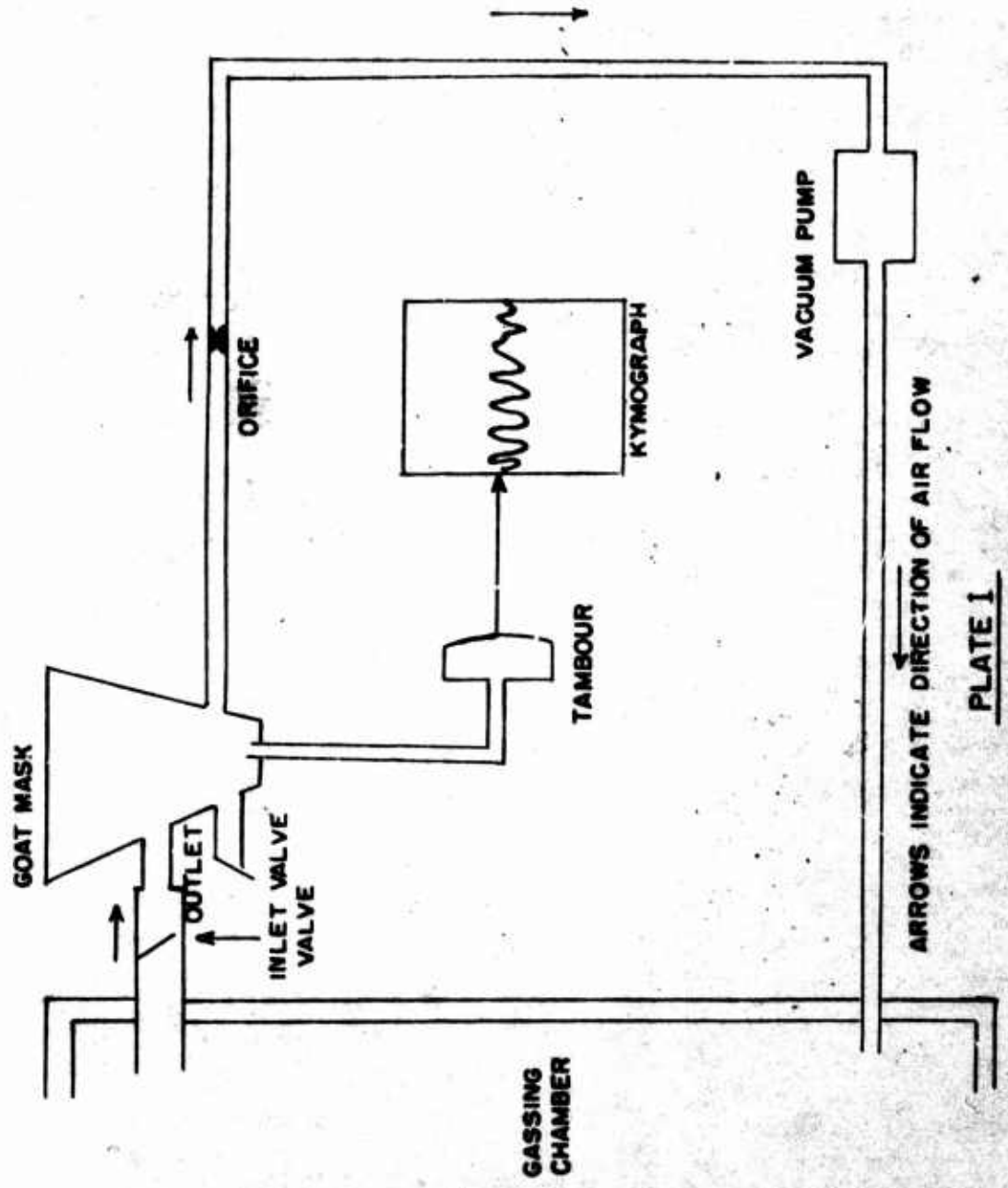
To determine the respiratory behavior of the animal during exposure to the gas in question, the apparatus shown in Plates 1 and 4 was used. After equilibrium was established, the intake hose of the goat mask was connected to the chamber and the chamber atmosphere circulated through the mask at a rate of 30 to 34 liters per minute for the desired interval. This was done to eliminate the dead space of the mask. The slight negative pressure so produced did not appear to affect the respiratory behavior of the "masked" goat. At the termination of the exposure period the inlet hose was disconnected from the chamber and the mask flushed with clean air. Tracings showing pressure differences due to the goats' respiration were taken before, during, and after the exposure by means of the recording tambour. During the experiments with CG the inlet was connected to an MIXA2 canister before the exposure to protect the animal from any gas in the room. The resistance of the canister was found to alter the respiratory pattern slightly and, since the canister was found unnecessary, its use was discontinued thereafter.

Samples of gas were withdrawn from the chamber in duplicate during the period of exposure. Samples were also withdrawn from the mask in four instances during the CK exposures in order to compare mask and chamber concentrations. The results are presented in Table IX, and show that the concentrations were essentially the same.

## 3. Analytical Methods.

Samples of the chamber atmosphere were collected at a flow rate of one liter per minute regulated by critical pressure orifices. Flow rates were checked frequently with a calibrated wet test meter. The absorbing solutions used were 4% hexamethylenetetramine for CG, 4% sodium hydroxide in 30% ethanol for CK (2 bubblers), and 4% sodium hydroxide\* for AC. Titrations for CG and CK content of the absorbing solution were made according to the mercuric nitrate method for chlorides in acid solution using diphenylcarbazone as indicator. Several drops of carbon tetrachloride were added to assist in seeing the end-point (Moody P.R. 2423 (1942)). AC was determined by the silver nitrate titration method of Liebig (Ann. Chem. und Pharm., 77, 102 (1851)), using potassium iodide as indicator.

\* 8% NaOH was used at concentrations of 13 mg./liter and greater.



ARROWS INDICATE DIRECTION OF AIR FLOW

PLATE I  
DIAGRAM OF GASSING APPARATUS

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PLATE 3

Dynamic Flow Gassing Chamber.

- A. Roller equipped carrier for introducing animals.
- B. Atomizer in ice bath.
- C. Manometer for measuring nitrogen flow.
- D. Vigreux type bubbler sampling from post.
- E. Bubbler sampling on carrier.
- F. Filter to protect orifice.

PLATE 4

Apparatus Used to Study Respiratory Behavior of Goats.

- A. Goat mask.
- B. Tambour.
- C. Recorder for tambour.
- D. Tube to vacuum pump.
- E. Tube to tambour.
- F. Outlet valve.
- G. Intake hose leading to chamber post.

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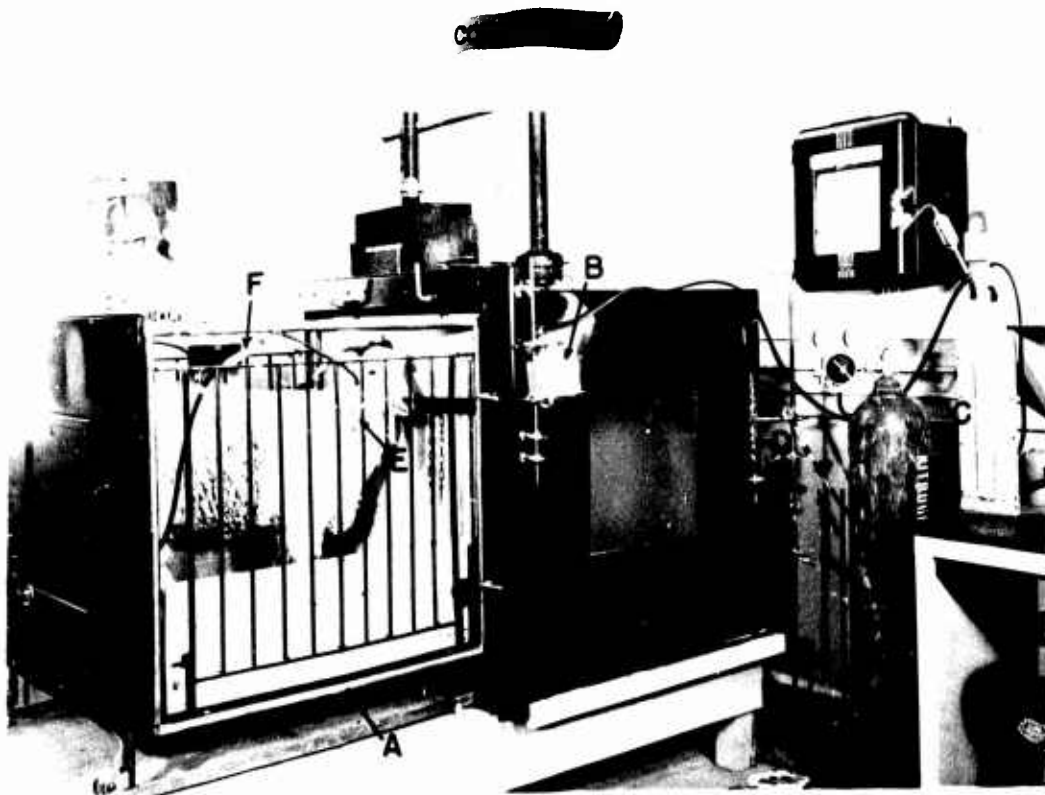


Plate 3. Dynamic Flow Gassing Chamber



Plate 4. Apparatus used to study  
Respiratory Behavior  
of Goats.

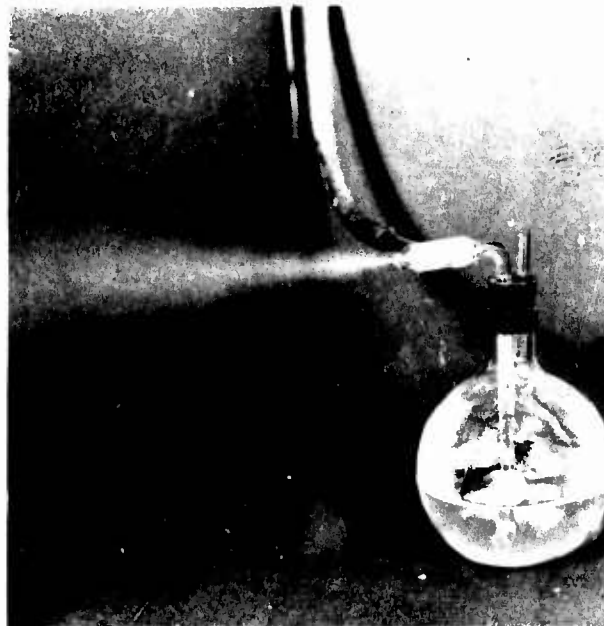


Plate 2. Atomizer for Dispersing  
CG, CK, and AC.

Photo No. 1585

████████████████████

#### 4. Operation of the Chamber.

The chamber flow rates and ratios of analytical to nominal concentrations for each series of runs are given in Table II. Analytical values are used in preference to nominal concentrations throughout this report for the following reasons: 1) The atomizers used for dispersing the agents tended to deliver more rapidly at the start of the run. 2) Evaporation losses occurred in weighing the agent. 3) Analytical samples were taken at a constant rate during the exact period of exposure and were thus not subject to errors caused by fluctuations in concentration.

TABLE II

<u>Agent</u>	<u>Study</u>	<u>Time of Sample minute</u>	<u>Chamber Flow l./minute</u>	<u>Average Ratio of Analytical to Nominal Concentration.</u>
CG	L(Ct)50	2	1,050	0.75
CG	L(Ct)50	0.5	1,050	0.79
CG	Respiratory	0.5, 2	1,000	0.66
CK	L(Ct)50	2	1,000	0.73
CK	Respiratory	0.5, 2	1000, 750, 1650	0.65
AC	Respiratory	0.5, 2	1000, 750, 500	0.76
AC	L(Ct)50	0.5	2,900	0.70

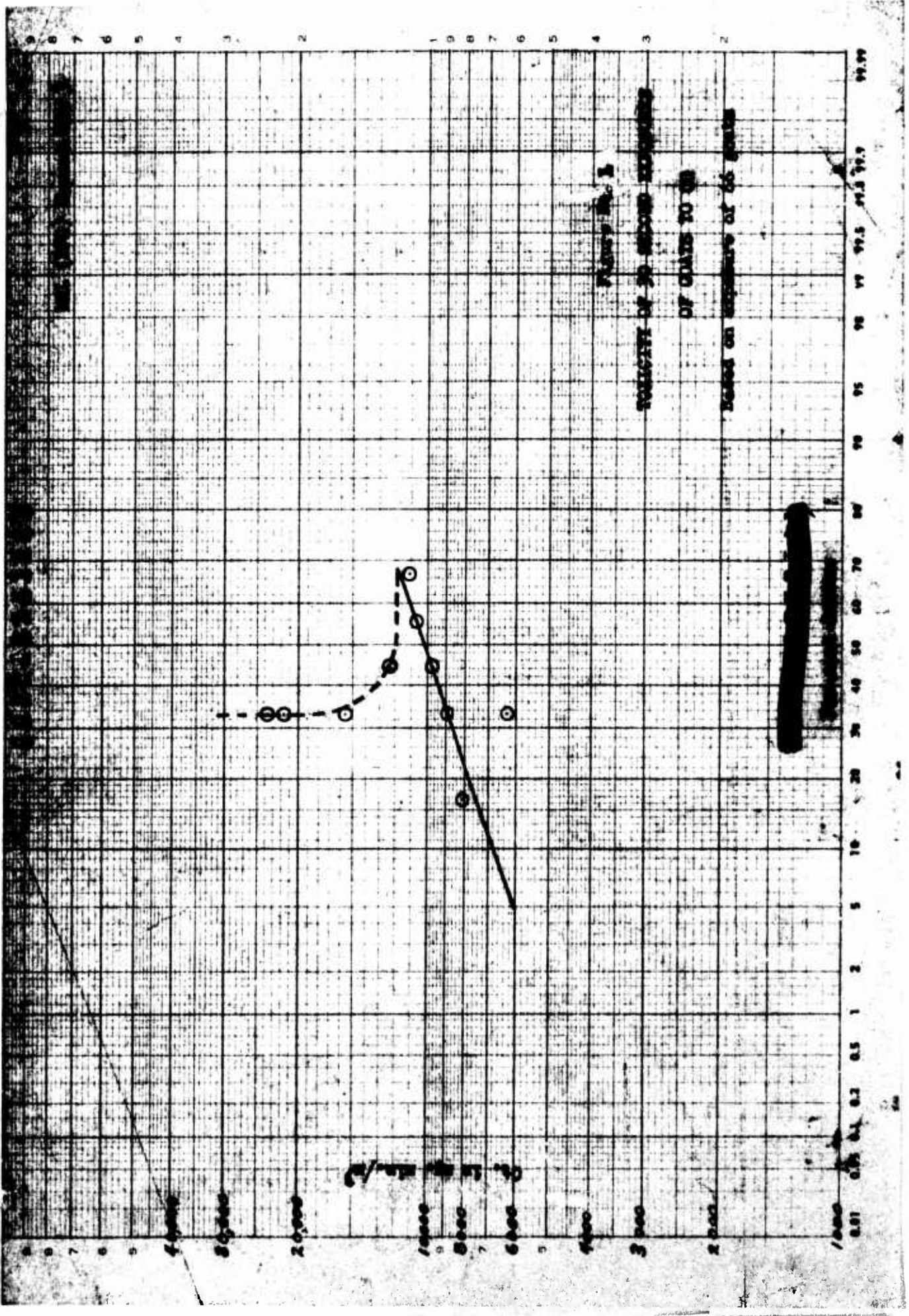
A further check on the accuracy of sampling in the chamber was made comparing results obtained from collection bubblers mounted on the carrier and bubblers sampling through ports of the chamber. The carrier with the bubblers operating and with 3 goats was introduced into a chamber concentration of AC for a 30 second period. Port samples were taken for the same interval. The results of 20 such experiments yielded an average ratio of carrier to port concentrations of 0.99 with a standard error ( $\sigma$ ) of 0.09. It is thus evident that the homogeneity of the chamber atmosphere was not appreciably disturbed by the introduction of animals, and that sampling on the carrier or from the ports was equally reliable.

#### D. Results.

##### 1. L(Ct)50 Determinations

##### a. CG (t = 2 minutes, 30 seconds)

The L(Ct)50 for 2 minute total exposures of unmasked goats to CG is  $6500 \pm 750$  mg.min./m<sup>3</sup>, calculated by the method of Bliss (C.I. Bliss, Quart. J. Pharm., 11, 192 - 216 (1938)). The determination is based on the exposure of 72 goats. For 30 second exposures using 66 goats, the L(Ct)50 was indeterminate because mortality greater than 50% was attained only at Ct's between 10,000 and 12,000 mg.min./m<sup>3</sup>. At greater Ct's the mortality probit curve exhibited a reverse trend. Detailed results are given in Tables III and IV, where the data are grouped for convenience in plotting. The Log Ct-probability curves are shown in Figures 1 and 2.



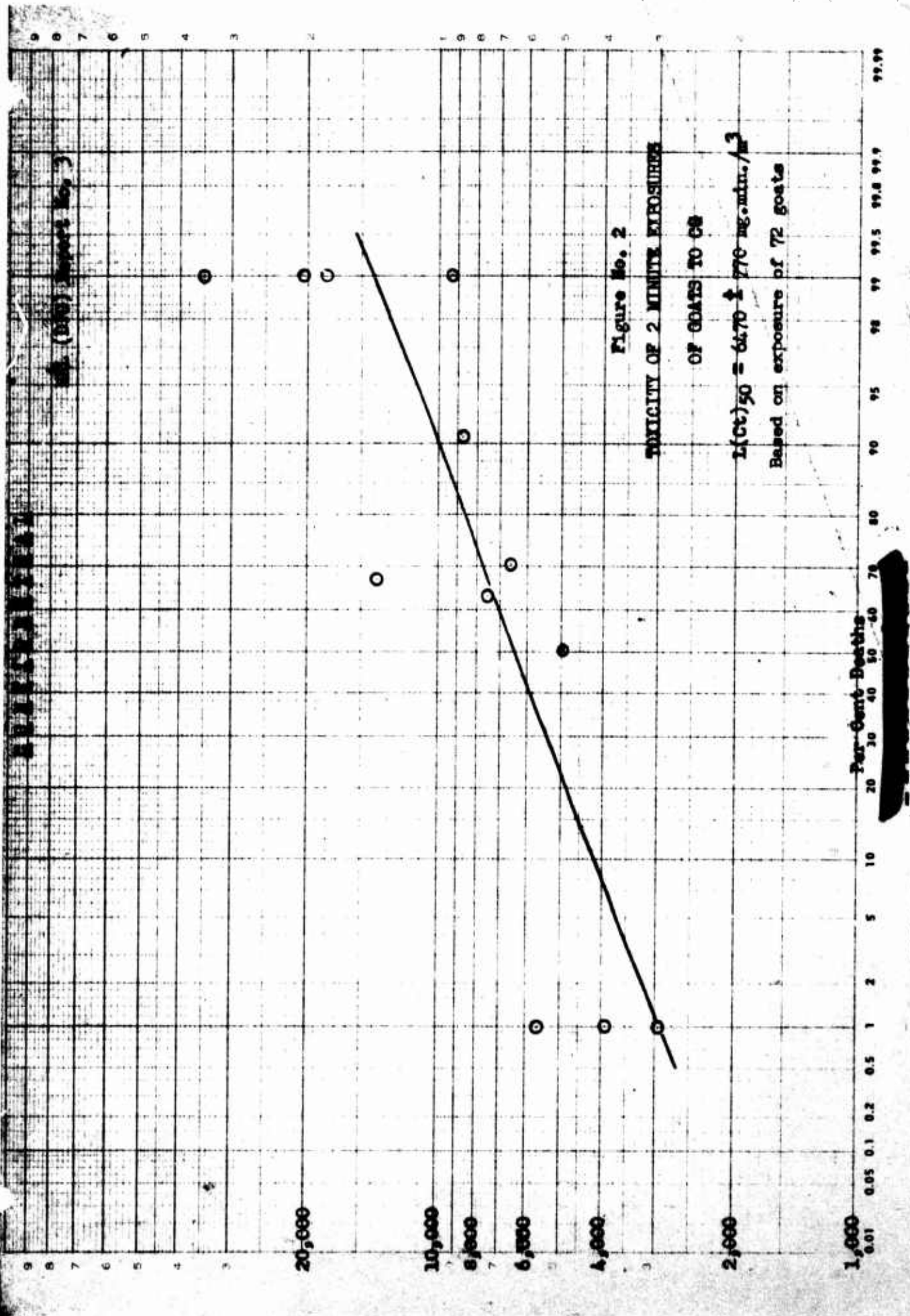


TABLE III

TOXICITY OF 30  
SECOND EXPOSURES OF GOATS TO PHOSGENE

<u>Run No.</u>	<u>Analytical Concentration</u> mg./l.	<u>Ct</u> mg.min./m <sup>3</sup>	<u>Mortality</u>	<u>Deaths</u> %
24	47.50	23,750	1/3	33.3
25	43.28	21,640	1/3	33.3
17	31.28	15,610	1/3	33.3
13	26.22	13,110	2/3	
18	23.70	11,850	1/3	
14	23.60	<u>11,800</u>	<u>1/3</u>	
		Av. 12,250	4/9	44.4
11	22.73	11,370	3/3	
19	22.26	11,130	2/3	
2	21.74	<u>10,870</u>	<u>1/3</u>	
		Av. 11,120	6/7	66.6
9	21.64	10,820	2/3	
10	21.32	10,660	1/3	
6	21.16	<u>10,580</u>	<u>2/3</u>	
		Av. 10,690	5/9	55.5
8	20.06	10,030	2/3	
16	19.70	9,850	1/3	
12	18.83	<u>9,420</u>	<u>1/3</u>	
		Av. 9,770	4/9	44.4
3	18.36	9,180	1/3	
15	18.10	9,050	1/3	
5	17.44	<u>8,720</u>	<u>1/3</u>	
		Av. 8,980	3/9	33.3
22	16.36	8,180	0/3	
1	16.04	<u>8,020</u>	<u>1/3</u>	
		Av. 8,100	1/6	16.6
4	13.80	6,900	1/3	
20	11.52	<u>5,760</u>	<u>1/3</u>	
		Av. 6,330	2/6	33.3

[REDACTED]

TABLE IV

TOXICITY OF TWO MINUTE EXPOSURES OF GOATS TO CG

<u>Run No.</u>	<u>analytical Concentration mg./l.</u>	<u>Ct mg.min./m<sup>3</sup></u>	<u>Mortality</u>	<u>Deaths %</u>
30	17.50	35,000	3/3	100
29	10.23	20,460	3/3	100
27	8.98	17,960	2/2	100
28	6.98	13,960	2/3	67
14	4.63	9,260	3/3	100
18	4.41	8,820	3/3	
15	4.39	8,780	3/3	
16	4.31	8,620	2/3	
19	4.20	<u>8,400</u>	<u>3/3</u>	
		Av. 8,645	11/12	92
20	3.93	7,860	2/3	
6	3.90	7,800	2/2	
5	3.69	7,380	1/2	
4	3.61	7,220	1/2	
21	3.55	<u>7,100</u>	<u>1/2</u>	
		Av. 7,500	7/11	64
24	3.44	6,880	2/3	
26	3.36	6,720	2/3	
7	3.32	6,640	2/2	
12	3.27	6,540	2/2	
23	3.24	6,480	2/3	
3	3.21	6,420	1/2	
17	3.07	<u>6,140</u>	<u>1/2</u>	
		Av. 6,570	12/17	71
13	2.96	5,920	0/3	
11	2.83	5,630	0/2	
25	2.68	<u>5,360</u>	<u>0/3</u>	
		Av. 5,590	0/8	0
8	2.46	4,920	1/2	50
9	1.97	3,940	0/2	
2	1.91	<u>3,820</u>	<u>0/2</u>	
		Av. 3,880	0/4	0
10	1.49	2,980	0/2	
1	1.46	<u>2,920</u>	<u>0/2</u>	
		Av. 2,950	0/4	0

[REDACTED]

b. CK (t = 2 minutes)

The L(Ct)50 for 2 minute total exposures of unmasked goats to CK is 7000  $\pm$  750 mg.min./m<sup>3</sup>, calculated by the method of Bliss. Fifty-nine goats were used. Detailed results are shown in Table V and Figure 3.

c. AC (t = 30 seconds)

The L(Ct)50 for 30 second total exposure of unmasked goats to AC is 1300 mg.min./m<sup>3</sup> (48 animals). Grouping of the data for plotting is shown in Table VI and the log Ct-probability curve used to determine the L(Ct)50 is given in Figure 4. As no correlation was found between weight of the animal and toxicity, weights are not given.

2. General Response of Goats.

a. CG.

Goats exposed to casualty producing concentrations of CG exhibited no early symptoms except struggling during exposure. Difficulty in expiration immediately following exposure was severe enough in some instances to cause retraction of the intercostal spaces. About four hours after gassing, difficulty in respiration had increased and there was audible and visible evidence of pulmonary edema. Cyanosis followed and all symptoms increased until the time of death.

b. CK and AC.

Animals exposed to CK and AC showed an essentially similar train of symptoms. The first noticeable effect was dilatation of the pupils, which was more marked after exposure to CK than to AC. Respiratory stimulation then occurred and after about 30 seconds the goat bleated and struggled violently. The abdomen usually became distended at this time. A few seconds after struggling started the goat collapsed (25 to 60 seconds from the start of exposure). Respiratory stimulation continued for about 30 seconds and was followed by respiratory paralysis. While the animal was comatose tetanic spasms occurred and then changed to clonic convulsions. The convulsions continued at intervals until death or start of recovery of the animal. The goats that died usually struggled briefly just before death. In some instances (with both CK and AC), pulmonary and nasal hemorrhage were noted. Deaths usually occurred within 10 minutes of exposure.

Those animals which recovered resumed normal respiration slowly. Return of consciousness was gradual, and animals frequently relapsed after making too great an effort to rise. Upon recovery, the forelegs were weak, but in a short time the goat was alert and apparently unaffected. There were no residual symptoms or delayed deaths due to AC. Three of the goats totally exposed to CK exhibited severe residual neurological signs.

Cyanosis was present in both AC and CK gassed animals but was more pronounced with CK. Animals totally exposed to CK also exhibited marked laceration.

TABLE V

TOXICITY OF TWO MINUTE EXPOSURES OF GOATS TO CK

<u>Run No.</u>	<u>Analytical Concentration mg./l.</u>	<u>Ct mg.min./m<sup>3</sup></u>	<u>Mortality</u>	<u>Deaths %</u>
21	8.10	16,200	3/3	100
22	5.89	11,780	3/3	100
1	5.38	10,760	3/3	100
2	4.90	9,800	3/3	
18	4.88	9,760	2/3	
11	4.70	<u>9,400</u>	<u>3/3</u>	
		Av. 9,650	8/9	89
16	4.34	8,680	2/3	
10	4.05	<u>8,100</u>	<u>1/3</u>	
		Av. 8,390	3/6	50
15	3.99	7,800	3/3	
20	3.60	7,200	3/3	
6	3.54	7,080	2/3(1)	
9	3.50	<u>7,000</u>	<u>2/3</u>	
		Av. 7,520	10/12	83
8	3.42	6,840	0/3(1)	
7	3.20	<u>6,400</u>	<u>1/3</u>	
		Av. 6,620	1/6	17
3	2.92	5,840	1/3	
5	2.81	<u>5,620</u>	<u>0/3</u>	
		Av. 5,730	1/6	17
12	2.33	4,660	0/3(2)	
13	2.17	4,340	0/3	
14	2.16	<u>4,320</u>	<u>1/3</u>	
		Av. 4,440	1/9	11
19	1.94	3,880	0/3	0
17	1.41	2,820	0/3	
4	1.11	<u>2,240</u>	<u>0/3</u>	
		Av. 2,530	0/6	0

- Notes: (1) One goat suffered severe neurological symptoms for three days after exposure. It was then sacrificed but counted as a survivor in the calculation of the L(Ct)50.  
 (2) One goat showed severe after effects for three days but slowly recovered.

MIL (DFG) Report No. 3

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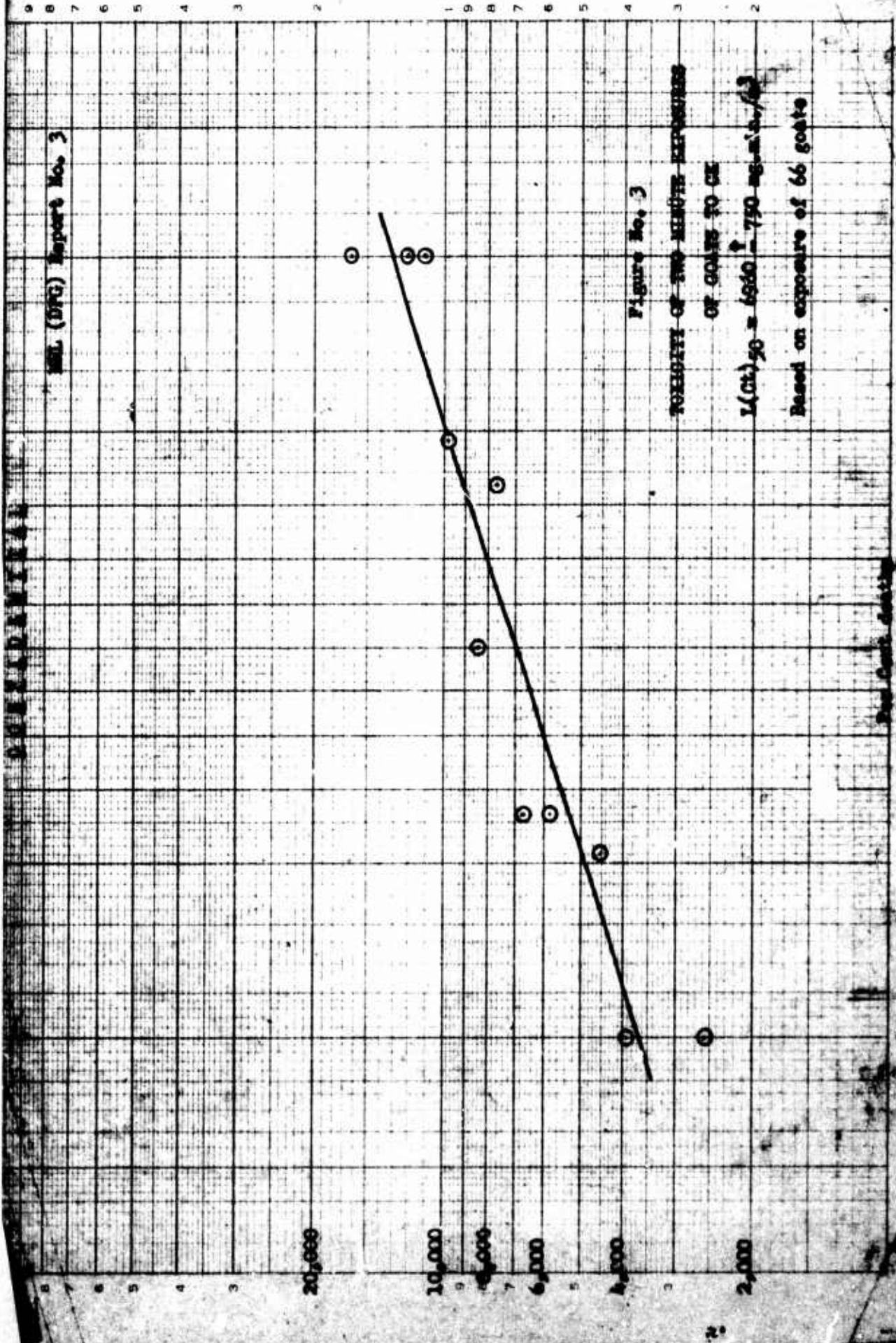


Figure No. 3

TOXICITY OF TWO-MINUTE EXPOSURES OF GASES TO CE

$$I(CE)_{90} = 6960 \sqrt{D}$$

Based on exposure of 66 goats

Dose Count Density

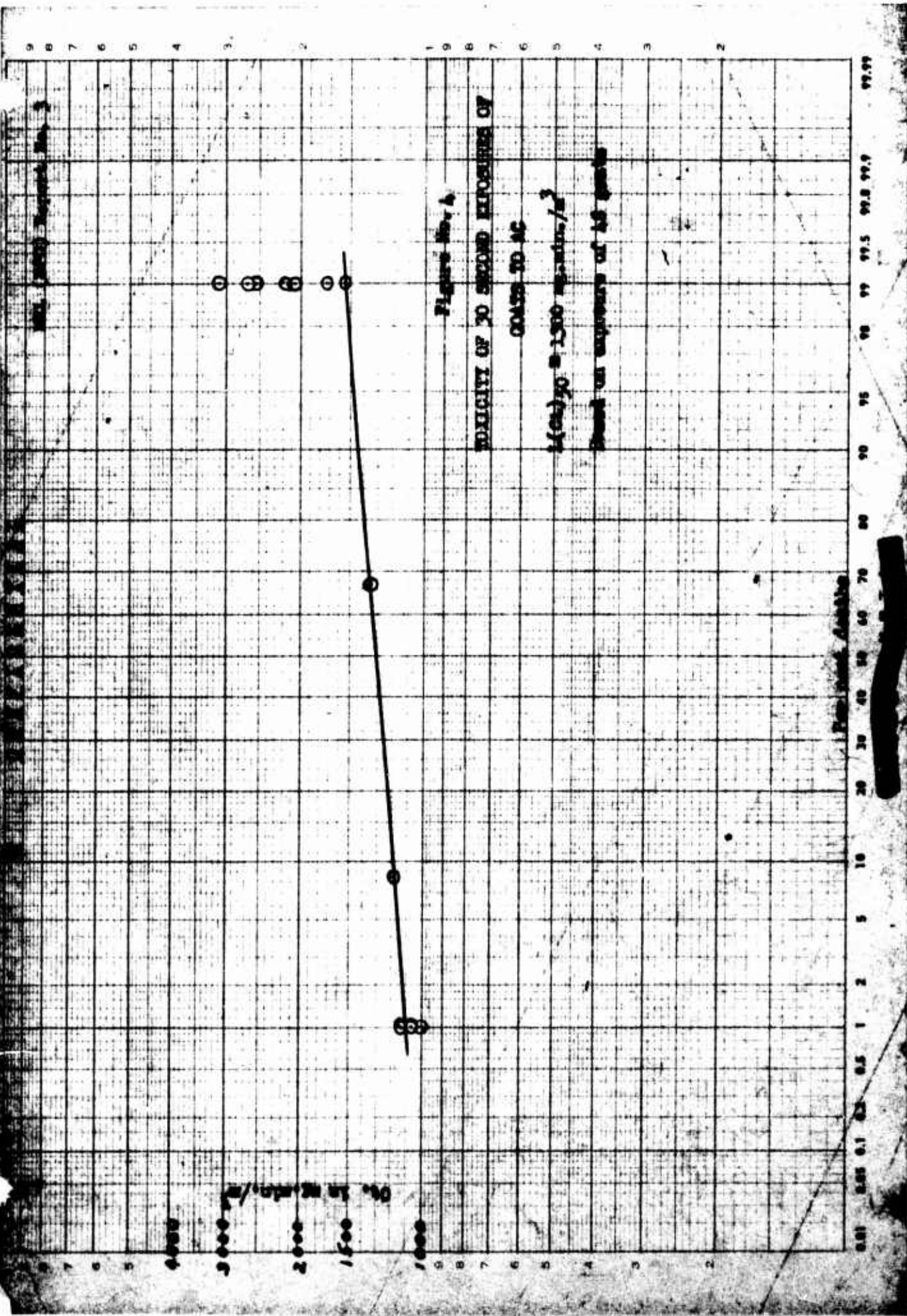
0.05 0.1 0.2 0.5 1 2 5 10 20 50 100 200 500 1000

2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20

**TABLE VI**

**TOXICITY OF 30 SECOND EXPOSURES OF GOATS TO AC**

<u>Run No.</u>	<u>Analytical Concentration</u> mg./l.	<u>Ct.</u> mg.min./m <sup>3</sup>	<u>Time from Start of Exposure for Death</u> Min.	<u>Mortality</u>	<u>Deaths</u> %
1	6.22	3,110	7, 8, 4	3/3	100
2	5.38	2,690	8, 7, 4	3/3	100
13	5.10	2,550	7	1/1	100
12	4.37	2,185	3	1/1	100
3	4.14	2,070	7, 8, 5	3/3	100
14	3.44	1,720	10, 10, 11	3/3	100
8	3.09	1,545	7, 6, 10	3/3	100
17	2.74	1,370	13	1/3	
20	2.72	1,360	--	0/1	
4	2.71	1,355	25, 7	2/3	
9	2.69	1,345	10	1/1	
10	2.64	1,320	7	1/1	
16	2.63	<u>1,315</u>	8, 12, 6	<u>3/3</u>	
		Av. 1,345		8/12	66.7
19	2.41	1,205	--	0/3	
15	2.39	1,195	--	0/3	
18	2.36	1,190	35	1/3	
7	2.27	<u>1,135</u>	--	<u>0/3</u>	
		Av. 1,180		1/12	8.4
11	2.24	1,120	--	0/1	0
5	2.12	1,060	--	0/3	0
6	1.99	995	--	0/3	0



[REDACTED]

### 3. Respiratory Behavior of "Masked" Goats.

#### a. CG.

Seven goats wearing the modified mask were exposed for 30 seconds to CG in concentrations of 25 to 50 mg./l. (Ct's of 12,500 to 25,000 mg.min./m<sup>3</sup>). Six of these animals showed complete breath holding during the entire exposure, and exhibited no symptoms of CG poisoning. One goat exposed to 35.3 mg./l. took 18 shallow breaths and died as a result.

In another series of experiments 19 "masked" goats were exposed to concentrations of 0.6 to 15.7 mg./l. of CG for the duration of breath holding plus 30 seconds thereafter. Breath holding of 15 to 139 seconds was a constant response to concentrations above 1.3 mg./l. Below this concentration breath holding was not present in animals exposed for two minutes but respiration was depressed. At 0.37 mg./l. breathing was essentially normal. In one instance a goat was exposed to a concentration of 1.5 mg./l. for 12 minutes (Ct = 18,000 mg.min./m<sup>3</sup>) without adverse effects, because of depression of the respiratory minute volume (Figure 7). Details of these results are shown in Table VII and representative tracings of the respiratory patterns are presented in Figures 5-8.

#### b. CK.

A total of 42 "masked" goats was exposed for 30 seconds or 2 minutes to concentrations of CK ranging from 0.54 to 51.6 mg./l. (Table VIII and IX). The general respiratory pattern for both exposure periods consisted of an initial period of respiratory depression with or without actual breath holding, followed by a period of respiratory stimulation and another period of depression. The initial depression (25 to 120 seconds) was observed in all exposures to concentrations of 2.0 mg./l. or higher. Eleven out of 42 goats exhibited breath holding. Below 2.0 mg./l. the initial respiratory phase was essentially normal. The depressed phase was followed by a stimulated phase characterized by deep, rapid, and regular breathing. The second depressed phase was characterized by slow, regular breathing of approximately normal depth. Representative tracings of these exposures are presented in Figures 9 to 15.

#### c. AC.

A total of 45 "masked" goats was exposed to AC for 2 minutes, 30 seconds or 15 seconds at concentrations of 0.8 to 45.0 mg./l. (Tables X and XI). With this gas, the immediate response to exposure differed from that to CG and CK in that respiratory depression occurred only in concentrations higher than 16.4 mg./l. In all other exposures respiration was normal for a brief initial period (5 to 60 seconds). This initial period of normal respiration was followed by progressive respiratory stimulation, usually occurring after the first 5 to 10 breaths. It was characterized by deep, rapid, and regular breathing. The stimulated phase was followed by marked respiratory depression.

TABLE VII

RESPIRATORY BEHAVIOR OF GOATS EXPOSED TO CG

Goat Number	Analytical Concentration Mg./l.	Total Exposure Time Sec.	Analytical Ct mg.min./m <sup>3</sup>	Time of Breath Holding Sec.	Respiratory Behavior Character of Resumed Respiration During Exposure	Response of Goat to Agent	Figure Number
737	50.1	30	25,000	30	Complete breath holding	No symptoms	
1396	35.3	30	17,700	0	18 shallow breaths	Died - 26 hours	
862	34.5	30	11,300	30	Complete breath holding	No symptoms	
440	32.5	30	16,300	30	Complete breath holding	No symptoms	
20	31.3	30	15,700	30	Complete breath holding	No symptoms	
242	26.8	30	13,400	30	Complete breath holding	No symptoms	
815	25.9	30	13,000	30	Complete breath holding	No symptoms	
144	15.7	65	17,000	35	11 shallow breaths	Died - 12 hours	
60	15.1	85	21,400	55	6 shallow breaths	No symptoms	
61	12.9	115	24,800	85	15 shallow breaths	Died - 12 hours	
818	11.9	79	15,700	49	11 shallow breaths	Died - 24 hours	
183	8.9	102	15,100	72	5 shallow breaths	No symptoms	
354	8.5	82	11,600	52	6 shallow breaths	No symptoms	
UMG	8.5	157	22,200	127	11 shallow breaths	Died - 24 hours	
403	8.2	68	9,300	38	13 shallow breaths	Moderate casualty-recovered	
1301	4.2	102	7,100	72	8 shallow breaths	No symptoms	
25	3.6	169	10,100	139	4 shallow breaths	No symptoms	
541	2.4	76	3,000	46	12 mod. shallow breaths	Died - 24 hours	
401	1.5	720	18,000	60	Extremely shallow, slow	No symptoms	
603	1.4	77	1,800	47	8 shallow breaths	No symptoms	7
389	1.3	45	1,000	15	7 shallow breaths	No symptoms	
73	1.0	120	2,000	0	Mod. shallow, irregular	No symptoms	
382	0.98	120	1,960	0	Mod. shallow, irregular	No symptoms	
762	0.85	120	1,690	0	Mod. shallow, slow, irreg.	No symptoms	
17	0.60	330	3,300	0	Shallow, slow, irregular	No symptoms	
711	0.37	120	740	0	Normal breathing	No symptoms	

\* Wearing masks  
All times are from start of exposure.

NORMAL RESPIRATION

START OF EXPOSURE

END OF EXPOSURE

ARI(276) R. PART NO. 3

FIGURE 5

AG 170 06  
CONT. NO. 443  
EXPOSURE TIME 10 min.  
CONC. 32.5 mg/l  
At 15,000 mg./min./l.<sup>3</sup>  
NO. 3 DETECTOR  
INHALE →  
EXHALE ←

715



NORMAL RESPIRATION

START OF EXPOSURE

SAMPLING PERIOD

30 sec.

END OF EXPOSURE

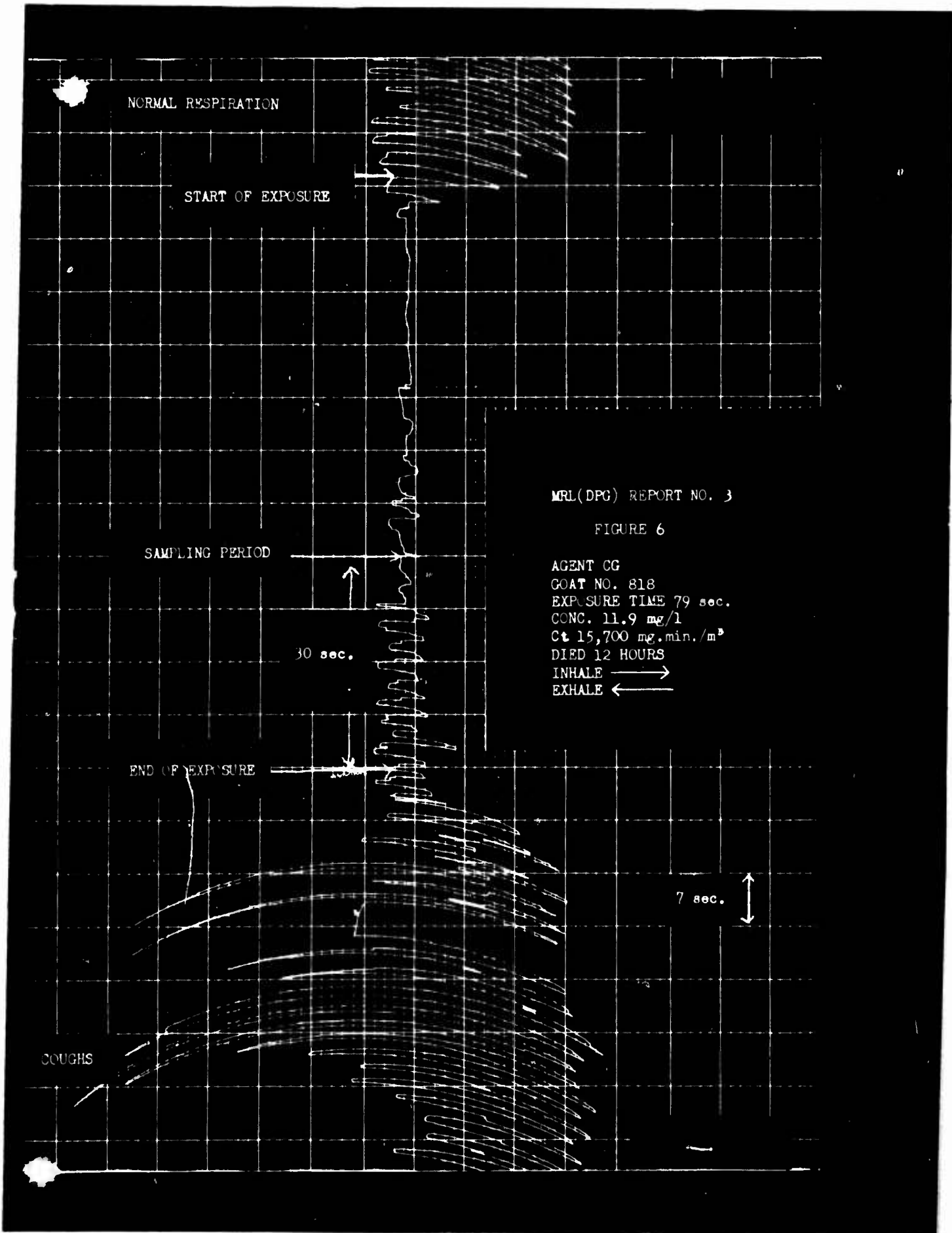
COUGHS

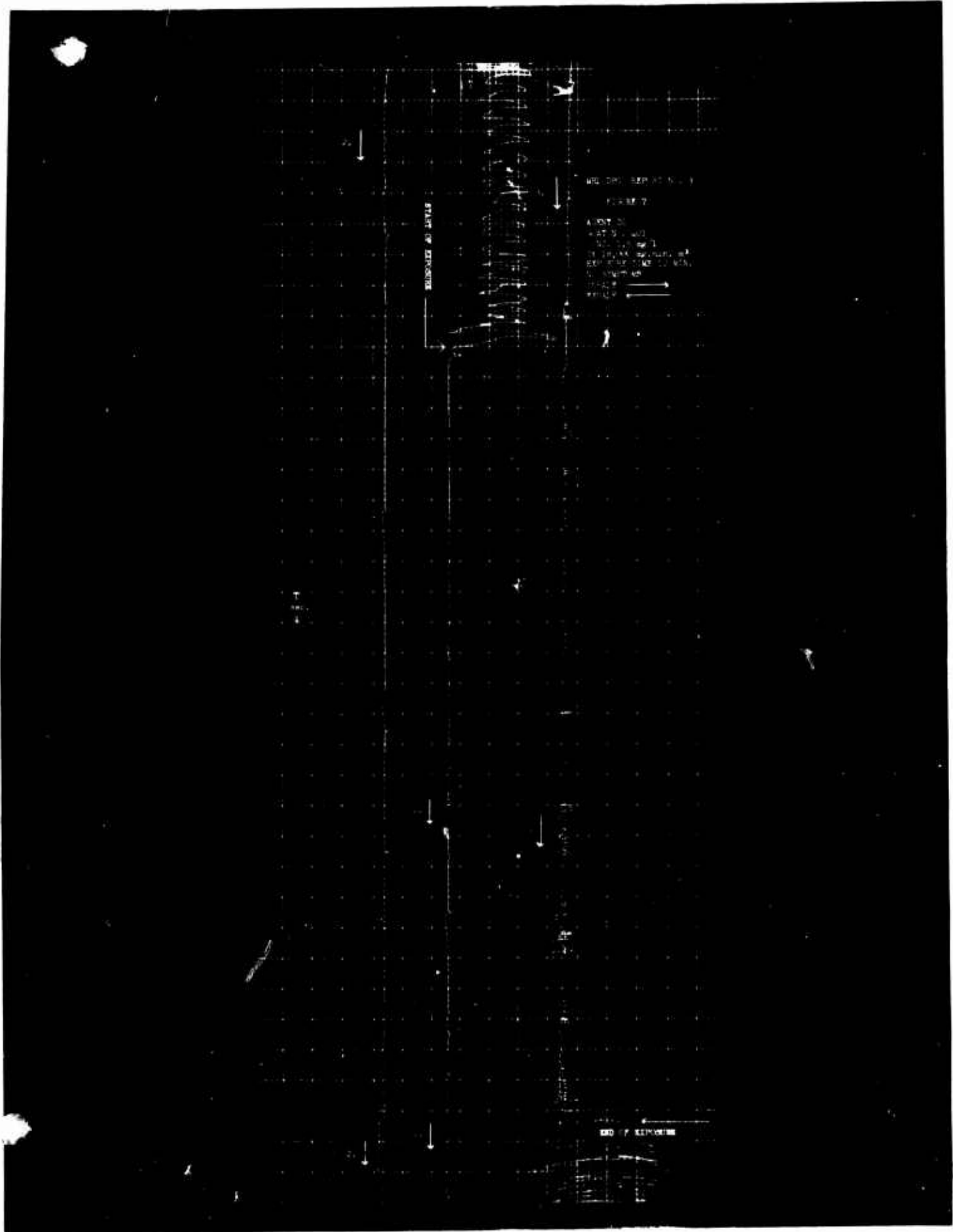
MRL(DPG) REPORT NO. 3

FIGURE 6

AGENT CG  
COAT NO. 818  
EXPOSURE TIME 79 sec.  
CONC. 11.9 mg/l  
Ct 15,700 mg.min./m<sup>3</sup>  
DIED 12 HOURS  
INHALE →  
EXHALE ←

7 sec.





MRL(DPG) REPORT NO. 3

FIGURE 8

AGENT CG  
CLOT NO. 382  
EXPOSURE TIME 2 MIN.  
CONC. 0.98 mg./l  
Ct 1960 mg.min./m<sup>3</sup>  
NO SYMPTOMS  
INHALE →  
EXHALE ←

7 sec.

START OF EXPOSURE

END OF EXPOSURE

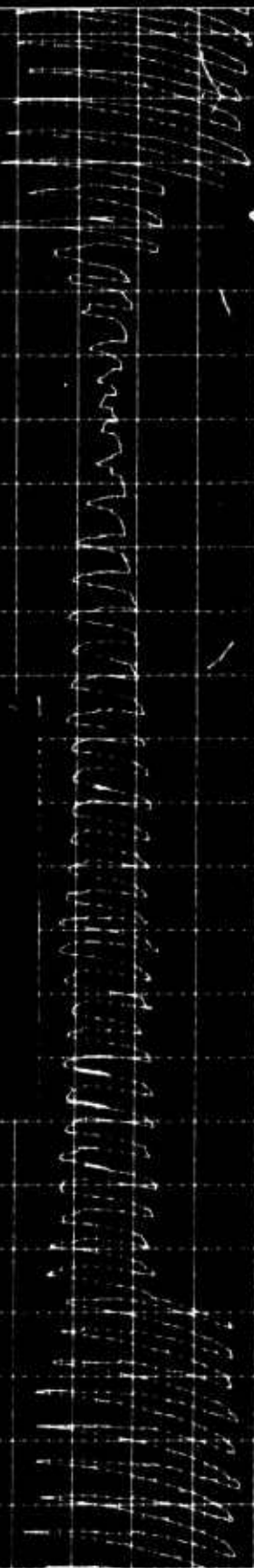


TABLE VIII

RESPIRATORY BEHAVIOR OF GOATS<sup>1</sup> EXPOSED TO CK FOR 22 SECONDS

Goat Number	Analytical Concentration Mg./l.	Analytical C <sub>3</sub> mg./l./hr <sup>3</sup>	Character of Respiration During Exposure	Response Other Than Cyanosis	Recovery Time Min.	Figure Number
832	51.6	25,800	Moderate depth, rapid, irregular	Died	--	
160	46.0*	23,000	Breath holding-12 sec. extremely shallow-18 seconds	None	I	
99	39.2	19,600	Shallow, rapid, irregular	None	I	
53	35.4	17,700	Shallow, rapid, irregular	None	I	
106	35.0	17,500	Extremely shallow, rapid, irregular	None	I	
494	21.9	10,950	Extremely shallow, rapid, irregular	None	I	
804	21.5	10,800	Normal depth, rapid, irregular	Died	--	
723	21.4	10,700	Slow, irregular, 2 deep breaths	None	I	
1311	21.1	10,550	Breath holding-6 sec. shallow, slow, irreg.-24 sec.	None	I	
54	19.7	9,850	Shallow, irregular, rapid, 2 deep breaths	Convulsions	23	
853	19.6	9,800	Extremely shallow, irregular	None	I	15
352	19.2	9,600	Breath holding-6 sec., shallow, rapid, irreg.-24 sec.	None	I	
170	18.2	9,100	Shallow, rapid, 22 sec., deep, rapid-6 sec.	Died	--	
UNG	18.2	9,100	Normal depth, irregular, rapid	Convulsions	14	13
428	17.3	8,650	Breath holding-17 sec., slow, 2 deep breaths-13 sec.	Convulsions	10	
107	16.8	8,400	Normal depth, rapid, irregular	Convulsions	20	
833	15.6	7,800	Breath holding-10 sec., rapid 3 deep breaths-20 sec.	Convulsions	10	14
91	13.2	6,600	Breath holding-20 sec., shallow, rapid-10 sec.	None	I	

1 Wearing masks  
 \* Analytical Sample Lost. Concentration calculated from an A/N ratio of 0.60  
 I Immediate recovery

All times are from start of exposure.  
 Deaths occurred within 5 minutes after start of exposure.

RESPIRATORY BEHAVIOR OF GUINEA PIGS EXPOSED TO CK FOR 2 MINUTES

Character of Respiration During Exposure

Goat No.	Analytical Concentration		Chamber-Mask Conc. Ratio	mg. min./m <sup>3</sup>	Analytical Ct (Chamber)	Depressed Phase	Duration Sec.	Stimulated Phase Duration Sec.	Response Other than Cyanosis	Recovery Time Min.	Figure No.
	mg./l.	Mask mg./l.									
829	12.5			27,300	Shallow, slow, irregular	60	60	Died			
437	8.51			17,020	Extremely shallow, irregular	60	60	Died			
838	8.10			16,200	Breath holding-40 sec., shallow irregular-35 sec.	75	45	Died			
1337	8.00	7.76	0.97	16,000	Mod. shallow, irregular	130*	After exposure	None		I	11
196	6.89			13,780	Extremely shallow, irregular	30	90	Convulsions		25	
737	6.83			13,600	Shallow, irregular	60	60	Convulsions		10	
565	6.75			13,500	Breath holding-60 sec. shallow-20 sec.	80	40	Convulsions		20	10
618	6.65			13,300	Shallow, irregular	30	90	Convulsions		18	
520	6.24	6.00	0.96	12,430	Breath holding-20sec.irreg.40sec.	60	60	Convulsions		90	
112	6.03	5.37	0.89	12,060	Shallow, slow	25	155	Convulsions		50	
326	5.30			-10,600	Shallow, irregular	60	60	Died			
577	4.41			8,820	Breath holding	70	50	Weakness		5	
351	4.25			8,500	Shallow, slow	60	60	None		I	
195	2.59			5,150	Breath holding	25	95	Died			9
29	2.54			5,080	Shallow, irregular	30	90	None		I	
53	2.41			4,820	Shallow, irregular	60	60	None		I	
650	1.98			3,960	Normal Respiration	30**	90	None		I	
411	1.90			3,800	Normal Respiration	60**	60	Weakness		5	
175	1.82			3,640	Normal Respiration	35**	85	Convulsions		9	
69	1.72			3,440	Normal Respiration	75**	45	None		I	12
32	1.55	1.46	0.94	3,100	Slow, irregular	85	35	None		I	
486	1.31			2,620	Normal Respiration			None		I	
561	1.18			2,360	Normal Respiration			None		I	
113	0.54			1,080	Normal Respiration			None		I	

\* Depressed phase lasted until after exposure ended.  
 \*\* Intervals of normal respiration before onset of stimulation.  
 \*\*\* All deaths were within 10 minutes of start of exposure.

USL(DP) REPORT NO. 1

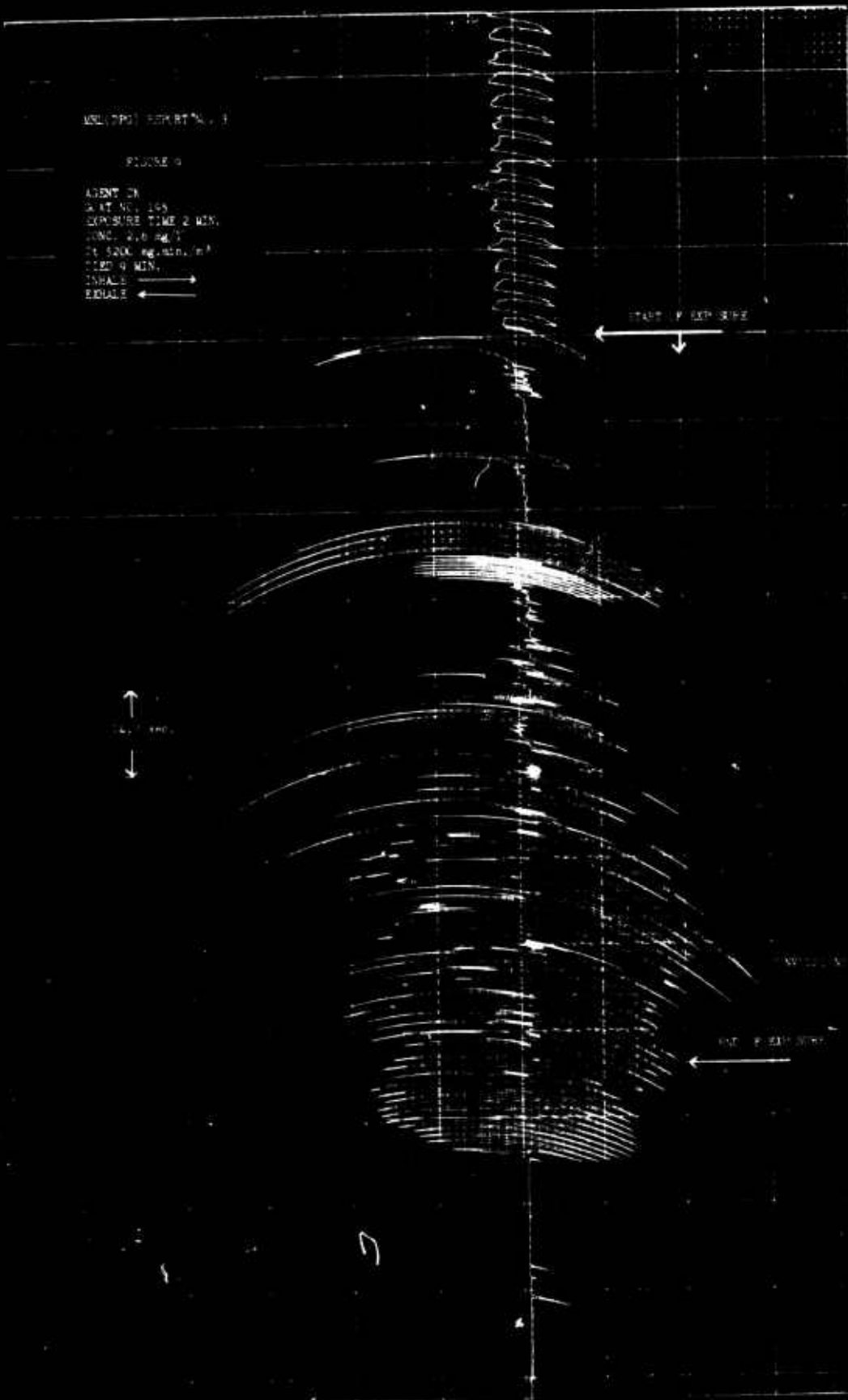
FIGURE 9

AGENT: CN  
SLAT NO. 169  
EXPOSURE TIME: 2 MIN.  
DUNG: 2.0 mg/l  
Ct: 5000 mg-min./m<sup>3</sup>  
TIDEL: 4 MIN.  
INHALE →  
EXHALE ←

4.0 cm

START OF EXPOSURE

END OF EXPOSURE



MIL(DMG) REPORT NO. 3

FIGURE 10

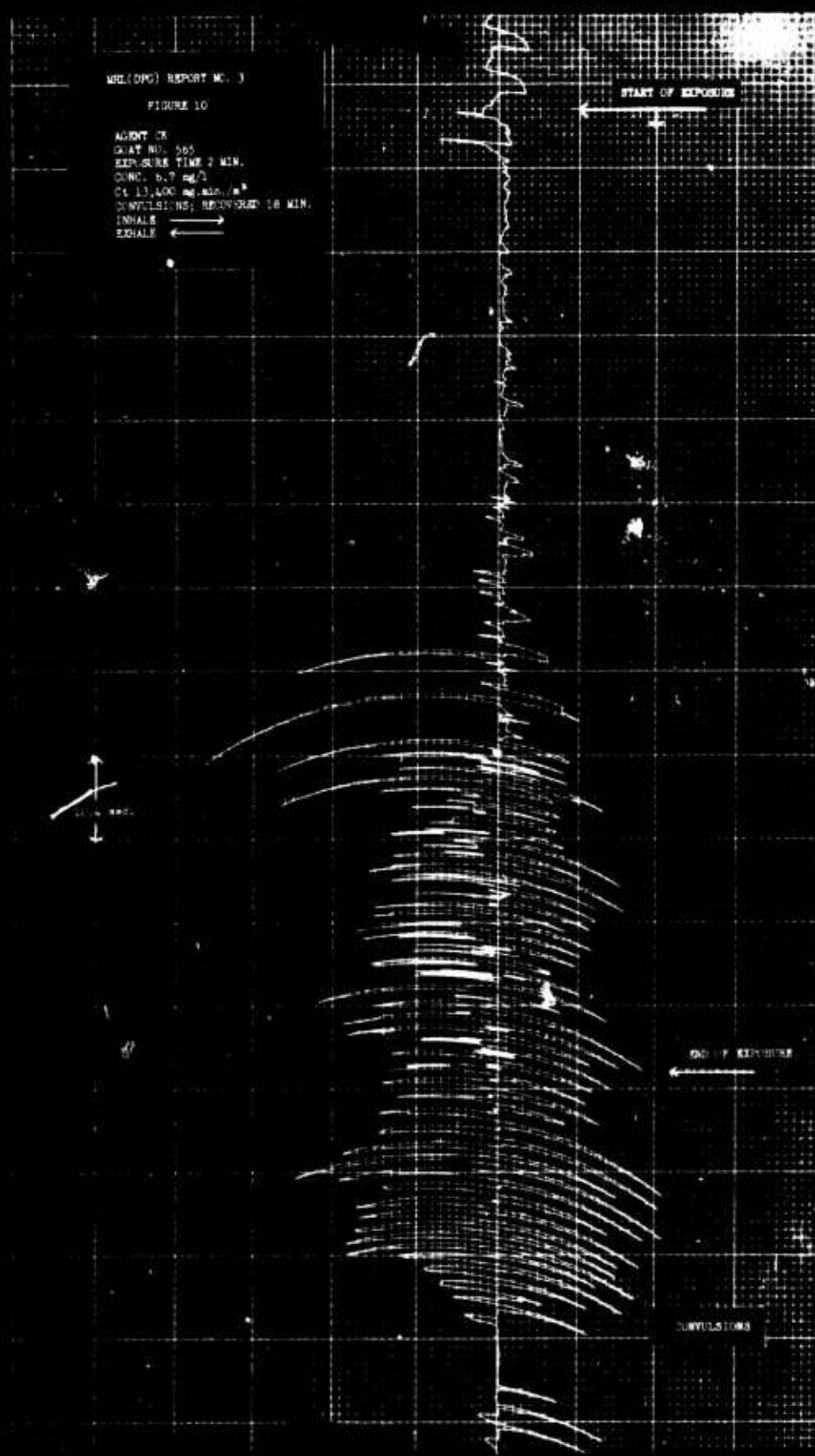
AGENT CA  
GRAT NO. 505  
EXPOSURE TIME 2 MIN.  
CINC. 6.7 mg/l  
CL 13,400 mg. min. / m<sup>3</sup>  
CONVULSIONS; RECOVERED 10 MIN.  
INHALE →  
EXHALE ←

← 100 →

START OF EXPOSURE

END OF EXPOSURE

CONVULSIONS



WR. (DPG) REP. NO. 1

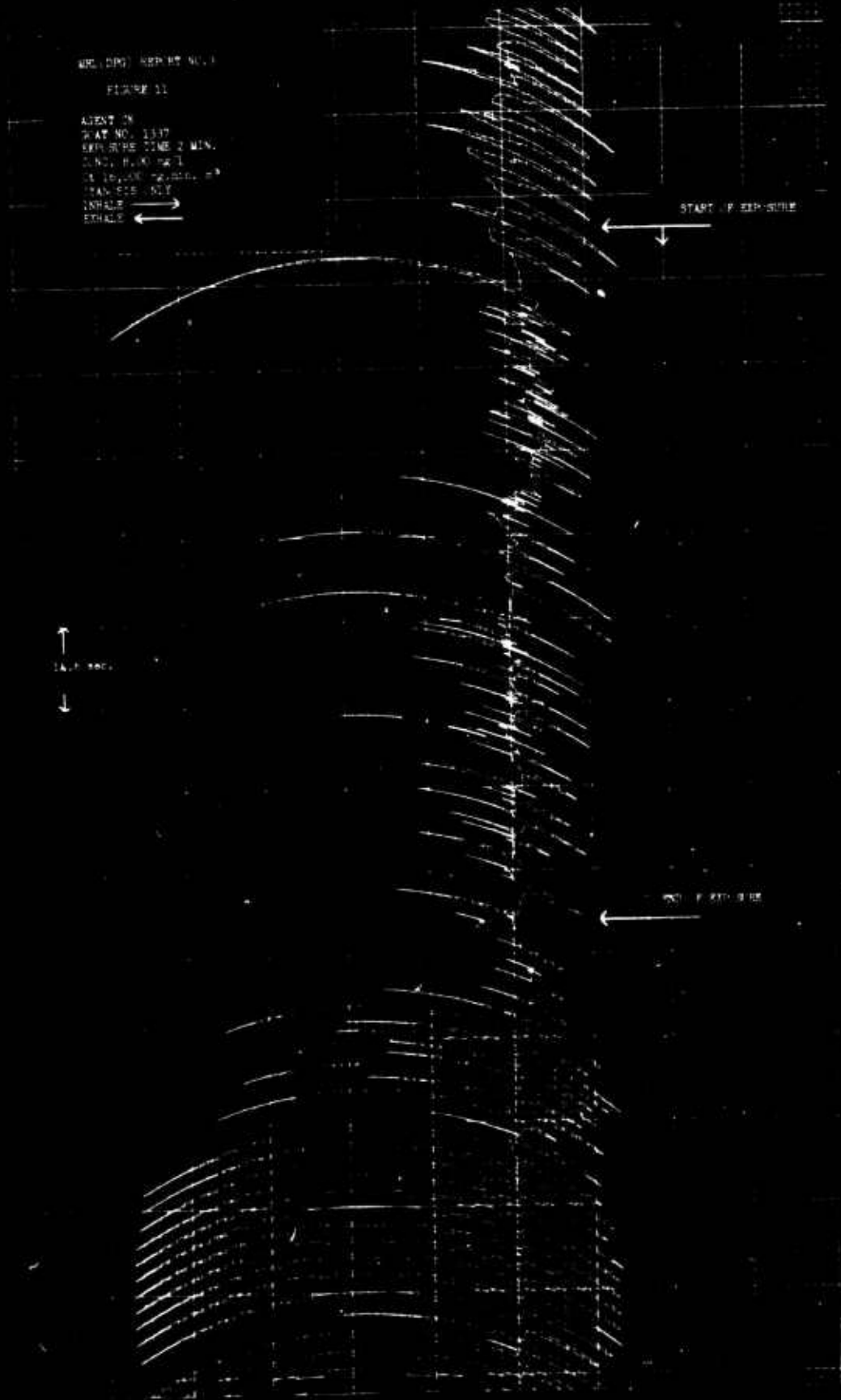
FIGURE 11

AGENT ON  
TRAY NO. 1337  
EXPOSURE TIME 2 MIN.  
DND: 8.0 mg/l  
A 10,000 72-000. 0  
TAN 515 - 517  
INHALE →  
EXHALE ←

START OF EXPOSURE

14.7 sec.

END OF EXPOSURE



MRL (DPG) REPORT NO. 3

FIGURE 12

AGENT OR  
GOAT NO. 69  
EXPOSURE TIME 2 MIN.  
CONC. 1.7 mg/l  
Ct 3400 mg.min./m<sup>3</sup>  
CYANOSIS ONLY  
INHALE →  
EXHALE ←

1000 mg

START OF EXH. PIPE

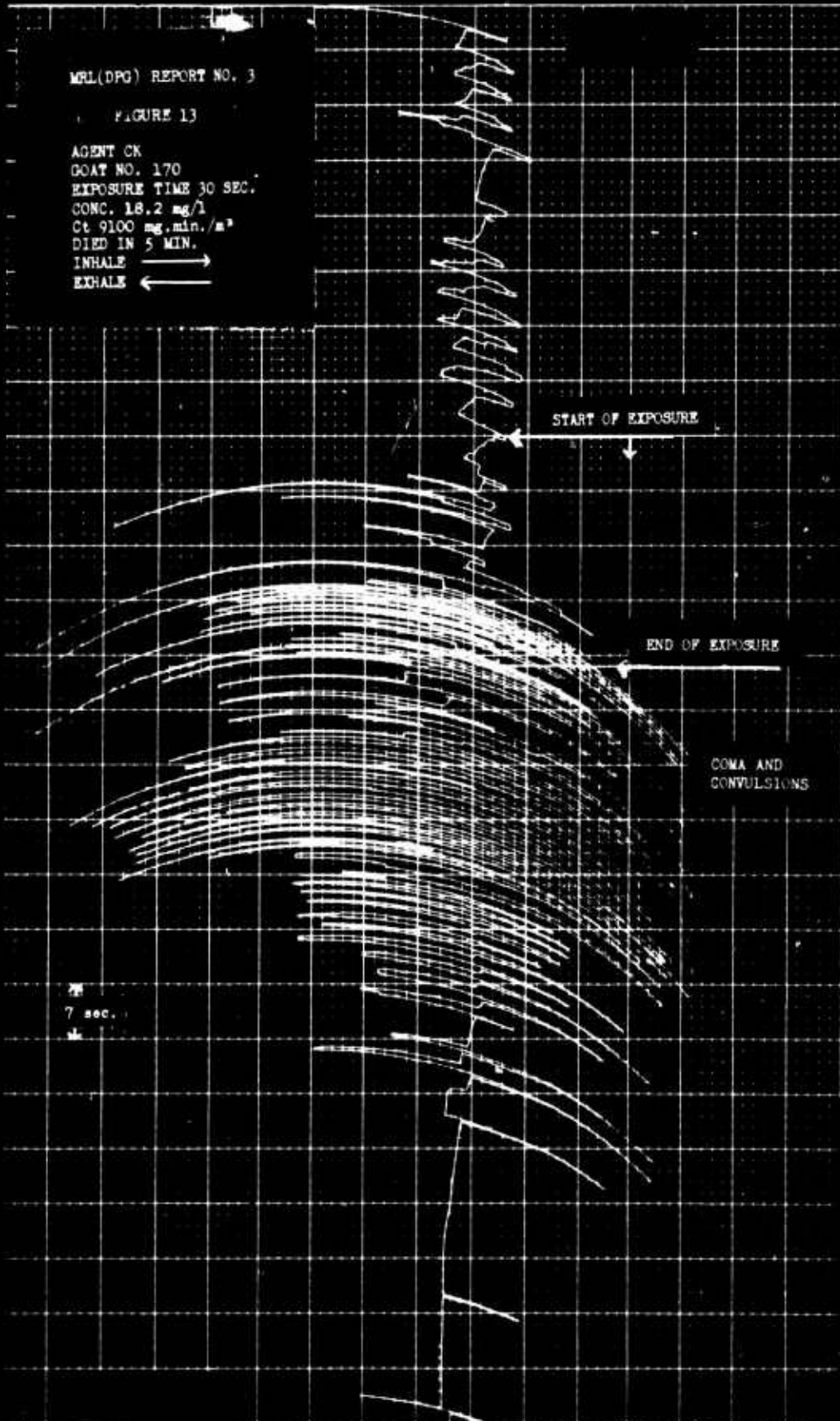
END OF EXH. PIPE



MRL(DPG) REPORT NO. 3

FIGURE 13

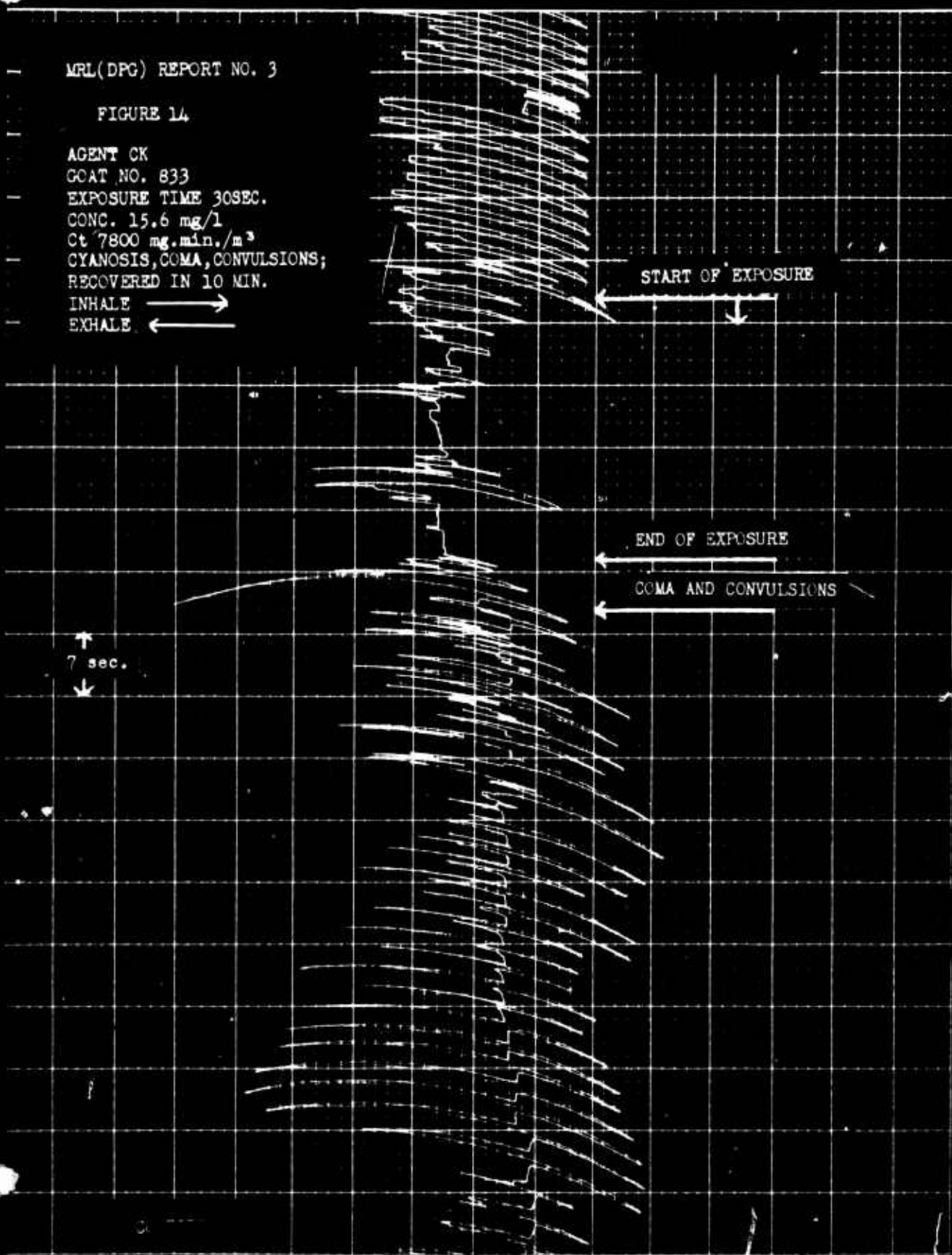
AGENT CK  
GOAT NO. 170  
EXPOSURE TIME 30 SEC.  
CONC. 18.2 mg/l  
Ct 9100 mg.min./m<sup>3</sup>  
DIED IN 5 MIN.  
INHALE →  
EXHALE ←



MRL(DPG) REPORT NO. 3

FIGURE 14.

AGENT CK  
GCAT NO. 833  
EXPOSURE TIME 30SEC.  
CONC. 15.6 mg/l  
Ct 7800 mg.min./m<sup>3</sup>  
CYANOSIS, COMA, CONVULSIONS;  
RECOVERED IN 10 MIN.  
INHALE →  
EXHALE ←



START OF EXPOSURE

END OF EXPOSURE

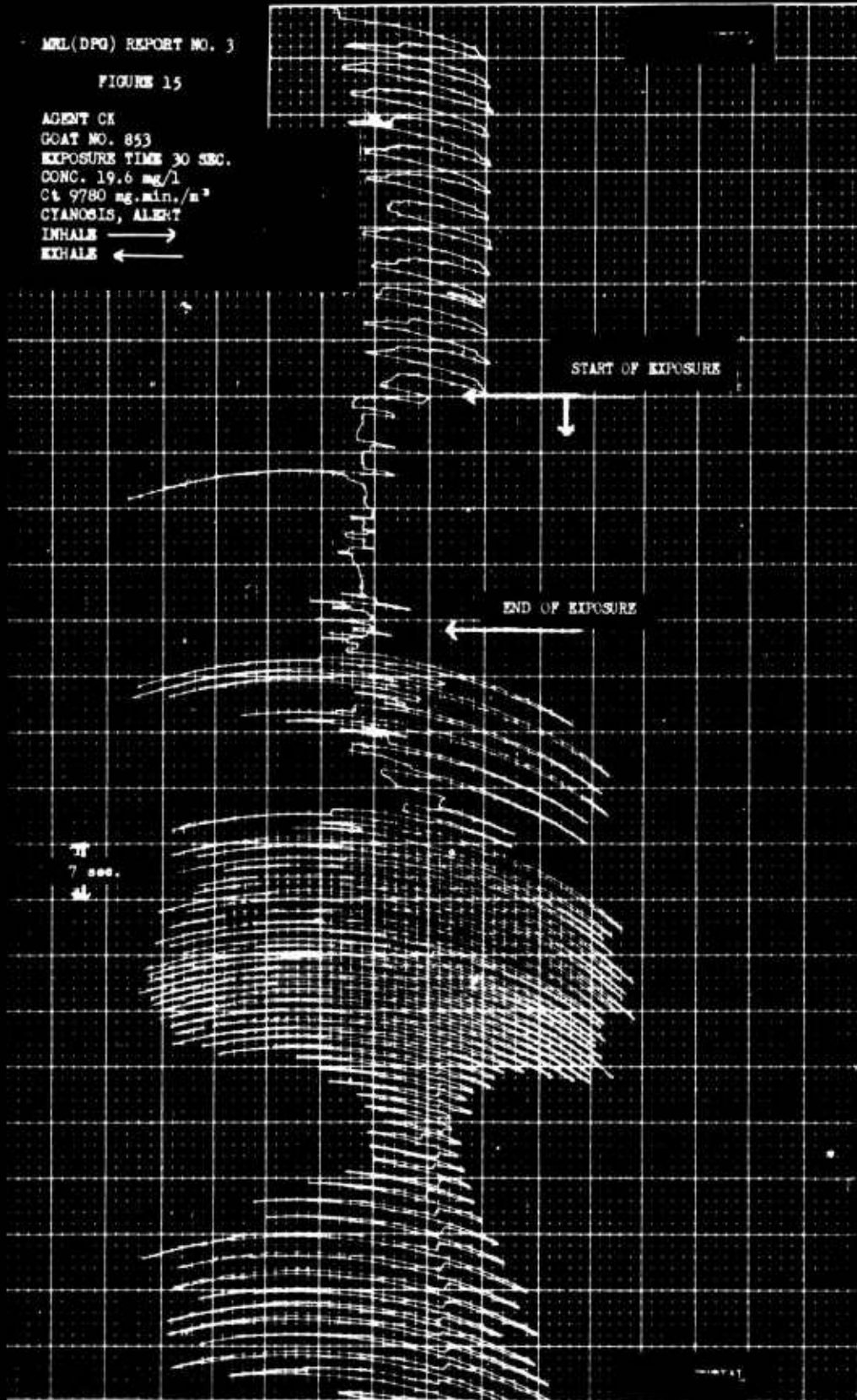
COMA AND CONVULSIONS

7 sec.

MRL(DPG) REPORT NO. 3

FIGURE 15

AGENT CX  
GOAT NO. 853  
EXPOSURE TIME 30 SEC.  
CONC. 19.6 mg/l  
Ct 9780 mg.min./m<sup>3</sup>  
CYANOSIS, ALERT  
INHALE →  
EXHALE ←



THE EFFECT OF  
RESPIRATORY BEHAVIOR OF GOATS EXPOSED TO AC FOR 15 SECONDS

Respiratory Behavior

Goat Number	Analytical Concentration	Analytical Conc. mg./m <sup>3</sup>	Depressed Phase		Duration	Onset of Stimulation	Onset of Collapse	Time of Death	Recovery Time	Remarks	Figure Number
			Character of Depressed Respiration	Sec.							
433	45.0	11,250	Shallow	15	15	40	12	—	Pulmonary hemorrhage	20	
12	35.5	8,970	Shallow	7	7	45	17	—	Pulmonary hemorrhage		
UMG*	32.7	8,170	Moderate shallow	10	10	30	3	—	Pulmonary hemorrhage		
440	26.4	7,100	Shallow	8	13	40	8	—	Coma and convulsions preceded death		
UMG	27.7	6,930	None	—	15	35	6	—	Coma and convulsions preceded death		
474	27.6	6,900	Shallow	7	7	35	4	—	Coma and convulsions preceded death		
84	27.4	6,850	None	—	7	35	8	—	Coma and convulsions preceded death		
494	26.9	6,720	None	—	18	45	—	30	Convulsions	17	
812	26.0	6,500	None	—	15	45	—	50	Convulsions		
575	25.4	6,350	Shallow, 8 sec., breath holding-7 sec.	15	21	None	—	1	No symptoms	22	
211	23.0	5,750	Shallow	15	15	60	—	12	Convulsions		
486	20.2	5,050	Shallow, slow	15	15	None	—	1	No symptoms		
35	18.4	4,600	None	—	8	30	7	—	Coma and convulsions preceded death		
143	16.4	4,100	None	—	7	40	7	—	Coma and convulsions preceded death	21	
173	14.9	3,720	None	—	8	45	—	30	Convulsions		
305	13.6	3,400	None	—	18	90	—	2	Convulsions		
860	13.0	3,250	None	—	15	40	—	3	Convulsions		

1 - Hearing masks  
 All times are from start of exposure  
 I - Immediate Recovery  
 \* Un-numbered Goat

TABLE 4  
RESPIRATORY BEHAVIOR OF GOATS EXPOSED TO AEROSOL FOR 2 MINUTES AND FOR 30 SECONDS  
Respiratory Behavior      Response of Goat

Goat Number	Time of Exposure Min.	Analytical Concentration mg./l.	Analytical Ct mg. min./m <sup>3</sup>	Onset of Stimulation Sec.	Duration of Stimulation Sec.	Onset of Depression Sec.	Onset of Collapse Sec.	Time of Death Min.	Recovery Time Min.	Remarks	Figure Number
336	2	8.10	16,200	14	30	44	45	4.5	—	Coma and convulsions preceded death	—
537	2	4.71	9,120	22	58	80	80	5	—	Coma and convulsions preceded death	—
847	2	4.15	8,300	15	44	59	50	6	—	Coma and convulsions preceded death	—
1316	2	2.64	5,280	22	58	60	55	—	27	Coma and convulsions preceded death	17
421	2	2.36	4,720	11	62	73	45	5	—	Coma and convulsions preceded death	—
200	2	2.32	4,640	25	75	100	85	—	77	Coma and convulsions preceded death	16
345	2	2.14	4,280	37	71	108	80	10	—	Coma and convulsions preceded death	—
118	2	2.08	4,160	22	57	79	65	4.5	—	Coma and convulsions preceded death	—
412	2	1.96	3,920	5	75	80	75	—	52	Coma and convulsions preceded death	—
UNG	2	1.63	3,260	30	93	123	85	8	—	Coma and Convulsions preceded death	—
286	2	1.62	3,240	15	56	71	50	—	52	Convulsions preceded death	—
305	2	1.24	2,480	59	>135	None	125	—	7	Convulsions	—
374	2	1.24	2,480	30	90	120	110	—	22	Convulsions	—
603	2	1.10	2,200	24	96	120	73	—	15	Convulsions	—
874	2	1.07	2,140	26	100	126	100	—	15	Convulsions	—
362	2	0.98	1,960	22	131	153	65	—	38	Convulsions	—
197	2	0.89	1,780	38	96	134	140	—	32	Convulsions	—
498	2	0.87	1,740	35	78	113	None	—	1	No symptoms	—

All times are from start of exposure  
I - Immediate recovery  
1 - Wearing masks



████████████████████

Depressed respiration occurred from the onset of exposure in 8 of 12 goats exposed to concentrations over 18.4 mg./l. It was characterized by complete breath holding in one goat and very shallow, slow respiration in the others. This phase continued for 7 to 15 seconds after initial exposure and was immediately followed by stimulated respiration. Respiratory depression as described above followed the stimulated phase. All goats exposed for 15 seconds to concentrations of 27.4 mg./l. or higher died regardless of the nature of their respiration during exposure. Representative tracings of the respiratory pattern for goats exposed to AC are presented in Figures 16 to 22.

#### 4. Toxicity for Exposures of "Masked" Goats.

From the results of studies on respiratory behavior it was possible to estimate the toxicity of CG, CK, and AC for short exposures of goats wearing the special mask. Since a relatively small number of animals were exposed, the values can be considered as only approximate. The following L(Ct)50's were obtained graphically.

<u>Agent</u>	<u>Time of Exposure</u>	<u>No. Goats Exposed</u>	<u>Approximate L(Ct)50</u> mg.min./m <sup>3</sup>
CG	Variable*; average 100 seconds	17	17,000
CK	Two minutes	24	14,000
AC	15 Seconds	17	6,000
AC	30 Seconds	10	3,000
AC	Two minutes	18	4,000

\* Results of 330 and 720 second exposures were not included.

Thirty second exposures to CG and CK showed no correlation between concentration and mortality (7 and 18 goats exposed, respectively). Use of a greater number of animals would not be expected to change this conclusion, since breath holding of 30 seconds duration or longer occurred in 20 out of 21 goats for CG concentrations of 1.3 mg./l. and higher; and since 31 out of 34 goats exposed to CK concentrations of 2.4 mg./l. and higher exhibited respiratory depression for 25 seconds or longer. For each of the three agents studied individual respiratory behavior accounted for every pronounced variation from the plotted log dosage-mortality probit curve.

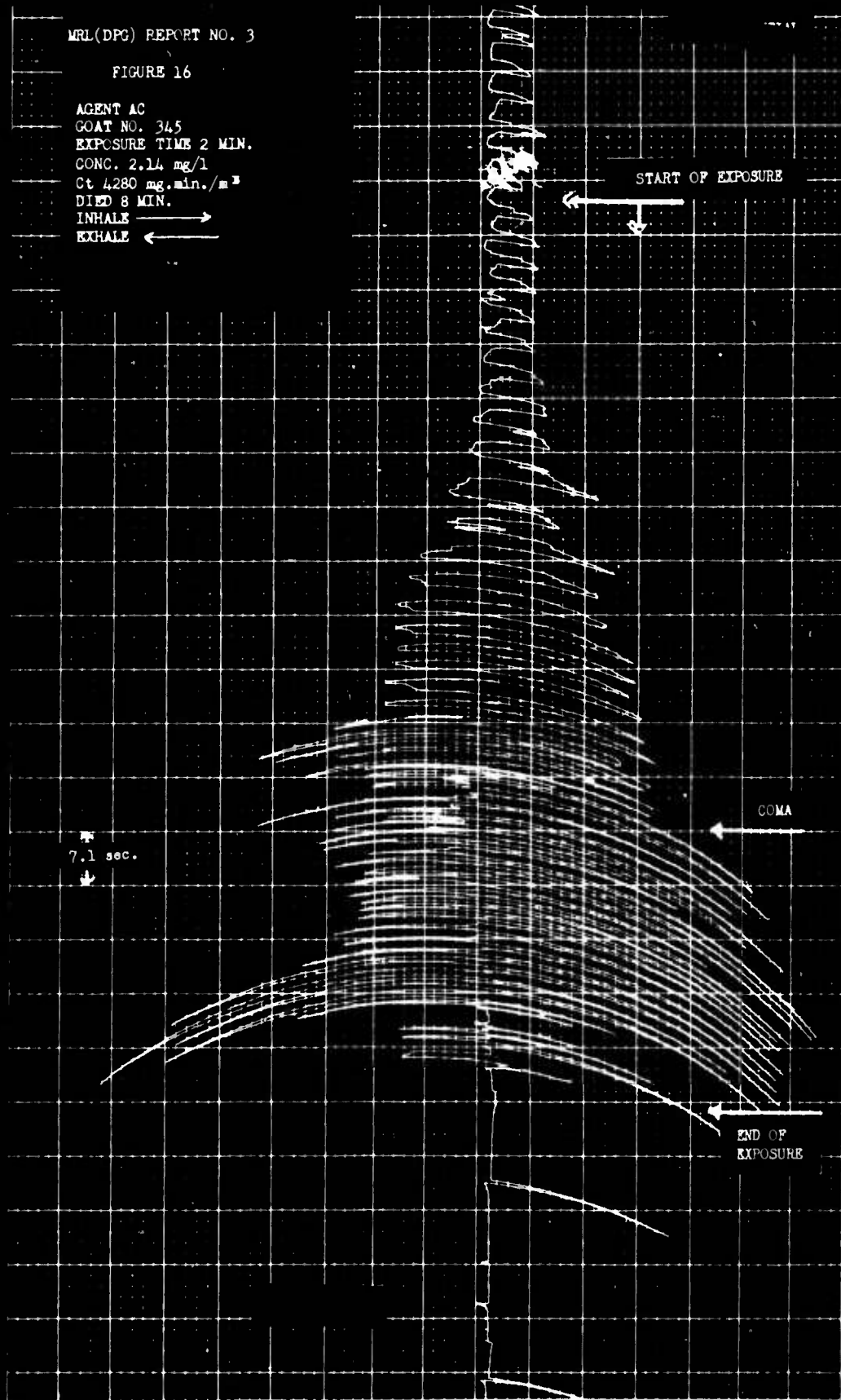
In order to evaluate the effects of skin absorption of AC during short total exposures, six "masked" goats were placed in the chamber for 30 seconds and the chamber atmosphere circulated through the mask at 34 l./min. No significant difference was found between the effects on these "masked" goats and "masked" goats placed outside the chamber (Table XII).

Eleven additional goats with their mouths taped shut to simulate the effect of the mask were placed in the chamber and exposed to AC for 30 seconds. In this manner possible absorption of agent through the mucous membranes of the mouth was eliminated. The approximate L(Ct)50 for these goats was 1700 mg.min./m<sup>3</sup>. The details are presented in Table XII.

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FIGURE 16

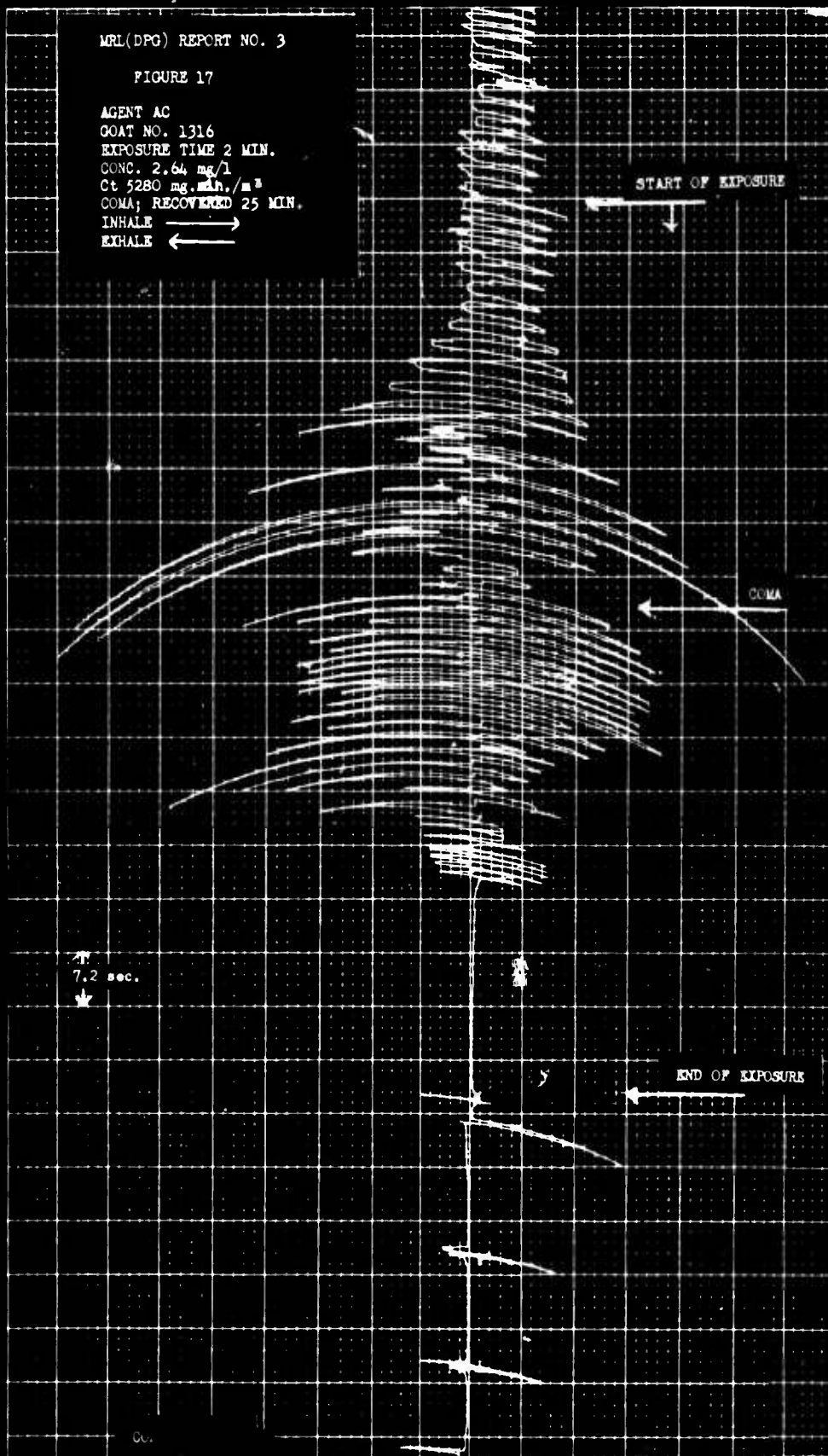
AGENT AC  
GOAT NO. 345  
EXPOSURE TIME 2 MIN.  
CONC. 2.14 mg/l  
Ct 4280 mg.min./m<sup>3</sup>  
DIED 8 MIN.  
INHALE →  
EXHALE ←



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FIGURE 17

AGENT AC  
GOAT NO. 1316  
EXPOSURE TIME 2 MIN.  
CONC. 2.64 mg/l  
Ct 5280 mg. $\cdot$ h./m<sup>3</sup>  
COMA; RECOVERED 25 MIN.  
INHALE  $\rightarrow$   
EXHALE  $\leftarrow$



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FIGURE 18

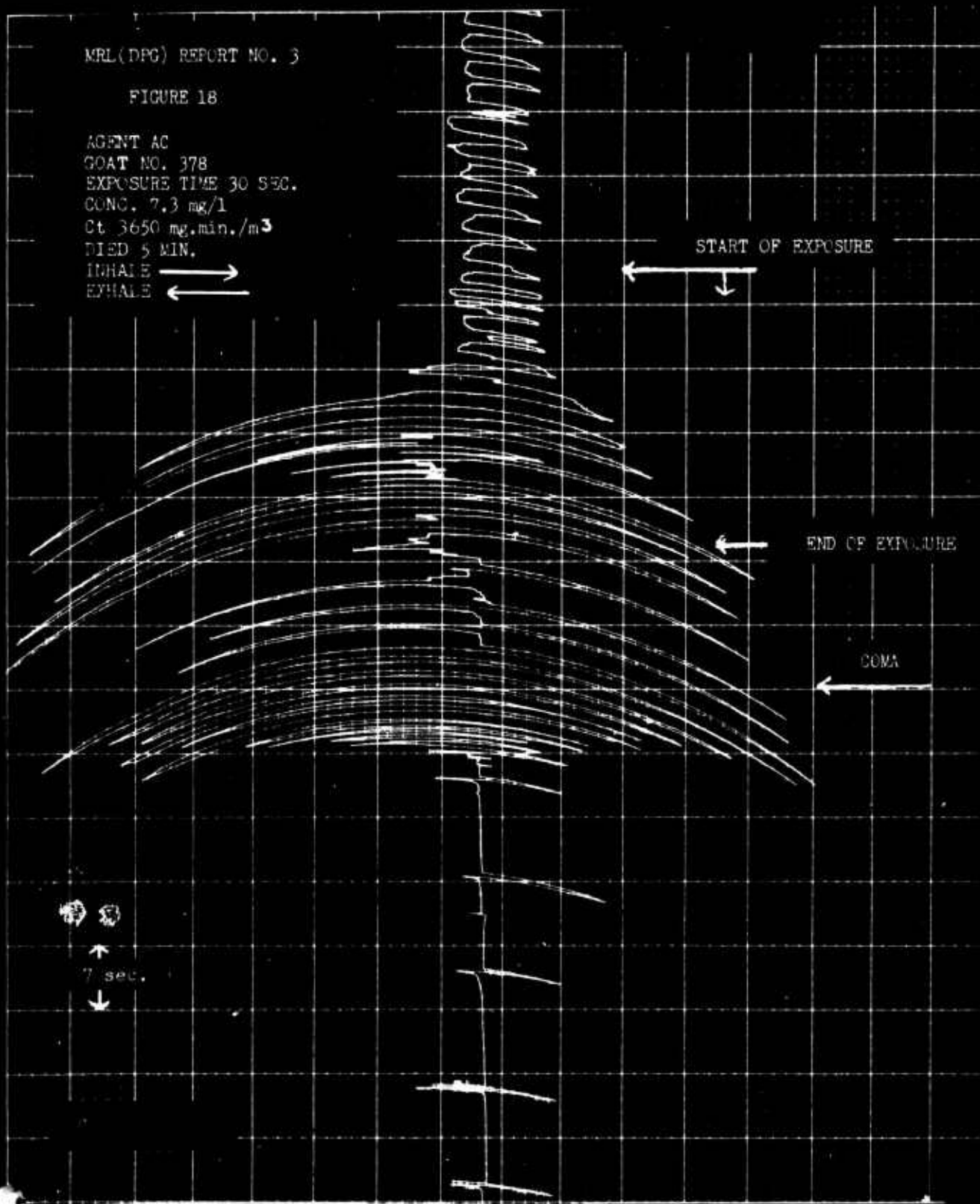
AGENT AC  
GOAT NO. 378  
EXPOSURE TIME 30 SEC.  
CONC. 7.3 mg/l  
Ct. 3650 mg.min./m<sup>3</sup>  
DIED 5 MIN.  
INHALE →  
EXHALE ←

START OF EXPOSURE

END OF EXPOSURE

COMA

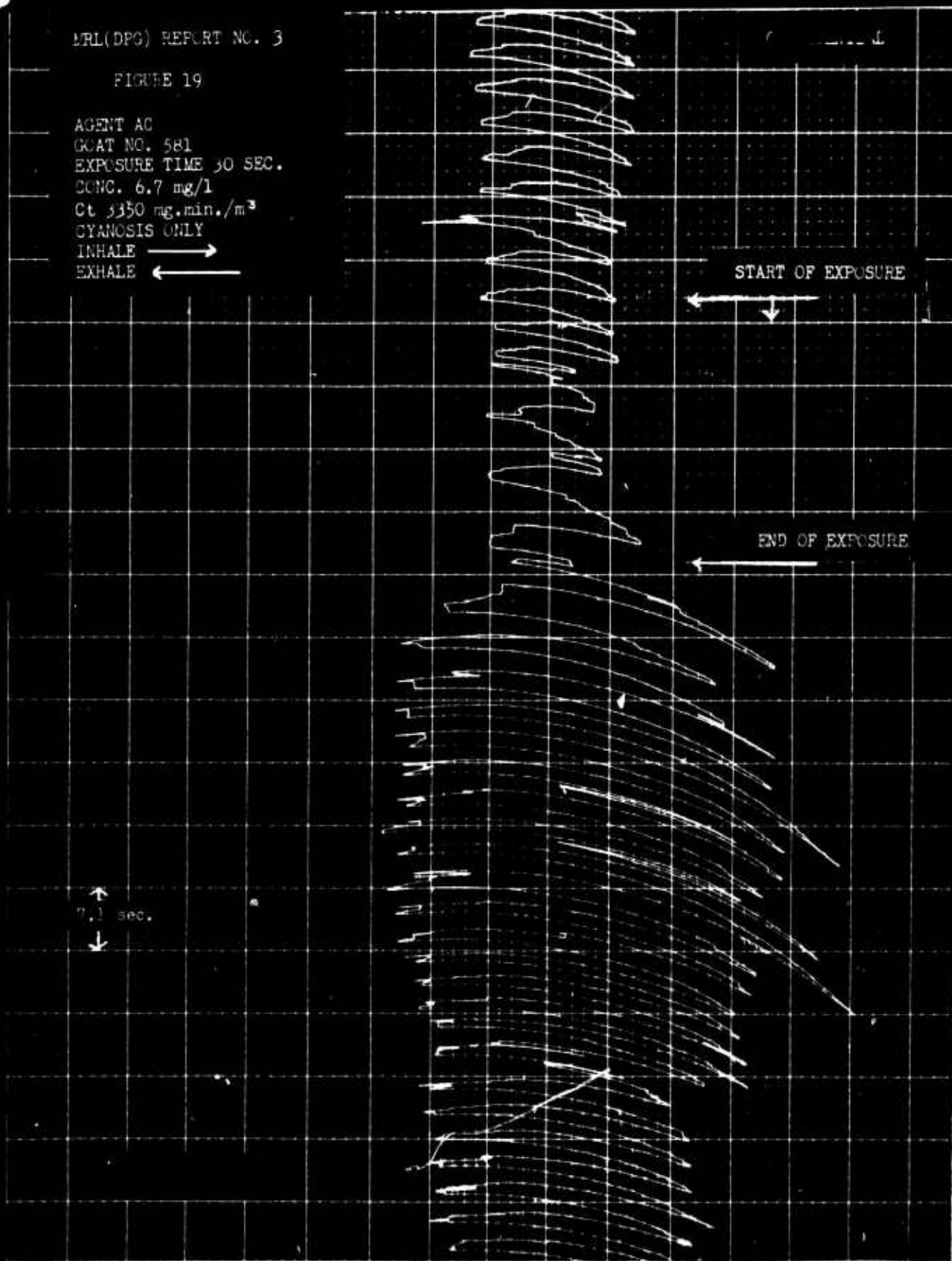
7 sec.



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FIGURE 19

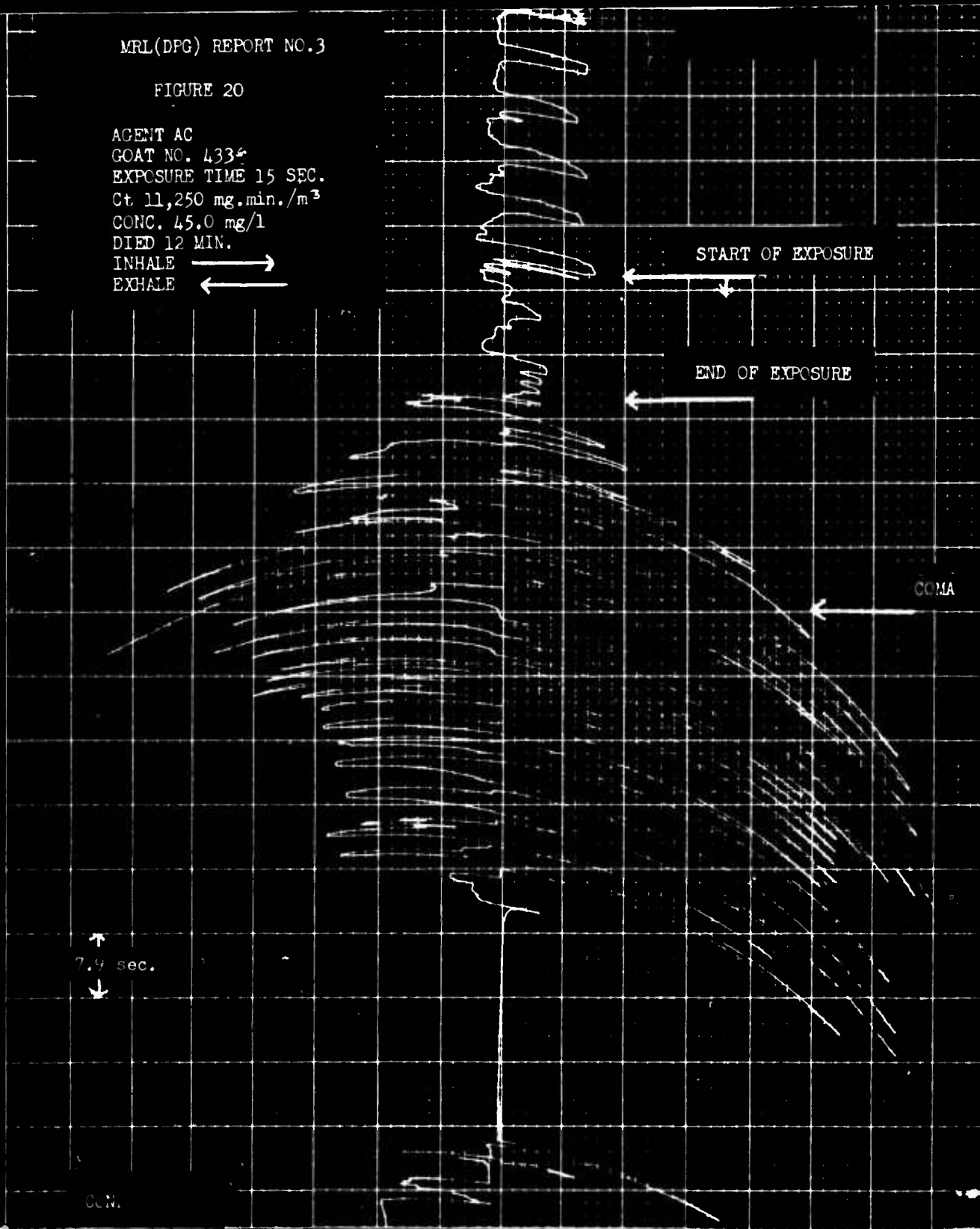
AGENT AC  
GCAT NO. 581  
EXPOSURE TIME 30 SEC.  
CCNC. 6.7 mg/l  
Ct 3350 mg.min./m<sup>3</sup>  
CYANOSIS ONLY  
INHALE →  
EXHALE ←



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FIGURE 20

AGENT AC  
GOAT NO. 4334  
EXPOSURE TIME 15 SEC.  
Ct 11,250 mg.min./m<sup>3</sup>  
CONC. 45.0 mg/l  
DIED 12 MIN.  
INHALE →  
EXHALE ←



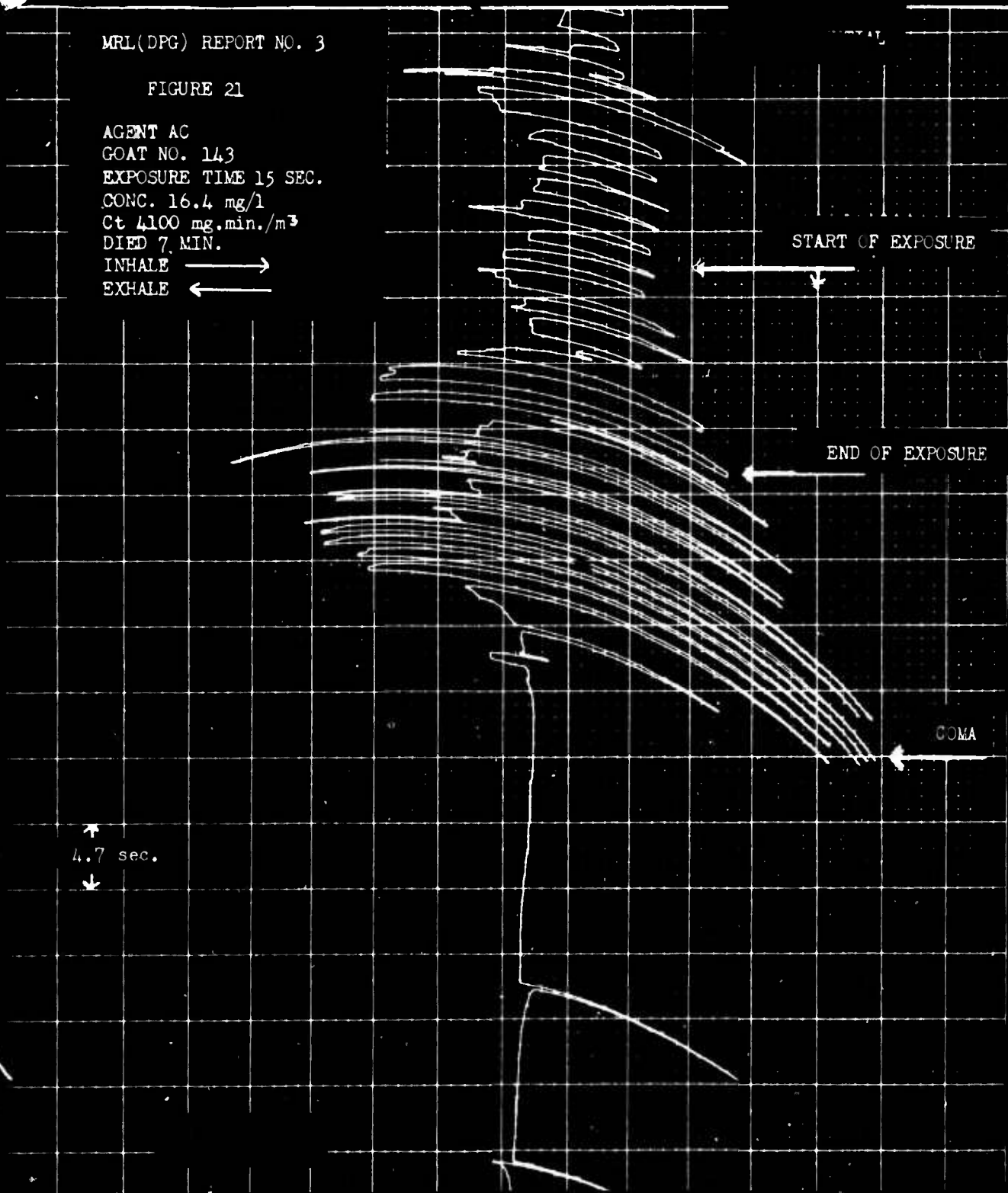
↑  
7.9 sec.  
↓

CCM.

MRL(DPG) REPORT NO. 3

FIGURE 21

AGENT AC  
GOAT NO. 143  
EXPOSURE TIME 15 SEC.  
CONC. 16.4 mg/l  
Ct 4100 mg.min./m<sup>3</sup>  
DIED 7 MIN.  
INHALE →  
EXHALE ←



MRL (DPG) REPORT NO. 3

FIGURE 22

LEVEL AC  
GOAT NO. 575  
EXPOSURE TIME 15 SEC.  
CONC. 25.4 mg/l  
Ct 6350 mg.min./m<sup>3</sup>  
NO SYMPTOMS  
INHALE →  
EXHALE ←

START OF EXPOSURE

END OF EXPOSURE

6.8 sec.

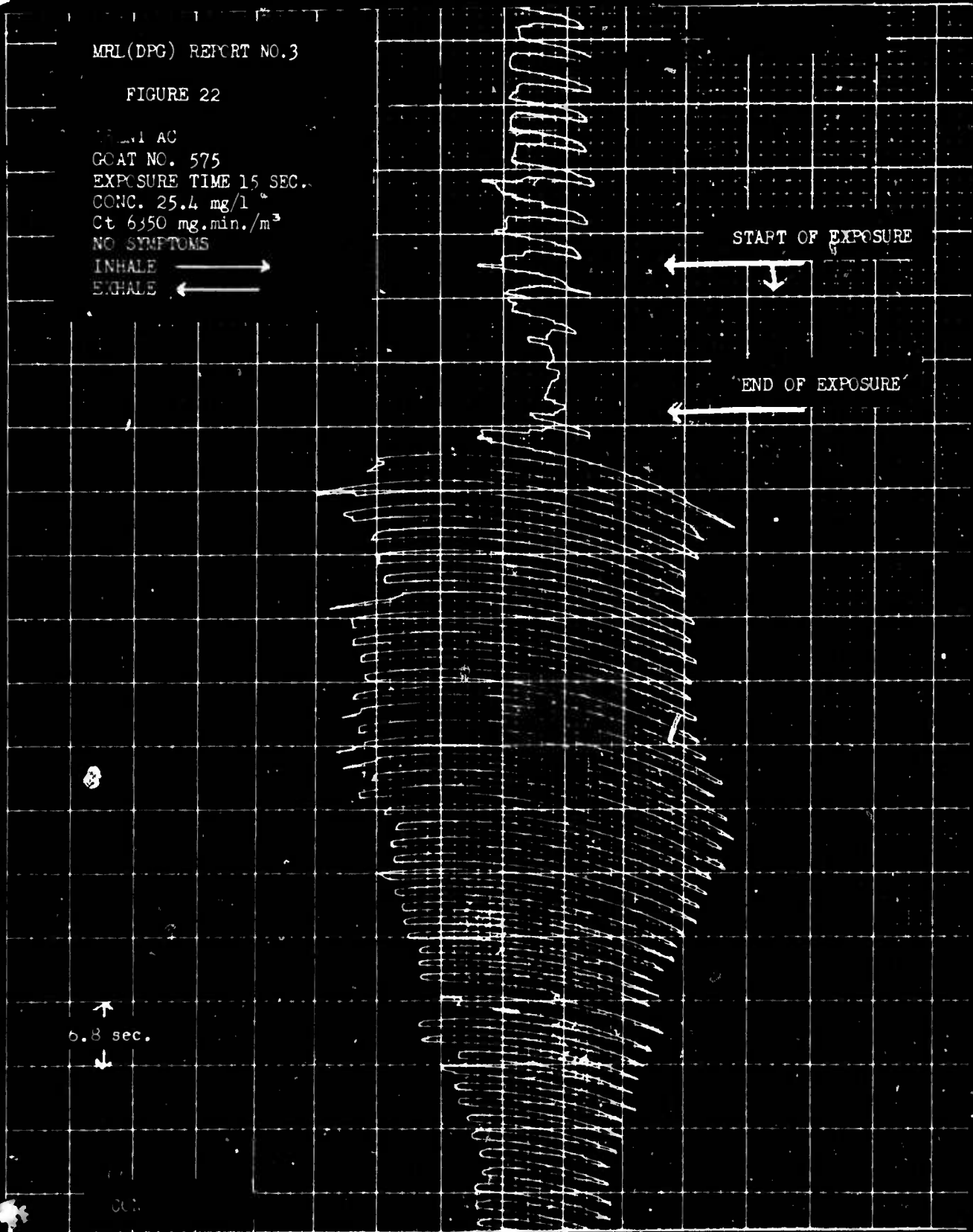


TABLE 211

EFFECT OF CLOSING MOUTH OF GOATS EXPOSED TO AC FOR 30 SECONDS

Goat Number	Method of Closing Mouth	Analytical Concentration mg./l.	Analytical Ct mg. min./m <sup>3</sup>	Time of Collapse Sec.	Time of Death Min.	Time of Recovery Min.	Remarks
42	Masked	5.10	2550	45	—	50	Chamber Gas Drawn Through Mask at 34 l./min. Goat Inside Chamber
389	Masked	4.57	2285	62	—	2	Coma, convulsions Cyanosis only
428	Masked	4.37	2165	40	30	—	Epistaxis
1307	Masked	4.27	2135	45	—	8	Coma, convulsions
167	Masked	2.69	1345	50	—	3	Cyanosis only
108	Masked	2.64	1320	40	—	2	Coma, convulsions
8	UNG Taped	4.04	2020	25	9	—	Mouth of Goat Taped Shut. Exposure Made in the Gas Chamber
1339	Taped	4.04	2020	25	—	90	Coma and convulsions preceded death
806	Taped	3.49	1745	41	30	—	Coma, convulsions preceded death
306	Taped	3.32	1660	35	—	9	Coma, convulsions
398	Taped	3.32	1660	45	—	23	Coma, convulsions
79	Taped	3.32	1660	44	—	60	Coma, convulsions
429	Taped	3.32	1660	37	—	8	Coma, convulsions
292	Taped	3.27	1635	35	15	—	Coma and convulsions preceded death
303	Taped	3.27	1635	35	15	—	Coma and convulsions preceded death
70	Taped	2.24	1120	45	—	5	Coma, convulsions

11

2

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#### IV. DISCUSSION.

##### A. Determination of Toxicity of Nonpersistent Agents for Short Exposures.

It is evident from these and other studies that the toxicity of nonpersistent agents is largely dependent upon the respiratory behavior of the subject during exposure. This is particularly true for short exposures; while in longer exposures (~5 min.) the effects due to initial changes of breathing assume decreasing importance. Because of differences in respiratory response to widely varying concentrations of CG, CK, and AC, it is likely that the log dosage-mortality probit relationships will not always be linear (e.g. 30 second CG exposures), and the L(Ct)50 value will not have its usual significance. For this reason it is most important that determinations of toxicity for short period exposures to these agents include a wide range of concentrations. Omission of the extremes has misled investigators, and has resulted in a misinterpretation of data. The individual differences in respiratory response of the animals, particularly to the irritant gases, CG and CK, often result in unusually wide dispersion of the mortality data. In these cases a determination of L(Ct)50 may be impractical.

The apparent failure of the L(Ct)50's of all of these agents to comply with Haber's Ct law can be accounted for by the respiratory behavior. Extremely high values found for short period exposures to CG and CK are due to respiratory depression during the initial part of the exposure. It is also evident that the relationship of the L(Ct)50 values for "masked" goats for 15 second, 30 second, and 2 minute exposures to AC cannot be fully accounted for by the usual equations (T.D.M.R. 699; Medical Division Report No. 22) taking detoxication into account. The value of 6,000 mg.min./m<sup>3</sup> for 15 second exposures is high because respiratory stimulation does not usually occur during that period. For 30 second and 2 minute exposures lower values of 3000 and 400 mg.min./m<sup>3</sup> are found because respiratory stimulation during that period results in a much higher respiratory volume.

##### B. Use of "Masked" Goats.

It is apparent that the toxicity figures for exposures of "masked" and unmasked goats are not in agreement. In each case where a comparison is afforded the L(Ct)50 values for "masked" goats are about two times greater. These are shown as follow:

<u>Agent</u>	<u>Time of Exposure</u> min.	<u>L(Ct)50 for Unmasked Goats</u> mg.min./m <sup>3</sup>	<u>Approximate L(Ct)50 for "Masked" Goats</u> mg.min./m <sup>3</sup>
CG	2	6500 ± 750	17,000*
CK	2	7000 ± 750	14,000
AC	1/2	1300	3,000
AC	2	2200**	4,000

\* t = 45 to 169 seconds, average 100 seconds

\*\* T.R.L.R. 23

[REDACTED] UNCLASSIFIED

It was found that total exposures of goats with their mouths bound shut resulted in slightly increased resistance to AC (approximate L(Ct)50 1700 mg.min./m<sup>3</sup>) when compared with total exposures of unmasked goats (L(Ct)50 1300 mg.min./m<sup>3</sup>). This increase was less in degree than for total exposures of "masked" goats with the chamber atmosphere circulating through the mask (Table XII).

Several possible sources were considered for this difference in toxicity. Possible dilution of the mask concentration by exhaled air was not thought to be a significant factor because of the rapid circulation rate used through the mask and because, in the case of CK, mask concentrations were found to vary by less than 10% from that of the chamber (Table I). Body absorption was shown not to be an important factor for short exposures. It was observed that unmasked goats frequently opened their mouths and licked their lips during exposure, whereas "masked" goats were unable to open their mouths. This could permit additional absorption of agent, particularly AC, through the mucous membrane of the mouth of unmasked goats. However, since the ratios of toxicities are identical (i.e. about 2 for each agent), it seems likely that the differences are caused by a similar factor for each agent. Mouth absorption for AC would therefore appear to be of minor importance. In view of all these observations, it seems most likely that the mask to some degree discourages the breathing effort of the goat. This would result in a decrease in the respiratory minute volume and, consequently, a decreased amount of agent inspired by the animals. There is, however, no reason to believe that the qualitative picture of respiratory behavior of the goat is essentially changed by the mask.

As a result of this investigation it is apparent that the use of "masked" goats for field bio-assay is subject to several marked limitations. Exposures of goats for 30 second intervals to the irritant gases yields no useful information. The toxicity data for comparison to field findings of all agents requires correction for the effect of the surprise mask upon the goat. Where this device is used, steps should be taken to reduce or eliminate dead space within the mask to prevent dilution of the inspired air through rebreathing effects.

### C. Limitations of Surprise Effects.

Exposure of goats to high concentrations of CK and CG caused marked respiratory depression of variable duration. That reflex action, mediated by the afferent fibers of the vagus nerve, accounts, at least in part, for this effect has been shown on anesthetized dogs (N.D.R.C. Div. 9 Report of U.C.T.L. 9-4-1-15 April 1944). In many cases, the duration of respiratory depression exceeded the presumed period of exposure to a crash concentration so that the amount of gas inhaled by the animal, and hence the effective dosage, was markedly reduced.

AC, on the other hand, appeared non-irritating in concentrations below 20 mg./l. Even above this level, where initial respiratory depression was observed, the amount of agent inhaled in 15 seconds was often enough to produce death. Its non-irritant properties, combined with respiratory stimulation, make AC the biologically preferable standard nonpersistent agent for obtaining surprise effects. Difficulties in its field dispersal however, reduce its usefulness at the present time.

[REDACTED] UNCLASSIFIED

The data herein presented emphasize the importance of non-irritancy in the use of respiratory lethal agents where surprise is sought.

V. CONCLUSIONS.

A. The toxicity of nonpersistent agents during short exposures is largely dependent on the respiratory response of the subject during exposure.

B. Exposures to high concentrations of the irritant gases, CG and CK, result in reflex respiratory depression. This respiratory depression reduces the effectiveness of crash concentrations of these agents for surprise effects.

C. On the basis of physiological response, AC is the most desirable standard nonpersistent agent for surprise effects.

D. Short interval exposures of "masked" goats to a nonpersistent gas cloud are subject to the following limitations:

1. The effectiveness of the agent is reduced approximately one-half by the presence of the mask under the conditions tested.

2. The dead space of the mask dilutes the agent, unless measures are taken to circulate the atmosphere through the mask.

3. Exposures to irritant gases of two minutes duration or less result in marked variation in response.

4. Exposures to irritant gases of 30 seconds duration or less show no correlation between the concentration of agent and mortality.

VI. RECOMMENDATIONS.

A. Field requirements for non-persistent agents should be re-examined in the light of these results to establish new criteria for lethal surprise effects.

B. New methods for controlled short exposures of goats in the field to nonpersistent agents should be investigated.

C. Field data obtained with unmasked and "masked" goats should be re-evaluated.

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MRL (DPG) REPORT NO. 3  
A STUDY OF SHORT INTERVAL EXPOSURES  
OF GOATS TO CG, CK, AND AC

Submitted by:

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Captain, CWS

Experimental Work:

Started: 15 November 1944  
Completed: 10 September 1945  
Notebooks on file in MRL, DPG

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REPLY TO  
ATTENTION OF

RDCB-DPS-RS

*MS 27 AUG 14*

AUG 27 2014

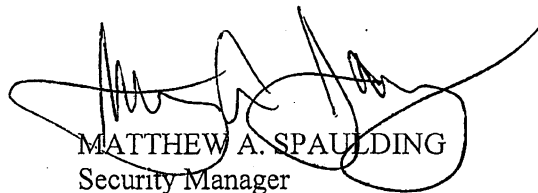
MEMORANDUM THRU Director, Edgewood Chemical Biological Center, (RDCB-D/Mr. Joseph Wienand), 5183 Blackhawk Road, Aberdeen Proving Ground, Maryland 21010-5424

FOR Defense Technical Information Center, 8725 John J. Kingman Road, Ft Belvoir, VA 22060

SUBJECT: Internal Request for Change in Distribution

1. This action is in response to an Edgewood Chemical Biological Center (ECBC) Internal Request for a Change in Distribution on documents related to cyanogen chloride.
2. The listed documents in the attachment have been reviewed by ECBC Subject Matter Experts and deemed suitable for the change in distribution to read "Approved for Public Release; distribution unlimited."
3. The point of contact is Adana L. Eilo, ECBC Security Specialist, (410) 436-2063, [adana.l.eilo.civ@mail.mil](mailto:adana.l.eilo.civ@mail.mil).

Encl

  
MATTHEW A. SPAULDING  
Security Manager

## Cyanogen Chloride References

[1] Armstrong, GC, *Toxicity of Cyanogen Chloride to White Mice by Inhalation*, War Department, Chemical Warfare Service, Edgewood Arsenal, MD, 03 March 1933. Unclassified, Dist. D. DoD/Contractors. AD# B956466.

[2] Fuhr, I., Krackow, E.H., *Cyanogen Chloride LC 50 for Rats: 2 min. Exposure*, **TRLR-27**, Edgewood Arsenal, Aberdeen Proving Ground, MD, 12 April 1944, Unclassified, Dist. D, DoD/Contractors. AD# B967754

[3] E.H. Krackow, Fuhr, I., *Cyanogen Chloride LC 50 for Rabbits: 2 min. Exposure*, **TRLR-33**, Edgewood Arsenal, MD, 31 May 1944, Unclassified, Dist. D, DoD/Contractors. AD# B967782.

[4] Bass, A.D., Tucker, V.J., *Cyanogen Chloride, Informal Progress Report No. 37*, **CB-186516**, National Defense Research Committee of the Office of Scientific Research and Development, Washington, DC, 22 June 1943, Unclassified, Dist. E, DoD Only.

[5] Kolls, AC, Kuhn, HA, and Todd, AJ, *Report on Toxicity Tests on Mice*, **Report No. 33** in Marshall, EK ed., **Pharmacological and Research Section Monographs**. War Department Chemical Warfare Service, Research Division, American University Experiment Station, Washington, DC, c. 1917. On file with the Historical Research and Response Team, Research, Development and Engineering Command, Aberdeen Proving Ground, MD. Unclassified, Dist. E, DoD Only.

[6] Franklin, R.C., Wilding, J.L., Stone, W., Franklin, R.T., *A Study of Short Interval Exposures of Goats to Cg, Ck, and Ac*, **CB-004057**, Dugway Proving Ground, UT, 28 November 1945, Unclassified, Dist. B, U.S. Gov't Agencies Only.

[7] Kolls, AC, Kuhn, HA, and Todd, AJ, *Report on Toxicity Tests on Mice*, **Report No. 41** in Marshall, EK ed., **Pharmacological and Research Section Monographs**. War Department Chemical Warfare Service, Research Division, American University Experiment Station, Washington, DC, c. 1917. On file with the Historical Research and Response Team, Research, Development and Engineering Command, Aberdeen Proving Ground, MD. Unclassified, Dist. E, DoD Only.