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ABSTRACT

AN ESTIMATE OF THE RELATIVE EXPOSURE OF U.S. AIR FORCE CREWMEMBERS TO AGENT ORANGE

by Stephen Langdon Meek

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The U.S. Air Force is conducting a major epidemiological investigation of the health status of personnel previously assigned to a herbicide spray unit. Of critical importance to this investigation is exposure information, particularly relative exposure, to allow examination of possible dose-response relationships. No such exposure information was available, thus this attempt to reconstruct the conditions existing and assess relative exposure. Four flights were conducted in spray aircraft with analyses made of internal airflow, vapor dispersal, and aerosol dispersal and deposition. It was determined that internal air movement was such to provide the potential for exposure to all crewmembers. Vapor dispersal was as predicted by the air movement. An aerosol generated in the vicinity of the spray tank would disperse and deposit particles on all crewmembers, but unequally. From

the air movement, vapor dispersal, and particle deposition evidence it was concluded that the flight mechanic experienced an exposure at least six times as great as the other crewmembers.

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INTRODUCTION

Agent Orange has come to be for many people symbolic of the controversial nature of the Vietnam war. Agent (or Herbicide) Orange was used extensively during the conflict for defoliation and crop destruction. It consisted of a 50-50 mixture of the n-butyl esters of 2,4-dichlorophenoxyacetic acid (2,4-D) and 2,4,5-trichlorophenoxyacetic acid (2,4,5-T), two commercially available and widely used herbicides. Partly by extension of the Vietnam controversy (guilt by association) and partly due to reports of human health effects, the continued civilian use of the herbicides has generated considerable critical interest and opposition.

The U.S. National Academy of Science[2] estimated that a total of 11.27 million gallons of Agent Orange was dropped on Vietnam between 1965 and 1971. Agent Purple, a similar formulation, was used in relatively small quantities from 1962 through 1964.

By far, the major part of these herbicides were expended by U.S. Air Force crews operating specially modified transport aircraft, an operation code-named Ranch Hand.

In 1970, the Secretaries of Agriculture, Health, Education and Welfare, and the Interior issued a joint suspension of some uses of 2,4,5-T. The Department of Defense suspended the use of Agent Orange shortly thereafter. These actions followed a report by Courtney et al[4] that 2,4,5-T was a teratogen in mice. Reports had appeared previously in the Vietnamese press that the herbicides caused malformations and stillbirths in humans, but these were largely disregarded as invalid and/or Viet Cong planted propaganda.

It was later found that early samples of 2,4,5-T were substantially contaminated with 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD or dioxin), an extremely toxic substance formed as a reaction by-product when trichlorophenol, a precursor of 2,4,5-T and other chemical products, is synthesized from tetrachlorobenzene. Young et al[10] compiled an excellent, and remarkably thorough, review of the literature pertinent to Herbicide Orange and an assessment of the human risk involved in the use of phenoxy herbicides. Major conclusions were that 2,4-D and 2,4,5-T are generally safe chemicals, that the human nervous and hematopoietic systems are sensitive to 2,4-D, that chloracne is the hallmark of TCDD exposure, that TCDD intoxication may cause hyperlipemia and an asthenic syndrome, that mutagenesis, carcinogenesis, and teratogenesis in man have not been confirmed although associations have been shown, and that the long-term effects of a chronic exposure to TCDD are unknown. TCDD concentrations were reported at 2 parts per million (ppm) in Agent Orange and at 45 ppm in Agent Purple.

Herbicide spraying in Vietnam by the Air Force was accomplished with modified C-123 (designated UC-123B) twin engine transport planes (Illustration I). The planes were internally equipped with a 1,000 gallon tank, pump, hosing, and associated controls (Illustration II). Externally, spray booms were mounted under each wing and the aft fuselage.

The normal flight crew included a pilot, co-pilot, and flight mechanic. Additionally, the lead aircraft in formation carried a navigator.

ILLUSTRATION I
UC-123B AIRCRAFT SPRAYING AGENT ORANGE

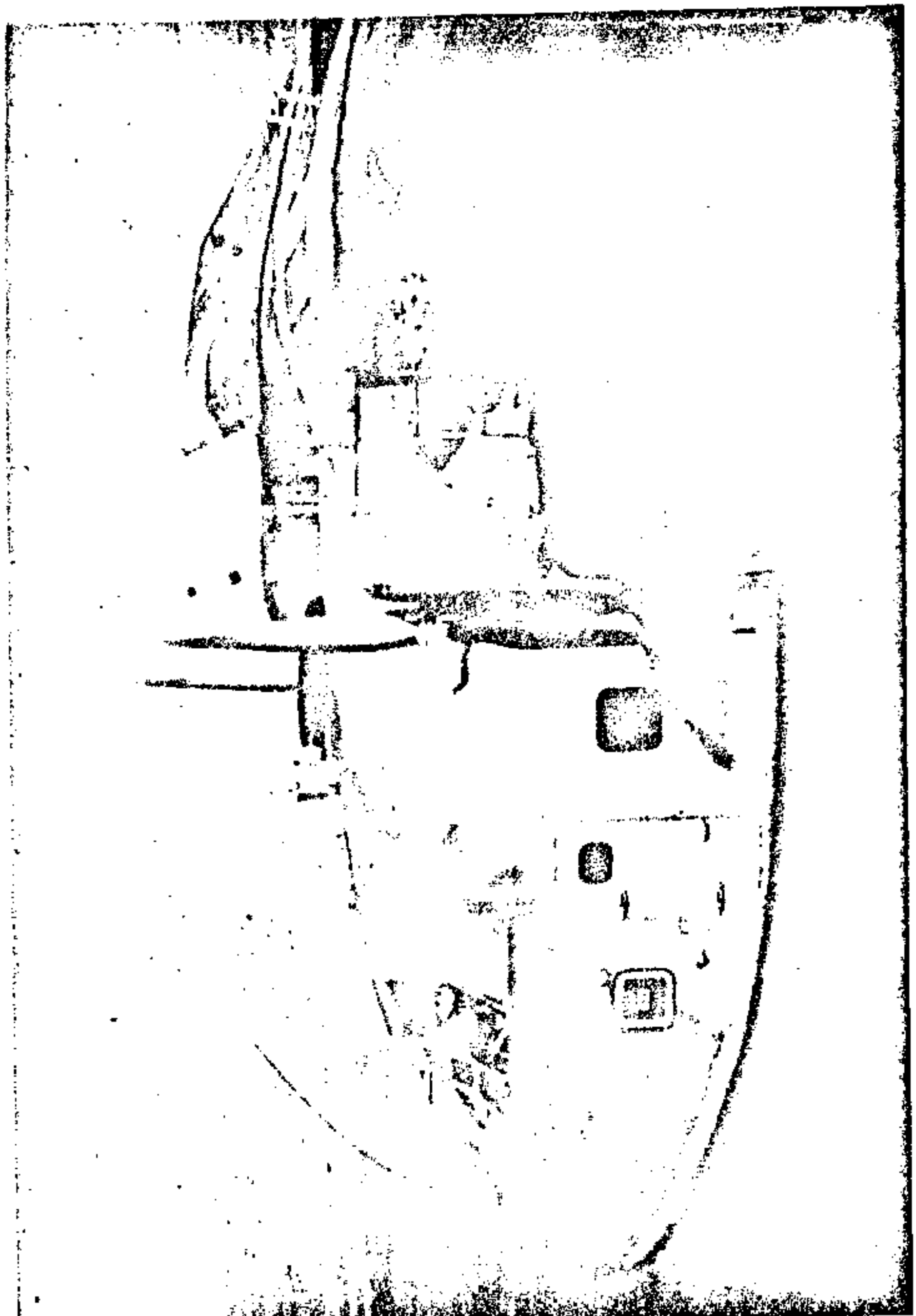
ILLUSTRATION II
FLIGHT MECHANIC AT SPRAY PUMP CONSOLE

A normal mission consisted of three or six aircraft flying approximately one hour enroute to a target area, spraying for five to ten minutes, then returning to base. The aircraft and crews frequently flew two missions per day.

The pilot and copilot remained in the cockpit throughout the mission, while the navigator and flight mechanic were free to move around except during the spraying. On target, the navigator positioned himself between the pilots to direct the spray path, while the flight mechanic took up his position at the spray pump control console in the aft cargo compartment.

While spraying, the pilot's and copilot's side windows were generally open for ventilation (Illustration III). Also open was the left aft troop door directly opposite the flight mechanic (enabling him to throw out smoke grenades to mark the location of anti-aircraft fire). An aeronautical engineer[7] estimated that this configuration would create forward air movement in the cargo compartment. The air would then enter the cockpit and exit the cockpit side windows. This corresponds with anecdotal information from Ranch

ILLUSTRATION III
COCKPIT WINDOW OPEN IN FLIGHT



Hand crews.[6] Thus, an air concentration of herbicide generated in the vicinity of the tank would likely have dispersed throughout the aircraft. Free herbicide as vapor or aerosol resulted from spills while filling the tank, pressurized leaks at fittings, bullet holes, etc. The crews therefore had potential exposures by inhalation and by skin deposition with subsequent absorption. Additionally, contact with herbicide dampened surfaces may have contributed to percutaneous absorption. Exposure would have generally been on a daily basis over a one year period.

PROBLEM

As it is possible there may have been, or will be, adverse health effects resulting from this exposure and as a response to the intense interest in, and controversy over, the use of herbicides, the U.S. Air Force is commencing a major epidemiological investigation of the health status of the Ranch Hand crews.

Of critical importance to such an investigation is exposure information. Assumptions have been made that Ranch Hand personnel were exposed and that their exposure was greater, of a chronic nature, and more easily documented than that of any other identifiable Vietnam veteran group. Unfortunately, it was not possible to ascertain actual exposures in terms of mg herbicide/Kg body weight. Nor was any specific information available on whether exposures varied as a function of crew duty position.

It was possible, however, to reconstruct the flight conditions existing during Ranch Hand missions and to evaluate some of the factors influencing exposure. This study did so with the specific intent of answering two questions:

(1) Did exposure to Agent Orange differ significantly as function of crew position?

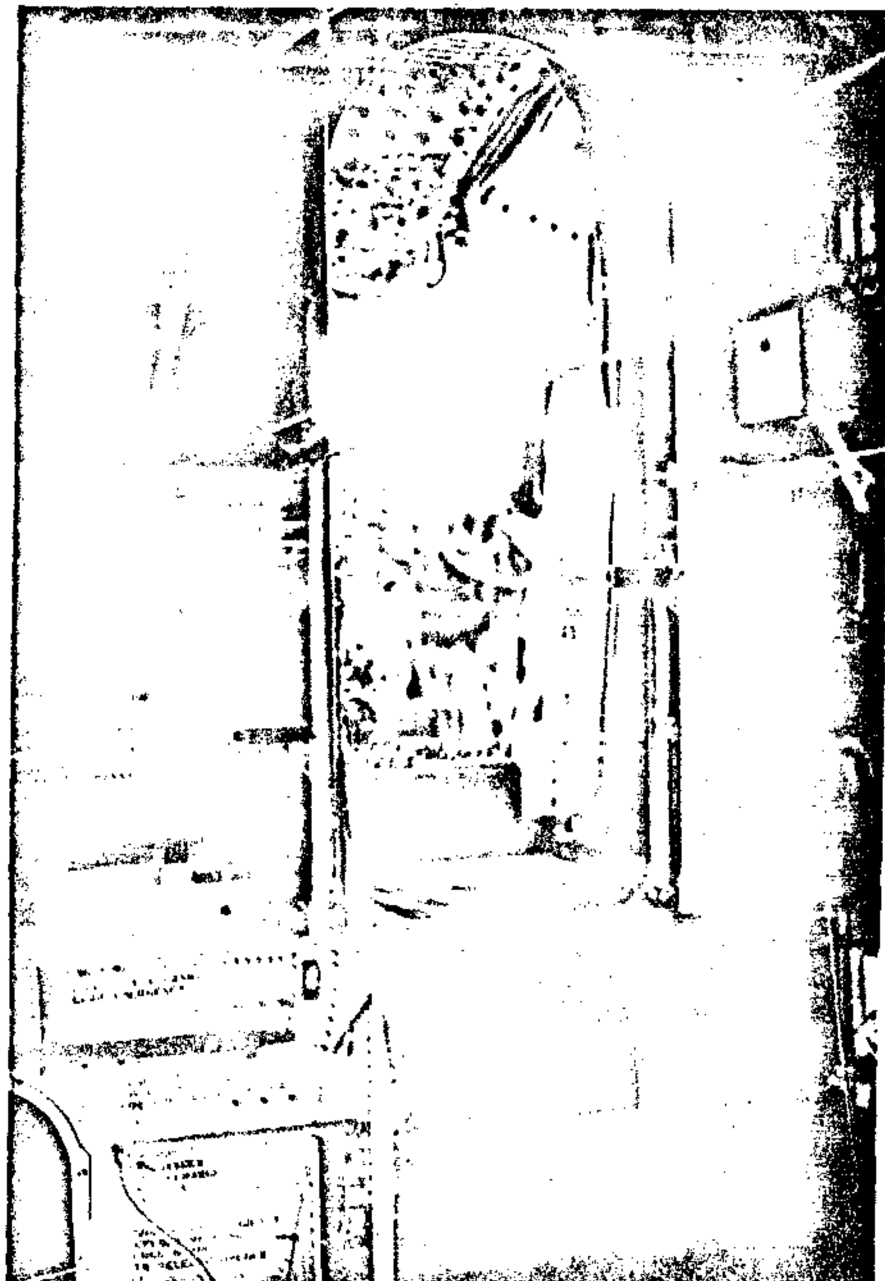
(2) If so, what was the magnitude of the difference?

METHODOLOGY

The U.S. Air Force provided UC-123 aircraft and crews for four flights (configured and flown to simulate spray missions) during which a three phase approach was taken to determine crew exposure. Phase one assessed internal airflow patterns. Smoke was used initially for gross evaluation of airflow. Physical dimensions of the aircraft were acquired. Air velocity at selected points in the cargo compartment and at the hatchway (Illustration IV) to the cockpit was measured with an Alnor Series 6000-P Velometer equipped with a 6070-P Probe. The hatchway was marked to facilitate measurements centered in six equal areas. Velocity readings were taken on all four flights in two different aircraft. Cabin air and internal surface temperatures were taken with a Tele-Thermometer. Relative humidity was measured with a Weksler psychrometer.

Phase two consisted of generating an aerosol of an Agent Orange simulant solution, then selectively collecting samples to assess dispersal and deposition

ILLUSTRATION IV
HATCHWAY FROM CARGO COMPARTMENT TO COCKPIT



of the particles. This phase was conducted during the third flight.

A portable generation system was developed, tested, and used. It consisted of a D oxygen cylinder containing 360 liters of medical oxygen with Puritan valve, regulator, and flowmeter equipment. This provided a pressure source for aerosol production by a Bard-Parker Model u-mid/hi Jet Nebulizer. Manufacturer's data indicated 95% of particles would be in the .8 to 6 micron range. On the aircraft the system was positioned just aft of the tank near the pump and hosing. The Agent Orange simulant solution was 10% glycerin in water containing 12 mg/ml sodium fluorescein as a marker. With oxygen flow set at seven (7) liters per minute and dilution with ambient air at 50%, the solution nebulized at the approximate rate of .6 ml/minute.

Sample collection included surface wipes, static skin deposition patches, and breathing zone air. The surface wipes and skin deposition patches were of Whatman #1 filter paper. The breathing zone air samples were collected using DuPont Model P-4000 Multi-Range High Flow Sampler Pumps drawing through

.8 μm Millipore membrane filters in closed-face cassette holders. The two pumps were adjusted to a flow rate near their maximum capacity. The copilot's pump was calibrated at 4.15 liters per minute; the flight mechanic's at 3.72 liters per minute. Both pumps were calibrated on the day of the flight using a bubble buret and with a duplicate sampling train attached.

The surface wipe locations were the copilot's arm rest and the flight mechanic's console. The skin deposition patches were securely attached to the copilot's and flight mechanic's left forearms. Air samples were taken by placing the pump in the lap, draping the hose around the neck, and positioning the filter cassette just under the chin. During the mission the copilot remained in his cockpit seat; the flight mechanic remained at the spray console during the simulated spraying period of ten (10) minutes, then was free to move around.

Aerosol generation time was ten (10) minutes, approximating that time during which the spray system was normally pressurized. The air sampling pumps were preset for fifteen (15) minutes of operation to bracket the aerosol generation time. Background wipes were taken and bottled prior to aerosol generation; collection wipes were taken and bottled immediately after aerosol generation ceased. Skin deposition patches were also collected and bottled. The filter cassettes were collected and capped at the end of the preset sampling time.

Fluorometric analysis of the samples was conducted under contract by Langston Laboratories, Incorporated of Leawood, Kansas. The filters were extracted with 20 ml of 1M sodium hydroxide. The analyses were performed on a Turner Model 111 Fluorometer with excitation at 365 mμ (Filter #7-60) and emission at 510 mμ (Filter #ZA-12).

Phase three, designed to evaluate the dispersal and concentration of volatile components using a tracer gas, was conducted during flights three and four, principally by Stone.[9] Sulfur hexafluoride (SF_6) was released from a small gas bottle, through a regulator and rotameter, positioned near the console aft of the spray tank. The release rate approximated 50 cubic centimeters per minute. Sampling for the tracer gas was accomplished through Teflon(R) tubing probes located near the console, center cargo area, and in the cockpit. The tubing was manually connectable to a two-way valve on an A.I.D. Model 511 portable gas chromatograph equipped with an electron capture detector. The valve selected either sample or internal standard gas to be drawn in for analysis. An Esterline Angus Model T171B Port-A-Graph was used to record detector response.

RESULTS

Inflight, the cabin air and internal surface temperatures were very uniform, seldom varying more than 2°C from each other and from outside air temperature. Relative humidity inside the cabin approximated that outside.

During the simulated Ranch Hand missions at 130 to 135 knots indicated air speed and with the pilot's windows and the troop door open, internal airflow was strongly directional, flowing from the vicinity of the troop doors and ramp, past the flight mechanic's console, along the sides of the tank, forward through the cockpit hatchway, and out the pilots' windows. Airflow in the immediate vicinity of the tank, pump, and console was swirling and turbulent.

The first two flights were in an aircraft fitted with an insecticide spray system that differed somewhat from the herbicide spray system. Air velocities taken on these flights yielded an average of 4993 cubic feet per minute total airflow through the hatchway into the cockpit. These findings were closely repeated on the third and fourth flights in an aircraft fitted with a Vietnam era herbicide spray system. Thus, the cargo compartment, with an approximate volume of 2896 cubic feet, experienced nearly two (2) air changes per minute supplied from outside. The cockpit, approximate volume 189 cubic feet, experienced more than twenty-five (25) air changes per minute supplied from the cargo compartment.

The pilots' windows alone virtually control the direction and velocity of internal airflow. With the windows closed, airflow patterns were essentially non-directional. Conversely, closing the troop door had little effect on internal airflow as there appeared to be sufficient leakage around the door seals and ramp to supply makeup air.

Analysis of the samples collected on the third flight following the release of the Agent Orange simulant aerosol showed the following measured quantities of recovered fluorescein corrected for background or blank values:

Skin Deposition	- Copilot	negligible
Skin Deposition	- Flight Mechanic	6.06 μg
Surface Wipe	- Copilot	negligible
Surface Wipe	- Flight Mechanic	.11 μg
Breathing Zone	- Copilot	30 $\mu g/M^3$
Breathing Zone	- Flight Mechanic	25 $\mu g/M^3$

The measured SF_6 levels during the fourth flight were:

Rear (Console) Area	145 ± 30 parts per billion (ppb)
Right (Center Cargo) Area	53 ± 12 ppb
Cockpit	43 ± ppb

A leakage problem in the gas release train was apparent on the third flight. Corrective measures taken on the fourth flight precluded an accurate flow rate determination. However, the release rate was less than 50 cubic centimeters per minute (cc/min) and may have approximated 25 cc/min. Given this approximation, these data were fairly consistent with predictable concentrations under the ventilation conditions determined in Phase one.

DISCUSSION

The results of the airflow studies indicate strongly that any concentrations of vapors or particles generated at or near the spray tank would have been quickly dispersed forward, and diluted, by the high volume of ventilating air. Thus, the pilots were exposed to an estimated one third of the concentration of air contaminants existing in the rear cargo compartment. Conway et al[3] reported the results of recent C-123K aircraft internal air sampling and analysis of residue found on interior surfaces. The residue showed traces of 2,4-D and 2,4,5-T while the air samples showed fairly significant levels of Herbicide Orange ($\sim$ .336 mg/m^3) vapor. Of interest was that the aircraft had not been used to spray herbicide since 1966, indicating probable heavy deposition on internal surfaces while so used and continuous volatilization occurring.

During the transfer operations in preparation for incineration of leftover Herbicide Orange, careful air monitoring was accomplished.[10] The highest level of Herbicide Orange vapor (combined 2,4-D and 2,4,5-T) recorded was .215 mg/m^3. These results in conjunction with those above may indicate an approximate level of constant exposure to all Ranch Hand crewmembers. To this background level exposure to vapor would be added the exposures resulting from skin deposition or contact and inhalation of aerosol.

Little is known of inhalation as an exposure route for any of the chemicals involved. However, other routes of exposure generally produce equivalent toxic effects with equivalent dosage of TCDD.[8] Inhalation may very well be an equally effective route. Frohberg et al[5] reported severe toxic effects in mice following inhalation trials with 2,4,5-T.

The results of the aerosol dispersal and sampling experiment were somewhat equivocal. Two significant problem areas developed. The first was the high background and blank levels of fluorescence. They rendered virtually unusable all but the skin deposition results. Contamination of the samples was first considered as a cause. However, Langston

Laboratory analyzed samples of their own stock Whatman #1 filter paper and got similar results. An attempt was made to analyze the samples on a Welch Chem-Anal Fluorimeter to investigate technique, but the detection range of this equipment was unacceptably high. Three samples were later analyzed on an Aminco SPF-125 Spectrofluorometer to determine if a more sophisticated instrument could achieve better results. Some photo decomposition had apparently occurred, but the relative values remained essentially the same.

The experimental and analytical techniques have previously been used successfully;[1] however, better sensitivity is needed. Fruitful areas for investigation might include alternate collection media, alternate solvents, the effect of filtering the solvent after desorption, and the importance of light scattering phenomena.

The second major problem area was interpretation of the breathing zone air sampling results. In addition to a high blank value, the results were not what would be expected given the other evidence (airflow, skin deposition, and tracer gas analyses).

These results must, then, be regarded with suspicion. A more extensive investigation, involving several trials, would be required to assess the many variables involved.

The skin deposition results were considered to be reasonably reliable, even given the fact of a single trial and the other problems noted. The aerosol production was visually monitored. The swirling, turbulent air around the flight mechanic was visibly and heavily contaminated with the aerosol. Not until the aerosol nearly reached the aisleway alongside the console and tank was it entrained and carried forward. This provided a graphic example of the potential results of pressurized leaks, agitated spills, etc.

There can be no doubt that the flight mechanic receives significantly greater exposure by contact and absorption than do the pilots and navigator. Further, the flight mechanic's exposure likely continues throughout the duty day by absorption from contaminated clothing. In contrast, the other crewmembers are only, or primarily, exposed during the mission(s).

The results of the SF_6 tracer gas experiment as reported by Stone[9] were very clearcut. A more than adequate demonstration of the dispersal and resulting concentrations of volatile components was made.

There were several notable constraints operative during this study. Foremost was the time and expense involved in conducting the simulated spray missions. This governing factor precluded multiple trial experiments. Additionally, most of the experimental apparatus had to be portable, self-energized, safe for flight, and not interfere with the operation of the aircraft in any way. There was no opportunity to refine techniques and equipment. Given these and other limitations the study achieved its purpose: to demonstrate that exposure to Agent Orange varied significantly as a function of crew position and to estimate the relative magnitude of the exposures.

CONCLUSIONS

An aerosol or vapor generated in the vicinity of the spray tank will be diluted and dispersed forward by the high volume internal airflow created by the aircraft ventilation configuration common to Ranch Hand missions.

There was most probably a background level air concentration of Agent Orange vapors to which all crew members were chronically exposed. To this exposure must be added exposures resulting from mission activities and events. These include an inhalation exposure to aerosol and a contact exposure with subsequent percutaneous absorption. Exposure differs significantly as a function of crew position. The flight mechanic's exposure most probably exceeds that of the pilots and navigators by a factor of six or greater.

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APPENDIX A

AIR MOVEMENT THROUGH HATCHWAY FROM CARGO COMPARTMENT INTO COCKPIT

(HATCHWAY DIVIDED INTO SIX EQUAL AREAS FOR VELOCITY MEASUREMENTS)

Sample Area (F+^{2})	Trials: 1		2		3		4	
	Velocity (FPM)	Flow (CFM)	Velocity (FPM)	Flow (CFM)				
(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)
1.4	580	812	720	1008	1000	1400	500	700
1.4	630	882	450	630	750	1050	500	700
1.4	400	560	350	490	720	1008	700	980
1.4	600	840	500	700	850	1190	500	700
1.4	620	868	500	700	750	1050	500	700
1.4	480	672	450	630	580	812	600	840
Total Flow		4634		4158		6510		4620
Average Q					4981			

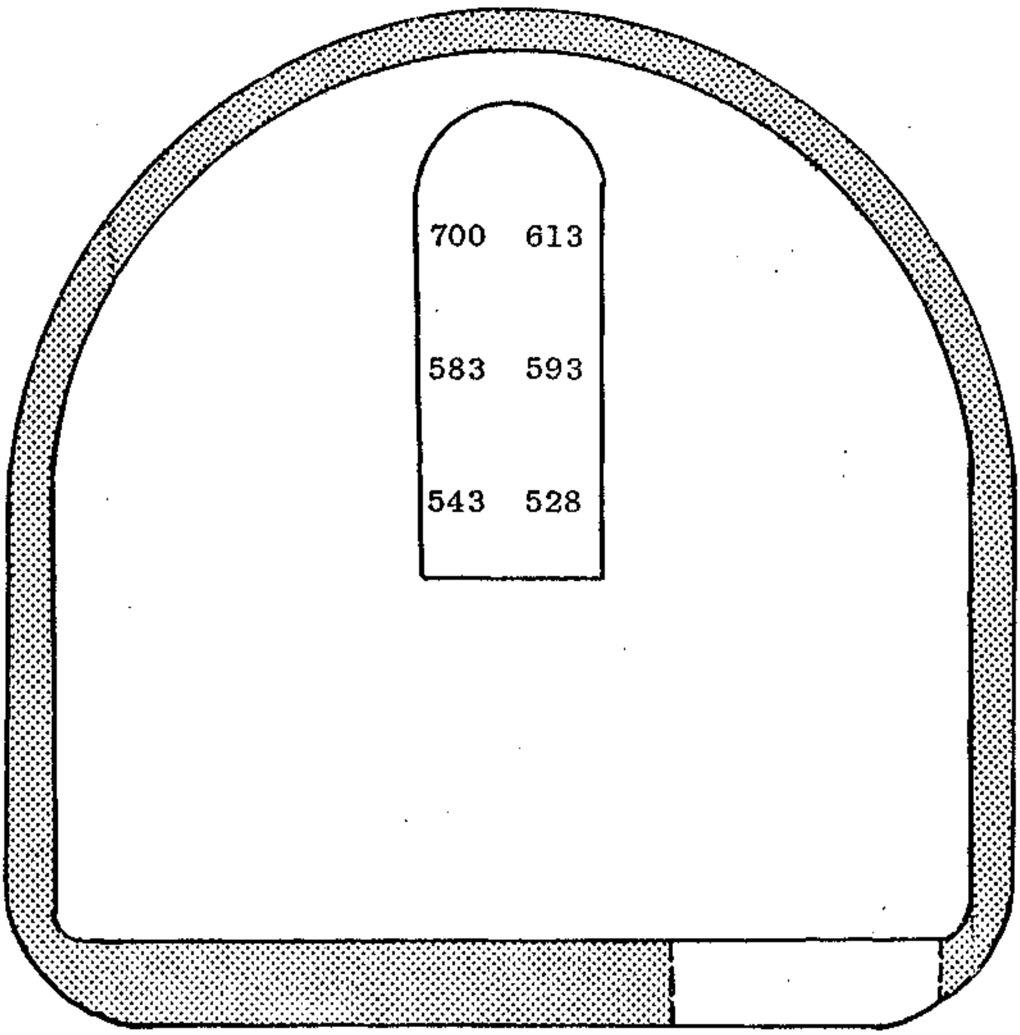
Source:
Columns 3, 5, 7, and 9: Column 1 times Columns 2, 4, 6, and 8, respectively.

Key:
FPM = Feet Per Minute
CFM = Cubic Feet Per Minute
Q = Total Flow in CFM (Q = Velocity X Area)

APPENDIX B

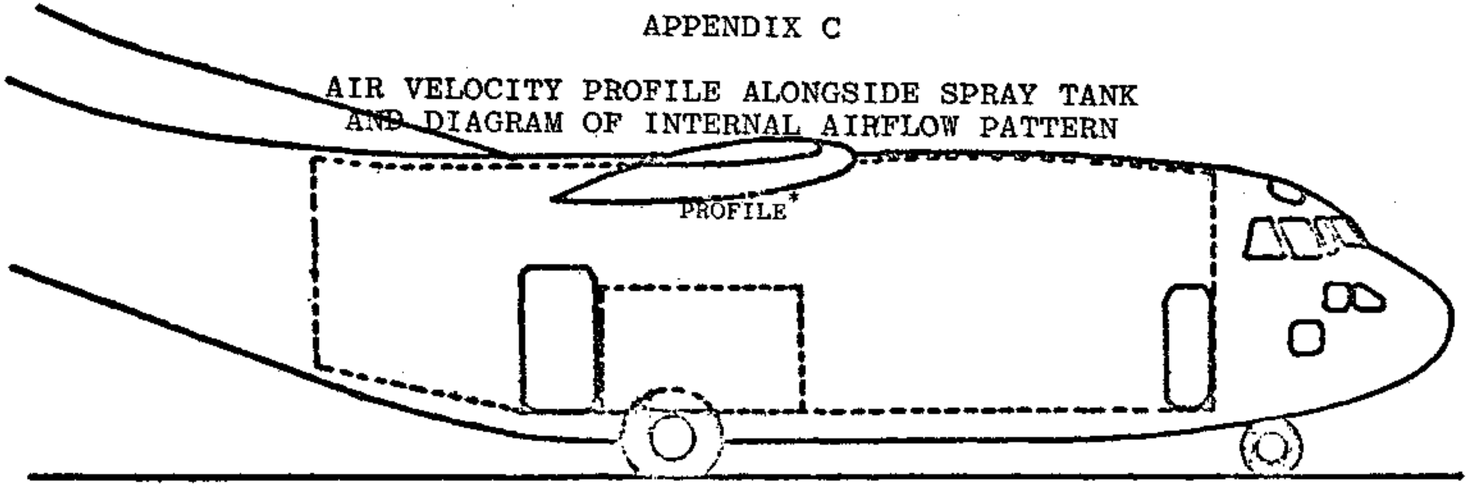
AIR MOVEMENT THROUGH HATCHWAY

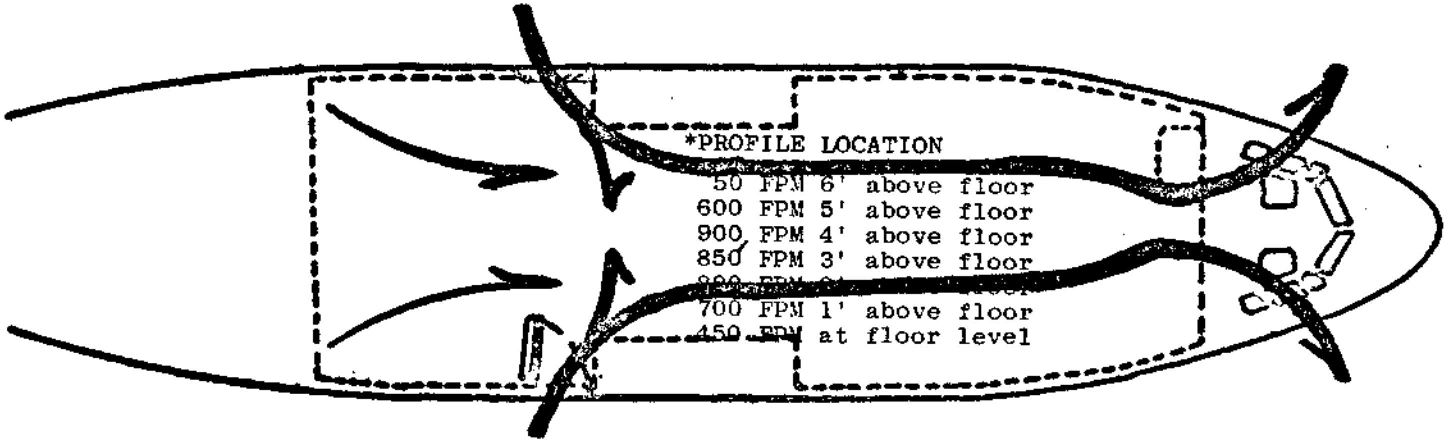
(AVERAGE VELOCITY [FPM] AND MEASUREMENT LOCATIONS)



APPENDIX C

AIR VELOCITY PROFILE ALONGSIDE SPRAY TANK
AND DIAGRAM OF INTERNAL AIRFLOW PATTERN





APPENDIX D

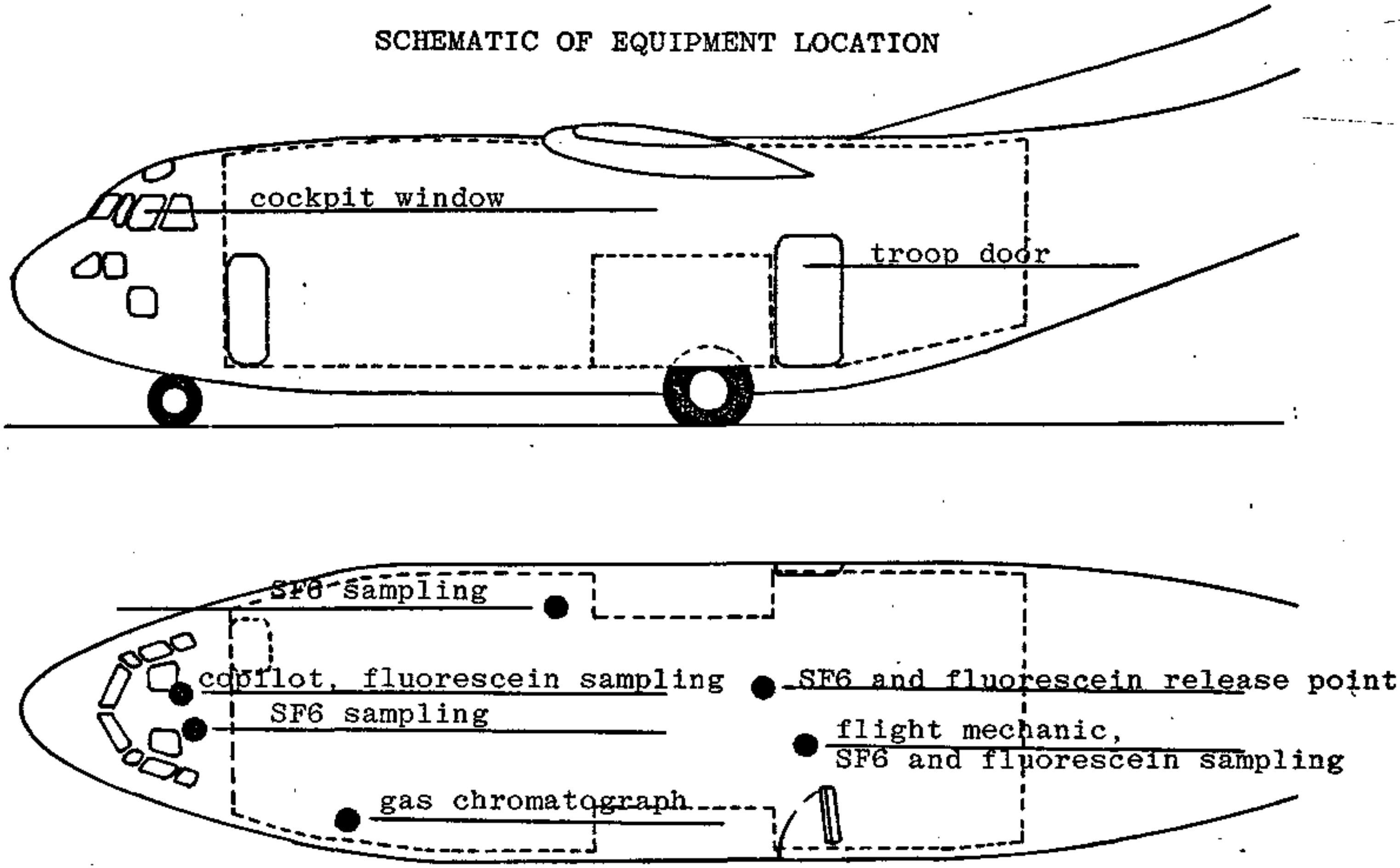
RECOVERY AND ANALYSIS OF FLUORESCEIN

Recovery of Fluorescein						Standard Curve	
Type Sample (1)	Sample Location (2)	Collection Medium (3)	Fluorescein (µg/ml) (4)	Blank/ Background (5)	Fluorescein (Corrected) (6)	Concentration (µg/ml) (8)	Absorbance (9)
Deposition	Copilot	Whatman #1 Filter Paper	1.58	1.75	<0	10.1	5.5
Deposition	Flight Mechanic	"	7.81	1.75	6.06	20.2	9.5
Surface Wipe	Copilot	"	.51	.63	<0	30.3	14.25
Surface Wipe	Flight Mechanic	"	.63	.52	.11	40.4	19
Breathing Zone	Copilot	Millipore AA Filter	1.72	.83	.89	60.6	28.5
Breathing Zone	Flight Mechanic	"	1.38	.83	.55	101.1	52

Sources:
Columns 4, 5, 8, and 9: Report of Langston Laboratories, Inc., Leawood, KS, Project No. 80-4343, June 11, 1980.
Column 6: Column 4 minus Column 5.

APPENDIX E

SCHEMATIC OF EQUIPMENT LOCATION



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by

Stephen Langdon Meek

A thesis submitted in partial fulfillment
of the requirements for the degree of

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(Chairperson of Supervisory Committee)

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to Offer Degree Public Health and Community Medicine

Date 26 February 1981

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