UNCLASSIFIED

AD NUMBER

ADB257280

NEW LIMITATION CHANGE

TO

Approved for public release, distribution unlimited

FROM

Distribution authorized to U.S. Gov't. agencies only; Proprietary Info.; Nov 99. Other requests shall be referred to US Army Medical Research and Materiel Comd., Fort Detrick, MD 21702-5012.

AUTHORITY

USAMRMC ltr, 1 Apr 2003

THIS PAGE IS UNCLASSIFIED

AD_____

Award Number: DAMD17-96-2-6015

TITLE: Female Reproductive Effects of Exposure to Jet Fuel at U.S. Air Force Bases

PRINCIPAL INVESTIGATOR: Grace K. Lemasters, Ph.D.

CONTRACTING ORGANIZATION: University of Cincinnati
Cincinnati, Ohio 45267-0182

REPORT DATE: November 1999

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Distribution authorized to U.S. Government agencies only (proprietary information, Nov 99). Other requests for this document shall be referred to U.S. Army Medical Research and Materiel Command, 504 Scott Street, Fort Detrick, Maryland 21702-5012.

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

20000828 112

DTIC QUALITY INSPECTED 4

NOTICE

USING GOVERNMENT DRAWINGS, SPECIFICATIONS, OR OTHER DATA INCLUDED IN THIS DOCUMENT FOR ANY PURPOSE OTHER THAN GOVERNMENT PROCUREMENT DOES NOT IN ANY WAY OBLIGATE THE U.S. GOVERNMENT. THE FACT THAT THE GOVERNMENT FORMULATED OR SUPPLIED THE DRAWINGS, SPECIFICATIONS, OR OTHER DATA DOES NOT LICENSE THE HOLDER OR ANY OTHER PERSON OR CORPORATION; OR CONVEY ANY RIGHTS OR PERMISSION TO MANUFACTURE, USE, OR SELL ANY PATENTED INVENTION THAT MAY RELATE TO THEM.

LIMITED RIGHTS LEGEND

Award Number: DAMD17-96-2-6015
Organization: University of Cincinnati

Those portions of the technical data contained in this report marked as limited rights data shall not, without the written permission of the above contractor, be (a) released or disclosed outside the government, (b) used by the Government for manufacture or, in the case of computer software documentation, for preparing the same or similar computer software, or (c) used by a party other than the Government, except that the Government may release or disclose technical data to persons outside the Government, or permit the use of technical data by such persons, if (i) such release, disclosure, or use is necessary for emergency repair or overhaul or (ii) is a release or disclosure of technical data (other than detailed manufacturing or process data) to, or use of such data by, a foreign government that is in the interest of the Government and is required for evaluational or informational purposes, provided in either case that such release, disclosure or use is made subject to a prohibition that the person to whom the data is released or disclosed may not further use, release or disclose such data, and the contractor or subcontractor or subcontractor asserting the restriction is notified of such release, disclosure or use. This legend, together with the indications of the portions of this data which are subject to such limitations, shall be included on any reproduction hereof which includes any part of the portions subject to such limitations.

THIS TECHNICAL REPORT HAS BEEN REVIEWED AND IS APPROVED FOR PUBLICATION.

Patricia C. Modron — 8/18/00

_____ _____

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 074-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503

1. AGENCY USE ONLY (Leave blank)	2. REPORT DATE	3. REPORT TYPE AND DATES COVERED
	November 1999	Annual (15 Oct 98 – 14 Oct 99)

4. TITLE AND SUBTITLE
Female Reproductive Effects of Exposure to Jet Fuel at U.S. Air Force Bases

5. FUNDING NUMBERS
DAMD17-96-2-6015

6. AUTHOR(S)
Grace Lemasters, Ph.D.

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
University of Cincinnati
Cincinnati, Ohio 45267-0182

e-mail:
grace.lemasters@uc.edu

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSORING / MONITORING AGENCY REPORT NUMBER

11. SUPPLEMENTARY NOTES

12a. DISTRIBUTION / AVAILABILITY STATEMENT
Distribution authorized to U.S. Government agencies only (proprietary information, Nov 99). Other requests for this document shall be referred to U.S. Army Medical Research and Materiel Command, 504 Scott Street, Fort Detrick, Maryland 21702-5012.

12b. DISTRIBUTION CODE

13. ABSTRACT *(Maximum 200 Words)*

One of the most prevalent exposures at all Air Force (AF) bases is to jet fuel. Total consumption ranks in the billions of gallons. Jet fuel is composed of aliphatic/aromatic hydrocarbons and traces of metals that have potential adverse effects on health including menstrual disorders, infertility, spontaneous abortions, and fetal effects. This study addresses whether or not women are experiencing menstrual symptoms and hormone change related to their workplace from fuel or other occupational exposures. Ten AF bases participated and have been visited. Approximately 1000 women were identified as potential participants. Of this group 170 were eligible and participated. Menstrual disorders (dysmenorrhea, hypermenorrhea, and abnormal cycle length) were evaluated in 170 employed by the USAF, 140 were military and 30 were civilians. The average age of the participants was 29.4 years, 61.8% were Caucasians, and 56.8 were married. Of this group, 66 had job activities involved with fuel handling and 104 did not. Results indicate a two-fold increase in dysmenorrhea for those women involved in fuel handling (OR 2.1, 95% CI 1.1-4.1). Stressful life events were significantly ($p \leq 0.05$) associated with all three menstrual disorders (O.R.-2.5-3.4). Relationship of occupational exposures to hormonal differences is currently being evaluated.

14. SUBJECT TERMS	15. NUMBER OF PAGES
Women's Health	83
	16. PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
Unclassified	Unclassified	Unclassified	Limited

NSN 7540-01-280-5500

Standard Form 298 (Rev. 2-89)
Prescribed by ANSI Std. Z39-18
298-102

FOREWORD

Opinions, interpretations, conclusions and recommendations are those of the author and are not necessarily endorsed by the U.S. Army.

_____ Where copyrighted material is quoted, permission has been obtained to use such material.

_____ Where material from documents designated for limited distribution is quoted, permission has been obtained to use the material.

_____ Citations of commercial organizations and trade names in this report do not constitute an official Department of Army endorsement or approval of the products or services of these organizations.

_____ In conducting research using animals, the investigator(s) adhered to the "Guide for the Care and Use of Laboratory Animals," prepared by the Committee on Care and use of Laboratory Animals of the Institute of Laboratory Resources, national Research Council (NIH Publication No. 86-23, Revised 1985).

_____ For the protection of human subjects, the investigator(s) adhered to policies of applicable Federal Law 45 CFR 46.

_____ In conducting research utilizing recombinant DNA technology, the investigator(s) adhered to current guidelines promulgated by the National Institutes of Health.

_____ In the conduct of research utilizing recombinant DNA, the investigator(s) adhered to the NIH Guidelines for Research Involving Recombinant DNA Molecules.

JKK In the conduct of research involving hazardous organisms, the investigator(s) adhered to the CDC-NIH Guide for Biosafety in Microbiological and Biomedical Laboratories.

Grace Semmelers 11-10-99

PI - Signature Date

(4) **Table of Contents**: Page

(1) Front Cover.....i

(2) Standard Form (SF) 298, Report Documentation.....ii

(3) Foreword.....iii

(4) Table of Contents.....iv

(5) Introduction.....1

(6) Body.....1

(7) Key Research Accomplishments.....24

(8) Reportable Outcomes.....24

(9) Conclusions.....25

(10) References.....25

(11) Appendices.....26

(5) Introduction:

Jet fuel (JF) constitutes at least two thirds of the turbine fuels used by the Department of Defense (DoD). It is one of the most common chemical exposures at all Air Force Bases. Jet fuel consists of a variable mixture of hydrocarbon compounds whose specifications are based on burn characteristics, and additives used to inhibit icing, corrosion, and static. JP-8 is a turbine engine fuel recently replacing JP-4. JP-8 is a kerosene-based distillate with a higher flash point, higher chain hydrocarbons and lower benzene; it is, therefore, presumed to be safer to use than its JP-4 predecessor.

The reproductive and developmental toxicity of the complex streams that comprise fuels has not yet been established. The literature does, however, contain both animal and human studies of exposure to various fuels and primary fuel components. While the paraffins and olefins, with the exception of n-hexane, are believed to be nontoxic at low doses, certain organic compounds in fuels and emissions are known or suspected human reproductive or developmental toxicants (Hersh JH et al., 1985; Plenge-Bönig A & Karmaus W; Page N & Mehlman, 1989; Harrington JM, 1987; Lemasters GK, 1999).

Hypothesis and Technical Objectives:

The primary null hypothesis of this study is that there will be no statistically significant difference in hormonal patterns and menstrual function between women exposed to jet fuel and an unexposed group. The secondary null hypothesis is that there will be no significant racial differences in either internal dose to JF exposure or reproductive health response.

The technical objectives of this study are 1) to identify and recruit jet fuel exposed and unexposed women group-matched with respect to race and age, 2) to characterize workplace exposures , 3) to determine if hormonal patterns differ significantly between the exposed and unexposed groups and to determine if there are differences between racial groups and, 4) to determine if prevalences of menstrual disorders differ significantly between the exposed and unexposed groups; and to determine if there are effect differences between racial groups. The statement of work (SOW) for all years can be found in Appendix IV.

(6) Body:

Overview of Air Force Base Participation and Subject Recruitment:

The employees recruited were both military and civilian women from ten Air Force Bases: Davis-Monthan, Hill, Langley, Luke, Moody, Nellis, Pope, Warner-Robins, Seymour Johnson, and Shaw. The recruitment of these Air Force Bases involved preliminary identification of a contact person at each base and mailing letters requesting study approval to each base commander. Recruiting and scheduling bases involved follow-up activities, such as confirming permission, scheduling base visits around exercises and deployments, identifying office space, arranging briefings and accessing phone recruitment lists.

Potential participants were contacted by telephone and in person at each base both prior to and during each base visit in order to ascertain personal interest and eligibility status and to inform the women of the voluntary nature of the study. The women were given a brief overview of the study with emphasis placed on the study requirements, which for the expanded study included collection of daily urine samples. Women on hormonal contraceptives, pregnant within the last six months, currently pregnant, or over age 45 were excluded from the study. Also excluded were those women with any of the following diagnosed disease conditions: endometriosis, chronic pelvic inflammatory disease, vaginal, cervical, uterine, or ovarian cancer, systemic lupus erythematosus, hypopituitarism, Cushing's syndrome, sarcoidosis, pituitary tumor, acute hepatitis, HIV or AIDS, cirrhosis of the liver, hypothyroidism, hyperthyroidism, multiple sclerosis, tuberculosis, or diabetes. Women that had one or both of their ovaries removed or women that had a hysterectomy were also excluded from the study. Appointments were scheduled for those women that were considered eligible after the initial screening.

At the appointment participation requirements and the eligibility criteria were discussed and informed consent was obtained. During the personal interviews all administrative forms along with the questionnaires were completed and all instructions for hormone sample collection and diary completion were given (Appendix I). Also the height and weight of each study participant were measured. These activities were completed during Year 01 thru Year 03 of the study.

UPDATED RESULTS AND DISCUSSION OF SOW ACTIVITIES (YEAR 02):

This section is an addendum to the second annual report and summarizes the outcome of Year 02 SOW activities completed after that report's submission (see Year 02 SOW items #1, 2, 3, 6, and 8). These activities extended to Year 3 in order to accommodate additional repeat visits to two of the 10 participating AF bases. Subsequent laboratory analysis of biological samples is also addressed. Subject recruitment (SOW items #2 and #6) occurred prior to shipping/ analyzing samples (SOW #1, 3 & 8), therefore the SOW activities are presented in that order.

Year 02 SOW Items #2 and #6:

Year 02 items two and six were as follows:

2. Perform items 15-19 (see SOW Year 01) at Base 3 on approximately 50 women (months 15–18).

6. Perform items 15-19 (see SOW Year 01) at Base 4 on approximately 50 women (months 21-24).

Items 15-19 in the SOW refer to subject participation activities that were enumerated in Year 01 of that document (Appendix IV). These activities included conducting breath analysis sampling (Item #15), administering occupational and menstrual history questionnaires (Item #16), implementing menstrual diaries and collecting daily biological samples (Item #17), shipping samples (Item #18) and preparing the annual report (Item #19, completed).

Year 02 items referenced above have been completed at this time. A summary of the number of participating women, by AF base and exposure group as defined by job title, is described in Table 1. As in the Year 02 report, ten AF bases participated. As described in the Year 02 report, we increased the number of AF bases sought from four to ten in order to increase our sample size of women to match our stringent eligibility requirements. Because of our intensive recruitment efforts, we were able to obtain a 1:2 ratio of exposed (n=57) to unexposed (n=113) subjects. Because of use of oral contraceptives and other criteria as well as deployment activities in progress during this study, we did not reach the targeted sample size of 200. Additional funds were requested to continue recruitment and base visits but this request was denied. It is recommended that 10 participants with a study outcome per independent variable are needed to achieve adequate power for multiple logistic regression and between 6 to 20 subjects per independent variable are required for multiple linear regression (M. Katz, 1999; Neter J. et al., 1989). Ample power is, therefore, available to test the most highly prevalent outcomes, including key menstrual and hormonal variables, with the stated caveat that power is likely inadequate to show effects after adjustment for multiple testing.

Table 1:

Participation Of Eligible Subjects By Exposure Status & Base

Base:	Location:	Exposed:	Non-exposed:
Davis	AZ	10	5
Hill	UT	4	17
Luke	AZ	10	13
Langley	VA	5	12
Moody	GA	2	12
Nellis	NV	6	2
Pope	NC	2	3
Robins	GA	12	21
Seymour Johnson	NC	4	17
Shaw	SC	2	11
Total (10 Bases)		**57**	**113**

In order to obtain 170 participants, attempts were made to recruit of 996 subjects (Table 2). Of this 996, 711 were reached, either by phone or in-person. Eligibility status could not be ascertained for 285 of these women as they were not available at the work-site due to deployment, leaves or illness. Of the remaining 711 women, 376 did not meet one or more eligibility requirements. Of the 335 who were eligible, 170 (50.7%) completed the baseline questionnaire interview (Table 2).

Table 2

Recruitment Status of Potential Subjects by Recruitment Outcome Category:

Recruitment Outcome:	Number
Eligible, participated:	170
Eligible, declined participation:	135
Scheduled, but no shows:	30
Ineligible:	376
Unavailable (absent or gone with eligibility undetermined):	285
Totals	**996**

Daily diaries were also collected for 120 (70.6%) of the 170 participants who completed baseline questionnaires (Table 3). The average number of recorded diary days per participant was 46 (range 3 to 103). All diary and questionnaire data have been standardized and cleaned in preparation for preliminary analyses.

Table 3

Number of Baseline Questionnaires, and Daily Diaries Completed by Exposed and Unexposed Status

Completed Study Items:	Exposed:	Non-Exposed:	Total :
Questionnaires:	57	113	170
Diaries:*	33	87	120

* Diaries = # of subjects who returned $\geq$ 1 day of diary information

Biological Samples:

Year 02 SOW Items #1, #3 & #8:

1. **Ship samples to NIOSH; perform laboratory analysis of IH and biological samples collected at Base 2; inventory and organize urine samples; store/conduct urinary LH & FSH fluoroimmunoassays; store/conduct urinary E13G and PD3G fluoroimmunoassays; store/conduct creatinine assays (months 3-16)**

3. **Ship samples to NIOSH; perform laboratory analysis of IH and biological samples collected at Base 3; inventory and organize urine samples; store/conduct urinary LH & FSH fluoroimmunoassays; store/conduct urinary E13G and PD3G fluoroimmunoassays; store/conduct creatinine assays (months 16-19)**

8. **Ship samples to NIOSH; perform laboratory analysis of IH and biological samples collected at Base 4; inventory and organize urine samples; store/conduct urinary LH & FSH fluoroimmunoassays; store/conduct urinary E13G and PD3G fluoroimmunoassays; store/conduct creatinine assays (months 23-25)**

Biological Sample Collection:

(As mentioned in last year's annual report we had numerous technical difficulties with collecting breath samples.) Of the 170 subjects who completed the baseline questionnaire, 112 provided urine samples for hormonal analysis and 96 provided breath samples for characterizing internal dose measures. Since 108 provided baseline diary, urine and breath and we have only 65 breath samples, work history will be used to primarily document exposure status. Only 65 subjects were fully compliant in providing baseline questionnaire, diary, urine and workweek breath samples (Table 4). Some subjects who provide properly collected diaries did not do so for the urine samples and visa-versa.

Table 4

Number of Biological Samples from 170 Participants

Completed Study Items	Exposed:	Non-Exposed:	Total:
Urine:	29	83	112
Breath:	29	67	96
Questionnaire, Diaries & Urine:	29	79	108
Questionnaire, Diaries, Urine & Breath:	16	49	65

Urine = # of subjects who returned urine samples from whom at least one of 16 endocrine endpoints were obtained.

Most women who disclosed reasons for ceasing urine and/or diary collection cited being "too busy" or collection involving "too much work" or unforeseen medical or work conditions including four subjects deployed to foreign countries and four subject's samples were discarded by others at their households. Table 5 describes the reasons for incomplete data. All valid urine samples that were ultimately received by NIOSH were inventoried and analyzed at NIOSH by Dr. Kesner's laboratory. Urine samples were stored initially in the participants' freezers in vials containing 7% glycerol to prevent freeze-induced activity loss of luteinizing hormone (LH) and follicle stimulating hormone (FSH) (Kesner et al, 1995). Participants shipped samples, chilled by freezer packs, to the laboratory by next-day courier. In the laboratory, samples were stored frozen at -80° C until assayed.

Urinary endocrine analytes were measured by trained personnel in the NIOSH laboratory using published protocols. LH and FSH were assayed in duplicate using non-competitive, two-site time-resolved immunofluorometric assays (Kesner et al, 1994a; Kesner et al, 1998). Estrone 3-glucuronide ($E_1$3G) and pregnanediol 3-glucuronide (Pd3G), the major urinary metabolites of estradiol and progesterone, were assayed in triplicate using competitive, double-antibody time-resolved fluoroimmunoassays (Kesner et al, 1994b). Creatinine was measured in duplicate using a modification of the Jaffe reaction in which creatinine and picric acid react in an alkaline environment to yield a red-orange tautomer creatinine-picrate to be measured spectrophotometrically (Jaffe 1886). An assay to measure salivary progesterone is currently under development. All urinary endocrine values were divided by the respective sample's creatinine concentration to adjust for urine dilution (Kesner et al, 1998).

Table 5

Number of Subjects with Incomplete Diary and Urine Sample Participation during Follow-up Period by Data Type, Reason and Fuel Exposure (Job Category)

Instrument:	Reasons for Incomplete Data:	Exposed:	Nonexposed:	Total:
Diary:	Quit post-questionnaire; no diaries returned to study; no known exclusions:	15	18	33
	Diaries reportedly "lost" post-completion, prior to study receipt:	9	8	17
	Diaries received but later excluded from analysis for medical reasons.	4	2	6
Total:	**# diaries not received/out for analysis:**	**28**	**28**	**56**
Urine:	Quit post-questionnaire; no samples returned to study; no known exclusions:	18	18	36
	Samples reportedly "lost" post-completion, prior to study receipt:	7	6	13
	Apparent wrongful aliquoting:	3	6	9
	Samples received by study, but *out* for hormone analysis because pregnancy/ medical exclusion found (post-questionnaire):	2	2	4
Total:	**# urines not received/out for analysis:**	**30**	**32**	**62**

In-house quality control urine pools (low, medium, & high levels) were included at the start and end of each microtiter plate for all LH, FSH, $E_1$3G, and Pd3G assays. In addition, Bio-Rad quality control serum pools (low, medium, & high) were run in all LH & FSH assays. Creatinine quality control included Beckman serum pools (low, medium, & high) and Bio-Rad urine pools (low & high).

Samples were re-assayed: 1) if the initial measurement was relatively imprecise ($\geq$10% coefficient of variation for LH, FSH, & creatinine; $\geq$ 20% coefficient of variation for $E_1$3G & Pd3G); 2) if the initial measurement exceeded the highest standard level (re-assayed as a dilution); or 3) the quality control measurements for an assay microtiter plate or an entire assay were $\geq$ 3 standard deviations from the mean for that specific assay or for all assays, respectively.

Intra- and inter-assay coefficients of variation for the study: 6.16% & 4.63% for LH; 2.84% & 3.53% for FSH; 15.36% & 10.14% for $E_1$3G; 11.57% & 8.44% for Pd3G; 0.97% & 3.44% for creatinine. All samples for each subject were measured in the same assay.

Menstrual periods were derived from the participants' daily records of vaginal bleeding using an algorithm developed by Paige Hornsby (personal communication; University of Virginia Health Sciences Center; Appendix III). In brief essence, the menstrual cycle and the menstrual period begin on the first of 2 consecutive days of bleeding, only one of which is spotting. Menses is preceded and followed by $\geq$ 3 consecutive days of non-bleeding or spotting. After day 2 of the period, 1-2 day intervals of non-bleeding or spotting are counted as part of the menses. In

addition, self-reported menses was accepted up to 14 days retrospectively. Urinary endocrine measurements and menses dates were used to derive a battery of endpoints using established algorithms (Appendix III).

RESULTS AND DISCUSSION OF SOW ACTIVITIES (YEAR 03):

SOW Item #1:

Data management: standardize and computerize data collected from air sampling, biological sampling and breath analysis at four military bases; reduce data onto spreadsheets importable for statistical and graphical analyses; generate graphic depictions of data; conduct preliminary statistical analyses, subsequent to complex analyses (months 25-36).

SOW Item #2: Prepare preliminary report (months 34-36)

Breath analysis *and industrial hygiene data* have (internal dose exposure data) have been entered into Excel and currently are being cleaned and the quality evaluated. Six personal (area) industrial hygiene samples collected from subjects after laboratory equipment problems were remedied. Analysis of breath and industrial samples proceeded according to the revised protocol and was accomplished by thermal desorption of the SS tubes with a Tekmar 3000 Purge and Trap. The Hewlett-Packard Model 5890 Series 2 Gas Chromatograph connected to a Hewlett-Packard Model 3396 Integrator was used and EZChrom software was purchase. Using EZChrom achieved lower detection limits and improved separation of compounds that co-eluted. We were also subsequently able to quantify the kerosene fraction in a subset of samples. All data from the 170 baseline questionnaires have been entered into the computer. Quality control checks are completed for data from our written instruments and the data analyses from the baseline questionnaire is described under SOW Item #2. Endocrine data have been reviewed, cleaned and computerized under the supervision of Dr. Kesner at NIOSH and sent to the University of Cincinnati for statistical analysis. Preliminary statistical analysis of diary and endocrine data are currently underway and the preliminary report is described below.

Baseline Questionnaire Report on Factors Related to Menstrual Disorders in Military Personnel:

Baseline questionnaire data were used for analysis of risk factors related to menstrual abnormalities. The menstrual function data collected included age at menarche, last menstrual period, and menstrual cycle characteristics including cycle length, bleeding patterns, and menstrual or premenstrual symptoms. The reproductive history included information on infertility, number of pregnancies and their outcomes, a history of female genital tract disorders such as polyps, uterine fibroids, pelvic infection, sexually transmitted diseases and any other reproductive abnormalities or surgeries. Also included in this questionnaire was information on potential covariates for the menstrual disorders being considered in this study. These factors include age, marital status, socioeconomic status, smoking status, ethnicity, race, gravida, parity, and age at menarche.

The dichotomous outcomes measured in this analysis are menstrual abnormalities. Menstrual dysfunction can be divided into three broad categories: 1) cycle length or rhythm, 2) hyper-menorrhea, which is excessively profuse or prolonged menstruation, and 3) dysmenorrhea or the presence of pain. If a woman's interval between menses is outside the limits considered normal than a woman may have either polymenorrhea or oligomenorrhea. Polymenorrhea was defined as menstrual cycles with less than 24 days between menses and oligomenorrhea is defined as menstrual cycles with more than 35 days between menses. The literature in the area of cycle length is ambiguous and there are no precise definitions on what is considered less than normal or abnormal. Based on a review of the literature, the lower limit was either 25, 24, or 23 days. A correlation coefficient was calculated to determine which lower limit, 25, 24, or 23 days, was most highly correlated with women reporting that their periods were "irregular". These results showed that less than 24 days was the most highly correlated (r=0.24) with this response and was therefore chosen as our lower limit for normal interval length.

Women were asked about their menstruation pattern over the previous three months. Hence, *abnormal cycle length* was defined as intervals less than 24 or greater than 35 days. Bleeding patterns can be abnormal either in the duration or amount of menstrual flow. The terms hypermenorrhea and menorrhagia are often used interchangeably. For this study the outcome *hypermenorrhea* was defined as bleeding patterns abnormal either in duration or amount. The normal duration of menses is defined as between 3 and 7 days. Therefore, hypermenorrhea was defined as menses excessive in duration (>7 days) or if the subject reported their amount of menstrual bleeding as "heavy" rather than "spotting", "light", or "moderate". The third menstrual outcome, dysmenorrhea, is the presence of pain and is among the most common of all gynecologic complaints. This study was concerned with primary dysmenorrhea. Women were excluded if they had any of the pathologic conditions contributing to secondary dysmenorrhea. Dysmenorrhea is generally recognized as a condition severe enough to warrant women to cease their daily activities, such as loss of time from work or school. For this study, *dysmenorrhea* was defined as ever having the need for bed rest or missing work due to menstrual pain.

The first step of this analysis was to obtain frequency counts on all variables of interest, including exposure variables, explanatory variables, and outcome measures. Next, single associations between the exposure factors and the outcome measures were examined. An analysis evaluated the correlations among the main effects and found that none of the exposure factors or explanatory variables remaining in the final model were highly correlated. Multiple logistic regression was the primary analysis method used to model the relationship between the binary outcome response variables, exposure factors, and other explanatory variables known or suspected of being associated with menstrual disorders. The following variables were evaluated in the logistic regression analysis but were not significant and therefore were excluded from any further analyses: age (<30=0, ≥30=1), income (≥$30,000=0, <$30,000=1), marital status (partner=0, no partner=1), and number of children (no children=0, one child=1, two or more children=2).

The main effects remaining in the model included the stress exposure variables life events (no life events=0, life events=1), non-work stressful activities (no non-work activities=0, non-work activities=1,) and job strain scores, race (Caucasian=0, non-Caucasian=1), education level (some high school, or high school and technical training=0, some college or associate's degree=1,

bachelor's or master's degree=2), military employee (civilian employee=0, military employee=1), and fuel handling (non-fuel handling=0, fuel handling=1).

The fuel exposure risk factor for this analysis was ascertained by asking women to categorize themselves as having a current job either in contact with fuels such as aircraft maintenance, fuel handling, or flightline positions or with no or limited contact with fuels such as clerical, education or health-care related jobs. A backward elimination approach was used. Adjusted odds ratios and the 95% confidence interval of the odds ratios were calculated for factors remaining in the model.

RESULTS

As Table 6 shows, the 170 participants in the baseline questionnaire ranged in age from 18 to 41 years old with a mean age of 29.4 ($\pm$ 6.4) years. The mean age at menarche for this population was 12.7 ($\pm$1.6) years and ranged from 9 to 17 years of age. Over half of the participants, 61.8% (n=105) were Caucasian. Most, 56.8% (n=96) were either married or had a permanent partner, while 43.2% (n=73) were either widowed, divorced, permanently separated or had never been married. The subjects were generally well educated with 75.9% (n=129) having had some college education while the other 24.1% (n=41) of the women had some high school, a high school diploma or G.E.D., or high school and technical or vocational training. Half the population, 50.6% (n=85) had a net family income of $30,000 or higher. Over half of the group, 58.3% (n=98) had children. The majority of this population, 82.4% (n=140) were in the military and 38.8% (n=66) of participants reported handling fuels as part of their work detail.

Table 6

Demographic Characteristics of the Participating Population

Demographic Characteristics		n
Mean age, years	29.4 ± 6.4	170
and Range	(18 – 41)	
Mean age at menarche, years	12.7 ± 1.6	170
and Range	(9 – 17)	
Race, %		
Caucasian	61.8	105
Non-Caucasian		
African-American	31.8	54
Hispanic	4.7	8
Other	1.8	3
Marital Status‡, %		
Never Married	26.0	44
Married or Have Permanent Partner	56.8	96
Widowed, Divorced, or Permanently Separated	17.2	29
Education, %		
Some HS/ HS or GED/ HS & Tech Training	24.1	41
Some College	61.8	105
College degree	14.1	24
Number of Children‡, %		
0	41.7	70
1	26.2	44
2+	32.1	54
Family Income‡, %		
< $30,000	49.4	83
≥ $30,000	50.6	85
Job Category, %		
Military	82.4	140
Civilian	17.6	30
Fuel Exposure, %		
Fuel Handling	38.8	66
Non-Fuel Handling	61.2	104

‡Marital status missing for 1 person; income and number of children missing for 2 people

Outcome Measures

The prevalence of menstrual outcomes were calculated and are shown in Table 7. Of the 170 participants, 46.1% (n=77), reported having one or more menstrual disorders. Based on their responses, 31.2% (n=53) of the participants had dysmenorrhea. Hypermenorrhea questionnaire data were complete for 168 participants and of these 17.9% (n=30) met the definition. Abnormal cycle length data were incomplete for four participants; of the 166 participants with completed information 12.0% (n=20) had an abnormal cycle length.

The first tests of association were to determine if there were any significant differences among the non-fuel handlers and the fuel-handlers with respect to the stress factors. Chi-square statistics showed that there were no statistically significant differences between the fuel-handlers and non-fuel handlers with regard to the stress exposure variables.

Table 7

Type of Menstrual Disorders Reported

Menstrual Abnormality	Percent	Subjects (n=170)
Dysmenorrhea	31.2	53
Hypermenorrhea‡	17.9	30
Abnormal Cycle Length‡	12.0	20
Any Menstrual Disorders	46.1	77

‡2 Missing from hypermenorrhea analysis and 4 missing from abnormal cycle length analysis

Multivariate Logistic Regression Analysis

Table 8 shows that being a fuel handler was significantly associated with dysmenorrhea (OR=2.09, 95% C.I. 1.05-4.13) but not hypermenorrhea or abnormal cycle length. Life events were significantly associated with dysmenorrhea (OR=2.46, 95% C.I. 1.22-4.95), hypermenorrhea (OR=2.99, 95% C.I. 1.20-7.42), abnormal cycle length (OR=3.42, 95% C.I. 1.12-10.50), and having one or more menstrual disorders (OR=3.10, 95% C.I. 1.58-6.05). Race also was significantly associated with hypermenorrhea (OR=4.99, 95% C.I. 2.07-12.05), abnormal cycle length (OR=4.12, 95% C.I. 1.47-11.55) and the report of one or more menstrual disorders (OR=2.82, 95% C.I. 1.42-5.50).

Table 8
Adjusted Logistic Regression Odds Ratios for
Life Events and Menstrual Disorders

Outcome	Life Event	Race	Fuel-Handling
Dysmenorrhea	2.46		2.09
(n = 53)	(1.22-4.95)		(1.05-4.13)
	0.90		0.74
Hypermenorrhea	2.99	4.99°	
(n = 30)†	(1.20-7.42)	(2.07-12.05)	
	1.09	1.61	
Abnormal Cycle Length	3.42	4.12°	
(n = 20)†	(1.12-10.50)	(1.47-11.55)	
	1.23	1.42	
Any Menstrual Disorders	3.10	2.82	
(n = 77)	(1.58-6.05)	(1.42-5.50)	
	1.13	1.04	

Results shown are odds ratios 95% confidence intervals in parentheses, and coefficients
All variables that were significant at the 0.10 level are included in the table – full model included job strain, life events, non-work activities, race, age, fuel exposure, education level, military employee, number of children, marital status, and income
2 Missing from abnormal bleeding patterns analysis and 4 missing from abnormal cycle length analysis

Based on the results of race as a risk factor for three outcomes further exploration was undertaken. As Table 9 shows, both Caucasians and non-Caucasians reported virtually the same prevalence of dysmenorrhea, 31.4% and 30.8% respectively. **Non-Caucasians compared to Caucasians reported a significantly greater prevalence of hypermenorrhea, 30.8% versus 9.7%, which was related to the report of "heavy" bleeding, 26.2% versus 9.7%, respectively**. Race was significantly associated with abnormal cycle length and report of any menstrual disorder (Table 9). Both groups reported the mean length of their period as approximately 5 days. **The prevalence of abnormal cycle length (<24 or >35 days) was higher in non-Caucasians (20.6%) than in Caucasians (6.8%).** Although both Caucasians and non-Caucasians had a mean cycle length close to 28 days (28.9 and 28.0, respectively) the variation was greater for non-Caucasians (6.4 days) compared to Caucasians (4.5) days. Of the non-Caucasians, 58.7% reported at least one of the three menstrual disorders compared to 38.5% Caucasians.

Table 9

Characteristics of Menstrual Patterns by Racial Status

	Caucasian (n = 105)*	Non-Caucasian‡ (n = 65)†
% Dysmenorrhea	31.4%	30.8%
% Hypermenorrhea §	9.7%	30.8%
Defined as:		
Mean (± 1 S.D.) days periods last	5.0 ± 1.2	5.2 ± 2.7
% Typical amount of bleeding reported		
Not Heavy	90.3%	73.8%
Heavy °	9.7%	26.2%
% Abnormal Cycle Length (<24 or >35 days)**	6.8%	20.6%
Mean (± 1 S.D.) of cycle length in days	28.9 ± 4.5	28.0 ± 6.4
% Reporting at least 1 Menstrual Disorder **	38.5%	58.7%
% Reporting regular periods 3 months prior to interview	88.1%	89.2%
Mean (± 1 S.D.) age at menarche in years	12.9 ± 1.6	12.5 ± 1.6
Mean (± 1 S.D.) age in years	29.8 ± 6.1	29.0 ± 6.9
Mean (± 1 S.D.) weight in pounds	150.0 ± 22.9	156.2 + 40.0
% Children		
No children	37.5%	47.7%
Children	62.5%	52.3%

‡Non-Caucasian group consisted of 54 African-Americans, 8 Hispanics, and 3 reported race as 'Other'

*1 Missing for one or more menstrual disorders, and number of children; 2 missing for typical amount of bleeding and abnormal cycle length; 5 missing mean weight

†2 Missing for abnormal cycle length, one or more menstrual disorders, and mean weight

**$P \leq 0.01$

°$P \leq 0.005$

§$P \leq 0.001$

Both groups had approximately the same percentages reporting regular periods in the three months prior to their interview date. The mean age at menarche for the non-Caucasian group (12.5 years of age) was slightly earlier than the Caucasian group (12.9 years of age). The mean age of both groups was approximately 29 years of age, the mean weight of both groups varied only slightly, 150 versus 156 pounds, however the non-Caucasian group were more likely to be childless, 47.7% compared to 37.5%

Preliminary Findings from Hormonal Analysis:

Table 10 describes the 104 subjects providing both diary and hormonal data. As can be seen from Table 10 this subgroup was similar to the total group of 170 participants (Table 6) Mean age at interview, age at menarche, and percent Caucasian, married, with college education, and in the military were almost identical. The total group of 170 had 38.8%, were fuel handlers compared to 26.9% in the hormonal analysis. This difference is likely associated with job demands and deployment activities.

Table 10

Demographic Characteristics of Participants Providing Diaries & Preovulatory LH, Mid-luteal E13G, Follicular PD3G, and/or Mid-luteal PD3G:

Demographic Characteristics	Exposed:	n:	Non-exposed:	n:	Total:	n
Mean age, years	27.4	28	30.1	76	29.4	104
Mean age at menarche, years	13.0	28	12.6	76	12.7	104
Race, %						
Caucasian	78.6%	22	55.3%	42	61.5%	64
Non-Caucasian	21.4%	6	44.7%	34	38.5%	40
African-American	17.8%	5	35.5%	27	30.8%	32
Hispanic	3.6%	1	6.6%	5	5.8%	6
Other	0.0%	0	2.6%	2	1.9%	2
Marital Status, %						
Never Married	44.4%	12	22.4%	17	28.2%	29
Married or Have Permanent Partner	37.0%	10	65.8%	50	57.7%	60
Widowed, Divorced , or Permanently Separated	18.5%	5	11.8%	9	13.6%	14
Education, %						
Some HS/HS or GED/HS & Tech Training	14.3%	4	19.7%	15	18.3%	19
Some college or associates degree	67.9%	19	61.8%	47	63.4%	66
Bachelors (or greater)	17.9%	5	18.4%	14	18.3%	19
Number of Children, %						
0	39.3%	11	38.2%	29	38.5%	40
1	32.1%	9	27.6%	21	28.8%	30
2	28.6%	8	34.2%	26	32.7%	34
Family Income, %						
<$30.000	71.4%	20	41.3%	31	49.5%	51
≥$30.000	28.6%	8	58.7%	44	50.5%	52
Job Category, %						
Military	89.3%	25	82.9%	63	84.6%	88
Civilian	10.7%	3	17.1%	13	15.4%	16
Fuel Exposure, %	28/104=26.9%	28	76/104=73.1%	76	100%	**104***

* 4 deleted due to medical conditions

Table 11 describes the distribution of urinary endocrine endpoints by dichotomous job exposure category. Job category assignment to exposed and unexposed category was based upon current job title and description. Most of these endocrine outcomes were available for each woman in this subgroup (n=104), but a few were not ascertained for every endpoint.. The four key

endocrine endpoints for the upcoming multivariable analyses include preovulatory LH, mid-luteal E13G, follicular PD3G, and mid-luteal PD3G. These hormones were chosen because they have been linked to a hormonal milieu favorable for conception to occur (Baird et al., 1999). As seen in Table 11, the samples sizes for these hormones are as follows: preovulatory LH (n=96), mid-luteal E13G (n=96), follicular PD3G (n=102) and mid-luteal PD3G (n=96). For this preliminary report, crude differences between exposed and nonexposed groups with regard to outcomes reported in Table 11 were evaluated using t-tests for normally distributed variables and Wilcoxon Rank Sum test for non-normally distributed variables. **No significant differences were found during the unadjusted analysis of these endocrine endpoints.**

Table 11

Number of Subjects Providing Hormonal Data with Unadjusted Means, Standard Deviations, Minimum & Maximum Levels by Fuel Exposure (Job Category):*

Urinary Endocrine Endpoint:	Exposed:	N:	Mean:	SD:	Min:	Max:
Follicular Phase Length:	Y	27	14.370	3.307	7.000	21.000
	N	68	15.765	5.241	9.000	40.000
Luteal Phase Length:	Y	27	12.963	1.581	10.000	16.000
	N	66	13.015	1.957	8.000	17.000
Preovulatory LH Level:	Y	27	16.732	10.212	3.034	38.736
	N	67	19.31	12.094	2.394	55.409
Level of LH Surge Peak:	Y	27	41.361	18.437	5.529	86.662
	N	68	46.945	21.399	9.972	101.547
Follicular LH Level:	Y	25	5.442	2.883	1.749	14.448
	N	65	6.151	4.331	0.980	29.635
Early-Follicular $E_1$3G Level:	Y	25	13.631	13.764	5.558	77.432
	N	70	11.928	6.531	3.177	38.824
Mid-Luteal $E_1$3G Level:	Y	26	30.035	14.671	12.659	68.146
	N	68	27.123	15.511	2.065	89.143
3-Day Periovulatory $E_1$3G Peak Level:	Y	28	42.823	18.185	22.515	92.510
	N	69	45.473	20.528	6.784	112.850
Early Follicular Pd3G Level:	Y	25	1.363	0.696	0.332	3.175
	N	70	1.602	1.030	0.160	4.547
Follicular Pd3G Level:	Y	27	1.124	0.552	0.305	2.621
	N	72	1.244	0.813	0.012	3.578
Mid-Luteal Pd3G Level:	Y	26	9.264	4.988	1.997	21.525
	N	68	11.269	7.652	0.123	37.865
$E_1$3G:Pd3G Day of Luteal Transition:	Y	23	15.739	3.558	7.000	22.000
	N	62	16.403	5.113	3.000	39.000
Early Follicular FSH Level:	Y	24	6.636	3.097	2.007	14.000
	N	67	6.839	3.610	0.736	18.201
Follicular LH:FSH Ratio:	Y	24	0.8145	0.460	0.165	1.883
	N	69	0.899	0.589	0.140	3.177
Mid-Luteal FSH Level:	Y	27	3.331	1.741	1.325	9.013
	N	72	3.531	2.343	0.940	13.994
FSH Rise Before Menses:	Y	24	0.242	0.660	-1.976	1.499
	N	74	0.426	0.627	-1.029	2.430

* Participants without properly aliquoted, complete data for at least one of these hormonal endpoints were excluded.

Prior to the multivariable analysis to be done in Year 04, bivariate analyses were conducted between the four key study hormone outcomes and candidate covariates. These potential covariates among the candidate covariates examined in preliminary bivariate analyses were: exposure to fuels, solvents, exhaust, age, age at first menses, income, education, racial/ethnic group, body mass index/unadjusted weight, stress (home and total), job strain (average and

maximum level), illness with fever, sleep, cold temperatures, caffeine, coffee, alcohol, sidestream smoke, cigarettes, and various exercise/activity measures. Spearman rank correlations were used to compare continuous and categorical (> 2 categories) candidate covariates that were not normally distributed to both non-normal and normally distributed (transformed) continuous hormone levels. Pearson correlations were used when comparing normally distributed, continuous candidate covariates and transformed hormone levels. A subset of continuous variables were also tested categorically against hormone levels using Spearman rank correlations. This analysis was done to control for the effects of extreme values, and/or to group data according to heuristically meaningful criteria. A p-value of 0.15 was chosen to select potential covariates for inclusion for the upcoming stepwise regression analyses. The significance or nonsignificance of relationships between covariates and hormones remained (exception: hours of sleep per day) regardless of transformation or correlation coefficient applied. Continuous covariates presented in Table 12 below, were significantly associated with at least one the four study hormones. Where extreme values for covariates were present, bivariate analyses were repeated with the extremes removed, as footnoted in Table 12. As shown in Table 12, hours of solvent exposure per week and days of fuel exposure per week were both associated with having dysmenorrhea. Hours of fuel exposure per week was also associated with preovulatory LH.

Table 12

Continuous & Ordinal Variables found to be Significantly Correlated ($p \leq 0.15$) with One or More Endocrine Outcomes during Preliminary Bivariate Analyses

Continuous Variable:	Hormone:	Correlation:	p-value:	n:
Hrs. of solvent/wk: (solwkout)	*Preovulatory LH*			
	Mid-luteal E13G			
	Follicular PD3G			
	Mid-luteal PD3G			
	Dysmenorrhea	*0.169*	*0.094**	*100*
Hrs. of fuel exposure/wk: (hrfulout)	*Preovulatory LH*	*-0.185*	*0.078**	*92*
	Mid-luteal E13G			
	Follicular PD3G			
	Mid-luteal PD3G			
	Dysmenorrhea			
Days of fuel exposure/wk: (dfwkout)	*Preovulatory LH*			
	Mid-luteal E13G			
	Follicular PD3G			
	Mid-luteal PD3G			
	Dysmenorrhea	*0.162*	*0.105**	*102*
Age: (age)	*Preovulatory LH*			
	Mid-luteal E13G			
	Follicular PD3G	*0.220*	*0.029*	*99*
	Mid-luteal PD3G	*0.265*	*0.010*	*94*
	Dysmenorrhea:	*-0.175*	*0.076*	*104*
Age at first menses: (menses)	*Preovulatory LH*			
	Mid-luteal E13G			
	Follicular PD3G			
	Mid-luteal PD3G			
	Dysmenorrhea:	*-0.188*	*0.057*	*104*
Education level: (schlevel)	*Preovulatory LH*			
	Mid-luteal E13G			
	Follicular PD3G			
	Mid-luteal PD3G	*-0.243*	*0.018*	*94*
	Dysmenorrhea	*-0.256*	*0.009*	*104*
Education level (6 groups): (schlevw)	*Preovulatory LH*			
	Mid-luteal E13G	*-0.158*	*0.129*	*94*
	Follicular PD3G			
	Mid-luteal PD3G			
	Dysmenorrhea	*-0.267*	*0.006*	*104*
Income level (5 groups): (incomew)	*Preovulatory LH*			
	Mid-luteal E13G			
	Follicular PD3G			
	Mid-luteal PD3G			
	Dysmenorrhea	*-0.212*	*0.031*	*103*
BMI: (bmi)	*Preovulatory LH*			
	Mid-luteal E13G			
	Follicular PD3G			
	Mid-luteal PD3G			
	Dysmenorrhea	*-0.277*	*0.004*	*104*

(continued next pg).

Weight: (subjwt)	*Preovulatory LH*			
	Mid-luteal E13G			
	Follicular PD3G			
	Mid-luteal PD3G			
	Dysmenorrhea	*-0.326*	*0.001*	*104*
Maximum job strain score: (mxstrain)	*Preovulatory LH*			
	Mid-luteal E13G			
	Follicular PD3G			
	Mid-luteal PD3G	*-0.212*	*0.041*	*94*
	Dysmenorrhea			
Sleep: (sleepday)	*Preovulatory LH*			
	Mid-luteal E13G	*0.177*	*0.088†*	*94*
	Follicular PD3G	*0.165*	*0.103*	*99*
	Mid-luteal PD3G	*0.197*	*0.057†*	*94*
	Dysmenorrhea			
Cold exposure: (hwmc_vdy)	*Preovulatory LH*	*0.201*	*0.055*	*92*
	Mid-luteal E13G			
	Follicular PD3G			
	Mid-luteal PD3G			
	Dysmenorrhea	*0.146*	*0.143**	*102*
Caffeine (mg/day, 4 groups) (mgcaf4)	*Preovulatory LH*			
	Mid-luteal E13G	*-0.176*	*0.090*	*94*
	Follicular PD3G			
	Mid-luteal PD3G			
	Dysmenorrhea			
Coffee (mg/day): (mgcofday)	*Preovulatory LH*			
	Mid-luteal E13G	*0.159*	*0.136*	*89*
	Follicular PD3G			
	Mid-luteal PD3G			
	Dysmenorrhea			
Alcohol (drinks/day): (etohday)	*Preovulatory LH*			
	Mid-luteal E13G			
	Follicular PD3G	*-0.162*	*0.111***	*98*
	Mid-luteal PD3G			
	Dysmenorrhea			
Cigarettes (~benzene from smoking/day, 4 groups): (cbenzout)	*Preovulatory LH*			
	Mid-luteal E13G			
	Follicular PD3G	*0.234*	*0.020**	*95*
	Mid-luteal PD3G	*0.191*	*0.072**	*90*
	Dysmenorrhea:			
Cigarettes (#/day): (cigtotdy)	*Preovulatory LH*			
	Mid-luteal E13G			
	Follicular PD3G			
	Mid-luteal PD3G	*0.164*	*0.115*	*94*
	Dysmenorrhea:	*0.193*	*0.050*	*104*
Side-stream smoke: (bysmkdy)	*Preovulatory LH*			
	Mid-luteal E13G			
	Follicular PD3G			
	Mid-luteal PD3G			
	Dysmenorrhea	*0.178*	*0.072*	*104*

(continued next page)

Running (miles/day): (runmidy)	*Preovulatory LH*			
	Mid-luteal E13G	*-0.212*	*0.043*	*92*
	Follicular PD3G			
	Mid-luteal PD3G			
	Dysmenorrhea			
Running + walking (miles per day,4 groups) (runwlk4)	*Preovulatory LH*			
	Mid-luteal E13G			
	Follicular PD3G	*0.163*	*0.107*	*99*
	Mid-luteal PD3G	*0.211*	*0.042*	*94*
	Dysmenorrhea			
Running + walking (miles/day): (runwlkdy)	*Preovulatory LH*			
	Mid-luteal E13G			
	Follicular PD3G			
	Mid-luteal PD3G	*0.248*	*0.016*	*94*
	Dysmenorrhea			
Heavy activity: (hvyactdy)	*Preovulatory LH*			
	Mid-luteal E13G			
	Follicular PD3G			
	Mid-luteal PD3G	*0.207*	*0.0456*	*94*
	Dysmenorrhea			

* Significant only after extreme values removed.
** Nonsignificant after extreme values removed.
‡ Significant only when hormonal outcome transformed

Also among the candidate covariates were nominal and dichotomous variables. Nominal variables with > 2 categories were compared to continuous (untransformed) hormonal outcomes using the Kruskall-Wallis test, while dichotomous covariates were compared to untransformed hormone levels using the Wilcoxon rank sum and to transformed hormones by t-tests. Significant results ($p \leq 0.15$) of bivariate analyses of candidate covariates compared to untransformed outcomes (Table 13) and transformed outcomes (Table 14) are shown. These above analyses will be used to determine variables in the stepwise regression analysis.

Table 13

Categorical Variables found to be Significantly Correlated ($p \leq 0.15$) with One or More Key Endocrine Outcomes during Preliminary Bivariate Analyses:

Categorical Variable:	Square Root of Preovulatory LH	Square Root of Mid-luteal E13G	Log of Follicular PD3G + 1	Square Root of Mid-luteal PD3G
Solvent exposure (< median, ≥ median):			0.092 (99) †	
Income groups (high, low):		*		
Race (Caucasian, Noncauc.):			*	0.095 (94)
Marital status (yes/no):	0.054 (93)	*		0.008 (93)
Education group (schl2):				0.044 (94)
Non-work:				0.007 (94)
BMI: (< 30, ≥30)				*
Home stress: (<median, ≥median):	*		0.102 (99) †	
Maximum job strain (high/rest):				0.092 (94)
Maximum job strain: (< median, ≥ median)		*		0.079 (94)
Cold exposure (yes/no):	0.054 (92) †			
Fever (yes/no):		0.057 (94)		0.144 (94)
Sleep (< median, ≥ median):			0.028 (99)	0.062 (94)
Run, walk and heavy activity:				0.098 (94)
Caffeine group (high/low):	0.148 (94)			
Caffeine group (<median, ≥ median):		0.064 (94)		
Coffee group (<median, ≥ median):		0.112 (94)		*
Alcohol (high vs. rest)	0.115 (94)†		0.119 (99) †	0.085 (94)
Alcohol (<median, ≥ median):		0.107 (99)†	*	
Alcohol (drinks/kg, high/low)		0.103 (94) †		
Smoker (yes/no):			0.094(99)	0.093 (94)

Dysmenorrhea nonnormal, not transformed (no interpretable transformation found)
† Not significant (Wilcoxon rank sum) before non-normal outcome variable transformed
* Not significant (t-test) after non-normal outcome variable transformed

Table 14

Categorical Variables found to be Significantly Correlated ($p \leq 0.15$) with Key Study Hormones during Preliminary Bivariate Analyses:

Categorical Variable:	Preovulatory LH	Mid-luteal E13G	Follicular PD3G	Mid-luteal PD3G
Solvent exposure (< median, ≥ median):			†	
Income groups (high, low):		0.044 (93)*		
Race (Caucasian, Noncauc.):			0.120 (99)*	0.023 (94)
Race (African American, Caucasian, Hispanic, Native American): **			0.042 (99)	0.048 (94)
Marital status (never married, married, prev. marriage):**	0.087 (93)		0.118 (98)	0.027 (93)
Marital status (yes/no):	0.073 (93)	0.137 (93)*		0.023 (93)
Education group (schl2):				0.017 (94)
Non-work:				0.002 (94)
BMI: (< 30, ≥30)				0.106 (94)*
Home stress: (<median, ≥median):	0.091 (94)*			†
Maximum job strain (high/rest):				0.085 (94)
Maximum job strain: (< median, ≥ median)		0.089 (94)*		0.061 (94)
Cold exposure (yes/no):	†			
Fever (yes/no):		0.121 (94)		0.106 (94)
Sleep (< median, ≥ median):			0.087 (99)	†
Run, walk and heavy activity:				0.085 (94)
Caffeine group (high/low):	0.124 (94)	†		
Caffeine group (<median, ≥ median):		0.054 (94)		
Coffee group (<median, ≥median):		0.022 (94)		0.069 (94)*
Alcohol (<median, ≥median):		†	0.130 (99)*	
Alcohol (high vs. rest)	†		†	0.145 (94)
Alcohol (drinks/kg, high/low)		†		
Smoker (yes/no):			0.101 (99)	0.105 (94)

† Not significant (Wilcoxon rank sum) before non-normal outcome variable transformed
* Not significant (t-test) after non-normal outcome variable transformed
** Kruskal-Wallis Test: performed for nominal data > 2 categories with non-normal (untransformed) outcomes only.

Next Step for Hormone Analysis

Covariates that were significantly associated with the key hormonal outcomes in Tables 12-14 will be examined to determine which are also associated with fuel exposure variables in bivariate analyses (i.e., potential confounders). Where multiple variables defining a single construct have been examined, the most useful variable for stepwise regression will be narrowed to select a single variable. The final variable to represent each construct will be that which maximizes control of possible confounding, minimizes collinearity, is most meaningful/interpretable and is the most significant in bivariate analysis with hormonal outcomes.

Analysis of Dysmenorrhea

Since having fuel exposure on the baseline questionnaire was found to be associated with dysmenorrhea (Table 8) further analysis is underway with the diary data for this outcome. The distribution of dysmenorrhea was non-normal. Dysmenorrhea (untransformed) was measured as the number of days dysmenorrhea was reported. As shown in Table 15, dysmenorrhea was significantly and directly correlated with measures of solvent exposure, but was most significant for solvent exposure, and only significantly (positively) related to weekly fuel exposure, when several women with extreme values for these measurements were included. With inclusion of these women with outlying values, solvent exposure remained significant, but weekly fuel exposure became non-significant. Dysmenorrhea was negatively and significantly related to several variables used to measure age, age at first menses, educational level, body mass index and unadjusted weight. Job strain, cold temperatures, side-stream smoke and smoking, as defined by at least one variable, all had a direct and significant relationship with dysmenorrhea.

Early follicular FSH level approached a significant correlation with dysmenorrhea (Spearman correlation coefficient 0.166, $p = 0.11$). Because a transformation to normalize dysmenorrhea was not found, this variable was dichotomized into ever/never diary-reported dysmenorrhea categories. Again, after dichotomizing dysmenorrhea, only early follicular FSH was significantly (positively) related to its presence (Wilcoxon rank sum, $p = 0.093$).

Table 15

Categorical Variables found to be Significantly Correlated ($p \leq 0.15$) with Dysmenorrhea during Preliminary Bivariate Analyses:

Categorical Variable:	Dysmenorrhea
Solvent exposure (< median, ≥ median):	0.105 (104)
Age groups (<30, ≥ 30):	0.010 (104)
Income groups (high, low):	0.110 (103)
Education group (schl2):	0.116 (104)
Military status (military, non)	0.087 (104)
Cold exposure (high, low):	0.053 (104)
Maximum job strain: (< median, ≥ median)	0.041 (104)
Sidestream smoke (yes/no):	0.102 (104)
Smoker (yes/no):	0.060 (104)

As shown in Table 16, there were significant, but moderately small correlations between mid-luteal E13G and both follicular PD3G and mid-luteal PD3G. The two measures of PD3G were correlated. Preovulatory LH levels were not correlated with these three hormones.

Table 16

Significant Correlations between Four Key Study Hormone Levels

	Mid-luteal E13G Level:	Follicular PD3G Level:	Mid-luteal PD3G Level:
Mid-luteal E13G Level:		0.178 (p = 0.088)	0.273 (p = 0.008)
Follicular PD3G Level:			0.627 (p = 0.000)
Mid-luteal PD3G Level:			

SOW Item #2: **Prepare preliminary report (months 34-36)**

Year 03 preliminary report is completed with this document.

(7) Key Research Accomplishments

- Gained participation from 10 base commanders
- Identified a potential cohort of ~1000 women working for the USAF
- Recruited 170 eligible subjects
- Developed a portable method for obtaining breath samples
- Completed analyses of menstrual symptom disorders from the baseline questionnaire
- Obtained assay results for >16 hormonal endpoints per women from consecutive daily urine collection

(8) Reportable Outcomes

- M.S. Degree in epidemiology obtained by student Lori Gordley. This grant funded her Master's Thesis
- Manuscript on menstrual symptoms submitted to peer-reviewed journal
- Current Ph.D. student funded for her dissertation research (Susan Simpson)
- Two current Ph.D. student traineeships funded in part based on this grant
- Three undergraduate students (two minority) funded by this grant
- One medical student received summer training and funding.
- Cooperative partnership established with the National Institute for Occupational Safety and Health (Co-investigator Dr. J. Kesner)

(9) Conclusions

a) Exposure to fuel handling job activities and life event stress was significantly associated with dysmenorrhea after adjustment for race, military status, age, education, number of children, marital status and income.

b) Stressful life events was significantly associated with dysmenorrhea, hypermenorrhea and abnormal cycle length.

(10) References

Baird DD, Weinberg CR, Zhou H, Kamel F, McConnaughey DR, Kesner JS, Wilcox AJ. Preimplantation urinary hormone profiles and the probability of conception in healthy women. Fertil Steril 71:40-49, 1999.

Harrington JM. The health experience of workers in the petroleum manufacturing and distribution industry 1987, [The Hague]: CONCAWE: report no.2/87, January, 1987

Hersh JH. Toluene embryopathy: two new cases. Journal of Medical Genetics 26(5):333-337, 1985

Katz MH. Multivariate Analysis: A Practical Guide for Clinicians. University Press: Cambridge. 1999

Kesner JS, Knecht EA, Krieg EF Jr. Time-resolved immunofluorometric assays for urinary luteinizing hormone and follicle stimulating hormone. *Analytica Chimica Acta* 285, 13-22. 1994a

Kesner JS, Knecht EA, Krieg EF Jr, Barnard G, Mikola H, Kohen F, Gani MM, Coley J. Validation of time-resolved fluoroimmunoassays for urinary estrone 3-glucuronide and pregnanediol 3-glucuronide. *Steroids* 58:205-211. 1994b

Kesner JS, Knecht EA, Krieg, EF Jr. Stability of urinary biomarkers of female reproductive hormones stored under various conditions. *Reprod Toxicol* 9:239-244. 1995

Kesner JS, Knecht EA, Krieg EF Jr, Wilcox AJ, O'Connor JF. Detecting preovulatory luteinizing hormone surges in urine. *Human Reprod* 13: 15-21. 1998

Jaffe M. Uber den niederschlag, welchen pikrinsaure im normalen harn erzeught und uber eine neue reaktion des kreatinins. *Z Physiol Chem* 10:391-400. 1886.

Lemasters GK, Olsen DM, Yiin JH, Lockey JE, Shukla R, Selevan SG, Schrader SM, Toth GP, Evenson DP & Huszar G. Male reproductive effects of solvent and fuel exposure during aircraft maintenance. Reproductive Toxicology 13(3): 155-166, 1999

Neter J, Wasserman W & Kutner MH. Applied Linear Regression Models, 2nd Edition. Irwin: Homewood, IL. 1989

Page N & Mehlman, Health effects of gasoline refueling vapors and measured exposures at service stations. Tox. Ind. Health 5:869-890,1989

Plenge-Bönig & Karmaus W. Exposure to toluene in the printing industry is associated with subfecundity in women but not in men. Occupational & Environmental Medicine 56:443-448, 1999.

(11) Appendixes:

Appendix I (Participant Instructions):

U.S.A.F. JET FUEL HEALTH PROJECT PROTOCOL
DAILY SALIVA COLLECTION INSTRUCTIONS

SALIVA COLLECTING PLAN:
For this study, you will start collecting your saliva tomorrow morning. You will continue collecting your early morning saliva samples every day through your next full menstrual cycle and for 2-3 days after your second menstrual period has ended. This is the same schedule as for collecting urine samples, as shown on the time line on the last page.

You should **use the gum** to collect your saliva **BEFORE** you eat, drink, or brush your teeth. If you must collect your saliva sample after eating, drinking, or brushing your teeth, wait at least 30 minutes after these activities and then collect the saliva.

Call Dr. James Kesner, the Study Laboratory Director (800-870-0201), if you ever have any questions. Also call him when you have finished collecting all your saliva samples.

THE SUPPLIES that you will receive today for daily saliva collection are:
- 1 cardboard box containing 84 labeled & capped vials & 1 plastic pearl
- 6 packs (90 sticks) of CareFree Sugarless gum

WHEN YOU RECEIVE YOUR SUPPLIES:
- The saliva sample vials are arranged in the box in rows by week; the vials in the top row are for this week. Vials for all the Sunday samples are in the left column, and so on. The vials for the last 2 weeks are arranged side-ways along the right side of the box. (Please see the diagram on last page).

- Look at the label on the very first vial in the top-left corner. The label contains:
  - your Study ID number,
  - the Sample # (this vial is for Sample #1),
  - the day of the week (this vial is for Sunday),
  - space to write the date(___/___/9__),
  - a jet icon and an arrow.

- Start with the top row of vials on the left corner and remove the vials up to and including the vial for today, i.e., if today is Thursday, remove the first 5 vials for Sunday through Thursday. These vials you remove are extras. You may store them in case you lose or need a spare vial.

- When you get home, remove tomorrow's vial and put it in the bathroom with the urine vial and collection cup, where they will remind you to collect your samples early tomorrow morning.

COLLECTING SALIVA:

1. Always store the sample box containing samples in the **freezer.**

2. Before you go to bed, take the next morning's vial out of the sample box in the freezer. You can transfer the pearl to the next vial cap to mark your place. Place the vial in the bathroom, ready for saliva collection when you awake in the morning. **Make sure the vial label matches tomorrow's day of the week.**

3. When you get up for the day, before you eat, drink, brush your teeth, or apply lipstick, **rinse your mouth out well with water.**

4. **Wait about 5 minutes.** While you are waiting, start chewing a stick of the Care-Free Sugarless gum. **Please use the gum, even if you don't need to.** Get the saliva vial with today's day of the week on the label. Take the lid off of the tube.

5. **After about 5 minutes has passed, and while still chewing the gum, begin to collect saliva by spitting into the tube.** You will need to do this for about 2-5 minutes to collect saliva up to the arrow on the label, not counting bubbles. This is about 2 milliliter (less than 1 teaspoon) of saliva. Looking into a mirror as you collect the first couple samples may make collection easier. Holding the vial with a tissue may make collection cleaner.

6. After collecting the sample, screw the cap **tightly** onto the tube.

7. **Write the date on the sample vial's label.** Use the water-proof study pen.

8. **Write in your diary:**
   - the sample # from the vial's label
   - the **military time** the sample was collected

9. Place the filled saliva vial in its slot in the sample box in the freezer and remove the next vial from the sample box. Check the label for tomorrow's day of the week and place the vial in the bathroom for your next morning sample.

10. Repeat this procedure for each day that you collect saliva.

11. Telephone Dr. Kesner, the Lab Director (800-870-0201), 1 week after your entry interview. This will allow you to discuss your study progress. Try to call between 8 a.m. & 5 p.m. eastern time. You may also leave a phone message.

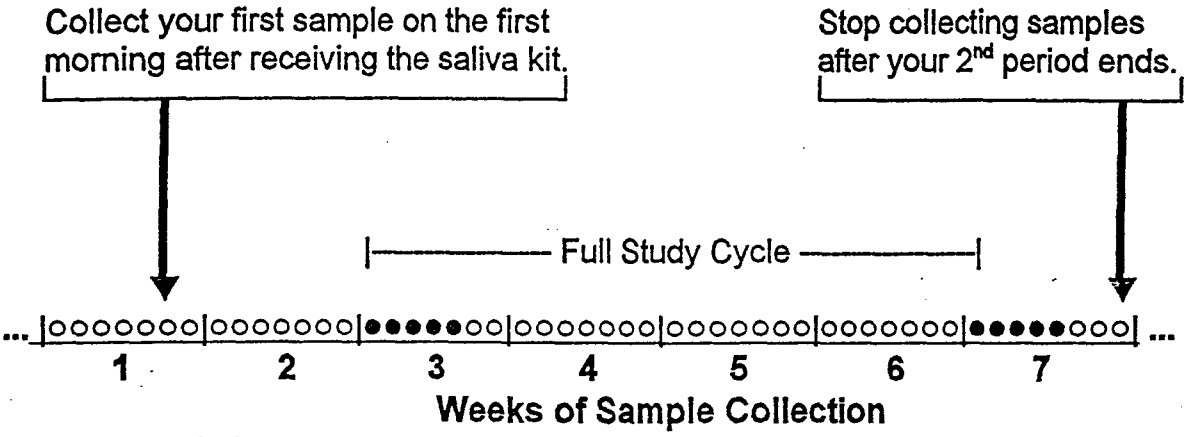
Immediately telephone Dr. Kesner (800-870-0201) if you have any questions.

SPECIAL NOTES:

- **Collect your saliva every morning.**
- **Keep all your samples frozen at all times.**
- **If you travel**, follow the same instructions as for urine.
- **Collect the saliva sample first thing in the morning**, when you collect your urine sample. If you must collect your saliva sample after eating, drinking, or brushing your teeth, wait at least 30 minutes after these activities, rinse your mouth, and then collect the saliva. Make a note in your diary describing these activities. Remember: **A late sample is better than no sample!**
- **If you do not collect saliva on a day**, leave that vial empty, make a note about this in your diary, and collect your sample for the next day in the next vial, as usual.
- **If you accidentally fill the wrong vial** or for some other reason must change the label, note the change on the plastic area of the test tube with your water-proof study marker. Make a note about this change in your diary.
- Record **military times.**
- **Some replacement materials** (pens, gum, etc.) may be available from your Base BEE Point of Contact. If you get replacement supplies, please note this in your diary or on the 800-870-0201 number.
- **Returning Your Saliva Samples:** Call Dr. Kesner, the Lab Director (800-870-0201), as soon as you are sure you are having your second menstrual period. You and he will determine if you are finished collecting your study samples and coordinate shipping your samples back to the Study Lab, using the written instructions you have already received.

Be sure to immediately contact Dr. Kesner at 800-870-0201 if you have any questions or problems.

EXAMPLE of COLLECTING DAILY SALIVA SAMPLES THROUGH A FULL MENSTRUAL CYCLE



●●●●● = period

Arrangement of Vials in the Saliva Box

Sun #1	Mon #2	Tue #3	Wed #4	Thu #5	Fri #6	Sat #7			
Sun #8	Mon #9	Tue #10	Wed #11	Thu #12	Fri #13	Sat #14			
Sun #15	Mon #16	Tue #17	Wed #18	Thu #19	Fri #20	Sat #21			
Sun #22	Mon #23	Tue #24	Wed #25	Thu #26	Fri #27	Sat #28		Sat #77	Sat #84
Sun #29	Mon #30	Tue #31	Wed #32	Thu #33	Fri #34	Sat #35		Fri #76	Fri #83
Sun #36	Mon #37	Tue #38	Wed #39	Thu #40	Fri #41	Sat #42		Thu #75	Thu #82
Sun #43	Mon #44	Tue #45	Wed #46	Thu #47	Fri #48	Sat #49		Wed #74	Wed #81
Sun #50	Mon #51	Tue #52	Wed #53	Thu #54	Fri #55	Sat #56		Tue #73	Tue #80
Sun #57	Mon #58	Tue #59	Wed #60	Thu #61	Fri #62	Sat #63		Mon #72	Mon #79
Sun #64	Mon #65	Tue #66	Wed #67	Thu #68	Fri #69	Sat #70		Sun #71	Sun #78

U.S.A.F. JET FUEL HEALTH PROJECT PROTOCOL
DAILY URINE COLLECTION INSTRUCTIONS

URINE COLLECTING PLAN:

For this study, you will start collecting your urine tomorrow morning. You will continue collecting your first morning urine every day through your next full menstrual cycle and for 2-3 days after your second menstrual period has ended. Please see the time-line on the last page for clarification.

Call Dr. James Kesner, the Study Laboratory Director (800-870-0201), if you ever have any questions. Also call him when you have finished collecting all your urine samples.

THE SUPPLIES that you will receive today for daily urine collection are:

- 2 cardboard boxes, each containing 42 labeled & capped vials
- 1 metal ring marker
- 2 plastic cup with pouring spout
- 1 water-proof marking pen
- 1 Styrofoam chest
- 2 freezer ice packs
- 1 instructions for shipping your samples to the Study Lab by Federal Express
- 1 Federal Express air bill & envelope
- 1 roll sealing tape

WHEN YOU RECEIVE YOUR SUPPLIES:

- Notice that the sample vials are arranged in the box in rows, week by week; the vials in the top row are for this week. Vials for all the Sunday samples are in the left column, and so on. (Please see the diagram on last page).

- Look at the label on the very first vial in the top-left corner. The label contains:
  - your Study ID number,
  - the Sample # (this vial is for Sample #1),
  - the day of the week (this vial is for Sunday),
  - space to write the date(___/___/9__),
  - a jet icon and an arrow.

- Start with the top row of vials on the left corner and remove the vials up to and including the vial for today, i.e., if today is Thursday, remove the first 5 vials for Sunday through Thursday. These vials you remove are extras. You may store them in case you lose or need a spare vial.

- When you get home, remove tomorrow's vial and put it with the plastic urine collection cup and saliva vial in the bathroom where they will remind you to collect your samples tomorrow morning.

COLLECTING URINE:

1. Always store the sample boxes containing samples in the **freezer**.

2. Each night before you go to bed, make sure you have taken the next morning's vial out of the sample box in the freezer. You can transfer the metal ring to the next vial cap to mark your place. Place the vial and plastic collection cup in the bathroom, ready for urine collection when you awake in the morning. **Make sure the label on the vial matches tomorrow's day of the week.**

3. When you get up for the day, collect some of this **first morning urination** in the plastic cup.

4. Carefully pour urine from the cup into the vial. **Fill the vial as close to the arrow on the label as possible.** Screw the lid **tightly** on the sample vial.

5. Turn the tube **upside-down three times** to mix the urine with preservative.

6. **Write the date on the sample vial's label.** Use the water-proof study pen.

7. **Write in your diary:**
   - the vial # from the sample label
   - the **military time** the sample was collected

8. Discard the urine remaining in the plastic collection cup and rinse the cup with warm water. Do <u>NOT</u> wash with soap or detergent. Place the cup upside down on clean tissue to drain for tomorrow's sample.

9. Place the filled urine vial in its slot in the sample box in the freezer and remove the next vial for tomorrow. Check the label for tomorrow's day of the week and place the vial in the bathroom for your next morning sample.

10. Repeat this procedure for each day that you collect urine.

11. Telephone the Dr. James Kesner, the Lab Director (800-870-0201), 1 week after your entry interview. This will allow you to discuss your study progress. Try to call between 8 a.m. & 5 p.m. eastern time. You may also leave a phone message.

Immediately telephone Dr. Kesner (800-870-0201) if you have any questions.

SPECIAL NOTES:

- **Collect your urine every morning**, even during your period or when you have had sexual intercourse.

- **Keep all your samples frozen at all times.** If this is not possible, keep them refrigerated or as cool as possible and then freeze them as soon as possible. Make notes every time that your samples are not immediately frozen.

- **Collecting & freezing your daily samples during travel:**
  - Take your **1)** sample vials for the travel days, **2)** the plastic collection cup, **3)** the water-proof pen, and **4)** one or more Aladdin thermoses (available upon request). These thermoses will each hold urine & saliva vials for 3 days. The thermos cap contains coolant material, so keep the thermos and samples in a freezer or refrigerator as much as possible during your travel. If possible, unscrew the thermos lid while in the freezer so the lid and samples will freeze. When you return home, place the sample vials in the freezer boxes and make notes about these activities in your diary.

  - If you are going to be traveling for a long period, use your study Styrofoam chest and ice packs to replace the Aladdin thermos. Otherwise, follow the instructions above. Call Dr. Kesner if you have questions.

- **If you miss your first morning urine**, collect the sample as early in the day as possible. Make a note about this in your diary. Remember: **A late sample is better than no sample!**

- **If you do not collect urine on a day**, leave that vial empty, make a note in your diary, and collect your sample for the next day in the next vial, as usual.

- **If you accidentally fill the wrong vial** or for some other reason must change the label, note the change on the plastic area of the test tube with your water-proof study marker. Make a note about this change in your diary.

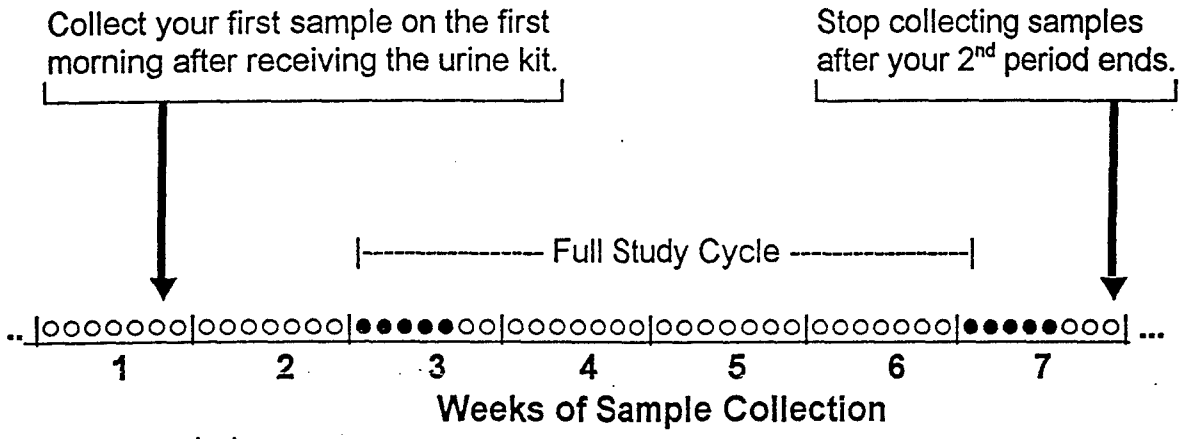
- **Record military times.**

- **Some replacement materials** (pens, beakers, etc.) may be available from your Base BEE Point of Contact. If you get replacement supplies, please note this in your diary or on the 800-870-0201 number.

- **Returning Your Urine Samples:** Call Dr. James Kesner, the Lab Director (800-870-0201), as soon as you are sure you are having your second menstrual period. You and he will determine if you are finished collecting your study samples and coordinate shipping your samples back to the Study Lab, using the written instructions you have already received.

Contact Dr. Kesner (800-870-0201) If You Have Any Questions or Problems.

EXAMPLE of COLLECTING DAILY URINE SAMPLES THROUGH A FULL MENSTRUAL CYCLE



●●●●● = period

Vial Arrangement in Urine Box #1

Sun #1	Mon #2	Tue #3	Wed #4	Thu #5	Fri #6	Sat #7
Sun #8	Mon #9	Tue #10	Wed #11	Thu #12	Fri #13	Sat #14
Sun #15	Mon #16	Tue #17	Wed #18	Thu #19	Fri #20	Sat #21
Sun #22	Mon #23	Tue #24	Wed #25	Thu #26	Fri #27	Sat #28
Sun #29	Mon #30	Tue #31	Wed #32	Thu #33	Fri #34	Sat #35
Sun #36	Mon #37	Tue #38	Wed #39	Thu #40	Fri #41	Sat #42

Vial Arrangement in Urine Box #2

Sun #43	Mon #44	Tue #45	Wed #46	Thu #47	Fri #48	Sat #49
Sun #50	Mon #51	Tue #52	Wed #53	Thu #54	Fri #55	Sat #56
Sun #57	Mon #58	Tue #59	Wed #60	Thu #61	Fri #62	Sat #63
Sun #64	Mon #65	Tue #66	Wed #67	Thu #68	Fri #69	Sat #70
Sun #71	Mon #72	Tue #73	Wed #74	Thu #75	Fri #76	Sat #77
Sun #78	Mon #79	Tue #80	Wed #81	Thu #82	Fri #83	Sat #84

U.S.A.F. JET FUEL HEALTH PROJECT PROTOCOL

ID. _____

INSTRUCTIONS FOR MAILING THE SAMPLES TO THE STUDY LABORATORY BY FEDERAL EXPRESS

When you are sure you are having your second menstrual period, call Dr. James Kesner, the Study Laboratory Director, at **800-870-0201.** You and he will determine if you are finished collecting your study samples and coordinate shipping your samples back to the Study Lab using the following instructions.

1. Prior to shipment, always keep your samples stored frozen.
2. When you and Dr. Kesner decide that you have completed collecting samples, identify the next Monday, Tuesday, or Wednesday that is convenient for you to send them by Federal Express. **DO NOT ship samples on a Thursday, Friday, Saturday, or Sunday.**
3. Place all the "ice packs" in your freezer, at least over night, in preparation for shipment. If you have an empty urine sample box that has not been frozen, put that in the freezer to get it cold, too.
4. At least one day before the shipment, phone Federal Express (**800-463-3339, option** *) and schedule them to come to your home or work for free pick-up. **Do not deliver your package. We have had many samples lost when participants took their package to "Federal Express."**
5. Be prepared to provide or discuss the following information:
   - the time for pick-up or delivery,
   - your home or work address,
   - the package weighs 7 pounds,
   - the shipment is government priority overnight on account number 0452-1271-8, and
   - the air bill number: _____.
6. Prepare the package as described below.
7. Make sure that you or someone you trust hands your sample package directly to the Federal Express courier to check the air bill. Do not leave the box for Federal Express to pick-up or with someone you don't completely trust. **Samples have been lost or destroyed these ways.**
8. Make sure the FedEx courier gives you the "Sender's" copy of the air bill.
9. Call Dr. Kesner (800-870-0201) to confirm that the samples were picked up.

PACKAGE PREPARATION:

1. Remove the Styrofoam chest from the cardboard box. Place your 2 frozen urine sample boxes and the frozen saliva sample box in the Styrofoam chest. Arrange the frozen "ice packs" around the sample boxes. Fill all remaining space with wadded newspaper to keep everything firmly in place and insulated.
2. Place your diaries inside the Styrofoam box.
3. Tape the Styrofoam lid tightly shut with the sealing tape that we gave you. Place the Styrofoam box into the cardboard crate and tape it closed very securely.
4. Write your **name, address, telephone number, and today's date** on the air bill form in the highlighted spaces in the upper left-hand corner.
5. Remove the clear envelope's larger adhesive backing and stick the envelope to the top of the shipping crate. Insert the air bill into the envelope. DO NOT seal the envelope!
6. If you have any questions, please telephone **Dr. James Kesner at 800-870-0201.**

SPECIAL MEASURES FOR THE WEEK OF BREATH SAMPLING:
FEMALE REPRODUCTIVE EFFECTS OF EXPOSURE
TO JET FUEL AT U.S. AIR FORCE BASES

The following measures will help us to obtain accurate estimates of your fuel exposure at work. We would like you to follow them for *ONE WEEK, i.e., from the Monday before your first breath sample until the Monday morning of your final breath sample.*

- **Avoid self-service refueling of your vehicle or lawn mower this week (outside of work).**
- **Avoid mowing the lawn.**
- **Avoid smoking sections of businesses and break rooms; try to lessen your exposure to cigarette smoke from friends and relatives as much as possible, especially indoors.**
- **If you are an occasional smoker, please do not smoke until after the final (Monday) breath sample is provided.**
- **Avoid smoke from fireplaces, grill-outs and grilled/smoked/charred foods**
- **Avoid using pesticides/insecticides, paints/solvents – this includes fingernail polish and polish remover.**
- **Please avoid using products containing alcohol. Especially, 24 hours prior to your breath sample, please do not use alcohol, mouthwash or cough syrup.**
- **Even the best-laid plans sometimes go awry. If you are unable to avoid one or more of the exposures on this page, please tell us when you provide your breath sample. This will help us to interpret the results.**
- **If you live with others, please ask them to read and, if acceptable, sign the form below. Bring the signed form with you when you arrive to provide your breath sample.**

TO OTHER MEMBERS OF THE HOUSEHOLD: *In order to obtain an accurate picture of the subject's internal exposure to fuel while at work, we need to enlist your help. During the week of testing, you can assist us in the following ways:*

Please protect her from exposure to smoke <u>for one week</u> during testing by:

- Helping her to avoid smoke from stoves, fireplaces or grilling food, even outdoors
- If you smoke, do so outdoors and please do not smoke when she is in the car with you
- Fuel-up the gas tank for her so she doesn't inhale the fumes
- If the lawn has to be mowed, fuel the lawn mower and mow the lawn for her
- Post-pone painting, spraying pesticides/insecticides or using solvents if she might be in the area and inhale the fumes

We realize these requests may cause some inconvenience. If you have any questions before you sign, please leave a phone message for Susan Simpson at (513) 558-0229. Include your name, phone number and days/times when you can be reached. IF YOU ARE WILLING TO PERFORM THESE MEASURES, PLEASE SIGN BELOW:

_____

Appendix II (Written Instruments):

Female Reproductive Study
Daily Diary

In this diary, "TODAY" means 1700 (5 pm) YESTERDAY to 1700 (5 pm) TONIGHT local time

Date

Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
Mnth Day Year	Mnth Day Year	Mnth Day Year	Mnth Day Year	Mnth Day Year	Mnth Day Year	Mnth Day Year

Today's Urine Sample

1a) Time the sample was obtained (record military time)

1b) Hours since last urination (record # of hours: 2 hrs=02)

1c) Sample number on today's urine vial (record sample #)

Today's Saliva Sample

2a) Time the sample was obtained (record military time)

For staff use only

ID: _____ Week: _____ Page # 1

	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
2b) Sample number on today's saliva vial (record sample #)	00 11 22 33 44 55 66 77 88 99	00 11 22 33 44 55 66 77 88 99	00 11 22 33 44 55 66 77 88 99	00 11 22 33 44 55 66 77 88 99	00 11 22 33 44 55 66 77 88 99	00 11 22 33 44 55 66 77 88 99	00 11 22 33 44 55 66 77 88 99

Today, did you have any problems with:

3a) Urine or saliva collection	Y N	Y N	Y N	Y N	Y N	Y N	Y N
3b) Sample storage or transport	Y N	Y N	Y N	Y N	Y N	Y N	Y N
3c) Explain if YES to 3a or 3b							
4) How many total hours did you sleep in the last 24 hrs. (hours between 1700 yesterday and 1700 today; 8 hours=08)	00 11 22 33 44 55 66 77 88 99	00 11 22 33 44 55 66 77 88 99	00 11 22 33 44 55 66 77 88 99	00 11 22 33 44 55 66 77 88 99	00 11 22 33 44 55 66 77 88 99	00 11 22 33 44 55 66 77 88 99	00 11 22 33 44 55 66 77 88 99

5) Did you have a cold, flu, other infection or fever of 101 or more today?

	Y N	Y N	Y N	Y N	Y N	Y N	Y N
6) Were you usually _____ today?	Hot H Warm W Comfortable M Cold C Very Cold V	Hot H Warm W Comfortable M Cold C Very Cold V	Hot H Warm W Comfortable M Cold C Very Cold V	Hot H Warm W Comfortable M Cold C Very Cold V	Hot H Warm W Comfortable M Cold C Very Cold V	Hot H Warm W Comfortable M Cold C Very Cold V	Hot H Warm W Comfortable M Cold C Very Cold V

Today, did you have any of the symptoms listed below?

M = yes, menstrual/Premenstrual symptom X = yes, *NOT* a menstrual/Premenstrual symptom N = No;

7) Lower Abdominal Cramping	M X N	M X N	M X N	M X N	M X N	M X N	M X N
8) Aching Back or Thighs	M X N	M X N	M X N	M X N	M X N	M X N	M X N
9) Bloating and/or Painful Breasts	M X N	M X N	M X N	M X N	M X N	M X N	M X N
10) Headache	M X N	M X N	M X N	M X N	M X N	M X N	M X N
11) Nausea	M X N	M X N	M X N	M X N	M X N	M X N	M X N
12) Loss of Appetite	M X N	M X N	M X N	M X N	M X N	M X N	M X N
13) Diarrhea	M X N	M X N	M X N	M X N	M X N	M X N	M X N

If you recorded "M" on any of the above, answer #14-#16; otherwise go directly to #17

	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday

14) Did you need to LIE DOWN due to any of the above menstrual/premenstrual symptoms today?

	Ⓨ Ⓝ	Ⓨ Ⓝ	Ⓨ Ⓝ	Ⓨ Ⓝ	Ⓨ Ⓝ	Ⓨ Ⓝ	Ⓨ Ⓝ

15) Did you MISS WORK due to any of the above menstrual/premenstrual symptoms today?

	Ⓨ Ⓝ	Ⓨ Ⓝ	Ⓨ Ⓝ	Ⓨ Ⓝ	Ⓨ Ⓝ	Ⓨ Ⓝ	Ⓨ Ⓝ

16) Did you take prescription or non-prescribed medication(s) for any of the above menstrual/premenstrual symptoms today?

	Ⓨ Ⓝ	Ⓨ Ⓝ	Ⓨ Ⓝ	Ⓨ Ⓝ	Ⓨ Ⓝ	Ⓨ Ⓝ	Ⓨ Ⓝ

17) Did you START taking any (OTHER) prescribed or non-prescribed medication(s) or supplements today?
If YES, please list the medication(s)

	Ⓨ Ⓝ	Ⓨ Ⓝ	Ⓨ Ⓝ	Ⓨ Ⓝ	Ⓨ Ⓝ	Ⓨ Ⓝ	Ⓨ Ⓝ

18) Did you have any MENSTRUAL BLEEDING or SPOTTING today? *(If NO go directly to # 22)*

	Ⓨ Ⓝ	Ⓨ Ⓝ	Ⓨ Ⓝ	Ⓨ Ⓝ	Ⓨ Ⓝ	Ⓨ Ⓝ	Ⓨ Ⓝ

19) How many TAMPONS and SANITARY NAPKINS did you use today? *(2 Sanitary Napkins = 02)*

	00 01 02 03 04 05 06 07 08 09	00 01 02 03 04 05 06 07 08 09	00 01 02 03 04 05 06 07 08 09	00 01 02 03 04 05 06 07 08 09	00 01 02 03 04 05 06 07 08 09	00 01 02 03 04 05 06 07 08 09	00 01 02 03 04 05 06 07 08 09
20) What was the AMOUNT of BLOOD?	Spotting ① Light ② Moderate ③ Heavy ④	Spotting ① Light ② Moderate ③ Heavy ④	Spotting ① Light ② Moderate ③ Heavy ④	Spotting ① Light ② Moderate ③ Heavy ④	Spotting ① Light ② Moderate ③ Heavy ④	Spotting ① Light ② Moderate ③ Heavy ④	Spotting ① Light ② Moderate ③ Heavy ④

21) Did you have any LEAKAGE around your pad or tampon while you last SLEPT?

	Ⓨ Ⓝ	Ⓨ Ⓝ	Ⓨ Ⓝ	Ⓨ Ⓝ	Ⓨ Ⓝ	Ⓨ Ⓝ	Ⓨ Ⓝ

22) Did you SMOKE today?
(if NO go to #27)

	Ⓨ Ⓝ	Ⓨ Ⓝ	Ⓨ Ⓝ	Ⓨ Ⓝ	Ⓨ Ⓝ	Ⓨ Ⓝ	Ⓨ Ⓝ

23-25) Please Record the Number of Cigarettes and Cigars Smoked Today

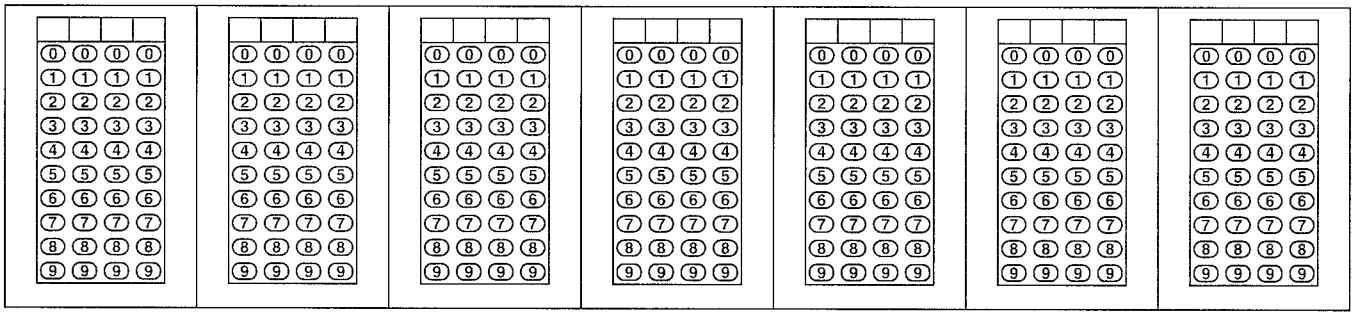
CF=Charcoal Filtered RF=Regular Filtered or Unfiltered Ci=Cigars

CF	RF	Ci	CF	RF	Ci	CF	RF	Ci	CF	RF	Ci	CF	RF	Ci	CF	RF	Ci	CF	RF	Ci
00 01 02 03 04 05 06 07 08 09	00 01 02 03 04 05 06 07 08 09	00 01 02 03 04 05 06 07 08 09	00 01 02 03 04 05 06 07 08 09	00 01 02 03 04 05 06 07 08 09	00 01 02 03 04 05 06 07 08 09	00 01 02 03 04 05 06 07 08 09	00 01 02 03 04 05 06 07 08 09	00 01 02 03 04 05 06 07 08 09	00 01 02 03 04 05 06 07 08 09	00 01 02 03 04 05 06 07 08 09	00 01 02 03 04 05 06 07 08 09	00 01 02 03 04 05 06 07 08 09	00 01 02 03 04 05 06 07 08 09	00 01 02 03 04 05 06 07 08 09	00 01 02 03 04 05 06 07 08 09	00 01 02 03 04 05 06 07 08 09	00 01 02 03 04 05 06 07 08 09	00 01 02 03 04 05 06 07 08 09	00 01 02 03 04 05 06 07 08 09	00 01 02 03 04 05 06 07 08 09

For staff use only ID: _____ Week: _____ Page # 3

Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday

26) IF your BREATH was SAMPLED today, what time was your last cigarette or cigar before the sample? *(record military time)*



27-28) How many HOURS were you NEAR OTHER SMOKERS at WORK or at HOME today?

(Darken "5" bubble on right if total hours includes an additional half hour, e.g. 7.5 hours; otherwise, leave blank)

(2 hrs = 02)

Work	Home	Work	Home	Work	Home	Work	Home	Work	Home	Work	Home	Work	Home
0 0 5	0 0 5	0 0 5	0 0 5	0 0 5	0 0 5	0 0 5	0 0 5	0 0 5	0 0 5	0 0 5	0 0 5	0 0 5	0 0 5
1 1	1 1	1 1	1 1	1 1	1 1	1 1	1 1	1 1	1 1	1 1	1 1	1 1	1 1
2 2	2 2	2 2	2 2	2 2	2 2	2 2	2 2	2 2	2 2	2 2	2 2	2 2	2 2
3 3	3 3	3 3	3 3	3 3	3 3	3 3	3 3	3 3	3 3	3 3	3 3	3 3	3 3
4 4	4 4	4 4	4 4	4 4	4 4	4 4	4 4	4 4	4 4	4 4	4 4	4 4	4 4
5 5	5 5	5 5	5 5	5 5	5 5	5 5	5 5	5 5	5 5	5 5	5 5	5 5	5 5
6 6	6 6	6 6	6 6	6 6	6 6	6 6	6 6	6 6	6 6	6 6	6 6	6 6	6 6
7 7	7 7	7 7	7 7	7 7	7 7	7 7	7 7	7 7	7 7	7 7	7 7	7 7	7 7
8 8	8 8	8 8	8 8	8 8	8 8	8 8	8 8	8 8	8 8	8 8	8 8	8 8	8 8
9 9	9 9	9 9	9 9	9 9	9 9	9 9	9 9	9 9	9 9	9 9	9 9	9 9	9 9

29-31) Did you drink any CAFFEINATED coffee drinks, tea, or soda today? If YES: list total number of ounces (oz) of:

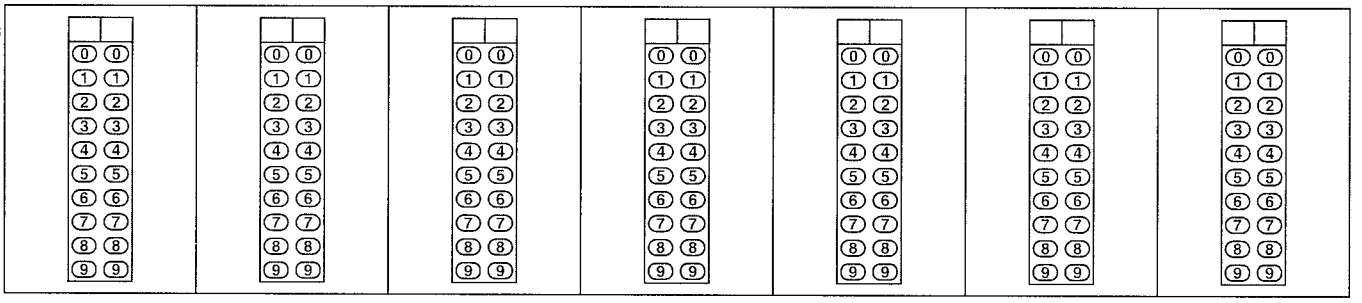
8 oz. = regular coffee cup; 12 oz. = mug, regular bottle or can (Do NOT include decaffeinated drinks)

(2 oz. = 02)

Y N																				
Coffee	Tea	Soda	Coffee	Tea	Soda	Coffee	Tea	Soda	Coffee	Tea	Soda	Coffee	Tea	Soda	Coffee	Tea	Soda	Coffee	Tea	Soda
0 0	0 0	0 0	0 0	0 0	0 0	0 0	0 0	0 0	0 0	0 0	0 0	0 0	0 0	0 0	0 0	0 0	0 0	0 0	0 0	0 0
1 1	1 1	1 1	1 1	1 1	1 1	1 1	1 1	1 1	1 1	1 1	1 1	1 1	1 1	1 1	1 1	1 1	1 1	1 1	1 1	1 1
2 2	2 2	2 2	2 2	2 2	2 2	2 2	2 2	2 2	2 2	2 2	2 2	2 2	2 2	2 2	2 2	2 2	2 2	2 2	2 2	2 2
3 3	3 3	3 3	3 3	3 3	3 3	3 3	3 3	3 3	3 3	3 3	3 3	3 3	3 3	3 3	3 3	3 3	3 3	3 3	3 3	3 3
4 4	4 4	4 4	4 4	4 4	4 4	4 4	4 4	4 4	4 4	4 4	4 4	4 4	4 4	4 4	4 4	4 4	4 4	4 4	4 4	4 4
5 5	5 5	5 5	5 5	5 5	5 5	5 5	5 5	5 5	5 5	5 5	5 5	5 5	5 5	5 5	5 5	5 5	5 5	5 5	5 5	5 5
6 6	6 6	6 6	6 6	6 6	6 6	6 6	6 6	6 6	6 6	6 6	6 6	6 6	6 6	6 6	6 6	6 6	6 6	6 6	6 6	6 6
7 7	7 7	7 7	7 7	7 7	7 7	7 7	7 7	7 7	7 7	7 7	7 7	7 7	7 7	7 7	7 7	7 7	7 7	7 7	7 7	7 7
8 8	8 8	8 8	8 8	8 8	8 8	8 8	8 8	8 8	8 8	8 8	8 8	8 8	8 8	8 8	8 8	8 8	8 8	8 8	8 8	8 8
9 9	9 9	9 9	9 9	9 9	9 9	9 9	9 9	9 9	9 9	9 9	9 9	9 9	9 9	9 9	9 9	9 9	9 9	9 9	9 9	9 9

32) How many DRINKS of ALCOHOL did you consume today (e.g. wine, beer, liquor)? *(List the total number of drinks)*

(2 drinks = 02)



33-38) On a scale of zero to four, please rate your FEELINGS today for the following states

e.g. no mood swings = 0 - 1 - 2 - 3 - 4 = severe mood swings

no depression = 0 - 1 - 2 - 3 - 4 = very depressed

| | | | | | | | | | | | | | | | | | | |

39) Did you work at the base today?

Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
Y N	Y N	Y N	Y N	Y N	Y N	Y N

40) If YES: How many TOTAL HOURS did you work today, including classes? *(If NO, go to #44.)*

(Darken "5" bubble on right if total hours includes an additional half hour, e.g. 7.5 hours; otherwise, leave blank)

(2 hrs = 02)

Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
0 0 1 1 2 2 3 3 4 4 5 5 6 6 7 7 8 8 9 9 5	0 0 1 1 2 2 3 3 4 4 5 5 6 6 7 7 8 8 9 9 5	0 0 1 1 2 2 3 3 4 4 5 5 6 6 7 7 8 8 9 9 5	0 0 1 1 2 2 3 3 4 4 5 5 6 6 7 7 8 8 9 9 5	0 0 1 1 2 2 3 3 4 4 5 5 6 6 7 7 8 8 9 9 5	0 0 1 1 2 2 3 3 4 4 5 5 6 6 7 7 8 8 9 9 5	0 0 1 1 2 2 3 3 4 4 5 5 6 6 7 7 8 8 9 9 5

41) What SHIFT did you work today? *(If worked a "double shift," record both shifts)*

Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
Day D Evening E Night N	Day D Evening E Night N	Day D Evening E Night N	Day D Evening E Night N	Day D Evening E Night N	Day D Evening E Night N	Day D Evening E Night N

42) In what SHOP or OFFICE did you work today? *(record name of shop or office)*

Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday

43) Did you perform an unusual JOB or JOB ACTIVITY(IES) today? *(If yes, describe job or activities)*

Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
Y N	Y N	Y N	Y N	Y N	Y N	Y N

44) Did you SMELL FUEL in the air today?

Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
Y N	Y N	Y N	Y N	Y N	Y N	Y N

45) IF YES: Did you SMELL FUEL while at work, outside of work? *(If NO, go to #49)*

Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
Work W Outside O Both B	Work W Outside O Both B	Work W Outside O Both B	Work W Outside O Both B	Work W Outside O Both B	Work W Outside O Both B	Work W Outside O Both B

46-47) How many HOURS were you exposed to...

Typical = TYPICAL levels of FUEL in the air today?

Higher = HIGHER than USUAL levels of FUEL in the air today?

(Darken "5" bubble on right if total hours includes an additional half hour, e.g. 7.5 hours; otherwise, leave blank)

(2 hrs = 02)

Monday		Tuesday		Wednesday		Thursday		Friday		Saturday		Sunday	
Typical	Higher	Typical	Higher	Typical	Higher	Typical	Higher	Typical	Higher	Typical	Higher	Typical	Higher
0 0 1 1 2 2 3 3 4 4 5 5 6 6 7 7 8 8 9 9 5	0 0 1 1 2 2 3 3 4 4 5 5 6 6 7 7 8 8 9 9 5	0 0 1 1 2 2 3 3 4 4 5 5 6 6 7 7 8 8 9 9 5	0 0 1 1 2 2 3 3 4 4 5 5 6 6 7 7 8 8 9 9 5	0 0 1 1 2 2 3 3 4 4 5 5 6 6 7 7 8 8 9 9 5	0 0 1 1 2 2 3 3 4 4 5 5 6 6 7 7 8 8 9 9 5	0 0 1 1 2 2 3 3 4 4 5 5 6 6 7 7 8 8 9 9 5	0 0 1 1 2 2 3 3 4 4 5 5 6 6 7 7 8 8 9 9 5	0 0 1 1 2 2 3 3 4 4 5 5 6 6 7 7 8 8 9 9 5	0 0 1 1 2 2 3 3 4 4 5 5 6 6 7 7 8 8 9 9 5	0 0 1 1 2 2 3 3 4 4 5 5 6 6 7 7 8 8 9 9 5	0 0 1 1 2 2 3 3 4 4 5 5 6 6 7 7 8 8 9 9 5	0 0 1 1 2 2 3 3 4 4 5 5 6 6 7 7 8 8 9 9 5	0 0 1 1 2 2 3 3 4 4 5 5 6 6 7 7 8 8 9 9 5

48) How many HOURS did you wear a respirator today? *(record total hours)*

(2 hrs = 02)

Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
0 0 1 1 2 2 3 3 4 4 5 5 6 6 7 7 8 8 9 9 5	0 0 1 1 2 2 3 3 4 4 5 5 6 6 7 7 8 8 9 9 5	0 0 1 1 2 2 3 3 4 4 5 5 6 6 7 7 8 8 9 9 5	0 0 1 1 2 2 3 3 4 4 5 5 6 6 7 7 8 8 9 9 5	0 0 1 1 2 2 3 3 4 4 5 5 6 6 7 7 8 8 9 9 5	0 0 1 1 2 2 3 3 4 4 5 5 6 6 7 7 8 8 9 9 5	0 0 1 1 2 2 3 3 4 4 5 5 6 6 7 7 8 8 9 9 5

For staff use only

ID: _____ Week: _____

Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday

49) Did your skin come into contact with liquid FUEL today? *(If NO, go to #53)*

Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
Y N	Y N	Y N	Y N	Y N	Y N	Y N

50) Was FUEL on your SKIN while at Work, Outside of Work, or Both?
(Darken "5" bubble on right if total hours includes an additional half hour, e.g. 7.5 hours; otherwise, leave blank)

Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
Work W Outside O Both B	Work W Outside O Both B	Work W Outside O Both B	Work W Outside O Both B	Work W Outside O Both B	Work W Outside O Both B	Work W Outside O Both B

51) How many hours was FUEL on your SKIN today?
(1 hr = 01; 0 hrs = 00)

52) How many HOURS did you wear GLOVES or COVERALLS today?
(2 hrs = 02; 0 hrs = 00)

53) How many MINUTES were you exposed to exhaust today?
(5 min = 005; 0 min = 000)

54) How many HOURS were you exposed to SOLVENTS or PESTICIDES IN THE AIR today?
(e.g., degreasing cleaner, glue, paint, nail polish, nail polish remover, oil, weed killer, insect killer, varnish, lacquer)
(Darken "5" bubble on right if total hours includes an additional half hour, e.g. 7.5 hours; otherwise, leave blank)
(2 hrs = 02; 0 hrs = 00)

55) How many HOURS was your skin in contact with SOLVENTS or PESTICIDES today?
(e.g., degreasing cleaner, glue, paint, nail polish, nail polish remover, oil, weed killer, insect killer, varnish, lacquer)
(2 hrs = 02; 0 hrs = 00)

Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday

56) How many FLIGHTS of STAIRS did you climb today? *(assume 10 stairs per flight)*

(5 flights = 005)

57-58) How many MILES did you...

(2 mi = 02: 0 mi = 00)

Walk	Run	Walk	Run	Walk	Run	Walk	Run	Walk	Run	Walk	Run	Walk	Run

59) How many MINUTES did you RUN today?

(10 min = 010)

60-61) Today, _____, how many HOURS did you do light to moderate physical activity?

at work	off work	at work	off work	at work	off work	at work	off work	at work	off work	at work	off work	at work	off work

62-63) Today, _____, how many MINUTES did you do heavy (to the point of perspiration or breathing) physical activity?

(do not include running here)

at work	off work	at work	off work	at work	off work	at work	off work	at work	off work	at work	off work	at work	off work

IF YOU WORKED DURING THE LAST WEEK, PLEASE ANSWER QUESTIONS #64-75 AT THE END OF YOUR WORK WEEK

(T) (F) 64) I had to work very hard this week?
(T) (F) 65) I had an excessive amount of work this week?
(T) (F) 66) I did not have enough time to get my work done this week?
(T) (F) 67) I had to do a lot of repetitive work this week?
(T) (F) 68) I had a job that allowed me to be creative this week?
(T) (F) 69) I had a job that allowed me to learn new things this week?
(T) (F) 70) I had a lot of say about what happened this week?
(T) (F) 71) I had a lot of freedom to decide how to do my work this week?
(T) (F) 72) I worked with helpful people this week?
(T) (F) 73) I worked with people who took a personal interest in me this week?
(T) (F) 74) My supervisor was helpful this week?
(T) (F) 75) My supervisor was concerned about my welfare this week?

IF YOU ARE PROVIDING A *HOME* BREATH SAMPLE ON A *THURSDAY* OR *FRIDAY* EVENING, PLEASE ANSWER QUESTIONS #76-79 AFTER THE SAMPLE IS PROVIDED; OTHERWISE GO TO #80-83

ON THE *MONDAY MORNING* THAT YOU PROVIDE A *HOME* BREATH SAMPLE, PLEASE ANSWER QUESTIONS #80-83

Thursday / Friday

What TIME did you collect your BREATH SAMPLE at HOME? *(record military time)*

76) Time (Thursday) OR Time (Friday)

After you left work, prior to your evening breath sample, were you exposed to:

Solvents, fuel odors or exhausts? *(if not exposed, record 0's in time & date blanks; otherwise, record date & time of last exposure before your first sample)*

77) Time / Date (Thursday) OR Time / Date (Friday)

Mouthwash, cough syrup or alcohol? *(if not exposed, record 0's in time & date blanks; otherwise, record date & time of last exposure before your first sample)*

78) Time / Date (Thursday) OR Time / Date (Friday)

79) Did you have any problems COLLECTING, STORING, OR TRANSPORTING your THURSDAY or FRIDAY EVENING BREATH SAMPLE?

If yes, please describe problem(s)
(Y) (N)

_____

_____

Monday Morning

80) Time

Within 24 hours prior to your Monday morning breath sample, were you exposed to:

81) Time / Date

82) Time / Date

83) Did you have any problems COLLECTING, STORING, OR TRANSPORTING your MONDAY MORNING BREATH SAMPLE?

If yes, please describe problem(s)
(Y) (N)

_____

_____

For staff use only ☞☞☞

ID: _____ Week: _____

Date: ___/___/___ Time Started: _____ Time Ended: _____ Interviewer Initials: _____	I.D.: _ _ _ _ _ _ _ _

BACKGROUND QUESTIONNAIRE
FOR THE
FEMALE REPRODUCTIVE STUDY:
UNIVERSITY OF CINCINNATI

READ INTRODUCTION: "Hello, my name is _____. You are Ms. _____. Is that correct? I am from the University of Cincinnati Medical Center. We are here to conduct a study of women's reproductive health."

"We are asking you if you wish to participate in this research study. Although your participation in this investigation is voluntary, it is very important that we obtain the cooperation of all the employees. Before we can proceed, please take a few minutes to read this informed consent." HAND FORM TO WORKER. "Your signature will give us permission to interview you, to collect urine samples from you before and during one menstrual cycle, and to obtain study diary information provided by you." AFTER WORKER HAS COMPLETED THE CONSENT FORM, ASK "Have you had enough time to consider the study?" IF NO, ALLOW MORE TIME TO REVIEW THE STUDY. "Do you have any questions?" IF NO, OBTAIN SIGNED FORM FROM THE WORKER AND WITNESS WITH A SIGNATURE. IF WORKER HAS A QUESTION, REFER TO "POTENTIAL QUESTIONS OF RESPONDENT GUIDE".

"IF WORKER REFUSES TO PARTICIPATE, ASK HIM/HER "Why do you not wish participate?" RECORD RESPONSE AT THE BOTTOM OF THIS PAGE. THANK WORKER FOR HIS/HER TIME.

"Thank you for your willingness to participate. Your cooperation is very important for the success of the study. Now we would like to ask you a number of questions about you, your work and your medical history."
(GO TO PAGE 2)

STATUS: INT REF ABS OTHER ("Please explain")_____
_____
_____

INSTRUCTIONS FOR INTERVIEWERS:

The **INTERVIEWER INSTRUCTIONS** throughout the questionnaire are written in **CAPITAL LETTERS (IN BOLD).** These are exclusively for your information. Do not read them out loud to the respondent.

The questionnaire has **SKIP PATTERNS** depending on the answers given or the personal characteristics of the respondent. If the skip pattern involves follow-up questions, the instruction will direct you as to which question(s) to ask next. For example:

IF YES, GO TO Q# 2-4 (continue with the next questions)
IF NO, GO TO Q#5 (skip questions two thru four & go on to number five)

If a respondent needs clarification on a given question, state **only** the information specified on the "Female Reproductive Study Question and Answer Sheet".

Record answers to open-ended questions **verbatim**. Record answers to close-ended questions by marking the appropriate box. Otherwise, record/code as:

"Don't know" If a participant is instructed, for a given question, to answer "no" if she does not know the answer, then record "don't know" responses by marking "**No ❐** ". If the question does not specify that a "don't know" answer is to be recorded as a "**No ❐** ", then record "don't know" responses by hand by writing "**DK**"; code as "**7**".

Refused responses Record refused responses by hand by writing "**R**"; code as "**8**".

Missing responses Contact the participant for the missing information. If unable to obtain the information post-interview, code as "**9**".

Dates are always recorded as either **month/year** or month/day/year

INTERVIEWER: **READ EACH QUESTION THEN LIST THE POSSIBLE RESPONSES. PLACE AN "X" IN THE APPROPRIATE BOX.**

READ: "the first set of questions are screening questions to determine if you have any conditions that might affect your study participation."

(#1) **"Please review this list. GIVE PARTICIPANT THE LIST. If a physician has diagnosed you with one or more of the following conditions, please answer 'yes'. If the you do not have the condition or you do not know, please answer 'no'."**

Yes ☐ No ☐

LIST:

Endometriosis
Chronic Pelvic Inflammatory Disease
Vaginal Cancer
Cervical Cancer
Uterine Cancer
Ovarian Cancer
Systemic Lupus Erythematosus
Hypopituitarism
Cushing's Syndrome
Sarcoidosis
Pituitary Tumor
Acute Hepatitis
HIV or AIDS
Cirrhosis of the Liver
Hypothyroidism (only if taking thyroid medication)
Hyperthyroidism
Multiple Sclerosis
Tuberculosis (confirmed by x-ray and/or sputum)
Diabetes
Have you had a hysterectomy?
Have one or both of your ovaries been removed?

(#2-9) "Do any of the following cases apply to you?"

(2) "I currently smoke three or more cigarettes or cigars per week?"	Yes ❒	No ❒
(3) "I was pregnant within the last three months?"	Yes ❒	No ❒
(4) "I am currently pregnant?"	Yes ❒	No ❒
(5) "I have used oral contraceptives within the last three months?"	Yes ❒	No ❒
(6) "I have used estrogen replacement therapy within the last three months?"	Yes ❒	No ❒
(7) "I have used at least one of the following drugs within the last three months?" SHOW LIST:	Yes ❒	No ❒
(8) "I breast-fed within the last three months?"	Yes ❒	No ❒
(9) "I had an intrauterine devise (IUD) inserted within the last three months?"	Yes ❒	No ❒

(10) "What is your.... 10a) date of birth?" ____/____/____
Mo. / Day / Year

10b) age in years?" _____ **YEARS**

(#11) "Is you race.....?"

(A) African American ❒
(B) Asian or Pacific Islander ❒
(C) Caucasian ❒
(D) Hispanic ❒
(E) Native American ❒
(F) Other ❒

IF OTHER, PLEASE DESCRIBE: _____

(#12) "What is your marital status?"

(A) Never Married ❒
(B) Married, or Have a Permanent Partner ❒
(C) Widowed, Divorced or Permanently Separated ❒

(#13) "What is the highest educational level you completed?"

(A) Some High School ❒

(B) High School or GED ❒

(C) High School + Technical School Vocat. Trng. ❒

(D) Some College or Associate's degree ❒

(E) Bachelor's degree ❒

(F) Master's degree ❒

(G) Doctorate ❒

(#14) "What was your total net family income for last year? Include any specialty pay, proficiency pay, housing and/or rations allowances. Was it..."

(A) Less than $15,000 ❒

(B) $15,000 - $29,999 ❒

(C) $30,000 - $44,999 ❒

(D) $45,000 - $59,999 ❒

(E) Over $60,000 ❒

INTERVIEWER: IF YES TO ANY ITEM, QUESTIONS #1 OR #9, STATE: "The/your (STATE STATUS/ CONDITION) is a condition which is beyond the scope of the current study. Because of the/your (STATE STATUS/CONDITION), we are unable to include you in this investigation. We do appreciate your answering of our questions and your time, though. We do not have any more questions. Thank you!"

IF OVER AGE 40 YEARS, STATE: "This is a study of women between the ages of 18 and 40 years. We are unable to include you because of this requirement. We do appreciate your answering of our questions and your time, though. We do not have any more questions. Thank you!"

IF NO TO ALL ITEMS, QUESTIONS #1 & #10, ASK "If you should move during or after the study, we would like to know how to contact you. Is there someone, other than your spouse, who will always know where you can be contacted?"

First Name: _____

M.I.: _____

Last Name: _____

Street: _____

City: _____

State: _____

Zip: _____

Phone: (_ _ _) _ _ _ - _ _ _ _

Relationship of Contact: _____

(#15-#27) ASK: "Has a doctor ever told you that you had any of the following gynecological conditions? If you do not know, please answer 'no'."

(15) "Uterine Fibroids?" Yes ❒ No ❒

(16) "Genital tract polyps?" Yes ❒ No ❒

(17) "Cervical or uterine hyperplasia?" Yes ❒ No ❒

(18) "Pelvic Infection?" Yes ❒ No ❒

(19) "Sexually Transmitted Disease?" Yes ❒ No ❒

(20) "Polycystic Ovarian Syndrome?" Yes ❒ No ❒

(21) "Premature Menopause?" Yes ❒ No ❒

(22) "Other reproductive abnormalities or conditions?" Yes ❒ No ❒

(22a) **IF YES**: " please describe"_____

(23) "Other reproductive system surgery not previously mentioned?" Yes ❒ No ❒

(23a) **IF YES**: " please describe the surgery"_____

(24) "Were you ever treated with radiation?" Yes ❒ No ❒

(24a) **IF YES**: "please describe the treatment"_____

(25) "Did your mother take DES when she was pregnant with you?" Yes ❒ No ❒

(26) "Do you currently have an intrauterine device (IUD)?" Yes ❒ No ❒

(26a) **IF YES**: " indicate month and year of insertion." ____/____

(27) "Have you underwent tubal sterilization?" Yes ❒ No ❒

(27a) **IF YES**: " indicate month and year of procedure" ____/____

(28) "If you are sexually active, are you and/or your partner currently using any method of contraception, including male birth control methods?"

Yes ❒ No ❒

(29) **READ: "Do you have any other chronic medical conditions, not previously mentioned, which were diagnosed by a physician?"** Yes ❒ No ❒

29a) IF YES, ASK: "Please list the condition(s)."

_____

_____

30) **"Before your first Air Force job, have you ever been unable to become pregnant after one year of frequent unprotected intercourse? Frequent means intercourse at least once per week."** Yes ❒ No ❒

31) **"Since your first Air Force job, have you ever been unable to become pregnant after one year of frequent unprotected intercourse? Frequent means at least once per week."** Yes ❒ No ❒

32) **"At what age did you start menstruating?"** AGE _____

33) **"Have your periods stopped due to menopause? IF YES, GO TO # 33a. IF NO, GO TO Q#34.** Yes ❒ No ❒

33a) At what age did your periods stop?" GO TO #40. AGE _____

34) **"When did your last menstrual period start? PROVIDE WITH A CALENDAR** _____/_____/_____ Mo. / Day / Yr.

35) **"During the past three months, how many days usually have passed from the start of one period to the start of the next?"** DAYS _____

36a) **"During the last three months, were your periods regular? That is, was the length of your cycles usually between (± FOUR DAYS AROUND DAYS REPORTED IN Q #35) ____ and ____ days apart?" (IF UNCLEAR, PROBE: did your cycles, which were typically ____ days, usually vary from month to month by less than four days?)** Yes ❒ No ❒

36b) **"During the last twelve months, were your periods regular? That is, was the length of your cycles usually between (± FOUR DAYS AROUND DAYS REPORTED IN Q #35) ____ and ____ days apart?** Yes ❒ No ❒

37) **"During the past three months, how many days have your periods usually lasted?"** DAYS _____

38) **"Would you describe the amount of bleeding during your typical menstrual period as...?"**

Spotting	❒
Light	❒
Moderate	❒
Heavy	❒

39)**"Do you usually have menstrual bleeding or spotting between periods?"** Yes ❒ No ❒

40) "Altogether, how many times have you been pregnant, including live births, stillbirths, miscarriages, abortions, tubal pregnancies, and a current pregnancy? IF NO PREGNANCIES, GO TO Q. #42. IF ONE OR MORE PREGNANCIES, GO TO Q. # 41. #_____

41) "Thinking about your pregnancy(ies)....."

FIRST PREGNANCY:

41a1) "What month and year did your (first) pregnancy end?" ____/____ Mo. / Yr.

41b1) "Was it a....."

Single birth?	☐	Miscarriage?	☐
Multiple birth?	☐	Stillbirth?	☐
Tubal pregnancy?	☐	Abortion?	☐

IF NOT A LIVE BIRTH, GO TO 41a2 OR, IF NO IF NO ADDITIONAL PREGNANCIES, GO TO Q#42. IF A SINGLE OR MULTIPLE BIRTH, ASK:

41c1) "How much did the baby('babies if multiple birth') delivered with this pregnancy weigh?"

____/____ lbs / oz ____/____ lbs / oz ____/____ lbs / oz

SECOND PREGNANCY:

41a2) "What month and year did your (second) pregnancy end?" ____/____ Mo. / Yr.

41b2) "Was it a....."

Single birth?	☐	Miscarriage?	☐
Multiple birth?	☐	Stillbirth?	☐
Tubal pregnancy?	☐	Abortion?	☐

IF NOT A LIVE BIRTH, GO TO 41a3 OR, IF NO IF NO ADDITIONAL PREGNANCIES, GO TO Q#42. IF A SINGLE OR MULTIPLE BIRTH, ASK:

41c2) "How much did the baby('babies if multiple birth') delivered with this pregnancy weigh?"

____/____ lbs / oz ____/____ lbs / oz ____/____ lbs / oz

THIRD PREGNANCY:

41a3) "What month and year did your (third) pregnancy end?" ____/____ Mo. / Yr.

41b3) "Was it a....."

Single birth?	☐	Miscarriage?	☐
Multiple birth?	☐	Stillbirth?	☐
Tubal pregnancy?	☐	Abortion?	☐

IF NOT A LIVE BIRTH, GO TO 41a4 OR, IF NO IF NO ADDITIONAL PREGNANCIES, GO TO Q#42. IF A SINGLE OR MULTIPLE BIRTH, ASK:

41c3) "How much did the baby('babies if multiple birth') delivered with this pregnancy weigh?"

____/____ lbs / oz ____/____ lbs / oz ____/____ lbs / oz

IF ADDITIONAL PREGNANIES, CONTINUE...

41) "Thinking about your pregnancy(ies)....."

FOURTH PREGNANCY:

41a4) "What month and year did your (fourth) pregnancy end?" ____/____
Mo. / Yr.

41b4) "Was it a....."

Single birth?	☐	Miscarriage?	☐
Multiple birth?	☐	Stillbirth?	☐
Tubal pregnancy?	☐	Abortion?	☐

IF NOT A LIVE BIRTH, GO TO 41a5 OR, IF NO IF NO ADDITIONAL PREGNANCIES, GO TO Q#42. IF A SINGLE OR MULTIPLE BIRTH, ASK:

41c4) "How much did the baby('babies if multiple birth') delivered with this pregnancy weigh?"

____/____ lbs / oz ____/____ lbs / oz ____/____ lbs / oz

FIFTH PREGNANCY:

41a5) "What month and year did your (fifth) pregnancy end?" ____/____
Mo. / Yr.

41b5) "Was it a....."

Single birth?	☐	Miscarriage?	☐
Multiple birth?	☐	Stillbirth?	☐
Tubal pregnancy?	☐	Abortion?	☐

IF NOT A LIVE BIRTH, GO TO 41a6 OR, IF NO IF NO ADDITIONAL PREGNANCIES, GO TO Q#42. IF A SINGLE OR MULTIPLE BIRTH, ASK:

41c5) "How much did the baby('babies if multiple birth') delivered with this pregnancy weigh?"

____/____ lbs / oz ____/____ lbs / oz ____/____ lbs / oz

SIXTH PREGNANCY:

41a6) "What month and year did your (sixth) pregnancy end?" ____/____
Mo. / Yr.

41b6) "Was it a....."

Single birth?	☐	Miscarriage?	☐
Multiple birth?	☐	Stillbirth?	☐
Tubal pregnancy?	☐	Abortion?	☐

IF NOT A LIVE BIRTH, GO TO 41a7 OR, IF NO IF NO ADDITIONAL PREGNANCIES, GO TO Q#42. IF A SINGLE OR MULTIPLE BIRTH, ASK:

41c6) "How much did the baby('babies if multiple birth') delivered with this pregnancy weigh?"

____/____ lbs / oz ____/____ lbs / oz ____/____ lbs / oz

IF ADDITIONAL PREGNANIES, CONTINUE...

41) "Thinking about your pregnancy(ies)....."

SEVENTH PREGNANCY:

41a7) "What month and year did your (seventh) pregnancy end?" ____/____ Mo. / Yr.

41b7) "Was it a....."

Single birth?	☐	Miscarriage?	☐
Multiple birth?	☐	Stillbirth?	☐
Tubal pregnancy?	☐	Abortion?	☐

IF NOT A LIVE BIRTH, GO TO 41a8 OR, IF NO IF NO ADDITIONAL PREGNANCIES, GO TO Q#42. IF A SINGLE OR MULTIPLE BIRTH, ASK:

41c7) "How much did the baby('babies if multiple birth') delivered with this pregnancy weigh?"

____/____ lbs / oz ____/____ lbs / oz ____/____ lbs / oz

EIGTH PREGNANCY:

41a8) "What month and year did your (eigth) pregnancy end?" ____/____ Mo. / Yr.

41b8) "Was it a....."

Single birth?	☐	Miscarriage?	☐
Multiple birth?	☐	Stillbirth?	☐
Tubal pregnancy?	☐	Abortion?	☐

IF NOT A LIVE BIRTH, GO TO 41a9 OR, IF NO IF NO ADDITIONAL PREGNANCIES, GO TO Q#42. IF A SINGLE OR MULTIPLE BIRTH, ASK:

41c8) "How much did the baby('babies if multiple birth') delivered with this pregnancy weigh?"

____/____ lbs / oz ____/____ lbs / oz ____/____ lbs / oz

NINTH PREGNANCY:

41a9) "What month and year did your (ninth) pregnancy end?" ____/____ Mo. / Yr.

41b9) "Was it a....."

Single birth?	☐	Miscarriage?	☐
Multiple birth?	☐	Stillbirth?	☐
Tubal pregnancy?	☐	Abortion?	☐

IF NOT A LIVE BIRTH, GO TO SUPPLEMENTAL PREGNANCY SHEET OR, IF NO IF NO ADDITIONAL PREGNANCIES, GO TO Q#42. IF A SINGLE OR MULTIPLE BIRTH, ASK:

41c9) "How much did the baby('babies if multiple birth') delivered with this pregnancy weigh?"

____/____ lbs / oz ____/____ lbs / oz ____/____ lbs / oz

IF ADDITIONAL PREGNANCIES, CONTINUE ON SUPPLEMENTAL PREGNANCY SHEETS, THEN GO TO Q#42.

(#42-48) "In the past three months, did you have one or more of the following symptoms...? READ THRU LIST AND ✓ YES OR NO. IF YES, AND IF PREMENOPAUSAL, ASK "Was this a menstrual symptom? Include premenstrual symptoms as menstrual"

	No	Yes, menstrual symptom	Yes, non-menstrual symptom
(42) Lower abdominal cramping	❐	❐	❐
(43) Aching back or thighs	❐	❐	❐
(44) Bloating and/or painful breasts	❐	❐	❐
(45) Headache	❐	❐	❐
(46) Nausea	❐	❐	❐
(47) Loss of Appetite	❐	❐	❐
(48) Diarrhea	❐	❐	❐

IF NO TO ALL OF THE ABOVE IN THE PREMENSTRUAL/MENSTRUAL SYMPTOM(S), GO TO Q#54. IF YES TO ONE OR MORE PREMENSTRUAL/MENSTRUAL SYMPTOMS, ASK:

49) "Did you miss work in the last three months due to _____(symptom(s))?" **Yes ❐** **No ❐**

50) "Did you need to lie down in the last three months due to _____(symptom(s))?" **Yes ❐** **No ❐**

51) "Did you take any prescribed medications for your _____(symptom(s))?" **Yes ❐** **No ❐**

52) "Did you take any over-the-counter medications for your _____(symptom(s))?" **Yes ❐** **No ❐**

53) "Please list all prescribed medications that you have taken since your last mentrual period."

NONE ❐ **OTHERWISE, LIST MED'S.:**

_____
_____
_____
_____
_____
_____

(#54 - #59) "Now we'd like to ask you some general questions related to your overall feelings of well-being. Please rate your usual feelings on a scale from zero to four for the following states." READ EACH STATE AND GIVE CARD FOR ACCOMPANYING SCALE.

	If zero equals:	And four equals:	What number between zero and four best describes how you usually feel?
54)	No energy	Very energetic	0 --- 1 --- 2 --- 3 --- 4
55)	No tension	Very tense	0 --- 1 --- 2 --- 3 --- 4
56)	No irritability	Very irritable	0 --- 1 --- 2 --- 3 --- 4
57)	No depression	Very depressed	0 --- 1 --- 2 --- 3 --- 4
58)	No mood swings	Severe mood swings	0 --- 1 --- 2 --- 3 --- 4
59)	No concentration	Excellent concentration	0 --- 1 --- 2 --- 3 --- 4

READ "The following questions refer to your non-work activities during the past 12 months."

60)	**"Did you have any accidental injuries when you were away from work during the past 12 months?"**	**Yes ❒**	**No ❒**
61)	**"Did you have primary responsibility for child care duties during the past 12 months?**	**Yes ❒**	**No ❒**
62)	**"Did you have primary responsibility for house cleaning duties during the past 12 months?"**	**Yes ❒**	**No ❒**
63)	**"Did you have primary responsibility for the care of an elderly or disabled person on a regular basis during the past 12 months?"**	**Yes ❒**	**No ❒**
64)	**"During the past 12 months, did you go to school and take courses for accreditation or credit towards a degree?"**	**Yes ❒**	**No ❒**
65)	**"During the past 12 months, did you belong to a voluntary or religious organization at which you spent at least 5-10 hours per week?"**	**Yes ❒**	**No ❒**
66)	**"During the last 12 months, about how many weeks did you work more than 40 hours per week?"**	**____ ____ wk(s).**	
67)	"How many children four years of age or less did you have living with you during the past 12 months?"	# _____	
68)	"How many children over age 4 years did you have living with you during the past 12 months?"	# _____	

(#69 - #80) Which of the following statements usually apply to you when you are at work?

69)	"I have to work very hard."	True ❒ False ❒
70)	"I have to do an excessive amount of work."	True ❒ False ❒
71)	"I do not have enough time to get my work done."	True ❒ False ❒
72)	"I have to do a lot of repetitive work."	True ❒ False ❒
73)	"I have a job which allows me to be creative."	True ❒ False ❒
74)	"I have a job which allows me to learn new things."	True ❒ False ❒
75)	"I have a lot of say about what happens."	True ❒ False ❒
76)	"I have a lot of freedom to decide how I do my work."	True ❒ False ❒
77)	"I work with helpful people."	True ❒ False ❒
78)	"I work with people who take a personal interest in me."	True ❒ False ❒
79)	"My supervisor is very helpful."	True ❒ False ❒
80)	"My supervisor is concerned about my welfare."	True ❒ False ❒

READ: "Have you had any unusually stressful events or experiences, which were not previously described in the past year, related to your...."

81) Situation at work? Yes ❒ No ❒

81a) IF YES: "please briefly describe the stressful event or experience"

_____

_____

_____

82) Situation outside of work? Yes ❒ No ❒

82a) IF YES: "please briefly describe the stressful event or experience"

_____
_____
_____
_____

83) Gender? Yes ❒ No ❒

83a) IF YES: "please briefly describe the stressful event or experience"

_____
_____
_____
_____

84) Race or ethnicity? Yes ❒ No ❒

84a) IF YES: "please briefly describe the stressful event or experience"

_____
_____
_____
_____

85) "If this (these) stressful event(s) had not occurred, how different would your life be now"?

READ:
Not different ❒
A little different ❒
Different in several ways ❒
Different in most ways ❒

(#86 - #90) STATE "The next group of questions are about your consumption patterns in the past two months."

86) "Have you consumed any caffeinated drinks in the past two months?" Yes ❒ No ❒

86a) IF YES, ASK: "During the past two months, how many caffeinated drinks did you usually drink or eat per day?" #_____

87) "At work, did you usually take breaks or have lunch indoors with people who were smoking in the past two months?" Yes ❒ No ❒

88) "At home, were you usually near people who were smoking indoors within the past two months?" Yes ❒ No ❒

89) "On average, how many alcoholic beverages drinks did you consume per week in the last two months?" # DRINKS: _____

READ: "The next set of questions are about recent life events. Please indicate which events, if any, have occurred within the past six months. We will then ask whether or not the event just happened, that is, within the last 30 days. Some events may have happened more than once in the past six months. If so, state the most recent time that the event happened. Some events may continue over a long period including the past six months. For these events, state the ending date. If you can't remember the exact dates, be as accurate as you can." CHECK THE BOX CORRESPONDING TO THE REPORTED TIME FRAME FOR EACH ITEM.

		A) Within 30 days:	B) 1 to 6 months ago:
90)	Death of a close loved one:		
1.	Mother	❐	❐
2.	Father	❐	❐
3.	Brother or sister	❐	❐
4.	Husband or lover	❐	❐
5.	Child	❐	❐
6.	Close friend or other important person	❐	❐
91)	Change in a relationship:		
1.	Argument with husband or lover	❐	❐
2.	Separation from husband or lover because of relationship problems	❐	❐
3.	Breaking off of an engagement	❐	❐
4.	A love affair outside your primary relationship	❐	❐
5.	Husband or lover being unfaithful	❐	❐
6.	Divorce from husband or break-up with lover	❐	❐
7.	Getting married or returning to husband or lover after separation	❐	❐
8.	Separation from a close friend	❐	❐
92)	Other changes:		
1.	The birth of a child or adoption	❐	❐
2.	An unwanted pregnancy	❐	❐
3.	A miscarriage	❐	❐

		A) Within 30 days:	B) 1 to 6 months ago:
93)	Work changes:		
1.	A big change at work or in school	❐	❐
2.	Trouble with your boss or other workers	❐	❐
3.	Being fired or laid off	❐	❐
4.	Taking an important examination	❐	❐
5.	Failing an important examination	❐	❐
94)	Illness or injuries:	❐	❐
1.	An illness or injury which kept you in bed for a week or more, or sent you to the hospital emergency room	❐	❐
2.	Hospitalization of a family member for a serious illness	❐	❐
3.	Attacked, raped or involved in violent acts	❐	❐
95)	Legal or financial troubles	❐	❐
1.	Trouble because of minor violations of the law	❐	❐
2.	Court appearance because of a serious violation	❐	❐
3.	Involvement in a law suit (other than divorce)	❐	❐
4.	Legal troubles leading you to be held in jail	❐	❐
5.	Financial difficulties	❐	❐
6.	Taking a large loan	❐	❐
7.	Loss of a personally valuable object	❐	❐
96)	Moves:		
1.	Moving of your home within the same city or town	❐	❐
2.	Moving to another town, city, state or country	❐	❐

READ: "The next set of questions concern substances you may have had contact with while on the Air Force base or elsewhere, such as during another job, hobby or at home. If you have breathed, swallowed or had skin or eye contact with any of the following substances, please answer 'yes'"

(97) "During the past three months, did you have contact with any of the following substances at or outside of work?"--------->

		IF YES, ASK: "During the past? three months, was your contact usually...?"		**IF YES, ASK:** "When in contact with _____, what % of the time did you usually wear/ use...?"
A) Oil (exclude cooking oil)	Yes ❒ No ❒	Daily 1-3 x's/week 1-3 x's/mo. < once/mo.	❒ ❒ ❒ ❒	Gloves ____ Respirator ____ Protective Clothes ____ Good Vent-illation ____
B) Degreasing cleaner	Yes ❒ No ❒	Daily 1-3 x's/week 1-3 x's/mo. < once/mo.	❒ ❒ ❒ ❒	Gloves ____ Respirator ____ Protective Clothes ____ Good Vent-illation ____
C) Paint Thinner/Stripper	Yes ❒ No ❒	Daily 1-3 x's/week 1-3 x's/mo. < once/mo.	❒ ❒ ❒ ❒	Gloves ____ Respirator ____ Protective Clothes ____ Good Vent-illation ____
D) Paint	Yes ❒ No ❒	Daily 1-3 x's/week 1-3 x's/mo. < once/mo.	❒ ❒ ❒ ❒	Gloves ____ Respirator ____ Protective Clothes ____ Good Vent-illation ____
E) Varnish	Yes ❒ No ❒	Daily 1-3 x's/week 1-3 x's/mo. < once/mo.	❒ ❒ ❒ ❒	Gloves ____ Respirator ____ Protective Clothes ____ Good Vent-illation ____
F) Lacquer	Yes ❒ No ❒	Daily 1-3 x's/week 1-3 x's/mo. < once/mo.	❒ ❒ ❒ ❒	Gloves ____ Respirator ____ Protective Clothes ____ Good Vent-illation ____

(Cont'd) ----------> **IF YES, ASK:**

		"During the past? three months, was your contact usually...?"	"When in contact with _____, what % of the time did you usually wear/ use...?"
G) Nail Polish Remover	Yes ❒ No ❒	Daily ❒ 1-3 x's/week ❒ 1-3 x's/mo. ❒ < once/mo. ❒	Good Vent-illation ____
H) Nail Polish	Yes ❒ No ❒	Daily ❒ 1-3 x's/week ❒ 1-3 x's/mo. ❒ < once/mo. ❒	Good Vent-illation ____
I) Jet Fuel	Yes ❒ No ❒	Daily ❒ 1-3 x's/week ❒ 1-3 x's/mo. ❒ < once/mo. ❒	Gloves ____ Respirator ____ Protective Clothes ____ Good Vent-illation ____
M) Kerosine	Yes ❒ No ❒	Daily ❒ 1-3 x's/week ❒ 1-3 x's/mo. ❒ < once/mo. ❒	Gloves ____ Respirator ____ Protective Clothes ____ Good Vent-illation ____
J) Gasoline and other fuels	Yes ❒ No ❒	Daily ❒ 1-3 x's/week ❒ 1-3 x's/mo. ❒ < once/mo. ❒	Gloves ____ Respirator ____ Protective Clothes ____ Good Vent-illation ____
K) Engine Exhaust	Yes ❒ No ❒	Daily ❒ 1-3 x's/week ❒ 1-3 x's/mo. ❒ < once/mo. ❒	Respirator ____ Good Vent-illation ____
L) Pesticides	Yes ❒ No ❒	Daily ❒ 1-3 x's/week ❒ 1-3 x's/mo. ❒ < once/mo. ❒	Gloves ____ Respirator ____ Protective Clothes ____ Good Vent-illation ____
N) Glue	Yes ❒ No ❒	Daily ❒ 1-3 x's/week ❒ 1-3 x's/mo. ❒ < once/mo. ❒	Gloves ____ Respirator ____ Protective Clothes ____ Good Vent-illation ____
O) Natural Gas	Yes ❒ No ❒	Daily ❒ 1-3 x's/week ❒ 1-3 x's/mo. ❒ < once/mo. ❒	Respirator ____ Good Vent-illation ____

(Cont'd) ----------> **IF YES, ASK:**

			"During the past? three months, was your contact usually...?"		"When in contact with _____, what % of the time did you usually wear/ use...?"
P) Other Solvents	Yes ☐	No ☐	Daily 1-3 x's/week 1-3 x's/mo. < once/mo.	☐ ☐ ☐ ☐	Gloves ____ Respirator ____ Protective Clothes ____ Good Vent-illation ____
Q) Smoke, other than tobacco smoke	Yes ☐	No ☐	Daily 1-3 x's/week 1-3 x's/mo. < once/mo.	☐ ☐ ☐ ☐	Respirator ____ Good Vent-illation ____

R) "How long (months/years) have you had direct or indirect contact with fuels at work?" _____(Yrs.) & _____ (Mos.)

IF MORE THAN ZERO MONTHS, ASK:

i) What month and year did you first have contact with fuels at work? First: ____/____ Mo. / Yr.

ii) What month and year did you last have contact with fuels at work? Last: ____/____ Mo. / Yr.

S) "How long (months/years) have you been working with fuels at this Air Force Base?" _____(Yrs.) & _____ (Mos.)

T) "How long have you been working at your current job activity?"

_____(Yrs.) & _____ (Mos.)

U) What is your current job title? _____ ID_____

V) What do you actually do? Please be specific.

_____

_____

_____

W) Which of the following categories best describes your job?

Aircraft Maintenance	☐
Fuel Handling	☐
Flightline Position	☐
Other (with fuel exposure)	☐
Other (without fuel exposure)	☐

98) Because there may be hormonal differences among racial and ethnic groups, we would like a brief history of your ancestry.

A) On your MOTHER'S side of the family, what race or races were your GREAT GRANDPARENTS? (IF GREAT GRANDPARENT WAS MULTIRACIAL, PROBE FOR % OF EACH RACE, AND RECORD IF KNOWN)

	Grandmother's Mother:	**Grandmother's Father:**	**Grandfather's Mother:**	**Grandfather's Father:**
African American	❒	❒	❒	❒
Asian or Pacific Islander	❒	❒	❒	❒
Caucasian	❒	❒	❒	❒
Hispanic	❒	❒	❒	❒
Native American	❒	❒	❒	❒
Don't Know	❒	❒	❒	❒
Refusal	❒	❒	❒	❒

2) On your FATHER'S side of the family, what race or races were your GREAT GRANDPARENTS? (IF GREAT GRANDPARENT WAS MULTIRACIAL, PROBE FOR % OF EACH RACE, AND RECORD IF KNOWN)

	Grandmother's Mother:	**Grandmother's Father:**	**Grandfather's Mother:**	**Grandfather's Father:**
African American	❒	❒	❒	❒
Asian or Pacific Islander	❒	❒	❒	❒
Caucasian	❒	❒	❒	❒
Hispanic	❒	❒	❒	❒
Native American	❒	❒	❒	❒
Don't Know	❒	❒	❒	❒
Refusal	❒	❒	❒	❒

INTERVIEWER'S SUPPLEMENT:

FOR THE ENTIRE QUESTIONNAIRE, HOW ACCURATE DO YOU FEEL THE RESPONDENTS ANSWERS WERE?

1) SEEMED COMPLETELY ACCURATE
2) SEEMED FAIRLY ACCURATE
3) DID NOT SEEM ACCURATE AT ALL

HOW COOPERATIVE WAS THE RESPONDENT?

1) VERY COOPERATIVE; RESPONSIVE
2) FAIRLY COOPERATIVE; RESPONSIVE
3) NOT COOPERATIVE AT ALL; UNINTERESTED; RETICENT

WERE THERE ANY UNUSUAL ASPECTS TO THIS RESPONDENT OR ANYTHING ELSE THAT SHOULD BE NOTED ABOUT THIS INTERVIEW?

WORK WEEK PRE-BREATH SAMPLE CHECKLIST ID ___ ___ ___

Record Time Left Work: ____ Record Date: __/__/__

1. *In the PAST 24 HOURS, that is, since this time yesterday, have you had any of the following foods?.....IF YES, RECORD:*

			# of Servings:	*Eaten at (time):*
a) Hamburger, cheeseburger, meatloaf	Yes ☐	No ☐	___ ___	_____ _____
b) Hot dogs, lunch meat	Yes ☐	No ☐	___ ___	_____ _____
c) Whole milk	Yes ☐	No ☐	___ ___	_____ _____
d) Doughnuts, cookies, cake, pastry, pies	Yes ☐	No ☐	___ ___	_____ _____
e) Other beef	Yes ☐	No ☐	___ ___	_____ _____
f) Eggs	Yes ☐	No ☐	___ ___	_____ _____
g) Cheese, cheese spreads (excluding cottage cheese)	Yes ☐	No ☐	___ ___	_____ _____
h) Margarine or butter on bread rolls or on vegetables	Yes ☐	No ☐	___ ___	_____ _____
i) Other pork	Yes ☐	No ☐	___ ___	_____ _____
j) French fries, fried potatoes	Yes ☐	No ☐	___ ___	_____ _____
k) Snacks such as chips, popcorn (exclude if low fat)	Yes ☐	No ☐	___ ___	_____ _____
l) Bacon, sausage	Yes ☐	No ☐	___ ___	_____ _____
m) Fried chicken	Yes ☐	No ☐	___ ___	_____ _____

2. *In the PAST WEEK, that is, one week ago today, did you...*

a)...use the self-service tank when refueling of your vehicle or lawn mower this week (outside of work)? Yes ☐ No ☐ *If yes, which date(s):* __/__/__ ; __/__/__ ; __/__/__

b)...mow the lawn? Yes ☐ No ☐ *If yes, which date(s):* __/__/__ ; __/__/__ ; __/__/__

c)...breathe smoke from stoves, fireplaces or grills? Yes ☐ No ☐
If yes, which date(s): __/__/__ ; __/__/__ ; __/__/__

d)...eat any grilled/smoked/charred foods? Yes ☐ No ☐
If yes, which date(s): __/__/__ ; __/__/__ ; __/__/__

e)...use pesticides/insecticides, paints/solvents – this includes fingernail polish and polish remover? Yes ☐ No ☐ *If yes, which date(s):* __/__/__ ; __/__/__ ; __/__/__

PLEASE REMOVE SHOES, HAT, JACKETS: *HT:* ____ ' ____ " *WT:* _____

Appendix III (NIOSH Endpoint Algorithm):

Menstrual Period Algorithm

adapted from Paige Hornsby personal communication

Participants recorded daily if there was bleeding (yes/no), bleeding amount (0-4), and number of tampons or napkins used.
Bleeding Amounts: 0 = none; 1 = spotting; 2 = light; 3 = medium; 4 = heavy.
Non-Bleeding = 0; **Bleeding** = 1-4; **Spotting** is a category of bleeding.

Onset of Menses: 3 consecutive days of Non-Bleeding or Spotting, followed by at least 2 consecutive days of Bleeding, only one of which is Spotting. After the Onset, 1-2 day intervals of Non-Bleeding or Spotting are part of Menses.

Self-reported menses was accepted up to 14 days retrospectively.

End of Menses: The last day of Menses is followed by at least 3 consecutive days of Non-Bleeding or Spotting. This is beyond the last 2 days of Menses, which can be Spotting. Spotting outside of this sequence is not Menses.

Missing Data:
If more than 7 consecutive days of missing data extend beyond 21 days after a previous Onset of Menses, interrupt the data, do not calculate cycle length, and calculate the cycle information before and after the interruption separately.

If more than 7 consecutive days of missing data do not extend beyond 21 days after a previous Onset of Menses, consider the missing data as Non-Bleeding days.

If less than 7 consecutive days: Use the definition above for Menses.

If not clear and ...

if missing days are bounded on both sides by Bleeding...

and if Onset and End of Menses can be determined, missing days are part of Menses;

and if only Onset of Menses can be determined, calculate cycle length, but not bleeding duration;

but if Onset of Menses can not be determined, interrupt the data (cycle length, bleeding duration of bleeding, etc. are missing).

if missing days are not bounded on both sides by Bleeding, then examine and define individually. If 1 missing day is separated from an apparent Menses by 1-2 Non-Bleeding day(s), the Onset or End of Menses can be interpreted as the first or last day of recorded bleeding.

Inconsistencies:
Bleeding variable priority: Bleeding Amt > Bleeding (Y/N) > Tampon #; data has priority to missing data.
Example 1: If Bleeding = 0, Bleeding Amt = 1, and Tampon # = 0, then change Bleeding = 1 and Tampon # = 0.
Example 2: If Bleeding = 1, Bleeding Amt = missing, and Tampon # = 0, then bleeding occurred, Amt is missing and Tampon # = 0.

Endocrine Endpoint Algorithms

A. Cycle Length Endpoints

1. **Cycle length.** Must have start and end menses.
2. **Follicular phase length** = day of LH surge onset or DLT (day of luteal transition). Equals luteal day 0. Must have start menses.
3. **Luteal phase length** = last day of cycle minus day after LH surge onset or after DLT. Must have end menses.
4. **Luteal phase length : Cycle length.** A3/A1. Must have start and end menses.

B. Urinary LH Endpoints

LH surge peak = highest value of the cycle that exceeds 8.5 mIU LH/mg CR. Omit if there is missing data on day adjacent to highest value. Omit if highest value is not ≤4 days after a rise >2.5-fold above the mean of the previous 7 days w/ no more than 3 missing days. Omit cycles w/o start menstrual period that do not have ≥17 days of sampling. Omit cycles w/o end menstrual period that do not have ≥20 days of sampling. Omit cycles w/ <35 days and no menstrual period.

LH surge onset = first rise >2.5-fold above the mean of the previous 7 days and ≤4 days before the peak. Omit [do not search further] if values missing on >3 of 7 preceding days or on day before onset. Omit cycles w/o start menstrual period that do not have ≥17 days of sampling. Omit cycles w/o end menstrual period that do not have ≥20 days of sampling. Omit cycles w/ <35 days and no menstrual period.

1. **Level of LH surge peak** = LH level on day of surge peak or on DLT.
2. **Day of LH surge peak.** May calculate, but not report w/o start menses.
3. **Day of LH surge onset** = follicular phase length. May calculate, but not report w/o start menses.
4. **Follicular LH level** = mean for cycle day 3 thru 4th day before LH surge onset or before DLT, or cycle days 6 thru 10 for cycles w/ ≥20 days of sampling. Omit if >2 missing days. Must have start menses.
5. **Duration of LH surge** = number of consecutive days from the LH surge onset, through the LH surge peak and last day LH is >8.5 mIU/mg CR. Omit if >1 missing value. Count the missing value day.
6. **Area under the LH surge** = AUC for duration of LH surge (B5) minus LH baseline (B4). Extrapolate 1 missing value; omit if >1 missing value.
7. **Preovulatory LH level** = geometric mean for the 3 days ending on DLT or day of LH surge onset. Omit if any days are missing.

C. Urinary $E_1$3G/Creatinine (ng/mg) Endpoints

1. **Early-luteal $E_1$3G level** = mean for days 1 thru 4 after $E_1$3G peak. Omit if >1 missing value.
2. **Mid-luteal $E_1$3G level** (before implantation) = geometric mean for days 5 & 6 after DLT or after day of LH surge onset. Omit if any missing values.
3. **Late-luteal $E_1$3G level** = mean of last 6 days of cycle. Omit if >1 missing value. Must have end menses.
4. **3-day periovulatory $E_1$3G peak level** = max 3-day mean. The peak day is ≤3 days from LH surge onset or DLT; if none, select highest cycle $E_1$3G value. Omit if values are missing on days adjacent to endpoint. Cycles w/o start menstrual period must have ≥17 days of samples. Cycles w/o end menstrual period must have ≥20 days of samples. Omit cycles w/ <35 days and no menstrual period. Cycles with both menstrual periods must have samples on ≥90% of either the first 22 cycle days or of the last 20 cycle days. Accept cycles shorter than 20 days.
5. **Preovulatory $E_1$3G rise** = slope for 3 days prior to day of $E_1$3G peak. Omit if any missing value.

6. **Mid-follicular $E_1$3G level** = mean from cycle day 5 thru day -2 from $E_1$3G peak. Omit if >1 missing value. Must have start menses.
7. **Onset of follicular $E_1$3G rise** = CUSUM (#1; Schiphorst et al, Fertil Steril 44:328, 1985), where K = mean & SD for days 3-8; H = 2 SD; Sum = max(0, S + [$E_1$3G] - K); Day = endpoint if S>H. Start counting on day 3 of cycle. Omit if values are missing on >2 of 6 preceding days or on day before endpoint. Omit cycles w/ <35 days and no menstrual period. Cycles w/o start menstrual period must have ≥27 days of sampling (may calculate, but not report w/o start menses). Cycles w/o end menstrual period must have ≥20 days of sampling.
8. **Days from $E_1$3G rise onset → LH surge onset** = B3 minus C7.
9. **Early-follicular $E_1$3G level** = mean from cycle days 3 thru 6. Omit if >1 missing value. Must have start menses.
10. **Day of $E_1$3G peak.** May calculate, but not report w/o start menses.

D. Urinary Pd3G/Creatinine (µg/mg) Endpoints

1. **Anovulatory cycles**. Modification of Lasley's rule: Lowest baseline w/ ≤1 missing value. Must have ≥5 samples within 10 days of end menses.
   Base1 (cycle method) = mean for cycle days 6 thru 10. Need start & end menses.
   Base2 (interval method) = low 5-day mean (collection days +3 → -3). Need end menses or 35 days of sampling.
   Base3 = cycle method for next cycle. Need end menses.
   Base4 = interval method for days 1-14 of next cycle. Need end menses.
   If $Pd3G_i$/Base >2 for ≥3 straight days, cycle is ovulatory=1; If not, cycle is anovulatory=0.
   If Base1 is not calculable (missing days or start menses), pick lowest of Base2-4.
2. **Lasley Baseline** = If no Base1, pick lowest of Base2-4.
3. **Pd3G Rise** = first rise >3.5 SD above mean of previous 7 days, with next day above same limit. Start counting on day 5. Omit if values are missing on >2 of 7 preceding days or on day before endpoint. Omit cycles w/ <35 days and no menstrual period. Cycles w/o start menstrual period must have ≥24 days of sampling; may calculate, but not report w/o start menses. Cycles w/o end menstrual period must have ≥20 days of sampling.
4. **Follicular Pd3G level** = geometric mean from cycle day 5 thru 3rd day before DLT or day of LH surge onset, or days 6-10. Omit if < 2 values present. Must have start menses.
5. **Mid-luteal Pd3G level** (before implantation) = geometric mean for days 5 & 6 after DLT or day of LH surge onset. Omit if any missing values.
6. **Area under the Pd3G curve, absolute** = AUC for day after LH surge onset or after DLT thru end of cycle. Extrapolate missing values; omit if >3 missing values or consecutive missing values. Must have end menses.
7. **Area under the Pd3G curve, absolute** = AUC for day after LH surge onset or after DLT thru end of cycle, or last 14 days of anovulatory cycles. Extrapolate missing values; omit if >3 missing value or consecutive missing values. Must have end menses.
8. **Area under the Pd3G curve, minus baseline** = AUC for day after LH surge onset or after DLT thru end of cycle, minus Lasley baseline. Extrapolate missing values; omit if >3 missing values or consecutive missing values. Must have end menses.
9. **Area under the Pd3G curve, minus baseline** = AUC for day after LH surge onset or after DLT thru end of cycle, or last 14 days of anovulatory cycles, minus Lasley baseline. Extrapolate missing values; omit if >3 missing values or consecutive missing values. Must have end menses.
10. **Periovulatory Pd3G rise** = slope for days 0 thru 2 after LH surge onset or after DLT. Omit if any missing values.
11. **Day of the Pd3G peak** = Highest value of cycle. Omit if missing values on days adjacent to endpoint or on consecutive days 1 day from endpoint. Cycles w/o start menstrual period must have ≥8 sample days; endpoint can not be 1st day of sampling. Cycles w/o end menstrual period must have ≥28 sample days. May calculate, but not report w/o start menses. Omit cycles w/ <35 days and no menstrual period.
12. **Early-mid luteal Pd3G rise** = slope for 3rd day after LH surge onset or after DLT thru Pd3G

peak. Omit if missing values on >2 days or on consecutive days.

13. **Mid-late luteal Pd3G drop** = slope for day of Pd3G peak thru end of cycle. Omit if missing values on >2 days or on consecutive days. Must have end menses.
14. **3-day Pd3G peak level, absolute** = max 3-day mean w/ peak. Omit if any missing values.
15. **3-day Pd3G peak level, minus baseline** = max 3-day mean w/ peak minus Lasley baseline. Omit if any missing values.
16. **Days from LH surge onset or DLT → Pd3G rise onset** = D3 minus B2 or E1.
17. **Days from Pd3G peak → end of cycle** = A1 minus D9. Must have end menses to calculate.
18. **Early follicular Pd3G** = mean of cycle days 3 thru 6. Omit if >1 missing value. Must have start menses.

E. Urinary $E_1$3G:Pd3G Day of Luteal Transition Endpoints (DLT). Calculate DLT (Baird et al., Stat Med 10: 255-266, 1991), impute DLT (Baird et al., Epidemiol 6:547-550, 1995) then calculate other endpoints.

Ratios: E1. NIEHS = $E_1$3G/Pd3G
E2. California = $E_1$3G/(Pd3G+1)
E3. NIOSH = ($E_1$3G/CR)/[(Pd3G/CR)+1] ≡ E/(P+Cr)

1. **DLT** = May calculate, but not report w/o start menses.
2. **Initial drop in $E_1$3G:Pd3G** = 3-day slope (day -1, DLT, day 1)
3. **Drop in $E_1$3G:Pd3G beginning on the DLT** = 3-day slope (DLT, day 1, day 2)
4. **Mid-luteal $E_1$3G:Pd3G** (before implantation) = days 5 & 6 after LH surge onset or after DLT
5. **$E_1$3G:Pd3G "peak" level** = value on day before DLT
6. **$E_1$3G:Pd3G level on DLT**

F. Urinary FSH Endpoints

1. **Early follicular FSH level** = mean from cycle days 1 thru 3. Omit if >1 missing value. Must have start menses.
2. **Follicular FSH drop** = slope for cycle day 4 thru day before LH surge onset or before DLT, or days 4-12. Omit if >2 missing value. Must have start menses.
3. **FSH rise before menses** = slope for last 4 days of cycle. Omit if values for 1st, 4th, or (2nd & 3rd) day is missing. Must have end menses.
4. **Mid-luteal FSH level** = mean for days -7 thru -4 from end of cycle. Omit if >1 missing value. Must have end menses.
5. **FSH surge peak level** = surge is highest value >5 days after menses onset (if only end menses, start counting on first day of sampling) and not on last day of cycle. Omit if missing values on days adjacent to endpoint. Omit cycles w/o start menstrual period that do not have ≥17 days of sampling. Omit cycles w/o end menstrual period that do not have ≥20 days of sampling. Omit cycles w/ <35 days and no menstrual period. Cycles with both menstrual periods must have samples on ≥90% of either the first 22 cycle days or of the last 20 cycle days. Accept cycles shorter than 20 days.
6. **Day of FSH surge peak.** May calculate, but not report w/o start menses.
7. **Follicular LH:FSH Ratio** = ratio of means for cycle day 4 thru the 4th day before the LH surge onset or before DLT, or cycle days 4 thru 10. Omit if >2 missing value. Must have start menses to calculate.

Appendix IV (Statement of Work):

1.G. REVISED STATEMENT OF WORK:

Note: Few SOW refinements in italics below. The major change is that we are doing/have done aspects of pilot testing at several sites, i.e., Hill AFB(during a separate study), Wright Patterson Air Force Base and the University of Cincinnati in order to permit us to go to two bases in the first year while staying within our revised budget.

Year 01

1. Develop questionnaires for collecting menstrual and occupational histories (months 1-4).
2. Adapt portable breath analysis system (months 1-6).
3. Develop protocols for breath analysis, industrial hygiene sampling, biological sampling (months 3-9).
4. Pilot test questionnaires on a representative sample of women (months 4-6).
5. Train personnel in use of breath analysis equipment, in teaching participants how to collect urine and saliva samples (months 4-5).
6. Recruit four military bases for participants in study (months 5-9).
7. Characterize the female populations within each selected base that are exposed to jet fuel and that are not exposed [comparison group]; determine the expected number of study participants (months 5-9).
8. Determine the optimal logistical approaches for distributing, monitoring, and collecting samples and supportive material (months 5-9).
9. Perform pilot study air sampling analysis at *Hill AFB* (months 6-*8*).
10. Conduct pilot study breath analysis sampling at *Hill AFB* (months 6-8).
11. Pilot test administration of occupational and menstrual history questionnaires and menstrual diaries at *WPAFB* (months 6-*7*).
12. Pilot test collection of collect daily urine and saliva samples at *from University of Cincinnati pilot test volunteers*: (months 6-*7*).
13. Collection of daily urine and saliva pilot test samples at the *University of Cincinnati pilot test volunteers* (months *7*-9).
14. Perform formal study air sampling at Base 1 (months 9-*11*).
15. Conduct breath analysis sampling at Base 1 (months 9-*11*).
16. Administer occupational and menstrual history questionnaires. Implement menstrual diaries at Base 1 (months 9-12).
17. Collect daily urine and saliva samples at Base 1 on approximately 50 women (months 9-*11*).
18. Ship samples to NIOSH; perform laboratory analysis of IH and biological samples collected at Base 1; inventory and organize urine samples; *store/*conduct urinary LH & FSH fluoroimmunoassays; *store/*conduct urinary $E_1$3G and Pd3G fluoroimmunoassays; *store/*conduct creatinine assays (months *10-13*).
19. Prepare year 01 summary report (months 10-12).
20. Perform items 15-19 at Base 2 on approximately 50 women (months *11-14*).

Year 2

1. Ship samples to NIOSH; perform laboratory analysis of IH and biological samples collected at Base 2; inventory and organize urine samples; *store/*conduct urinary LH & FSH fluoroimmunoassays; *store/*conduct urinary $E_1$3G and Pd3G fluoroimmunoassays; *store/*conduct creatinine assays (months *13-16*).
2. Perform items 15-19 at Base 3 on approximately *50* women (months 15-18).
3. Ship samples to NIOSH; perform laboratory analysis of IH and biological samples collected at Base 3; inventory and organize urine samples; conduct urinary LH & FSH fluoroimmunoassays; conduct urinary $E_1$3G and Pd3G fluoroimmunoassays; conduct creatinine assays (months *16*-19).
4. Abstract military personnel and occupational history data for validity subanalysis (month 16).
5. Conduct validity subanalysis: questionnaire *vs.* military records and prepare valididty subanalysis report (months 18-21).
6. Perform items 15-19 at Base 4 on approximately *50* women (months 21-24).
7. Prepare year 02 summary report (months 22-24).
8. Ship samples to NIOSH; perform laboratory analysis of IH and biological samples collected at Base 4; inventory and organize urine samples; conduct urinary LH & FSH fluoroimmunoassays; conduct urinary $E_1$3G and Pd3G fluoroimmunoassays; conduct creatinine assays (months 23-25).

Year 3

1. Data management: Standardize and computerize data collected from air sampling, biological sampling and breath analysis at four military bases; reduce data onto spreadsheets importable for statistical and graphic analyses; generate graphic depictions of data; conduct preliminary statistical analyses, preparatory to subsequent, complex analyses (months 25-36).
2. Prepare preliminary report (months 34-36).

Year 04

1. Conduct final statistical analysis for menstrual, hormonal and jet fuel data (months 37-39).
2. Distribute preliminary report for review and comments (months 39-41).
3. Begin preparation of papers for publication and scientific presentation (months 39-43).
4. Send results to bases and participating subjects (months 42-44).
5. Present study to bases as requested (months 42-48).
6. Prepare and distribute final report (months 45-48).

Appendix V (IRB Approval Form):

UNIVERSITY OF CINCINNATI MEDICAL CENTER
INSTITUTIONAL REVIEW BOARD
NOTIFICATION FORM

PRINCIPAL INVESTIGATOR: Grace K. Lemasters, Ph.D.

CO-INVESTIGATOR(S):

TITLE: #95-10-27-2--"Female Reproductive Effects of Exposure to Jet Fuel at U.S. Air Force Bases"

xxx APPROVED - INCLUDES INFORMED CONSENT*
DISAPPROVED

DATE: January 10, 1996

1. If the study involves a drug, you must complete the Pharmacy Committee Drug Information Sheet (available at the In-Patient Pharmacy, University Hospital).

2. You are required to immediately report any adverse reactions or complications of the project to the Institutional Review Board.

3. An annual progress report form must be filed with the Institutional Review Board. If the progress report is not returned by the specified date, your department head will be notified.

4. There may be no change or addition to the project, or changes of the investitgators involved, without prior approval of the IRB.

5. If this protocol has not been initiated within two years of this date, you will be required to resubmit the study for reconsideration by the Institutional Review Board.

6. Notification of approval by the Institutional Review Board does not necessarily indicate approval by other committees of the Medical Center with the exception of Radiation Safety.

7. You are required to modify this study, subject to IRB approval, if subsequent information regarding any drug, device or procedure utilized in the study is received from the manufacturer or any other reliable source, that could reasonably increase or alter potential harm to subjects. The informed consent statement must be modified to include this new information or an addendum must be prepared as a means to assure subject notification. In cases where the subject has completed the study, the modification or addendum is only necessary if the additional information received could impact the subjects in the future.

Harry Rudney
Chairperson, Institutional Review Board

DHHS Assurance No. M1138
Identification No. 01

*The attached consent has been approved by the IRB. Please copy this ICS document and use for all subjects entered into the study.

DEPARTMENT OF THE ARMY
US ARMY MEDICAL RESEARCH AND MATERIEL COMMAND
504 SCOTT STREET
FORT DETRICK, MARYLAND 21702-5012

REPLY TO
ATTENTION OF:

MCMR-RMI-S (70-1y) 1 Apr 03

MEMORANDUM FOR Administrator, Defense Technical Information Center (DTIC-OCA), 8725 John J. Kingman Road, Fort Belvoir, VA 22060-6218

SUBJECT: Request Change in Distribution Statement

1. The U.S. Army Medical Research and Materiel Command has reexamined the need for the limitation assigned to technical reports written for this Command. Request the limited distribution statement for the enclosed accession document numbers be changed to "Approved for public release; distribution unlimited." Copies of these reports should be released to the National Technical Information Service.

2. Point of contact for this request is Ms. Judy Pawlus at DSN 343-7322 or by e-mail at judy.pawlus@det.amedd.army.mil.

FOR THE COMMANDER:

Encl

PHYLLIS M. RINEHART
Deputy Chief of Staff for
Information Management

ADB277986
ADB263450
ADB267669
ADB277564
ADB261754
ADB257280
ADB283722
ADB249627
ADB282841
ADB266235
ADB283529
ADB283519
ADB256683
ADB262564
ADB271045
ADB283537
ADB257204
ADB283513
ADB281571
ADB262777
ADB270818
ADB283748
ADB274588
ADB283788
ADB259015
ADB266031