U.S. DEPARTMENT OF HEALTH, EDCUATION, AND WELFARE
CENTER FOR DISEASE CONTROL
NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH
CINCINNATI, OHIO 45226

HEALTH HAZARD EVALUATION DETERMINATION

REPORT NO. HE 77-75-494

DAWES LABORATORIES
CHICAGO HEIGHTS, ILLINOIS

JUNE 1978

I. TOXICITY DETERMINATION

Based on the results of biological testing, medical histories, and physical examinations, a health hazard did exist at Dawes Laboratories, Chicago Heights, Illinois, in May 1977, from worker exposure to diethylstilbestrol (DES).

A complete discussion of the results of the testing conducted at Dawes as well as recommendations for medical surveillance are included in the body of this report.

II. DISTRIBUTION AND AVAILABILITY

Copies of this determination report are currently available upon request from NIOSH, Division of Technical Services, Information Resources and Dissemination Section; 4676 Columbia Parkway, Cincinnati, Ohio 45226. After 90 days this report will be available through the National Technical Information Service (NTIS); Springfield, Virginia. Information regarding its availability through NTIS can be obtained from the NIOSH Publications Office at the Cincinnati address.

Copies of this report have been sent to:

A. Dawes Laboratories, Chicago Heights, Illinois
B. Authorized representative of Local No. 7-765 of the Oil, Chemical, and Atomic Workers Union
C. U.S. Department of Labor, Region V
D. NIOSH, Region V
E. International Office, Oil, Chemical, and Atomic Workers Union

For the purpose of informing approximately 50 affected employees, the employer shall promptly post for a period of 30 calendar days the determination report in a prominent place(s) near where the exposed employees work.

III. INTRODUCTION

Section 20(a)(6) of the Occupational Safety and Health Act of 1970 29 U.S.C. 669(a)(6), authorizes the Secretary of Helath, Education and Welfare following a written request by an employer or authorized representative of employees, to determine whether any substance normally found in the place of employment has potentially toxic effects in such concentrations as used or found.

The National Institute for Occupational Safety and Health received such a request from the Oil, Chemical, and Atomic Workers Union Local 7-765 as well as the International Office of the Oil, Chemical, and Atomic Workers Union to investigate the problems that were allegedly occurring at the Dawes Laboratories. In this request, workers in the area where DES was being manufactured, processed, and packaged were having a variety of symptoms and signs, including breast enlargement, breast tenderness, and changes in sexual libido especially in the male workers employed in the DES areas.

Since an OSHA inspection, including environmental measurements, had been conducted 30 days prior to the HHE request, NIOSH was requested to perform only a medical evaluation of the exposed workers.

IV. HEALTH HAZARD EVALUATION

A. Description of Process - Conditions of Use

Dawes Laboratories is a formulator of a variety of biologically active chemical agents. The laboratory is located in Chicago Heights, Illinois. According to the request, approximately 15 to 25 individuals were directly or indirectly exposed to the DES production, processing, and packaging operations at Dawes Laboratories.

DES is manufactured in Dawes Laboratory at the Chemical Process Department. The chemical process is initiated by the formation of propionyl chloride from propionic acid and aluminum trichloride. Propionyl chloride then is reacted with the phenol P-hydroxy propiophenone. The propiophenone undergoes further processing until the final synthesis of DES is obtained. The final stages include filtration, atmospheric drying, and high temperature drying. The dry DES crystals are then packed in 37.5 kg cardboard boxes or dissolved in polyethylene glycol to be used in the blending and packing department.

Based on a previous OSHA environmental survey and a discussion with several members of the local union, a rank order estimate of potential exposure to DES was made by job category. The following job titles were ranked with respect to potential DES exposure on a scale of 1 to 10. One was the lowest potential exposure, ten the highest potential exposure in this ranking profile. The following is a list of the job titles and their relative ranking with respect to potential diethylstilbestrol exposure:

Laboratory Technician - 2
Pellatizer - 2
Utility Man - 2
Chemical Operator - 2
Shipping Clerk - 3
Janitor - 4
Mainline Operator Blending Building - 6
Panel Operator - 8
Production Supervisor - 8
Maintenance Man - DES - 8
Production Helper - 8
DES Operator - 10

B. Background Medical Information

Workers in the Chemical Department in the Blending and Packaging Department reported 5 cases of gynecomastia (breast enlargement) several years prior to this survey. These individuals were evaluated at the National Institutes of Health in the early 70's and underwent treatment with a variety of formulations of injectible testosterone. In March of 1977 a number of complaints of gynecomastia were reported in the Dawes facilities. Many cases of gynecomastia as well as breast tenderness and reports of impotence were reported. Because of the high incidence of abnormalities in workers in this area of the plant, a health hazard evaluation request was submitted.

NIOSH physicians toured the area in question and conducted an indepth investigation involving the workers in this part of the plant.

C. Medical Criteria Toxic Substances Data

DES is a synthetic estrogen with a variety of therapeutic as well as other biological applications. It has been used in humans as a replacement estrogen, and in pregnancy it was thought to prevent spontaneous abortion. It has been used in animals because of its anabolic activity which enables the animal treated with DES to gain weight at a much faster rate with less food consumption than a non DES treated control animal.

In recent years it was discovered that pregnant females who consumed this drug in the early stages of their pregnancy to prevent early spontaneous abortion, experienced a number of abnormalities in their offspring. The female children of these DES treated women have a much higher than normal incidence of a clear cell carcinoma of the vagina, and male offspring have been found to have a high incidence of a variety of congenital abnormalities of the genito-urinary tract, including reduced fertility.

When ingested, especially in the male, DES produces a number of effects primarily related to the estrogenic activity of this chemical. In males, gyneocomastia, breast tenderness, lactation, increased pigmentation of the areola as well as diminished libido and sexual performance capabilities have been reported. In females exposed to DES, abnormalities occur including enlargement of the breasts, lactation, breakthrough bleeding, and marked irregularity in menstrual periods have been reported.

DES has been categorized by NIOSH as a suspected carcinogen and therefore exposure to this particular compound is to be kept at as low a level as is technologically possible.

D. Medical Examination Protocol

Because of the known estrogenic effects of DES a protocol was developed to determine the physical, historical, and biological abnormalities created by exposure to this material. Each worker involved in the manufacture, processing, and packaging of DES as well as those who might likely have exposure were tested.

Each worker was evaluated using the following testing procedures:

1. Complete occupational and pertinent medical history
2. Physical examination with emphasis on the genito-urinary tract, breasts, and secondary sex characteristics
3. Detailed biological evaluation including,
    a. serum prolactin
    b. serum luteinizing hormone (LH)
    c. serum progesterone
    d. serum 17 hydroxy progesterone
    e. serum estrone (E_1)
    f. serum estradiol (E_2)
    g. serum follicle stimulating hormone (FSH)
    h. serum serum testosterone
    i. serum free androgen index
    j. serum percent testosterone bound
    k. serum total androgens

In addition to the blood tests that were performed, a 24-hour urine was collected for testosterone level and both blood and urine specimens were submitted on selected workers for DES levels. These measurements were made using a special radioimmunoassay technique.

All biological analyses were performed at the Metabolism laboratory at the University of Cincinnati College of Medicine, except the blood and urine specimens that were analyzed for diethylstilbestrol. These were performed at Emory University using a radioimmunoassay technique. A description of the technique and procedural format is included in Appendix A at the end of this report.

V. RESULTS AND DISCUSSION

A. Results

A total of 25 workers were examined in this survey. Two of the workers could not be included in the final statistical evaluation of the data becuase of confounding medical abnormalities. As was discussed in an earlier section of the report, the workers were divided into 2 categories -- a low exposure group and a high exposure group. The categorization of a worker into the low or high exposure groups was done using the results of an OSHA environmental survey conducted one month prior to the NIOSH study, and a rank ordering of exposures by job title provided by 4 individual members of the local union. Any worker who received a rating of five or less was considered in the low exposure group, and those who were six or greater were considered high exposure.

The low exposure group consisted of 12 individuals. Their mean age was 30 years with a range of 20 to 59 years, and their mean length of employment at Dawes Laboratories was 43 months. The high exposure group consisted of 11 individuals with a mean age of 36 years, a range of 22 to 58 years and a mean length of employment at Dawes Laboratories of 122 months.

Table I shows the results of the biological testing done on the workers at Dawes Laboratories. Each individual test with the normal for the reference laboratory and each individual workers' results are included on this table. Each worker's exposure category is designated by either LE-low exposure or HE-high exposure. Individuals who did not supply a urine specimen are indicated by the absence of a number in that particular column.

Table II shows the mean values of the tests performed on this group of workers. The statistical significance of these values is represented in the third column with p-values so noted.

Table III and Table IV represent the results from the assays of blood and urine for DES performed at Emory University.

Tables V and VI show the results of the workers' responses to the questionnaire as well as the differences in the groups with respect to the findings on physical examination.

B. Discussion

This investigation included the measurement of a wide variety of hormones and gonadotropins. In addition, urinary testosterone, excretion, and concentrations of DES in blood and urine were measured.

Table II shows that of the many tests done and the comparisons of the results of these tests in the high and low exposure groups only two values showed results that were statistically significant at the $p < .05$ value. These were the total androdens and the free androgen index. Although some of the other tests approached statistical significance, none of the additional tests were less than $p = .05$.

The measurement of diethylstilbestrol by radioimmunoassay in the blood and urine showed no statistically significant differences between the high exposure and low exposure groups.

The results of the response of workers to the questionnaire and the results of the physical examinations of all workers showed no statistically significant differences present between the low exposure and high exposure. However, breast tenderness approached statistical significance and was reported more frequently in the group classified as high exposure. Gynecomastia, a classic physical finding in estrogen absorption, was present to a greater degree in the high exposure group than in the low exposure, but, again no statistically significant difference was observed. However, the degree of gynecomastia was minimal in the low exposure group. All of those workers were felt to have only sub-areolar thickening. The high exposure group showed more evidence of not only sub-areolar thickening but of actual breast tissue enlargement away from the areolar areas.

There is very little evidence in the scientific literature as to the effect of long term estrogen overexposure and absorption on hormone values in males. A number of aspects of this study are complicated and a wide variety of variables were present. It has been shown that the levels of luteinizing hormone and follicle stimulating hormone as well as testosterone can vary substantially over a 24-hour period. Because of this, there is a possibility that the true hormonal parameters were different than those measured in this study.

The designation of workers into the high and low exposure categories were done on an arbitrary basis. The categorization was accomplished by using previously selected OSHA data as well as a subjective rank ordering of job categories with respect to potential DES exposure provided by several local union members independently of one another.

Despite the fact that the laboratory tests were analyzed by a competent laboratory, the possibility of laboratory error still exists. Although this is not likely, it is still a possibility. These and many other less significant complicating factors were present in this particular study. Given all of the potential problems involved, the study is as good as could be done given the confounding variables.

Many researchers have looked at the effects of estrogens on gonadatropins and testosterone levels in males during estrogen therapy for patients with carcinoma of the prostate. In one study[2] it was found that a combined therapy of orchidectomy with subsequent administration of estrogen hormones caused a rapid fall in the plasma levels of FSH, LH, and testosterone, whereas in the early stage the pituitary continued to respond to luteinizing hormone-releasing hormone loading. These researchers found that after more than 6 months of estrogen therapy the plasma level of testosterone began to rise toward normal. In another series of patients[3] DES and premarin were used alone without orchidectomy. In this study DES produced a significant increase in plasma concentration of growth hormone in prolactin and a decrease in plasma concentration of testosterone luteinizing hormone, and follicle stimulating hormone.

In a more recent study[4] alterations in the metabolism of testosterone and dihydrotestosterone induced by DES were studied. With both of the dosage regimens of DES, production rates, plasma concentrations, and metabolic clearance rates of both testosterone and dihydrotestosterone declined. Testosterone was suppressed to a much greater extent than dihydrotesterone. This was attributed to a direct suppression of testicular androgen synthesis and possibly by decreased gonadatropin stimulation caused by the estrogen.

An in-vitro study[5] showed that testosterone synthesis may be effected within as little as 24 hours following exposure to DES, but usually takes in the range of 4 to 8 days to manifest its effects. These investigators showed that longer term exposure to low level exposures of DES demonstrated a return to normal of hormonal parameters.

It is apparent from these studies done mostly in men with prostatic carcinoma and in experimental animals that exposure to DES does indeed produce changes in serum testosterone and gonadatropin levels. However, these exposures are to relatively high concentrations of orally administered DES over relatively short periods of time. While there may be a similar change in serum testosterone, FSH, and LH in workers occupationally exposed to DES, it is apparent from this investigation that persistent abnormalities in testosterone and gonadatropins are not likely to occur. What is apparent from this study is that there are statistically significant differences in the total androgen measurements in these workers and in the free androgen index. While this may represent some artifact, it is more likely that it represents a change in the metabolism of the total androgen picture in the male exposed to DES. Further investigations are obviously needed to substantiate the use of total serum androgens and free androgen index as an indicator of DES toxicity.

VI. CONCLUSIONS

Based on the measurement of DES in blood and urine and history and physical examination results, a health hazard existed at the time of this study from worker overexposure to DES. The physical presence of gynecomastia in virtually all of the high exposure group and even in several of the low exposure group, indicates that enough DES was absorbed to create these feminization effects. The fact that any DES was measured in blood and urine indicates that increased absorption of DES and presumably overexposure of workers to DES existed at the time of this study.

VII. RECOMMENDATIONS

1. That Dawes Labortory in conjunction with the local Oil, Chemical, and Atomic Workers Union contract with a physician experienced in internal-occupational medicine and or endocrinology to provide medical surveillance to the workers at Dawes Laboratories

2. That this individual physician or group of physicians use the information contained in this report to further study workers exposed to DES and determine whether or not the total serum androgen and free androgen index is a reliable way to follow workers exposed to DES.

3. Careful records be maintained of those individuals who are exposed to DES so that morbidity and mortality studies will be more easily performed in the future. This is because of the fact that DES has been shown to be a human carcinogen and its effects after long-term low exposure have not been fully delineated.

4. An industrial hygiene consultant be retained to recommend engineering changes and personal protective equipment so that exposures to DES may be reduced to the lowest possible limit.

5. Workers be educated as to the potential harmful effects of DES and be educated as to proper work practices in dealing with this material.

6. No worker should be treated with testosterone or any other hormone for any sign or symptom unless by an expert in the field of internal-occupational medicine and/or endocrinology.

VIII. REFERENCES

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IX. AUTHORSHIP AND ACKNOLWEDGEMENT

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TABLE I

DAWES LABORATORIES
HHE 77-75

MAY 16 & 17, 1977

INDIVIDUAL WORKERS' RESULTS

Worker Number	Prolactin 7-12 ng/ml	FSH 7-27 uU/ml	LH 2-32 uU/ml	Testosterone ng/ml	Percent Bound % 32-69	Total Androgens ug% .53-1.35	Free Androgen Index ug% .27-.65	Progesterone 50-180 pg/ml	17 OH PRO Gesterone 400-2500 pg/ml	Estrone E_1 10-79 pg/ml	Estradiol E_2 10-63 pg/ml	Urinary Testos Terone 37-165 ug/24 hrs
LE 1	7.7	6.2	8.8	6.62	23	0.64	.492	110	1353	51	33	129.6
HE 2	8.6	4.8	6.3	7.04	18	0.50	.410	235	1845	86	45	80.0
LE 3	12.9	6.9	12.5	9.16	24	0.71	.539	395	2142	48	31	144.9
LE 4	9.1	5.7	5.9	5.09	17	0.32	.265	150	835	75	39	54.9
HE 5	7.7	4.8	10.5	2.82	37	0.54	.340	201	666	50	16	-----
LE 6	16.6	2.4	11.5	6.32	37	0.81	.510	220	763	50	15	78.9
HE 7	18.6	6.5	9.3	8.88	35	0.62	.403	95	1181	87	38	75.3
HE 8	21.7	10.5	24.0	10.89	22	0.77	.600	119	1494	104	80	92.7
HE 9	6.2	3.6	10.5	4.38	15	0.38	.323	115	1078	31	29	52.5
HE 10	6.1	5.3	7.8	6.10	21	0.64	.505	144	1354	67	41	59.1
LE 11	14.4	8.6	9.0	12.04	31	1.18	.814	293	2105	62	67	48.7
HE 12	6.1	7.6	6.5	7.14	31	0.74	.510	223	832	57	28	152.3
HE 13	3.4	8.1	12.0	10.10	25	0.67	.502	153	2500	75	71	74.1
HE 14	11.2	<2.0	3.6	1.54	58	0.30	.132	203	730	55	26	8.7
HE 15	12.7	6.9	14.5	6.92	17	0.38	.315	91	1817	67	64	14.2
HE 16	16.8	12.0	14.5	6.61	19	0.49	.396	97	1198	31	30	42.0
LE 17	10.3	2.8	9.9	3.17	27	0.32	.233	62	883	79	36	354.0
LE 18	21.5	16.0	14.0	7.99	36	1.10	.704	165	683	54	16	-----
LE 19	29.2	7.5	12.5	8.16	29	1.10	.781	139	707	59	17	152.5
LE 20	21.8	10.5	19.0	7.64	30	1.06	.742	165	1577	66	16	86.2
LE 21	7.9	17.5	14.5	3.65	22	0.36	.280	155	633	72	16	54.1
LE 22	10.9	4.9	10.5	10.22	32	1.03	.700	184	1800	57	18	-----
LE 23	9.2	4.9	14.5	8.46	27	0.88	.642	167	1379	44	14	-----
*LE 24	17.3	84.0	65.0	0.84	38	0.04	.010	146	526	30	15	-----
*LE 25	9.9	65.0	110.0	1.02	52	0.15	.072	111	211	74	16	-----

HE - High Exposure Group
LE - Low Exposure Group

* Worker not included in group for statistical comparison because of underlying medical problems unrelated to occupation.

TABLE II

DAWES LABORATORIES
HHE 77-75

MAY 16 & 17, 1977

COMPARISON OF HIGH AND LOW EXPOSURE GROUP MEANS

See Table I for Units

TEST	LOW EXPOSURE MEAN	HIGH EXPOSURE MEAN	SIGNIFICANCE STD T TEST
Prolactin	14.3	10.8	$p > .05$
LH	11.9	10.9	$p > .05$
FSH	7.8	6.5	$p > .05$
Testosterone	7.4	6.6	$p > .05$
% Binding	27.9	27.1	$p > .05$
Total Androgens	0.79	0.55	$p < .05$**
Free Androgen Index	0.560	0.400	$p < .05$**
Progesterone	183	152	$p > .05$
17 OH Progesterone	1238	1336	$p > .05$
Estrone (E_1)	60	64	$p > .05$
Estradiol (E_2)	26.5	42	$p > .05$
Urinary Testosterone	93	55	$p > .05$
STD DEV Testosterone	± 43	± 28	

** Statistically significant differences at the $p < .05$ level.

TABLE III

DAWES LABORATORIES

HHE 77-75

MAY 16 & 17, 1977

Mean values of duplicate determinations for DES obtained from plasma samples. The sensitivity of this assay was 21 pg/ML.

Sample designation	DES pg/ml
1	124
1-2	120
2	91
2-2	<56
3	118
3-2	136
5	83
5-2	111
6	<56
6-2	<56
7	108
7-2	159
12	<56
12-2	171
17	<56
17-2	98
19	<56
19-2	<56
20	<56
20-2	<56
21	83
21-2	<56

TABLE IV

DAWES LABORATORIES
HHE 77-75

MAY 16 & 17, 1977

Mean value of duplicate determinations for diethylstilbestrol obtained from urine samples. The sensitivity of this assay was 21 pg/ml.

Sample designation	Specific Gravity	DES pg/ml
1β	1.024	177
2β	1.032	67
3β	1.015	194
5A	1.027	<21
6β	1.010	<21
7β	1.020	112
12β	1.027	<21
17A	1.032	83
19A	1.025	190
20A	1.015	286
21A	1.030	<21

TABLE V

DAWES LABORATORIES
HHE 77-75

MAY 16 & 17, 1977

COMPARISON OF HIGH AND LOW EXPOSURE GROUPS' RESPONSES
TO THE QUESTIONNAIRE

SYMPTOM OR SIGN	LOW EXPOSURE	HIGH EXPOSURE
1. Change in Breast Size in Last 6 Months	Yes 7 of 12 (58%)	Yes 8 of 11 (73%)
2. Breast Tenderness	Yes 7 of 12 (58%)	Yes 10 of 11 (91%)
3. Change in Color of Nipple	Yes 2 of 12 (17%)	Yes 4 of 11 (36%)
4. Lactation	Yes 1 of 12 (8%)	Yes 2 of 11 (18%)
5. Decreased Libido	Yes 6 of 12 (50%)	Yes 6 of 11 (55%)
6. Decreased Sexual Performance	Yes 3 of 12 (25%)	Yes 4 of 11 (36%)
7. Weight Gain	Yes 4 of 12 (33%)	Yes 2 of 11 (18%)

TABLE VI

DAWES LABORATORIES
HHE 77-75

MAY 16 & 17, 1977

COMPARISON OF HIGH AND LOW EXPOSURE GROUPS
IN PHYSICAL EXAMINATION ABNORMALITIES

PHYSICAL FINDING		LOW EXPOSURE		HIGH EXPOSURE
1. Increased Pigmentation	Yes	1 of 12 (8%)	Yes	1 of 11 (9%)
2. Gynecomastia	Yes	5 of 12 (42%)	Yes	8 of 11 (73%)
3. Breast Tenderness	Yes	1 of 12 (8%)	Yes	2 of 11 (18%)
4. Galactorrhea	Yes	0 of 12 (0%)	Yes	0 of 11 (0%)
5. Abnormal Hair Distribution	Yes	0 of 12 (0%)	Yes	0 of 11 (0%)

APPENDIX A

Analysis of Diethylstilbestrol by Radioimmunoassay

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Materials and Methods

Nonradioactive steroids and diethylstilbestrol (DES) were obtained from Steraloids, Hanover, N.H., or Sigma Chemical Co., St. Louis, Mo. and recrystallized and prepared as previously described (1,2). ^{3}H-DES was obtained from New England Nuclear Co., Boston, Mass. The assay procedure for DES was similar to that previously described in our laboratory for several other steroids (1-4). The antisera against DES was obtained from Dr. Guy Abraham of Harbor General Hospital, Anaheim, Calif. (5). Aliquots containing 50-100 pg standard DES were pipetted into assay tubes for a standard curve. The antiserum and ^{3}H-DES solutions in phosphate-buffered saline were added, mixed thoroughly and incubated overnight at 4°C. Bound and free DES were separated by a 10 min incubation with 1.0 ml dextran-coated charcoal at 4°C and centrifuged at 2500 rpm for 5 min at 4°C. The supernatant containing the bound DES was decanted into a scintillation vial and counted.

Extractions:

Plasma: Approximately 2000 cpm ^{3}H-DES was added to each 1.0 ml aliquot and diluted to 3 ml with distilled water. The diluted plasma was extracted 2 x 5 ml with diethyl ether and dried *in vacuo* and aliquots taken for recovery.

Urine: 5.0 ml of each urine sample was diluted with 5.0 ml and 0.1 M acetate buffer (pH 5.2) and 0.25 ml of an β-glucuronidase/aryl sulfatase preparation (Calbiochem:

cat 34742 with 100,000 unit/ml β-glucuronidase and 50,000 unit/ml sulfatase activity). After overnight incubation at 37°C, the free DES was extracted 2 x 20 ml with ether. Aliquots were taken for recovery and the DES was quantitated by radioimmunoassay.

Calculations: Values were calculated from the standard curve using a logit as described by Rodbard (6). Recovery for each aliquot was used in calculating the concentration of DES (pg/ml).

Results

Radioimmunoassay:

The specificity of the antiserum was tested by competition with ^{3}H-DES. None of the steroids tested showed any significant cross reaction (<0.1%). The steroids tested were estradiol-17β, estrone, estriol, testosterone, androstenedione, progesterone, dehydroepiandrosterone, cortisol cholesterol, ethinyl estradiol and mestranol.

The accuracy of the method was determined by adding various amounts of standard DES ranging from 100-500 pg/ml to male plasma. When the values expected were compared with the values analyzed, a linear regression of 0.98 with a correlation coefficient of 0.96 and an intercept not significantly different from zero was obtained.

The intra-assay coefficient of variation varied from 6.2% at 400 pg/ml to 9.4% at 100 pg/ml. The inter-assay coefficient of variation was 12.1% at mean value of 124 pg/ml and 8.7% at a value of 379 pg/ml. The sensitivity of the standard curve was 40 pg/ml. Significant blanks were obtained when the ether extracts of urine and male plasma was added to the assay tube. Therefore, these extracts were added to the standard curve when the samples were analyzed.

The values obtained for the plasma samples are shown in Table III. The sensitivity of this assay was 56 pg/ml. Values of 56 pg or less were indicated as <56 pg/ml. Significant levels of DES were seen in a number of samples.

The values obtained for urine samples are shown in Table IV. The values are calculated as pg DES/ml of urine. The specific gravity of the urine samples are also shown in Table IV.

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INDIVIDUAL WORKERS' RESULTS

Worker Number	Prolactin 7-12 ng/ml	FSH 7-27 uU/ml	LH 2-32 uU/ml	Testosterone ng/ml	Percent Bound % 32-69	Total Androgens ug% .53-1.35	Free Androgen Index ug% .27-.65	Progesterone 50-180 pg/ml	17 OH PRO Gesterone 400-2500 pg/ml	Estrone E1 10-79 pg/ml	Estradiol E_2 10-63 pg/ml	Urinary Testos Terone 37-165 ug/24 hrs
LE 1	7.7	6.2	8.8	6.62	23	0.64	.492	110	1353	51	33	129.6
HE 2	8.6	4.8	6.3	7.04	18	0.50	.410	235	1845	86	45	80.0
LE 3	12.9	6.9	12.5	9.16	24	0.71	.539	395	2142	48	31	144.9
LE 4	9.1	5.7	5.9	5.09	17	0.32	.265	150	835	75	39	54.9
HE 5	7.7	4.8	10.5	2.82	37	0.54	.340	201	666	50	16	-----
LE 6	16.6	2.4	11.5	6.32	37	0.81	.510	220	763	50	15	78.9
HE 7	18.6	6.5	9.3	8.88	35	0.62	.403	95	1181	87	38	75.3
HE 8	21.7	10.5	24.0	10.89	22	0.77	.600	119	1494	104	80	92.7
HE 9	6.2	3.6	10.5	4.38	15	0.38	.323	115	1078	31	29	52.5
HE 10	6.1	5.3	7.8	6.10	21	0.64	.505	144	1354	67	41	59.1
LE 11	14.4	8.6	9.0	12.04	31	1.18	.814	293	2105	62	67	48.7
HE 12	6.1	7.6	6.5	7.14	31	0.74	.510	223	832	57	28	152.3
HE 13	3.4	8.1	12.0	10.10	25	0.67	.502	153	2500	75	71	74.1
HE 14	11.2	<2.0	3.6	1.54	58	0.30	.132	203	730	55	26	8.7
HE 15	12.7	6.9	14.5	6.92	17	0.38	.315	91	1817	67	64	14.2
HE 16	16.8	12.0	14.5	6.61	19	0.49	.396	97	1198	31	30	42.0
LE 17	10.3	2.8	9.9	3.17	27	0.32	.233	62	883	79	36	354.0
LE 18	21.5	16.0	14.0	7.99	36	1.10	.704	165	683	54	16	-----
LE 19	29.2	7.5	12.5	8.16	29	1.10	.781	139	707	59	17	152.5
LE 20	21.8	10.5	19.0	7.64	30	1.06	.742	165	1577	66	16	86.2
LE 21	7.9	17.5	14.5	3.65	22	0.36	.280	155	633	72	16	54.1
LE 22	10.9	4.9	10.5	10.22	32	1.03	.700	184	1800	57	18	-----
LE 23	9.2	4.9	14.5	8.46	27	0.88	.642	167	1379	44	14	-----
*LE 24	17.3	84.0	65.0	0.84	38	0.04	.010	146	526	30	15	-----
*LE 25	9.9	65.0	110.0	1.02	52	0.15	.072	111	211	74	16	-----

HE - High Exposure Group
LE - Low Exposure Group

* Worker not included in group for statistical comparison because of underlying medical problems unrelated to occupation.