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Report No. V 82.276/291099

LIFE-SPAN ORAL CARCINOGENICITY STUDY WITH VINYL CHLORIDE IN RATS

(seventh interim report: week 132 - study termination)

Authors : Dr H.P. Til
H.R. Immel

At the request of : Verband Kunststofferzeugende Industrie E.V.
Frankfurt am Main

Approved by : Dr V.J. Feron

Project number : B79-1099

Assay number : 125

Date : October, 1982

SUMMARY

1. The oral carcinogenicity of vinyl chloride monomer (VCM) was examined in a life-span study with Wistar rats. VCM was administered by incorporating PVC-powder with a high VCM content into the diet. The test substance was fed at various dietary levels to provide oral exposure levels of approximately 0, 0.017, 0.17, or 1.7 mg VCM/kg body weight/day. Each of the dose levels was given to groups of 100 male and 100 female rats, except for the top dose which was given to 50 male and 50 female rats. An extra control group of 100 male and 100 female rats was housed in a separate room. The results obtained in the period of week 132 to termination of the study (week 149) are presented in this report.

2. General health, behaviour, and body weight were not adversely affected by the test compound. The mortality in the top-dose group was relatively high during the final stage of the study, especially in females.

3. At gross pathological examination the number of liver nodules in males as well as in females of the 1.7 mg/kg group was found to be higher than in controls.

4. Preliminary histopathological examination revealed a clearly higher incidence of "foci of cellular alterations" in the liver of males and females of the 1.7 mg/kg group than in rats of the other groups including both control groups. More neoplastic liver nodules were found in females of the top-dose group than in any of the other groups.

VINYL CHLORIDE / CANCER

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Report No. V 83.285/291099

LIFESPAN ORAL CARCINOGENICITY STUDY OF VINYL CHLORIDE IN RATS

(Final Report)

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Report No. V 83.285/291099

LIFESPAN ORAL CARCINOGENICITY STUDY OF VINYL CHLORIDE IN RATS

(Final report)

Authors : Dr H.P. Til
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At the request of : Verband Kunststofferzeugende Industrie E.V., Frankfurt am Main, B.R.D.

Project number : B 79-1099

Start of the study : August 21, 1979

Termination of the study: June 29, 1982

Study director : Dr H.P. Til

Study supervisor : Dr V.J. Feron

Approved by : Dr A.P. de Groot

Date : September, 1983

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SUMMARY

1. The oral carcinogenicity of vinyl chloride monomer (VCM) was examined in a lifespan study (149 weeks) with five groups of Wistar rats, each consisting of 100 males and 100 females, except for the top-dose group which comprised 50 males and 50 females. VCM was administered by incorporating polyvinyl chloride (PVC) powder with a high VCM content into the diet. The diet was provided daily for a period of 4 consecutive hours, whereas food was withdrawn during the other 20 hours. The use of this way of oral VCM administration resulted in the following exposure levels: 0 (control), 0.014, 0.13 and 1.3 mg VCM/kg body weight/day. An extra control group of 100 rats/sex was housed in a separate room.
Additional satellite groups of 10 male and 10 female rats, each receiving the same treatment as the main groups were used for determinations of glutathione levels in the liver after 9 and 18 months.
Observations were made of general appearance mortality, growth, food intake, thrombocyte count, prothrombin time, glutathione levels in the liver, gross pathology and microscopic pathology of the liver and of all grossly visible tumours or presumable tumours in the abdominal cavity, the glands of Zymbal and the mammary glands.

2. General health, behaviour, body weight and food intake were not adversely affected by the test substance.

3. In the second half of the experimental period, mortality in the extra control group was higher than in all other groups. This was most probably due to a high incidence of chronic respiratory disease in the extra control group. In the final stage of the study, the mortality in the top-dose group was slightly higher than in the lower dose groups and the controls.

4. Thrombocyte count, prothrombin time and liver glutathione levels did not show treatment-related differences among the groups.

5. A clearly higher incidence of grossly visible, tumourous, liver nodules was found in both males and females of the top-dose group than in any of the other groups. Moreover, in females of the top-dose group the incidence of hepatic cysts was considerably higher than in controls.

6. Microscopic examination of the liver revealed increased incidences of liver-cell polymorphism, hepatic cysts, foci of cellular alteration, neoplastic nodules and hepatocellular carcinomas in the top-dose group as compared to the control group. Moreover, a hepatic angiosarcoma was found in one male and two females of the top-dose group, whereas no such tumours were encountered in any of the other groups.
The number of animals bearing foci of cellular alteration in the liver was also statistically significantly increased in females of the mid-dose group as compared to controls. In addition, in females but not in males, the incidence of basophilic foci of cellular alteration in the liver was statistically significantly higher in both the low- and the mid-dose group than in the control group.

7. There was no evidence of VCM-feeding affecting the incidence of abdominal mesotheliomas or the type and incidence of mammary gland tumours. No Zymbal gland tumour was found.

8. It was concluded that under the conditions of the present experiment:

   - VCM at a level of 1.3 mg/kg body weight/day induces neoplastic and non-neoplastic changes in the liver of rats,

   - VCM at a level of 0.13 mg/kg body weight/day may lead to more female rats bearing foci of cellular alteration in the liver,

   - VCM at levels of 0.014 or 0.13 mg/kg body weight/day may result in an increased incidence of basophilic foci of cellular alteration in the liver of female rats,

   - 0.13 mg VCM/kg body weight/day is a "no-observed-adverse-effect-level" with respect to the induction of tumours in rats.

9. Risk estimation based on the results of the present rat study and taking into account the prudence of the linear model applied and a lesser sensitivity of humans to the carcinogenic action of VCM in comparison with rats, indicates that the cancer risk of a likely maximum oral daily intake of 0.1 µg VCM per person per day can be practically neglected.

LIFE-SPAN ORAL CARCINOGENICITY STUDY OF VINYL CHLORIDE IN RATS

1. INTRODUCTION

From a previous life-span oral toxicity study of vinyl chloride monomer (VCM) in rats with dose levels of 1.7, 5.0 and 14.1 mg/kg body weight/day (Feron et al., 1978; 1981), it appeared that hepatic angiosarcomas occurred at dose levels of 5.0 mg/kg body weight/day and above, while hepatocellular tumours (neoplastic nodules and carcinomas) were found at all dose levels. Zymbal gland tumours were found at VCM levels of 5.0 and 300 mg/kg body weight/day. Moreover, there was some evidence that VCM enhanced the formation of intra-abdominal mesotheliomas and adenocarcinomas of the mammary gland. In females of the low-dose group there was still a high incidence of liver-cell tumours, viz. 28/58. Thus, this study showed

a) that VCM is a carcinogen in rats when administered orally, and
b) that the "no observed-adverse-effect level" of VCM in rats with respect to the induction of tumours was lower than 1.7 mg/kg body weight/day.

For extrapolating experimental data to man in a reliable way the information obtained from such a test system ideally should include both a "minimum tumour-level" and a "no tumour-level". Therefore, a similar life-span oral carcinogenicity study with VCM in rats was carried out, at lower dose levels, viz. nominally 0.017, 0.17 and 1.7 mg VCM/kg body weight/day (actual oral exposure levels 0.014, 0.13 and 1.3 mg VCM/ kg body weight/day) and two control groups. Based on the pathological findings of the previous long-term study, histopathological examinations in the present experiment were focused on the detection of liver lesions, Zymbal gland tumours, mammary gland carcinomas and abdominal mesotheliomas. A proposal for the present study - dated 19-02-1979 - was accepted by the sponsor. The present experiment and results are described in this report.

2. MATERIAL AND METHODS

2.1 Materials

Vinyl chloride monomer (VCM), from Akzo Zout Chemie, Rotterdam, The Netherlands. Physical chemical constants:
MW = 62.50; m.p. = -153.8 °C; b.p. = -13.37 °C; density = 0.9106; n_D = 1.3700. The product (colourless, clear, free of suspended matter) was delivered in pressurized stainless-steel cylinders, and was specified by the supplier as:
Vinyl chloride monomer ≥ 99.97 wt % min.; acetylene ≤ 2 µl/l (gas); mono-vinylacetylene ≤ 15 µl/l (gas); 1,3-butandiene ≤ 10 µl/l (gas); methyl chloride ≤ 75 µl/l (gas); ethyl chloride ≤ 50 µl/l (gas); chloroprene ≤ 1 µl/l (gas); 1,1-dichloroethane ≤ 1 µl/l (gas); 1,2-dichloroethane ≤ 20 µl/l (gas); acetaldehyde ≤ 5 mg/kg; hydrochloric acid ≤ 1 mg/kg; iron ≤ 0.5 mg/kg; water ≤ 100 mg/kg; evaporation residue ≤ 10 mg/kg.

PVC-powder, commercial name Carina S 65-02, was supplied by Shell Nederland Chemie, Pernis, The Netherlands, in closed steel barrels. The particle size distribution (by weight), specified by the supplier, was: 0.1 % max. > 300 µm; 4 % max. > 200 µm; 90 % max. > 88 µm; 95 % max. 40 µm.
The remaining part of a batch of 500 kg PVC-powder (VCM content 3 ppm) received on January 13, 1977 from Shell, which had been partly used in the previous study (Feron et al., 1978), was used.
Part of this PVC-powder was freed from residual VCM by keeping it in layers of 4 to 6 cm thick in a vacuum oven at 60 °C for a period of 3 to 4 days. The so treated PVC-powder (VCM content less than 0.2 ppm) was used for control purposes.
An amount of about 50 kg PVC powder was mixed with a calculated amount of the liquid VCM in a closed steel barrel to raise the VCM content of the PVC-powder to approximately 4600 ppm.
This PVC-powder was repacked and stored in tightly closed steel containers (containing about 10 kg PVC) in a freezer at -20 °C until a few minutes before mixing with each diet.

2.2 Preparation and administration of the diets

Preparation and administration of the diets were done in the same way as in the previous life-span study (Feron et al., 1978). Only one distinction has to be made. In that study the dietary levels of VCM were obtained by incorporating into the diets 10 % PVC-powder with varying proportions of VCM-containing and "VCM-free" powder. In the present study, the diets were prepared to a total concentration of PVC-powder of 1 % only. The proportions of PVC-powder with or without VCM for each of the diets are specified below:

group	PVC-powder in the diet (%)	
	PVC-powder containing about 4600 ppm VCM	PVC-powder without VCM[1)]
control group	0	1
low-dose group	0.01	0.99
mid-dose group	0.1	0.9
top-dose group	1	0
extra control group	0	1

1) PVC-powder freed from VCM. The VCM-content was lower than 0.2 ppm

Diets were prepared daily - by mixing appropriate amounts of PVC-powder (with or without VCM) with the Institute's rat stock diet - just prior to offering the diets to the rats. The composition of the stock diet is presented in Annex 1. The level of nutrients and contaminants in the stock diet are determined twice a year. The contaminants determined are tabulated, together with detection limits and tentative maxima in Annex 2. Actual levels in batches produced on January 24, 1980, September 9, 1980, February 27, 1981, September 9, 1981 and February 9, 1982 are given in Annexes 3 to 7 (nutrients) and in Annexes 8 to 12 (contaminants).

As in the previous study, the powdered diets were available to the rats each day for a period of four hours (generally between 10.00 a.m. and 02.00 p.m.), in such quantities that the animals did not consume all the feed. At the end of the four-hour feeding period the feeders were removed from the cages and the remainder of the diets was destroyed.

The rats had constant access to bottled tap water. The contaminants in the drinking water which are determined twice a year, are given in Annex 13. The actual levels determined in November-December 1979, January-April 1980, September-November 1980, March-May 1981, September-November 1981 and January-March 1982 are given in Annexes 14 to 19.

2.3 Animals and housing

Five hundred and twenty-five male and 525 female, SPF-bred, weanling rats (Cpb:WU; Wistar random) were obtained from the Central Institute for the Breeding of Laboratory Animals TNO, Zeist, The Netherlands. The animals arrived on August 14, 1979, when they were about 25 days old. The body weight range was 38-71 g for males and 42-66 g for females.
Upon arrival, the animals were checked for overt signs of ill health and anomalies. One rat showing hydrocephalus, one rat with closed eyes and two rats with a dirty yellow fur were discarded. The healthy animals were allocated to five main groups by a computer randomisation program. Four of the groups, viz. the control group, the low- and mid-dose group and the extra control group, each consisted of 100 males and 100 females. The top-dose group consisted of 50 males and 50 females. To each dietary group a satellite group, comprising 10 males and 10 females each, was attached. The rats of the satellite groups, which received the same diets as the rats of the corresponding main groups, were killed for determinations of glutathione levels in the liver, half of the animals when they had been on their diets for nine months and the remaining half after an experimental period of 18 months.
The rats which were not allocated to the main or satellite groups were kept in reserve for a period of four weeks. One female rat of the extra control group showing epileptic fits had to be exchanged for a reserve two days after the start of the study. None of the other reserved were used.

The rats were housed under conventional conditions, five rats per sex per cage, in suspended stainless steel cages (17 x 44 x 32 cm), fitted with wire mesh floors and fronts.

Animals which were in bad condition were housed individually in separate cages until they died or until they were killed because their condition was so bad that they were not expected to last out the night, (or, when observed on Friday, the weekend). If the condition of the singly housed rats improved they were returned to their original cage.
The male rats of the control-, low-, mid- and top-dose groups were housed in one room, the females of these groups in a second room and the males and females of the extra control group in a third room. The rooms were ventilated with about 10 air changes per hour. The temperature was kept at 23 $\pm$ 1 °C, the relative humidity was 40-80 % and a 12 hour light/dark cycle was maintained (light from 06.00 a.m. till 06.00 p.m.). After an acclimatisation period of 7 days, the animals were placed on the test diets for four hours a day during the entire test period. During a period of 3 days, prior to the start of the experiment, the rats received stock diet without PVC for four to six hours each day. This was done to adapt the animals to the daily feeding-period of four hours.

Drinking water was supplied in glass bottles, which were filled daily with fresh tap water, except for the weekend, and cleaned once weekly.

2.4 Identification of the test system

The individual animals were identified in the following way. Each group of rats (the control, low-dose, mid-dose, top-dose and extra control group) was fitted with a letter and colour code.
A table showing the group letter, colour code, exposure level and number of animals is given on the next page.

group letter	colour code	nominal exposure levels (mg VCM/kg b.w./day)	actual exposure levels (mg VCM/kg b.w./day)	number of rats: main groups study no. 125 males	main groups study no. 125 females	satellite groups study no. 126 males	satellite groups study no. 126 females
A	white	0	0	100	100	10	10
B	blue	0.017	0.014	100	100	10	10
C	green	0.17	0.13	100	100	10	10
D	red	1.7	1.3	50	50	10	10
E	brown	0	0	100	100	10	10

Each rat was identified by a six digit computer reference number, which was even for males and odd for females. Within each subgroup of 10 rats, each rat was individually identified by sex and one out of 10 different V-shaped earmarks according to the following code:

Z = zero
R_1 = one right
R_2 = two right
L_1 = one left
L_2 = two left
R_1L_1 = one right plus one left
R_1L_2 = one right plus two left
R_2L_1 = two right plus one left
R_2L_2 = two right plus two left
R_3 = three right

See also the cross reference listing (Annexes 20 and 21).

Each cage was provided with a coloured card showing the computer reference number range, the earmark range, the cage number, the group letter and the study number.

2.5 Experimental conduct

The experiment (main and satellite groups) was started on August 21, 1979. Half of the rats of the satellite groups (assay no. 126) was killed on May 20 or 22, 1980 and the remaining half on February 26 or 27, 1981 for determinations of glutathione in the liver. The final autopsy of the rats in the main groups (assay no. 125) was carried out on June 24 to 29, 1982, when about 80 % of the control-, low-dose and mid-dose rats had died.

The following determinations were made:

a) Analysis of VCM in the diets

The VCM content of freshly prepared diets was generally determined once every fortnight. During the course of the study, 72 determinations for each dose level were carried out. At the same time the VCM content of the PVC-powder was determined.

The rate of evaporation of VCM from the diets was determined by measuring the VCM content of the diets at the beginning of the feeding-period and after 1 hour and after 2, 3 and 4 hours. The diet samples to be analysed were taken at random from the feeders. In this way samples of each of the test diets were taken in week 3, 12, 27, 56, 79, 105 and 132, and were analysed for their VCM content. At the same time samples from the control diets were taken at the beginning of the feeding-period only and also analysed.

The analyses were carried out by means of gas-liquid chromatography according to a method described by Feron et al. (1975).

b) Analysis of VCM in the faeces

Freshly produced faeces from 5 rats of each dietary group were collected 24 hours after the start of the feeding-period at about 10.00 a.m. in week 6, 28, 52, 80 and 106. Fresh faeces was obtained by squeezing the lower part of a rat's abdomen. The droppings were weighed, submerged in 10 ml ethylacetate, and stored at 4 °C in a closed vessel until analysis of the supernatant liquid by gas chromatography.

c) Calculation of the actual oral intake and oral exposure levels of VCM

The amount of food eaten by the rats of each test group (g/kg body weight/day) was calculated for males and females separately from the grand averages of body weight (table 7) and food intake (table 9) of each test group over the whole experimental period.

The VCM intake (mg/kg body weight/day) was calculated from the rate of evaporation of VCM from the diets (table 2) and the rate of overall food consumption over the four-hour feeding-period for males and females (table 10). Both the rate of evaporation and the rate of food intake were assumed to be linear within each hour of the feeding-period. The actual VCM intake for each group during each of these four periods was calculated by multiplying the amount of food eaten during a one-hour period by the average VCM content of the food eaten in that period. The total actual VCM intake was obtained by adding the VCM intakes during the four one-hour periods of the feeding-period.

To obtain the actual oral exposure levels of VCM, the actual VCM intakes were corrected for the VCM excreted with the faeces. For that purpose, the faeces production (g/kg body weight/day) was calculated based on an average of 36 g wet faeces/100 g food consumed. The amount of VCM in the wet faeces (mg/kg body weight/day) was calculated by multiplying the amount of faeces produced/kg body weight with the VCM content measured in the faeces (table 3). The amount of VCM excreted with the faeces, expressed in mg VCM/kg body weight/day, was substracted from the actual oral intake of VCM (also expressed in mg VCM/kg body weight/day) to find the actual oral exposure level of VCM.

d) Clinical signs (main groups)

The animals were observed daily and carefully examined for signs of illness and tumours once every two weeks. All signs of ill-health or toxicity with any changes in behaviour were recorded, together with the progression or regression of such abnormalities, as well as mortality and the time of onset, dimensions and location of palpable tumours.

e) Body weight (main and satellite groups)

The weight of each animal was recorded when the administration of the test substance was started and further in week 2 and 4 and once every four weeks thereafter. From these individual figures the mean body weight of the animals of each group was calculated.

f) Food consumption; amount and rate (main groups)

The food consumption was measured in 20 animals/sex/group, in week 1, 2, 3 and 4, 11 and 12, 23 and 24, 35 and 36, 47 and 48, 59 and 60, 73 and 74, 85 and 86, 97 and 98, 109 and 110 and 121 and 122.
The rate of food consumption was determined by weighing the feeders initially and after periods of 1 hour, 2 hours, 3 hours and 4 hours. This was done for each of the diet groups on one day in week 4, 12, 25, 38, 52, 64, 77, 90, 103, 116 and 129. The number of rats involved in these determinations was 20/sex/group.

g) Haematology (satellite groups)

Samples of blood were collected from the tip of the tail of 10 rats/sex/group on days 94 and 185 and of five rats/sex/group on day 367. All blood samples were examined for the following parameters.

- thrombocyte count, by means of the Sysmex Platelet Counter Pl 110 using the manual of Toa Medical Electronics Co., Ltd., Japan
- prothrombin time using Normo-test reagents from Nyegaard & Co. As, Oslo, Norway (Owren, 1959).

h) Glutathione in the liver (satellite group)

In week 40 and 80, five rats/sex/group were killed by decapitation. The livers were quickly removed and cooled to 0 °C and cut into two, about equal, pieces; both were weighed and stored in a freezer at -20 °C until analysis. After thawing, each sample was homogenised in ice-cold 0.1 M EDTA(Na_2) solution. A part of the homogenates was centrifuged at 2800 rpm for 5 minutes. The non-protein bound sulfhydryl ('glutathione') content of the supernatants was determined with 5,5'-dithiobis-(2-nitrobenzoic acid) by means of an AutoAnalyser.

1) Pathology

All males still alive in week 149 (June 24 and 25, 1982) and all females in week 150 (June 28 and 29, 1982) were killed by decapitation, autopsied and subjected to a careful gross examination. At that time a mortality of about 80 % had been reached in the control, low- and mid-dose groups. A thorough autopsy was also performed on rats found dead or killed in extremis.

All superficial tissues, including the urogenital orifices and tail, each pinna, eye and external auditory meatus, were examined visually and by palpation for distortion, swelling or evidence of tumour formation; similar attention was given to the mammary tracts and subcutaneous structures. The external nares, buccal cavity and tongue were then examined, and the cranial roof removed to allow observation of the brain, pituitary gland and cranial nerves. After ventral midline incision and skin reflection, all subcutaneous tissues were examined, including regional lymph nodes, mammary and thyroid/parathyroid glands. The condition of the thoracic viscera was noted, and attention was given to the thymus, lymph nodes and heart.
The abdominal viscera were examined before and after removal. The lungs were removed and all pleural surfaces examined.
The kidneys were incised and examined.
Any abnormalities in the appearance and size of the gonads, adrenals, uterus, intra-abdominal lymph nodes and accessory reproductive organs were recorded. Any lesion suggestive of neoplasia was noted, including details of location, size and multiplicity. Any evidence of adhesion or possible invasion to adjacent structures was noted.
Samples of the following tissues and organs of all animals were preserved in 4 % aqueous neutral phosphate-buffered formaldehyde solution:

adrenals	ovaries
aorta	pancreas
axillary lymph nodes	parotid salivary glands
brain	preputial glands
caecum	pituitary
cervix	prostate
coagulating glands	seminal vesicles

colon	skeletal muscle
duodenum	skin
epididymides	spinal cord
exorbital lachrymal glands	spleen
eyes	sternum (with bone marrow)
sciatic nerve	stomach
heart	submaxillary salivary glands
ileum	sublingual salivary glands
jejunum	testes
kidneys	thymus
liver	thyroid
lungs	trachea
mammary glands	urinary bladder
mesenteric lymph nodes	uterus
nose	Zymbal glands
oesophagus	all gross lesions

Tissues required for microscopic examination were embedded in paraffin wax, sectioned at 5 µm and stained with haematoxylin and eosin. Histopathology was restricted to the liver, all grossly visible tumours or presumable tumours in the abdominal cavity, the glands of Zymbal, and the mammary glands. As to the liver, of each rat three liver pieces, each taken from a different lobe, were studied; these pieces were always taken from the same three lobes at about the same sites; in addition sections were prepared from liver tissue showing gross changes.

2.6 Statistical analysis

Data on body weights were subjected to one-way analysis of (co-)variance, followed by Dunnett's multiple comparison test.
Thrombocyte counts and prothrombin time values were analysed by the Mann Whitney U-test. Levels of glutathione in the liver were evaluated by the Student t-test.
Data on mortality and microscopical observations were analysed by the Fisher exact probability test.
Grossly visible masses were evaluated by the Chi square test.

2.7 Contributors

Major contributions to this study were made by:

Animal handling and diet preparation	Ms. M.M. Andringa
	J.M. Blom
	Ms. A. Dijkstra
	Ms. G.G.M. Fleer
	Ms. A.A. van Tuyl
	D.C. Veldhuysen
Diet analysis	: A. Schouten
Clinical chemistry	: Dr H.E. Falke
	J.F. Catsburg
Biochemistry	: Dr D.C. Leegwater
Histotechnique	: Ms. M.T. v. Rijswijk
	Ms. J. Wisman
	Ms. A.P.M. v. Tuyl-Fonville
	Ms. N. Hagemeyer
Pathology	: H.R. Immel
	Dr V.J. Feron
Study director	: Dr H.P. Til
Study supervisor	: Dr V.J. Feron

2.8 Deviations from the protocol

- At the request of the sponsor, the glutathione determinations in the liver were carried out after 9 and 18 months instead of after 6, 12 and 24 months.

- Prothrombin time and thrombocyte count in rats of the satellite groups after 24 months could not be carried out, because all rats of the satellite group had already been killed before that time.

3. RESULTS

3.1 Analysis of VCM in the diets (tables 1 and 2)

The average VCM content of freshly prepared test diets appeared to be 0.49, 4.49 and 44.1 ppm for the low-, mid- and top-dose group, respectively (table 1).

The VCM content in all three test diets decreased with time during the four-hour feeding-period (table 2). The greatest losses were observed during the first hour. Proportionally, the losses of VCM were virtually the same in all three test diets at the corresponding points of time during the four-hour period. On average, the cumulative losses were 22, 30, 39 and 38 % after 1, 2, 3 and 4 hours, respectively.

3.2 Levels of VCM in the faeces (table 3)

The VCM content of the faeces increased with increasing dietary levels of VCM. No appreciable differences in VCM content of the faeces were found within one particular test group. The average amount of VCM found in the faeces expressed as percentage of the actual oral VCM intake, was found to be 23.5, 25.9 and 23.9 % for the low-, mid-, and top-dose groups, respectively.

3.3 Actual oral exposure levels of VCM (table 4)

The VCM content of the freshly prepared test diets (table 1) formed the basis for calculating the average VCM content of the various diets. Since the loss of VCM from the diets during the four-hour feeding-period (table 2), the rate of food intake (table 10) and the VCM content of the faeces (table 3) were known, the actual oral exposure levels of VCM for each group could be calculated (see section 2.5). They were found to be 0.014, 0.13 and 1.3 mg VCM/kg body weight/day for the low-, mid-, and top-dose groups, respectively (table 4).

When the actual oral intake of VCM was expressed as percentage of the theoretical intake, the values found were 81.5, 81.2 and 81.3 % for males, and 80.1, 79.8 and 79.8 % for females of the low-, mid- and top-dose groups, respectively. The overall average for males and females of the various test groups was calculated to be 80.6 %. This percentage was in good agreement with the 80 % found in the previous life-span study using much higher dietary levels of VCM (Feron et al., 1978; 1981).

3.4 Symptomatology and survival (tables 5 and 6)

There were no overt signs of reaction to treatment with VCM. The behaviour of the rats during the first 18 months of the experiment was unremarkable. After 18 months ageing symptoms developed in all groups and the number of unthrifty rats increased, more rapidly in males than in females. The poor condition started with a humpbacked position and slight emaciation, followed by dyspnoea, pale eyes, lethargy, filthiness and in many cases severe emaciation.
Randomly distributed major abnormalities due to ageing included malocclusion of incisors, stained coats, a bloody discharge around nostrils and eyes, wet stools, focal alopecia, focal dermatitis, paresis of hind legs, loss of one or both eyes and white opaque cornea.

Macroscopically visible or palpable masses occurred in all groups. The total number of rats which showed such a lesion at any time, together with the number of masses is given in table 5. In females both the incidence and the total number of these gross lesions was considerably higher than in males. Taking into account that the top-dose group comprised only 50 rats of each sex, the total number of masses in females of the top-dose group was higher than in the other groups. This remarkable difference appeared to be caused by the high number of top-dose females with liver cysts (see also tables 13 and 14), which are easily detected by palpation of the abdomen.
In the extra control group the total number and the incidence of masses was relatively low as compared to the other groups, the control group included. The low figures for the extra control group are undoubtedly related to the relatively high and early mortality in this group, giving fewer animals of this extra control group the time to develop lesions associated with old age.

The cumulative mortality is given in table 6. Up to week 68 mortality was very low. Thereafter, mortality gradually increased, more quickly in the extra control group than in the other groups. The extra control animals - which were housed in a separate room - were much more severely affected by chronic respiratory disease than the animals in the other groups (see also 3.9.1). This phenomenon undoubtedly explains the higher and earlier mortality in the extra control group.

3.5 Body weights (tables 7 and 8; figures 1 and 2)

In the three test groups, the mean body weights were generally comparable to those of the controls. Some isolated changes were observed, but there was no evidence of a dose-related response.
In the extra control group mean body weights were statistically significantly decreased throughout the study in males and from day 674 and onwards in females as compared to the standard control group. In males the lower body weights were accompanied by lower intake of food (see 3.6). Since the extra controls were housed in a separate room, the lower body weights and food consumption might be due to unknown differences in environmental condition (see also 3.4), although this separate room was conditioned in the same way as the other rooms.

3.6 Food intake (tables 9 and 10)

Food intake showed wide variations among the different weighings within one group. There was, however, no evidence that food intake was affected by VCM-feeding (table 9). Males of the extra control group had a lower food intake than the other groups from week 3 onward.

No appreciable variations were encountered in the rate of food consumption in the various groups (table 10). Females consumed their food slightly less quickly than males.

3.7 Haematology (table 11)

Thrombocyte count did not show dose-related differences between the test groups and the controls. The slight, though statistically significant increase in females of the top-dose group on day 366 was not apparent when compared to the extra controls.
Prothrombin time of females of the top-dose group was slightly increased after 3 and 6 months. However, prothrombin time of females of the extra control group was even higher at the same stages. No differences between the groups occurred after a feeding-period of 12 months.

3.8 Glutathione levels of the liver (table 12)

There were no significant differences in liver glutathione levels between the various test groups and the controls, either after 9 or 18 months.

3.9 Pathology

3.9.1 Gross examination (table 13)

The incidence of liver nodules suspected of being tumours was higher in males and females of the top-dose groups than in controls or lower dose animals. Most of these tumourous masses were small (diameter up to 1 cm), solid and pale or had the same colour as the adjacent liver tissue; some were large (diameter 2 to 4 cm), soft or firm and occasionally slightly haemorrhagic. Cysts in the liver of old rats, particularly in females, is a common finding in the strain of rats used. However, the incidence of such cysts was much higher in females of the top-dose group than in females of the other groups, the control group included. The cysts varied widely in size, were often multiple and generally contained a turbid, watery liquid.
There was no evidence that any of the other gross lesions observed and summarised in table 13 were related to the administration of VCM.

Severe chronic respiratory disease (CRD) often accompanied by focal emphysema (spongy lungs) was seen much more frequently in the extra control group than in the other groups. Many of the rats affected by advanced CRD lost weight and emaciated before they died or were killed in extremis.

Other conspicuous findings in animals of the extra control group were the high incidences of bilateral testicular atrophy and atrophy of the coagulating glands and seminal vesicles. Atrophy of the testes and of the secondary sexual glands were often seen in the same animals, but these lesions also occurred separately. Moreover, a relatively high number of females of this group showed protrusion of the eye balls; this was almost exclusively observed in severely emaciated rats.

3.9.2 Microscopic examination

Liver (table 14)

Increased incidences of foci of cellular alteration, neoplastic nodules, hepatocellular carcinomas, liver-cell polymorphism and cysts have been observed in the top-dose group. Moreover, in the top-dose group two females and one male had developed a hepatic angiosarcoma, whereas such tumours have not been seen in any of the other groups. Since the morphology of the hepatocellular lesions was essentially the same as that of the liver lesions described in full detail in our previous report on the long-term effects of oral administration of VCM in rats (Feron et al., 1981), no further discription of these alterations is presented in this report. The morphology of VCM-induced hepatic angiosarcomas has also been described in a previous report (Spit et al., 1981).

Table 14 also shows that in females, but not in males, of both the low- and mid-dose group the incidence of basophilic foci of cellular alteration was significantly higher than in controls. In addition, in the mid-dose group the number of females bearing foci of cellular alteration was statistically significantly higher than in the control group.

There was no evidence that any of the other hepatic lesions observed, was related to the feeding of VCM. There were a few statistically significant differences between test groups and the control group, but this concerned decreases in incidence in the test groups (e.g. slight cholangiofibrosis in males), or the differences were not statistically significant as compared to the extra controls (e.g. single cell necrosis in females), or there was no dose-response relationship (e.g. foci of degenerated hepatocytes in males).
As compared to controls lower incidences of several hepatic abnormalities were found in the extra control group. Examples of such lesions are cysts, bile duct proliferation, cholangiofibrosis and vacuolisation of periportal hepatocytes in females, and liver cell polymorphism in males. Such changes might be associated with old age and their relatively low incidences in the extra control group is most probably due to the much lower average survival time of these animals (118 weeks) in comparison with that of the controls (129 weeks).

Mammary glands (table 15)

The number of females bearing a mammary gland tumour was considerably lower in the extra control group and in the low- and mid-dose groups than in the control group. In the same groups the number of females with a mammary fibroadenoma was also lower than in the control group. There was no indication that the incidence of mammary gland carcinomas increased with increasing VCM dose.

Abdominal tumours (table 15)

All intra-abdominal tumours found at autopsy were examined histologically. The numbers of mesotheliomas detected in rats of the different groups indicate that there was no evidence of a relationship between the administration of VCM and the development of this type of tumour.

Zymbal gland tumours

All gross tumours in the head region were studied by light microscopy. No Zymbal gland tumour was found.

4. DISCUSSION

In the present study no effects attributable to VCM were observed other than liver changes, and a higher mortality in the top-dose group as compared to the control group during the last 6 to 9 months of the experimental period.

The differences in mortality between the top-dose group and the control group were slight and attained a level of statistical significance only at a few points of time. This slightly increased mortality in the top-dose group might be due to the increased incidence of neoplastic and non-neoplastic liver changes in this group. A similar adverse effect has been observed in females, but not in males, of the low-dose group (1.7 mg VCM/kg body weight/day) used in the previous long-term oral rat study with VCM (Feron et al., 1981).

From the previous study (Feron et al., 1981) it appeared that oral exposure to VCM at a level of 1.7 mg/kg body weight/day resulted in a series of changes in the hepatic parenchyma. These changes included an increased incidence of cellular alteration and neoplastic nodules, a few hepatocellular carcinomas, an increased incidence and degree of liver-cell polymorphism, and an increased incidence of hepatic cysts. In the present study the same type of treatment-related liver changes were found in the top-dose group receiving 1.3 mg VCM/kg body weight/day. In addition, one male and two females of the top-dose group had developed a hepatic angiosarcoma; in the previous experiment hepatic angiosarcomas were observed at VCM levels of 5.0 mg/kg body weight/day and above but not at the lowest exposure level of 1.7 mg/kg body weight/day.

As compared to controls increased incidences of basophilic foci of hepatocellular alteration occurred in males of the top-dose group and in females of each of the dose groups. In females the incidence of this type of foci of cellular alteration in the liver increased with increasing dose levels. Moreover, the number of rats bearing foci of cellular alteration in the liver (all type of foci) was significantly higher in males of the top-dose group and in females of the mid- and top-dose group than in controls. These findings suggest a relationship between the oral exposure to VCM at levels of 0.014 and 0.13 mg/kg body weight/day and the increased occurrence of foci of cellular alteration in the liver of female rats.

The incidence of basophilic foci of hepatocellular alterations in females of the control group (9/98 or 9 %) was clearly lower than the incidence of this type of foci in female controls used in the previous long-term oral rat study with VCM (10/57 or 18 %; Feron et al., 1981). Similar incidences were also found in females of control groups of three other long-term rat studies carried out in our Institute more or less simultaneously with the study of Feron et al. (1981); the incidences being 11/95 or 12 %, 3/20 or 15 % and 17/99 or 17 %. These data seem to indicate that the incidence of basophilic foci (9 %) in females of the control group of the present VCM study is unusually low, and, thus, would seem to throw doubt upon the toxicological significance of the slight increase in incidence of this type of foci of cellular alterations in the low- and mid-dose groups. However, the incidences of basophilic foci of hepatocellular alterations in females of control groups of other long-term rat studies performed in our Institute in the same period as the present VCM-study were: 0/20 or 0 %, 1/20 or 5 %, 5/69 or 7 % and 4/50 or 8 %. Compared to these figures an incidence of 9/98 or 9 % as found in the present group of female controls is not unusually low, and, thus support the suggestion that the feeding of VCM at levels of 0.014 or 0.13 mg/kg body weight/day may have resulted in more basophilic foci of cellular alteration in the liver of female rats.

The directive of the European Community (EC) of January 30, 1978 (78/142/EEC) imposes a maximum permitted limit of 1 ppm residual VCM in finished plastic materials or articles intended for use in contact with foodstuffs. The same EC-directive stipulates that any migration of VCM to the food must not produce a concentration in the food of greater than 10 ppb VCM which is or is very close to the detection limit of VCM in foodstuffs.

Calculations based on a survey of residual levels of VCM in PVC bottles, films and foods in the period of 1974-1977, suggest that the intake of VCM from the average diet will be less than 0.1 µg per person per day (Crosby, 1982; Ministry of Agriculture, Fisheries and Food, 1978). What does this maximum oral daily intake of VCM by humans mean in terms of cancer risk?

Extrapolation of the results of the present rat study to humans using the linear extrapolation model and taking into account an acceptable cancer risk from oral VCM exposure for man of 10^{-6}, leads to an acceptable oral intake of 0.4 µg VCM per person per day. Since the estimated maximum oral daily intake is only 0.1 µg VCM/person/day, the estimated cancer risk is at least a factor 4 lower. Moreover, the extrapolation model used is a conservative and prudent one, which implies that the actual cancer risk might be (considerably) lower than that calculated by means of the linear model. In addition, comparison of the results of an epidemiological study of vinyl chloride workers with the predicted cancer risk in the cohort of workers based on the results of VCM studies in rats suggested that humans are less sensitive to the carcinogenic action of VCM than rats (Gehring et al., 1979). Translated into practical terms this means that the cancer risk of a maximum oral daily intake of 0.1 µg VCM/person/day is small enough to be practically neglected.

5. CONCLUSIONS

The results of the present oral study allow the following conclusions:

- VCM at a level of 1.3 mg/kg body weight/day induces neoplastic and non-neoplastic changes in the liver of male and female rats,

- VCM at a level of 0.13 mg/kg body weight/day may lead to more female rats bearing foci of cellular alteration in the liver,

- VCM at levels of 0.014 or 0.13 mg/kg body weight/day may result in an increased incidence of basophilic foci of cellular alteration in the liver of female, but not of male, rats, and

- 0.13 mg VCM/kg body weight/day is a "no-observed-adverse-effect-level" with respect to the induction of tumours in rats.

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7. AUTHENTICATION

This report was prepared by:

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and approved by:

Dr A.P. de Groot date: 28 September 1983
(Head Dept. Biological Toxicology)

8. RETENTION OF RECORDS, SAMPLES AND SPECIMENS

All records concerning the dietary formula, daily observations, body weights, food intake, haematology, clinical chemistry and gross- and microscopical examinations and all other information relevant to the quality and integrity of the study have been filed in the archives of the Department of Biological Toxicology together with the master copy of this report. Materials (samples of the test substance, wet specimens, blocks) have been stored, and will be retained for a period of eight years, i.e. till July 1990. The slides will be retained for a period of 15 years, i.e. till July 1997.

QUALITY ASSURANCE UNIT TNO - P.O. Box 360, 3700 AJ ZEIST, Netherlands

STATEMENT OF GLP COMPLIANCE

On : Lifespan oral carcinogenicity study of vinyl chloride in rats
Report no.: V 83.285/291099
Date : September, 1983

The study was carried out under conditions of good laboratory practice. Within reason there have been no circumstances that might have affected the quality and integrity of the results obtained.

Dates and number of inspections:		Dates of reports to management:
19 November 1979	(1)	19 November 1979
22 and 25 February 1980	(1)	25 February 1980
12 May 1980	(1)	12 May 1980
12 November 1980	(1)	12 November 1980
17 November 1980	(2)	18 November 1980
23 January 1981	(1)	26 January 1981
3-4 March 1981	(2)	5 March 1981
14-15 May 1981	(3)	18 May 1981
18 August 1981	(1)	18 August 1981
27 October 1981	(3)	27 October 1981
22 January 1982	(3)	26 January 1982
12-13 May 1982	(2)	13 May 1982
24 June 1982	(1)	24 June 1982
8 July 1982	(3)	8 July 1982
8-11 March 1983	(2)	16 March 1983
10 March 1983	(1)	24 March 1983
Draft report audit:		
10-11 March 1983		24 March 1983
Final report audit:		
20 September 1983	(1)	20 September 1983

C. N. v. S.

Drs S. van Straten
Quality Assurance Manager

date: 28 September 1983

CIVO/TNO

STUDY NO 125 CARCINOGENICITY STUDY IN RATS WITH VCM IN THE DIET

TABLE 1 LEVELS OF VCM IN THE DIET IMMEDIATELY AFTER PREPARATION OF THE DIETS[1)]

Group	Intended oral exposure levels of VCM (mg/kg b.w./day)	Dietary level of VCM (ppm) MEAN	SEM	N
A	0	< 0.1		72
B	0.017	0.487	0.013	72
C	0.17	4.487	0.097	72
D	1.7	44.07	0.926	72
E	0	< 0.1		65

1) The VCM content of the PVC-powder with VCM was on average 4582 ± 98 ppm.

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TABLE 2 LOSSES OF VCM FROM THE DIET DURING A PERIOD OF FOUR HOURS

Group	Intended oral exposure levels of VCM (mg/kg b.w./day)	VCM levels in the diet during the four-hour feeding-period at different points of time [1]								
		expressed as ppm [2]					expressed as percentage of t_0			
		t_0	t_1	t_2	t_3	t_4	t_1	t_2	t_3	t_4
A	0	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1				
B	0.017	0.48	0.37	0.32	0.27	0.28	77	67	56	58
		0.037 [3]	0.039	0.024	0.021	0.016				
C	0.17	4.2	3.3	3.0	2.7	2.7	79	71	64	64
		0.36	0.23	0.13	0.20	0.15				
D	1.7	41.3	33.3	29.9	26.7	25.3	81	72	65	61
		1.94	1.85	1.70	1.66	1.96				
E	0	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1				
Grand Mean							79	70	62	62

1) Samples taken immediately after preparation of the diets (t_0) and further from the feeders in the cages of the rats one hour (t_1), two hours (t_2), three hours (t_3) and four hours (t_4) after preparation

2) The values are the means of 7 different analyses.

3) Standard error of the mean.

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STUDY NO 125 CARCINOGENICITY STUDY IN RATS WITH VCM IN THE DIET

TABLE 3 LEVELS OF VCM IN THE FAECES

Group	Intended oral exposure levels of VCM (mg/kg b.w./day)	Level of VCM (ppm) found in the faeces 24 hours after the start of the feeding-period[1)]		
		MEAN	SEM	N
A	0	< 0.1		5
B	0.017	0.26	0.028	5
C	0.17	2.64	0.273	5
D	1.7	23.6	2.968	5
E	0	< 0.1		5

1) Faeces were collected by squeezing the lower part of the rat's abdomen; they were immediately submerged in 10 ml ethylacetate and then stored at 4 °C in a closed vessel until analysis for the VCM content.

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TABLE 4 DESIGN AND ACTUAL DOSE LEVELS OF VCM IN RATS FED DIETS CONTAINING PVC POWDER

Group	Intended oral exposure levels of VCM		Actual dietary VCM levels at the start of the feeding period[1] (ppm)	Theoretical oral intake of VCM[2] (mg/kg b.w./day)	Actual oral intake of VCM[3] (mg/kg b.w./day)	Actual oral exposure level of VCM[4] (mg/kg b.w./day)
	ppm in diet	mg/kg b.w./day				
A	0	0	0	0	0	0
B	0.34	0.017	0.49	0.022	0.018	0.014
C	3.4	0.17	4.5	0.21	0.17	0.13
D	34	1.7	44.1	2.1	1.7	1.3
E	0	0	0	0	0	0

1) Average dietary VCM contents determined immediately after preparation of the diets.
2) Assuming no loss of VCM by evaporation from the diets (see also table 1).
3) Taking into account the loss of VCM from the diets.
4) Oral intake of VCM diminished by the faecal VCM. The VCM excreted in the faeces was considered to be still enclosed in the PVC granules, and thus not to have been in contact with the body.

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TABLE 5 GROSSLY VISIBLE OR PALPABLE SUPERFICIAL OR INTRA-ABDOMINAL MASSES OBSERVED IN THE COURSE OF THE STUDY

Group	Intended exposure levels of VCM (mg/kg b.w./day)	Total no. of rats at start	No. of rats with masses		No. of masses	
			Total	Non-survivors	Total	disappeared in course of time
	MALES					
A	0	100	35	32	55	10
B	0.017	100	45	40	55	10
C	0.17	100	36	31	42	7
D	1.7	50	18	17	23	6
E	0	100	14***	14**	16	1
	FEMALES					
A	0	100	68	59	112	3
B	0.017	100	80	69	119	8
C	0.17	100	63	49	115	6
D	1.7	50	38	36	87	2
E	0	100	48**	48	79	4

STATISTICS: CHI-square test: ** $P < 0.01$, *** $P < 0.001$

TABLE 6 MORTALITY

M A L E S

	CONTROL INCIDENCES		0.017 MG/KG INCIDENCES		0.17 MG/KG INCIDENCES		1.7 MG/KG INCIDENCES		CONTROL INCIDENCES	
DAY 0	0	0%	0	0%	0	0%	0	0%	0	0%
DAY 28	0	0%	0	0%	0	0%	0	0%	0	0%
DAY 56	0	0%	0	0%	0	0%	0	0%	0	0%
DAY 84	1	1%	1	1%	0	0%	0	0%	0	0%
DAY 112	1	1%	1	1%	0	0%	0	0%	0	0%
DAY 140	1	1%	1	1%	0	0%	0	0%	0	0%
DAY 168	1	1%	1	1%	0	0%	0	0%	0	0%
DAY 196	1	1%	1	1%	0	0%	0	0%	0	0%
DAY 224	1	1%	1	1%	0	0%	0	0%	0	0%
DAY 252	1	1%	1	1%	0	0%	0	0%	0	0%
DAY 280	1	1%	1	1%	0	0%	0	0%	0	0%
DAY 308	1	1%	1	1%	1	1%	0	0%	0	0%
DAY 336	1	1%	1	1%	1	1%	0	0%	0	0%
DAY 364	2	2%	1	1%	1	1%	0	0%	0	0%
DAY 392	2	2%	1	1%	2	2%	0	0%	0	0%
DAY 420	2	2%	1	1%	2	2%	0	0%	0	0%
DAY 448	3	3%	1	1%	3	3%	0	0%	0	0%
DAY 476	4	4%	1	1%	3	3%	0	0%	2	2%
DAY 504	4	4%	4	4%	4	4%	1	2%	8	8%
DAY 532	4	4%	4	4%	5	5%	1	2%	8	8%
DAY 560	4	4%	4	4%	6	6%	2	4%	9	9%
DAY 588	6	6%	7	7%	7	7%	2	4%	8	9%
DAY 616	6	6%	8	8%	7	7%	2	4%	9	10%
DAY 644	6	6%	8	8%	7	7%	3	6%	10	10%
DAY 672	6	6%	12	12%	8	8%	3	6%	13	13%
DAY 700	11	11%	15	15%	9	9%	4	8%	17	17%
DAY 728	13	13%	15	15%	13	13%	7	14%	22	22%
DAY 756	13	13%	15	15%	14	14%	10	20%	29**	29%

STATISTICS: FISHER EXACT PROBABILITY TEST * P<0.05 ** P<0.01 *** P<0.001 TWO SIDED

R&S 006504

TABLE 6 MORTALITY (CONTINUED 1)

M A L E S

	CONTROL INCIDENCES		0.017 MG/KG INCIDENCES		0.17 MG/KG INCIDENCES		1.7 MG/KG INCIDENCES		CONTROL INCIDENCES	
DAY 784	15	15%	17	17%	16	16%	15	30%	37***	37%
DAY 812	21	21%	25	25%	23	23%	18	36%	47***	47%
DAY 840	28	28%	28	28%	28	28%	21	42%	58***	58%
DAY 868	31	31%	34	34%	34	34%	24	48%	71***	71%
DAY 896	38	38%	43	43%	38	38%	24*	48%	76***	76%
DAY 924	44	44%	51	51%	44	44%	29*	56%	88***	88%
DAY 952	53*	53%	54	54%	53	53%	32**	64%	100***	100%
DAY 980	59	59%	63	63%	59	59%	35**	70%	100***	100%
DAY 1008	72	72%	69	69%	72	72%	39***	78%	100***	100%
DAY 1036	80	80%	80	80%	82	82%	42***	84%	100***	100%

STATISTICS: FISHER EXACT PROBABILITY TEST * P<0.05 ** P<0.01 *** P<0.001 TWO SIDED

TABLE 6 MORTALITY (CONTINUED 2)

F E M A L E S

	CONTROL INCIDENCES		0.017 MG/KG INCIDENCES		0.17 MG/KG INCIDENCES		1.7 MG/KG INCIDENCES		CONTROL INCIDENCES	
DAY 2	0	0%	0	0%	0	0%	0	0%	0	0%
DAY 30	0	0%	0	0%	0	0%	0	0%	0	0%
DAY 58	0	0%	0	0%	0	0%	0	0%	0	0%
DAY 86	0	0%	0	0%	0	0%	0	0%	0	0%
DAY 114	0	0%	0	0%	0	0%	0	0%	0	0%
DAY 142	0	0%	0	0%	0	0%	0	0%	0	0%
DAY 170	0	0%	0	0%	0	0%	0	0%	0	0%
DAY 198	0	0%	0	0%	0	0%	0	0%	0	0%
DAY 226	0	0%	0	0%	0	0%	0	0%	0	0%
DAY 254	0	0%	0	0%	0	0%	0	0%	0	0%
DAY 282	0	0%	0	0%	0	0%	0	0%	0	0%
DAY 310	1	1%	0	0%	0	0%	0	0%	0	0%
DAY 338	1	1%	0	0%	0	0%	0	0%	0	0%
DAY 366	1	1%	0	0%	0	0%	0	0%	0	0%
DAY 394	1	1%	0	0%	1	1%	0	0%	0	0%
DAY 422	1	1%	0	0%	1	1%	0	0%	0	0%
DAY 450	1	1%	0	0%	2	2%	1	2%	0	0%
DAY 478	1	1%	1	1%	2	2%	1	2%	0	0%
DAY 506	2	2%	2	2%	3	3%	2	4%	0	0%
DAY 534	2	2%	2	2%	3	3%	2	4%	0	0%
DAY 562	4	4%	4	4%	3	3%	2	4%	0	0%
DAY 590	5	5%	4	4%	4	4%	5	10%	1	1%
DAY 618	6	6%	4	4%	4	4%	6	12%	2	2%
DAY 646	7	7%	5	5%	7	7%	6	12%	2	2%
DAY 674	10	12%	8	8%	10	10%	6	12%	2*	2%
DAY 702	12	12%	8	8%	12	12%	6	12%	3*	3%
DAY 730	15	15%	11	11%	14	14%	12	24%	7	7%
DAY 758	20	20%	13	13%	19	19%	14	28%	14	14%

STATISTICS: FISHER EXACT PROBABILITY TEST * P<0.05 ** P<0.01 *** P<0.001 TWO SIDED

TABLE 6 MORTALITY (CONTINUED 3)

F E M A L E S

	CONTROL INCIDENCES		0.017 MG/KG INCIDENCES		0.17 MG/KG INCIDENCES		1.7 MG/KG INCIDENCES		CONTROL INCIDENCES	
DAY 786	20	20%	15	15%	19	19%	15	30%	16	16%
DAY 814	26	26%	25	25%	22	22%	16	32%	25	25%
DAY 842	28	28%	32	32%	27	27%	19	38%	37	37%
DAY 870	30	30%	36	36%	30	30%	21	42%	50**	50%
DAY 898	35	35%	41	41%	35	35%	24	48%	58**	58%
DAY 926	41	41%	51	51%	45	45%	28	56%	92***	92%
DAY 954	47	47%	60	60%	52	52%	32*	64%	100***	100%
DAY 982	58	58%	66	66%	61	61%	36**	72%	100***	100%
DAY 1010	66	66%	72	72%	67	67%	43**	86%	100***	100%
DAY 1038	76	76%	77	77%	74	74%	45***	90%	100***	100%

STATISTICS: FISHER EXACT PROBABILITY TEST * P<0.05 ** P<0.01 *** P<0.001 TWO SIDED

TABLE 7 MEAN BODY WEIGHTS (G)

M A L E S

	CONTROL			0.017 MG/KG			0.17 MG/KG			1.7 MG/KG			CONTROL		
	MEAN	SEM	N	MEAN	SEM	N	MEAN	SEM	N	MEAN	SEM	N	MEAN	SEM	N
DAY 0	53.9	0.5	100	53.2	0.5	100	53.2	0.5	100	54.3	0.6	50	51.5	0.5	100
DAY 14	95.7	0.8	100	96.9*	1.0	100	95.8	0.8	100	98.2	1.1	50	89.3**	0.7	100
DAY 28	149.8	1.4	100	147.8	1.6	100	148.9	1.3	100	149.2	1.8	50	141.7*	1.1	100
DAY 56	233.4	2.4	100	223.0**	2.4	100	232.0	2.5	100	224.5*	2.9	50	214.6**	1.5	100
DAY 84	286.4	3.1	99	271.8**	3.0	99	283.3	3.0	100	279.0	3.6	50	251.1**	2.0	100
DAY 112	326.5	3.4	99	309.2**	3.3	99	323.8	3.1	100	316.6	3.9	50	278.1**	2.2	100
DAY 140	344.7	3.5	99	340.2	3.6	99	343.0	3.4	100	348.8	4.4	50	297.5**	2.3	100
DAY 168	367.5	3.7	99	357.0	3.7	99	364.7	3.4	100	364.1	4.7	50	314.5**	2.6	100
DAY 196	376.6	3.7	99	370.8	3.9	99	372.8	3.6	100	384.3	4.8	50	318.5**	2.8	100
DAY 224	386.5	3.9	99	377.7	4.0	99	385.7	3.7	100	389.3	4.9	50	339.8**	2.6	100
DAY 252	388.5	4.0	99	381.2	4.0	99	387.8	3.4	100	387.3	4.7	50	351.4**	2.7	100
DAY 280	403.4	4.0	99	400.0	4.1	99	405.2	3.6	100	408.3	5.1	50	365.0**	2.7	100
DAY 308	411.2	4.2	99	403.3	4.2	99	407.7	3.7	99	414.6	5.2	50	371.0**	2.8	100
DAY 336	416.5	4.2	99	406.5	4.2	99	415.0	3.8	99	417.9	5.0	50	371.3**	3.3	100
DAY 364	413.3	4.2	98	409.1	4.3	99	411.7	3.9	99	418.6	5.1	50	377.8**	3.0	100
DAY 392	410.8	4.2	98	403.6	4.3	99	407.4	3.9	98	419.4	4.9	50	385.2**	3.1	100
DAY 420	404.2	4.1	98	397.3	4.3	99	402.8	3.9	98	411.9	4.8	50	370.9**	2.9	100
DAY 448	404.2	4.2	97	399.0	4.4	99	404.7	4.1	97	413.1	4.8	50	368.0**	2.9	100
DAY 476	405.9	4.4	96	403.3	4.4	99	410.9	4.1	97	414.8	5.1	50	377.3**	3.0	99
DAY 504	400.4	4.2	96	395.2	4.3	96	404.0	4.4	96	409.2	5.0	49	364.0**	3.7	92
DAY 532	415.6	4.1	96	407.5	4.4	96	416.1	4.2	95	420.6	5.0	49	380.7**	3.3	92
DAY 560	419.4	4.1	96	414.9	4.3	96	422.6	4.2	94	426.7	5.5	49	384.3**	3.3	92
DAY 588	414.5	4.1	94	412.5	4.5	93	418.4	4.3	93	423.5	5.3	48	379.9**	3.3	92
DAY 616	419.4	4.2	94	415.9	4.5	92	425.2	4.3	93	429.3	5.5	48	376.7**	3.7	92
DAY 644	428.8	4.3	94	425.9	4.5	92	431.5	4.4	93	438.5	5.8	47	379.7**	4.1	90
DAY 672	431.1	4.2	94	427.5	4.7	89	437.8	4.5	92	446.5	6.1	47	381.2**	4.3	87
DAY 700	427.8	4.0	89	424.8	4.8	86	431.4	4.4	91	440.4	5.8	46	365.9**	4.5	83
DAY 728	425.4	4.0	88	421.2	4.8	85	428.0	4.4	87	428.8	7.4	44	357.2**	4.9	78
DAY 756	419.8	4.2	87	418.5	4.7	85	423.3	4.6	86	423.9	6.9	40	344.8**	5.5	71

STATISTICS: COVAR + DUNNETT TESTS * P<0.05 ** P<0.01 TWO SIDED (EXP.UNIT = ANIMAL)

R&S 006508

TABLE 7 MEAN BODY WEIGHTS (G) (CONTINUED 1)

M A L E S

	CONTROL			0.017 MG/KG			0.17 MG/KG			1.7 MG/KG			CONTROL		
	MEAN	SEM	N	MEAN	SEM	N	MEAN	SEM	N	MEAN	SEM	N	MEAN	SEM	N
DAY 784	408.6	4.0	85	406.3	4.8	83	409.4	4.6	84	414.9	6.7	35	322.9**	5.4	63
DAY 812	394.8	3.9	79	395.5	4.9	75	402.9	4.5	77	403.5	7.1	32	302.5**	5.5	58
DAY 840	393.3	3.9	72	400.0	4.7	72	400.6	4.7	72	398.3	5.9	29	297.9**	7.0	41
DAY 868	387.4	3.8	69	390.6	5.0	67	394.8	4.7	66	393.7	5.7	26	299.3**	7.8	29
DAY 896	376.6	4.3	62	383.7	5.6	59	386.3	4.5	62	382.5	6.1	26	288.1**	9.0	24
DAY 924	365.6	4.3	56	372.9	5.8	49	371.2	4.4	56	380.0	7.8	21	329.8	20.4	2
DAY 952	361.7	4.1	47	368.7	6.4	47	363.4	4.7	47	368.6	7.7	18	--	--	0
DAY 980	352.9	4.4	41	359.5	6.1	38	360.2	4.9	43	363.3	8.0	16	--	--	0
DAY1008	346.5	5.2	30	360.7	6.5	31	358.6	6.3	28	354.2	7.4	11	--	--	0
DAY1036	341.3	5.2	21	356.6	5.5	20	356.3	6.2	19	366.7	7.8	8	--	--	0
DAY1043	343.8	5.3	20	359.3	5.6	20	358.1	6.3	18	368.7	7.9	8	--	--	0

STATISTICS: COVAR + DUNNETT TESTS * P<0.05 ** P<0.01 TWO SIDED (EXP.UNIT = ANIMAL)

TABLE 7 MEAN BODY WEIGHTS (G) (CONTINUED 2)

F E M A L E S

	CONTROL			0.017 MG/KG			0.17 MG/KG			1.7 MG/KG			CONTROL		
	MEAN	SEM	N	MEAN	SEM	N	MEAN	SEM	N	MEAN	SEM	N	MEAN	SEM	N
DAY 0	52.8	0.5	100	52.9	0.5	100	51.5	0.5	100	51.2	0.7	50	52.8	0.4	100
DAY 16	92.7	0.8	100	92.5	0.7	100	90.1	0.7	100	88.5*	1.2	50	90.4**	0.8	100
DAY 30	118.9	0.9	100	120.2	0.9	100	120.1	0.9	100	117.9	1.3	50	117.4	0.9	100
DAY 58	151.4	1.1	100	153.4	1.1	100	153.6	1.0	100	152.0	1.5	50	160.0**	1.2	100
DAY 86	164.7	1.3	100	166.2	1.4	100	168.6*	1.2	100	167.8	1.8	50	167.3	1.4	100
DAY 114	178.0	1.4	100	175.2	1.5	100	178.5	1.3	100	178.8	2.0	50	176.3	1.5	100
DAY 142	183.3	1.5	100	183.4	1.7	100	184.0	1.5	100	187.8	2.1	50	182.8	1.5	100
DAY 170	188.4	1.6	100	187.2	1.7	100	190.6	1.5	100	194.3*	2.2	50	188.9	1.6	100
DAY 198	189.6	1.6	100	192.9	1.8	100	190.8	1.6	100	194.8	2.4	50	193.0	1.6	100
DAY 226	193.9	1.7	100	192.7	1.8	100	195.6	1.7	100	195.4	2.3	50	195.8	1.6	100
DAY 254	199.0	1.6	100	201.0	1.7	100	201.8	1.6	100	203.3	2.4	50	205.2	1.8	100
DAY 282	202.9	1.6	100	203.7	1.9	100	205.9	1.6	100	205.5	2.6	50	206.7	1.8	100
DAY 310	210.2	1.7	99	209.7	2.0	100	210.8	1.7	100	212.3	2.8	50	212.3	1.9	100
DAY 338	209.2	1.7	99	208.1	2.0	100	210.8	1.9	100	213.1	2.8	50	210.0	1.8	100
DAY 366	211.5	1.8	99	212.4	2.1	100	211.6	1.8	100	214.6	3.1	50	211.5	1.9	100
DAY 394	212.1	1.9	99	210.8	2.1	100	212.9	1.9	99	217.3	3.1	50	213.2	1.9	100
DAY 422	207.9	1.9	99	207.6	2.1	100	209.0	1.9	99	212.7	3.0	50	209.7	1.8	100
DAY 450	210.1	1.9	99	210.3	2.1	100	213.4	1.9	98	217.0	3.2	49	211.2	1.9	100
DAY 478	214.0	2.1	99	212.6	2.2	99	215.4	2.0	98	217.9	3.3	49	215.9	2.0	100
DAY 506	213.8	2.0	98	213.1	2.2	98	216.0	2.0	97	217.0	3.3	48	210.8	2.0	100
DAY 534	218.6	2.3	98	217.6	2.5	98	218.4	2.2	97	222.2	3.6	48	219.1	2.0	100
DAY 562	220.7	2.5	96	219.0	2.5	96	221.8	2.2	97	223.3	3.7	48	219.3	2.1	100
DAY 590	225.3	2.8	95	222.7	2.7	96	226.5	2.4	96	228.0	3.5	46	221.9	2.1	99
DAY 618	226.3	2.5	94	227.0	2.8	96	230.3	2.5	96	232.9	3.8	44	223.2	2.2	98
DAY 646	231.7	2.7	93	231.9	2.9	95	235.8	2.6	93	240.8	4.0	44	227.7	2.2	98
DAY 674	237.0	2.7	90	236.0	3.0	93	241.0	2.7	91	245.1	4.2	44	226.8*	2.4	98
DAY 702	235.8	2.7	89	234.4	3.0	92	240.0	2.8	89	242.8	4.4	44	224.0**	2.6	98
DAY 730	232.5	2.7	86	232.3	3.0	90	238.8	2.7	86	237.0	4.0	38	21[illegible].8**	2.4	94
DAY 758	232.9	3.0	80	234.6	3.2	87	240.2	2.9	81	237.4	4.2	36	219.0**	2.5	86

STATISTICS: COVAR + DUNNETT TESTS * P<0.05 ** P<0.01 TWO SIDED (EXP.UNIT = ANIMAL)

TABLE 7 MEAN BODY WEIGHTS (G) (CONTINUED 3)

F E M A L E S

	CONTROL			0.017 MG/KG			0.17 MG/KG			1.7 MG/KG			CONTROL		
	MEAN	SEM	N	MEAN	SEM	N	MEAN	SEM	N	MEAN	SEM	N	MEAN	SEM	N
DAY 786	230.7	2.8	80	230.7	3.2	85	235.4	2.8	81	232.9	3.7	35	209.8**	2.8	84
DAY 814	224.0	2.6	74	227.0	3.1	78	232.1	2.7	78	227.9	3.7	34	207.7**	2.8	77
DAY 842	224.2	2.7	72	224.0	3.4	69	231.8	2.8	74	227.4	4.4	31	203.1**	3.4	65
DAY 870	222.7	2.9	70	222.7	3.6	65	227.3	2.9	70	227.1	4.2	29	203.3**	3.7	50
DAY 898	217.9	2.9	66	221.0	3.9	59	223.3	3.2	66	227.0	4.9	26	200.6**	4.0	42
DAY 926	216.6	2.8	59	217.7	3.8	49	220.8	2.9	55	224.6	5.4	22	217.6	4.3	8
DAY 954	212.3	3.0	54	212.8	4.3	41	215.1	3.0	48	217.2	5.5	19	--	--	0
DAY 982	211.1	3.3	43	214.4	4.6	34	212.1	3.8	42	194.2	4.8	14	--	--	0
DAY1010	212.7	3.4	36	216.0	5.1	28	221.1	3.5	33	208.6	3.7	7	--	--	0
DAY1038	212.4	3.6	23	215.1	5.7	23	218.4	4.1	25	214.2	3.1	4	--	--	0
DAY1042	214.9	3.3	21	215.2	5.7	23	217.7	4.2	25	212.2	3.8	4	--	--	0

STATISTICS: COVAR + DUNNETT TESTS * P<0.05 ** P<0.01 TWO SIDED (EXP.UNIT = ANIMAL)

[illegible] IN RATS WITH TCP IN THE DIET

TABLE 8 MEAN BODY WEIGHTS (G).

MALES

	CONTROL			0.017 MG/KG			0.17 MG/KG			1.7 MG/KG			CONTROL	
	MEAN	SEM	N	MEAN	SEM	N	MEAN	SEM	N	MEAN	SEM	N	MEAN	SEM
DAY 0	51.4	2.0	10	53.4	2.1	10	55.5	1.5	10	56.4	1.0	10	54.9	1.5
DAY 14	89.4	2.5	10	94.0	2.4	10	96.9	2.0	10	97.0	1.0	10	96.4	2.3
DAY 28	141.6	3.1	10	146.3	3.2	10	139.5	9.1	10	149.5	2.0	10	147.7	4.[illegible]
DAY 56	229.2	4.6	10	232.8	5.4	10	230.4	4.3	9	224.9	3.2	10	218.1	8.4
DAY 84	276.4	4.8	10	288.7	6.3	10	289.4	6.5	9	280.3	5.0	10	246.0**	9.0
DAY 112	312.1	5.1	10	325.9	7.3	10	325.7	8.8	9	321.0	7.2	10	270.3**	9.2
DAY 140	336.1	5.4	10	354.7	10.2	10	350.7	9.6	9	341.9	6.3	10	286.9**	9.6
DAY 168	360.4	7.1	10	374.5	8.3	10	372.3	10.6	9	360.8	6.1	10	306.5**	9.7
DAY 196	373.5	6.2	10	384.2	9.7	10	377.5	9.5	9	379.6	4.9	10	314.6**	8.8
DAY 224	383.4	7.4	10	385.5	12.2	10	388.4	8.5	9	391.1	5.5	10	337.8**	9.5
DAY 252	382.6	12.7	10	395.4	9.7	10	394.2	9.4	9	394.1	7.0	10	340.6*	8.1
DAY 280	417.1	11.9	5	425.5	8.5	5	393.1	6.5	4	412.3	10.1	5	352.3**	16.3
DAY 308	424.6	9.4	5	434.3	12.2	5	392.4	6.5	4	415.1	10.0	5	361.3**	16.7
DAY 336	430.3	10.3	5	439.9	13.2	5	400.1	7.8	4	418.4	8.2	5	364.1**	16.3
DAY 364	413.0	9.7	5	440.0	13.0	5	395.6	5.6	4	421.4	8.9	5	373.1	14.9
DAY 392	419.7	8.1	5	436.0	11.9	5	391.0	5.8	4	421.8	8.4	5	372.9*	15.6
DAY 420	416.5	6.6	5	432.6	10.4	5	379.2	12.7	4	413.2	8.8	5	359.2**	18.1
DAY 448	413.7	10.1	5	434.0	10.9	5	382.4	9.3	4	417.9	8.1	5	356.0**	16.9
DAY 476	422.1	10.8	5	421.8	8.8	5	381.5	12.1	4	421.8	7.5	5	359.6**	16.5
DAY 504	413.5	9.8	5	405.4	10.2	5	374.9	14.1	4	408.7	4.8	5	353.1**	15.7
DAY 532	426.6	11.6	5	423.2	9.2	5	395.1	14.9	4	422.7	6.8	5	369.2*	17.9

STATISTICS: ANOVA + DUNNETT TESTS * P<0.05 ** P<0.01 TWO SIDED (EXP.UNIT = ANIMAL)

STUDY NO 126 18-MONTH STUDY IN RATS WITH VCM IN THE DIET

TABLE 8 MEAN BODY WEIGHTS (G). (CONTINUED)

F E M A L E S

	CONTROL			0.017 MG/KG			0.17 MG/KG			1.7 MG/KG			CONTROL	
	MEAN	SEM	N	MEAN	SEM	N	MEAN	SEM	N	MEAN	SEM	N	MEAN	SEM
DAY 0	53.3	1.4	10	54.3	1.7	10	54.7	1.6	10	52.5	1.6	10	50.4	1.6
DAY 16	95.4	1.8	10	92.2	2.7	10	95.2	1.9	10	87.2	2.9	10	85.7*	2.1
DAY 30	119.8	2.5	10	119.3	2.8	10	123.1	2.4	10	116.2	3.3	10	111.8	2.4
DAY 58	150.3	2.7	10	154.5	3.7	9	154.4	3.1	10	147.9	4.0	10	152.2	2.9
DAY 86	161.7	3.8	10	168.9	3.6	9	166.3	3.3	10	162.7	4.8	10	160.9	4.4
DAY 114	172.3	4.0	10	179.5	3.4	9	178.5	4.1	10	175.6	5.8	10	173.6	4.9
DAY 142	177.8	4.9	10	185.3	3.4	9	185.9	4.6	10	182.1	5.5	10	179.6	4.3
DAY 170	187.8	5.1	10	193.3	3.9	9	190.7	4.9	10	195.9	6.1	10	184.8	5.4
DAY 198	185.9	5.4	10	193.9	3.4	9	191.0	4.2	10	188.9	6.0	10	186.2	4.8
DAY 226	187.7	5.5	10	195.9	3.6	9	196.7	5.0	10	191.0	5.6	10	190.4	5.4
DAY 254	195.3	5.5	10	204.8	3.2	9	201.3	4.3	10	199.4	6.1	10	198.3	5.7
DAY 282	195.7	3.2	5	209.8	3.0	5	195.1	7.2	5	198.3	11.3	5	204.7	5.0
DAY 310	197.3	4.5	5	214.3	5.1	5	202.2	8.3	5	202.3	11.9	5	211.4	5.8
DAY 338	198.7	3.0	5	213.2	4.4	5	199.5	6.9	5	201.7	10.5	5	211.6	6.0
DAY 366	200.7	5.2	5	220.3	5.5	5	198.2	8.1	5	201.6	10.4	5	215.4	5.6
DAY 394	203.1	5.3	5	216.5	6.1	5	198.7	8.4	5	204.0	10.6	5	214.0	6.4
DAY 422	198.8	5.5	5	215.6	6.4	5	199.6	8.1	5	199.5	10.1	5	210.7	5.3
DAY 450	201.4	5.9	5	217.1	6.8	5	201.0	7.5	5	204.2	11.0	5	212.2	5.7
DAY 478	208.0	6.4	5	219.1	7.8	5	200.7	8.1	5	205.2	11.2	5	217.2	6.4
DAY 506	209.8	5.5	5	225.2	7.9	5	202.2	8.8	5	205.8	11.3	5	214.2	5.1
DAY 534	214.5	7.0	5	226.6	9.1	5	204.3	9.0	5	209.4	12.4	5	223.0	6.0

STATISTICS: ANOVA + DUNNETT TESTS * P<0.05 ** P<0.01 TWO SIDED (EXP.UNIT = ANIMAL)

CIVO/TNO
STUDY NO 125 CARCINOGENICITY STUDY IN RATS WITH VCM IN THE DIET

TABLE 9 MEAN FOOD INTAKE

Group	Intended intake levels of VCM (mg/kg b.w./day	Food intake (g/rat/day) in week 1	2	3	4	11	12	23	24	35	36	47	48	59
	MALES													
A	0	8.9	10.3	12.3	14.4	16.1	16.1	16.5	16.3	15.3	16.7	15.7	17.0	17.1
B	0.017	7.4	9.7	11.1	13.5	14.0	14.5	14.5	14.0	14.8	15.5	14.6	15.3	16.6
C	0.17	7.7	10.3	11.9	14.7	15.6	15.6	17.4	17.0	15.5	16.6	15.8	17.1	15.9
D	1.7	7.8	10.4	12.1	14.5	14.7	15.3	17.4	17.0	15.9	15.5	15.5	16.4	17.0
E	0	8.2	10.3	12.4	13.5	12.5	13.3	12.5	11.9	13.3	12.9	12.3	13.0	12.5
	FEMALES													
A	0	8.9	10.0	9.9	10.7	10.4	10.2	9.2	9.1	9.3	9.8	10.6	10.2	9.9
B	0.017	8.3	9.8	10.4	11.0	10.2	10.0	9.0	9.2	10.3	10.5	9.4	9.8	9.6
C	0.17	8.5	9.7	11.5	12.0	11.0	10.8	10.8	10.4	10.3	11.3	10.3	10.6	10.0
D	1.7	8.3	9.4	10.4	10.6	11.0	10.7	9.3	9.6	10.8	11.1	9.3	10.4	10.3
E	0	8.3	9.3	10.2	9.9	9.4	10.3	9.1	9.2	9.9	9.7	9.8	9.9	10.0

CIVO/TNO
STUDY NO 125 CARCINOGENICITY STUDY IN RATS WITH VCM IN THE DIET

TABLE 9 MEAN FOOD INTAKE (CONT.)

Group	Intended intake levels of VCM (mg/kg b.w./day	Food intake (g/rat/day) in week 60	73	74	85	86	97	98	109	110	121	122
	MALES											
A	0	16.2	16.5	16.6	14.4	16.2	14.7	14.2	15.2	15.0	15.9	16.1
B	0.017	15.2	15.9	16.1	13.6	14.6	14.6	15.2	15.4	14.5	14.6	15.0
C	0.17	16.1	17.5	17.3	15.0	16.3	15.4	15.9	15.7	15.7	15.8	15.8
D	1.7	15.8	18.2	17.5	15.7	14.9	15.7	15.6	16.1	15.4	14.2	15.8
E	0	12.6	13.3	13.3	13.0	12.4	12.3	11.6	11.4	11.2	12.3	12.5
	FEMALES											
A	0	9.7	10.4	9.0	8.9	9.7	9.7	9.6	10.1	10.2	10.8	10.8
B	0.017	10.0	10.9	10.5	9.9	9.3	10.4	11.8	10.5	10.4	11.7	12.1
C	0.17	9.9	12.0	11.0	9.8	10.8	10.4	10.9	11.0	10.4	11.4	11.6
D	1.7	9.7	11.1	10.6	10.1	9.9	10.8	10.9	11.4	10.5	11.3	13.3
E	0	9.5	9.8	10.3	9.2	9.2	8.8	8.7	9.7	9.2	10.0	11.0

CIVO/TNO
STUDY NO 125 CARCINOGENICITY STUDY IN RATS WITH VCM IN THE DIETS

TABLE 10 FOOD INTAKE DURI.G THE FOUR-HOUR FEEDING PERIOD

Group	Intended oral intake levels of VCM (mg/kg b.w./day)	Food intake during the feeding-period over periods of one hour[1] expressed as g/rat					expressed as %-tage of total food consumed per rat over the 4-hr period			
		0-1	1-2	2-3	3-4	TOTAL	0-1	1-2	2-3	3-4
	MALES									
A	0	11.6[2]	2.7	2.0	1.9	18.2	64	15	11	10
		0.87	0.29	0.27	0.31	0.62				
B	0.017	9.9	3.2	2.3	1.8	17.2	58	19	13	10
		0.66	0.29	0.11	0.17	0.71				
C	0.17	10.5	3.0	2.5	1.7	17.7	59	17	14	10
		0.58	0.27	0.23	0.16	0.60				
D	1.7	10.7	3.6	2.3	2.0	18.5	58	19	12	11
		0.90	0.34	0.25	0.29	0.95				
E	0	8.8	2.6	1.7	1.6	14.6	60	18	11	11
		0.66	0.24	0.17	0.15	0.69				
overall							60	18	12	10
	FEMALES									
A	0	6.6	2.1	1.7	1.7	12.1	55	17	14	14
		0.32	0.19	0.10	0.26	0.40				
B	0.017	6.5	2.4	1.6	1.5	12.0	54	20	13	13
		0.44	0.23	0.19	0.18	0.53				
C	0.17	6.5	2.3	1.9	1.6	12.3	53	19	15	13
		0.30	0.20	0.18	0.24	0.30				
D	1.7	7.1	2.3	1.8	1.6	12.8	55	18	14	13
		0.46	0.21	0.16	0.17	0.62				
E	0	6.2	2.1	1.5	1.6	11.4	54	19	13	14
		0.36	0.13	0.14	0.18	0.31				
overall							54	19	14	13

1) Food intake figures are the means of 11 different determinations.
2) Standard error of the mean

TABLE 11 MEAN HAEMATOLOGICAL FINDINGS RECORDED AT DAY 94,185 AND 367

M A L E S

		DAY 94 THROMBOC (10E9/L)	DAY 185 THROMBOC (10E9/L)	DAY 367 THROMBOC (10E9/L)	DAY 94 PTT (SEC)	DAY 185 PTT (SEC)	DAY 367 PTT (SEC)
CONTROL	MEAN	982.	898.	946.	55.0	36.8	49.3
	SEM	27.	17.	23.	1.7	0.8	1.4
	N	10	10	5	10	10	5
0.017 MG/KG	MEAN	1036.	915.	855.	52.9	35.2	50.1
	SEM	33.	43.	43.	1.5	0.4	2.7
	N	10	8	5	10	8	5
0.17 MG/KG	MEAN	1008.	860.	895.	53.0	37.2	50.5
	SEM	23.	45.	21.	2.2	0.6	0.6
	N	8	9	4	9	9	4
1.7 MG/KG	MEAN	996.	825.	930.	50.8	37.0	50.2
	SEM	25.	51.	63.	1.3	0.7	1.8
	N	10	10	5	10	8	5
CONTROL	MEAN	866.	879.	872.	54.2	39.0	52.5
	SEM	50.	31.	32.	2.3	0.5	1.2
	N	9	10	5	8	10	5

STATISTICS: MANN/WHITNEY U-TEST * P<0.05 ** P<0.02 *** P<0.002 TWO SIDED (EXP.UNIT = ANIMAL)
THROMBOC = THROMBOCYTE
PTT = PROTHROMBIN TIME

STUDY NO. 126 18-MONTH STUDY IN RATS WITH VCM IN THE [illegible]

TABLE 11 MEAN HAEMATOLOGICAL FINDINGS RECORDED AT DAY 97,184 AND 366

F E M A L E S

		DAY 97	DAY 184	DAY 366	DAY 97	DAY 184	DAY 366
		THROMBOC (10E9/L)	THROMBOC (10E9/L)	THROMBOC (10E9/L)	PTT (SEC)	PTT (SEC)	PTT (SEC)
CONTROL	MEAN	927.	972.	879.	41.6	33.2	40.1
	SEM	19.	27.	26.	0.8	0.5	1.2
	N	10	10	5	10	9	3
0.017 MG/KG	MEAN	915.	1032.	930.	40.2	32.8	43.6
	SEM	27.	34.	106.	0.8	0.4	2.8
	N	9	9	3	9	9	4
0.17 MG/KG	MEAN	904.	871.**	904.	43.1	33.0	39.4
	SEM	14.	23.	24.	1.6	1.0	1.2
	N	10	9	4	10	8	5
1.7 MG/KG	MEAN	863.	1018.	986.*	47.4**	36.2	38.6
	SEM	34.	22.	20.	2.1	1.7	1.7
	N	10	9	4	8	9	5
CONTROL	MEAN	943.	1010.	929.	51.3***	37.0***	39.9
	SEM	28.	29.	131.	1.9	0.7	1.0
	N	10	10	3	10	9	4

STATISTICS: MANN/WHITNEY U-TEST * P<0.05 ** P<0.02 *** P<0.002 TWO SIDED (EXP.UNIT = ANIMAL)
THROMBOC = THROMBOCYTE
PTT = PROTHROMBIN TIME

TABLE 12 MEAN NON-PROTEIN BOUND SULFHYDRYL ("GLUTATHIONE") CONTENT OF LIVERS OF RATS FED VCM FOR 9 AND 18 MONTHS

Group	Intended exposure levels of VCM (mg/kg/day)	Non-protein bound liver SH in umol glutathione/g liver in months			
		9	18	9	18
		MALES		FEMALES	
A	0	7.58	7.52	6.05	5.58
		0.34	0.38	0.34	0.63
B	0.017	7.32	7.57	5.66 (4)	5.69
		0.38	0.47	0.18	0.14
C	0.17	7.38	7.33 (4)	5.95	5.95
		0.29	0.28	0.29	0.31
D	1.7	7.30	7.63	6.57	6.13
		0.22	0.22	0.36	0.43
E	0	7.31	7.44	6.52	6.30
		0.36	0.38	0.58	0.29

Under each mean the standard error of the mean is given.

In brackets number of rats if not 5.

:IVO/TNO

STUDY NO 125 CARCINOGENICITY STUDY IN RATS WITH VCM IN THE DIET

ABLE 13. MACROSCOPIC PATHOLOGY

Site and type of observations	Incidence of observations									
	MALES					FEMALES				
	mg VCM/kg b.w./day					mg VCM/kg b.w./day				
	0	.017	0.17	1.7	0	0	.017	0.17	1.7	0
Initial number of animals	100	100	100	50	100	100	100	100	50	100
Effective number of animals	99	100	99	49	100	98	100	96	49	100
MODE OF DEATH:										
a. found dead	26	26	25	16	10	8	15	9	5	8
b. killed in extremis	54	54	57	27	90	71	62	67	41	92
c. terminal sacrifice	20	20	18	7	0	21	23	24	4	0
AUTOLYSIS/CANNIBALISM:										
a. slightly autolytic	10	15	13	8	9	3	6	4	2	6
b. partially lost	11	4	4	9	1	0	6	4	2	5
c. completely lost	1	0	1	1	0	2	0	4	1	0
SKIN / SUBCUTIS										
1. tumour or suspected of tumour	5	7	9	3	3	5	3	3	2	3
2. alopecia	4	1	7	2	3	10	9	9	4	8
3. edema	2	3	2	1	0	1	1	1	0	0
4. haemorrhage	0	0	1	0	0	0	0	0	0	0
5. injury	0	0	2	0	1	0	0	0	0	1
AXILLARY LYMPH NODES										
1. tumour or suspected of tumour	3	2	0	0	0	0	0	0	1	0
2. enlarged	2	2	0	0	0	0	1	2	0	1
3. reddish	1	0	0	0	0	0	0	0	0	0
PREPUTIAL -/CLITORAL GLANDS										
1. tumour or suspected of tumour	3	5	2	1	2	3	1	0	2	0
2. evidence of inflammation	7	6	11	2	2	5	5	1	3	5
3. enlarged	0	1	1	0	0	0	0	1	1	0
4. small	0	0	2	0	0	0	0	0	0	0
5. cyst	0	0	0	0	0	0	1	0	0	0
MAMMARY GLANDS										
1. tumour or suspected of tumour	8	14	7	3	3	39	25	28	18	23
2. evidence of secretory activity	12	6	8	2	6	53	35	41	21	29
3. haemorrhage	0	0	1	0	0	0	0	0	0	0
ABDOMINAL CAVITY										
1. tumour or suspected of tumour	1	2	1	1	0	6	8	5	2	6
2. ascites	3	5	3	2	0	5	5	5	4	6

TABLE 13. MACROSCOPIC PATHOLOGY (CONTINUED 1)

Site and type of observations	Incidence of observations									
	MALES					FEMALES				
	mg VCM/kg b.w./day					mg VCM/kg b.w./day				
	0	.017	0.17	1.7	0	0	.017	0.17	1.7	0
SPLEEN										
1. tumour or suspected of tumour	0	1	0	1	0	0	1	0	0	3
2. splenomegaly	8	14	7	3	2	4	2	4	3	2
3. atrophy	0	0	0	0	1	0	0	0	1	0
4. granular surface	2	0	1	1	0	0	0	1	1	0
5. small	1	0	0	1	1	0	0	2	0	0
6. small nodule	0	0	0	0	1	0	0	0	0	0
7. dark	0	0	0	0	0	0	1	0	0	0
ADRENALS										
1. tumour or suspected of tumour	7	5	2	0	1	5	5	2	0	1
2. small (unilateral)	1	0	1	0	1	1	1	0	0	0
3. haemorrhagic	0	0	0	0	0	1	1	1	0	0
4. discoloured a. pale	1	0	1	1	13	2	0	1	2	1
b. dark	3	6	1	0	2	4	2	7	4	7
5. spotted	9	8	7	1	2	26	25	27	14	23
6. enlarged a. unilateral	6	2	8	2	1	21	9	6	4	7
b. bilateral	3	2	2	2	1	1	1	5	1	4
KIDNEYS										
1. tumour or suspected of tumour	0	2	3	0	0	0	2	0	0	0
2. granular surface	11	10	9	1	8	5	2	2	0	0
3. unilateral hydronephrosis	1	1	0	1	0	3	2	3	0	0
4. discoloured a. pale	5	2	7	2	3	3	1	1	0	0
b. dark	1	0	2	0	1	0	1	0	0	1
c. greenish	1	1	2	0	0	3	3	1	3	0
d. reddish	0	0	0	0	1	0	0	0	0	0
5. cyst(s)	5	4	4	2	4	1	4	3	0	1
6. enlarged	3	2	4	0	2	1	1	2	0	0
7. small	0	0	0	0	0	0	1	0	0	0
8. spotted	1	0	0	0	1	0	0	0	0	1
STOMACH										
1. enlarged/swollen	4	1	6	3	6	1	4	3	2	0
2. haemorrhage/erosion	1	6	5	4	1	0	6	1	2	2
3. rough inner surface	1	0	0	0	0	0	0	0	0	0
4. thickened cardial/fundic wall	0	1	0	0	0	1	0	0	0	0
5. thin fundic wall	0	0	1	0	0	0	0	0	0	0
6. trichobezoar	0	2	1	0	1	0	2	2	1	2

CIVO/TNO

STUDY NO 125 CARCINOGENICITY STUDY IN RATS WITH VCM IN THE DIET

TABLE 13. MACROSCOPIC PATHOLOGY (CONTINUED 2)

Site and type of observations	Incidence of observations									
	MALES					FEMALES				
	mg VCM/kg b.w./day					mg VCM/kg b.w./day				
	0	.017	0.17	1.7	0	0	.017	0.17	1.7	0
SMALL INTESTINES										
1. tumour or suspected of tumour	0	2	0	0	0	0	0	0	0	0
2. prominent Peyers's patches	3	4	0	0	0	1	0	0	1	2
3. enlarged/swollen	3	3	3	1	0	3	1	0	0	0
4. haemorrhage	1	2	2	1	0	0	1	0	0	0
5. reddish	1	0	1	0	0	0	0	0	0	0
6. filled with watery fluid	0	0	1	0	1	0	0	0	0	0
COECUM										
1. tumour or suspected of tumour	0	0	1	0	0	0	0	0	0	0
2. enlarged/swollen	8	5	7	5	3	3	3	0	0	0
3. small	0	1	0	0	0	0	0	0	0	0
4. filled with watery fluid	0	0	0	0	1	0	0	0	0	0
COLON										
1. tumour or suspected of tumour	1	0	0	0	0	1	0	0	0	0
2. enlarged/swollen	0	2	2	2	0	1	0	0	0	0
3. filled with watery fluid	0	0	0	0	1	0	0	0	0	0
4. accreted to the cervix	0	0	0	0	0	0	0	1	0	0
MESENTERY										
1. tumour or suspected of tumour	0	1	2	0	0	2	2	4	0	3
2. edema	0	0	4	0	0	1	0	0	0	0
3. dilated blood-vessel	4	4	3	1	0	5	4	1	1	3
4. thrombus in blood-vessel	0	0	1	0	0	0	0	0	0	0
5. haemorrhage	0	0	0	0	0	0	0	1	0	0
PANCREAS										
1. tumour or suspected of tumour	2	1	1	0	0	4	4	2	4	5
2. discoloured a. pale	2	0	0	2	1	0	0	0	1	2
b. dark	4	0	3	0	1	1	2	2	0	2
c. reddish	1	0	1	0	0	0	0	0	1	0
3. edema	0	1	1	0	0	0	0	0	0	0
4. spotted	3	0	0	0	0	0	0	0	0	0
5. small haemorrhages	0	0	0	0	0	1	0	0	0	0
MESENTERIC LYMPH NODES										
1. tumour or suspected of tumour	4	2	2	0	0	4	4	2	3	2
2. enlarged	3	3	1	1	1	6	1	3	0	0
3. small	0	1	1	0	1	2	1	2	1	1
4. edema	0	0	2	0	3	2	1	1	0	3
5. haemorrhagic	1	0	0	0	0	0	0	0	0	1

13. MACROSCOPIC PATHOLOGY (CONTINUED 3)

...ce and type of observations		Incidence of observations									
		MALES					FEMALES				
		mg VCM/kg b.w./day					mg VCM/kg b.w./day				
		0	.017	0.17	1.7	0	0	.017	0.17	1.7	0
...iscoloured	a. pale	1	0	0	1	0	0	0	0	0	0
	b. dark	1	0	1	0	0	0	0	0	0	0
	c. greenish	0	0	0	0	0	0	0	1	0	0
	d. reddish	0	0	2	0	0	0	0	2	1	1
...EY BLADDER											
...our or suspected of tumour		0	0	1	0	0	1	1	0	0	0
...morrhage		1	2	0	0	0	0	0	2	0	0	0
...rged/swollen		1	2	0	0	2	3	2	1	0	0
...culus/concrements		0	0	1	0	0	0	0	0	0	0
...L VESICLES											
...ur or suspected of tumour		0	1	0	0	0	-	-	-	-	-
...ence of inflammation		2	1	1	0	0	-	-	-	-	-
...rged		1	0	0	0	0	-	-	-	-	-
...phy		4	5	10	3	27	-	-	-	-	-
...TION GLANDS											
...ur or suspected of tumour		1	1	0	0	0	-	-	-	-	-
...ence of inflammation		1	0	0	0	0	-	-	-	-	-
...rged		0	0	0	0	0	-	-	-	-	-
...phy		3	5	9	3	27	-	-	-	-	-
...E											
...our or suspected of tumour		0	5	3	0	1	-	-	-	-	-
...dence of inflammation		1	2	0	0	0	-	-	-	-	-
...arged		1	1	0	0	1	-	-	-	-	-
...rophy		4	1	2	1	8	-	-	-	-	-
...S											
...our or suspected of tumour		3	0	4	0	0	-	-	-	-	-
...rophy	a. unilateral	14	10	18	5	7	-	-	-	-	-
	b. bilateral	10	9	6	5	22	-	-	-	-	-
...larged (unilateral)		2	0	2	1	0	-	-	-	-	-
...ptochismus		1	0	1	1	2	-	-	-	-	-
...DYMIDES											
...our or suspected of tumour		1	0	0	0	0	-	-	-	-	-
...idence of inflammation		0	0	1	0	0	-	-	-	-	-
...rophy		2	0	0	0	1	-	-	-	-	-
...Haemorrhage		1	0	0	0	0	-	-	-	-	-

STUDY NO 125 CARCINOGENICITY STUDY IN RATS WITH VCM IN THE DIET

TABLE 13. MACROSCOPIC PATHOLOGY (CONTINUED 4)

Site and type of observations	Incidence of observations									
	MALES					FEMALES				
	mg VCM/kg b.w./day					mg VCM/kg b.w./day				
	0	.017	0.17	1.7	0	0	.017	0.17	1.7	0
OVARIES										
1. tumour or suspected of tumour	-	-	-	-	-	6	4	2	3	5
2. cyst(s)	-	-	-	-	-	8	11	15	3	7
3. enlarged	-	-	-	-	-	5	2	4	2	7
4. reddish	-	-	-	-	-	2	1	1	1	0
UTERUS										
1. tumour or suspected of tumour	-	-	-	-	-	21	29	28	11	33
2. hydrometra	-	-	-	-	-	2	1	1	3	2
3. evidence of inflammation	-	-	-	-	-	1	1	0	0	0
4. pyometra	-	-	-	-	-	0	2	0	0	0
5. enlarged/swollen	-	-	-	-	-	10	2	2	2	7
LIVER										
1. tumour or suspected of tumour	1	1	2	7	1	2	1	3	8	0
2. prominent lobular pattern	1	4	2	0	0	0	1	3	1	0
3. swollen/enlarged	2	4	5	1	0	3	2	0	0	0
4. discoloured a. pale	3	2	0	1	0	1	3	1	2	1
b. dark	3	3	0	0	1	0	0	0	1	0
5. cyst(s)	2	1	5	4	0	17	14	22	33	3
6. small	0	1	1	0	2	0	0	2	0	0
7. small surface lesions (rosette, constriction)	1	0	1	0	1	3	0	0	0	1
8. spotted	5	6	8	2	3	2	1	6	2	2
9. granular surface	2	0	0	2	0	0	1	2	0	0
THORACIC CAVITY										
. tumour or suspected of tumour	0	0	0	0	0	0	0	0	0	0
. hydrothorax	3	5	8	3	0	2	6	2	1	0
. haemothorax	4	8	7	4	0	5	1	0	0	0
THYMUS										
. tumour or suspected of tumour	1	1	0	0	0	0	0	0	2	0
. enlarged	0	1	0	0	0	1	0	0	0	1
. spotted	1	0	0	0	0	0	0	0	0	0
HEART										
. enlarged (atria)	14	19	16	5	3	6	7	5	0	1
. thrombus	3	7	6	5	0	4	5	4	0	0
. pale	0	0	1	0	0	0	0	0	0	0

IVO/TNO

TUDY NO 125 CARCINOGENICITY STUDY IN RATS WITH VCM IN THE DIET

ABLE 13. MACROSCOPIC PATHOLOGY (CONTINUED 5)

ite and type of observations	Incidence of observations									
	MALES					FEMALES				
	mg VCM/kg b.w./day					mg VCM/kg b.w./day				
	0	.017	0.17	1.7	0	0	.017	0.17	1.7	0
IEDIASTINAL LYMPH NODES										
. tumour or suspected of tumour	3	1	0	1	0	0	0	0	0	0
2. enlarged	1	2	2	0	1	0	2	2	2	0
LUNGS										
1. tumour or suspected of tumour	0	1	0	0	1	0	0	0	0	1
2. evidence of CRD *)	4	6	4	5	72	4	3	10	9	67
3. spongy	6	8	11	1	50	5	5	4	3	36
4. spotted	18	18	26	9	6	20	17	9	6	4
5. haemorrhage	1	0	4	0	1	0	0	1	0	1
6. discoloured a. pale	1	2	0	4	2	5	6	4	0	2
b. dark	1	0	0	0	0	0	0	0	0	0
c. reddish	1	3	1	0	0	0	2	0	0	0
7. atelectasis (partially)	1	2	4	0	0	1	0	3	2	2
8. pleuritis	0	0	0	0	2	1	0	0	0	1
TRACHEA										
1. filled with blood	0	1	0	0	0	0	0	0	0	0
AORTA										
1. dilated	5	9	9	1	0	5	2	1	1	2
2. calcified	1	0	0	0	0	0	0	0	0	0
DIAPHRAGM										
1. tumour or suspected of tumour	1	0	0	0	0	0	1	1	0	1
2. spotted surface	0	0	0	1	0	0	0	0	0	0
CERVICAL LYMPH NODES										
1. tumour or suspected of tumour	1	0	0	0	0	0	0	0	0	0
2 enlarged	0	1	1	0	0	0	0	0	0	0
SUBMAXILLARY SALIVARY GLANDS										
1. tumour or suspected of tumour	1	1	1	0	0	0	0	0	0	1
2. edema	1	2	1	1	1	0	0	0	1	0
3. discoloured a. dark	1	0	0	0	0	0	0	0	0	0
b. reddish	0	0	1	0	0	0	1	0	0	0
4. enlarged/swollen	1	1	0	0	0	0	0	0	0	0

* CRD = chronic respiratory disease

CIVO/TNO

STUDY NO 125 CARCINOGENICITY STUDY IN RATS WITH VCM IN THE DIET

TABLE 13. MACROSCOPIC PATHOLOGY (CONTINUED 6)

Site and type of observations	Incidence of observations									
	MALES					FEMALES				
	mg VCM/kg b.w./day					mg VCM/kg b.w./day				
	0	.017	0.17	1.7	0	0	.017	0.17	1.7	0
SUBLINGUAL SALIVARY GLANDS										
1. tumour or suspected of tumour	1	0	0	0	0	0	0	0	0	0
2. enlarged/swollen	0	1	0	0	0	0	0	0	0	0
3. haemorrhage	1	0	0	0	0	0	0	0	0	0
4. edema	0	1	1	0	0	0	0	0	0	0
5. discoloured a. pale	1	0	0	0	0	0	0	0	0	0
b. reddish	0	0	0	0	0	0	1	0	0	0
PAROTID SALIVARY GLANDS										
1. discoloured, pale	3	0	0	1	0	0	0	0	0	0
2. spotted	0	0	0	1	3	0	0	0	0	0
3. enlarged	0	1	0	0	0	1	0	0	0	0
THYROID										
1. tumour or suspected of tumour	2	6	3	1	0	1	2	0	0	0
2. enlarged	3	0	1	1	0	0	0	0	0	1
3. discoloured a. pale	1	0	0	0	0	0	0	0	0	0
b. dark	2	1	3	0	1	0	1	0	0	1
c. reddish	0	0	0	0	0	0	0	1	0	0
PARATHYROID										
1. enlarged	1	0	0	0	0	0	0	0	0	0
EYES										
1. haemorrhagic scabs around eyes	2	2	0	2	4	0	2	1	1	1
2. evidence of inflammation	1	6	6	2	3	2	2	10	1	3
3. protruding	3	3	0	0	2	6	9	9	2	21
4. pale	8	6	6	2	0	12	12	3	7	3
5. opaque	13	1	13	7	9	16	2	14	3	5
BRAIN										
1. tumour or suspected of tumour	0	0	0	0	0	1	0	0	0	0
2. haemorrhage	0	1	1	1	0	0	0	0	0	0
3. a pale spot	0	0	0	1	0	0	0	0	0	0
MENINGES										
1. haemorrhage	0	0	2	0	1	0	0	0	0	0

IVO/TNO

IOGY NO 125 CARCINOGENICITY STUDY IN RATS WITH VCM IN THE DIET

TABLE 13. MACROSCOPIC PATHOLOGY (CONTINUED 7)

Site and type of observations	Incidence of observations									
	MALES					FEMALES				
	mg VCM/kg b.w./day					mg VCM/kg b.w./day				
	0	.017	0.17	1.7	0	0	.017	0.17	1.7	0
PITUITARY										
1. tumour or suspected of tumour	8	9	10	5	3	13	13	17	10	5
2. haemorrhagic (cyst)	1	2	3	1	1	5	10	11	4	2
3. discoloured a. pale	3	1	1	1	0	2	4	0	0	0
b. dark	1	1	0	0	1	0	0	0	0	1
4. enlarged/swollen	1	0	2	0	1	1	1	0	0	1
NOSE										
1. tumour or suspected of tumour	0	0	0	0	0	0	0	3	0	0
2. haemorrhagic scabs around nose	6	6	2	1	1	4	3	2	0	0
ORAL CAVITY										
1. malocclusion of incisors	5	3	2	1	1	2	1	0	0	1
EXORBITAL LACHRYMAL GLANDS										
1. pale	18	12	10	8	13	0	0	0	0	0
2. granular appearence	6	9	6	1	7	0	0	0	0	0
ZYMBAL's GLANDS										
1. tumour or suspected of tumour	0	1	0	1	0	0	0	0	0	0
2. enlarged	0	0	0	0	0	1	0	1	0	0
3. evidence of inflammation	0	0	0	0	1	0	0	0	0	0
4. haemorrhage	0	0	0	0	0	0	1	0	0	0
ABDOMINAL/LUMBAL LYMPH NODES										
1. tumour or suspected of tumour	1	1	0	0	0	0	0	1	0	0
2. enlarged	2	1	0	0	0	0	0	0	0	0
ABDOMINAL WALL										
1. small cysts	0	0	0	0	0	1	0	0	0	0
TAIL										
1. ulcer	2	1	1	1	0	0	0	0	0	0
2. abscess	0	0	0	0	0	0	0	1	0	0
EAR DUCT										
1. compact debris	0	1	0	0	0	0	0	0	0	0
2. evidence of inflammation	0	0	1	0	0	0	0	0	0	0
LIMBS										
1. tumour or suspected of tumour	2	0	0	0	0	0	0	0	0	0
2. abscess	0	0	0	0	1	0	0	0	1	0
3. deformed	4	2	1	0	1	1	1	1	0	0

STUDY NO 129 CARCINOGENICITY STUDY IN RATS WITH VCM IN THE DIET

TABLE 13: MACROSCOPIC PATHOLOGY (CONTINUED 8)

Site and type of observations	Incidence of observations									
	MALES					FEMALES				
	mg VCM/kg b.w./day					mg VCM/kg b.w./day				
	0	.017	0.17	1.7	0	0	.017	0.17	1.7	0
MISCELLANEOUS										
1. emaciated	15	19	17	7	48	32	22	26	14	55
2. deformed spine	1	3	0	0	0	0	1	0	0	0
3. deformed dorsal vertebrae	0	0	1	0	0	0	0	0	0	0

CIVO/TNO
STUDY NO 125 CARCINOGENICITY STUDY IN RATS WITH VCM IN THE DIETS

TABLE 14 TYPE AND INCIDENCE OF HISTOPATHOLOGICAL CHANGES IN THE LIVER

Type of changes[1)]	Incidence of changes									
	Males					Females				
	mg VCM/kg b.w./day					mg VCM/kg b.w./day				
	0	0.017	0.17	1.7	0	0	0.017	0.17	1.7	0
Number of animals examined	99	99	99	49	100	98	100	96	49	99
1. Foci of cellular alteration										
a. clear cell foci										
I one or a few	12	8	8	16**	5	4	5	3	13***	1
II several	0	0	0	3*	0	0	0	0	6***	0
b. basophilic foci										
I one or a few	4	2	3	8*	0	9	20*	26***	19***	4
II several	0	0	0	0	0	0	1	0	2	0
c. mixed cell foci										
I one or a few	0	1	2	2	0	6	6	4	8*	0
d. eosinophilic foci										
I one or a few	1	1	2	1	0	0	0	1	10***	2
All type of foci:										
Total	17	12	15	30	5	19	32	34	58	7
Number of foci-bearing animals	16	12	15	23***	5**	19	27	31*	32***	7**

CIVO/TNO
STUDY NO 125 CARCINOGENICITY STUDY IN RATS WITH VCM IN THE DIETS

TABLE 14 TYPE AND INCIDENCE OF HISTOPATHOLOGICAL CHANGES IN THE LIVER - CONTINUED 1

Type of changes	Incidence of changes									
	Males					Females				
	mg VCM/kg b.w./day					mg VCM/kg b.w./day				
	0	0.017	0.17	1.7	0	0	0.017	0.17	1.7	0
2. Neoplastic nodules										
a. one	0	0	0	1	0	0	1	1	9***	0
b. a few	0	0	0	2	0	0	0	0	1	0
3. Hepatocellular carcinoma	0	0	0	3*	0	1	0	1	3	0
4. Angiosarcoma	0	0	0	1	0	0	0	0	2	0
5. Liver-cell polymorphism										
a. slight	27	23	26	19	12**	46	41	49	23	38
b. moderate	4	4	7	10**	1	14	13	8	15*	15
c. severe	1	1	1	3	0	2	3	4	9***	3
6. Prominent sinusoidal cells										
a. slight	1	1	1	0	1	4	9	3	1	6
b. moderate/marked	1	2	1	1	0	3	8	5	2	0
7. Cysts										
a. one	1	0	1	0	0	3	2	4	1	1
b. a few	4	4	3	4	1	11	11	12	7	2**
c. many	0	0	0	0	0	3	4	9	24***	1
8. Bile duct proliferation										
a. slight	37	26	35	14	21**	27	23	36	18	14*
b. moderate	9	9	8	3	1**	11	6	10	2	3*
c. severe	2	0	0	0	1	1	2	1	1	4

CIVO/TNO
STUDY NO 125 CARCINOGENICITY STUDY IN RATS WITH VCM IN THE DIETS

TABLE 14 TYPE AND INCIDENCE OF HISTOPATHOLOGICAL CHANGES IN THE LIVER - CONTINUED 2

Type of changes	Incidence of changes									
	Males					Females				
	mg VCM/kg b.w./day					mg VCM/kg b.w./day				
	0	0.017	0.17	1.7	0	0	0.017	0.17	1.7	0
9. Cholangiofibrosis										
a. slight	33	19*	20*	15	23	16	13	17	15	2***
b. moderate	2	6	8*	2	1	6	2	4	0	0*
10. Periportal fibrosis										
a. slight	1	2	2	3	5	0	0	0	0	1
b. moderate	2	0	0	0	2	0	0	0	0	0
11. Periportal/centrolobular infiltrates of mononuclear cells										
a. slight	14	10	8	3	7	3	2	1	2	4
b. moderate	1	1	1	0	0	0	0	2	0	0
c. severe	0	1	1	0	0	0	0	0	0	0
12. Foci of RES-cells occasionally accompanied by a few necrotic hepatocytes										
a. one or a few	18	15	27	5	12	39	28	42	12*	25*
b. several	5	8	3	0	1	6	3	5	0	3
13. Slight haematopoietic activity	2	0	0	0	1	1	0	3	0	0

CIVO/TNO
STUDY NO 125 CARCINOGENICITY STUDY IN RATS WITH VCM IN THE DIETS

TABLE 14 TYPE AND INCIDENCE OF HISTOPATHOLOGICAL CHANGES IN THE LIVER - CONTINUED 3

Type of changes	Incidence of changes									
	Males					Females				
	mg VCM/kg b.w./day					mg VCM/kg b.w./day				
	0	0.017	0.17	1.7	0	0	0.017	0.17	1.7	0
14. Single cell necrosis										
a. slight	2	3	1	0	4	2	3	13**	5*	9*
b. moderate/severe	2	1	0	0	0	1	3	4	2	2
15. Focal necrosis										
a. slight	11	3*	8	2	4*	4	4	6	6	3
b. moderate	1	2	1	0	0	3	1	2	0	3
c. severe	1	0	0	2	0	3	0	1	0	1
16. Centrolobular liver-cell degeneration	1	3	3	1	0	3	2	2	0	0
17. One or a few foci of degenerated hepatocytes	1	0	7*	3	0	1	2	0	0	0
18. Haemorrhagic areas	1	0	1	0	0	0	0	1	0	0
19. Peliosis-like changes	0	1	0	2	0	1	1	0	0	0
20. Small granuloma	0	0	0	0	0	2	0	0	0	0
21. Vacuolization of hepatocytes mainly										
a. periportal										
I slight	3	6	11*	3	4	24	22	29	4*	6***
II moderate	0	2	5*	0	0	3	2	6	0	1
III severe	0	1	1	0	0	0	0	0	0	0

CIVO/TNO
STUDY NO 125 CARCINOGENICITY STUDY IN RATS WITH VCM IN THE DIETS

TABLE 14 TYPE AND INCIDENCE OF HISTOPATHOLOGICAL CHANGES IN THE LIVER - CONTINUED 4

Type of changes	Incidence of changes									
	Males					Females				
	mg VCM/kg b.w./day					mg VCM/kg b.w./day				
	0	0.017	0.17	1.7	0	0	0.017	0.17	1.7	0
b. diffuse										
I slight	1	0	1	0	0	0	0	0	0	0
II moderate	1	0	2	0	0	2	0	0	0	0
III severe	0	2	0	0	0	1	0	0	0	2
c. centrolobular										
I slight	0	1	0	0	0	0	0	0	0	0

1) Specific hepatocellular lesions were classified according to Squire and Levitt (1975).

* P < 0.05; ** P < 0.01; *** P < 0.001, according to the Fishers' exact test (one tailed).

CIVO/TNO
STUDY NO 125 CARCINOGENICITY STUDY IN RATS WITH VCM IN THE DIET

TABLE 15 TYPE AND INCIDENCE OF TUMOURS OF THE MAMMARY GLANDS AND INCIDENCES OF ABDOMINAL MESOTHELIOMAS

Site and type of tumours	Incidence of tumours									
	Males					Females				
	mg VCM/kg b.w./day					mg VCM/kg b.w./day				
	0	0.017	0.17	1.7	0	0	0.017	0.17	1.7	0
Number of animals examined	99	99	99	49	100	98	100	96	48	98
Mammary glands										
- No of tumour-bearing animals	5	8	3	0	3	41	21***	28*	21	20***
1. Adenoma										
a. single	0	0	0	0	0	6	4	2	5	2
b. two	0	0	0	0	0	1	1	1	0	0
2. Intraductal papilloma	0	0	0	0	0	0	0	0	1	0
3. Fibroadenoma										
a. single	0	1	0	0	0	25	10**	15	14	11**
b. two	0	0	0	0	0	2	3	2	2	4
c. multiple	0	0	0	0	0	3	1	1	1	1

CIVO/TNO
STUDY NO 125 CARCINOGENICITY STUDY IN RATS WITH VCM IN THE DIET

TABLE 15 TYPE AND INCIDENCE OF TUMOURS OF THE MAMMARY GLANDS AND INCIDENCES OF ABDOMINAL MESOTHELIOMAS CONTINUED

Site and type of tumours	Incidence of tumours									
	Males					Females				
	mg VCM/kg b.w./day					mg VCM/kg b.w./day				
	0	0.017	0.17	1.7	0	0	0.017	0.17	1.7	0
4. Fibroma										
a. single	4	6	2	0	3	1	4	1	2	2
b. two	0	0	1	0	0	0	0	0	0	0
c. multiple	0	0	0	0	0	1	0	0	0	0
5. Adenocarcinoma										
a. single	0	1	0	0	0	3	0	5	1	0
b. two	1	0	0	0	0	0	0	2	0	1
Abdomen										
1. Mesothelioma	0	1	2	0	0	3	2	2	1	1

* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$, according to the Fishers' exact test (one tailed)

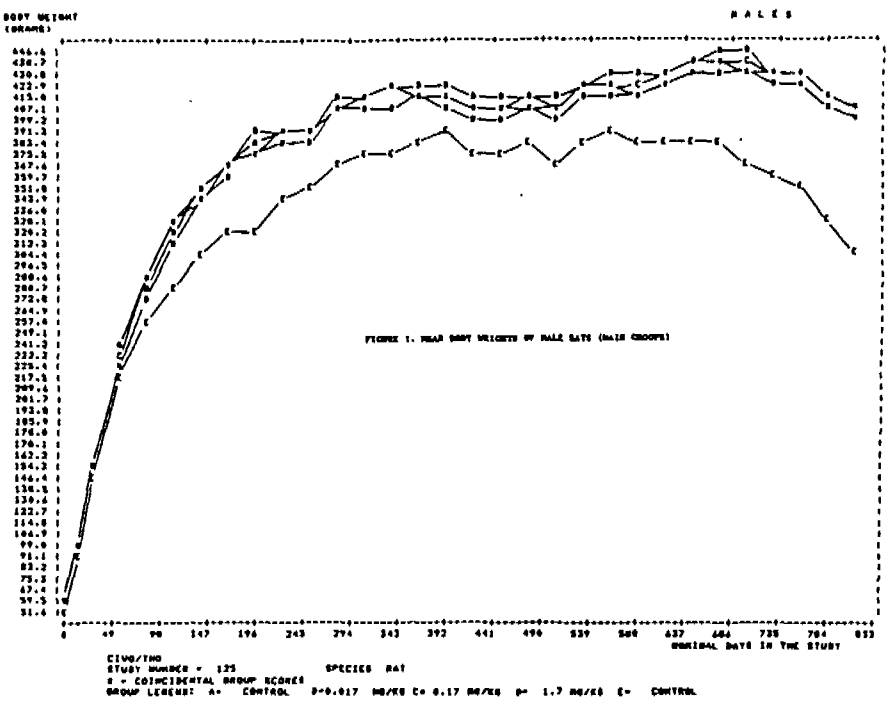

FIGURE 1

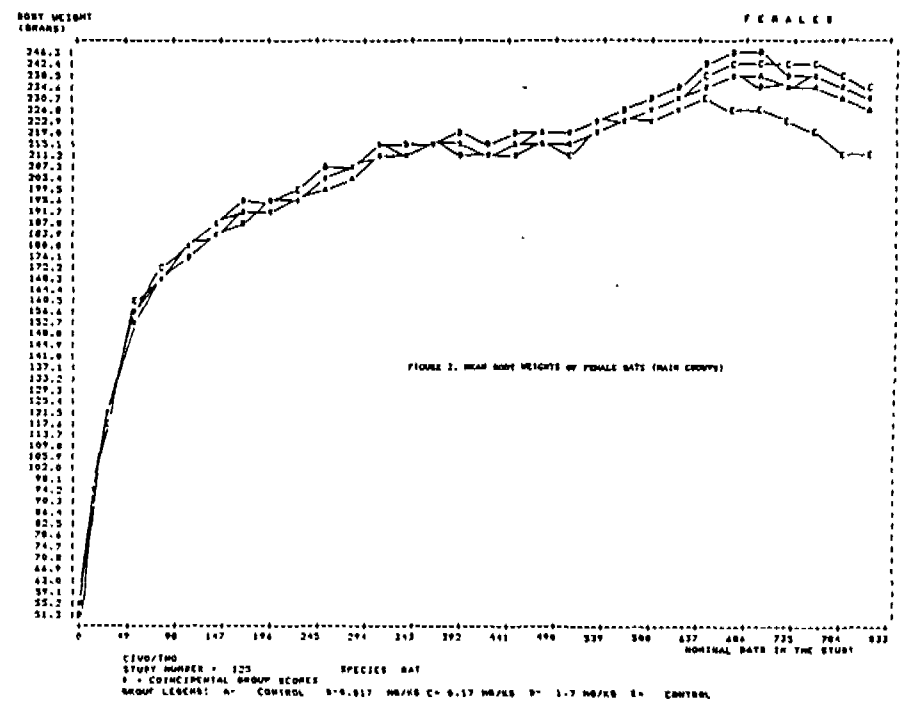

FIGURE 2

PERCENTAGE COMPOSITION OF BASAL DIET FOR RATS AND MICE

soya bean oil meal	11
fish meal	7
meat and bone scraps	4
wheat (whole ground)	36
maize (whole ground)	29.7
brewer's yeast	3
grass meal	3
whey powder	2
defatted bone meal	0.4
salt with trace elements[1])	0.5
B-vitamin mixture[2])	0.1
vitamin ADEK mixture[3])	0.3
soya bean oil	3
	100.0

[1]) Trace elements in salt

	Batch		added to 1 kg diet	
$MnSO_4.H_2O$	2380	g	41	mg Mn
$ZnCl_2$	250	g	12	mg Zn
KJ	20	g	1.5	mg J
$FeSO_4.7H_2O$	1250	g	25	mg Fe
$CoCl_2.6H_2O$	20	g	0.7	mg Co
$CuSO_4.5H_2O$	400	g	8	mg Cu
NaCl	45680	g		
	50000	g		

[2]) B-vitamin mixture

	Batch		added to 1 kg diet	
Thiamin-HCl	25	g	2.5	mg
Riboflavin	30	g	3.0	mg
Pyridoxin-HCl	100	g	10.0	mg
Niacin	125	g	12.5	mg
Ca-pantothenate	75	g	7.5	mg
Biotin	1.5	g	0.15	mg
Folic acid	5	g	0.5	mg
Vitamin B_{12}-prep. (0.1 %)	50	g	5.0	mg (= 5 µg B_{12})
Ground sucrose	9588.5	g		
	10000	g		

[3]) Vitamin ADEK mixture

	Batch		added to 1 kg diet	
Vit. AD_3-prills (Farmix):				
2250 IU vit. A,			6339	IU vit. A
750 IU vit. D_3/g	25000	g	2112	IU vit. D_3
Vit. E-dry powder (Merck)				
50 %	800	g	45	mg vit. E
Menadion-Na-bisulphite				
(Vit. K_3)	27	g	3	mg vit. K_3
Wheat starch	800	g		
	26627	g		

CONTAMINANTS REGULARLY DETERMINED IN BASAL DIET

1. Contaminants in basal diet

contaminant	detection limit	tentative maximum
- inorganic substances (mg/kg)		
arsenic	0.01	0.25
cadmium	0.005	0.05
lead	0.05	1.0
mercury	0.005	0.05
selenium	0.01	0.5
tin	1	25
potassium nitrate	25	500
sodium nitrite	5	10
- organochlorine compounds (mg/kg)		
HCB	0.005	0.02
lindane (γ-HCH)	0.01	0.1
α-HCH	0.01	0.1
β-HCH	0.02	0.02
heptachlor	0.01	0.02
heptachlorepoxide	0.02	0.02
α-chlordane	0.02	0.02
γ-chlordane	0.02	0.05
aldrin	0.01	0.01
dieldrin	0.01	0.01
endrin	0.02	0.02
methoxychlor	0.05	0.5
p,p'-DDE	0.02	0.02
p,p'-TDE	0.03	0.03
o,p'-DDT	0.03	0.05
p,p'-DDT	0.04	0.05
PCBs	0.3	0.5
- organophosphorus compounds (mg/kg)		
chlorpyrifos	0.01	0.05
diazinon	0.01	0.05
dichlorvos	0.01	0.05
fenitrothion	0.01	0.05
malathion	0.01	0.5
mevinfos	0.01	0.05
parathion	0.01	0.05
sulfotep	0.01	0.05
- dithiocarbamates, in total, determined as carbondisulfide (mg/kg)	0.5	1.0
ferbam		
mancozeb		
maneb		
nabam		
thiram		
zineb		
ziram		

Contaminants in basal diet (cont.)

contaminant	detection limit	tentative maximum
- polycyclic aromatic hydrocarbons (ug/kg)		
benzo(b)fluoranthene	0.2	10
benzo(k)fluoranthene	0.4	10
benzo(a)pyrene	0.2	10
fluoranthene	1.0	50
indeno(1,2,3-cd)pyrene	0.4	10
- nitroso compounds (ug/kg)		
nitrosodiethylamine	0.5-1.5	10
nitrosodimethylamine	0.3-0.9	10
nitrosodipropylamine	1.5-4.5	10
nitrosomethylbutylamine	1.5-4.5	10
nitrosomethylpropylamine	1.0-3.0	10
nitrosomorpholine	3.0-9	10
nitrosopiperidine	1.5-4.5	10
nitrosopyrrolidine	1.5-4.5	10
- mycotoxins (mg/kg)		
aflatoxin B_1	0.01	0.05
- miscellaneous determinations		
oestrogenic activity (Tiecco test)		negative
urease activity (ΔpH)		0.3
trypsin inhibitors (mg trypsin/g food)		8.0
haemagglutinins		
negative reaction at dilution		1:200

NUTRIENT COMPOSITION OF BASAL DIET FOR RATS

Analyses of a 1000 kg batch produced January 24, 1980

moisture	12.6	%	iron	175	ppm
crude protein (N x 6.25)	20.9	%	manganese	95	ppm
crude fat	8.9	%	copper	15	ppm
crude fibre	3.6	%	zinc	50	ppm
total ash	5.6	%	cobalt	2	ppm
calcium	0.89	%	chromium	3	ppm
phosphorus	0.72	%	selenium	0.24	ppm
magnesium	0.14	%			
potassium	0.75	%			
sodium	0.28	%			

vitamin A	5200	I.U./kg	vitamin B_1	4.7	mg/kg
vitamin D	1380	I.U./kg	vitamin B_2	5.8	mg/kg
vitamin E	44	mg/kg	vitamin B_6	12.0	mg/kg
carotene	2.0	mg/kg	niacin	66	mg/kg
vitamin K_3	1.6	mg/kg	pantothenic acid	15.5	mg/kg
			folic acid	1.25	mg/kg
			choline	1600	mg/kg
			biotin	0.22	mg/kg
			vitamin B_{12}	8	µg/kg

	g/100 g	g/16 g N		g/100 g	g/16 g N
isoleucine	0.85	4.1	valine	1.00	4.8
leucine	1.60	7.7	arginine	1.16	5.6
lysine	1.03	5.0	histidine	0.45	2.2
methionine	0.39	1.89	alanine	1.09	5.3
cystine	0.36	1.75	aspartic acid	1.74	8.4
phenylalanine	0.89	4.3	glutamic acid	3.69	17.9
tyrosine	0.64	3.1	glycine	1.11	5.4
threonine	0.81	3.9	proline	1.40	6.8
tryptophan	0.21	1.01	serine	1.10	5.3

NUTRIENT COMPOSITION OF BASAL DIET FOR RATS

Analyses of a 1000 kg batch produced September 9, 1980.

moisture	11.9 %	iron	135 ppm
crude protein (N x 6.25)	22.2 %	manganese	95 ppm
crude fat	6.4 %	copper	16 ppm
crude fibre	3.1 %	zinc	55 ppm
total ash	5.4 %	cobalt	2 ppm
calcium	0.90 %	chromium	2 ppm
phosphorus	0.78 %	selenium	0.40 ppm
magnesium	0.15 %	iodine	2.0 ppm
potassium	0.82 %		
sodium	0.29 %		

vitamin A	7000 I.U./kg	vitamin B_1	6.2 mg/kg
vitamin D	I.U./kg	vitamin B_2	5.4 mg/kg
vitamin E	55 mg/kg	vitamin B_6	11.8 mg/kg
carotene	mg/kg	niacin	74 mg/kg
vitamin K_3	1.8 mg/kg	pantothenic acid	11.5 mg/kg
		folic acid	2.4 mg/kg
		choline	1600 mg/kg
		biotin	0.20 mg/kg
		vitamin B_{12}	16.5 µg/kg

	g/100 g	g/16 g N		g/100 g	g/16 g N
isoleucine	0.98	4.4	valine	1.14	5.2
leucine	1.78	8.0	arginine	1.21	5.4
lysine	1.13	5.1	histidine	0.44	2.0
methionine	0.41	1.8	alanine	1.19	5.4
cystine	0.38	1.7	aspartic acid	1.93	8.7
phenylalanine	0.98	4.4	glutamic acid	4.20	18.9
tyrosine	0.69	3.1	glycine	1.12	5.1
threonine	0.85	3.9	proline	1.42	6.4
tryptophan	0.23	1.0	serine	1.17	5.3

ANNEX 5

NUTRIENT COMPOSITION OF BASAL DIET FOR RATS

Analyses of a 1000 batch produced February 27, 1981

moisture	12.6	%	iron	150	ppm
crude protein (N x 6.25)	20.6	%	manganese	90	ppm
crude fat	6.1	%	copper	17	ppm
crudefiber	3.8	%	zinc	45	ppm
total ash	5.6	%	cobalt	0.6	ppm
calcium	1.05	%	chromium	3	ppm
phosphorus	0.74	%	selenium	0.4	ppm
magnesium	0.13	%	iodine	1.5	ppm
potassium	0.75	%			
sodium	0.32	%			

vitamin A	6600	I.U./kg	vitamin B_1	7.5	mg/kg
vitamin D	-[1]	I.U./kg	vitamin B_2	5.7	mg/kg
vitamin E	57	mg/kg	vitamin B_6	12.1	mg/kg
carotene	1.6	mg/kg	niacin	55	mg/kg
vitamin K_3		mg/kg	pantothenic acid	14.7	mg/kg
			folic acid	5.1	mg/kg
			choline	1500	mg/kg
			biotin	0.25	mg/kg
			vitamin B_{12}	15.5	µg/kg

	g/100 g	g/16 g N		g/100 g	g/16 g N
isoleucine	0.81	4.0	valine	0.95	4.7
leucine	1.52	7.5	arginine	1.13	5.6
lysine	1.03	5.1	histidine	0.46	2.3
methionine	0.38	1.9	alanine	1.08	5.3
cystine	0.33	1.6	aspartic acid	1.74	8.6
phenylalanine	0.88	4.3	glutamic acid	3.70	18.2
tyrosine	0.63	3.1	glycine	1.13	5.6
threonine	0.78	3.8	proline	1.46	7.2
tryptophan	0.19	0.9	serine	1.06	5.2

[1] not analysed

CIVO-TNO, June 1981

NUTRIENT COMPOSITION OF CIVO-BASAL DIET FOR RATS

Analyses of a 4000 kg batch produced by Hope Farms on Sept. 9, 1981

moisture	11.3	%	iron	220	ppm
crude protein (N x 6.25)	20.2	%	manganese	105	ppm
crude fat	6.9	%	copper	18	ppm
crude fiber	3.9	%	zinc	55	ppm
total ash	5.3	%	cobalt	1	ppm
calcium	0.65	%	chromium	1	ppm
phosphorus	0.7	%	selenium	0.25	ppm
magnesium	0.21	%	iodine	3.0	ppm
potassium	0.8	%			
sodium	0.32	%			

vitamin A	5700	I.U./kg	vitamin B_1	9.0	mg/kg
vitamin D	-[1]	I.U./kg	vitamin B_2	7	mg/kg
vitamin E	56	mg/kg	vitamin B_6	12	mg/kg
carotene	13	mg/kg	niacin	70	mg/kg
vitamin K_3	< 3	mg/kg	pantothenic acid	18.6	mg/kg
			folic acid	3.3	mg/kg
			choline	1700	mg/kg
			biotin	0.24	mg/kg
			vitamin B_{12}	13	g/kg

	g/100 g	g/16 g N		g/100 g	g/16 g N
isoleucine	0.81	4.0	valine	1.05	5.2
leucine	1.60	7.9	arginine	1.13	5.6
lysine	1.07	5.3	histidine	0.49	2.4
methionine	0.40	2.0	alanine	1.14	5.6
cystine	0.34	1.69	aspartic acid	1.73	8.6
phenylalanine	0.89	4.4	glutamic acid	3.51	17.4
tyrosine	0.65	3.2	glycine	1.07	5.3
threonine	0.78	3.9	proline	1.27	6.3
tryptophan	0.23	1.14	serine	1.01	5.0

[1] not analysed

CIVO-TNO, June 1981

ANNEX 7

NUTRIENT COMPOSITION OF CIVO-BASAL DIET FOR RATS

Analyses of a 4000 kg batch produced by van Eck, Cothen, on Febr. 9, 1982

moisture	11.3	%	iron	315	ppm
crude protein (N x 6.25)	19.8	%	manganese	95	ppm
crude fat	6.2	%	copper	19	ppm
crude fiber	4.1	%	zinc	65	ppm
total ash	5.5	%	cobalt	0.5	ppm
calcium	0.95	%	chromium	1.0	ppm
phosphorus	0.66	%	selenium	0.3	ppm
magnesium	0.16	%	iodine	0.9	ppm
potassium	0.73	%			
sodium	0.32	%			

vitamin A	8000	I.U./kg	vitamin B_1	7	mg/kg
vitamin D	-[1]	I.U./kg	vitamin B_2	5	mg/kg
vitamin E	56	mg/kg	vitamin B_6	12	mg/kg
carotene	12.5	mg/kg	niacin	55	mg/kg
vitamin K_3	< 2	mg/kg	pantothenic acid	15	mg/kg
			folic acid	4	mg/kg
			choline	1600	mg/kg
			biotin	0.21	mg/kg
			vitamin B_{12}	26.8	µg/kg

	g/100 g	g/16 g N		g/100 g	g/16 g N
isoleucine	0.79	4.0	valine	1.00	5.1
leucine	1.52	7.7	arginine	1.08	5.5
lysine	0.99	5.0	histidine	0.43	2.2
methionine	0.40	2.0	alanine	1.02	5.2
cystine	0.32	1.62	aspartic acid	1.65	8.4
phenylalanine	0.84	4.3	glutamic acid	3.48	17.6
tyrosine	0.51	2.6	glycine	1.06	5.4
threonine	0.77	3.9	proline	1.22	6.2
tryptophan	0.22	1.11	serine	0.94	4.8

[1] not analysed

CIVO-TNO, June 1982

CONTAMINANTS IN BASAL DIET FOR RATS AND MICE

Sample of a 1000 kg batch produced on January 24, 1980

lead	0.95	mg/kg
cadmium	0.06	mg/kg
mercury	0.02	mg/kg
tin	2	mg/kg
arsenic	0.4	mg/kg
selenium	0.24	mg/kg
organo-P-compounds	ND	
organo-Cl-compounds	ND	
dithiocarbamates (as CS_2)	0.5	mg/kg
aflatoxin B_1,B_2,G_1,G_2	< 5	µg/kg
oestrogenic activity (Tiecco test)	ND	
benzo(a)pyrene	2.5	µg/kg
benzo(b)fluoranthene	4.4	µg/kg
indeno (1,2,3-c,d) pyrene	2.8	µg/kg
benzo(k)fluoranthene	2.6	µg/kg
fluoranthene	12.0	µg/kg
K-nitrate	163	mg/kg
Na-nitrite	1	mg/kg
nitrosodimethylamine	< 0.4	µg/kg
nitrosopyrrolidine	< 2	µg/kg
other nitrosamines	ND	
urease activity	0.15	ΔpH
trypsin inhibitor	< 0.6	mg tryps/g sample
haemagglutinins positive dilution	none	

ND = not detectable

CIVO-TNO-May, 1980

CONTAMINANTS IN BASAL DIET FOR RATS

(1000 kg batch produced 27 February 1981)

lead		0.3	mg/kg
cadmium		0.07	mg/kg
mercury		0.25	mg/kg
tin		< 1.0	mg/kg
arsenic		0.35	mg/kg
selenium		0.4	mg/kg
organo-P-compounds		ND	
organo-Cl-compounds		ND	
PCB's		ND	
dithiocarbamates		ND	
aflatoxin B_1, B_2, G_1, G_2		< 5	µg/kg
oestrogenic activity (Tiecco test)		ND	
benzo(a)pyrene		0.8	µg/kg
benzo(b)fluoranthene		0.9	µg/kg
indeno (1,2,3-c,d) pyrene		0.6	µg/kg
benzo(k)fluoranthene		0.3	µg/kg
fluoranthene		5.7	µg/kg
K-nitrate		77	mg/kg
Na-nitrite		1	mg/kg
nitrosodimethylamine		1.2	µg/kg
nitrosopyrrolidine		1.7	µg/kg
other nitrosamines		ND	
urease activity		0.05	Δ pH
trypsin inhibitor		< 0.6	mg tryps/g sample
haemagglutinins	positive dilution	1 : 10	
	negative dilution	1 : 20	

ND = not detectable

CIVO-TNO, June 1981

ANNEX 10

CONTAMINANTS IN BASAL DIETS FOR RATS

(1000 kg batch, produced 9 September 1980)

lead		0.25	mg/kg
cadmium		0.045	mg/kg
mercury		0.025	mg/kg
tin		< 1.0	mg/kg
arsenic		0.45	mg/kg
selenium		0.40	mg/kg
organo-P-compounds		ND	
organo-Cl-compounds		ND	
dithiocarbamates		ND	
aflatoxin B_1,B_2,G_1, and G_2		< 5	µg/kg
oestrogenic activity (Tiecco test)		ND	
benzo(a)pyrene		2.0	µg/kg
benzo(b)fluoranthene		2.7	µg/kg
indeno (1,2,3-c,d) pyrene		2.0	µg/kg
benzo(k)fluoranthene		1.0	µg/kg
fluoranthene		16.0	µg/kg
K-nitrate		80	mg/kg
Na-nitrite		1	mg/kg
nitrosodimethylamine		0.5	µg/kg
nitrosopyrrolidine		1.5	µg/kg
other nitrosamines		ND	
urease activity		0.05	Δ pH
trypsin inhibitor		< 0.6	mg tryps/g sample
haemagglutinins	positive dilution	none	
	negative dilution	-	

ND = not detectable

CIVO-TNO december 1980

ANNEX II

CONTAMINANTS IN CIVO BASAL DIET FOR RATS

(4000 kg batch, produced by Hope Farms on September 9, 1981).

lead	0.9	mg/kg
cadmium	0.07	mg/kg
mercury	0.005	mg/kg
tin	< 1.0	mg/kg
arsenic	0.45	mg/kg
selenium	0.25	mg/kg
organo-P-compounds	ND	
malathion	0.08	mg/kg
organo-Cl-compounds	ND	
PCB's	ND	
dithiocarbamates (as CS_2)	< 0.5	mg/kg
aflatoxin B_1, B_2, G_1, G_2	< 5	µg/kg
oestrogenic activity (Tiecco test)	ND	
benzo(a)pyrene	0.4	µg/kg
benzo(b)fluoranthene	0.7	µg/kg
indeno (1,2,3-c,d) pyrene	< 0.5	µg/kg
benzo(k)fluoranthene	0.1	µg/kg
fluoranthene	0.9	µg/kg
benz(ghi) perylene	0.3	µg/kg
K-nitrate	83	mg/kg
Na-nitrite	< 1	mg/kg
nitrosodimethylamine	0.9	µg/kg
nitrosopyrrolidine	1.0	µg/kg
other nitrosamines	ND	
urease activity	0.05	Δ pH
trypsin inhibitor	0.51	mg tryps/g sample
haemagglutinins positive dilution	1 : 50	
haemagglutinins negative dilution	1 : 100	

ND = not detectable

CIVO-TNO, November 1981

ANNEX 12

CONTAMINANTS IN CIVO BASAL DIET FOR RATS

(4000 kg batch, produced by van Eck, Cothen, on Febr. 9, 1982)

lead		1.4	mg/kg
cadmium		0.09	mg/kg
mercury		0.005	mg/kg
tin	<	1.0	mg/kg
arsenic		0.3	mg/kg
selenium		0.3	mg/kg
organo-P-compounds		ND	
organo-Cl-compounds		ND	
PCB's		ND	
dithiocarbamates	<	0.5	mg/kg
aflatoxin B_1,B_2,G_1,G_2	<	5	µg/kg
oestrogenic activity (Tiecco test)		ND	
benzo(a)pyrene		0.5	µg/kg
benzo(b)fluoranthene		0.1	µg/kg
indeno (1,2,3-c,d) pyrene	<	0.1	µg/kg
benzo(k)fluoranthene	<	0.2	µg/kg
fluoranthene		0.2	µg/kg
benz(ghi) perylene	<	0.3	µg/kg
K-nitrate		34	mg/kg
Na-nitrite		ND	
nitrosodimethylamine		ND	
nitrosopyrrolidine		0.7	µg/kg
other nitrosamines		ND	
urease activity		0.00	Δ pH
trypsin inhibitor		1.4	mg tryps/g sample
haemagglutinins	positive dilution		none
	negative dilution		-

ND = not detectable

CIVO-TNO, June 1982

Contaminants in drinking water

contaminant	detection limit	tentative maximum
- inorganic substances (µg/l)		
arsenic	10	50
cadmium	1	5
chromium	10	50
copper	1	50
cyanide	100	100
lead	1	50
mercury	1	1
selenium	1	10
zinc	1	100
potassium nitrate	1,000	50,000
sodium nitrite	1,000	1,000
ammonia	500	1,000
- organochlorine compounds (µg/l)		
1,1-dichloroethane	1	1
dichloromethane	5	1
tetrachloroethene	1	1
tetrachloromethane	0.1	1
1,1,1-trichloroethane	0.1	1
trichloroethene	0.5	1
trichloromethane	0.3	1
HCB	0.01	1
lindane (γ-HCH)	0.01	1
α-HCH	0.01	1
β-HCH	0.03	1
heptachlor	0.01	1
heptachlorepoxide	0.02	1
α-chlordane	0.03	1
γ-chlordane	0.03	1
aldrin	0.02	1
dieldrin	0.03	1
endrin	0.05	1
methoxychlor	0.15	1
p,p'-DDE	0.03	1
p,p'-TDE	0.06	1
o,p'-DDT	0.06	1
p,p'-DDT	0.1	1
PCBs	0.8	1
- organophosphorus compounds (µg/l)		
chlorpyrifos	0.1	0.1
diazinon	0.1	0.1
dichlorvos	0.1	0.1
fenitrothion	0.2	0.1
malathion	0.2	0.1
mevinfos	0.1	0.1
parathion	0.2	0.1
sulfotep	0.1	0.1

Contaminants in drinking water (cont.)

contaminant	detection limit	tentative maximum
- polycyclic aromatic hydrocarbons (ng/l)		
benzo(b)fluoranthene	5	200
benzo(k)fluoranthene	5	200
benzo(ghi)perylene	5	200
benzo(a)pyrene	5	200
fluoranthene	10	200
indeno(1,2,3-cd)pyrene	5	200

CONTAMINANTS IN TAP WATER (determined in period Nov.-Dec. 1979)

	ppb		ppm
lead	< 1	ammonia	< 0.01
cadmium	< 1	nitrate	9.6
mercury	< 5	nitrite	< 0.01
arsenic	2	chloride	23
selenium	< 1	sodium	14.5
copper	50	calcium	31
chromium	< 1	potassium	1.2
zinc	5	iron	0.04
cyanide --	3		

	ppb		ppb
dichloromethane	< 5	HCB	< 0.01
1,1-dichloroethane	absent	α-HCH	< 0.01
chloroform	0.8	lindane	< 0.01
1,1,1-trichloroethane	0.2	heptachlor	< 0.01
tetrachloromethane	0.5	heptachl. epoxide	< 0.02
trichloroethene	absent	aldrin	< 0.02
tetrachloroethene	absent	dieldrin	< 0.03
	ppt	α-chlordane	< 0.03
benzo(a)pyrene	< 5	γ-chlordane	< 0.03
benzo(b)fluoranthene	< 5	endrin	< 0.05
indeno (1,2,3,-c,d) pyrene	< 5	p,p'-DDE	< 0.03
benzo (k) fluoranthene	< 5	o,p'-DDT	< 0.06
fluoranthene	< 10	p,p'-TDE	< 0.06
benzo (g,h,i) perylene	< 5	p,p'-DDT	< 0.10
		β-HCH	< 0.03
		PCB's	< 0.8
		DDVP	< 0.1
		mevinfos	< 0.1
		diazinon	< 0.1
		malathion	< 0.2
		parathion	< 0.2
		chlorpyrifos	< 0.1
		sulfotep	< 0.1
		fenitrothion	< 0.2

CONTAMINANTS IN TAP WATER (determined in period Jan.-April 1980)

	ppb		ppm
lead	1	ammonia	0.01
cadmium	< 0.1	nitrate	11
mercury	0.1	nitrite	< 0.01
arsenic	2	chloride	30
selenium	< 1	sodium	18.5
copper	55	calcium	31.0
chromium	< 1	potassium	1.3
zinc	3	iron	0.08
cyanide	< 2		

	ppb		ppb
dichloromethane	< 5	HCB	< 0.01
1,1-dichloroethane	< 1	α-HCH	< 0.01
chloroform	0.3	lindane	< 0.01
1,1,1-trichloroethane	< 0.1	heptachlor	< 0.01
tetrachloromethane	< 0.1	heptachl. epoxide	< 0.02
trichloroethene	0.3	aldrin	< 0.02
tetrachloroethene	< 0.2	dieldrin	< 0.03
	ppt	α-chlordane	< 0.03
benzo(a)pyrene	< 5	γ-chlordane	< 0.03
benzo(b)fluoranthene	< 5	endrin	< 0.05
indeno (1,2,3,-c,d) pyrene	< 5	p,p'-DDE	< 0.03
benzo (k) fluoranthene	< 5	o,p'-DDT	< 0.06
fluoranthene	<10	p,p'-TDE	< 0.06
benzo (g,h,i) perylene	< 5	p,p'-DDT	< 0.10
		β-HCH	< 0.03
		PCB's	< 0.8
		DDVP	< 0.1
		mevinfos	< 0.1
		diazinon	< 0.1
		malathion	< 0.2
		parathion	< 0.2
		chlorpyrifos	< 0.1
		sulfotep	< 0.1
		fenitrothion	< 0.2

CONTAMINANTS IN TAP WATER (determined in period Sept.- Nov. 1980)

	ppb		ppm
lead	< 1	ammonia	< 0.01
cadmium	< 0.1	nitrate	8.0
mercury	0.1	nitrite	< 0.01
arsenic	1	chloride	25
selenium	< 1	sodium	15.0
copper	50	calcium	28.5
chromium	< 1	potassium	1.2
zinc	10	iron	0.01
cyanide	< 1		

	ppb		ppb
dichloromethane	< 5	HCB	< 0.01
1,1-dichloroethane	0.3	α-HCH	< 0.01
chloroform	0.3	lindane	< 0.01
1,1,1-trichloroethane	0.1	heptachlor	< 0.01
tetrachloromethane	< 0.1	heptachl. epoxide	< 0.02
trichloroethene	0.4	aldrin	< 0.02
tetrachloroethene	< 0.2	dieldrin	< 0.03
	ppt	α-chlordane	< 0.03
benzo(a)pyrene	< 5	γ-chlordane	< 0.03
benzo(b)fluoranthene	< 5	endrin	< 0.05
indeno (1,2,3,-c,d)pyrene	< 5	p,p'-DDE	< 0.03
benzo(k)fluoranthene	< 5	o,p'-DDT	< 0.06
fluoranthene	< 10	p,p'-TDE	< 0.06
benzo(g,h,i)perylene	< 5	p,p'-DDT	< 0.1
		β-HCH	< 0.03
		methoxychlor	< 0.15
		PCB's	< 0.8
		DDVP	< 0.1
		mevinfos	< 0.1
		diazinon	< 0.1
		malathion	< 0.2
		parathion	< 0.2
		chlorpyrifos	< 0.1
		sulfotep	< 0.1
		fenitrothion	< 0.2

CIVO-TNO December, 1980

ANNEX 17

CONTAMINANTS IN TAP WATER (determined in period March - May 1981)

	ppb		ppm
lead	1	ammonia	< 0.01
cadmium	< 0.1	nitrate	16
mercury	< 0.1	nitrite	< 0.01
arsenic	2	chloride	25
selenium	< 1	sodium	14.0
copper	30	calcium	30.0
chromium	< 1	potassium	1.1
zinc	2	iron	0.03
cyanide	6		

	ppb		ppb
dichloromethane	< 5	HCB	< 0.01
1,1-dichloroethane	< 1	α-HCH	< 0.01
chloroform	< 0.1	lindane	< 0.01
1,1,1-trichloroethane	< 0.1	heptachlor	< 0.01
tetrachloromethane	< 0.05	heptachl. epoxide	< 0.02
trichloroethene	1.0	aldrin	< 0.02
tetrachloroethene	< 0.4	dieldrin	< 0.03
	ppt	α-chlordane	< 0.03
benzo(a)pyrene	< 5	γ-chlordane	< 0.03
benzo(b)fluoranthene	< 5	endrin	< 0.05
indeno (1,2,3,-c,d)pyrene	< 5	p,p'-DDE	< 0.03
benzo(k)fluoranthene	< 5	o,p'-DDT	< 0.06
fluoranthene	<10	p,p'-TDE	< 0.06
benzo(g,h,i)perylene	< 5	p,p'-DDT	< 0.1
		ß-HCH	< 0.03
		methoxychlor	< 0.15
		PCB's	< 0.8
		DDVP	< 0.1
		mevinfos	< 0.1
		diazinon	< 0.1
		malathion	< 0.2
		parathion	< 0.2
		chlorpyrifos	< 0.1
		sulfotep	< 0.1
		fenitrothion	< 0.2

CIVO-TNO May 1981

CONTAMINANTS IN CIVO TAP WATER (determined in period Sept. - Nov. 1981)

	ppb		ppm
lead	< 1	ammonia	< 0.01
cadmium	< 1	nitrate	9.3
mercury	< 5	nitrite	< 0.01
arsenic	< 10	chloride	30
selenium	< 1	sodium	17.5
copper	50	calcium	30.0
chromium	< 10	potassium	1.2
zinc	5	iron	0.03
cyanide	< 10		

	ppb		ppb
dichloromethane	< 5	HCB	< 0.01
1,1-dichloroethane	< 1	α-HCH	< 0.01
chloroform	< 0.1	lindane	< 0.01
1,1,1-trichloroethane	0.2	heptachlor	< 0.01
tetrachloromethane	0.2	heptachl. epoxide	< 0.02
trichloroethene	1.5	aldrin	< 0.02
tetrachloroethene	< 0.5	dieldrin	< 0.03
	ppt	α-chlordane	< 0.03
benzo(a)pyrene	< 2	γ-chlordane	< 0.03
benzo(b)fluoranthene	< 2	endrin	< 0.05
indeno (1,2,3,-c,d)pyrene	<10	p,p'-DDE	< 0.03
benzo(k)fluoranthene	< 2	o,p'-DDT	< 0.06
fluoranthene	< 1	p,p'-TDE	< 0.06
benzo(g,h,i)perylene	< 3	p,p'-DDT	< 0.1
		β-HCH	< 0.03
		methoxychlor	< 0.15
		PCB's	< 0.8
		DDVP	< 0.1
		mevinfos	< 0.1
		diazinon	< 0.1
		malathion	< 0.2
		parathion	< 0.2
		chlorpyrifos	< 0.1
		sulfotep	< 0.1
		fenitrothion	< 0.2

CIVO-TNO May 1982

ANNEX 19

CONTAMINANTS IN TAP WATER (determined in period Jan - March 1982)

	ppb		ppm
lead	< 1	ammonia	< 0.01
cadmium	< 1	nitrate	8.3
mercury	< 5	nitrite	< 0.01
arsenic	<10	chloride	23
selenium	< 1	sodium	13.0
copper	40	calcium	30.0
chromium	< 10	potassium	1.1
zinc	10	iron	0.02
cyanide	< 10		

	ppb		ppb
dichloromethane	< 5	HCB	< 0.01
1,1-dichloroethane	< 5	α-HCH	< 0.01
chloroform	< 0.5	lindane	< 0.01
1,1,1-trichloroethane	< 0.2	heptachlor	< 0.01
tetrachloromethane	< 0.1	heptachl. epoxide	< 0.02
trichloroethene	0.4	aldrin	< 0.02
tetrachloroethene	< 0.2	dieldrin	< 0.03
	ppt	α-chlordane	< 0.03
benzo(a)pyrene	< 1.3	γ-chlordane	< 0.03
benzo(b)fluoranthene	< 0.5	endrin	< 0.05
indeno (1,2,3,-c,d)pyrene	< 1.3	p,p'-DDE	< 0.03
benzo(k)fluoranthene	< 0.7	o,p'-DDT	< 0.06
fluoranthene	< 0.5	p,p'-TDE	< 0.06
benzo(g,h,i)perylene	< 5.4	p,p'-DDT	< 0.1
		β-HCH	< 0.03
		methoxychlor	< 0.15
		PCB's	< 0.8
		DDVP	< 0.1
		mevinfos	< 0.1
		diazinon	< 0.1
		malathion	< 0.2
		parathion	< 0.2
		chlorpyrifos	< 0.1
		sulfotep	< 0.1
		fenitrothion	< 0.2

CIVO-TNO May 1982

D/INO

O S S R E F E R E N C E L I S T I N G

SY NO. 125 0 ZERO REFERENCE DATE = 21/ M[illegible]Y

	MALES					FEMALES			
JMK	EXPR	SGP	CAGE	EARR	COMR	EXPR	SGP	CAGE	EARR
0002K	A 2	(0)	2	Z	770001D	A 1	(0)	1	Z
0004K	A 4	(0)	2	R1	770003D	A 3	(0)	1	R1
0006D	A 6	(0)	2	R2	770005D	A 5	(0)	1	R2
0008K	A 8	(0)	2	L1	770007D	A 7	(0)	1	L1
0010D	A 10	(0)	2	L2	770009D	A 9	(0)	1	L2
0012K	A 12	(0)	4	R1L1	770011K	A 11	(0)	3	R1L1
0014D	A 14	(0)	4	R1L2	770013D	A 13	(0)	3	R1L2
0016D	A 16	(0)	4	R2L1	770015D	A 15	(0)	3	R2L1
0018I	A 18	(0)	4	R2L2	770017K	A 17	(0)	3	R2L2
0020D	A 20	(0)	4	R3	770019D	A 19	(0)	3	R3
0022D	A 22	(0)	6	Z	770021D	A 21	(0)	5	Z
0024D	A 24	(0)	6	R1	770023D	A 23	(0)	5	R1
0026D	A 26	(0)	6	R2	770025K	A 25	(0)	5	R2
0028D	A 28	(0)	6	L1	770027D	A 27	(0)	5	L1
0030D	A 30	(0)	6	L2	770029D	A 29	(0)	5	L2
0032D	A 32	(0)	8	R1L1	770031D	A 31	(0)	7	R1L1
0034D	A 34	(0)	8	R1L2	770033K	A 33	(0)	7	R1L2
0036K	A 36	(0)	8	R2L1	770035D	A 35	(0)	7	R2L1
0038D	A 38	(0)	8	R2L2	770037K	A 37	(0)	7	R2L2
0040D	A 40	(0)	8	R3	770039D	A 39	(0)	7	R3
0042I	A 42	(0)	10	Z	770041K	A 41	(0)	9	Z
0044D	A 44	(0)	10	R1	770043D	A 43	(0)	9	R1
0046D	A 46	(0)	10	R2	770045K	A 45	(0)	9	R2
0048D	A 48	(0)	10	L1	770047K	A 47	(0)	9	L1
0050D	A 50	(0)	10	L2	770049D	A 49	(0)	9	L2
0052D	A 52	(0)	12	R1L1	770051K	A 51	(0)	11	R1L1
0054D	A 54	(0)	12	R1L2	770053D	A 53	(0)	11	R1L2
0056D	A 56	(0)	12	R2L1	770055D	A 55	(0)	11	R2L1
0058D	A 58	(0)	12	R2L2	770057D	A 57	(0)	11	R2L2
0060D	A 60	(0)	12	R3	770059D	A 59	(0)	11	R3
0062D	A 62	(0)	14	Z	770061D	A 61	(0)	13	Z
0064D	A 64	(0)	14	R1	770063I	A 63	(0)	13	R1
0066K	A 66	(0)	14	R2	770065K	A 65	(0)	13	R2
0068D	A 68	(0)	14	L1	770067I	A 67	(0)	13	L1
0070D	A 70	(0)	14	L2	770069D	A 69	(0)	13	L2
0072D	A 72	(0)	16	R1L1	770071D	A 71	(0)	15	R1L1
0074D	A 74	(0)	16	R1L2	770073D	A 73	(0)	15	R1L2
0076K	A 76	(0)	16	R2L1	770075D	A 75	(0)	15	R2L1
0078K	A 78	(0)	16	R2L2	770077D	A 77	(0)	15	R2L2
0080D	A 80	(0)	16	R3	770079I	A 79	(0)	15	R3
0082D	A 82	(0)	18	Z	770081D	A 81	(0)	17	Z
0084D	A 84	(0)	18	R1	770083K	A 83	(0)	17	R1
0086D	A 86	(0)	18	R2	770085D	A 85	(0)	17	R2
0088D	A 88	(0)	18	L1	770087D	A 87	(0)	17	L1
0090D	A 90	(0)	18	L2	770089D	A 89	(0)	17	L2
0092D	A 92	(0)	20	R1L1	770091D	A 91	(0)	19	R1L1
0094D	A 94	(0)	20	R1L2	770093D	A 93	(0)	19	R1L2
0096K	A 96	(0)	20	R2L1	770095D	A 95	(0)	19	R2L1
0098D	A 98	(0)	20	R2L2	770097D	A 97	(0)	19	R2L2

K = killed D = dead I = ill = (dead)

ANNEX 20 (CONT. 1)

O S S R E F E R E N C E L I S T I N G

SS NO. 125 0 ZERO REFERENCE DATE = 21/ 8/ 77

MALES					FEMALES				
OMR	EXPR	SGP	CAGE	EARR	COMR	EXPR	SGP	CAGE	EARR
0100D	A100	(0)	20	R3	770099D	A 99	(0)	19	R3
0102D	A102	(0)	22	Z	770101D	A101	(0)	21	Z
0104D	A104	(0)	22	R1	770103D	A103	(0)	21	R1
0106D	A106	(0)	22	R2	770105D	A105	(0)	21	R2
0108D	A108	(0)	22	L1	770107D	A107	(0)	21	L1
0110D	A110	(0)	22	L2	770109D	A109	(0)	21	L2
0112D	A112	(0)	24	R1L1	770111I	A111	(0)	23	R1L1
0114D	A114	(0)	24	R1L2	770113I	A113	(0)	23	R1L2
0116D	A116	(0)	24	R2L1	770115K	A115	(0)	23	R2L1
0118D	A118	(0)	24	R2L2	770117D	A117	(0)	23	R2L2
0120D	A120	(0)	24	R3	770119D	A119	(0)	23	R3
0122D	A122	(0)	26	Z	770121I	A121	(0)	25	Z
0124D	A124	(0)	26	R1	770123I	A123	(0)	25	R1
0126D	A126	(0)	26	R2	770125K	A125	(0)	25	R2
0128D	A128	(0)	26	L1	770127D	A127	(0)	25	L1
0130D	A130	(0)	26	L2	770129D	A129	(0)	25	L2
0132D	A132	(0)	28	R1L1	770131D	A131	(0)	27	R1L1
0134D	A134	(0)	28	R1L2	770133K	A133	(0)	27	R1L2
0136D	A136	(0)	28	R2L1	770135D	A135	(0)	27	R2L1
0138K	A138	(0)	28	R2L2	770137D	A137	(0)	27	R2L2
0140K	A140	(0)	28	R3	770139D	A139	(0)	27	R3
0142D	A142	(0)	30	Z	770141K	A141	(0)	29	Z
0144D	A144	(0)	30	R1	770143D	A143	(0)	29	R1
0146D	A146	(0)	30	R2	770145D	A145	(0)	29	R2
0148D	A148	(0)	30	L1	770147D	A147	(0)	29	L1
0150D	A150	(0)	30	L2	770149D	A149	(0)	29	L2
0152D	A152	(0)	32	R1L1	770151D	A151	(0)	31	R1L1
0154I	A154	(0)	32	R1L2	770153D	A153	(0)	31	R1L2
0156D	A156	(0)	32	R2L1	770155D	A155	(0)	31	R2L1
0158D	A158	(0)	32	R2L2	770157D	A157	(0)	31	R2L2
0160D	A160	(0)	32	R3	770159K	A159	(0)	31	R3
0162K	A162	(0)	34	Z	770161D	A161	(0)	33	Z
0164K	A164	(0)	34	R1	770163D	A163	(0)	33	R1
0166K	A166	(0)	34	R2	770165D	A165	(0)	33	R2
0168K	A168	(0)	34	L1	770167K	A167	(0)	33	L1
0170K	A170	(0)	34	L2	770169D	A169	(0)	33	L2
0172D	A172	(0)	36	R1L1	770171D	A171	(0)	35	R1L1
0174D	A174	(0)	36	R1L2	770173K	A173	(0)	35	R1L2
0176D	A176	(0)	36	R2L1	770175D	A175	(0)	35	R2L1
0178K	A178	(0)	36	R2L2	770177D	A177	(0)	35	R2L2
0180K	A180	(0)	36	R3	770179D	A179	(0)	35	R3
0182D	A182	(0)	38	Z	770181D	A181	(0)	37	Z
0184D	A184	(0)	38	R1	770183D	A183	(0)	37	R1
0186D	A186	(0)	38	R2	770185D	A185	(0)	37	R2
0188D	A188	(0)	38	L1	770187D	A187	(0)	37	L1
0190K	A190	(0)	38	L2	770189K	A189	(0)	37	L2
0192D	A192	(0)	40	R1L1	770191K	A191	(0)	39	R1L1
0194K	A194	(0)	40	R1L2	770193D	A193	(0)	39	R1L2
0196D	A196	(0)	40	R2L1	770195D	A195	(0)	39	R2L1
0198D	A198	(0)	40	R2L2	770197D	A197	(0)	39	R2L2
0200D	A200	(0)	40	R3	770199K	A199	(0)	39	R3

STING

O S S R E F E R E N C E L I S T I N G

ST NO. 125 0 ZERO REFERENCE RATE = [illegible]

MALES					FEMALES				
OMR	EXPR	SGP	CAGE	EARR	COMR	EXPR	SGP	CAGE	EARR
0202D	B 2	(0)	42	Z	770201K	B 1	(0)	41	Z
0204D	B 4	(0)	42	R1	770203K	B 3	(0)	41	R1
0206D	B 6	(0)	42	R2	770205D	B 5	(0)	41	R2
0208D	B 8	(0)	42	L1	770207D	B 7	(0)	41	L1
0210D	B 10	(0)	42	L2	770209D	B 9	(0)	41	L2
0212D	B 12	(0)	44	R1L1	770211D	B 11	(0)	43	R1L1
0214D	B 14	(0)	44	R1L2	770213D	B 13	(0)	43	R1L2
0216D	B 16	(0)	44	R2L1	770215D	B 15	(0)	43	R2L1
0218D	B 18	(0)	44	R2L2	770217K	B 17	(0)	43	R2L2
0220K	B 20	(0)	44	R3	770219D	B 19	(0)	43	R3
0222D	B 22	(0)	46	Z	770221D	B 21	(0)	45	Z
0224D	B 24	(0)	46	R1	7702231	B 23	(0)	45	R1
0226K	B 26	(0)	46	R2	770225D	B 25	(0)	45	R2
0228D	B 28	(0)	46	L1	770227D	B 27	(0)	45	L1
0230D	B 30	(0)	46	L2	770229D	B 29	(0)	45	L2
0232D	B 32	(0)	48	R1L1	770231D	B 31	(0)	47	R1L1
0234K	B 34	(0)	48	R1L2	770233D	B 33	(0)	47	R1L2
0236D	B 36	(0)	48	R2L1	770235D	B 35	(0)	47	R2L1
0238D	B 38	(0)	48	R2L2	770237D	B 37	(0)	47	R2L2
0240D	B 40	(0)	48	R3	770239K	B 39	(0)	47	R3
0242K	B 42	(0)	50	Z	770241D	B 41	(0)	49	Z
0244D	B 44	(0)	50	R1	770243D	B 43	(0)	49	R1
0246K	B 46	(0)	50	R2	770245D	B 45	(0)	49	R2
0248D	B 48	(0)	50	L1	770247K	B 47	(0)	49	L1
0250D	B 50	(0)	50	L2	770249D	B 49	(0)	49	L2
0252K	B 52	(0)	52	R1L1	770251D	B 51	(0)	51	R1L1
0254D	B 54	(0)	52	R1L2	770253D	B 53	(0)	51	R1L2
0256D	B 56	(0)	52	R2L1	770255D	B 55	(0)	51	R2L1
0258K	B 58	(0)	52	R2L2	770257K	B 57	(0)	51	R2L2
0260D	B 60	(0)	52	R3	770259D	B 59	(0)	51	R3
0262D	B 62	(0)	54	Z	770261K	B 61	(0)	53	Z
0264D	B 64	(0)	54	R1	770263K	B 63	(0)	53	R1
0266D	B 66	(0)	54	R2	770265D	B 65	(0)	53	R2
0268D	B 68	(0)	54	L1	770267K	B 67	(0)	53	L1
0270D	B 70	(0)	54	L2	770269D	B 69	(0)	53	L2
0272D	B 72	(0)	56	R1L1	770271K	B 71	(0)	55	R1L1
0274K	B 74	(0)	56	R1L2	770273D	B 73	(0)	55	R1L2
0276K	B 76	(0)	56	R2L1	770275K	B 75	(0)	55	R2L1
0278D	B 78	(0)	56	R2L2	770277D	B 77	(0)	55	R2L2
0280D	B 80	(0)	56	R3	770279D	B 79	(0)	55	R3
0282D	B 82	(0)	58	Z	770281D	B 81	(0)	57	Z
0284D	B 84	(0)	58	R1	770283D	B 83	(0)	57	R1
0286D	B 86	(0)	58	R2	770285D	B 85	(0)	57	R2
0288I	B 88	(0)	58	L1	770287K	B 87	(0)	57	L1
0290K	B 90	(0)	58	L2	770289D	B 89	(0)	57	L2
0292D	B 92	(0)	60	R1L1	770291D	B 91	(0)	59	R1L1
0294K	B 94	(0)	60	R1L2	770293D	B 93	(0)	59	R1L2

/TNO

O S S R E F E R E N C E L I S T I N G

SY NO. 125 0 ZERO REFERENCE DATE [illegible]

MALES					FEMALES				
JMR	EXPR	SGP	CAGE	EARR	COMR	EXPR	SGP	CAGE	EARR
02960	B 96	(0)	60	R2L1	770295K	B 95	(0)	59	R2L1
02980	B 98	(0)	60	R2L2	770297D	B 97	(0)	59	R2L2
03000	B100	(0)	60	R3	770299D	B 99	(0)	59	R3
03020	B102	(0)	62	Z	770301D	B101	(0)	61	Z
03040	B104	(0)	62	R1	7703031	B103	(0)	61	R1
03060	B106	(0)	62	R2	770305K	B105	(0)	61	R2
0308K	B108	(0)	62	L1	770307D	B107	(0)	61	L1
03100	B110	(0)	62	L2	770309K	B109	(0)	61	L2
03120	B112	(0)	64	R1L1	770311D	B111	(0)	63	R1L1
03140	B114	(0)	64	R1L2	7703131	B113	(0)	63	R1L2
03161	B116	(0)	64	R2L1	770315D	B115	(0)	63	R2L1
03180	B118	(0)	64	R2L2	770317D	B117	(0)	63	R2L2
03200	B120	(0)	64	R3	770319D	B119	(0)	63	R3
03220	B122	(0)	66	Z	7703211	B121	(0)	65	Z
03240	B124	(0)	66	R1	7703231	B123	(0)	65	R1
03260	B126	(0)	66	R2	770325D	B125	(0)	65	R2
03280	B128	(0)	66	L1	770327K	B127	(0)	65	L1
03300	B130	(0)	66	L2	770329D	B129	(0)	65	L2
03320	B132	(0)	68	R1L1	770331D	B131	(0)	67	R1L1
03340	B134	(0)	68	R1L2	770333D	B133	(0)	67	R1L2
03360	B136	(0)	68	R2L1	770335D	B135	(0)	67	R2L1
03380	B138	(0)	68	R2L2	770337D	B137	(0)	67	R2L2
03401	B140	(0)	68	R3	770339I	B139	(0)	67	R3
03420	B142	(0)	70	Z	770341D	B141	(0)	69	Z
03440	B144	(0)	70	R1	770343D	B143	(0)	69	R1
03460	B146	(0)	70	R2	770345D	B145	(0)	69	R2
03480	B148	(0)	70	L1	770347K	B147	(0)	69	L1
03500	B150	(0)	70	L2	770349D	B149	(0)	69	L2
03520	B152	(0)	72	R1L1	770351K	B151	(0)	71	R1L1
03540	B154	(0)	72	R1L2	770353K	B153	(0)	71	R1L2
03560	B156	(0)	72	R2L1	770355D	B155	(0)	71	R2L1
03580	B158	(0)	72	R2L2	770357D	B157	(0)	71	R2L2
03600	B160	(0)	72	R3	770359D	B159	(0)	71	R3
03620	B162	(0)	74	Z	770361D	B161	(0)	73	Z
03640	B164	(0)	74	R1	7703631	B163	(0)	73	R1
03660	B166	(0)	74	R2	770365K	B165	(0)	73	R2
03680	B168	(0)	74	L1	770367D	B167	(0)	73	L1
03700	B170	(0)	74	L2	770369K	B169	(0)	73	L2
03720	B172	(0)	76	R1L1	770371D	B171	(0)	75	R1L1
03740	B174	(0)	76	R1L2	770373D	B173	(0)	75	R1L2
03760	B176	(0)	76	R2L1	770375D	B175	(0)	75	R2L1
03780	B178	(0)	76	R2L2	770377D	B177	(0)	75	R2L2
03800	B180	(0)	76	R3	770379D	B179	(0)	75	R3
03820	B182	(0)	78	Z	770381D	B181	(0)	77	Z
03840	B184	(0)	78	R1	770383D	B183	(0)	77	R1
03860	B186	(0)	78	R2	770385D	B185	(0)	77	R2
03880	B188	(0)	78	L1	770387K	B187	(0)	77	L1
03901	B190	(0)	78	L2	770389K	B189	(0)	77	L2
03920	B192	(0)	80	R1L1	770391D	B191	(0)	79	R1L1
03940	B194	(0)	80	R1L2	770393D	B193	(0)	79	R1L2
03960	B196	(0)	80	R2L1	770395D	B195	(0)	79	R2L1
03980	B198	(0)	80	R2L2	770397D	B197	(0)	79	R2L2
04000	B200	(0)	80	R3	7703991	B199	(0)	79	R3

R&S 006561

O S S R E F E R E N C E L I S T I N G

SY NO. 125 0 ZERO REFERENCE DATE - [illegible]

MALES					FEMALES				
OMR	EXPR	SGP	CAGE	EARR	COMR	EXPR	SGP	CAGE	EARR
70402D	C 2	(0)	82	Z	770401K	C 1	(0)	81	Z
70404K	C 4	(0)	82	R1	770403D	C 3	(0)	81	R1
70406D	C 6	(0)	82	R2	770405D	C 5	(0)	81	R2
70408D	C 8	(0)	82	L1	770407D	C 7	(0)	81	L1
70410D	C 10	(0)	82	L2	770409K	C 9	(0)	81	L2
70412K	C 12	(0)	84	R1L1	770411D	C 11	(0)	83	R1L1
70414K	C 14	(0)	84	R1L2	770413D	C 13	(0)	83	R1L2
70416K	C 16	(0)	84	R2L1	770415K	C 15	(0)	83	R2L1
70418K	C 18	(0)	84	R2L2	770417D	C 17	(0)	83	R2L2
70420D	C 20	(0)	84	R3	770419D	C 19	(0)	83	R3
70422D	C 22	(0)	86	Z	770421D	C 21	(0)	85	Z
70424D	C 24	(0)	86	R1	770423D	C 23	(0)	85	R1
70426D	C 26	(0)	86	R2	770425I	C 25	(0)	85	R2
70428D	C 28	(0)	86	L1	770427D	C 27	(0)	85	L1
70430D	C 30	(0)	86	L2	770429D	C 29	(0)	85	L2
70432D	C 32	(0)	88	R1L1	770431K	C 31	(0)	87	R1L1
70434D	C 34	(0)	88	R1L2	770433D	C 33	(0)	87	R1L2
70436D	C 36	(0)	88	R2L1	770435I	C 35	(0)	87	R2L1
70438D	C 38	(0)	88	R2L2	770437K	C 37	(0)	87	R2L2
70440D	C 40	(0)	88	R3	770439K	C 39	(0)	87	R3
70442D	C 42	(0)	90	Z	770441D	C 41	(0)	89	Z
70444D	C 44	(0)	90	R1	770443D	C 43	(0)	89	R1
70446D	C 46	(0)	90	R2	770445D	C 45	(0)	89	R2
70448D	C 48	(0)	90	L1	770447D	C 47	(0)	89	L1
70450K	C 50	(0)	90	L2	770449K	C 49	(0)	89	L2
70452D	C 52	(0)	92	R1L1	770451D	C 51	(0)	91	R1L1
70454D	C 54	(0)	92	R1L2	770453D	C 53	(0)	91	R1L2
70456D	C 56	(0)	92	R2L1	770455D	C 55	(0)	91	R2L1
70458D	C 58	(0)	92	R2L2	770457D	C 57	(0)	91	R2L2
70460D	C 60	(0)	92	R3	770459D	C 59	(0)	91	R3
70462K	C 62	(0)	94	Z	770461K	C 61	(0)	93	Z
70464D	C 64	(0)	94	R1	770463K	C 63	(0)	93	R1
70466K	C 66	(0)	94	R2	770465I	C 65	(0)	93	R2
70468K	C 68	(0)	94	L1	770467K	C 67	(0)	93	L1
70470K	C 70	(0)	94	L2	770469D	C 69	(0)	93	L2
70472D	C 72	(0)	96	R1L1	770471D	C 71	(0)	95	R1L1
70474K	C 74	(0)	96	R1L2	770473D	C 73	(0)	95	R1L2
70476D	C 76	(0)	96	R2L1	770475K	C 75	(0)	95	R2L1
70478D	C 78	(0)	96	R2L2	770477D	C 77	(0)	95	R2L2
70480D	C 80	(0)	96	R3	770479D	C 79	(0)	95	R3
70482D	C 82	(0)	98	Z	770481D	C 81	(0)	97	Z
70484D	C 84	(0)	98	R1	770483D	C 83	(0)	97	R1
70486D	C 86	(0)	98	R2	770485K	C 85	(0)	97	R2
70488D	C 88	(0)	98	L1	770487D	C 87	(0)	97	L1
70490D	C 90	(0)	98	L2	770489D	C 89	(0)	97	L2

O/TNO

O S S R E F E R E N C E L I S T I N G

AY NO. 125 0 ZERO REFERENCE DATE = 217 0779

MALES					FEMALES				
OMR	EXPR	SGP	CAGE	EARR	COMR	EXPR	SGP	CAGE	EARR
0492D	C 92	(0)	100	R1L1	770491D	C 91	(0)	99	R1L1
0494D	C 94	(0)	100	R1L2	770493D	C 93	(0)	99	R1L2
0496K	C 96	(0)	100	R2L1	770495K	C 95	(0)	99	R2L1
0498I	C 98	(0)	100	R2L2	770497K	C 97	(0)	99	R2L2
0500K	C100	(0)	100	R3	770499K	C 99	(0)	99	R3
0502I	C102	(0)	102	Z	770501D	C101	(0)	101	Z
0504D	C104	(0)	102	R1	770503K	C103	(0)	101	R1
0506K	C106	(0)	102	R2	770505D	C105	(0)	101	R2
0508D	C108	(0)	102	L1	770507K	C107	(0)	101	L1
0510D	C110	(0)	102	L2	770509D	C109	(0)	101	L2
0512D	C112	(0)	104	R1L1	770511K	C111	(0)	103	R1L1
0514D	C114	(0)	104	R1L2	770513D	C113	(0)	103	R1L2
0516D	C116	(0)	104	R2L1	770515D	C115	(0)	103	R2L1
0518D	C118	(0)	104	R2L2	770517K	C117	(0)	103	R2L2
0520D	C120	(0)	104	R3	770519D	C119	(0)	103	R3
0522D	C122	(0)	106	Z	770521D	C121	(0)	105	Z
0524D	C124	(0)	106	R1	770523K	C123	(0)	105	R1
0526D	C126	(0)	106	R2	770525K	C125	(0)	105	R2
0528D	C128	(0)	106	L1	770527D	C127	(0)	105	L1
0530K	C130	(0)	106	L2	770529I	C129	(0)	105	L2
0532D	C132	(0)	108	R1L1	770531D	C131	(0)	107	R1L1
0534D	C134	(0)	108	R1L2	770533D	C133	(0)	107	R1L2
0536D	C136	(0)	108	R2L1	770535D	C135	(0)	107	R2L1
0538D	C138	(0)	108	R2L2	770537D	C137	(0)	107	R2L2
0540D	C140	(0)	108	R3	770539D	C139	(0)	107	R3
0542D	C142	(0)	110	Z	770541D	C141	(0)	109	Z
0544K	C144	(0)	110	R1	770543K	C143	(0)	109	R1
0546D	C146	(0)	110	R2	770545I	C145	(0)	109	R2
0548D	C148	(0)	110	L1	770547D	C147	(0)	109	L1
0550D	C150	(0)	110	L2	770549D	C149	(0)	109	L2
0552K	C152	(0)	112	R1L1	770551D	C151	(0)	111	R1L1
0554D	C154	(0)	112	R1L2	770553D	C153	(0)	111	R1L2
0556D	C156	(0)	112	R2L1	770555D	C155	(0)	111	R2L1
0558D	C158	(0)	112	R2L2	770557D	C157	(0)	111	R2L2
0560D	C160	(0)	112	R3	770559I	C159	(0)	111	R3
0562D	C162	(0)	114	Z	770561D	C161	(0)	113	Z
0564D	C164	(0)	114	R1	770563D	C163	(0)	113	R1
0566D	C166	(0)	114	R2	770565D	C165	(0)	113	R2
0568I	C168	(0)	114	L1	770567D	C167	(0)	113	L1
0570D	C170	(0)	114	L2	770569D	C169	(0)	113	L2
0572D	C172	(0)	116	R1L1	770571D	C171	(0)	115	R1L1
0574D	C174	(0)	116	R1L2	770573D	C173	(0)	115	R1L2
0576D	C176	(0)	116	R2L1	770575D	C175	(0)	115	R2L1
0578D	C178	(0)	116	R2L2	770577D	C177	(0)	115	R2L2
0580D	C180	(0)	116	R3	770579D	C179	(0)	115	R3
0582K	C182	(0)	118	Z	770581D	C181	(0)	117	Z
0584D	C184	(0)	118	R1	770583D	C183	(0)	117	R1
0586I	C186	(0)	118	R2	770585K	C185	(0)	117	R2
0588D	C188	(0)	118	L1	770587D	C187	(0)	117	L1
0590D	C190	(0)	118	L2	770589D	C189	(0)	117	L2
0592D	C192	(0)	120	R1L1	770591K	C191	(0)	119	R1L1
0594D	C194	(0)	120	R1L2	770593D	C193	(0)	119	R1L2
0596D	C196	(0)	120	R2L1	770595D	C195	(0)	119	R2L1
0598D	C198	(0)	120	R2L2	770597K	C197	(0)	119	R2L2
0600D	C200	(0)	120	R3	770599D	C199	(0)	119	R3

O/TNO

O S S R E F E R E N C E L I S T I N G

AY NO. 125 0 ZERO REFERENCE DATE = 21/ 87 /

MALES					FEMALES				
OMK	EXPR	SGP	CAGE	EARR	COMK	EXPR	SGP	CAGE	EARR
0602D	D 2	(0)	122	Z	770601D	D 1	(0)	121	Z
0604D	D 4	(0)	122	R1	770603D	D 3	(0)	121	R1
0606D	D 6	(0)	122	R2	770605D	D 5	(0)	121	R2
0608D	D 8	(0)	122	L1	770607D	D 7	(0)	121	L1
0610D	D 10	(0)	122	L2	770609K	D 9	(0)	121	L2
0612D	D 12	(0)	124	R1L1	770611D	D 11	(0)	123	R1L1
0614D	D 14	(0)	124	R1L2	770613D	D 13	(0)	123	R1L2
0616D	D 16	(0)	124	R2L1	770615D	D 15	(0)	123	R2L1
0618K	D 18	(0)	124	R2L2	7706171	D 17	(0)	123	R2L2
0620D	D 20	(0)	124	R3	770619D	D 19	(0)	123	R3
0622D	D 22	(0)	126	Z	770621D	D 21	(0)	125	Z
0624D	D 24	(0)	126	R1	770623D	D 23	(0)	125	R1
0626D	D 26	(0)	126	R2	770625K	D 25	(0)	125	R2
0628K	D 28	(0)	126	L1	770627D	D 27	(0)	125	L1
0630D	D 30	(0)	126	L2	770629D	D 29	(0)	125	L2
0632D	D 32	(0)	128	R1L1	770631D	D 31	(0)	127	R1L1
0634D	D 34	(0)	128	R1L2	770633D	D 33	(0)	127	R1L2
0636D	D 36	(0)	128	R2L1	770635D	D 35	(0)	127	R2L1
0638D	D 38	(0)	128	R2L2	770637D	D 37	(0)	127	R2L2
0640D	D 40	(0)	128	R3	770639D	D 39	(0)	127	R3
0642D	D 42	(0)	130	Z	770641D	D 41	(0)	129	Z
0644K	D 44	(0)	130	R1	770643D	D 43	(0)	129	R1
0646D	D 46	(0)	130	R2	770645D	D 45	(0)	129	R2
0648D	D 48	(0)	130	L1	770647D	D 47	(0)	129	L1
0650D	D 50	(0)	130	L2	770649D	D 49	(0)	129	L2
0652K	D 52	(0)	132	R1L1	770651D	D 51	(0)	131	R1L1
0654D	D 54	(0)	132	R1L2	770653D	D 53	(0)	131	R1L2
0656D	D 56	(0)	132	R2L1	770655D	D 55	(0)	131	R2L1
0658D	D 58	(0)	132	R2L2	770657D	D 57	(0)	131	R2L2
0660D	D 60	(0)	132	R3	770659D	D 59	(0)	131	R3
0662D	D 62	(0)	134	Z	770661I	D 61	(0)	133	Z
0664K	D 64	(0)	134	R1	770663K	D 63	(0)	133	R1
0666D	D 66	(0)	134	R2	7706651	D 65	(0)	133	R2
0668K	D 68	(0	134	L1	770667D	D 67	(0)	133	L1
0670K	D 70	(0)	134	L2	0669K	D 69	(0)	133	L2
0672D	D 72	(0)	136	R1L1	770671D	D 71	(0)	135	L1
0674K	D 74	(0)	136	R1L2	770673D	D 73	(0)	135	R1L2
0676D	D 76	(0)	136	R2L1	770675D	D 75	(0)	135	R2L1
0678D	D 78	(0)	136	R2L2	7706771	D 77	(0)	135	R2L2
0680D	D 80	(0)	136	R3	770679D	D 79	(0)	135	R3
0682D	D 82	(0)	138	Z	770681D	D 81	(0)	137	Z
0684D	D 84	(0)	138	R1	770683D	D 83	(0)	137	R1
0686I	D 86	(0)	138	R2	770685D	D 85	(0)	137	R2
0688D	D 88	(0)	138	L1	770687D	D 87	(0)	137	L1
0690D	D 90	(0)	138	L2	770689D	D 89	(0)	137	L2
0692D	D 92	(0)	140	R1L1	770691D	D 91	(0)	139	R1L1
0694D	D 94	(0)	140	R1L2	770693D	D 93	(0)	139	R1L2

'O/TNO

'OSS REFERENCE LISTING

AY NO. 125 0 ZERO REFERENCE DATE [illegible]

MALES					FEMALES				
COMR	EXPR	SGP	CAGE	EARR	COMR	EXPR	SGP	CAGE	EARR
770696D	D 96	(0)	140	R2L1	770695D	D 95	(0)	139	R2L1
770698D	D 98	(0)	140	R2L2	770697D	D 97	(0)	139	R2L2
770700D	D100	(0)	140	R3	770699D	D 99	(0)	139	R3
770702K	D102	(0)	142	Z	770701K	D101	(0)	141	Z
770704K	D104	(0)	142	R1	770703K	D103	(0)	141	R1
770706K	D106	(0)	142	R2	770705K	D105	(0)	141	R2
770708K	D108	(0)	142	L1	770707K	D107	(0)	141	L1
770710K	D110	(0)	142	L2	770709K	D109	(0)	141	L2
770712K	D112	(0)	144	R1L1	770711K	D111	(0)	143	R1L1
770714K	D114	(0)	144	R1L2	770713K	D113	(0)	143	R1L2
770716K	D116	(0)	144	R2L1	770715K	D115	(0)	143	R2L1
770718K	D118	(0)	144	R2L2	770717K	D117	(0)	143	R2L2
770720K	D120	(0)	144	R3	770719K	D119	(0)	143	R3
770722K	D122	(0)	146	Z	770721K	D121	(0)	145	Z
770724K	D124	(0)	146	R1	770723K	D123	(0)	145	R1
770726K	D126	(0)	146	R2	770725K	D125	(0)	145	R2
770728K	D128	(0)	146	L1	770727K	D127	(0)	145	L1
770730K	D130	(0)	146	L2	770729K	D129	(0)	145	L2
770732K	D132	(0)	148	R1L1	770731K	D131	(0)	147	R1L1
770734K	D134	(0)	148	R1L2	770733K	D133	(0)	147	R1L2
770736K	D136	(0)	148	R2L1	770735K	D135	(0)	147	R2L1
770738K	D138	(0)	148	R2L2	770737K	D137	(0)	147	R2L2
770740K	D140	(0)	148	R3	770739K	D139	(0)	147	R3
770742K	D142	(0)	150	Z	770741K	D141	(0)	149	Z
770744K	D144	(0)	150	R1	770743K	D143	(0)	149	R1
770746K	D146	(0)	150	R2	770745K	D145	(0)	149	R2
770748K	D148	(0)	150	L1	770747K	D147	(0)	149	L1
770750K	D150	(0)	150	L2	770749K	D149	(0)	149	L2
770752K	D152	(0)	152	R1L1	770751K	D151	(0)	151	R1L1
770754K	D154	(0)	152	R1L2	770753K	D153	(0)	151	R1L2
770756K	D156	(0)	152	R2L1	770755K	D155	(0)	151	R2L1
770758K	D158	(0)	152	R2L2	770757K	D157	(0)	151	R2L2
770760K	D160	(0)	152	R3	770759K	D159	(0)	151	R3
770762K	D162	(0)	154	Z	770761K	D161	(0)	153	Z
770764K	D164	(0)	154	R1	770763K	D163	(0)	153	R1
770766K	D166	(0)	154	R2	770765K	D165	(0)	153	R2
770768K	D168	(0)	154	L1	770767K	D167	(0)	153	L1
770770K	D170	(0)	154	L2	770769K	D169	(0)	153	L2
770772K	D172	(0)	156	R1L1	770771K	D171	(0)	155	R1L1
770774K	D174	(0)	156	R1L2	770773K	D173	(0)	155	R1L2
770776K	D176	(0)	156	R2L1	770775K	D175	(0)	155	R2L1
770778K	D178	(0)	156	R2L2	770777K	D177	(0)	155	R2L2
770780K	D180	(0)	156	R3	770779K	D179	(0)	155	R3
770782K	D182	(0)	158	Z	770781K	D181	(0)	157	Z
770784K	D184	(0)	158	R1	770783K	D183	(0)	157	R1
770786K	D186	(0)	158	R2	770785K	D185	(0)	157	R2
770788K	D188	(0)	158	L1	770787K	D187	(0)	157	L1
770790K	D190	(0)	158	L2	770789K	D189	(0)	157	L2
770792K	D192	(0)	160	R1L1	770791K	D191	(0)	159	R1L1
770794K	D194	(0)	160	R1L2	770793K	D193	(0)	159	R1L2
770796K	D196	(0)	160	R2L1	770795K	D195	(0)	159	R2L1
770798K	D198	(0)	160	R2L2	770797K	D197	(0)	159	R2L2
770800K	D200	(0)	160	R3	770799K	D199	(0)	159	R3

OSS REFERENCE LISTING

SY NO. 125 0 ZERO REFERENCE DATE = 21 [illegible]

MALES					FEMALES				
DMR	EXPR	SGP	CAGE	FARR	COMR	EXPR	SGP	CAGE	FARR
0802D	E 2	(0)	162	Z	770801D	E 1	(0)	161	Z
0804D	E 4	(0)	162	R1	770803D	E 3	(0)	161	R1
0806D	E 6	(0)	162	R2	770805D	E 5	(0)	161	R2
0808D	E 8	(0)	162	L1	770807D	E 7	(0)	161	L1
0810D	E 10	(0)	162	L2	770809D	E 9	(0)	161	L2
0812D	E 12	(0)	164	R1L1	770811D	E 11	(0)	163	R1L1
0814D	E 14	(0)	164	R1L2	770813D	E 13	(0)	163	R1L2
0816D	E 16	(0)	164	R2L1	770815D	E 15	(0)	163	R2L1
0818D	E 18	(0)	164	R2L2	770817D	E 17	(0)	163	R2L2
0820D	E 20	(0)	164	R3	770819D	E 19	(0)	163	R3
0822D	E 22	(0)	166	Z	770821D	E 21	(0)	165	Z
0824D	E 24	(0)	166	R1	770823D	E 23	(0)	165	R1
0826D	E 26	(0)	166	R2	770825D	E 25	(0)	165	R2
0828D	E 28	(0)	166	L1	770827D	E 27	(0)	165	L1
0830D	E 30	(0)	166	L2	770829D	E 29	(0)	165	L2
0832D	E 32	(0)	168	R1L1	770831D	E 31	(0)	167	R1L1
0834D	E 34	(0)	168	R1L2	770833D	E 33	(0)	167	R1L2
0836D	E 36	(0)	168	R2L1	770835D	E 35	(0)	167	R2L1
0838D	E 38	(0)	168	R2L2	770837D	E 37	(0)	167	R2L2
0840D	E 40	(0)	168	R3	770839D	E 39	(0)	167	R3
0842D	E 42	(0)	170	Z	770841D	E 41	(0)	169	Z
0844D	E 44	(0)	170	R1	770843D	E 43	(0)	169	R1
0846D	E 46	(0)	170	R2	770845D	E 45	(0)	169	R2
0848D	E 48	(0)	170	L1	770847D	E 47	(0)	169	L1
0850D	E 50	(0)	170	L2	770849D	E 49	(0)	169	L2
0852D	E 52	(0)	172	R1L1	770851D	E 51	(0)	171	R1L1
0854D	E 54	(0)	172	R1L2	770853D	E 53	(0)	171	R1L2
0856D	E 56	(0)	172	R2L1	770855D	E 55	(0)	171	R2L1
0858D	E 58	(0)	172	R2L2	770857D	E 57	(0)	171	R2L2
0860D	E 60	(0)	172	R3	770859D	E 59	(0)	171	R3
0862D	E 62	(0)	174	Z	770861D	E 61	(0)	173	Z
0864D	E 64	(0)	174	R1	770863D	E 63	(0)	173	R1
0866D	E 66	(0)	174	R2	770865D	E 65	(0)	173	R2
0868D	E 68	(0)	174	L1	770867D	E 67	(0)	173	L1
0870D	E 70	(0)	174	L2	770869D	E 69	(0)	173	L2
0872D	E 72	(0)	176	R1L1	770871D	E 71	(0)	175	R1L1
0874D	E 74	(0)	176	R1L2	770873D	E 73	(0)	175	R1L2
0876D	E 76	(0)	176	R2L1	770875D	E 75	(0)	175	R2L1
0878D	E 78	(0)	176	R2L2	770877D	E 77	(0)	175	R2L2
0880D	E 80	(0)	176	R3	770879D	E 79	(0)	175	R3
0882D	E 82	(0)	178	Z	770881D	E 81	(0)	177	Z
0884D	E 84	(0)	178	R1	770883D	E 83	(0)	177	R1
0886D	E 86	(0)	178	R2	770885D	E 85	(0)	177	R2
0888D	E 88	(0)	178	L1	770887D	E 87	(0)	177	L1
0890D	E 90	(0)	178	L2	770889D	E 89	(0)	177	L2
0892D	E 92	(0)	180	R1L1	770891D	E 91	(0)	179	R1L1
0894D	E 94	(0)	180	R1L2	770893D	E 93	(0)	179	R1L2

ANNEX 20 (CONT. 9)
TNO

) S S R E F E R E N C E L I S T I N G

· NO. 125 0 ZERO REFERENCE DATE - 21/ 8/7

MALES					FEMALES				
MF	EXPR	SGP	CAGE	EARR	COMR	EXPR	SGP	CAGE	EARR
896D	E 96	(0)	180	R2L1	770895D	E 95	(0)	179	R2L1
898D	E 98	(0)	180	R2L2	770897D	E 97	(0)	179	R2L2
900D	E100	(0)	180	R3	770899D	E 99	(0)	179	R3
902D	E102	(0)	182	Z	770901D	E101	(0)	181	Z
904D	E104	(0)	182	R1	770903D	E103	(0)	181	R1
906D	E106	(0)	182	R2	770905D	E105	(0)	181	R2
908D	E108	(0)	182	L1	770907D	E107	(0)	181	L1
910D	E110	(0)	182	L2	770909D	E109	(0)	181	L2
912D	E112	(0)	184	R1L1	770911D	E111	(0)	183	R1L1
914D	E114	(0)	184	R1L2	770913D	E113	(0)	183	R1L2
916D	E116	(0)	184	R2L1	770915D	E115	(0)	183	R2L1
918I	E118	(0)	184	R2L2	770917D	E117	(0)	183	R2L2
920D	E120	(0)	184	R3	770919D	E119	(0)	183	R3
922D	E122	(0)	186	Z	770921D	E121	(0)	185	Z
924D	E124	(0)	186	R1	770923D	E123	(0)	185	R1
926I	E126	(0)	186	R2	770925D	E125	(0)	185	R2
928I	E128	(0)	186	L1	770927D	E127	(0)	185	L1
930I	E130	(0)	186	L2	770929D	E129	(0)	185	L2
932D	E132	(0)	188	R1L1	770931D	E131	(0)	187	R1L1
934D	E134	(0)	188	R1L2	770933D	E133	(0)	187	R1L2
936D	E136	(0)	188	R2L1	770935D	E135	(0)	187	R2L1
938I	E138	(0)	188	R2L2	770937D	E137	(0)	187	R2L2
940I	E140	(0)	188	R3	770939D	E139	(0)	187	R3
942D	E142	(0)	190	Z	770941D	E141	(0)	189	Z
944D	E144	(0)	190	R1	770943D	E143	(0)	189	R1
946D	E146	(0)	190	R2	770945D	E145	(0)	189	R2
948D	E148	(0)	190	L1	770947D	E147	(0)	189	L1
950D	E150	(0)	190	L2	770949D	E149	(0)	189	L2
952I	E152	(0)	192	R1L1	770951D	E151	(0)	191	R1L1
954D	E154	(0)	192	R1L2	770953D	E153	(0)	191	R1L2
956D	E156	(0)	192	R2L1	770955D	E155	(0)	191	R2L1
958D	E158	(0)	192	R2L2	770957D	E157	(0)	191	R2L2
960D	E160	(0)	192	R3	770959D	E159	(0)	191	R3
962D	E162	(0)	194	Z	770961D	E161	(0)	193	Z
964D	E164	(0)	194	R1	770963D	E163	(0)	193	R1
966D	E166	(0)	194	R2	770965D	E165	(0)	193	R2
968D	E168	(0)	194	L1	770967D	E167	(0)	193	L1
970D	E170	(0)	194	L2	770969D	E169	(0)	193	L2
972D	E172	(0)	196	R1L1	770971D	E171	(0)	195	R1L1
974D	E174	(0)	196	R1L2	770973D	E173	(0)	195	R1L2
976I	E176	(0)	196	R2L1	770975D	E175	(0)	195	R2L1
978D	E178	(0)	196	R2L2	770977D	E177	(0)	195	R2L2
980I	E180	(0)	196	R3	770979D	E179	(0)	195	R3
982D	E182	(0)	198	Z	770981D	E181	(0)	197	Z
984D	E184	(0)	198	R1	770983D	E183	(0)	197	R1
986D	E186	(0)	198	R2	770985D	E185	(0)	197	R2
988D	E188	(0)	198	L1	770987D	E187	(0)	197	L1
990I	E190	(0)	198	L2	770989D	E189	(0)	197	L2
992D	E192	(0)	200	R1L1	770991D	E191	(0)	199	R1L1
994D	E194	(0)	200	R1L2	770993D	E193	(0)	199	R1L2
996D	E196	(0)	200	R2L1	770995D	E195	(0)	199	R2L1
998D	E198	(0)	200	R2L2	770997D	E197	(0)	199	R2L2
1000D	E200	(0)	200	R3	770999D	E199	(0)	199	R3

JTAL MALES = 500 TOTAL FEMALES = 500

R&S 006567

ANNEX 21
VD/1ND

R O S S R E F E R E N C E L I S T I N G

ISAY NO. 126 0

MALES					FEMALES				
COMR	EXPR	SGP	CAGE	EARR	COMR	EXPR	SGP	CAGE	EARR
780002	A 2	(0)	2	Z	780001	A 1	(0)	1	Z
780004	A 4	(0)	2	R1	780003	A 3	(0)	1	R1
780006	A 6	(0)	2	R2	780005	A 5	(0)	1	R2
780008	A 8	(0)	2	L1	780007	A 7	(0)	1	L1
780010	A 10	(0)	2	L2	780009	A 9	(0)	1	L2
780012	A 12	(0)	4	R1L1	780011	A 11	(0)	3	R1L1
780014	A 14	(0)	4	R1L2	780013	A 13	(0)	3	R1L2
780016	A 16	(0)	4	R2L1	780015	A 15	(0)	3	R2L1
780018	A 18	(0)	4	R2L2	780017	A 17	(0)	3	R2L2
780020	A 20	(0)	4	R3	780019	A 19	(0)	3	R3
780022	B 2	(0)	6	Z	780021	B 1	(0)	5	Z
780024	B 4	(0)	6	R1	780023	B 3	(0)	5	R1
780026	B 6	(0)	6	R2	780025	B 5	(0)	5	R2
780028	B 8	(0)	6	L1	780027	B 7	(0)	5	L1
780030	B 10	(0)	6	L2	780029	B 9	(0)	5	L2
780032	B 12	(0)	8	R1L1	780031	B 11	(0)	7	R1L1
780034	B 14	(0)	8	R1L2	780033	B 13	(0)	7	R1L2
780036	B 16	(0)	8	R2L1	780035	B 15	(0)	7	R2L1
780038	B 18	(0)	8	R2L2	780037	B 17	(0)	7	R2L2
780040	B 20	(0)	8	R3	780039	B 19	(0)	7	R3
780042	C 2	(0)	10	Z	780041	C 1	(0)	9	Z
780044	C 4	(0)	10	R1	780043	C 3	(0)	9	R1
780046	C 6	(0)	10	R2	780045	C 5	(0)	9	R2
780048	C 8	(0)	10	L1	780047	C 7	(0)	9	L1
780050	C 10	(0)	10	L2	780049	C 9	(0)	9	L2
780052	C 12	(0)	12	R1L1	780051	C 11	(0)	11	R1L1
780054	C 14	(0)	12	R1L2	780053	C 13	(0)	11	R1L2
780056	C 16	(0)	12	R2L1	780055	C 15	(0)	11	R2L1
780058	C 18	(0)	12	R2L2	780057	C 17	(0)	11	R2L2
780060	C 20	(0)	12	R3	780059	C 19	(0)	11	R3
780062	D 2	(0)	14	Z	780061	D 1	(0)	13	Z
780064	D 4	(0)	14	R1	780063	D 3	(0)	13	R1
780066	D 6	(0)	14	R2	780065	D 5	(0)	13	R2
780068	D 8	(0)	14	L1	780067	D 7	(0)	13	L1
780070	D 10	(0)	14	L2	780069	D 9	(0)	13	L2
780072	D 12	(0)	16	R1L1	780071	D 11	(0)	15	R1L1
780074	D 14	(0)	16	R1L2	780073	D 13	(0)	15	R1L2
780076	D 16	(0)	16	R2L1	780075	D 15	(0)	15	R2L1
780078	D 18	(0)	16	R2L2	780077	D 17	(0)	15	R2L2
780080	D 20	(0)	16	R3	780079	D 19	(0)	15	R3
780082	E 2	(0)	18	Z	780081	E 1	(0)	17	Z
780084	E 4	(0)	18	R1	780083	E 3	(0)	17	R1
780086	E 6	(0)	18	R2	780085	E 5	(0)	17	R2
780088	E 8	(0)	18	L1	780087	E 7	(0)	17	L1
780090	E 10	(0)	18	L2	780089	E 9	(0)	17	L2
780092	E 12	(0)	20	R1L1	780091	E 11	(0)	19	R1L1
780094	E 14	(0)	20	R1L2	780093	E 13	(0)	19	R1L2
780096	E 16	(0)	20	R2L1	780095	E 15	(0)	19	R2L1
780098	E 18	(0)	20	R2L2	780097	E 17	(0)	19	R2L2
780100	F 20	(0)	20	R3	780099	E 19	(0)	19	R3

TOTAL MALES = 50

TOTAL FEMALES = 50