

STERLING DRUG INC.
80 PARK AVENUE, NEW YORK, N.Y. 10016

ANTHONY E. ANZALONE
CORPORATE DIRECTOR FOR
OF GOVERNMENT AFFAIRS

August 18, 1978

TELEPHONE: (212) 972-1000
TELEX: 121928

Mr. Lawrence J. Nadler
Chief, Chemical Systems Section
New York State Department of
Environmental Conservation
30 Wolf Road
Albany, New York

Dear Mr. Nadler:

In response to your March 16, 1977 letter Sterling Drug Inc. has conducted wastewater monitoring of the effluent from the following operations:

1. Sterling Drug Inc. - 33 Riverside Avenue, Rensselaer, New York, 12144.
2. Sterling Drug Inc. - Red Mill Road, East Greenbush, New York, 12144.
3. Sterling-Winthrop Research Institute, Columbia Turnpike, Rensselaer, New York, 12144.

In addition, the parameters requested by Mr. F. Wurtemberger in his September 28, 1976 letter to Mr. Donald Shepherd were also tested. An outside consultant was retained to perform the necessary sampling and analytical work for Sterling.

Attached please find a report for each of the three operations. These reports include the method of sampling, the analytical procedures utilized and the test results found.

Please note since the original survey of the Substances of Concern by New York State we have deleted Methylene Chloride and 1,1,1-Trichloroethane from the substances handled at the Riverside Avenue plant.

./.

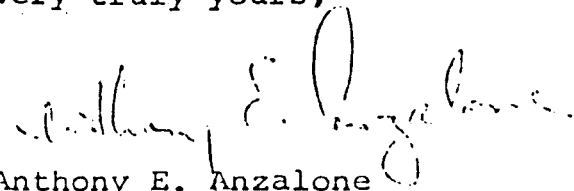
Anthony E. Anzalone to
Mr. Lawrence J. Nadler

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August 18, 1978

By carbon copy we are forwarding these reports to the Rensselaer
County Sewer District.

Very truly yours,


Anthony E. Anzalone

cc: Mr. F. Wurtemberger (Riverside Avenue and Columbia Turnpike facilities)
Rensselaer County Sewer District
Rensselaer, New York

Mr. J. Daly (letter only)
New York State
Department of Health

Enclosures

AEA/eab

WASTEWATER MONITORING

STERLING DRUG INC.

33 Riverside Avenue

Rensselaer, New York 12144

August 18, 1978

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I. MONITORING PROGRAM

A wastewater monitoring program was conducted at the Sterling Drug Inc., Riverside Avenue plant in Rensselaer, New York, in order to provide: (1) the necessary wastewater characterization data required by the Rensselaer County Sewer District No. 1 for their SPDES Industrial Compliance Schedule and (2) the specific chlorinated organic compound analyses requested in a March 16, 1977 letter from the New York Department of Environmental Conservation.

A two week sampling program was conducted by an outside consultant at the Riverside Avenue plant between January 16 and 30, 1978. Twenty-four hour composite samples were taken of the raw Hudson River water entering the Sterling filter plant which comprises the majority of the water used at this plant. These samples of influent were analyzed to provide a baseline.

II. METHODOLOGY

A. Sample Acquisition and Handling

The samples of the effluent from the Riverside Avenue Plant site and the raw river water were taken using automatic, flow proportioned compositing samplers. High fluid velocities were maintained in the sampling system during sampling action, and the collection bottles were kept refrigerated to prevent loss of volatile organic compounds or other sample deterioration.

The samples were collected every day, and various aliquots were prepared in suitable glass bottles and shipped under refrigerated conditions to the analytical labs. Standard sample preservation techniques were used for certain aliquots as indicated in the Appendix. Analyses were performed as soon as possible, always making sure to keep the samples refrigerated.

B. Analytical Procedures

The analyses for the conventional wastewater parameters were performed according to Standard Methods.¹ The analyses for specific chlorinated organics were performed using published methods, adapted for the particular characteristics of the wastewater.

Most of the organic compounds were determined by a method known as Volatile Organic Analysis (VOA).² This is a technique which concentrates volatile organics by bubbling an inert gas through the wastewater sample, then passing the gas through adsorbent material. Organic vapors which have been "purged" from the wastewater are "trapped" on the adsorbent, while the inert gas and water vapor pass through.

¹Standard Methods for the Determination of Water and Wastewater, 14th Edition, 1975, APHA-AWWA-WACF.

²Bellar, T.A., J.J. Lichtenberg, "Determining Volatile Organics at the Microgram per Litre Levels by Gas Chromatography." Journal AWWA, 66, 739(1974).

The organic vapors can then be transferred into a gas chromatographic (GC) column using heat to desorb them from the absorbent. Conventional GC procedures can be utilized to separate and measure the various organic constituents in the desorbed gas.

Two of the chlorinated organics - benzyl chloride and hexachlorophene - were extracted from the Riverside Avenue Plant wastewater with organic solvents and either analyzed directly, or after derivatization, by gas chromatography.

A detailed description of the Volatile Organic method, as well as the methods used for benzyl chloride and hexachlorophene is included in the Appendix.

III. RESULTS AND DISCUSSION

A. General Discussion

1. Conventional Wastewater Parameters

The following parameters were quantified for the Sterling samples at the Riverside Avenue Plant and the raw river water.

pH	Phosphate	Cyanide
BOD	TSS	Phenol
5		
COD	TDS	Chloride demand
TKN	MBAS (detergents)	

BOD analyses were performed using "seed from the
5
Rensselaer County Sewer District No. 1 WWTP. COD
analyses were performed in accordance with Standard
Methods, 14th Edition

2. Chlorinated Organic Compounds

The following parameters were quantified for the Sterling samples at the Riverside Avenue plant and the raw river water.

Chloroform

Hexachlorophene

Methylene Iodine

Monochlorobenzene

Methylene Chloride

Cyclohexyl Chloride

Ethylene Dichloride

1,1,1 - Trichloroethane

Benzyl Chloride (plant effluent only)

Most of the quantitative analyses were performed using a gas chromatograph (GC) equipped with a flame ionization detector (FID). However, for numerous effluent samples, compounds which were not to be quantitated were found to interfere with the analyses for methylene chloride. These compounds were detected by gas chromatography-mass spectrometry (GC/MS). They eluted from the gas chromatographic column within seconds of the methylene chloride. The results of the methylene chloride quantitation by GC/FID were therefore erroneously high. GC/MS with selected ion monitoring was used to quantitate methylene chloride in composites of these effluent samples. The results of the methylene chloride analyses by GC/FID are listed in the tables for comparison purposes only.

B. Analytical Results

1. Raw River Water

The conventional parameter results are listed in Table I. Table II lists the results of the VOA determination for seven organics in river water over a 2-week period. No interferences were seen. All the results obtained by GC/FID are valid. Ethylene dichloride was the only compound found at a quantifiable level in the river water. Hexachlorophene was analyzed in a weekly composite (1/23-29), but none was detected.

2. Riverside Avenue Plant Effluent

The conventional parameter results are listed in Table III. There was difficulty in determining the chlorine demand for most samples. Although chlorine dosages considerably higher than normally used for this analysis on municipal wastewater were added, breakpoint was not always reached. In some cases, an apparent initial demand level was reached and is reported as such. It is felt that the levels of TKN and organics contributed to these chlorine demand results.

The results of the analyses for the specific chlorinated organics in the Main Plant effluent are listed in Table IV.

The asterisked results are those obtained for methylene chloride and 1,1,1-trichloroethane by GC/FID in the presence of interferences. Table V lists the results of the GC/MS analyses of Riverside Avenue Plant weekly composites. The comparison of the methylene chloride results by the two methods is very dramatic. The results by GC/FID are grossly high due to the presence of a compound peak which coincides with the methylene chloride retention time. The GC/MS confirmed that very low levels methylene chloride are present in the Riverside Avenue effluent.

TABLE I
RIVER WATER
CONVENTIONAL PARAMETER ANALYSES

<u>Date</u>	<u>pH</u>	<u>COD</u>	<u>BOD₅</u>	<u>TKN</u>	<u>T-PO₄-P</u>	<u>TSS</u>	<u>TDS</u>	<u>MBAS</u>	<u>Cyanide</u>	<u>Phenol</u>	<u>Chlorine Demand</u>
1-16-78	5.8	14	9	0.61	0.03	40	105	-	0.013	0.002	10
1-17-78	5.6	24	3	0.42	0.03	32	96	0.05	0.003	0.003	-
1-18-78	5.6	19	4	0.40	0.03	35	105	0.05	0.003	0.018	0
1-19-78	5.9	15	2	0.50	0.03	32	102	0.05	0.004	0.003	11
1-20-78	5.9	4	2	0.45	0.03	30	105	0.05	0.003	0.006	10
1-21-78	6.1	6	1	0.49	0.03	36	114	0.05	0.005	0.001	4
1-22-78	5.7	4	1	0.39	0.03	28	94	0.05	0.001	0.001	7
1-23-78	5.3	8	1	0.49	0.03	--	--	0.05	--	--	3

All values in mg/l except pH

TABLE II

RIVER WATER ANALYSIS BY GC/FID

Date	Methylene Chloride (ppb)	Chloroform (ppb)	Ethylene Dichloride (ppb)	1,1,1-Tri- Chloroethane (ppb)	Methylene Iodide (ppb)	Monochloro- Benzene (ppb)	Chloro- Cyclohexane (ppb)
1-16-78	<5	<5	5	<10	<20	<5	<5
1-17-78	<5	<5	9	<10	<20	<5	<5
1-18-78	<5	<5	17	<10	<20	<5	<5
1-19-78	<5	<5	26	<10	<20	<5	<5
1-20-78	<5	<5	10	<10	<20	<5	<5
1-21-78	<5	<5	6	<10	<20	<5	<5
1-22-78	<5	<5	5	<10	<20	<5	<5
Composite 1-23 to 1-29-78	<5	<5	5	<10	<20	<5	<5

TABLE III

STERLING DRUG INC. - RIVERSIDE AVENUE PLANT EFFLUENT
CONVENTIONAL PARAMETER ANALYSES

<u>Date</u>	<u>pH</u>	<u>COD</u>	<u>BOD₅</u>	<u>TKN</u>	<u>T-PO₄-P</u>	<u>TSS</u>	<u>TDS</u>	<u>MBAS</u>	<u>Cyanide</u>	<u>Phenol</u>	<u>Chlorine Demand</u>
1-16-78	3.9	680	570	15.1	0.13	11	480	0.6	0.003	0.03	NR
1-17-78	3.8	910	550	15.4	0.16	7	360	0.7	0.007	0.06	-
1-18-78	2.9	900	550	12.2	0.30	10	320	0.4	0.003	0.07	NR
1-19-78	3.4	640	520	19.8	0.31	3	670	1.4	0.009	0.03	27
1-20-78	3.9	580	440	43.2	0.29	4	380	0.5	0.003	0.09	14
1-21-78	6.3	200	130	1.8	0.44	7	150	0.1	0.005	0.03	10
1-22-78	6.7	72	48	0.8	0.62	4	120	0.1	0.001	0.01	7
1-23-78	3.1	480	480	35.2	0.31	-	-	1.3	-	-	6 ¹

All values in mg/l except pH

NR = not reached

¹ Apparent initial demand; ultimate demand not reached

TABLE IV

STERLING DRUG INC. - RIVERSIDE AVENUE PLANT EFFLUENT
GAS CHROMATOGRAPHIC ANALYSES FOR SPECIFIC ORGANICS

Date	MeCl ₂ (ppb)	CHCl ₃ (ppb)	EDC (ppb)	TCE (ppb)	MeI ₂ (ppb)	MCB (ppb)	CCH (ppb)	BzCl (ppb)	HCP (ppb)
1-16-78	2270*	26	6400	<10	55	28	<5	<50	12
1-17-78	1330*	20	7690	<10	30	40	<5	<50	68
1-18-78	2850*	20	8990	20	<20	2210	<5	<50	<10
1-19-78	3570*	140	775	100*	<20	60	40	<50	110
1-20-78	2500*	60	340	<10	30	60	<5	<50	<10
1-21-78	840*	11	350	<10	<20	20	<5	<50	<10
1-22-78	200*	15	270	<10	<20	<5	<5	<50	<10
1-23-78	1010*	235	605	<10	<20	<5	<5	<50	91
1-24-78	2190*	55	3320	<10	<20	27	<5	<50	84
1-25-78	2860*	120	440	<10	<20	32	<5	<50	150
1-26-78	3500*	100	8020	<10	<20	31	<5	<50	77
1-27-78	90*	140	8830	<10	<20	26	<5	<50	83
1-28-78	450*	29	52	<10	<20	22	<5	<50	<10
1-29-78	380*	36	330	<10	<20	18	<5	<50	10

*Interference from adjoining peak

TABLE V

STERLING DRUG INC. - RIVERSIDE AVENUE PLANT EFFLUENT
SELECTED VOLATILE ORGANIC ANALYSES BY GC/MS

<u>Date</u>	<u>Methylene Chloride (ppb)</u>	<u>1,1,1-Tri- Chloroethane (ppb)</u>
1-19-78	50	<5
Composite 1-16 to 1-22-78	8	4
Composite 1-23 to 1-29-78	1	1

C. Wastewater Flow

Flow determinations were made during the 2-week sampling program. The Riverside Avenue Plant effluent, which originates mostly from Hudson River water, was measured using existing metering instruments in the wastewater pretreatment plant. The Main Plant flow averaged 1.6 million gal/day. Flow during weekend periods was considerably lower due to decreased activity. The maximum daily flow was 2.5 million gal/day; the minimum daily flow was 0.8 million gal/day.

APPENDIX A
ABBREVIATION INDEX

ABBREVIATION INDEX

Abbreviation	Definition	
TSS	Total Suspended Solids	
BOD ₅	Biochemical Oxygen Demand - 5 day	
COD	Chemical Oxygen Demand	
TKN	Total Kjeldahl Nitrogen	
T-PO ₄ -P	Total Phosphate as Phosphorous	
TDS	Total Dissolved Solids	
MBAS	Methylene Blue Active Substances (detergents)	
MeCl ₂	Methylene Chloride	CH ₂ Cl ₂
CHCl ₃	Chloroform	CHCl ₃
EDC	Ethylene Dichloride	CH ₂ ClCH ₂ Cl
TCE	1,1,1-Trichloroethane	CH ₃ CCl ₃
MeI ₂	Methylene Iodide	CH ₂ I ₂
CCH	Chlorocyclohexane	C ₆ H ₁₁ Cl
MCB	Monochlorobenzene	C ₆ H ₅ Cl
BzCl	Benzyl Chloride	C ₆ H ₅ CH ₂ Cl
HCP	Hexachlorophene	(C ₆ HCl ₃ OH) ₂ CH ₂
GC/FID	Gas Chromatograph with Flame Ionization Detector	
GC/EC	Gas Chromatograph with Electron Capture Detector	
GC/MS	Gas Chromatograph with Mass Spectrometer	
VOA	Volatile Organic Analysis (Purge and Trap Technique)	
WWTP	Wastewater Treatment Plant	

APPENDIX B
ANALYTICAL METHODS DESCRIPTION FOR
ORGANIC COMPOUNDS

The analytical procedures given herein have been adapted from literature sources or developed upon the basis of experimental data believed to be reliable. In the hands of a qualified analyst they are expected to yield results of sufficient accuracy for their intended purposes. Users are cautioned to confirm the suitability of the methods by appropriate tests.

VOLATILE ORGANICS ANALYSIS (VOA) - THE PURGE AND TRAP METHOD

Scope

A modified Bellar purge and trap method utilizing a gas chromatograph equipped with a flame ionization detector was used to quantitatively determine a number of specific volatile organics. The compounds monitored by this method in the waste effluent and river water were: methylene chloride; chloroform; ethylene dichloride; 1,1,1-trichloroethane; methylene iodide; chlorocyclohexane; and monochlorobenzene. The sensitivity of this method to these compounds is 5-20 parts per billion (ppb).

Procedure

A 5-ml sample was injected into a glass purging device which has been described by Bellar and Lichtenberg.² A glass frit installed at the base of the sample device allowed finely divided gas bubbles to pass through the sample while it was restrained above the frit.

The volatile organics were purged from the sample over a period of twelve minutes onto a Tenax-silica gel trap at room temperature. The trap was then rapidly heated to 180°C by means of a six-way valve (see attached drawing) and trapped organics were eluted over a four-minute period onto the injector end of a gas chromatographic column maintained at room temperature. When the desorption period was over, the column was temperature programmed to achieve separation of the volatiles.

Variations in purging efficiencies between sample runs were corrected for by use of internal standards, bromochloromethane and 2-bromo-1-chloroethane. Quantitation was achieved by comparison with external standards whose response closely approximated the sample response. Aqueous standards were purged and analyzed under identical conditions as the unknowns in order to compensate for purging or desorption losses.

Interferences

Numerous volatile organics are amenable to the purge and trap method. Often, these organics will elute at or near the retention times of those compounds which are of primary interest. Therefore, confirmatory analyses must be performed using dissimilar columns or mass spectrometry.

In this work, selected samples and composited samples were analyzed by gas chromatography-mass spectrometry (GC/MS) to confirm the presence and to quantify methylene chloride. The technique was also used to identify interferences.

Purge and Trap Parameters

Purge Gas - Nitrogen (prepurified grade) for GC/FID
 - Helium (prepurified grade) for GC/MS

Purge Flow - 20 ml/minute

Purge Time - 12 minutes

Trap Dimensions - 6 in. x 1/8 in. O.D. (S.S.)

Trap Sorbent - Tenax GC 60/80 mesh (4 in.)
 - Davidson 12 silica gel 80/100 mesh (2 in.)

Desorption Flow - 40 ml/minute

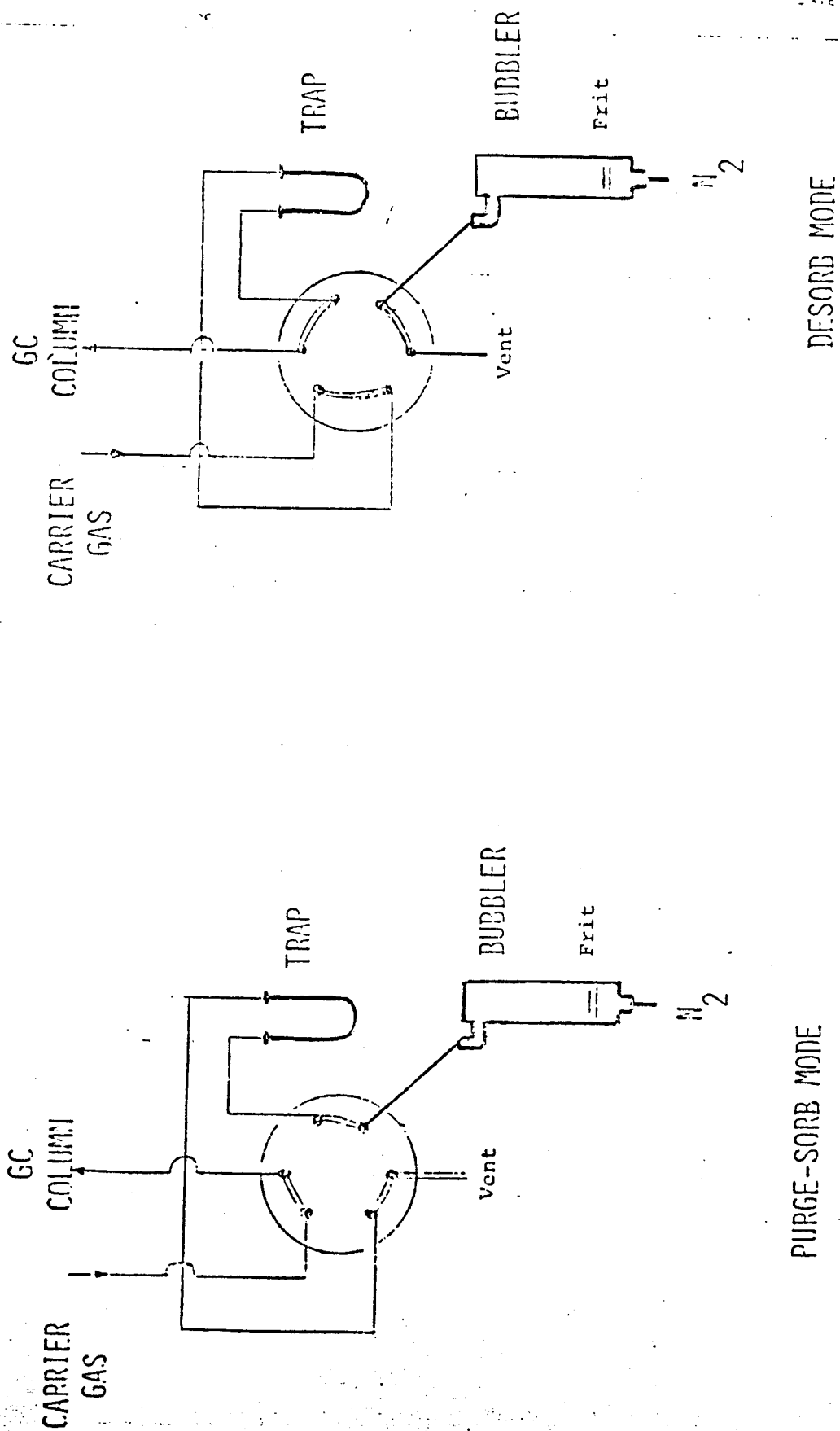
Desorption Time - 4 minutes

Desorption Temperature - 180°C

Gas Chromatographic Parameters

	A	B
Detector	Flame Ionization	Mass Spectrometer
Column	10' x 1/8" O.D. stainless steel 0.25 Carbowax 1500 on Carbopack C (60/80 mesh) preceded by a 1' x 1/8" O.D. stainless steel 3% Carbowax 1500 m Chromosorb W	8' x 2 mm glass 7' of 0.2% Carbowax 1500 on Carbopack C preceded by 1' 3% Carbowax 1500 on Chromosorb W
Column Temperature	Ambient during injection Rapid heating to 60°C Holding at 60°C at 40 minutes Program to 165°C at 8°/min Post-hold at 165°C until all peaks are eluted	Ambient during injection Rapid heating to 60°C Hold at 60°C for 4 minutes Program to 165°C at 10°C/min Post-hold at 165°C until all peaks are eluted
Carrier Gas	Nitrogen at 40 cc/min	Helium at 20 cc/min
Detector Temperature	220°C	80°C
Electron Energy	-	70 eV
Emission Current	-	500 ua
Mass Range	-	24-27, 33-260 amu

PURGE-TRAP SYSTEM



THE DETERMINATION OF HEXACHLOROPHENE IN WATER AND
WASTEWATER BY GAS CHROMATOGRAPHY

Scope

This method is applicable to the determination of hexachlorophene in both water and wastewater. The method is a modification of a Sterling Drug method.

Procedure

Transfer 500 ml of sample into a one-liter separatory funnel and mix with 2.5 ml of 6N HCL. Extract the aqueous portion with 100 ml of diethyl ether. Record the recovered volume of diethyl ether and dilute a 5-ml portion of the extract with 5 ml of n-hexane.

Place 2 ml of this (1-1) ether-hexane solution into a 2-ml Reacti-vial and add three drops of a (1-1) pyridine-acetic anhydride solution. Replace the septum top and heat the vial for 15 minutes in a water bath (80°C). After allowing the solution to return to room temperature, it is ready for analysis by gas chromatography.

Standardization

A response curve should be developed that encompasses the concentration range of the samples as injected. These standards should be made up in diethyl ether and then carried through the hexane dilution and subsequent derivatization.

Samples should also be spiked with hexachlorophene and carried through this entire analytical procedure.

Discussion

A sample of deionized water was spiked with 21.6 ppb and carried through this procedure. The analytical resultant was 18.7 ppb. The Riverside Avenue Plant effluent sample for 1/17/78 was spiked with 35 ppb hexachlorophene, and 39 ppb was the recovered value by analysis.

Gas Chromatographic Parameters

Column - 0.46 meters x 3.18 mm O.D. (SS)

3% OV-1 on 100/120 mesh GCQ

Column temperature - 180°C

Injector temperature - 195°C

Detector temperature - 200°C

Carrier gas - 5% methane in Argon at 25 cc/min.

Detector - electron capture

Injection size - 3 μ l

Approximate retention time - 14 min. (see Figure 4)

THE DETERMINATION OF BENZYL CHLORIDE IN WATER AND
WASTEWATER BY GAS CHROMATOGRAPHY

Scope

This method is applicable to the determination of benzyl chloride in both water and wastewater. The benzyl chloride is extracted using diethyl ether and analyzed by gas chromatography.

Procedure

Transfer 500 ml of sample into a one-liter separatory funnel and mix with 2.5 ml of 6N HCl. Extract the aqueous portion with 100 ml of diethyl ether. Record the recovered volume of diethyl ether. By evaporation under a nitrogen stream, concentrate 25 ml of the ether extract down to 2.5 ml. This concentration is performed in a 10-ml graduate, using successive additions until the 25 ml addition has been achieved. This concentrated extract is now ready for gas chromatographic analysis.

Standardization

A response curve should be developed that encompasses the concentration range of the samples as injected. The standards should be made up in diethyl ether.

Samples should be spiked with benzyl chloride and carried through this entire analytical procedure.

Interferences

No direct interference by retention time was observed, but some samples contained a high concentration unknown that eluted just prior to benzyl chloride; therefore, trace levels of benzyl chloride eluted on the backside slope of the unknown. Because of this interference with the quantitation, dissimilar columns were used for some of the analysis.

Discussion

The Main Plant effluent (1/27/28) sample was spiked with 28 ppb benzyl chloride and the recovery was 25 ppb.

Gas Chromatographic Parameters

Condition A (see Figure 5)

Column - 1 meter x 3.18 mm O.D. (SS)

20% OV-17 on 100/120 GCQ

Column temperature - 80°C

Injector temperature - 150°C

Detector temperature - 200°C

Carrier gas - N₂ at 25 cc/min.

Detector - flame ionization

Injection size - 3 µl

Condition B (see Figure 6)

Column - 1 meter x 3.18 mm O.D. (SS)

Porapak Q, 100/120 mesh

Column temperature - 190°C

Injector temperature - 210°C

Detector temperature - 225°C

Carrier gas - N₂ at 20 cc/min

Detector - flame ionization

Injection size - 3 µl

Quality Assurance Program

1. Purge and Trap Method

- a. Standardization was done over a concentration range that encompassed each sample concentration.
- b. Two internal standards were added to each sample and external standard prior to analysis.
- c. Every fifth sample was run in duplicate.
- d. A standard representative of the sample concentration was run every fifth sample.
- e. Every tenth Sterling wastewater sample was spiked with the cited compounds to determine recovery efficiencies.

2. Benzyl Chloride and Hexachlorophene by Gas Chromatography

- a. Standardization was done over a concentration range that encompassed each sample concentration.
- b. A standard representative of sample concentration was run every fifth sample.
- c. The extraction efficiencies of benzyl chloride and hexachlorophene were determined.
- d. Representative Sterling wastewater samples were spiked in order to determine the recovery efficiencies of the procedure.

APPENDIX C
SAMPLE PRESERVATION TECHNIQUES

SAMPLE PRESERVATION TECHNIQUES PRIOR TO SHIPMENT

Refrigeration Only

All 40 ml sample vials which are completely filled - No air space

1 - Quart bottle for extraction, in the analysis of hexachlorophene and benzyl chloride

2 - Quart bottles for:

BOD ₅	Chlorine Demand
pH	MBAS
TSS	TD5

Refrigeration + H₂SO₄ to pH <2

1 - Quart bottle for COD, TKN, and T-OP₄

Refrigeration + NaOH to pH 12

1 - Quart bottle for Cyanide

Refrigeration + H₃PO₄ to pH <2 + 1 Gram CuSO₄

1 - Quart bottle for phenol by 4-AAP

Appendix C

USPAX

drugs (440.25) (see *Antibiotics* (1011)). It has a potency equivalent to not less than 810 μg of ampicillin ($\text{C}_{16}\text{H}_{19}\text{N}_3\text{O}_4\text{S}$) per mg.

Packaging and storage—Preserve in tight containers.

Reference standards—U. S. Ampicillin Reference Standard; U. S. Hetacillin Reference Standard.

pH: between 2.5 and 5.5, in a solution containing 10 mg per ml.

Water: not more than 1.0%.

Hetacillin content: between 90.0% and 105.0%.

Other requirements—It complies with the tests for identification, safety, and crystallinity.

Hetacillin for Oral Suspension

» Hetacillin for Oral Suspension conforms to the regulations of the federal Food and Drug Administration concerning antibiotic drugs (440.125b) (see *Antibiotics* (1011)). It contains the equivalent of not less than 90.0 percent and not more than 120.0 percent of the labeled amount of ampicillin ($\text{C}_{16}\text{H}_{19}\text{N}_3\text{O}_4\text{S}$), the labeled amount being 22.5, 45, or 112.5 mg per ml when constituted as directed. It contains one or more suitable colors, flavors, preservatives, sweeteners, and suspending agents.

Packaging and storage—Preserve in tight containers.

pH: between 2.0 and 5.0, in the suspension constituted as directed in the labeling.

Water: not more than 2.0%.

Hetacillin Tablets

» Hetacillin Tablets conform to the regulations of the federal Food and Drug Administration concerning antibiotic drugs (440.125a, hetacillin chewable tablets) (see *Antibiotics* (1011)). Hetacillin Tablets contain the equivalent of not less than 90.0 percent and not more than 120.0 percent of the labeled amount of ampicillin ($\text{C}_{16}\text{H}_{19}\text{N}_3\text{O}_4\text{S}$), the labeled amount being 112.5 mg.

Packaging and storage—Preserve in tight containers.

Labeling—Label Tablets to indicate that they are to be chewed before swallowing.

Water: not more than 2.0%.

Hetacillin Potassium

$\text{C}_{19}\text{H}_{32}\text{KN}_3\text{O}_4\text{S}$ 427.56

4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-(2,2-dimethyl-5-oxo-4-phenyl-1-imidazolidinyl)-3,3-dimethyl-7-oxo-, monopotassium salt, [2S-[2 α ,5 α ,6 β -(S*)]]-

Potassium 6-(2,2-dimethyl-5-oxo-4-phenyl-1-imidazolidinyl)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate [5321-32-4].

» Hetacillin Potassium conforms to the regulations of the federal Food and Drug Administration concerning antibiotic drugs (440.29; 440.29a, sterile hetacillin potassium) (see *Antibiotics* (1011)). It has a potency equivalent to not less than 735 μg of ampicillin ($\text{C}_{16}\text{H}_{19}\text{N}_3\text{O}_4\text{S}$) per mg and, if sterile and packaged for dispensing, it contains the equivalent of not less than 90.0 percent and not more than 120.0 percent of the labeled amount of ampicillin.

Packaging and storage—Preserve in tight containers.

Reference standards—U. S. Ampicillin Reference Standard; U. S. Hetacillin Reference Standard.

pH: between 7.0 and 9.0, in a solution containing 10 mg per ml (or, if sterile and packaged for dispensing, in the solution constituted as directed in the labeling).

Water: not more than 1.0%.

Hetacillin content: between 82.0% and 95.5%.

Other requirements—It complies with the tests for identification, safety, and crystallinity. In addition, the sterile form complies with the tests for pyrogen and sterility.

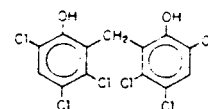
Hetacillin Potassium Capsules

» Hetacillin Potassium Capsules conform to the regulations of the federal Food and Drug Administration concerning antibiotic drugs (440.129) (see *Antibiotics* (1011)). Capsules contain the equivalent of not less than 90.0 percent and not more than 120.0 percent of the labeled amount of ampicillin ($\text{C}_{16}\text{H}_{19}\text{N}_3\text{O}_4\text{S}$), the labeled amount being 112.5, 225, or 450 mg in each Capsule.

Packaging and storage—Preserve in tight containers.

Water: not more than 3%.

Hexachlorophene



$\text{C}_{13}\text{H}_6\text{Cl}_6\text{O}_2$ 406.91

Phenol, 2,2'-methylenebis[3,4,6-trichloro-2,2'-Methylenebis[3,4,6-trichlorophenol] [70-30-4].

» Hexachlorophene contains not less than 98.0 percent and not more than 100.5 percent of $\text{C}_{13}\text{H}_6\text{Cl}_6\text{O}_2$, calculated on the dried basis.

Packaging and storage—Preserve in tight, light-resistant containers.

Reference standard—USP Hexachlorophene Reference Standard—Dry at 105° for 4 hours before using.

Identification—

A: The infrared absorption spectrum of a potassium bromide dispersion of it, previously dried, exhibits maxima only at the same wavelengths as that of a similar preparation of USP Hexachlorophene RS.

B: To a solution of about 5 mg in 5 ml of alcohol add 1 drop of ferric chloride TS: a transient purple color is produced immediately.

Melting range (741): between 161° and 167°.

Loss on drying (731)—Dry it at 105° for 4 hours: it loses not more than 1.0% of its weight.

Residue on ignition (281): not more than 0.1%.

Assay—Weigh accurately about 1.5 g of Hexachlorophene, dissolve in 25 ml of alcohol, and titrate with 0.1 N sodium hydroxide VS, determining the end-point potentiometrically. Perform a blank determination, and make any necessary correction. Each ml of 0.1 N sodium hydroxide is equivalent to 40.69 mg of $\text{C}_{13}\text{H}_6\text{Cl}_6\text{O}_2$.

Hexachlorophene Cleansing Emulsion

» Hexachlorophene Cleansing Emulsion is Hexachlorophene in a suitable aqueous vehicle. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of $C_{13}H_6Cl_6O_2$. It contains no coloring agents.

Packaging and storage—Preserve in tight, light-resistant, non-metallic containers.

Reference standard—USP Hexachlorophene Reference Standard—Dry at 105° for 4 hours before using.

Identification—Place a volume of Cleansing Emulsion, equivalent to about 150 mg of hexachlorophene, in a glass-stoppered, 25-ml graduated cylinder, dilute with a mixture of equal volumes of chloroform and methanol to volume, mix, and allow to stand for about 5 minutes. On a suitable thin-layer chromatographic plate (see *Chromatography* (621)), coated with a 0.25-mm layer of silica gel, spot 10 μ l of this solution and 10 μ l of a solution of USP Hexachlorophene RS in the same chloroform-methanol mixture containing 6 mg per ml. Develop the chromatogram in a solvent system consisting of a mixture of benzene and glacial acetic acid (9:1) until the solvent ascends to about 10 cm above the point of application. Remove the plate, mark the solvent front and evaporate the solvent in a current of warm air. Spray the plate with dilute nitric acid (1 in 5), and warm on a hot plate until yellow spots appear: the R_f value of the main spot obtained from the solution under test corresponds to that obtained from the Standard solution.

pH (791)—Place 20 ml of the well-shaken Cleansing Emulsion and 10 ml of water in a glass-stoppered, 50-ml graduated cylinder, mix, and determine the pH in a suitable pH meter, using a glass electrode and preferably a sleeve-type calomel electrode: the pH is between 5.0 and 6.0.

Assay—

Standard preparation—Weigh accurately about 50 mg of USP Hexachlorophene RS into a 50-ml volumetric flask, add 10 ml of methanol, shake until dissolved, add methanol to volume, and mix. Pipet 3 ml of this solution into a 100-ml volumetric flask, add 1 ml of dilute hydrochloric acid (1 in 10), add methanol to volume, and mix.

Assay preparation—Transfer an accurately weighed portion of Hexachlorophene Cleansing Emulsion, equivalent to about 30 mg of hexachlorophene, to a 100-ml volumetric flask, add methanol to volume, and mix. Filter the solution through paper, taking adequate precautions to prevent evaporation. Pipet a 10-ml aliquot of the filtrate into a 100-ml volumetric flask, add 1 ml of dilute hydrochloric acid (1 in 10), and add methanol to volume.

Procedure—Concomitantly determine the absorbances of the Assay preparation and the Standard preparation in 1-cm cells at the wavelength of maximum absorbance at about 299 nm, with a suitable spectrophotometer, using a mixture of 99 volumes of methanol and 1 volume of hydrochloric acid as the blank. Calculate the quantity, in mg, of $C_{13}H_6Cl_6O_2$ in the portion of Cleansing Emulsion taken by the formula $C(A_t/A_s)$, in which C is the concentration, in μ g per ml, of USP Hexachlorophene RS in the Standard preparation, and A_t and A_s are the absorbances of the Assay preparation and the Standard preparation, respectively.

Hexachlorophene Liquid Soap

» Hexachlorophene Liquid Soap is a solution of Hexachlorophene in a 10.0 to 13.0 percent solution of a potassium soap. It contains, in each 100 g, not less than 225 mg and not more than 260 mg of $C_{13}H_6Cl_6O_2$. It may contain suitable water hardness controls.

Note—The inclusion of non-ionic detergents in Hexachlorophene Liquid Soap in amounts greater than 8 percent on a total weight basis may decrease the bacteriostatic activity of the Soap.

Packaging and storage—Preserve in tight, light-resistant containers.

Labeling—Solutions of higher concentrations of hexachlorophene

and potassium soap, in which the ratios of these components are consistent with the official limits, may be labeled "For the preparation of Hexachlorophene Liquid Soap, USP," provided that the label indicates also that the soap is a concentrate, and provided that directions are given for dilution to the official strength.

Reference standard—USP Hexachlorophene Reference Standard—Dry at 105° for 4 hours before using.

Identification—

A: Pour about 2 g into a beaker, and add, with stirring, dilute hydrochloric acid (1 in 100) until the mixture is just acid to litmus. To 10 ml of the mixture, in a beaker, add 10 ml of chloroform, and mix. Add 3 or 4 drops of ferric chloride TS, mix, and allow to stand: the chloroform layer becomes purple.

B: To 2 ml of the mixture prepared in Identification test A, in a test tube, add 2 ml of acetone, and mix. Add 1 ml of titanium trichloride solution (1 in 5), and shake vigorously: a yellow oil separates.

Water—Place about 5 g, quickly weighed to the nearest centigram, in the distilling flask of the apparatus for Water Determination—Azeotropic Method (921). (The Soap is most conveniently weighed in a boat of metal foil, of a size that will just pass through the neck of the flask.) Place 250 ml of toluene and 10 g of anhydrous barium chloride in the flask, connect the flask through a ground-glass joint to the distilling apparatus, fill the receiving tube with toluene, and determine the water as directed, beginning with "Heat the flask gently." The volume of water found corresponds to between 86.5% and 90.0% by weight of the portion of Soap taken.

Alcohol-insoluble substances—Dissolve about 5 g, rapidly and accurately weighed, in 100 ml of hot neutralized alcohol, collect the residue, if any, on a tared filter, thoroughly wash it with hot neutralized alcohol, and dry at 105° for 1 hour: the weight of the residue obtained does not exceed 3.0% of the weight of Soap taken. Retain the solution and the residue.

Free alkali hydroxides—To the combined filtrate and washings obtained in the test for Alcohol-insoluble substances add 0.5 ml of phenolphthalein TS. If a pink color is produced, titrate the solution with 0.1 N sulfuric acid VS until the pink color is just discharged. Each ml of 0.1 N sulfuric acid is equivalent to 5.61 mg of KOH. The volume of 0.1 N sulfuric acid consumed corresponds to not more than 0.05% of KOH.

Alkali carbonates—Wash the filter containing the Alcohol-insoluble substances with 50 ml of boiling water, cool, add methyl orange TS, and titrate the filtrate with 0.1 N sulfuric acid VS. Not more than 0.5 ml of 0.1 N sulfuric acid per g of Soap originally taken is required (0.35% calculated as K_2CO_3).

Assay for hexachlorophene—

Alkaline buffer—Dissolve 6.07 g of tris(hydroxymethyl)aminomethane in 900 ml of methanol. Add 25.0 ml of dilute hydrochloric acid (1 in 10), dilute with water to 1 liter, and mix.

Standard preparation—Place about 50 mg of USP Hexachlorophene RS, accurately weighed, in a 100-ml volumetric flask, dissolve in 10 ml of alcohol, and dilute with Alkaline buffer to volume. Preserve in a tight container.

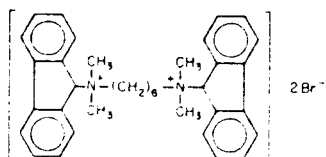
Standard hexachlorophene graph—To 50-ml volumetric flasks add, by pipet and in duplicate, 2-, 3-, 4-, 5-, 6-, and 7-ml portions of the Standard preparation. To one flask of each pair of duplicates add to volume acidified 90 percent methanol containing, in each 100 ml, 5 ml of acetic acid and 0.3 ml of hydrochloric acid, and mix. To the second flask of each pair add Alkaline buffer to volume.

Arrange the two series of standard hexachlorophene solutions in pairs according to their hexachlorophene content, and determine the absorbances of the alkaline solutions at 312 nm, with a suitable spectrophotometer, using the corresponding acid solution as the blank. Plot the observed absorbance on the ordinate scale against the corresponding concentration of hexachlorophene, in mg per 100 ml, on the abscissa scale.

Procedure—Weigh accurately a portion of Hexachlorophene Liquid Soap, containing the equivalent of about 100 mg of hexachlorophene, and transfer to a 100-ml volumetric flask. Add alcohol to volume, and mix. Transfer 25.0 ml of this solution to a 100-ml volumetric flask, add 90 percent methanol to volume, mix, and filter if necessary. Add 10.0 ml of this solution to each of two 50-ml volumetric flasks, and fill one flask to volume with 0.3 M acetic acid in 90 percent methanol containing 0.1% of hydrochloric acid, and mix. Fill the other flask to volume with Alkaline buffer, and mix. Determine the absorbance of the alkaline solution at 312

nm with the same spectrophotometer used in preparing the *Standard hexachlorophene graph*, using the control as the blank. From the observed absorbance, calculate the weight of hexachlorophene in the Hexachlorophene Liquid Soap taken.

Hexafluorenium Bromide



$C_{36}H_{42}Br_2N_2$ 662.55
1,6-Hexanediaminium, *N,N'*-di-9*H*-fluoren-9-yl-*N,N,N',N'*-tetramethyl-, dibromide.
Hexamethylenebis[fluoren-9-ylidimethylammonium] dibromide [317-52-2].

» Hexafluorenium Bromide contains not less than 98.0 percent and not more than 100.5 percent of $C_{36}H_{42}Br_2N_2$, calculated on the dried basis.

Packaging and storage—Preserve in well-closed, light-resistant containers.

Reference standard—USP Hexafluorenium Bromide Reference Standard—Dry at 105° for 4 hours before using.

Identification—

A: The infrared absorption spectrum of a potassium bromide dispersion of it, previously dried, exhibits maxima only at the same wavelengths as that of a similar preparation of USP Hexafluorenium Bromide RS.

B: The ultraviolet absorption spectrum of a solution (1 in 100,000) exhibits maxima and minima at the same wavelengths as that of a similar solution of USP Hexafluorenium Bromide RS, concomitantly measured, and the respective absorptivities, calculated on the dried basis, at the wavelength of maximum absorbance at about 275 nm do not differ by more than 3.0%.

C: It responds to the tests for *Bromide* (191).

Loss on drying (731)—Dry it at 105° for 4 hours; it loses not more than 2.0% of its weight.

Residue on ignition (281): not more than 0.1%.

Bromide content—Dissolve about 500 mg, accurately weighed, in 25 ml of methanol. Add 75 ml of water and 1.5 ml of nitric acid, and titrate with 0.1 *N* silver nitrate VS, determining the end-point potentiometrically, using suitable electrodes. Each ml of 0.1 *N* silver nitrate is equivalent to 7.991 mg of Br; the content of Br is between 23.7% and 24.5%.

Assay—Dissolve about 300 mg of Hexafluorenium Bromide, accurately weighed, in 10 ml of methanol. Add 10 ml of acetic anhydride, 60 ml of glacial acetic acid, and 10 ml of mercuric acetate TS, and titrate with 0.1 *N* perchloric acid VS, determining the end-point potentiometrically. Perform a blank determination, and make any necessary correction. Each ml of 0.1 *N* perchloric acid is equivalent to 33.13 mg of $C_{36}H_{42}Br_2N_2$.

Hexafluorenium Bromide Injection

» Hexafluorenium Bromide Injection is a sterile solution of Hexafluorenium Bromide in an aqueous polyethylene glycol vehicle. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of $C_{36}H_{42}Br_2N_2$.

Packaging and storage—Preserve in single-dose or in multiple-dose containers, preferably of Type I glass, protected from light.

Reference standard—USP Hexafluorenium Bromide Reference Standard—Dry at 105° for 4 hours before using.

Identification—

A: The ultraviolet absorption spectrum of the *Assay preparation*, prepared as directed in the *Assay*, exhibits maxima and minima at the same wavelengths as that of the *Standard preparation*, prepared as directed in the *Assay*, concomitantly measured.

B: It responds to the tests for *Bromide* (191).

Pyrogen—When diluted with Sodium Chloride Injection to a concentration of 200 µg of hexafluorenium bromide per ml, it meets the requirements of the *Pyrogen Test* (151).

pH (791): between 4.0 and 7.0, in a solution (1 in 5).

Other requirements—It meets the requirements under *Injections* (1).

Assay—

Chromatographic column—Pack a pledget of fine glass wool in the base of a standard 5- × 100-mm chromatographic tube. Add to the tube 2.0 g of strongly basic quaternary ammonium (polystyrene) type anion-exchange resin that has been made into a slurry with water, washing the slurry with water into the column. Backwash the column with water until all the trapped air is removed. Convert the resin to the hydroxyl form by percolating 10 ml of 2.5 *N* sodium hydroxide through the resin. Wash the column so prepared with water until the washings are neutral to pH indicator paper and show no ultraviolet absorbance at 275 nm.

Standard preparation—Transfer about 30 mg of USP Hexafluorenium Bromide RS, accurately weighed, to a 50-ml volumetric flask. Dissolve in water, dilute with water to volume, and mix. Transfer 3.0 ml of this solution to a 100-ml volumetric flask, dilute with water to volume, and mix.

Assay preparation—Transfer an accurately measured volume of Hexafluorenium Bromide Injection, equivalent to about 60 mg of hexafluorenium bromide, to a 100-ml volumetric flask, dilute with water to volume, and mix. Transfer 3.0 ml of this solution to the top of the *Chromatographic column*. After almost all of the solution has passed into the column, complete the elution of the hexafluorenium by addition of water until 100 ml of eluate has been collected in a 100-ml volumetric flask, and mix.

Procedure—Concomitantly determine the absorbances of the solutions in 1-cm cells at the wavelength of maximum absorbance at about 275 nm, with a suitable spectrophotometer, using water as the blank. Calculate the quantity, in mg, of $C_{36}H_{42}Br_2N_2$ in each ml of the Injection taken by the formula $(3.33C/V)(A_t/A_s)$, in which *C* is the concentration, in µg per ml, of USP Hexafluorenium Bromide RS in the *Standard preparation*, *V* is the volume, in ml, of Injection taken, and *A_t* and *A_s* are the absorbances of the *Assay preparation* and the *Standard preparation*, respectively.

Hexavitamin Capsules

» Hexavitamin Capsules contain, in each capsule, not less than 1.5 mg (5000 USP Units) of retinol in the form of vitamin A; not less than 10 µg (400 USP Units) of vitamin D as ergocalciferol or cholecalciferol obtained by the activation of ergosterol or 7-dehydrocholesterol or from natural sources; not less than 75 mg of ascorbic acid ($C_6H_8O_6$) or its equivalent as sodium ascorbate ($C_6H_7NaO_6$); not less than 2 mg of thiamine hydrochloride ($C_{12}H_{17}ClN_4OS \cdot HCl$) or its equivalent as thiamine mononitrate ($C_{12}H_{17}N_5O_4S$); not less than 3 mg of riboflavin ($C_{17}H_{20}N_4O_6$); and not less than 20 mg of niacinamide ($C_6H_6N_2O$).

Packaging and storage—Preserve in tight, light-resistant containers.

Labeling—The labeling includes no claim based upon any quantity of vitamin in excess of that specified in this monograph. Label Capsules to state the identity of the forms of vitamin A, vitamin D, and thiamine that are present.

Reference standards—USP Ergocalciferol Reference Standard or USP Cholecalciferol Reference Standard—Store in a cold place, protected from light. Allow it to attain room temperature before opening ampul. Use the material promptly, and discard the unused portion. USP Niacinamide Reference Standard—Dry over silica gel for 4 hours before using. USP Thiamine Hydrochloride Ref-

Hepatitis B Immune Globulin

Change to read:

Expiration date—Its Δ minimum Δ_{1a} expiration date is not later than 1 year after the date of manufacture, such date being that of the first valid potency test of the product.

Hexachlorophene

Add the following:

Δ 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin—[Caution—Since 2,3,7,8-tetrachlorodibenzo-*p*-dioxin is an extremely toxic substance, exercise all necessary precautions in the conduct of this procedure.]—Dissolve 10.0 g of Hexachlorophene in 50 ml of methanol, transfer to a 1-liter separator with the aid of 25 ml of methanol, add 25 ml of 2.5 *N* lithium hydroxide and 225 ml of water, and extract with two 200-ml portions of freshly distilled *n*-hexane. Dry the combined *n*-hexane extracts over anhydrous sodium sulfate, filter, and evaporate to a volume of about 15 ml on a rotary evaporator at a bath temperature not higher than 40°. Transfer this solution in portions to a 12-ml centrifuge tube, concentrating each time to a volume of 1 ml in a gentle stream of nitrogen in a warm water bath. Rinse the flask with 15 ml of *n*-hexane, and evaporate similarly. Wash down the walls of the tube with 10 ml of *n*-hexane, and again evaporate to a volume of 1.0 ml. Cool, and transfer to a micro-column that has been prepared in the following manner: Place a small plug of glass wool in a 5 × 15-mm pipet, add a small amount of sand and 1.0 g of basic alumina, tap several times to pack down the alumina, and heat in a vacuum oven at 110° for 3 hours. Store under vacuum.

Elute the column with 10 ml of a mixture of methylene chloride and *n*-hexane (1:9), using a portion to rinse the tube. Collect the eluate in a 12-ml graduated centrifuge tube, and concentrate in a gentle stream of nitrogen in a warm water bath to a volume of 1.0 ml.

Inject 2.0 μ l of the concentrated eluate into a suitable gas chromatograph connected to a mass spectrograph equipped with a multiple-ion detector. The gas chromatograph is fitted with a 2-mm × 1-m glass column containing liquid phase G1 on support S1. The carrier gas is helium flowing at the rate of 40 ml per minute. The column temperature is maintained at 250° and the injection port at 300°. Similarly inject 2.0 μ l of a Standard solution of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin containing 0.5 μ g per ml.* The sum of the peak heights at mass values of 320, 322, and 324 obtained with the solution under test is not greater than the sum of the peak heights at the same mass values obtained with the Standard solution. The limit is 50 ppb.

* A solution in anisole is available commercially from KOR Isotopes, Div. of ECO, Inc., 56 Rogers St., Cambridge, Mass. 02142. This solution may be diluted with a mixture of *n*-hexane and methylene chloride (9:1) to the required concentration. Δ_{2a}

Hexachlorophene Cleansing Emulsion

Add the following:

Microbial limits—It meets the requirements of the tests for absence of *Staphylococcus aureus* and *Pseudomonas aeruginosa* under *Microbial Limit Tests* (61). Δ_2

Hexachlorophene Liquid Soap

Add the following:

Microbial limits—It meets the requirements of the tests for absence of *Staphylococcus aureus* and *Pseudomonas aeruginosa* under *Microbial Limit Tests* (61). Δ_2

Hexafluorenum Bromide

Change to read:

Bromide content—Dissolve about 500 mg, accurately weighed, in 25 ml of methanol. Add 75 ml of water and 1.5 ml of nitric acid, and titrate with 0.1 *N* silver nitrate VS, determining the end-point potentiometrically, using suitable electrodes. Each ml of 0.1 *N* silver nitrate is equivalent to Δ 7.990 Δ_{1a} mg of Br; the content of Br is between 23.7% and 24.5%, Δ calculated on the dried basis. Δ_1

Hexobarbital Tablets

Delete the following:

Disintegration (701): 15 minutes. Δ_1

Add the following:

Dissolution (711)—

Medium: water; 900 ml.

Apparatus 1: 100 rpm.

Time: 45 minutes.

Procedure—Determine the amount of $C_{12}H_{16}N_2O_4$ dissolved from ultraviolet absorbances at the wavelength of maximum absorbance at about 240 nm of filtered portions of the solution under test, suitably diluted with *Dissolution Medium*, if necessary, in comparison with a Standard solution having a known concentration of USP Hexobarbital RS in the same medium.

Tolerances—Not less than 75% (Q) of the labeled amount of $C_{12}H_{16}N_2O_4$ is dissolved in 45 minutes. Δ_3

Hexylcaine Hydrochloride

Change to read:

Identification—

A: The infrared absorption spectrum of a mineral oil dispersion of it, previously dried, exhibits maxima only at the same wavelengths as that of a similar preparation of USP Hexylcaine Hydrochloride RS.

B: The ultraviolet absorption spectrum of a 1 in 100,000 solution in dilute hydrochloric acid (1 in 120) exhibits maxima and minima at the same wavelengths as that of a similar solution of USP Hexylcaine Hydrochloride RS, concomitantly measured, and the respective absorptivities, calculated on the dried basis, at the Δ wavelength Δ_3 of maximum absorbance at about 232 nm Δ_3 do not differ by more than 3.0%.

C: Dissolve about 50 mg in 5 ml of water, add 2 ml of 6 *N* ammonium hydroxide, and filter. Neutralize the clear filtrate with nitric acid, and add 2 drops in excess: the solution responds to the tests for *Chloride* (191).

Histamine Phosphate Injection

Change to read:

Identification—

A: Evaporate a volume of Injection, equivalent to about 2 mg of histamine phosphate, on a steam bath to dryness, dissolve the residue in 0.5 ml of water, and add 0.5 ml of 1 *N* sodium hydroxide. Add Δ 2 drops of sodium nitrite solution (1 in 10), and add Δ_1 1 ml of a solution prepared by mixing 50 mg of sulfanilic acid with 10 ml of water containing 2 drops of hydrochloric acid; Δ_1 an orange-red color is produced.

B: To 1 ml of Injection, equivalent to not less than 1 mg of histamine phosphate (concentrate a larger volume by evaporation, if necessary), add Δ_1 ammonium molybdate TS dropwise; Δ_1 a yellow precipitate, which is soluble in ammonia TS, Δ_1 is formed.

CONFIDENTIAL

ANALYSIS OF G-11[®] (GIVAUDAN'S HEXACHLOROPHENE)

1.) Introduction:

The present report summarizes an analysis of G-11, Givaudan's brand of hexachlorophene. All impurities present at 0.02% or more are accounted for. The work was done by a team of Research Chemists of Givaudan Corp. (Clifton, N.J.), mainly by Mr. P. J. Porcaro, Mr. P. Shubiak, Mr. P. Vallon and Dr. H. Brandman.

The sample(s) used in this study were randomly selected from commercial grade G-11, i.e. the quality as sold to our customers. The lots used were manufactured in 1969 and 1970.

It should be mentioned at this point that previous studies have clearly demonstrated that 2,3,7,8-tetrachloro-dibenzo-p-dioxin is not present in G-11 (sensitivity level 0.03 ppm). It has also been shown that the non-phenolic impurities do not contain any highly toxic chemical in any appreciable amount. These studies will not be dealt with in the present report. For details please be referred to a report by Hans U. Doeniker, dated August 5, 1970, entitled "Investigations concerning the possible presence of 2,3,7,8-tetrachloro-dibenzo-p-dioxin in Givaudan's commercial hexachlorophene".

It is our opinion that the present study has gone as far as is necessary and feasible for all practical purposes.

Letters

Industrial chemistry course

SIR: Your recent discussion (C&EN, Feb. 9, page 43) regarding academic vs. industrial or chemical engineering thinking and preparation of students was read with much interest. I have been concerned with the matter for some time, and have spent many an hour with my industrial friends in discussion regarding graduates and how much training was necessary to "fit" them for their new job.

Our department has begun to attack the problem by implementing a new "Industrial chemistry" major. This program has been met with much enthusiasm and cooperation from our local industry, and is apparently being met with equal enthusiasm by our students and administration. We expect to share some of our costs, ideas, and personnel—through seminars, laboratory interaction, guest (industry) lectures, and internships.

I know that others have had successful experiences along similar lines, and would not be a bit surprised to see that the traditional "standoffishness" (on both sides) will soon give way to a spirit of cooperation. After all, whenever I have discussed the matter one-on-one I have found that we are not so far from our brothers after all; it is the larger group meeting which leads to arguments—perhaps that is the nature of the human being.

Thomas Neil

Associate Professor of Chemistry, Keene State College, N.H.

On studying cancer causes

SIR: I read with interest the report called Science Update—Biochemistry in the March 2 issue. On page 29 the subject of research into causes for cancer is discussed.

I wonder if the reason our nation has failed to find the means by which cancer is started is because most of the effort, such as that of the National Cancer Institute, has been directed towards finding a "chemicals" cause instead of a natural biological cause, as discussed in the article?

As a result of Congress and the Delaney clause of the Food & Drug Act, we have been in a position of their having predetermined that there are indeed sinister causes for cancer. Too bad research cannot be conducted in the proper atmosphere instead of being directed by people with no knowledge of science.

Consultant, Orinda, Calif.

R. W. Lillie

More on nuclear arms race

SIR: You will no doubt receive several letters which state that the article on the nuclear arms race does not belong in C&EN. As a reason the writers will state that it is not chemical or scientific in nature, and thus has no connection with the American Chemical Society.

Let me suggest to these people, and others, another point of view, another way of thinking.

As a chemist (or other scientist) you are practicing a science which is of great interest to you, of great value to you, other than as a mere means of livelihood. Most of you think that it is important that chemistry (and all science) continue to exist and continue to progress. The existence of science and the progress of science are something to which you attach a high valuation.

Those who have studied the nuclear war situation agree that the degree of probability of a nuclear war is pretty much a random phenomenon: The chance of nuclear catastrophe increases as the number of weapons increases, as the proliferation increases, and as time goes on. The chance of nuclear catastrophe is now high and constantly increasing: It is now "four minutes to midnight."

A major nuclear war will not destroy mankind, but will demolish the technologically advanced nations. Chaos will reign. Transportation will come virtually to a standstill. Energy supplies, including electricity, will almost vanish. When you flip the switch the NMR instrument will not come on, the centrifuge will not spin, the accelerator will not bombard nuclei. Most science libraries will disappear in smoke, because most are located in or near cities. *Chemical Abstracts* will not get the information to abstract, and its computers will not alphabetize. A large percentage of chemists will be dead, because they too are located in or near cities. The science of chemistry will come virtually to a standstill.

Please, if you have any love of chemistry (and science in general), and a desire for its continued development, then join in the efforts to reduce the possibility of nuclear catastrophe.

Kent State University

R. Thomas Myers

TCDD in hexachlorophene

SIR: I have previously called attention to the 2,3,7,8-tetrachlorodibenzodioxin (TCDD, dioxin) contamination of 2,4,5-T and its "effects" on Vietnam veterans exposed to agent orange as being insignificant owing to the low and brief exposures involved (C&EN, Nov. 12, 1979, page 50). In particular I pointed out that the Seveso, Italy, accident with TCDD involved a factory making hexachlorophene, which was and still is used by many doctors and nurses and which was removed from general use in antiseptic soaps in the early seventies after being implicated in the deaths of newborns (C&EN, July 7, 1980, page 50). However, I could not find any literature references to show hexachlorophene being analyzed for TCDD, although Whiteside, in his *New Yorker* article "The Pendulum and the Toxic Cloud," July 25, 1977, page 30, mentions the association of contaminated 2,4,5-trichlorophenol being common to both 2,4,5-T and hexachlorophene, and the detection of very low levels of TCDD in hexachlorophene in 1976.

I now have found mention in an analytical procedure for hexachlorophene residues (Van Auken, O. W., Hulse, M., "Hexachlorophene,"

Continued on page 58



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Letters

Continued from page 2

"Analytical Methods for Pesticides and Plant Growth Regulators," Vol. X, Ed., G. Zweig, Academic Press, New York, 1978) that some commercial hexachlorophene did have TCDD contamination, but no data on frequency or quantity and no references to such data were given. The Food & Drug Administration's "Pesticide Analytical Manual" has a method for TCDD in hexachlorophene submitted in 1974, and correspondence with the Environmental Protection Agency (E. Johnson, March 9, 1981) indicates that hexachlorophene used as an agricultural fungicide-bactericide is supposed to have less than 0.1 ppm of TCDD. However, EPA's "Manual of Chemical Methods for Pesticides and Devices" omits methods for hexachlorophene formulations, as well as methods for TCDD, which raises the question as to when the 0.1-ppm level went into effect.

Obviously, the presence of TCDD as a contaminant in hexachlorophene has been known for some time, and the time has come to drag this skeleton out of the closet to try to find the levels and frequency of contamination before 1970. The past silence on TCDD contamination of hexachlorophene (out of perhaps a dozen articles in the popular literature and scientific news reports on TCDD, only Whiteside has mentioned the 2,4,5-trichlorophenol as the actual contaminated material and the possibility of TCDD in hexachlorophene) does not bode well for perhaps millions of Americans in view of the following uses of hexachlorophene.

As mentioned before, hexachlorophene containing (3%) soaps have been used to scrub before operations by almost all doctors since the early 1950's. From then to the early 1970's, many hexachlorophene-based antiseptic materials were widely advertised and used for acne and scalp conditions. Doctors prescribed at least one soap for douching to control certain vaginal infections. Up until the curtailing of uses in the early 1970's, these products certainly contained some TCDD on some occasions, as no one knew before, and some was found afterwards. While one soap has been monitored carefully since then, the former standard procedure of a douche with it before vaginal operations has just recently been dropped from the list of accepted uses by the company. From these exposures, the women of America who douched with the soaps ought to be our major concern for reproduction difficulties, birth defects in their children, and cancer, rather than the Vietnam veterans.

Beside the direct antiseptic exposures, two new groups—agricultural fungicide applicators and hexachlorophene plant workers—are now identified as having possible chronic exposures to TCDD over many years. Hexachlorophene has been used in a variety of fungicide-bactericide formulations for crops with a wide range of uses in the 1960's (Thomson, W. T., "Agricultural Chemicals—Book IV, Fungicides, Thomson Pub., Davis, Calif., 1967, page 215). By 1976 the uses had been reduced considerably, but no information whatsoever seems to be available on the contamination in the products or in the manufacturing of them.

At the present time EPA has registrations for a hexachlorophene formulation with uses in tomatoes, peppers, and cucumbers for applications made weekly up to three to five days

before harvest, but without tolerances assigned for hexachlorophene residues in the crops.

When compared to the exposures noted above and in 2,4,5-T plants and applicators noted before, the low and brief exposure of the Vietnam veterans has to be considered insignificant, until some people in these severely exposed groups start to show the effects, so far unnoticed in some of these groups, that are claimed by so many veterans. Some people in these groups were exposed to TCDD before the Vietnam war directly using or handling practically daily for years products with possible contamination much greater than in one or two agent orange spray drifts. The doctors and nurses who used hexachlorophene soaps several times a day with vigorous scrubbing certainly had much more effective and frequent exposure to TCDD than the veterans.

The women who douched with the hexachlorophene soaps had such direct contact with their reproductive systems that immediate epidemiologic studies seem to be required. I think these studies should include a reassessment of the connection between vaginal cancer occurring in daughters and diethylstilbestrol taken by their mothers to see if douching with a hexachlorophene soap might be implicated.

I hope that the Vietnam veterans will start realizing that their claims are badly diverting attention from possible serious exposures to TCDD. If the veterans continue to pursue their claims heedlessly, a great deal of time and money will be sacrificed that could otherwise be used by scientists and doctors to find if these more severe exposures have any low latent effects that have so far escaped notice. Throughout this letter the toxicology is based on the concept of higher and/or longer exposures causing greater and/or faster responses. With exposures of hexachlorophene noted here, the TCDD contamination of it requires putting aside its contamination in 2,4,5-T for now.

Rio Piedras, P.R. James A. Singmaster III

Regulatory madness

SIR: Regarding M. Jeffrey Shoemaker's recent letter (C&EN, Jan. 19, page 106) about the regulation of phenylacetone availability, I became aware of the classification of this common chemical on Schedule II of the Schedules of Controlled Substances recently when our order for a small amount of phenylacetone, which has traditionally been used as one of the unknowns in our undergraduate organic chemistry laboratory, was bounced by a major chemical supplier. Since I do not have Drug Enforcement Administration authorization to possess controlled substances, we had to drop this chemical from our list of unknowns.

I found myself wondering how many more of our organic unknowns would soon be unavailable for the same reason. Will we soon be unable to purchase acetyl chloride simply because it can be used to convert morphine to heroin? Something must be done about this regulatory madness and I wholeheartedly agree with Shoemaker that ACS should take the lead in such an effort.

Kenneth L. Brown
Associate Professor of Chemistry, University of Texas, Arlington

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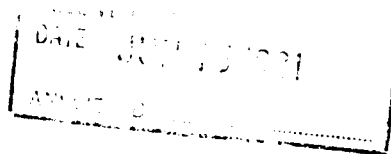
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LETTERS



Credit to Burg

SIR: Prof. Anton B. Burg has requested that I
clarify his contribution to the study of the reac-
tion of diborane with organic compounds con-
taining carbonyl groups. As described in my
Priestley Medal Address (C&EN, April 6, page
24), the presentation of Alfred Stock's book by
my girlfriend, Sarah Baylen, interested me in
doing my doctorate research in the boron hydride
area. Accordingly, I decided to do my doctorate
research with Prof. H. I. Schlesinger. As de-
scribed in my address, "Following discussions
with Schlesinger and his research assistant,
Anton B. Burg, I decided [or was persuaded] to
explore the reaction of diborane with aldehydes
and ketones [and other compounds containing
carbonyl groups]. . . .

"My thesis was completed in 1938 and the
results were published in 1939: Hydrides of
Boron. XI. 'The Reaction of Diborane with Or-
ganic Compounds Containing a Carbonyl Group'
[H. C. Brown, H. I. Schlesinger, and A. B. Burg,
J. Am. Chem. Soc., 61, 673 (1939)]."

Two of the experiments described in this joint
paper, the reaction of diborane with acetalde-
hyde and with methyl formate, were carried out
by Anton B. Burg. They were unpublished ex-
periments carried out in the summer of 1934
(see Anton B. Burg, *Chem. Tech.*, January 1977,
page 50). Consequently, I was wrong in stating
that, "I soon discovered that simple aldehydes
and ketones react readily with diborane at 0 °C
to give alkoxyboranes." Anton Burg feels that
credit for this discovery should go not to our joint
publication, but to his earlier unpublished ex-
periments.

Herbert C. Brown

Purdue University, West Lafayette, Ind.

Hexachlorophene facts

SIR: I read with great irritation and alarm the
letter of James A. Singmaster III concerning
TCDD in hexachlorophene (C&EN, May 4, page
2). Irritation because Singmaster has created a
tale of a potent health hazard based on an er-
roneous assumption. Alarm because the repu-
table C&EN dedicated two columns of valuable
journal space to inflammatory rhetoric that has
no factual foundation.

The essence of the letter appears to be that
TCDD is a contaminant of hexachlorophene at
a level representing a major health threat—past,
present, and future. The letter also attacks the

regulatory agencies and the scientific commu-
nity for ignoring this hazard. In reply to these
speculations and accusations I would submit the
facts. Hexachlorophene, through the years, has
been analyzed repeatedly for TCDD by various
industrial and regulatory laboratories. Significant
levels of TCDD were not found in these analyses.
Our routine analyses of all production batches
of hexachlorophene during recent years using
a method sensitive to 1.0 ppb normally show no
detectable TCDD. Samples of our hexachloro-
phene were analyzed by the Food & Drug Ad-
ministration in 1970 and many times in recent
years by the Environmental Protection Agency,
the Occupational Safety & Health Administration,
and the New Jersey Department of Environ-
mental Protection Agency, which have never
reported significant levels of TCDD present.

Corroborating the analytical results is the
clinical history of hexachlorophene as it relates
to the incidence of chloracne, an early-warning
dermatological symptom of the presence of
TCDD contamination. We are not aware of a
single reported incidence of chloracne attributed
to the use or manufacture of hexachlorophene
through its entire 35-year history.

Singmaster's groundless conjecture of a
possible connection between vaginal cancer,
DES, and douching with hexachlorophene soaps
requires no further comment. I would inform him,
however, that hexachlorophene was not carci-
nogenic in bioassays conducted by the National
Cancer Institute. He should also be apprised that
the Seveso factory, referred to in his letter, did
not manufacture hexachlorophene.

It is unfortunate that Singmaster did not con-
tact us in his quest for facts on TCDD and hex-
achlorophene, rather than use the *New Yorker*
magazine and other publications as his source
of information. I suggest that he obtain more
valid information prior to launching attacks
against any future targets.

M. Manowitz, Ph.D.

Givaudan Corp., Clifton, N.J.

To correct a misstatement

SIR: In the Editor's Page of May 4 on page 3,
Philip Handler, president of the National Acad-
emy of Sciences, stated that "Creationists and
Right to Lifers and the Moral Majority will seek
to have education concerning evolution and
human reproduction expunged from the sec-
ondary schools while exercising pressure to
secure removal from the appropriations to NSF
and NIH of any funds that might be used for re-
search on evolution or reproductive biology." I
have no affiliation with organizations of crea-
tionists or the Moral Majority, but I am a staunch
supporter of the pro-life movement and wish to
correct this misstatement of facts.

Pro-life organizations take no stand on evo-
lution, nor do they discourage teaching about
human reproduction in the secondary schools.
We do support complete, scientifically accurate
descriptions of human development during
pregnancy so that all people, including those of
high school age, will protect human life in all

Correction

• May 18, page 33: The number of
initial users of EPA's Chemical Sub-
stance Information Network has not
been determined at this time, nor have
the agreements been completed for use
of the commercial data bases in the
system. Both of these decisions had
been reported as final.