



Cyclohexylamine

Method number: PV2016

Target concentration:
ACGIH TWA PEL 10 ppm (41 mg/m³)

Procedure: Samples are collected by drawing a known volume of air through a 10% phosphoric acid coated XAD-7 tube. Samples are desorbed with 1 mL of 1:1 solution of methanol:deionized water for one-half hour with shaking, then 0.5 mL of the sample is removed and added to 0.5 mL of 1:4 solution of 1.0 N NaOH:methanol and analyzed by gas chromatography using a flame ionization detector (GC-FID). An alternate desorbing solvent is 1 mL of 0.888 N NH₄OH in methanol on a shaker for 30 minutes then analysis by GC-FID.

Recommended air volume
and sampling rate: 100 minutes at 0.1 L/min (10 L)
Maximum 20 liters at 0.2 L/min

Reliable quantitation limit: 0.04 ppm (0.16 mg/m³)

Status of method: Partially Evaluated Method. This method has been subjected to established evaluation procedures, and is presented for information and trial use.

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1 General Discussion

1.1 Background

1.1.1 History

The partially validated NIOSH method 221 for aliphatic amines suggests cyclohexylamine can be collected on silica gel tubes, but no validation studies have been performed. (Ref. 5.1) Silica gel tubes adsorb water readily, and there was some dilution of the sample when humid air was drawn through the tubes due to the adsorbed water, making recoveries appear lower. A media which was not affected by the humidity was desired. XAD-7 tubes were explored initially, but there was 6.7% breakthrough when 20 liters of humid air (87% RH) was drawn through them. The 10% phosphoric acid coated XAD-7 tubes were then tried and found to have desorption, retention, and storage recoveries above 95%. Desorption with a 1:4 solution of 1.0 N NaOH:water was initially tried and found to give 96% recovery, but something on the XAD-7 resin, or the resin itself, appeared to react with the NaOH causing a sticky residue to build up in the syringe on the autosampler, despite using a solvent wash. To avoid this problem, desorption with 1:1 water:methanol was used (30 minutes of shaking was necessary), then 0.5 mL was removed from the resin and neutralized with 0.5 mL of 1:4 solution of 1.0 N NaOH:methanol before analysis. After this study was completed, a new desorbing solvent was found. Samples desorbed with 0.888 N NH₄OH in methanol gave an overall desorption of 97.0% without the stickiness in the autosampler syringe. This generates ammonia, which may become interference on some columns.

1.1.2 Toxic effects (This section is for information only and should not be taken as the basis of OSHA policy.) (Ref. 5.2 and 5.3)

Cyclohexylamine is moderately toxic and intensely irritating to the skin, and may cause sensitization. Human subjects exposed to 125 mg using skin patch tests over 48 hours showed a severe reaction. Workers, wearing personal protective equipment, exposed to 4-10 ppm cyclohexylamine showed no ill effects. Cyclohexylamine has been reported to cause human mutation in sperm. Symptoms of exposure are lightheadedness, drowsiness, anxiety and apprehension, nausea, slurred speech, vomiting, and pupillary dilation.

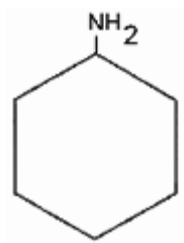
1.1.3 Workplace exposure (Ref. 5.2 and 5.4)

Cyclohexylamine is used in synthesis, manufacture of insecticides, plasticizers, rubber chemicals, dyestuffs, emulsifying agents, dry cleaning soaps, acid gas adsorbents, and as a corrosion inhibitor in boiler feed water.

1.1.4 Physical properties and other descriptive information (Ref. 5.3 and 5.4)

Synonyms:	Aminocyclohexane; Amino-hexahydrobenzene; Cyclohexanamine; Hexahydroaniline
CAS number:	108-91-8
IMIS:	0842
RTECS:	GX0700000; 28789
DOT:	UN 2357 (flammable liquid and corrosive)
Molecular weight:	99.20
Flash point:	31 °C (88 °F) (cc)
Boiling point:	134.5 °C
Melting point:	-17.7 °C
Odor: strong	fishy or amine odor

Color: clear to light yellow
 Autoignition temperature: 293 °C (560 °F)
 Density: 0.8647
 Molecular formula: C₆H₁₃N
 Structural formula:



The analyte air concentrations throughout this method are based on the recommended sampling and analytical parameters of 10 liters and a desorption volume of 1 mL. Air concentrations listed in ppm are referenced to 25 °C and 101.3 kPa (760 mmHg).

1.2 Limit defining parameters

1.2.1 Detection limit of the overall procedure (DLOP)

The detection limit of the overall procedure is 0.5 µg per sample (0.01 ppm or 0.05 mg/m³). This is the amount of analyte spiked on the sampler that will give a response that is significantly different from the background response of a sampler blank.

The DLOP is defined as the concentration of analyte that gives a response (Y_{DLOP}) that is significantly different (three standard deviations (SD_{BR})) from the background response

$$Y_{DLOP} - Y_{BR} = 3(SD_{BR})$$

The direct measurement of Y_{BR} and SD_{BR} in chromatographic methods is typically inconvenient and difficult because Y_{BR} is usually extremely low. Estimates of these parameters can be made with data obtained from the analysis of a series of samples whose responses are in the vicinity of the background response. The regression curve obtained for a plot of instrument response versus concentration of analyte will usually be linear. Assuming SD_{BR} and the precision of data about the curve are similar, the standard error of estimate (SEE) for the regression curve can be substituted for SD_{BR} in the above equation. The following calculations derive a formula for the DLOP:

$$SEE = \sqrt{\frac{\sum (Y_{obs} - Y_{est})^2}{n - k}}$$

Y_{obs} = observed response
 Y_{est} = estimated response from regression curve
 n = total number of data points
 k = 2 for a linear regression curve

At point Y_{DLOP} on the regression curve

$$Y_{DLOP} = A(DLOP) + Y_{BR}$$

A = analytical sensitivity (slope)

Therefore:

$$DLOP = \frac{(Y_{DLOP} - Y_{BR})}{A}$$

Substituting $3(SEE) + Y_{BR}$ for Y_{DLOP} gives

$$DLOP = \frac{3(SEE)}{A}$$

Table 1.2.1
Detection Limit of the Overall Procedure

µg mass per sample	area counts (µV-s)
0	0
1.038	634
2.076	1094
3.114	1514
4.152	2207
5.190	2761
6.228	3313
7.266	3894
8.304	4595
9.342	5000
10.38	5549

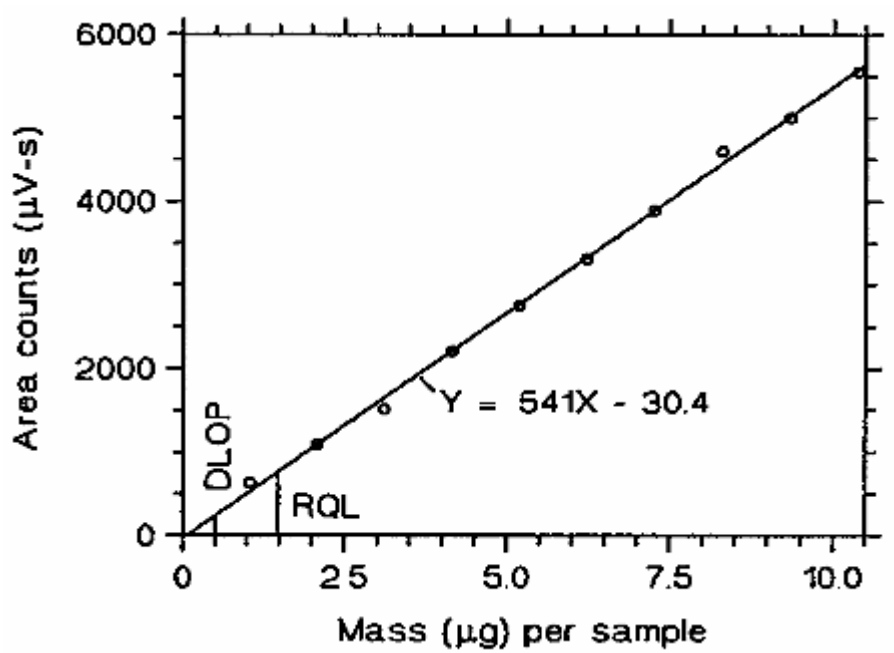


Figure 1.2.1 Plot of data to determine the DLOP/RQL.

- 1.2.2 The reliable quantitation limit is 1.5 µg per sample (0.04 ppm). This is the amount of analyte spiked on a sampler that will give a signal that is considered the lower limit for precise quantitative measurements.

The RQL is considered the lower limit for precise quantitative measurements. It is determined from the regression line data obtained for the calculation of the DLOP (Section 1.2.1), providing at least 75% of the analyte is recovered. The RQL is defined as the concentration of analyte that gives a response (Y_{RQL}) such that

$$Y_{RQL} - Y_{BR} = 10(SD_{BR})$$

Therefore:

$$RQL = \frac{10(SEE)}{A}$$

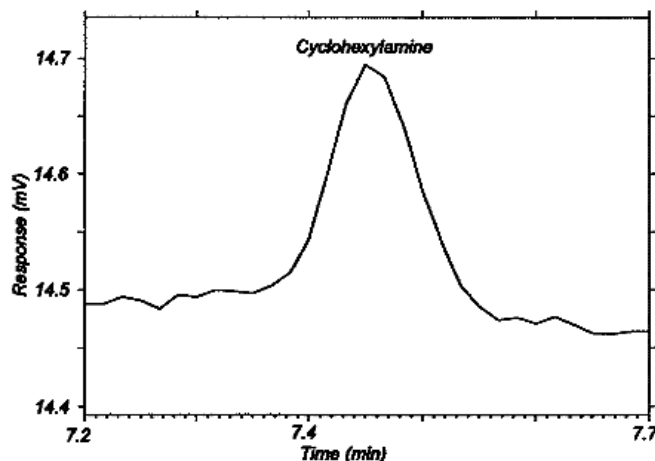


Figure 1.2.3 Chromatogram of the RQL.

2 Sampling Procedure

2.1 Apparatus

- 2.1.1 Samples are collected using a personal sampling pump calibrated, with the sampling device attached, to within $\pm 5\%$ of the recommended flow rate.
- 2.1.2 Samples are collected on 10% phosphoric acid coated XAD-7 tubes, lot 540, containing 80 mg adsorbing section with a 40 mg backup section separated by a 2-mm portion of urethane foam, with a silanized glass wool plug before the adsorbing section and a 3-mm plug of urethane foam at the back of the backup section. The ends are flame sealed and the glass tube containing the adsorbent is 7-cm x 6-mm o.d., SKC tubes, or equivalent.

2.2 Technique

- 2.2.1 Immediately before sampling, break off the ends of the sampling tube. All tubes should be from the same lot.
- 2.2.2 Attach the sampling tube to the pump with flexible tubing. It is desirable to utilize sampling tube holders which have a protective cover to shield the employee from the sharp, jagged end of the sampling tube. Position the tube so that sampled air passes through the reference, larger, section of the tube first.
- 2.2.3 Air being sampled should not pass through any hose or tubing before entering the sampling tube.

- 2.2.4 Attach the sampler vertically with the reference (larger section) pointing downward, in the worker's breathing zone, and positioned so it does not impede work performance or safety.
- 2.2.5 After sampling for the appropriate time, remove the sample and seal the tube with plastic end caps. Wrap each sample end-to-end with a Form OSHA-21 seal.
- 2.2.6 Submit at least one blank sample with each set of samples. Handle the blank sampler in the same manner as the other samples except draw no air through it.
- 2.2.7 Record sample time, flow rate, and air volumes (in liters of air) for each sample, along with any potential interference.
- 2.2.8 Ship any bulk samples separate from the air samples.
- 2.2.9 Submit the samples to the laboratory for analysis as soon as possible after sampling. If delay is unavoidable, store the samples in a refrigerator.

2.3 Desorption efficiency

2.3.1 The desorption efficiencies (DE) of cyclohexylamine were determined by liquid spiking the sampling tubes with 43.2 µg (1.07 ppm), 216 µg (5.33 ppm), 432 µg (10.7 ppm), and 865 µg (21.3 ppm) cyclohexylamine. These samples were stored overnight at ambient temperature and then desorbed with 1 mL of 1:1 solution of deionized water:methanol for 30 minutes on the shaker. An aliquot of 0.5 mL of each sample was removed and added to 0.5 mL of 1:4 solution of 1.0 N NaOH:methanol and analyzed by GC-FID. The average desorption efficiency over the studied range was 95.9%.

Table 2.3.1
Desorption Efficiency of Cyclohexylamine

	43.2	216	432	865
	µg	µg	µg	µg
DE (%)	97.2	95.6	96.7	94.0
lost	96.7	96.6	97.7	95.2
	96.7	95.5	94.5	93.4
	94.9	94.1	96.1	95.6
	97.5	93.6	96.4	98.0
	94.7	96.7	96.2	98.4
mean	96.2	95.4	96.3	95.8

overall average = 95.9%
standard deviation = ±1.42

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Table 2.3.2
Desorption Efficiency Using
0.888 N NH₄OH in Methanol

	43.2	216	432	865
	μg	μg	μg	μg
DE (%)	97.4	98.3	97.7	95.7
	98.1	95.4	98.7	97.1
	94.0	99.0	97.0	96.6
	96.6	97.7	96.3	96.9
	95.8	98.8	97.4	96.8
	96.9	97.6	95.8	96.0
mean	96.5	97.8	97.2	96.5

overall average = 97.0%
standard deviation = ±1.19

2.4 Retention efficiency

Six sampling tubes were spiked with 865 μg (21.3 ppm) cyclohexylamine, allowed to equilibrate overnight at room temperature, and then had 20 L humid air (87% RH at 23 °C) pulled through them at 0.2 Lpm. They were then opened, desorbed, and analyzed by GC-FID. The results were corrected for desorption efficiency. The retention efficiency averaged 99.1%. There was no cyclohexylamine found on the backup portions of the tubes.

Table 2.4
Retention Efficiency of Cyclohexylamine

tube #	% recovery		
	'A' section	'B' section	total
1	97.9	0.0	97.9
2	96.9	0.0	96.9
3	99.2	0.0	99.2
4	102	0.0	102
5	98.9	0.0	98.9
6	99.4	0.0	99.4

mean = 99.1%

2.5 Sample storage

The front sections of six sampling tubes were each spiked with 432 μg (10.7 ppm) of cyclohexylamine. Six more tubes had 10 liters of humid air (83% RH at 23 °C) drawn through them before they were spiked with 432 μg (10.7 ppm) of cyclohexylamine. They were sealed and stored at room temperature. Three dry samples and three humid air samples were analyzed after 7 days and the remaining three samples of each after 14 days. The amounts recovered, corrected for desorption efficiency; indicate good storage stability for the time period studied.

Table 2.5
Storage Test for Cyclohexylamine

dry samples		humid air samples	
time (days)	% recovered	time (days)	% recovered
7	101	7	100
7	99.6	7	100
7	98.5	7	101
14	100	14	98.1
14	99.3	14	100
14	101	14	100
mean	98.8	mean	99.8

2.6 Precision

The precision was calculated using the area counts from six injections of each standard at concentrations of 21.6, 108, 216, and 432 µg/mL cyclohexylamine in the desorbing solution.

Table 2.6
Cyclohexylamine Precision Study

injection #	µg/mL			
	21.6	108	216	432
1	10986	44698	84534	182682
2	11166	45444	82640	184770
3	10954	44654	81126	182416
4	10866	45826	78582	183678
5	10760	47110	78290	182946
6	10754	46176	77620	181338
mean	10914	45651	80465	182972
standard deviation	±156	±936	±2760	±1166

2.7 Recommended air volume and sampling rate.

Based on the data collected in this evaluation, 10 L air samples should be collected at a sampling rate of 0.1 L/min.

2.8 Interferences

2.8.1 It is not known if any compounds will severely interfere with the collection of cyclohexylamine on the sampling tubes. In general, the presence of other contaminant vapors in the air will reduce the capacity of 10% phosphoric acid coated XAD-7 tubes to collect cyclohexylamine.

2.8.2 Suspected interferences should be reported to the laboratory with submitted samples.

2.9 Safety precautions (sampling)

2.9.1 The sampling equipment should be attached to the worker in such a manner that it will not interfere with work performance or safety.

- 2.9.2 All safety practices that apply to the work area being sampled should be followed.
- 2.9.3 Protective eyewear should be worn when breaking the ends of the glass sampling tubes.

3 Analytical Procedure

3.1 Apparatus

- 3.1.1 The instrument used in this study was a gas chromatograph equipped with a flame ionization detector, specifically a Hewlett Packard model 5890.
- 3.1.2 A GC column capable of separating the analyte from any interference. The column used in this study was a 60-m x 0.32 mm i.d. with (1.0 μm dr Stabilwax DB) capillary.
- 3.1.3 An electronic integrator or some suitable method of measuring peak areas.
- 3.1.4 Two milliliter vials with PTFE-lined caps.
- 3.1.5 A 1- μL syringe or other convenient size for sample injection.
- 3.1.6 Pipettes for dispensing the desorbing solution.
- 3.1.7 Volumetric flasks, 10-mL and other convenient sizes for preparing standards.

3.2 Reagents

- 3.2.1 GC grade nitrogen, hydrogen, and air.
- 3.2.2 Cyclohexylamine, Reagent grade
- 3.2.3 Deionized water
- 3.2.4 Methanol, HPLC grade
- 3.2.5 Sodium hydroxide, Reagent grade
- 3.2.6 Ammonium hydroxide, concentrated, Reagent grade
- 3.2.7 Desorbing solution 1:1 methanol:deionized water. Neutralization solution (1:4) 1.0 N NaOH:methanol.
- 3.2.8 An alternate desorbing solution that requires no further neutralization is a solution of 0.888 N ammonium hydroxide in methanol. Solution is prepared by placing 3 mL of the concentrated ammonium hydroxide in 50 mL methanol.

3.3 Standard preparation

- 3.3.1 At least two separate stock standards are prepared by diluting a known quantity of cyclohexylamine with 1:4 solution of water:methanol, pH adjusted to 7.
- 3.3.2 Dilutions of the stock standards should be prepared to bracket the range of the samples. The standards used in this study ranged from 1 to 864 $\mu\text{g/mL}$.

3.4 Sample preparation

- 3.4.1 Sample tubes are opened and the front and back section of each tube are placed in separate 2-mL vials.
- 3.4.2 Each section is desorbed with 1 mL of 1:1 solution of water:methanol.
- 3.4.3 The vials are sealed immediately and allowed to desorb for 30 minutes with constant shaking.
- 3.4.4 A 0.5 mL aliquot of each sample is removed, being careful to leave the media behind, placed into a 2 mL vial, and 0.5 mL of 1:4 solution of 1.0 N NaOH:methanol is added to neutralize the sample. The vial is sealed and shaken briefly to mix well, and then analyzed.
- 3.4.5 An alternate desorbing solution, which requires no further neutralization, is a solution of 0.888 N ammonium hydroxide in methanol. After the contents of the tubes are placed in separate 2 mL vials, they are desorbed with 1 mL of this solution and placed on a shaker for 30 minutes.

3.5 Analysis

3.5.1 Gas chromatograph conditions.

Injection size: 1 μ L

Flow rates (mL/min)

Nitrogen (make-up):	30
Hydrogen (carrier):	2
Hydrogen (detector):	60
Air:	450

Temperatures (°C)

Injector:	180
Detector:	220
Temp program:	70 ° for 2 min then 10 °/min to 150 ° for 3 min

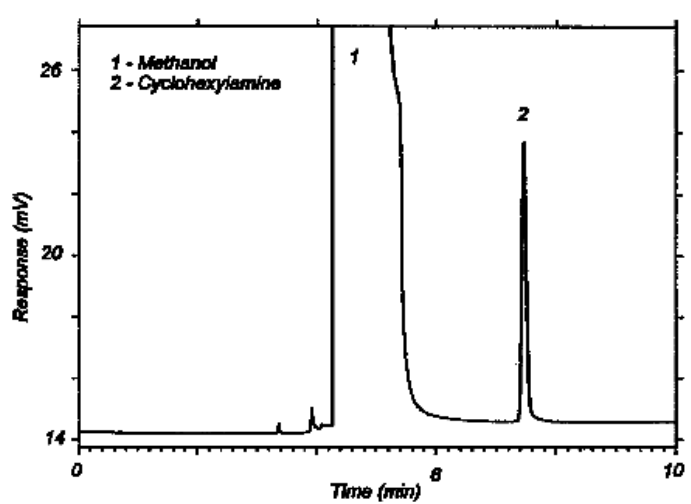


Figure 3.5.1 Chromatogram of the target concentration.

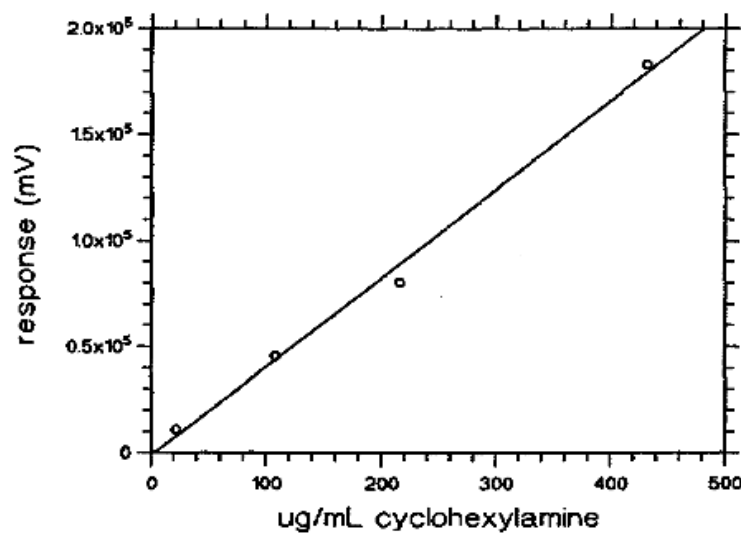


Figure 3.5.2 Calibration curve for cyclohexylamine based on standards presented in Section 2.6

3.5.2 Peak area is measured by an integrator or other suitable means.

3.6 Interferences (analytical)

3.6.1 Any compound that produces a response and has a similar retention time as the analyte is a potential interference. If any potential interference were reported, they should be considered before samples are desorbed. Generally, chromatographic conditions can be altered to separate interference from the analyte.

3.6.2 When necessary, the identity or purity of an analyte peak may be confirmed by GC-Mass spec or by another analytical procedure.

3.7 Calculations

3.7.1 The instrument was calibrated with a standard of 216 $\mu\text{g/mL}$ cyclohexylamine in the desorbing solution. The linearity of the calibration was checked with standards over the range of 1 to 864 $\mu\text{g/mL}$.

3.7.2 If the calibration is non-linear, two or more standards, at different concentrations, must be analyzed, bracketing the samples, so a calibration curve can be plotted and sample values obtained.

3.7.3 To calculate the concentration of analyte in the air sample the following formulas are used:

$$\text{mass of analyte, } \mu\text{g} = \frac{(\mu\text{g} / \text{mL})(\text{desorption volume, mL})}{(\text{desorption efficiency, decimal})}$$

$$\text{moles of analyte} = \frac{(\text{mass of analyte, } \mu\text{g})(1 \text{ g})}{(\text{molecular weight})(10^6 \mu\text{g})}$$

$$\text{volume of analyte} = (\text{moles of analyte})(\text{molar volume})$$

$$\text{ppm} = \frac{(\text{volume of analyte})(10^6)}{(\text{air volume, L})}$$

* All units must cancel.

3.7.4 The above equations can be consolidated to the following formula.

$$\text{ppm} = \frac{(\mu\text{g / mL})(DV)(24.46)}{(10 \text{ L})(DE)(MW)}$$

$\mu\text{g/mL}$ = concentration of analyte in sample or standard
 24.46 = Molar volume (liters/mole) at 25 °C and 760 mmHg.
 MW = Molecular weight (g/mole)
 DV = Desorption volume, mL
 10 L = 10 liter air sample
 DE = Desorption efficiency, decimal

3.7.5 This calculation is done for each section of the sampling tube and the results added together.

3.8 Safety precautions

3.8.1 Avoid skin contact and inhalation of all chemicals.

3.8.2 Wear safety glasses, gloves and a lab coat at all times while in the laboratory areas.

4 Recommendations for Further Study

Collection studies need to be performed.

5 References

- 5.1 "NIOSH Manual of Analytical Methods," U.S. Department of Health, Education, and Welfare, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, Second Edition, Vol. 1, Method 221.
- 5.2 Lewis, R., "Hawley's Condensed Chemical Dictionary," Twelfth Edition, Van Nostrand Reinhold Co., New York, 1993, p. 338.
- 5.3 Windholz, M., "The Merck Index," Eleventh Edition, Merck & Co., Rahway N.J., 1989, p. 427.
- 5.4 "Documentation of the Threshold Limit Values and Biological Exposure Indices," Fifth Edition, American Conference of Governmental Industrial Hygienists Inc., Cincinnati, OH, 1986, p.161.