Comparison of Three Methods of Breath Sampling for Biological Monitoring of Volatile Organic Chemicals

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Abstract

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This study compared three methods of breath sampling for assessment of exposure to volatile organic chemicals. Eleven healthy volunteers were exposed to four of these five chemicals: ethanol, acetone, methyl isobutyl ketone (MIBK), toluene, and halothane. After exposure, venous blood and mixed-exhaled breath, end-exhaled breath, and rebreathed gas were sampled ten times in four hours. The relationship between the concentrations of these chemicals in blood and each type of breath were calculated by linear regression. The calculated blood/gas partition coefficients and the goodness of fit for each breath sampling method were compared in order to evaluate which type of breath sample could best be used to predict blood concentrations. The effect of carbon dioxide correction and the effect of lung function on this relationship were investigated. Rebreathed gas concentrations predicted blood concentrations as well as end-exhaled concentrations and in most cases better than mixed-exhaled concentrations with or without carbon dioxide correction. Rebreathing gave the lowest calculated blood/gas partition coefficients, which were also closest to the literature values *in vitro*. Carbon dioxide correction lowered partition coefficients nearer to the end-exhaled and rebreathed coefficients for all but the most soluble chemical, but the coefficients did not match coefficients from the rebreathed and end-exhaled methods. Carbon dioxide correction did not generally improve the fit between blood and breath concentrations. The ratio between blood and breath concentrations is significantly lower for the rebreathed than for the mixed-exhaled methods, and the difference grows

clearer as water solubility decreases. The ratio between blood and breath concentrations is lower for the rebreathed than for the end-exhaled methods, which is more likely to be a significant difference between rebreathed and end-exhaled methods as water solubility decreases.

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Introduction:

This study compared three methods of breath sampling for assessment of exposure to volatile organic chemicals. Eleven healthy volunteers were exposed to four of these five chemicals: ethanol, acetone, methyl isobutyl ketone (MIBK), toluene, and halothane. After exposure, venous blood and mixed-exhaled breath, end-exhaled breath, and rebreathed gas were sampled ten times in four hours. The relationship between the concentrations of these chemicals in blood and each type of breath were calculated by linear regression. The calculated blood/gas partition coefficients and the goodness of fit for each breath sampling method were compared in order to evaluate which type of breath sample could best be used to predict blood concentrations. The effect of carbon dioxide correction and the effect of lung function on this relationship were investigated. Rebreathed gas concentrations predicted blood concentrations as well as end-exhaled concentrations and in most cases better than mixed-exhaled concentrations with or without carbon dioxide correction. Rebreathing gave the lowest calculated blood/gas partition coefficients, which were also closest to the literature values *in vitro*. Carbon dioxide correction lowered partition coefficients nearer to the end-exhaled and rebreathed coefficients for all but the most soluble chemical, but the coefficients did not match coefficients from the rebreathed and end-exhaled methods. Carbon dioxide correction did not generally improve the fit between blood and breath concentrations. The ratio between blood and breath concentrations is significantly lower for the rebreathed than for the mixed-exhaled methods, and the difference grows clearer as water solubility decreases. The ratio between blood and breath concentrations is lower for the rebreathed than for the end-exhaled methods, which is more likely to be a significant difference between rebreathed and end-exhaled methods as water solubility decreases.

Background and Significance:

Various methods can be used to assess exposure to environmental chemicals and the health risk associated with these exposures. It is common to estimate chemical exposure from measurements taken outside the body, such as concentrations in gases collected from the breathing zone or the general area, dermal contact and absorption rates, or concentrations in ingested materials. However, these methods may not take into account factors such as breathing rates, personal protective equipment, or unusual exposure pathways such as after-work exposure. Dermal contact and absorption rates are also difficult to calculate accurately. A more direct measurement of absorbed dose may be obtained by biological monitoring, or collecting and analyzing bodily fluids. One can estimate exposure by measuring concentrations of the chemical to which the person was exposed or concentrations of metabolites of these chemicals. One may also be able to estimate health risks from these exposures by measuring concentrations of DNA adducts or other types of evidence of effects on the body. Since the concentrations of chemicals in the body change during and after exposure, one must know the pharmacokinetics of this chemical and the period of exposure to calculate an absorbed dose and must know the routes and pharmacokinetics of exposure to calculate exposure from biological monitoring. Metcalf (2004), Mutti (1999) and Lauwerys (1995) provide a more thorough discussion of biological monitoring for exposure assessment.

Every exhaled breath contains gas that has had recent, intimate contact with blood. Some part of each inhaled breath reaches the alveoli, where gas exchange with blood is most efficient. Venous blood enters the lungs and is guided into alveolar capillaries only slightly wider than a red blood cell. The blood traveling through these capillaries passes through the lung in about one second normally (Caudill 1998), long enough to allow dissolved gases to diffuse into and out of the blood. The end-capillary pulmonary blood becomes arterial blood and is pumped out to interact with the tissues in the rest of the body. Gas concentrations in alveolar breath and arterial blood equilibrate in the alveoli, which means that a gas has the same partial pressure in alveolar breath as in arterial blood. Consequently, the measurement of chemical concentrations in breath can be valuable in the assessment of blood concentration, which is an indicator for exposure, dose and body burden of a volatile chemical. Blood carries volatile chemicals to and from the lungs and any organ where the chemicals may be stored, and the time course of chemical concentrations in blood after exposure can be known well enough to allow calculation of dose, exposure or body burden. Breath analysis for volatile chemicals has the potential to augment the information gained from other forms of exposure assessment. This form of biological monitoring can allow calculation of the absorbed dose of a chemical, which is more relevant to health risk than a simple measurement of environmental concentration. Absorbed dose and body burden may not be easy to ascertain from exposure measurements in air because of varying breathing rates, personal protective equipment, dermal exposure, or after-hours exposure.

Biological monitoring methods include measurement of concentrations in blood, urine, breath, or in rarer cases, bone, fat, hair or saliva. Any tissue that absorbs a chemical and for which the pharmacokinetics are known can be used to estimate absorbed dose. Some of these bodily fluids are easier and safer to collect than others. Blood analysis is standard for lead exposure assessment, but blood collection requires a medical procedure with some level of risk of infection or disease transmission. Blood and urine analysis also carry the stigma associated with drug testing, and people may question what is actually being tested. Traditional methods of exposure assessment also have their difficulties: Personal sampling requires some amount of equipment attached to the person, whether as small as a two-inch badge or as large as a pump hanging on a belt with a tube attached to sampling media. Area sampling may interfere less with the activity of the person whose exposure is sampled, but it is also less accurate when used to estimate personal exposure. Breath sampling has the advantage of being relatively easy and not requiring much time or pain for the subject. It also has not traditionally been used to detect drugs other than alcohol. Breath sampling may therefore be more practical than other types of biological monitoring samples.

Many researchers have used breath sampling in controlled studies and in the field, but the environmental and occupational health community has not agreed on a standard method of collecting breath. Often the terms "mixed," "end-expired" or "alveolar" are used to describe the breath collection method, but without enough description to determine the exact method. The contaminant concentration in breath may differ depending on the breathing pattern because of multiple factors: First, a normal exhalation will not contain the same proportion of "dead space," or gas that never reached the gas-exchange region of the lung, as a deeper or more shallow exhalation, and this depth of exhalation varies with each breath depending on respiratory drive. Second, breath holding can increase the exhaled concentration of any gas dissolved in blood, and hyperventilation can decrease the concentration, because exhaled gas has spent more or less time in contact with blood. This relationship between breathing pattern and exhaled concentration varies with the water solubility of the chemical, because more water soluble compounds dissolve in airway tissue to a greater extent so that the airways become another region of gas exchange.

Untrained subjects asked to breathe normally often breathe larger volumes than they normally would because of psychogenic hyperventilation, and trained subjects who are aware of this tendency may also hypoventilate in an effort to compensate for it (Guillemin 1982). End-expired air that is collected at the end of a normal expiration may contain different chemical concentrations from that collected at the end of a forced full expiration (Guillemin 1982). For example, an end-tidal sample during a normal expiration yields a carbon dioxide partial pressure very close to the mean arterial partial pressure, but a sample collected at the end of a forced expiration will yield a higher P_{CO_2}, and breath holding yields an even higher P_{CO_2}. However, both end-tidal and end-forced-expired air have been described as "alveolar" air by one or more researchers.

Chemical concentrations in breath have also been corrected to “alveolar” concentrations by adjustment for carbon dioxide concentrations (Guillemin 1982), but this correction may not be adequate in all cases.

Physiologists have collected alveolar breath by the rebreathing technique (Piiper 1979), while the environmental health community has relied on end-exhaled or end-tidal samples or on carbon dioxide correction of mixed-exhaled samples for alveolar breath collection. To give a breath sample by rebreathing, the subject must breathe back and forth into a bag for long enough to allow mixing of air from all regions of the lung and allow equilibration between the gas in the alveoli, the gas in the bag, and the dissolved gases in the arterial and venous blood. If the rebreathing continues for a sufficient amount of time, the arterial and venous partial pressures of these “inert” contaminants that are not actively being produced or consumed by the body should be equal. Venous blood is important because it is much more easily sampled and more commonly sampled for exposure assessment and pharmacokinetic studies. Furthermore, a device that collects gas by rebreathing while keeping the collected gas at the temperature of the body will keep gases in breath from dissolving out of breath into condensate on the surfaces of the collection bags or tubing. This isothermal rebreathing apparatus should also allow the rebreathed air to reach the core body temperature and minimize the effect of soluble gases being captured from breath being exhaled and dissolved into the cooler airway tissue before the gas is exhaled. No study has shown definitively that rebreathing gives an alveolar sample, although rebreathing has become common in several types of measurements. Pulmonary **diffusing capacities** for oxygen or carbon monoxide are commonly measured with rebreathing in order to reduce the effect of inhomogeneous lung function (Piiper 1979), but the only experimental situation for which rebreathing has been used to determine a dose or body burden of a chemical is the determination of the blood concentration of ethanol (Ohlsson 1990).

Ohlsson (1990) measured blood alcohol concentration (BAC) and used breath samples from isothermal rebreathing and from single breaths into a commercially available breath alcohol analyzer to predict blood alcohol concentrations. The commercially available breath analyzer, which required a single breath, predicted blood alcohol concentrations ranging from 14% above the measured BAC to 55% below the measured BAC. This study did not compare isothermally rebreathed samples to the more uniform samples that may be produced using the more carefully controlled mixed or end-forced-exhaled methods which have been used in exposure assessment.

Breath collection methods in the literature:

Many breath collection methods have been used to approximate contaminant concentrations in blood. Some researchers have collected one or more entire breaths, called "mixed-expired" breath because the breath collected includes both gas that has been in close contact with blood in the alveoli and gas from the dead space that was unable to exchange gases with the blood. Dead space is generally assumed to be equivalent to the volume of the conducting airways and any non-perfused alveoli. Figure 1 shows that an exhaled breath contains very low CO_2 concentrations during the first part of the exhalation, while the air flowing out of the mouth has only reached the airways (and thus has only traversed the dead space). This is followed by a rapid rise in concentration, while the air flowing out of the mouth is the shallowest part of the breath that reached the gas exchange region. After the initial rise in concentration, the carbon dioxide concentration in a normal person continues to rise slowly until the end of the breath. Other researchers have collected the last parts of one or more breaths in an attempt to capture only the alveolar air which has equilibrated with blood. A few researchers have collected rebreathed air in order to allow full equilibration with blood, considering the equilibrated, rebreathed air to have the same contents as alveolar air which is in contact with blood. The environmental health community and the physiology community apply the term "alveolar breath" to samples collected by different methods. Alveolar breath collection is further complicated by the differing behaviors of chemicals of varying blood/air partition coefficients. Highly water soluble chemicals in breath will undergo gas exchange with airway tissue, so that there is no dead space in which gas exchange has not occurred. This is true of ethanol and is likely to be true to a lesser extent of chemicals of medium to high water solubility. When breath has been exchanging gases with the airways over its entire path from the alveoli to the mouth, it is impossible to assume that the last part of an exhaled breath contains the same concentration that it did when it left the alveoli.

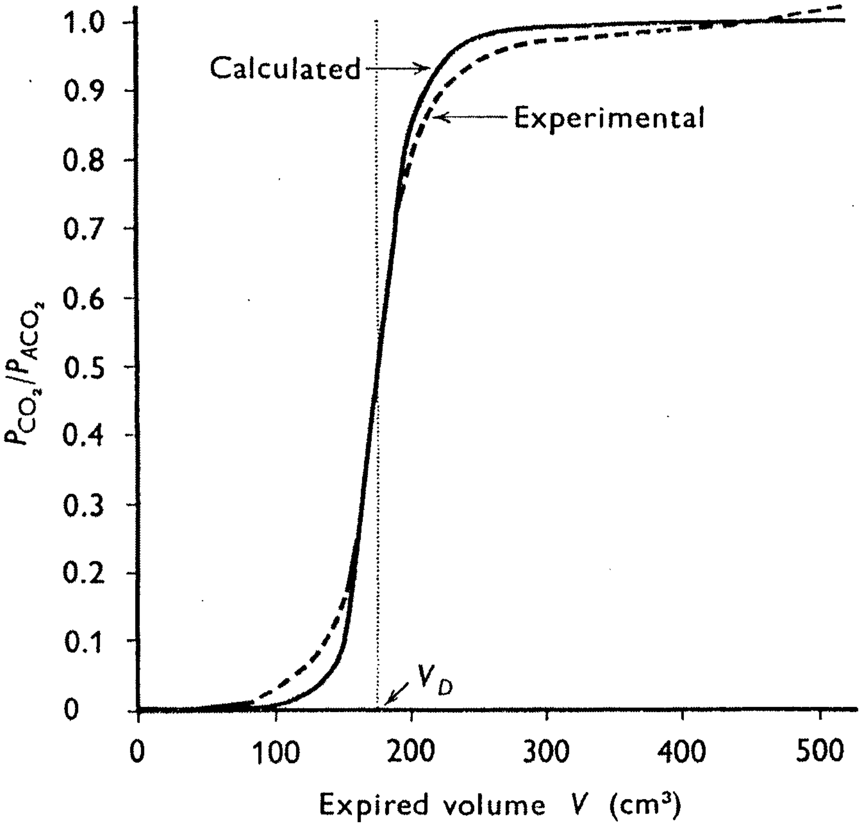

Figure 1: A "calculated" curve for P_{CO2} at the lips based upon back-mixing alone compared with a typical "experimental" curve. From Hills & Kuonen (1973).

The following sections will describe the methods and challenges of breath collection methods used by previous researchers. The technical requirements of breath sampling for high-solubility chemicals will be reviewed, followed by the requirements of low-solubility chemicals.

Mixed-Exhaled Air

Although it is well known that mixed-exhaled air contains a variable proportion of dead space gas which has not equilibrated with blood, mixed-exhaled breath is easy to collect and has been widely used. Some of these authors have corrected for carbon dioxide content of breath in order to approximate the alveolar contaminant concentration or correct for the variable proportion of dead space. This carbon dioxide correction assumes that the contaminant only interacted with blood in the gas exchange region and that the chemical concentration over the course of a breath changes in the same pattern seen for carbon dioxide in Figure 1. The chemical concentrations in mixed breath are divided by their carbon dioxide concentrations and multiplied by the end-exhaled carbon dioxide concentration of the subject or a standard alveolar carbon dioxide concentration from the literature. If the chemical of interest follows the same pattern of concentration as carbon dioxide over an exhaled volume of breath, the resulting number will closely approximate the concentration in alveolar breath.

Pleil and Lindstrom (1997) developed a very simple method for breath collection: a person exhales directly through a 5-cm diameter mouthpiece into an evacuated 1 L or 1.8 L stainless steel canister with a critical orifice so that the breath was collected into the canister at a controlled rate. This is sometimes known as the Single Breath Canister (SBC) method. The subject is required to pinch her own nose, open the canister valve by hand, breathe into the canister until it reaches ambient pressure, and close the valve. The breath is later pressurized with zero grade air to 40 psig to allow multiple analyses by the EPA method of cryogenic preconcentration and injection into a GC-MS. The SBC can be used to collect "alveolar" breath if the sampler valve is opened at the end of a normal exhalation. While this method controls the volume of the collected breath, it does not control the depth of the inhalation before collection. This method also requires the subject to perform some potentially difficult operations on the canister while holding her breath. This may change the chemical concentration because of slight hypoventilation during the period immediately before exposure or slight hyperventilation during the inhalation in preparation for this operation. For a shallow inhalation, the canister may collect air past the point where the subject would ordinarily have stopped exhaling. The vacuum is also impossible to shut off until the canister is full, so that it would be possible to catch a tongue or a lip in the suction.

Glaser et al. (1990) developed a stainless steel sampler that divides mixed exhaled breath into parallel streams and draws each stream through a different sorbent - one through Tenax sorbent and one through charcoal cloth. Exhaled volumes (5-20 L) being collected from the main tube onto charcoal cloth were recorded using a Wright respirometer, and the parallel sidestream was pumped at a rate of 50 mL/min onto Tenax adsorbent. Carbon dioxide concentrations were measured by an infrared detector. They compared ratios of carbon dioxide concentration and xylene concentration between methods and found reasonable agreement between mainstream-mixed and alveolar breath concentrations but found the sidestream sampling method to be relatively inaccurate. They concluded that the sidestream method was less accurate and precise because of the inaccurate and imprecise determination of sidestream sample volume.

The most common method for collecting mixed-exhaled breath is simple bag sampling, in which the subject is simply asked to breathe into a bag. It is used very commonly, especially for qualitative studies, and has been used in this laboratory for previous studies. This requires no coaching and no standardization of method between sample collecting personnel. Breaths are likely to be of variable size and depth because of changes in the subject's need for ventilation and in the subject's depth of inhalation. It is useful to make sure that the bag has a wide enough opening to allow easy exhalation without back pressure. This laboratory has collected multiple breaths into a bag by asking the subject to exhale into the bag once, block off the bag and take three normal breaths without being connected to the bag, and exhale into the bag again. The process of averaging multiple breaths into one sample eliminates some of the variability between breaths.

End-Exhaled Air:

Many researchers have used the Haldane-Priestley method or one of its variants (described by Wilson, 1986) to collect the air exhaled at the end of the breath. The subject exhales into a long tube, and at the end of the exhalation, a small volume of air is withdrawn from the end of the tube closest to the mouth – representing the last air exhaled. The purpose of this collection method is to collect only the last part of the breath, excluding dead space and collecting only air that has interacted with blood. The volume of air collected, the time during the breath at which the air is collected, and the tube dimensions vary by researcher. The sampling apparatus may collect the end of one or more tidal breaths or the end of one or more forced breaths, with or without breath holding. Several such apparatus types are described below.

End-Tidal Samplers:

Glaser et al. (1990) compared their mixed-exhaled parallel stream sampling method to an "alveolar" method in which the subject hyperventilated several times, breath was held for 30 seconds, and only the last ~50% of the breath was collected into a Teflon or Tedlar bag. The collection of only the last part of the breath was achieved by having the subject cup his mouth onto the mouthpiece and open the clamp on the Tygon tubing attached to the bag before exhaling the remainder of the breath into the bag. The bag was sealed by reclamping the Tygon tube, and the gas was connected directly to a sample loop in a gas chromatograph.

Dyne, Cocker and Wilson (1997) designed a sampler that captures the last 85 mL of a breath inside a small bag contained in a metal cylinder. Air is exhaled through a one way valve into the bag and through another one way valve into the outside air. The last 85 mL is captured in the bag at the end of the breath. A brass ring on the outside of the cylinder and attached to the mouthpiece end of the bag allows the captured breath to be expelled manually from the bag onto an adsorption tube. Subjects were encouraged to breathe as normally as possible and not to hold their breath before sampling.

Raymer (1990) reported on a system that draws air continuously from a tube with dimensions of 760 cm × 1.27 cm i.d. into an evacuated 1.8-L polished metal canister (with flow controlled by a critical orifice) while the subject exhales into the tube. The subject inhales air through a pair of respirator cartridges via one-way valves. The tube is meant to hold 0.96 L of alveolar breath at the end of an exhalation. The subject is asked to control volume as well as possible and to control the duration of each inhalation and exhalation with the aid of timers. Sampling starts after the first breath and continues for 1.5 to 2 minutes. This is end-tidal air with some caveats: The velocity of exhaled air is fastest at the beginning of the exhalation, as shown in Figure 2. Since the dead space air at the beginning of the exhalation moves past the orifice faster than the air from the gas exchange region which appears later in the breath, this collected a lower proportion of the dead space air and a higher proportion of the alveolar air than can be found in mixed-exhaled breath. Raymer calculated the fraction of dead space in the collected breath using CO_2 levels from a fast mass spectrometer. Alveolar breath was defined as the part of the collected breath with elevated CO_2 levels, and dead space air was defined as the part of the collected breath that showed a downward spike in CO_2 concentration. Wallace and Pellizzari (1995) used this system in the laboratory and in the field but do not mention the use of timers to control breath volume.

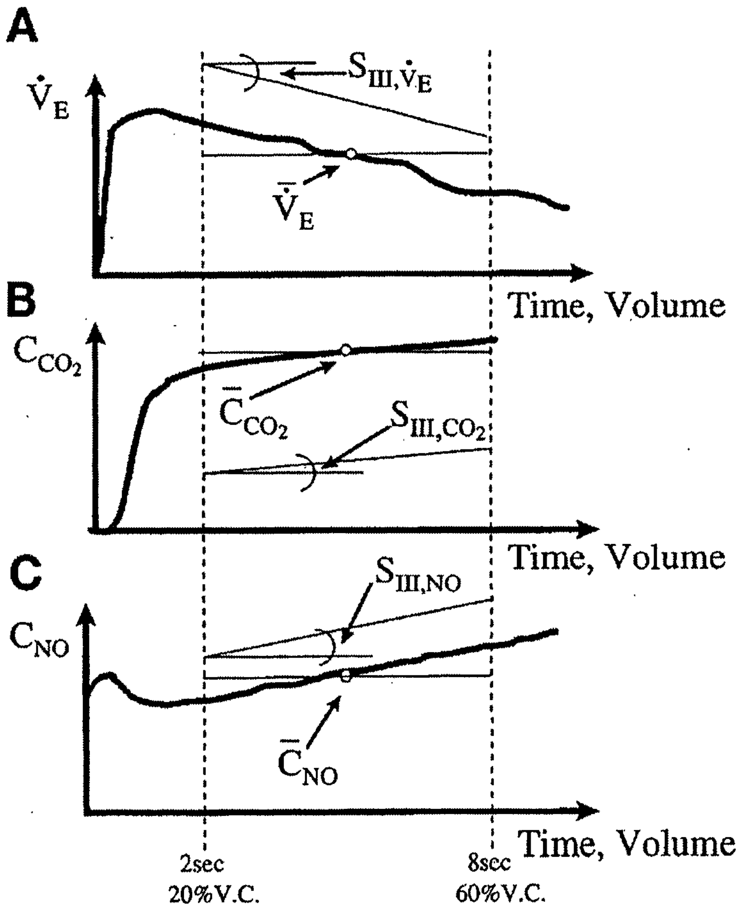

Figure 2: Schematic detailing analysis of exhalation profiles for concentration and flow rate. Average concentrations and flow rates were estimated for exhaled volume and exhaled time by use of interval of 20-60% of vital capacity (VC) or 2-8 s, respectively. Phase III slope was calculated using linear least squares over this same interval and then normalized by average value over interval. V(overdot)$_E$, exhalation flow rate; C_{CO2} and C_{NO}, CO_2 and NO concentration, respectively; V(overbar)$_E$, C(overbar)$_{CO2}$, and C(overbar)$_{NO}$, average V_E, C_{CO2}, and C_{NO}, respectively; $S_{III,VE}$, $S_{III,CO2}$, and C_{NO}, phase III slopes for NO, CO_2, and V_E respectively. (Tsoukias 1998)

Periago et al. (1992) have designed a breath sampler that uses a heated (40-45°C) 1 m × 26 mm diameter (531 mL) aluminum tube with a one-way valve and an automated syringe and valve system to combine the end-exhaled air from more than one exhalation. This is fully automated, with a motor controlling a three-way valve that alternately draws in exhaled air and expels it through glass charcoal tubes. At the end of each breath, an operator switches the machine so that it draws a set volume from near the one-way valve and mouthpiece into a syringe. The apparatus then switches the valve and moves the plunger to expel the sample through an adsorbent cartridge. In theory, the cartridge connection could be replaced with a bag. The tube is storable in two sections, and the prototype sampler weighs 5 kg. External electrical power is required. The amount of breath taken from each exhalation can be varied, and the investigators used 0.2 L or 0.3 L per breath.

Ljungkvist and Nordlinder (1995) developed a sampler based on a peak expiratory flow meter with an exchangeable paper mouthpiece, attached to a one-way spring-loaded valve leading to a 90 cm × 2.5 cm i.d. plastic tube. The subject was asked to breathe in through the nose and exhale into the sampler for four normal breaths. A handheld fast digital thermometer measured breath temperature, and for each breath, when the breath reached its maximum temperature of 34.5°C (which was used in this case as an indication of alveolar breath), a 100 mL sample was drawn with a manual sampling pump through an adsorbent (Tenax) tube.

Franzblau et al. (1992) used CO_2 content of breath to determine whether samples were "true" end-tidal air. They collected breath in an apparatus consisting of two bags, a 500-mL trapping volume bag and a 500-mL Mylar sample bag, attached to a T-valve into which the subject exhaled. The first 500 mL was collected in the trapping volume bag, which triggered the opening of the one-way valve on the sampling bag once the first bag was full. The sampling bag collected the last 200-500 mL of breath, which was tested for CO_2 content. Samples with CO_2 concentrations at or above 6% and samples of less than 200 mL were excluded, and the procedure was repeated after several minutes of rest. They chose the 6% concentration cutoff to represent "the plateau level that most normal subjects attain in a "true" end-tidal air sample" by using this respiratory maneuver.

End-forced-exhalation Samplers:

Brugnone et al. (1980) monitored the exposures of workers during their shifts by environmental sampling and "alveolar" sampling immediately beforehand using the Haldane-Priestly method. They sampled breath by asking workers to give a forced expiration through a 70-mL glass tube. Screw caps at each end of the tube were sealed immediately after the end of the expiration. The environmental samples were taken at the same time by drawing air from the worker's breathing zone into the same type of container. Air samples were all kept at 37°C and analyzed within 4 hours. Correlations between breath concentrations and concurrent spot environmental concentrations were generally high, ranging from 0.7634 to 0.9835. Correlations for the more water-soluble compounds tested were noticeably lower than the correlations for less soluble compounds: Correlations for the five less soluble compounds ranged from 0.9664 to 0.9835, while correlations for the five more soluble compounds ranged from 0.7634 to 0.8733. All of these correlations may be artificially high because the air the subjects inhaled while giving breath samples was the same air from which the environmental samples were taken. Breath sampling while the inhaled air carries elevated concentrations of a chemical is different from breath sampling during washout. Particularly for highly soluble chemicals, the airway tissue would be affected by the inhaled concentration and would in turn affect the exhaled concentration.

LeBlanc et al. (1995) have developed a breath sampling device for sampling of chloroform in breath. The subject exhaled to residual volume, inhaled to total lung capacity, held breath for 20 seconds "so as to achieve equilibrium between blood and alveolar air concentration of the chloroform," and then exhaled into the device, where only the last 20 mL were captured in a syringe. A simple mouthpiece was connected to the 25 mL syringe with 5-mm holes drilled near the 23 mL mark to let air escape. When further exhalation was impossible, the syringe piston was pushed to the 20 mL mark to close the holes, stop the flow of gas and trap the last 20 mL of air inside the syringe. That 20 mL was injected from this syringe into a headspace gas chromatography vial. This sampling method would seem to require a syringe with an opening at the needle end that is wide enough to allow all the breath to enter the syringe without requiring excessive backpressure but narrow enough to not lose significant amounts of the sample while the syringe is being removed from the mouthpiece and fitted with a needle for injection. Despite these practical issues and an analytical method that had a relatively high coefficient of variation (18.5%), they achieved a correlation coefficient of 0.83 between these breath samples and blood samples collected at the same time.

Stein et al. (1996) collected breath in 40-mL glass silanized tubes with stainless steel shutoff valves at each end, one of which included a septum for removal of aliquots of the gas by syringe. The subject inhaled normally, held his breath for 10 seconds, and then exhaled forcefully into the tube. When the subject was no longer able to exhale, the valves were shut off. It is unclear from the article whether the subject or another operator closed the valves, and it seems evident that these were not automated valves.

Rebreathed air:

Rebreathing has been used in limited situations for exposure assessment by physiologists.

In 1950, R.N. Harger et al. used rebreathing to measure breath alcohol levels and found breath collected by rebreathing to contain the same concentration of alcohol as alveolar air collected by filling a 600 mL bag with the first part of the breath and collecting the remainder in another bag, with the use of a T-shaped tube and a one-way valve. They also found that rebreathing estimated blood alcohol concentration much better than their previous method of mixed-expired breath collection with correction for CO_2 and that "the weight of alcohol present in 1 cc. of a subject's blood (a) is found in 2100 cc of his alveolar air, (b) accompanies 190 mg. of CO_2 in his mixed expired air or in his alveolar air; and (c) is present in about 3200 cc of his mixed expired air after removal of CO_2

and collection over water at 25°C." They recommended rebreathing as a precise way to find the alveolar alcohol concentration.

In 1990, J. Ohlsson et al. collected breath using an isothermal rebreathing apparatus that kept a collection bag and the tube leading to the mouthpiece warm while rebreathed breath was collected. The apparatus was designed to allow measurement of body temperature, calibration of a separate infrared analyzer immediately before measurement, and measurement of all breath volumes. The apparatus would stop collection and force the subject to start over if breath volumes did not reach a minimum level of 1.5-2 liters depending on self-reported height. Samples were transferred for analysis by a needle that punctured the tube leading to the mouthpiece.

Effect of blood solubility:

The solubility of a chemical in blood, water or airway tissue can affect the behavior of the chemical as it moves through the respiratory and cardiovascular systems and the results of breath samples as they relate to venous blood samples. Highly soluble gases may be retained and exchanged in airway tissue, which may make sampled breath differ from alveolar air. Poorly soluble gases will be extracted from the pulmonary circulation in such a large fraction that the arterial blood, with which the alveolar breath is in equilibrium, has a much different concentration from the venous blood. Details of these processes, their consequences and methods used or proposed to deal with them are described below.

Sampling for very blood-soluble chemicals:

Chemicals with very high partition coefficients, such as alcohols, present their own challenges to investigators attempting to determine blood concentration from breath concentration. In particular, the highly soluble compounds undergo gas exchange with the airways and not just the blood in the pulmonary capillaries. Rebreathing has been used to collect alveolar samples of ethanol and has been compared to other methods in two cases.

In 1983, A.W. Jones compared end-expired air to rebreathed air from subjects exposed to ethanol and found that rebreathing gives lower blood-breath ratios, closer to the ratios found *in vitro*. This implies that rebreathed samples more closely resemble gas in equilibrium with venous blood than do end-exhaled samples. He also found that although concentrations in rebreathed and end-expired air both correlated well with blood ethanol levels, end-expired air concentrations were also correlated with expired air temperature, while rebreathed air concentrations were unaffected by breath temperature.

In 1990, J. Ohlsson et al. investigated the effect of breathing pattern and air temperature on the isothermal rebreathing and single breath methods of breath collection. Breath alcohol levels increased during a single exhalation, never reaching a plateau where the concentration was constant as more air was exhaled. This implies that the true alveolar level was not reached during the single exhalation and that variations in how close an exhalation is to residual volume can make end-exhaled breath concentrations more variable than rebreathed breath. They also showed that changing the breathing pattern (hyperventilation vs. breath holding) affected breath ethanol levels taken in single breaths but not by rebreathing. In this case, the single breath method was based on the requirements of commercially available breath alcohol analyzers: After an inhalation to total lung capacity, the subject exhaled until airway inlet pressure had exceeded 15 cm H2O for at least 4 seconds. A minimum exhalation concentration was measured by an infrared detector when these criteria had been reached, and the subject continued to exhale. A maximum exhalation concentration was measured after a full exhalation to residual volume. This same single breath method was repeated after hyperventilation, after a 15 second breath hold, after three deep breaths of cold, dry air, and after three deep breaths of warm, dry air. The rebreathing method gave the lowest blood-breath ratio (BBR) (closest to the directly measured partition values) with the lowest standard deviations. A statistically significant relationship was also found between BBR and end-rebreathing breath temperature. It was hypothesized that the effects of breathing pattern on breath alcohol levels was caused by the differences in the temperature of the airway surfaces and resulting differences in alcohol solubility in airway tissue.

Schrikker et al. (1989) examined the excretion of highly soluble gases during a four-minute wash-in period, when venous concentrations were near zero as subjects were starting to absorb the gases. Excretion is important in this case as a measure of how gas in the lung exchanges with the various lung tissues and the blood perfusing the lungs. The solvents examined were ethyl acetate ($\lambda \approx 75$), acetone ($\lambda \approx 330$), ethanol ($\lambda \approx 2000$), and acetic acid ($\lambda \approx 20000$). They found that gas exchange in the airways cannot be ignored, that the excretion and absorption of the gases varied between rest and exercise for the two less soluble gases but not for the two most soluble gases, and that physiological dead space also depends on the value of the blood-gas partition coefficient (λ). (Physiological dead space is the volume of gas that does not undergo gas exchange, consisting of any volume that is ventilated but not well perfused.) Ethyl acetate and acetone showed differences in excretion between rest and exertion and between normal breath patterns and patterns that included a one-second post-inspiratory breath hold, while ethanol and acetic acid showed hardly any difference in excretion for either of these comparisons. The gas exchange properties of ethanol and acetic acid were different enough from those of the less soluble gases that it was suspected that most of the gas exchange for these very soluble gases was confined to the airways.

Sampling for chemicals with low blood solubilities:

At the opposite end of the scale of blood-gas partition coefficients (λ), there starts to be a noticeable difference between partial pressures of inert gases in alveolar gas and mixed venous blood. (Venous samples are another step removed from mixed venous blood in most cases, because the blood taken from an available skin surface has not passed through a path representative of the whole body.) Farhi used the following equation to describe the relationship between solubility, alveolar and mixed venous partial pressures, and ventilation-perfusion relationships under steady-state conditions:

$$P_A/P_V = \lambda / (\lambda + \bar{V}/\bar{Q})$$

where $\bar{V}$ is the alveolar ventilation and $\bar{Q}$ is the blood flow of the lung region being considered. This equation suggests that solvents with low water solubilities show greater differences between partial pressures in alveoli and in the veins, and that this ratio will be affected more by ventilation/perfusion ratios for less soluble chemicals (Wilson 1986). Even for a perfectly efficient lung, where $\bar{V}/\bar{Q}$ would equal 1, the alveolar and venous concentrations will never be exactly the same under steady-state conditions. Highly water soluble compounds will have large values of λ, so that the difference between venous and arterial blood attributable to the ventilation/perfusion ratio, which is usually near 1, is negligible. This starts to become more of an issue at below λ=8, at which point partial pressures of the gas in the alveoli drop below 90% of the venous partial pressures.

Hlastala and Robertson (1978) have used theory and dog experiments to illustrate the effects of ventilation-perfusion inhomogeneity, shunt, and dead space on the differences between arterial, venous and expired breath, showing that ventilation-perfusion inhomogeneity has its greatest effect at blood-gas partition coefficients near 1, with much less effect at blood-gas partitions below 0.01 or above 100. G.R. Kelman (1982) illustrates these points by modeling gas transport using the equation above and shows that a breath holding period can bring the partial pressures of inert gases in alveolar breath and venous blood closer together. During a breath hold, the ventilation rate drops to zero, allowing the ventilation/perfusion ratio to drop out of the equation so that $P_A/P_V = 1$. He argues that breath holding is unnecessary for end-forced-exhaled sampling at partition coefficients above 5 because during the exhalation (which he models as taking about 8 seconds), the cardiac output continues to supply venous blood at the same rate to a shrinking lung volume. He shows that a Haldane-Priestley tube, as described in many of the end-exhaled sampling descriptions above, "is likely to provide an alveolar solvent partial pressure of within 95% of the mixed venous pressure" for solvents with partition coefficients above 5. He mentions rebreathing as a way to determine a solvent's mixed venous pressure, but the method he describes is a different method with a bag already containing air or oxygen with "an appropriate concentration of solvent vapour" to ensure that the system reaches a plateau in concentration. Starting from any concentration above zero seems unsuitable for exposure assessment because one cannot know the dose received in advance well enough to pick an appropriate starting concentration: any inhaled concentration that is higher than the concentration in alveolar air exposes the subject to more of the chemical and may change the system. This paper does not consider airway gas exchange, so the conclusions may not apply to very high solubility gases.

Correcting exhaled concentrations for CO_2 content

Guillemin and Gubéran (1982) analyzed end-forced-exhaled breath for both 1,1,1-trichloroethane and carbon dioxide, using carbon dioxide concentrations in the samples to correct the 1,1,1-trichloroethane concentrations to "alveolar" concentrations. They used the following equation to convert their observed concentrations to a value that correlated to 38 mmHg, which is the mean normal value of P_{CO_2} at their altitude. At sea level, the value to use for this correction would be 40 mmHg.

$$^{C}\text{CORR} = {}^{C}\text{OBS} \times (\text{mean normal value}/P_{CO_2}\text{OBS})$$

They note that an end-tidal sample from a normal expiration has been shown to yield a P_{CO_2} close to the mean arterial P_{CO_2}, while the Haldane-Priestley method and breath holding methods yield P_{CO_2} values higher than mean arterial values. The sampling apparatus was a heated coil with a three-way valve to separate inspired air from expired air, in which 10 ml of breath was piped into a gas chromatograph when a continuous measurement of carbon dioxide concentration showed a plateau. The three breathing patterns tested included collection of the last part of a prolonged breath following a normal inspiration ("standard method"), hyperventilation followed by a forced expiration, and a ten-second breath hold followed by a forced expiration. Carbon dioxide concentrations did show correlation with those of 1,1,1-trichloroethane, and it was obvious that breath pattern before sampling affected both concentrations in a fairly similar manner. The relationship between carbon dioxide concentrations and 1,1,1-trichloroethane concentrations was as strong for mixed-expired samples as for alveolar samples for the same subjects. The intercept of the relationship between 1,1,1-trichloroethane concentrations and carbon dioxide concentrations was always slightly negative, so that for a theoretical P_{CO2} of zero, a negative solvent concentration would be calculated. They suggest that this nonzero intercept might be due to a different behavior of carbon dioxide and 1,1,1-trichloroethane when passing between the alveoli and either the blood or the mouth.. The P_{CO_2} measurements from 40 unselected and untrained workers who gave breath by the standard and breath-hold methods were spread widely around the value of 38 mm Hg suggested for correction, showing that normal P_{CO_2} values vary from person to person. While correction for carbon dioxide may improve the correlation between exhaled breath concentration of an inert gas and true alveolar concentration, it may not be satisfactory for chemicals of all solubilities. The blood-gas partition coefficients and Bohr dead spaces of 1,1,1-trichloroethane and carbon dioxide are very similar, which is unlikely to be true of gases with higher water solubilities. (Bohr dead space is calculated by the equation $V_D/V_E=(C_A-C_E/C_A$, where V_D is dead space, V_E is tidal volume, C_A is alveolar gas, and C_E is expired gas.) It has been illustrated by Ohlsson (1990) that not all chemicals show concentration plateaux over the course of a breath. Some chemicals, such as ethanol, continue to increase in concentration no matter how long the forced exhalation continues.

Strocchi et al. (1991) investigated the reproducibility of breath concentrations of trace gases. Their commercially available end-alveolar sampler used the same two-bag collection method as that of Franzblau et al. (1992). Four sets of instructions were compared, with duplicates of each method within 1 minute: no instructions, expiration at the end of a normal inspiration and avoidance of hyperventilation, maximal inspiration followed by immediate expiration, and maximal inhalation followed by 15 seconds of breath holding and an expiration. The variability of methane and hydrogen measurements decreased by half or more with the breath holding, even with normalization to 5% carbon dioxide. Normalization to 5% carbon dioxide decreased the variability in the breath holding method and in most other cases but increased the variability for methane in the maximal inspiration and immediate expiration case. The percentage of variability of CO_2 concentrations between duplicate measurements in individual subjects was 6.0%±4.6% for the breath holding method and around 10%±10% for all the other methods. They note that breath holding will supply samples with a higher concentration of hydrogen or methane than can be found in alveolar air, but they advocate its use as in the interest of reproducibility.

Summary and Questions Still Unanswered

Breath sampling has been undertaken in many circumstances in the laboratory and in the field, but it has not become a common method of exposure assessment because there is no standard sampling method that can be used to reliably estimate blood concentration for inert gases of all blood solubilities. The available evidence suggests that rebreathing has the potential to reliably predict alveolar gas concentration and venous blood concentration as no other breath sampling method has done. Mixed-expired, end-tidal, and end-expired breath samples are all affected by the breathing pattern before sampling and by the pattern of the particular breaths that are sampled. Hyperventilation or hypoventilation before any of these types of samples can affect their concentrations. Since many chemicals show increasing concentrations without a plateau as a subject continues to exhale to residual volume, the distinction between end-tidal and end-forced-expired samples and the amount of breath collected can affect the concentration in the sample. All these methods are also affected by ventilation/perfusion inhomogeneity and by the blood:gas partition coefficient of the contaminant being measured. High-solubility chemicals dissolve in airway tissue so that the concentration at the mouth is different from the alveolar concentration, because some of the soluble solvent in the breath in the alveoli will diffuse out into the airway tissue before it reaches the mouth. Exhaled concentrations of low-solubility chemicals are affected with statistical significance by ventilation-perfusion inhomogeneity so that the concentrations are lower in exhaled breath than in arterial blood.

Rebreathing accomplishes two goals: it mixes air from all regions of the lung (Piiper 1979) and allows time for inert gas partial pressure equilibration between the arterial blood and the alveolar gas. If one were to rebreathe for long enough, arterial and venous blood levels for any inert gas would be equal because excretion would stop when the blood and alveolar concentrations reached equilibrium, and the exhaled concentration of the chemical would be equal to that in the alveoli.

As for how long is long enough, Ohlsson (1990) found satisfactory results using 8 rebreathed breaths for ethanol. Highly soluble and less soluble gases may require different amounts of rebreathing to achieve the same goal of equilibration of breath with blood, because the more soluble compounds must have enough exposure to heated gas to equilibrate concentrations in the airway tissue and the breath with concentrations in the pulmonary capillary blood, while the less soluble compounds must have enough time without ventilation to reach equilibrium between alveolar gas and venous blood. Rebreathing may be considered to have the same effect on the equilibrium between alveolar and venous blood as a breath hold, with the added benefit of mixing air between well-ventilated and well-perfused parts of the lung and airways. Ventilation can be considered to drop to zero in rebreathing because no fresh air is entering the lungs. Kelman (1982) showed that it takes longer for chemicals with solubilities near 1 to approach equilibrium with venous blood than for chemicals with solubilities above 10: After ten seconds of hyperventilation in a modeled human at rest, gas with a partition coefficient of 10 should reach equality of partial pressures after 15-20 seconds of breath holding. The alveolar partial pressure of a gas with a partition coefficient of 5 reaches 95% of venous concentrations by the 15-20 second mark and 100% after a 30 second breath hold. The alveolar partial pressure of a gas with a partition coefficient of 2 reaches 80% at 15-20 seconds of breath holding, 90% at about 30 seconds, and over 95% at 40 seconds. In this study, rebreathing samples that required 8 breaths took 20-60 seconds depending on the subject's breathing speed.

Isothermal rebreathing also keeps the airway surfaces at core body temperatures, keeping airways from absorbing more of the inert gases by cooling. This is particularly important for gases that are very soluble in water (and thus in airway tissue) because their solubility varies with temperature. Rebreathing is thus the most promising method to collect true alveolar gas and is likely to be a more reliable predictor of arterial concentration of an inert gas than any of the existing methods. Venous concentration should be related predictably to arterial blood and thus to alveolar gas collected by this method.

Goals and Hypotheses:

The broad general goal of this research is to make breath sampling more feasible and reliable as a method to determine exposure to and dose of volatile chemicals. To reach this goal, Ohlsson's (1990) isothermal rebreathing technique was evaluated as a means of obtaining a valid breath sample representing blood concentration. This method was compared to an end-exhaled breath collection technique similar to the most common of the methods described above and a mixed-exhaled breath collection technique that is more carefully controlled than normal. Carbon dioxide corrected mixed-exhaled samples were also included in the comparison. Healthy volunteers were exposed to low concentrations of volatile organic chemicals with blood/gas partition coefficients ranging from 2.5 to around 2000. Over the course of several hours after exposure, the subjects gave up to ten sets of venous blood samples and breath samples by all three techniques. Concentrations of each chemical in each type of breath sample were compared to concentrations in blood. The goal was to determine which breathing method produced samples with concentrations that best matched concentrations in the blood.

Three related hypotheses were tested:

1. Rebreathed samples better predict blood concentrations than end-exhaled or mixed-exhaled samples. This was tested by linear regression of blood concentrations on one type of breath concentration at a time, one chemical at a time, treating the subject who gave each set of samples as a random effect. The standard deviation within subjects was compared for each method.
2. Carbon dioxide correction for mixed-exhaled gas concentrations does not correct to alveolar concentrations for all chemicals and does not improve accuracy of prediction to the level of rebreathed gas or end-exhaled gas. This was tested by comparing the slopes of the regressions described above to each other for each chemical.

The accuracy of prediction of blood concentration by rebreathed gas sampling is less affected by ventilation inhomogeneity than other methods. This was examined by plotting the slope and R^2 of individual subjects' regressions of blood concentration on each type of breath concentration against a measure of ventilation inhomogeneity.

Methods:

Eleven healthy subjects were recruited to participate in this study. Each subject agreed to be exposed to ethanol, acetone, methyl isobutyl ketone (MIBK), toluene, and/or halothane and supply samples of breath by three different methods and blood through an in-dwelling catheter in an antecubital vein. The procedure and the recruitment process were approved by the University of Washington's Institutional Research Board (IRB) and Human Subjects committee. The six male subjects were between 21 and 73 years old, and the five female subjects were between 19 and 35 years old.
Each subject was exposed on two occasions, to two different chemicals each time for a total of four chemicals per person. The exposures were at least two weeks apart. Subjects who were not project investigators were exposed to ethanol, acetone, MIBK and toluene. Investigators were exposed to an additional solvent, halothane, and three other chemicals selected from the above list. Halothane was not among the solvents originally approved by the UW Human Subjects Division, and was added to the protocol later to expand the range of solubility to be studied. Project investigators, by definition, gave informed consent for exposure to halothane.

Acetone, MIBK, toluene and halothane were delivered by inhalation for two hours using a controlled atmosphere generator that delivered breathing air with concentrations of the chemicals to a mouthpiece with a one-way valve. Up to two chemicals at a time were mixed in the appropriate proportions for that day's exposure, and a syringe filled with that mixture was metered at a slow, controlled rate into a heated compartment using a precision drive. The solvent vapors were diluted with USP breathing air to achieve concentrations of ½ the Threshold Limit Value (TLV), or in the case of MIBK, the full TLV. MIBK required a higher exposure concentration to assure samples would be above the limit of detection during the elimination phase after exposure. The generation system produced excess air mixture so that the subject could inhale on demand. When the subject breathed, the one-way valve ensured that the inhaled gas was from the controlled atmosphere and the exhaled gas was exhausted into a laboratory hood. A carbon dioxide meter (Novametrics Corp., Wallingford, CT) monitored the CO_2 concentration in the exhaled air.

Exposure to ethanol was delivered by ingestion. The subject was provided with a dose of vodka mixed with fruit juice. The dose for earlier subjects was up to 2 oz of 80 proof vodka, but most of the subjects were given a dose calculated by the Widmark method (Klaunig and Kamendulis, 2003) to achieve a blood alcohol concentration of about 0.022%. This dose was arrived at by experimentation, and the first few subjects were exposed to different doses of ethanol. The BAC of 0.022% was settled upon as a level that allowed breath and blood concentrations to be above the limits of detection for most of the post-exposure period but did not overload the blood analysis system at the highest concentrations. Ethanol had to be delivered by ingestion because its TLV for inhalation exposure is too low and its metabolism too fast to maintain blood and breath concentrations above background during the post-exposure sampling period. Doses were considered acceptable if they were within the range of what a subject would drink socially. Subjects did not leave the laboratory before their concentrations were well below the legal definition of intoxication, which is 0.08% in the state of Washington.

After exposure, subjects were allowed to rest for half an hour until the rate of decrease of the chemical concentrations diminished so that successive samples could be taken without large differences in concentration. At thirty minutes post-exposure, the first set of samples was collected. Each set of samples consisted of a blood sample followed by a mixed-exhaled sample, an end-exhaled sample, a rebreathed sample, and a second blood sample. This order of breath sampling was used to avoid interaction among sampling methods: mixed-exhaled breath is similar enough to normal breathing that it should not affect end-exhaled breath, and rebreathing could be performed last because Ohlsson has shown previously that hypoventilation and hyperventilation do not affect concentrations given by rebreathing. Blood samples were collected before and after breath samples so that all three breath methods could be compared to an average blood concentration that represented the time over which the breath samples were collected. Blood and breath were collected a total of ten times, twenty minutes apart. These samples were analyzed for chemical concentrations.

After the sampling was completed, homogeneity of ventilation was measured by multiple-breath nitrogen washout. During a multiple breath nitrogen washout measurement, a subject inhales oxygen for multiple breaths while the tidal volume of each breath and the nitrogen concentration at the end of each breath is measured. The speed at which the nitrogen washes out of the lungs is an indicator of the uniformity of ventilation throughout the lung. (Comroe 1965, West 1974) Nitrogen content in the subject's breath was measured using a mass spectrometer. The signal with a mass to charge ratio of 14 was used to calculate nitrogen concentrations. The subject inhaled pure oxygen from one side of a nonrebreathing valve connected to a large Tedlar bag filled with oxygen from a cylinder and exhaled into the room through the other side of the valve. The subject was asked to inhale and exhale every 6 seconds and to breathe a consistent tidal volume calculated from the subject's height and gender. The constant tidal volume was requested so that subjects' measurements could be compared to one another more easily: Each breath was the same proportion of vital capacity, so that the number of breaths to reach a certain nitrogen level was comparable between subjects. Between the mouthpiece and the one-way valve was a pneumotachometer which measured the velocity of breath passing through it. This was attached to a computer that integrated the velocity of breath and logged volumes. This pneumotachometer system was calibrated to measure volumes correctly for oxygen and used to measure the subject's breathing pattern. The computer displayed the subject's breathing pattern superimposed on the requested tidal volume as pictured in Figure 3. The computer also produced audible tones to aid the subject in maintaining a consistent pattern of inhalation and exhalation. The subject's breathing pattern and exhaled nitrogen signal were recorded for up to 8 minutes, or until the exhaled nitrogen concentration fell to 2% of the original concentration. This allowed calculation of the number of liters and the number of breaths required to reach 5%, 3% and 2% of the original nitrogen content.

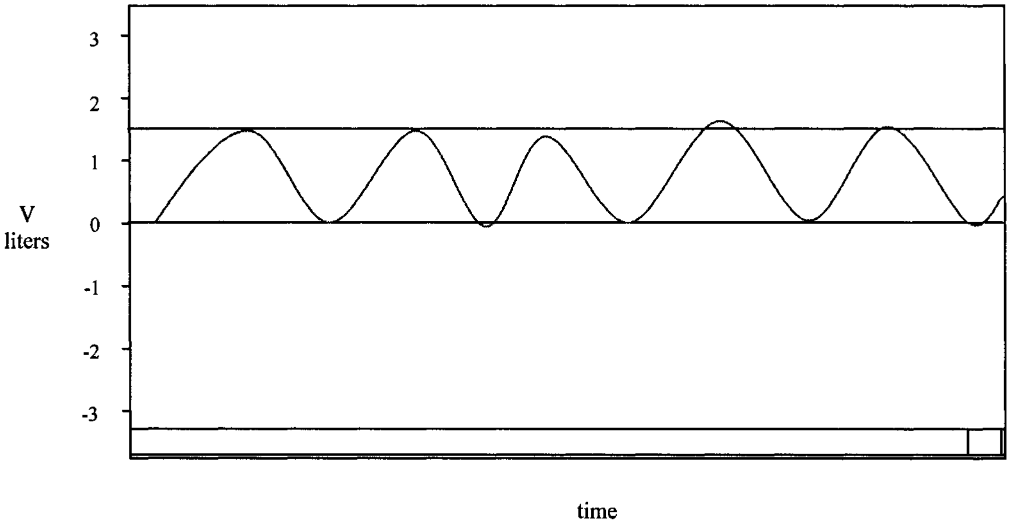

Figure 3: Computer display for nitrogen washout measurement. The subject was asked to inhale to the top line and exhale back to the bottom line in time with beeps timed three seconds apart. The curve shown is an example of how a resulting pattern might appear.

Breath collection and analysis:

Nose clips were used for all exposures and all breath collection methods to keep all the breath inside the measured system and prevent inhalation or exhalation through the nose. All three methods and equipment for breath collection were designed to create minimal backpressure for the subject. Heated Teflon tubing and stainless steel fittings were used, in the widest diameters that were practical. All sample transfer lines and collection compartments were kept at approximately 37°C using heating tape and heating pads. The breath was collected and stored in Tedlar bags at 37°C until analysis as soon as possible on the same day. Typically all samples were analyzed within 6 hours of collection.

Carbon dioxide concentrations were measured immediately after collection by hooking the bags up to the carbon dioxide meter for 15 seconds. Samples that had obviously changed in carbon dioxide concentrations by the time they were analyzed for solvent concentrations were noted and their analysis results discarded if they appeared to have leaked or lost carbon dioxide content while being stored.

All sample collection bags were cleaned and reused by flushing with solvent-free nitrogen. Mixed-exhaled and end-exhaled sample bags were flushed three times with nitrogen and incubated for at least an hour in between flushes. The rebreathing bag had a unique connection and had to be reused for each sample, so it was flushed with nitrogen three times after each sampling and analysis and held at 40 C during theday. Each of these flushing methods was evaluated, and after three nitrogen flushes, concentrations of solvents in the bags were undetectable. Any bag that was found to have broken or leaked was replaced.

For each of these breath collection methods, the subject was coached through the process, and evaluated as to whether the sample had been collected correctly.

Mixed-exhaled:

Mixed-exhaled breath samples were collected in a carefully controlled fashion. This controlled procedure was an effort to collect a consistent but natural breath pattern. Many untrained subjects tend to hyperventilate when asked for a breath sample. A diagram of this system may be found in Figure 4. At the beginning of a day of exposure and sampling, subjects were asked to don nose clips, sigh deeply, and then breathe into a tube in a relaxed manner with their eyes closed. The sigh was meant to reset their breath pattern to a similar point each time they sighed so that they started each maneuver with the same amount of ventilatory drive, and the closed eyes were meant to keep the subject from thinking about visual distractions or the visual representation of the pattern that was appearing on the screen in front of him. Between five and eight breaths were recorded, depending on the size of the breaths. Breath flow rate was measured with a pneumotachometer (Vacumed) connected to a pressure transducer and a carrier demodulator with an analog-to-digital input system that fed information to an Apple Macintosh computer. Flow rate was integrated over time to produce tidal volume measurements, and the breath flow rate pattern was stored and displayed over time as it was produced. The subject was asked to reproduce the original breath pattern for all subsequent breath samples. The subject was asked to match the original pattern, by following the flow rate recording displayed together with the actual flow rate for the sample.

The subject breathed through a heated pneumotachometer, a heated T-shaped nonrebreathing valve to allow subjects to inhale from the room and exhale into the bag, and heated Teflon tubing into a heated Styrofoam box. Inside the box, exhaled breath was collected in a 20-25 liter custom made Tedlar bag inside a heated Styrofoam box. The Tedlar bag had a standard stainless steel fitting on one end and a ¾” OD fiberglass reinforced Teflon fitting on the other end.

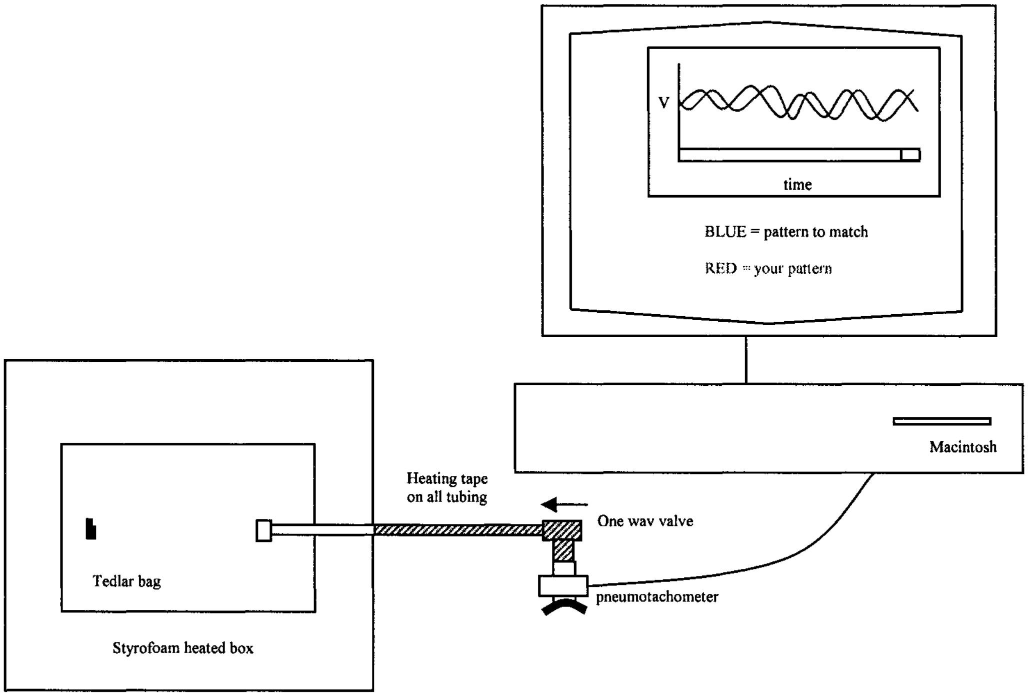

Figure 4: Mixed-exhaled sampling system.

End-exhaled:

End-exhaled samples were collected by a method based on the common Haldane-Priestley tube method. A diagram of this system may be found in Figure 5. The subject wore nose clips, inhaled to total lung capacity, held his/her breath for fifteen seconds, and exhaled to residual volume into a one-way valve connected to a three meter long, 2.54 cm outside diameter Teflon tube wrapped with heating tape to keep the tube at or above 37°C. After the exhalation, the final 1.0 liter of the breath in the tube was drawn into a Tedlar bag (SKC) from a port located just downstream of the one-way valve.

In order to collect the last liter of exhaled breath in a bag, a 64 mm internal diameter Teflon tube was connected from near the mouthpiece into a 5 L Tedlar bag inside an airtight box. A 1.5 liter plastic syringe was used to draw 1 liter of air out of the box, thus drawing 1 liter of air from the exhalation tube into the bag.

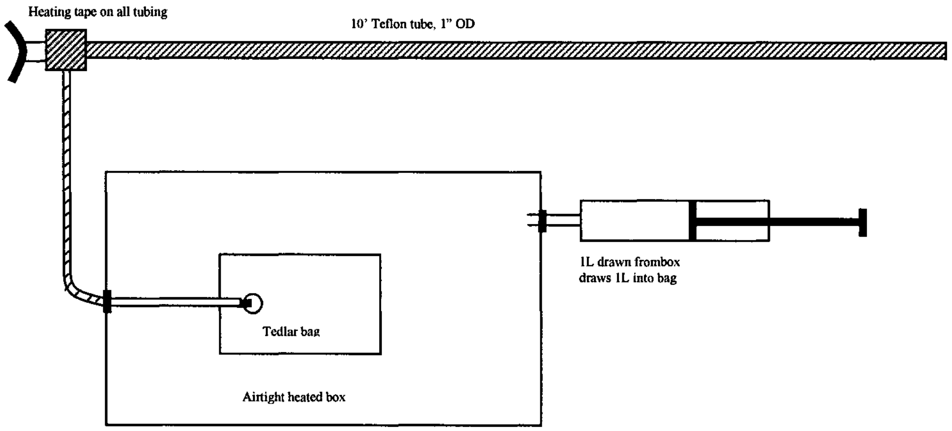

Figure 5: End-exhaled sampling system.

Isothermal Rebreathing:

For the early part of data collection, rebreathed breath was collected with an isothermal rebreathing apparatus described by Ohlsson but refitted with Teflon tubing and stainless fittings. An additional Teflon tube was connected from the sample bag outlet to a valve leading to the sample loop inside the gas chromatograph. This rebreathing apparatus measured breath volume and required each breath to be at least 1.5-2 liters, depending on the height of the subject. The device collected eight exhalations, counting down to zero and giving instructions via an LED panel. It also kept the transfer lines warm and the sample contained and warm until analysis.

After pilot studies and data collection for the first two subjects using this apparatus, the rest of the data was collected with a much simpler apparatus, which is shown in a diagram in Figure 6: A 5 liter Tedlar bag was placed inside a Styrofoam box with a heating pad, and a ½" OD flexible Teflon tube like the one that had been installed in the rebreather was connected to the bags via a bulkhead fitting. The inside of the box was kept at or above 37°C, and the part of the tubing that was outside the box was heated using heating tape. All that this system lacked was the measurement of breath volume to assure that each breath was of a sufficient size.

The subject exhaled directly into the Teflon tube instead of a mouthpiece, since no one-way valve was necessary for this method. Subjects were asked to don nose clips, inhale "a moderately deep breath" of room air, exhale into the bag, and breathe in from and out into the bag seven more times. An investigator counted down the breaths to help the subject keep track.

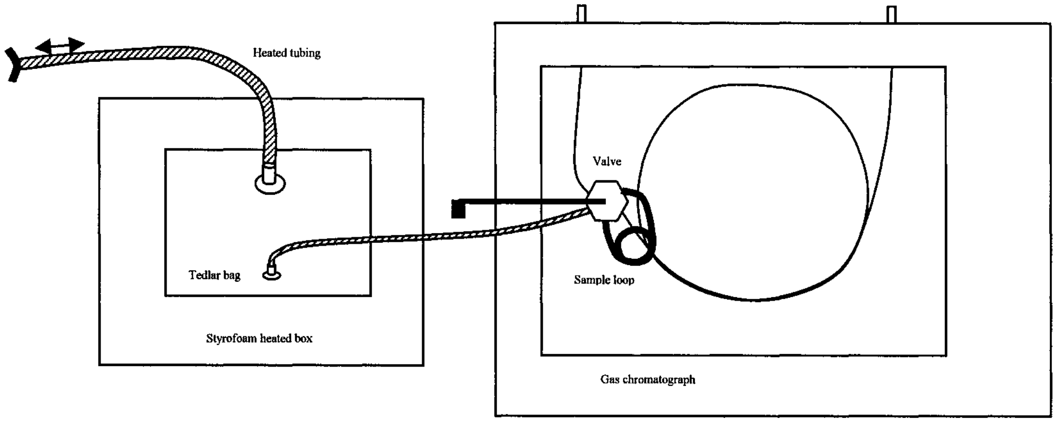

Figure 6: Rebreathed sampling and breath analysis system.

Breath Analysis:

A heated 32 mm internal diameter Teflon tube was connected from a standard stainless steel bag fitting on each bag to a valve leading into the gas chromatograph. Air was drawn by vacuum from the bag through heated Teflon and stainless steel tubing into a 1 milliliter sample loop inside the gas chromatograph oven. After 30 seconds, a valve downstream of the sample loop was used to shut off the flow. Once the pressure in the line had returned to atmospheric pressure, the 1 mL of gas in the sample loop was injected onto the 30 meter megabore (0.54 mm ID) DB-Wax (J & M) column using a hand-operated six-way valve (Valco). The carrier gas was helium, and the carrier velocity was about 30 m/minute. The oven temperature spent one minute at 37°C and rose at 10°C per minute until the temperature was 120°C, at which point the run ended. The column effluent was directed to a flame ionization detector operated at 225°C. The signal was integrated by an HP integrator, and peak areas were used to calculate concentrations.

Breath Concentration Standards:

Standard concentrations of gases were generated using a Dynacalibrator (VICI Metronics). Each solvent was evaporated in a constant temperature chamber in capillary vials (VICI) or permeation tubes. The evaporation rate was constant once the vial or tube reached themal equilibrium after a day in the chamber. Solvent-free dilution air was varied to produce desired reproducible concentrations. Calibration curves were prepared using bags of the resulting air, which was collected from an output port and delivered to the gas chromatograph.

Carbon dioxide corrected mixed-exhaled concentrations were calculated by multiplying the mixed-exhaled concentration by the subject's average end-tidal carbon dioxide concentration during exposure and dividing by the carbon dioxide concentration of the breath sample:

$$C_{corr} = C_{mixed} * CO_{2\ mean\ end\text{-}tidal} / CO_{2\ sample}$$

Blood:

Sampling:

Each subject had a 20 gauge catheter installed in an antecubital vein by the UWMC Clinical Research Center prior to exposure. Before exposure, six 5-mL samples were collected. All blood was collected in Vacutainers (B-D) with oxalate anticoagulant, which had been found to interfere the least with trace organic chemical assays in the past. After exposure, one 5-mL sample of blood was collected from the catheter before and after each series of breath samples.

Blood samples were stored at 4 C in their Vacutainers during the sample collection period. Blood samples were divided into 1-mL aliquots, which were placed in glass EPA vials (National Scientific, Duluth, GA) with Teflon and silicone septa (Eagle-Picher, Phoenix, AZ) that same evening. Calibration standards were prepared using the subject's blood from before the exposure. Blood was analyzed within 5 days of collection and refrigerated until analyzed.

Analysis:

Blood was analyzed by headspace gas chromatography/mass spectrometry (GC-MS). A purge and trap system (Tekmar, Mason, OH) was used to concentrate and dewater the headspace and transfer the sample onto the GC column. A K trap was chosen because it was consistent with sufficient sensitivity to the compounds of interest without allowing the column to be overloaded by the samples with the highest concentrations. Blood vials were heated to 45°C for headspace collection. The sample was cryogenically trapped at the column inlet and injected splitlessly onto a 60 meter 0.25 mm ID Rtx-5 column. The inlet temperature was 100°C and the detector temperature was 280°C. The oven temperature started at 35°C for two minutes and rose at 10°C/minute to 200°C, where it stayed for another two minutes. The carrier gas pressure started at 5.0 psi and rose at 10°C per minute to a pressure of 20.0 psi, where it stayed for two minutes. The pressure then rose at 0.75 psi per minute up to 25 psi, where it stayed for the duration of the run. After gas chromatographic separation, the sample was injected into a mass spectrometer.

Peaks were integrated and stored by HP DataChem software on an attached computer. An internal standard, 5 microliters of a 10^{-6} dilution by volume of d8 toluene in dimethyl sulfoxide, was added to each sample and standard aliquot. Concentrations were determined using peak areas of specific ions for each compound at its experimentally determined retention time. These peak areas were divided by the area of the internal standard peak for the same sample, and the resulting response factor was used to determine concentrations. From vial heating to recorded data, about 45 minutes were required for each sample analysis. The purge and trap system and the data logging system were both automated to allow operation overnight.

Blood Concentration Standards:

All standard concentrations were prepared using dimethyl sulfoxide (DMSO) solutions. DMSO was chosen as a standard preparation solvent after water and methanol solutions proved insufficiently stable. Standard solutions were prepared the day of exposure to avoid evaporative losses. The stock internal standard solutions were prepared in large batches and stored at -180°C. All standard solutions in DMSO were stored in GC vials with Teflon-lined crimp-top caps until they were ready to be used.

Blood was transferred from Vacutainers into EPA vials using an adjustable Eppendorf repeater with a disposable 12.5 mL long-tipped pipet tip, set to deliver 1 mL at a time. The EPA vials were capped immediately after the blood was injected. Injections of the standard and internal standard solutions into blood sample aliquots were performed using the open-cap method. This method was chosen to avoid leakage of volatile chemicals through small holes in the septa while the 90 or so other samples were being analyzed. Caps were kept open as little as possible to preserve sample integrity.

Calibration curves:

Calibration curves for breath were prepared using the concentrations from Dynacalibrator samples and the corresponding peak areas of the GC/FID system. The data were fit by least-squares linear regression. The intercept was not forced through zero, and the regression was not weighted by the inverse square of the concentration. This was because gas chromatography with a flame ionization detector is expected to produce a linear relationship between concentration and peak area and because the data seemed to fit this method best for the vast majority of the samples.

Standard curves prepared using the subject's own blood were used to determine sample concentrations. Calibration curves for blood were prepared using the known spiked concentrations in the standards and using the method of standard additions to calculate the concentrations in the subject's blank blood samples. The purge and trap system with GC/MS did not always produce a linear relationship between breath and blood. Curves were fit using linear regression without weighting, linear regression weighted by the inverse of the concentration of the standard, a power curve fit by Excel ($y=ax^b$), and an inverse concentration weighted polynomial curve of the form $y = ax^{1.2}+bx+c$. Whichever method best fit the calibration data over the range of the sample data was used to fit the data. When two methods fit visually the same, preference was given to the simpler method. No uniform method adequately fit the data for every exposure. If one type of calibration curve had been applied to all chemicals, or even to all data sets for a given chemical, some calibration curves would not have fit their associated data well enough to allow reliance on sample concentrations based on those curves.

Validity:

Data sets were assessed for validity. Some data were rejected for a variety of reasons described below that made the data seem untrustworthy. The blood analysis system was complex and delicate, and some data were unusable because of equipment malfunction or user error.

Data above and below the range of the calibration curves were excluded from the analysis. Breath concentrations that were much lower than the concentrations of the preceding and subsequent samples, or that had improbably low CO_2 concentrations, were assumed to be from bags that had leaked and were removed from analysis. Individual blood samples were removed if there was an identifiable physical problem with the sample. MIBK concentrations were very close to the limit of quantitation of this system and were not much above the noise, and an entire data set had to be removed when the sensitivity of the system dropped so that MIBK peaks were in the noise and unreliable. Ethanol and acetone concentrations were also sometimes much higher than the concentrations of other chemicals to which the subject had been exposed at the same time. In some early data sets, ethanol or acetone peaks were large enough to overwhelm either the mass spectrometer or the capillary column. All these types of nonstandard peaks had to be excluded from the analysis because they were too different from the normal peaks. The blood analysis process was therefore optimized over the course of the first third of the data collection to resolve these problems.

Some data sets were also removed for problems with the data that implied an invalid blood analysis. When breath concentrations showed a washout and blood concentrations showed no washout at all, the data set was removed under the theory that something was wrong with the system that day. When all the data was below the blank concentrations and many of the spiked standards, the data set was removed because the calibration was suspect. When calculated partition coefficients were wildly different from the rest, they were excluded under the theory that something likely went wrong with the analysis.

Calibration curve problems were addressed in as consistent a manner as possible. Some contained anomalous samples clearly different from the rest of the curve, which were excluded only if the rest of the data were noticeably uniform and the anomalous data pulled the calibration curve away from the pattern of the data. If the calibration curve was simply noisy, the standards were all used to calculate the curve. If instrument response did not reliably rise with spiked standard concentration, the data set was removed.

The data used in this study, after exclusion for the above criteria, is shown in Appendix B in graphical form.

Data Analysis:

Statistical analysis was conducted using STATA statistical software (Stata Press, College Station, TX).

Blood concentrations were regressed on breath concentrations separately for each chemical and for each method of breath collection. Data from all subjects were included, and subject ID was treated as a random effect. The statistical output is included in Appendix D.

The effects of age and gender on the relationship between blood and breath concentrations of the various types were evaluated by two methods. First, the apparent partition coefficient and the R^2 from the individual data set regressions were regressed on the age or gender of the subject for that data set. Second, age and gender were added to the regressions of blood concentration on breath concentration with subject ID treated as a random effect. This statistical output can be found in Appendix E.

The effect of ventilation inhomogeneity on the relationship between blood and breath concentrations was examined by plotting the slope and R^2 of individual subjects' regressions of blood concentration on each type of breath concentration against the lung clearance index. These scatterplots can be found in Appendix F.

Results and analysis:

After validation, nineteen of the fifty-four data sets collected could not be used because of technical deficiencies in the chemical analysis. All calibration curves for data sets included in this study may be found in Appendix A. Appendix B contains graphs of all calibration curves, blood and breath washout curves, and graphs of blood concentration against breath concentration for all data sets. Appendix C shows the list of data sets and their individual partition coefficients by breath collection type, date, chemical and subject code. These partition coefficients are from a linear regression of average blood concentration on breath concentration with robust variance estimates.

For this discussion, a data set will be defined as a group of blood and breath concentration data from one chemical to which one subject was exposed on one day.

Inhomogeneity of ventilation:

Ventilation homogeneity information was collected as an estimate of lung function. The measures calculated from this data were calculated from the number of liters required for the subject's exhaled nitrogen concentration to drop to 2% of its original value. Functional residual capacity (FRC) was also calculated from the nitrogen washout, and the lung clearance index (LCI) was calculated as the liters exhaled before 2% of the original concentration was reached divided by the FRC. These data are presented in Table 1. This group of subjects had an average lung clearance index of 8.7 with a standard deviation of 2.7, which is consistent with a group with normal lung function.

Table 1: Measures calculated for inhomogeneity of variation: volume exhaled while breathing oxygen before reaching 2% of the original end-tidal N_2 concentration. Only nine subjects are listed here because two subjects did not have a successful measurement in which they reached 2% of the original nitrogen concentration.

Date	Subject	liters to 2%	FRC	Lung clearance index: 2%
12/10/2003	3	37.0	3.5	10.5
3/19/2003	4	27.0	2.8	9.8
8/26/2003	6	21.6	1.5	14.3
8/21/2003	7	15.3	2.0	7.7
8/6/2003	8	32.1	5.4	5.9
7/10/2003	9	42.6	8.3	5.2
10/22/2003	10	38.2	4.9	7.9
12/17/2003	10	11.6	1.2	9.4
10/29/2003	11	54.7	7.6	7.2

Data set level analysis:

Figures 7-14 below illustrate the analysis that was performed for each data set. The data set shown is for the halothane exposure for Subject 1.

Figures 7 and 8 show the calibration curves calculated from the spiked calibration standards. For breath, a linear regression was performed in which the dependent variable was the calculated concentrations from the Dynacalibrator and the independent variable was the peak areas from chromatographic analysis of standard samples. The concentrations of the breath standards were calculated by dividing the measured emission rate of the chemicals in the heated chamber by the flow rate of the dilution gas. For blood, a linear regression, weighted by the inverse of the concentration of the standards, was performed in which the dependent variable was the spiked standard concentrations and the independent variable was the response factors from chromatographic analysis of the standards. The blood regression was weighted because that was the type of curve that best fit the standard regression in the range of the data. The method of standard additions was used to calculate the concentration of the subject's blank pre-exposure blood samples.

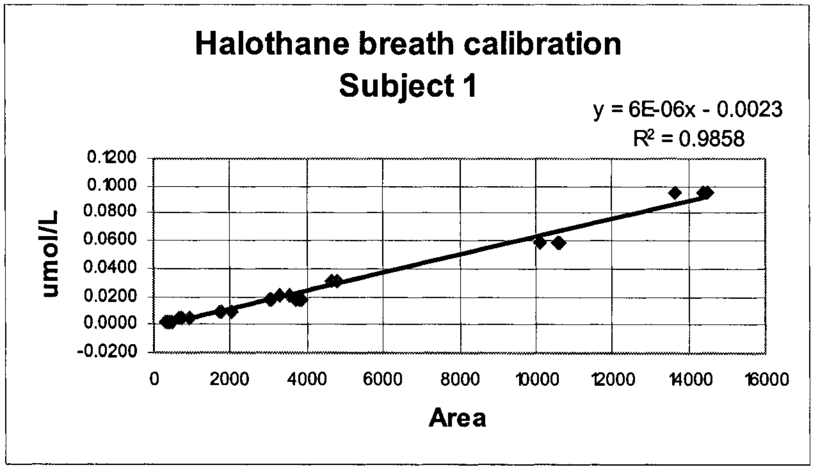

Figure 7: Breath calibration for Subject 1 for halothane.

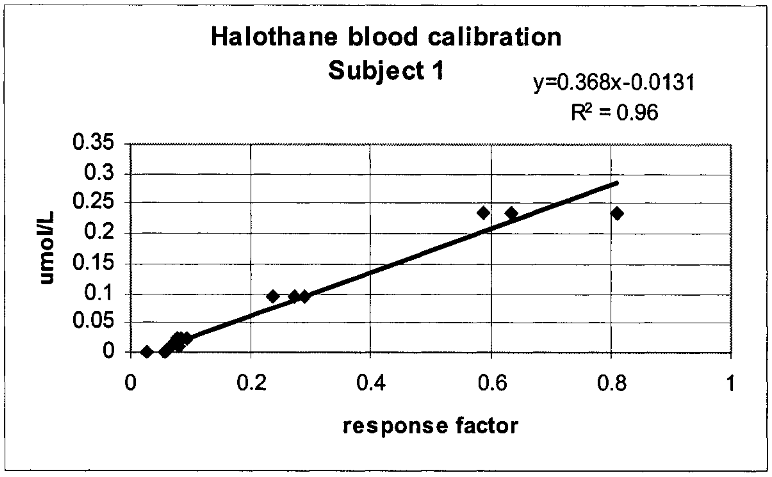

Figure 8: Blood calibration for subject 1 for halothane.

Figures 9 and 10 show the breath and blood washout curves. Concentrations of each type of breath were plotted against time post-exposure. Concentrations of the blood samples taken before and after each set of breath samples were also plotted against time post-exposure. It is expected that these concentrations would decrease over time and that the rebreathed concentrations would be the highest for each set of breath samples, followed by the end-exhaled and mixed-exhaled concentrations. One end-exhaled data point was removed from this data set because the bag showed indications of leakage.

The concentrations in the blood samples taken before and after each set of breath samples were averaged for all further analyses.

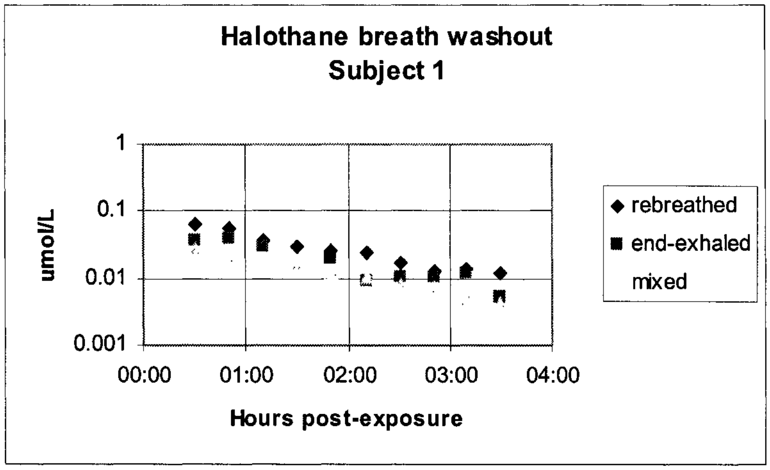

Figure 9: Breath washout for halothane for subject 1.

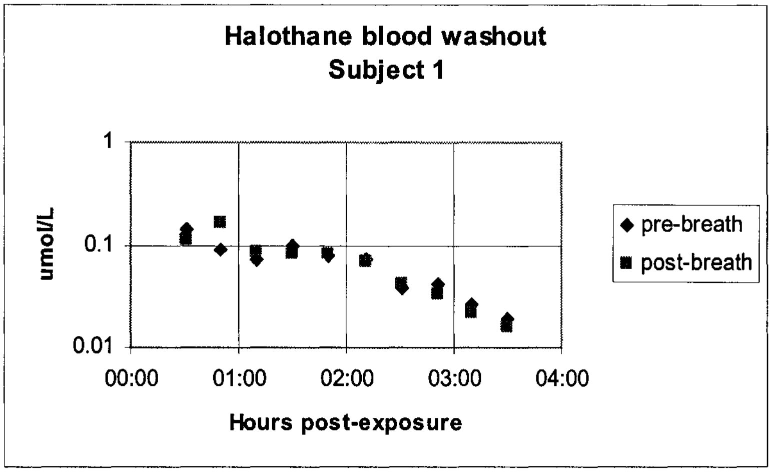

Figure 10: Blood washout for halothane for subject 1.

Figures 11 through 14 show blood concentrations plotted against breath concentrations of each type considered here. In this case, the correlation with blood concentrations is highest for mixed-exhaled concentrations and lowest for end-exhaled concentrations. The slope listed on each of these graphs is the apparent blood/gas partition coefficient for venous blood for that type of breath. In this case, the partition coefficient is lowest for rebreathed samples and highest for mixed-exhaled samples. Carbon dioxide correction of mixed-exhaled concentrations lowers the partition coefficient to between that of the end-exhaled breath and the level of the rebreathed breath. The rebreathed partition coefficients can be found in Table 2, and the full list of individual partition coefficients for each breathing method can be found in Appendix C. The robust standard error reported in these tables is the standard error from an individual's linear regression with robust variance estimates and is reported as an indicator of the variability of the relationship between blood and breath concentrations.

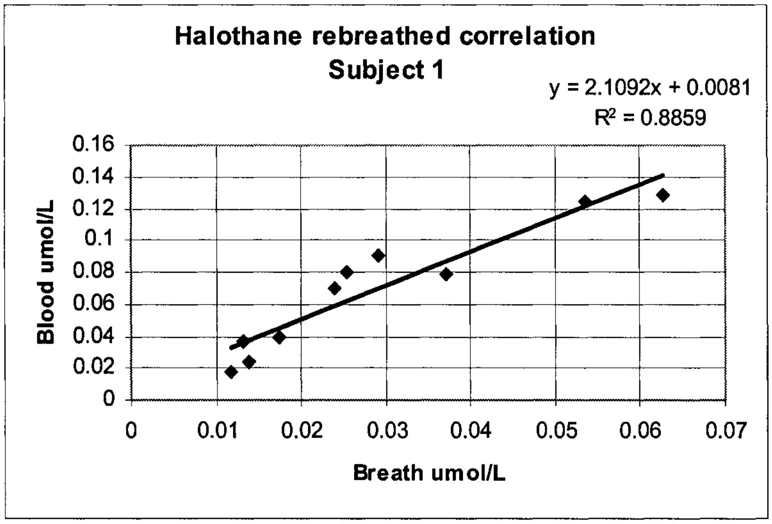

Figure 11: Correlation between blood halothane concentration and rebreathed halothane concentration for subject 1.

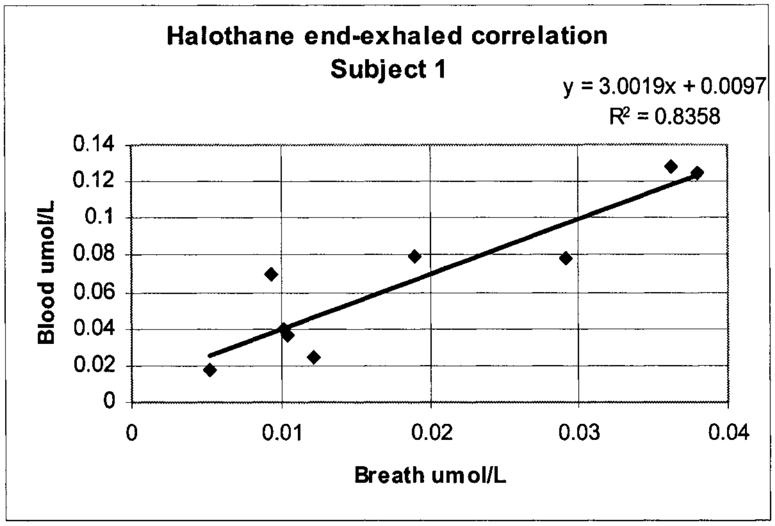

Figure 12: Correlation between blood halothane concentration and end-exhaled halothane concentration for subject 1.

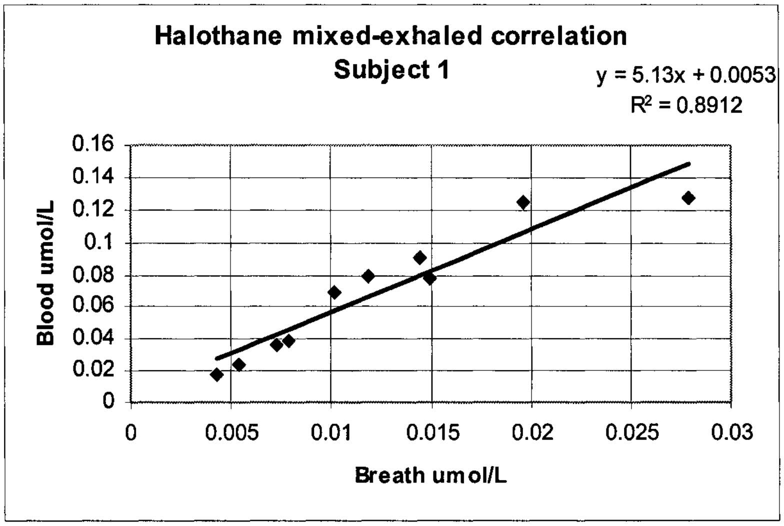

Figure 13: Correlation between blood halothane concentration and mixed-exhaled halothane concentration for subject 1.

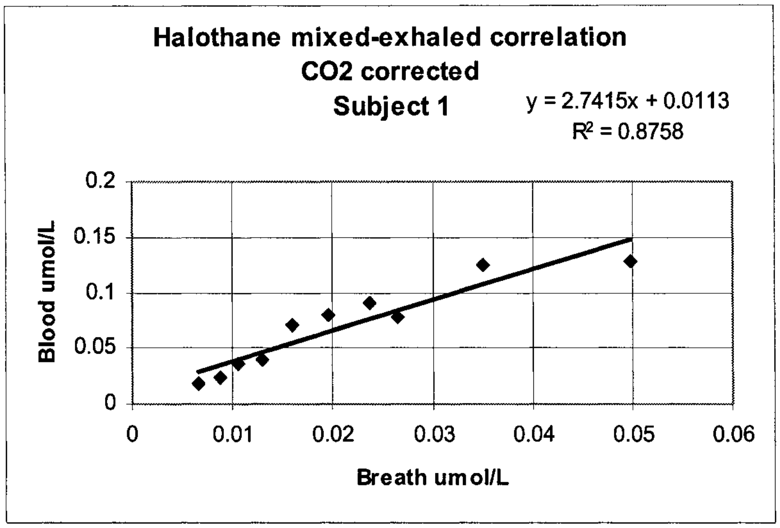

Figure 14: Correlation between blood halothane concentration and mixed-exhaled carbon dioxide corrected halothane concentration for subject 1.

Table 2: Rebreathed blood/gas partition coefficients as calculated by individual . "Average coefficients" are the averages of the individual slopes for one subject and one chemical each. "Coefficients by random effects" are the slopes obtained by using all the data for one chemical in a regression and treating subject as a random effect.

Table 2: Rebreathed blood/gas partition coefficients as calculated by individual . "Average coefficients" are the averages of the individual slopes for one subject and one chemical each. "Coefficients by random effects" are the slopes obtained by using all the data for one chemical in a regression and treating subject as a random effect.

Rebreathed:		Ethanol		Acetone		MIBK		Toluene		Halothane	
Individual partition coefficients:		individual partition coefficient	robust SE	individual partition coefficient	robust SE	individual partition coefficient	robust SE	individual partition coefficient	robust SE	individual partition coefficient	robust SE
Date:	Subject										
10/23/2002	1							36.9	2.36		
3/7/2003	1									3.4	0.48
5/21/2003	1									2.11	0.23
12/12/2002	2	1940	234							5.32	0.63
1/24/2003	2	3120	25.2	322	39.4						
10/7/2002	3					161	37				
12/10/2003	3									4.24	2.7
3/19/2003	4	1310	82	248	55.1						
8/1/2003	4							18.6	4.69		
5/1/2003	5							33.1	3.01		
5/29/2003	5	1780	72.6	120	95.1						
6/18/2003	6	3000	43.7			42.2	8.81				
8/26/2003	6			223	36.8			39	5.03		
6/25/2003	7			277	95.4			7.93	1.66		
8/21/2003	7	3150	579			13.1	2.64				
7/3/2003	8			378	93.1			43.9	2.5		
8/6/2003	8	2800	826			181	58.9				
7/10/2003	9			205	103			21.2	2.64		
8/11/2003	9	1810	168			441	57.6				
10/22/2003	10							22.7	0.372		
12/17/2003	10					110	11.7				
10/29/2003	11							55	5.34		
11/19/2003	11					25.1	2.07				
Average coefficients:		2364		253		139.1		30.9		3.77	
Slope by random effects:		2239		251		55.7		31.1		3.16	

Hypothesis testing:

Hypotheses were tested by statistical methods described above. The hypotheses tested were as follows:

- rebreathed samples better predict blood concentrations than end-exhaled or mixed-exhaled samples
- carbon dioxide correction for mixed-exhaled gas does not correct to alveolar concentrations for all chemicals and does not improve accuracy of prediction to the level of rebreathed gas or end-exhaled gas
- the accuracy of prediction of blood concentration by rebreathed gas sampling is less affected by ventilation inhomogeneity than other methods

The results of the regressions of blood concentrations on breath concentrations, treating subject ID as a random effect, are found in Table 3. The statistical output can be found in Appendix D. The root mean square error (MSE) within subject is a measure of the error remaining in the prediction of blood concentrations by breath concentrations, after differences between subjects are accounted for. The root MSE between subjects is a measure of the variation between the individual subjects' relationships between blood and breath concentrations. There is no variance estimate for the difference between these variances, so it is impossible to tell whether there is a significant difference in the different breath collection methods' ability to predict blood concentrations.

The root MSE between subjects, shown in Table 3, was larger than that within subjects for acetone, toluene, and the mixed-exhaled methods for MIBK, indicating that these cases showed higher variation between subjects than within. No uniform pattern is present for differences in root MSE between the different methods, but for three of the four cases for which there was enough data, the root MSE was larger for the mixed methods than the other methods and smallest for the rebreathed sample. This would indicate that the relationships to blood of concentrations in mixed-exhaled samples tend to vary more between subjects than do samples taken by other methods and that rebreathed samples vary less between subjects than do other methods.

Based on the root MSE within subject, shown in Table 3, rebreathed gas concentrations generally predict blood concentrations with less error than the other methods for acetone and toluene, and with less error than any uncorrected method for MIBK. For the highest and lowest solubilities, the rebreathed concentration was not the least variable of the methods. Since this standard error comparison does not have a standard error, it is difficult to interpret how real or relevant these differences are. It should also be noted that the mixed-expired method used here is more carefully controlled than other mixed-expired samples in the literature and is likely to be much less variable than typical uncontrolled mixed-exhaled breath samples. More details follow after the table.

Table 3: Results of regressions of blood concentration on breath concentration treating subject ID as a random effect. R^2 within subject refers to the average correlation of blood and breath concentrations for any given subject.

Ethanol:	Slope	R^2 within subjects	R^2 total	Root MSE within subjects	Root MSE between subjects
Rebreathed	2239	0.9166	0.9155	172.6	29.9
End-exhaled	2618	0.9197	0.9169	174.8	35.4
Mixed-exhaled	3052	0.9273	0.9265	161.7	24.7
Mixed-exhaled CO2 corrected	1598	0.6954	0.673	330.9	104.3
Acetone:					
Rebreathed	251	0.5846	0.5021	7.74	22.4
End-exhaled	265	0.3883	0.5197	9.67	22.0
Mixed-exhaled	554	0.4602	0.6861	8.69	17.1
Mixed-exhaled CO2 corrected	361	0.2925	0.5762	9.95	20.5
MIBK:					
Rebreathed	55.7	0.4691	0.1136	0.185	0.122
End-exhaled	68.1	0.4463	0.1064	0.192	0.154
Mixed-exhaled	87.3	0.3817	0.0343	0.185	0.274
Mixed-exhaled CO2 corrected	74.3	0.4176	0.0265	0.180	0.266
Toluene:					
Rebreathed	31.1	0.8051	0.6193	0.050	0.106
End-exhaled	39.1	0.6921	0.5749	0.067	0.116
Mixed-exhaled	81.9	0.6356	0.3654	0.064	0.157
Mixed-exhaled CO2 corrected	49.9	0.6931	0.4579	0.058	0.148
Halothane:					
Rebreathed	3.16	0.861	0.8522	0.024	0.011
End-exhaled	3.56	0.9397	0.9261	0.017	0
Mixed-exhaled	5.29	0.8464	0.8466	0.023	0.011
Mixed-exhaled CO2 corrected	4.49	0.74	0.7839	0.030	0

For ethanol, mixed-exhaled variation within subjects is lower than the other methods, and the end-exhaled variation within subjects is the highest of the uncorrected breath methods. The mixed-exhaled CO_2 corrected variation is far higher than any other method, meaning that the prediction is less reliable than other methods.

For acetone, rebreathed variation within subjects is lower than the other methods, and the end-exhaled variation is the highest of the uncorrected breath methods. After CO2 correction, the mixed-exhaled variation is the highest of all the methods.

For MIBK, rebreathed variation within subjects is lower than that of any other uncorrected method, and end-exhaled variation is the highest. The mixed-exhaled CO_2 corrected variation is the lowest of all the methods, meaning that in this case, CO2 correction of mixed-breath concentrations allows the prediction of blood values to be at least as precise as any other method.

For toluene, rebreathed variation within subjects is lower than that of any other uncorrected method, and end-exhaled variation is the highest of the uncorrected breath methods. The mixed-exhaled CO_2 corrected variation is lower than for any type of breath except rebreathed.

For halothane, the end-exhaled breath prediction shows the least variation within subjects, and rebreathed variation is slightly more variable than mixed-exhaled variation. The mixed-exhaled carbon dioxide corrected variation is the largest of the methods, which is not necessarily what would have been expected, since halothane has the partition coefficient closest to that of carbon dioxide. Halothane was used in too few subjects to allow the use of subject as a random effect, so the calculated variance due to the random subject effect dropped to zero, and all the variation was interpreted as within-subject variation.

Means and 95% confidence intervals for the overall within-subject apparent partition coefficients calculated using this method are presented in Figures 15a-15e. Overall, the apparent partition coefficient of rebreathed gas tends to be statistically significantly lower than that of mixed-expired gas but not distinguishable from that of end-expired gas. The apparent end-expired partition coefficients are higher than those from rebreathed gas on average, but not statistically significantly so. Carbon dioxide correction does not reliably correct the apparent blood-gas partition coefficient to that of rebreathed gas. For ethanol, it overcorrects so that the apparent partition coefficient is statistically significantly lower than that of rebreathed or end-expired gas. For all other chemicals, carbon dioxide correction changes the apparent partition coefficients so that they are higher than apparent end-expired coefficients, but not statistically significantly so. Therefore it can be said that carbon dioxide correction can help bring the mixed-expired concentration nearer to the end-expired concentration, except for very soluble gases such as ethanol. Note that the two lowest solubility gases (closest to the blood-gas partition coefficient of carbon dioxide) do show statistically significant differences in apparent blood-gas partition coefficient between CO_2 corrected mixed-exhaled gas and rebreathed gas.

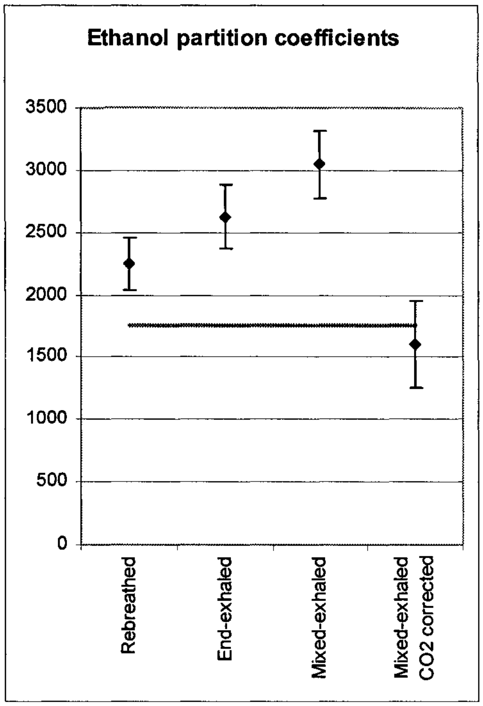

Figure 15a: Apparent ethanol partition coefficients (using venous blood and particular types of breath samples) as calculated with subject as a random variable. Error bars are drawn as ±1.96 × robust standard error of the mean slope. The literature value for the partition coefficient, as indicated by the horizontal line, is 1756 when directly measured from contact with blood. (Jones 1983)

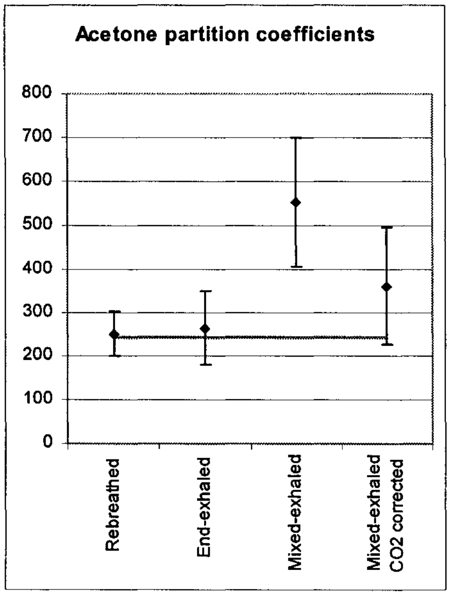

Figure 15b: Apparent acetone partition coefficients as calculated with subject as a random variable. The partition coefficient from the literature, as indicated by the horizontal line, is 245 (Sato 1979).

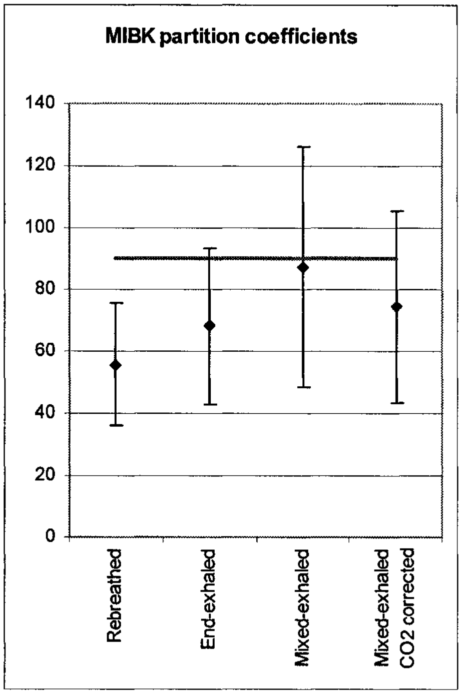

Figure 15c: Apparent MIBK partition coefficients as calculated with subject as a random variable. The partition coefficient from the literature, as indicated by the horizontal line, is 90 (Sato and Nakajima 1979).

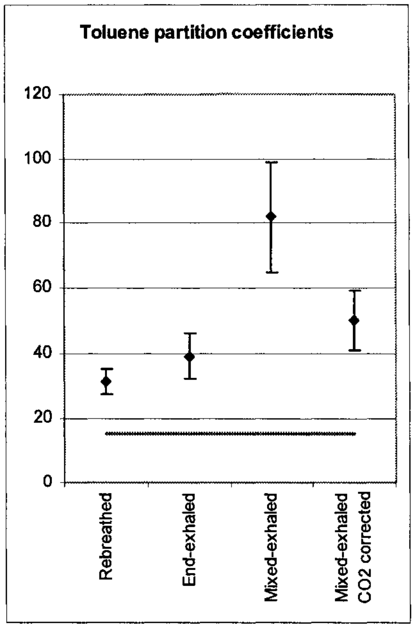

Figure 15d: Apparent toluene partition coefficients as calculated with subject as a random variable. The partition coefficient from the literature, as indicated by the horizontal line, is 15.6 (ACGIH).

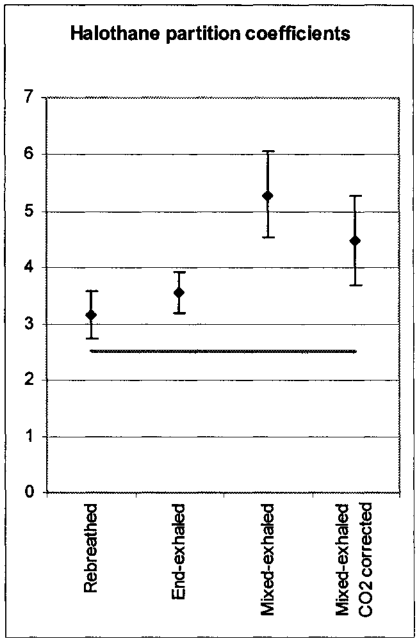

Figure 15e: Apparent halothane partition coefficients as calculated with subject as a random variable. The partition coefficient from the literature, as indicated by the horizontal line, is 2.5 (Yasuda 1989).

Gender made no difference in the slope or correlation of the blood/breath regressions for individual exposures: the regressions of gender on either slope or correlation never achieved a statistical significance of $p<0.1$. Age made no difference in correlation. Linear regressions showed that slopes did tend to decrease with age, but these correlations were rarely statistically significant. Slope was inversely correlated with age to $p<0.05$ only for rebreathed ethanol ($p=0.012$). Age and gender did statistically significantly affect the regressions between blood concentration and breath concentration when added as predictors, although the data was likely overfit when subject ID was included as a random effect. Lung clearance index (LCI) could not be added to this regression because it was collinear with subject ID. However, when subject ID was removed from the regression and age and gender were left in, lung clearance index was a highly significant predictor of blood concentration for a given breath sample for MIBK and acetone but not for ethanol, and for toluene the only type of breath for which LCI was a significant predictor was mixed-exhaled breath with carbon dioxide correction. (Gender was dropped from these regressions by the statistical software, presumably because it was collinear with LCI.) This statistical output can be found in Appendix E.

The effect of ventilation inhomogeneity on the relationship between blood and breath concentrations was examined by plotting the slope and R^2 of individual subjects' regressions of blood concentration on each type of breath concentration against the lung clearance index. The scatter plots can be found in Appendix F. Not every subject reached 2% of the original nitrogen level every time. Some subjects' data were excluded from this analysis because their washout curves showed evidence of nitrogen leakage in the system, perhaps around the mouthpiece. Nitrogen washouts that did not reach 2% of the original end-tidal nitrogen concentration were excluded from analysis because of suspicion of problems with the measurement. No significant relationship was found by linear regression between this measure of lung function and either the slope or the goodness of fit of an individual's blood/breath relationship for any breath sampling method or any chemical. The linear regressions of slopes and correlations for individuals' blood-breath relationships on lung clearance index can be found in Appendix F following the scatter plots.

While the LCI data was available for only half the exposures, limiting the inference that can be drawn, these comparisons indicate that lung inhomogeneity has a small effect on the relationship between individual blood and breath samples when age is also considered. The fact that lung clearance index is not significantly associated with the regression parameters of individuals' regressions may mean that it has a small influence only seen when other larger predictors are removed from the equation.

DISCUSSION

In summary:

- Rebreathed concentrations predict blood concentration with less within-subject variance than do other methods, for chemicals of intermediate solubility. For the highest and lowest solubility chemicals, the rebreathed variance within subjects was higher than some other methods.
- Rebreathed blood-gas partition coefficients are not distinguishable from end-exhaled blood-gas partition coefficients but are statistically significantly different from mixed-expired gas partition coefficients.
- There is a statistically significant difference in the relationship between blood and breath concentrations between the rebreathed and mixed-exhaled methods, increasing in significance as water solubility decreases. There is more likely to be a statistically significant difference between rebreathed and end-exhaled methods as water solubility decreases.
- Carbon dioxide correction can help bring the partition coefficient nearer to the end-expired or rebreathed coefficient, but it overcorrects for very soluble gases such as ethanol and undercorrects for less soluble gases. For some chemicals, it can bring partition coefficients close enough to not show statistically significant differences.
- Inhomogeneity of ventilation does not show a relationship with either blood/breath partition coefficient or goodness of fit in the blood/breath regressions.

Carbon dioxide correction:

Carbon dioxide correction of mixed-expired breath concentrations is intended to allow calculation of an accurate alveolar concentration. In this case, the mixed-expired breath concentration of a chemical was corrected to the average end-tidal concentration measured during part of the exposure period. So this calculation would have been expected to correct concentrations to end-tidal concentrations rather than end-forced-exhaled concentrations. End-forced-exhaled samples from a method with a breath hold will have higher CO_2 concentrations than end-tidal samples because of the added time for carbon dioxide production and excretion. End-forced-exhaled samples are also expected to have higher chemical concentrations than end-tidal samples for many chemicals because the breath hold allows additional time for equilibration with blood, because the breath at the end of the forced exhalation includes less gas from less ventilated acini with lower concentrations, or because gas interacts with the airways enough before the end of the exhalation that the last gas exhaled has not had as much soluble chemical content removed as gas exhaled earlier. So it can be expected that correction using end-tidal carbon dioxide concentrations would result in a slightly lower calculated chemical concentration than correction to end-forced-exhaled levels. This matches what is seen in this data for all but the most soluble chemicals.

Inhomogeneity of ventilation:

The measured LCI values agree fairly well with the values from the literature for healthy subjects. This group of subjects had an average lung clearance index of 8.7 with a standard deviation of 2.7. Cutillo et al. (1985) reported LCI values of 8.0 with a standard deviation of 1.6 for healthy subjects and 13.5 with a standard deviation of 4.3 for COPD patients. Bouhuys (1963) reported average LCI values for healthy males that ranged from 9.0 for subjects 44 years of age or younger to 10.0 for subjects between 55 and 65 years of age. Chiang and Wang (1970) reported LCI values of 9.02 average with a standard deviation of 1.13 for nonsmokers before smoking a cigarette and 12.20 average with a standard deviation of 2.16 for the same subjects after smoking two cigarettes in 10 minutes. Becklake first introduced the Lung Clearance Index in 1952 and reported an average LCI value of 7.02 with a standard deviation of 1.68 for normal subjects and values above 10.38 for emphysema patients.

Blood-breath partition coefficients:

The literature values for the blood-breath partition coefficients are around 1756-2100 for ethanol, 186-245 for acetone, 90 for MIBK, 15.6-17 for toluene, and 2.5 for halothane. This study's apparent *in vivo* partition coefficients with rebreathed gas, as shown in Table 1 in the previous section, were higher than the literature values by a factor of 2 for toluene, slightly higher for ethanol and halothane, very close for rebreathed acetone, and lower but very variable for methyl isobutyl ketone. The lower value listed above for ethanol is an *in vitro* measurement, and *in vivo* partition coefficients have been in the range near 2100. The measured apparent MIBK partition coefficients were most likely low and variable because of analytical problems. This is probably an effect of the difficulty of analyzing MIBK concentrations in blood on this headspace system. It is the least volatile of the chemicals, and it had the smallest peak on average at the concentrations of interest. Some MIBK data sets were removed at least in part because of unreasonably high apparent partition coefficients that implied equipment problems.

The toluene measurements showed few obvious signs of problems, so it is unclear why the apparent partition coefficients measured here for toluene are so much higher than the literature value. For all other chemicals, the coefficients from the regression of blood concentrations on rebreathed concentrations that treated subject as a random variable were reasonably close to the literature values. The coefficient for toluene was about 50% greater than the literature value. No good reason for this is evident; further research would be required to find out why these toluene partition coefficients differed so much. Investigation could include use of other methods or equipment to check calibration curves and measurement of the *in vitro* partition coefficient for toluene in the blood of these subjects.

Blood-breath partition coefficients varied between individuals by larger proportions than those measured *in vitro* for a similar range of volatile chemicals in studies by Dills et al (1994). This implicates some error component from the larger amount of equipment involved in the determination or user error in chemical analysis of blood or breath. Blood-air partition coefficient can vary between individuals because of such factors as blood content of lipid, albumin or other dissolved solutes. The *in vivo* relationship between breath and blood may vary further between individuals because of differences in airway gas exchange, the condition of the gas exchange tissue and its effect on diffusion between breath and blood, and the efficiency of ventilation throughout the lung. If a significant fraction of alveolar space is poorly ventilated, the venous/alveolar concentration gradient will be lower on average, and the fraction of an expired breath sample that has been in contact with blood may be lower. If the alveoli are scarred so that the diffusion distance between capillary blood and alveolar gas is farther or injured so that there is less surface area in which blood can be exposed to breath, the excretion will be slower and the breath concentration may be lower for the same blood concentration than for an uninjured lung. Diffusion-related differences will be most important for chemicals that have particularly large molecular size or mass. If one person has higher levels of a chemical such as ethanol in the airways or the blood, that chemical may alter the solubility of other chemicals in the tissue or blood and thus alter the chemical concentration in air that has passed by that tissue or been exposed to that blood. Fat soluble chemicals will have higher blood/gas partition coefficients in blood with high lipid content than in blood with lower lipid content, as detailed by Lin et al (2002). These factors do not seem to fully explain the wide range of ratios observed in this study between blood concentration and breath concentration.

It was expected that the blood-gas partition coefficients calculated from measured venous blood and exhaled breath concentrations would be near equal to the *in vitro* partition coefficient for rebreathed breath if indeed rebreathed breath were alveolar breath. The end-exhaled partition coefficients were expected to be higher for more water soluble compounds because the added interaction with airways would lower the chemical concentration by the time the exhaled air from the alveoli reached the mouth. The end-exhaled partition coefficients were also expected to be higher than *in vitro* partition coefficients for less water soluble compounds if the breath hold was inadequate to raise arterial partial pressures to the level of venous partial pressures. The mixed-exhaled partition coefficients were expected to be considerably higher than coefficients from the other methods because the dead space included in the sample, or in the case of ethanol the lower-concentration gas from the airways, would lower breath concentrations. Carbon dioxide correction was expected to lower the mixed-exhaled partition coefficient to near the end-tidal partition coefficient by raising the calculated breath concentration for all chemicals which transferred between blood and air in a manner similar to carbon dioxide, including chemicals with partition coefficients near 7. This corrected partition coefficient would be somewhat higher than the end-forced-exhaled partition coefficient because it would not reflect the added breath hold or the deep exhalation. For very water soluble compounds, the correction was expected to overcorrect the partition coefficient to one lower than the end-tidal partition coefficient because the carbon dioxide concentration and chemical concentration distributions would be different for a chemical that dissolved in airway tissue.

The observed partition coefficients largely followed this pattern with a few exceptions. Rebreathed partition coefficients did not match the *in vitro* partition coefficients from the literature, although they were the lowest and, in all but MIBK, closest to the literature partition coefficients. The partition coefficients from rebreathed and end-exhaled samples were fairly close together, and the means for end-exhaled samples were higher than for rebreathed samples for every chemical. For more water soluble chemicals, this is likely to be because an end-exhaled sampling method allows the chemical concentration to change between the alveoli and the mouth as some of the sample dissolves into the cooler airways. The isothermal rebreathing method is intended to allow the airways to warm enough not to scavenge chemicals from the breath and to allow the chemical concentrations to equilibrate throughout the lung, thus delivering breath with concentrations that are closer to alveolar concentrations and likely higher than the end-exhaled samples. For less water soluble chemicals, rebreathing is intended to lower the effective ventilation rate enough to raise the alveolar partial pressure of a chemical to the level of the venous partial pressure, making the rebreathed sample higher in concentration than the end-exhaled samples. The 15 second breath hold in the end-exhaled method used here also sets ventilation to zero for a short time, but rebreathing allows a longer period without net ventilation and without discomfort for the subject. The subjects in this study tended to take 30 to 60 seconds to give a rebreathed breath sample. It appears that the rebreathing method met many of its goals in this data.

Limitations of this study:

The applicability of these results may be limited by the following factors. Some were foreseen and accepted as part of the study design. Others were only apparent during or after data collection.

First, the mixed-exhaled breath collection method used here is much more carefully controlled than the typical method for collecting mixed-exhaled breath. The subjects' relaxed breathing patterns were monitored, and subjects were asked to control their breathing pattern for later samples. The computer used to measure and display breath pattern is far too bulky and time-consuming to use in the field, and it seems unrealistic to take a spirometer or pneumotachometer and computer into the field when other methods require so much less complicated equipment. The rationale behind this choice was to make the mixed-exhaled breath samples as uniform as possible in order to give mixed-exhaled breath the best chance of competing with the other methods. So instead of a mixed-exhaled breath sample similar to what one would find in the field, this method should supply a sample that is physiologically similar to normal mixed-exhaled samples but less variable in breath pattern. This assumption has not been tested. If the predictions from this method are less precise than rebreathed breath, the predictions from the more variable ordinary mixed-exhaled breath collection method used in other studies would likely be much less precise.

The small sample of subjects does not represent the general population. Six of the subjects were male, ranging in age from 21 to 73. The female subjects had ages ranging between 19 and 35. All subjects here were required to be healthy, free of respiratory conditions and free of medications that might be interfered with by this chemical exposure. This represents the working population better than the general population, and a sample this small would be unlikely to match the demographics of a larger general population.

The measure of ventilation inhomogeneity was only available for about half of the exposures because of problems such as mouthpiece leaks in some measurements and because of the assumption that was made in planning that one good measurement of ventilation inhomogeneity could be applied to other data sets for the same person. It was later decided that readings on different days for the same subject were too different to allow application of one day's inhomogeneity measure to another day's data sets.

The half-lives of concentration in people's blood and breath varied widely between chemicals, because of metabolism or excretion. Ethanol is metabolized the most quickly of these chemicals, with zero order kinetics. The other chemicals are metabolized more slowly. Highly lipid-soluble compounds tend to be excreted less quickly than more hydrophilic compounds because they dissolve into the fat compartment, where they are much more soluble than in blood, and take longer to leave the body than a more hydrophilic solvent residing in more water-filled compartments where it is soluble to a similar extent as in blood. This meant that some chemical concentrations varied during the sampling period over a much wider range than others. Ethanol concentrations varied over several orders of magnitude for most subjects, while acetone and MIBK concentrations varied over less than a factor of two for some subjects. These chemicals were chosen because they are commonly used, are not very toxic, and have pharmacokinetics that allowed breath monitoring for a few hours after exposure. The wide range of concentrations seen within one post-exposure period for ethanol means that higher correlations are achievable for ethanol than for chemicals with less variation in concentration. Acetone concentrations, for example, showed a much smaller amount of variation, as little as twofold. If acetone concentrations had varied over as wide a range as ethanol concentrations, with the same coefficient of variation that acetone had showed for any given time, the acetone correlations would have been considerably higher. With such low amounts of variation over the course of one sampling period, all that could be obtained was a small section of a larger relationship.

Only four data sets are available for halothane because only investigators could be exposed. There is therefore less data available for halothane than for the other chemicals. It is more difficult to interpret the statistical significance of results associated with halothane because there are so few subjects. Analysis of subject-specific information such as ventilation inhomogeneity and age may not be appropriate for halothane because with only three subjects, statistical power was relatively low.

Arm venous blood may not represent mixed venous blood, which is defined as the mixture of all the blood that has passed through each of the organs and which is drawn from the pulmonary artery. The relationship between mixed venous blood concentrations and arterial blood concentrations can be calculated using Farhi's equation,

$$P_A/P_v = \lambda / (\lambda + \bar{V}/\bar{Q}),$$

and alveolar breath is by definition in equilibrium with arterial blood. But the relationship between arm venous blood and arterial blood is more difficult to estimate because arm venous blood has perfused tissue that does not represent the whole body.

One can arterialize blood by heating up the arm it is taken from, but since it is rarely if ever done in environmental studies, it was not pursued here either.

Blood measurements were considerably more variable over the course of a subject's washout than breath measurements. This was true both for the calibration curves and the washout curves. This probably arises from a variety of factors. The chemical analysis process was considerably more complex for blood than for breath. The breath was drawn into a gas chromatograph without concentration or processing of any kind. The blood was injected into a vial and heated, the headspace was purged, a trap was used to capture the chemicals from the headspace, the water was removed as much as possible, and the remaining sample was cryogenically concentrated on the column inlet before injection by thermal desorption. The blood analysis system was more delicate and susceptible to changes or variation between vials. MIBK concentrations were near and sometimes below the limit of quantitation. So while the blood concentration is treated as the gold standard because it is what breath concentration is supposed to reflect, it was often more variable than the breath concentration.

No personal blood-air partition coefficients were measured *in vitro.* Thus the only partition coefficients available are the apparent *in vivo* coefficients from the subjects' venous blood and breath samples. Therefore, if ventilation inhomogeneity affects the relationship between blood and breath concentrations, it is difficult to tell how much of the difference in apparent partition coefficients between subjects comes from lung function and how much comes from other physiological differences. If it had been possible to directly measure partition coefficients *in vitro* from air in contact with blood using the available equipment, it would be possible to compare individual *in vitro* partition coefficients to *in vivo* coefficients from the corresponding subjects and look for a source of error in the chemical analysis. All that was possible with this data was exclusion of data sets that gave partition coefficients so far from the literature values that they were not believable. Some of the variation was likely to be real, and indeed regressions of blood and breath concentration that included age and ventilation inhomogeneity found that age and inhomogeneity were both predictors that explained some of the ventilation for some chemicals. Some of the variation was likely due to error from the analytical process.

CONCLUSIONS:

Isothermal rebreathing is a valid method of collecting alveolar gas. It performed as well as end-exhaled gas in this study, and considerably better than mixed-exhaled gas corrected for carbon dioxide concentration. Rebreathing showed the lowest *in vivo* blood-breath partition coefficients, which were also closest to the *in vitro* partition coefficients from the literature.

Based on the within-subjects variation, rebreathed breath concentrations tend to predict blood concentrations with somewhat more precision than either mixed-exhaled breath concentrations with or without CO_2 correction or end-exhaled breath concentrations. This is not true of the most or least water-soluble compounds in this data, which could mean either that overall there is no difference in precision between rebreathing and the other methods or that the most and least soluble compounds in the class of volatile organic compounds are affected differently by the method of breath sampling.

For any given blood sample, there is a statistically significant difference in the relationship between blood and breath concentrations between the rebreathed and mixed-exhaled methods, increasing in significance as water solubility decreases. There is more likely to be a statistically significant difference between rebreathed and end-exhaled methods as water solubility decreases.

Carbon dioxide correction of mixed-exhaled breath concentrations is acceptable as a way to analyze gases of most solubilities but should be avoided for very water soluble gases such as ethanol, for which it is an overcorrection. For most chemicals, it corrects the calculated blood-breath partition coefficient to one higher than but statistically indistinguishable from the end-exhaled partition coefficients.

Variation in lung function, as measured by ventilation homogeneity, does not affect the relationship between breath and blood concentrations in this data set.

Rebreathed gas is theoretically more likely to be equivalent to alveolar gas for more chemicals than is either end-exhaled gas or mixed-exhaled gas. For every chemical except MIBK, the rebreathed partition coefficient was the closest to the literature partition coefficient, which tends to support the idea. Carbon dioxide correction is an imperfect correction for mixed-exhaled gas, so that carbon dioxide corrected mixed-exhaled concentrations cannot be considered equivalent to alveolar air.

Rebreathing has been shown here to be a reliable method of obtaining alveolar breath samples that are representative of blood concentrations. Rebreathed concentration was not always the predictor with the highest precision in this data. The utility and precision of rebreathing as an exposure assessment method for volatile chemicals should be investigated further. More research is warranted on the highest and lowest solubility solvents by rebreathing, particularly to see whether a collection scheme that uses eight inhalations and exhalations allows sufficient time for the full equilibration at each end of the scale of partition coefficients of common industrial volatile organic compounds. More research into field studies of rebreathing is also warranted, to evaluate usability and validate its precision outside the laboratory.

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Appendix A: Calibration Curves

Part 1: Breath calibration equations from a linear regression of spiked sample concentrations on peak areas. These regressions were all unweighted and of the form *concentration = slope(peak area)+intercept.*

Ethanol

Date	intercept	slope	R^2
12/17/2003	0.2533	0.000245	0.9957
12/10/2003	-0.3734	0.000249	0.9978
11/19/2003	-0.2055	0.000261	0.9955
8/21/2003	0.1896	0.000226	0.9951
8/11/2003	0.1117	0.000237	0.9978
6/18/2003	0.0072	0.000274	0.9987
5/29/2003	-0.1391	0.000248	0.9976
3/19/2003	-0.0828	0.000240	0.9981
1/24/2003	0.1330	0.000291	0.9916
12/12/2002	-0.2785	0.000282	0.9831
10/23/2002	-0.0164	0.000299	1
10/7/2002	-0.0201	0.000299	1

Acetone

Date	intercept	slope	R^2
8/26/2003	-1.6781	0.000286	0.9401
7/10/2003	-0.0876	0.000192	0.9995
7/3/2003	0.1842	0.000169	0.9625
6/25/2003	-0.1459	0.000212	0.9991
5/29/2003	-0.0817	0.000243	0.9493
5/21/2003	-0.0824	0.000206	0.9979
3/19/2003	-0.1157	0.000212	0.9947
1/24/2003	-0.0914	0.000247	0.9996

MIBK

Date	intercept	slope	R^2
12/17/2003	-0.0404	0.0000848	0.7194
11/19/2003	-0.0460	0.0000719	0.9431
8/21/2003	-0.0112	0.0000701	0.9912
8/11/2003	-0.0171	0.0000386	0.996
8/6/2003	-0.0171	0.0000386	0.996
6/18/2003	-0.0516	0.0000627	0.8345
10/7/2002	0.0119	0.000103	0.998

Toluene

Date	intercept	slope	R^2
10/29/2003	-0.0366	0.0000425	0.9387
10/22/2003	-0.0366	0.0000425	0.9387
8/26/2003	-0.0440	0.0000468	0.7613
8/1/2003	-0.2233	0.0000842	0.9317
7/10/2003	-0.0177	0.0000567	1
7/3/2003	0.0046	0.0000248	0.9982
6/25/2003	0.0058	0.0000514	1
5/1/2003	-0.0088	0.000025	0.9241
10/23/2002	-0.0171	0.000057	0.9955

Halothane

Date	intercept	slope	R^2
12/10/2003	0.0113	0.000113	0.9971
5/21/2003	-0.0585	0.000165	0.9858
3/7/2003	-0.0474	0.000152	0.9989
12/12/2002	0.0196	0.000197	0.9885

Part II: Blood calibration equations from a linear regression of spiked sample concentrations on response factors from GC/MS peaks. These differ in magnitude because the concentration in the internal standard was not always alike between runs due to solvent evaporation in storage. The “best match” column refers to the determination of which type of curve best fit the data. “Linear” refers to unweighted linear regression. “Weighted linear” refers to linear regression weighted by the inverse of the concentration. “RF^1.2” refers to an equation of the form $concentration=a(response\ factor)^{1.2}+b(response\ factor)+c$.

MIBK

Date	R^2	Best Match	Equation
12/17/2003	0.956	RF^1.2	y = -1.994x^1.2+4.239x-0.00565
11/19/2003	0.8844	RF^1.2	y = -0.00562x^1.2+3.834x-1.6751
8/21/2003	0.9781	linear	y = 6.8275x - 0.0017
8/11/2003	0.8273	RF^1.2	y = -4.820x^1.2+11.873x+0.0334
8/6/2003	0.8459	RF^1.2	y = -4.809x^1.2+9.589x-0.00767
6/18/2003	0.7411	weighted linear	y = 10.68257x - 0.1975092
10/7/2002	0.9853	power	y = 0.5206x^1.2482

Halothane

Date	R^2	best match

12/10/2003	0.9753	linear	y = 0.6464x - 0.0264
5/21/2003	0.9595	weighted linear	y = .3682325x - .0131793
3/6/2003	0.9562	weighted linear	y = 0.2457009x - 0.017207
12/12/2002	0.9894	linear	y = 3.064907x + 0.002291

Toluene

Date	R^2	best match	
10/29/2003	0.9935	linear	y = 5.508E-04x - 3.452E-03
10/22/2003	0.8936	weighted linear	y = 0.7256x + 0.0259
8/26/2003	0.9997	linear	y = 1.0302x + 0.0131
8/1/2003	0.9668	weighted linear	y = 0.2928x - .005442
7/10/2003	0.9917	weighted linear	y = 0.5649x + 0.0025
7/3/2003	0.9854	weighted linear	y = 0.4427x + .00056
6/25/2003	0.9684	linear	y = 0.1662x - 2.476E-05
5/1/2003	0.983	linear	y = 0.1073x - 0.0259
10/23/2002	0.9858	weighted linear	y = 0.3047442x - 0.0099278

Acetone

Date	R^2	best match	
8/26/2003	0.9955	linear	y = 5.8296x - 5.1026
7/10/2003	0.9911	linear	y = 3.0202x - 30.387
7/3/2003	0.9921	linear	y = 1.9445x - 7.493
6/25/2003	0.9868	linear	y = 7.8001x - 3.2588
5/29/2003	0.9941	linear	y = 5.5862x + 0.0884
5/21/2003	0.9899	linear	y = 3.1325x + 3.4683
3/19/2003	0.9765	weighted linear	y = 69.4573x + 28.5012
1/24/2003	0.9755	power	y = 2026x^1.7671

Part III: A selection of early breath and blood calibrations with coefficients of variation calculated for each level. This was used to tell whether the blood or breath method produced more variable results for the same spiked concentration.

Halothane breath:			**Halothane blood:**		
Halothane 9/4/02			12/12/2002		
area	umol/L	CV	RF 117	umol/L	CV
5961	0.0576499	0.03357	0.0113566	0.04713	0.219528
6244	0.0576499		0.0177389	0.04713	
3277	0.0297941	0.035771	0.0147656	0.04713	
3048	0.0297941		0.0609368	0.18852	0.092326
3301	0.0297941		0.0657613	0.18852	
3263	0.0297941		0.0541204	0.18852	
1517	0.0131176	0.041966	0.1229123	0.4713	0.047721
1394	0.0131176		0.1346727	0.4713	
1427	0.0131176		0.1318896	0.4713	
	average				
	CV	0.037103	0.4338518	1.8852	0.052817
Halothane 12/12/02			0.4661954	1.8852	

area	umol/L	CV	0.4198525	1.8852	
7364	0.073595	0.251062	0.5910542	4.713	0.084334
10652	0.073595		0.6901839	4.713	
10473	0.073595		0.603385	4.713	
2618	0.0234768	0.213631	4.6663875	18.852	0.053651
2362	0.0234768		4.4808374	18.852	
3433	0.0234768		4.1801534	18.852	
1682	0.0168975	0.293803		average CV	0.091729
1561	0.0168975		9/4/2002		
2471	0.0168975		RF 117	umol/L	CV
1541	0.0137927	0.21773	0.1790479	0.0009303	0.023866
1466	0.0137927		0.1851949	0.0009303	
2081	0.0137927		0.3472852	0.0093035	0.06955
	average CV	0.244056	0.3104301	0.0093035	
			0.3523243	0.0093035	
			2.0425466	0.0930348	0.324894
			1.2988497	0.0930348	
			2.3555924	0.0930348	
			0.4548732	0.9303483	2.002504
			2.299587	0.9303483	
			5.8790025	0.9303483	
			124.53534	9.3034826	0.160043
			164.61148	9.3034826	
			164.61148	9.3034826	
					0.445431
Toluene breath:			**Toluene blood:**		
Toluene 10/23/02			5/1/2003		
area	umol/L	CV	RF 91	umol/L	CV
11159	0.02451	0.002345	0.6988312	0.0468034	0.026228
11122	0.02451		0.725242	0.0468034	
6020	0.012667	0.008809	1.9924014	0.1872137	0.09166
6095	0.012667		1.79559	0.1872137	
4729	0.0091171	0.054278	2.141712	0.1872137	
4366	0.0091171		5.0990465	0.4680342	0.098566
2204	0.0038075	0.083095	4.37936	0.4680342	
2463	0.0038075		4.2232986	0.4680342	
945	0.0017117	0.193545	16.801069	1.8721369	0.150893
912	0.0017117		19.274555	1.8721369	
613	0.0017117		22.237309	1.8721369	
	average CV	0.068414	57.880621	4.6803422	0.177231
Toluene 5/1/03			41.680381	4.6803422	
area	umol/L	CV	43.724037	4.6803422	
1618	0.0009444	0.02491		average CV	0.108916
1675	0.0009444		10/23/2002		

2355	0.002054	0.051212	RF 91	umol/L	CV
2169	0.002054		97598	0	0.156602
2129	0.002054		78138	0	
3273	0.0030448	0.013827	45216	0.0046814	0.331319
3209	0.0030448		86478	0.0046814	
4055	0.0034137	0.005231	53561	0.0046814	
4025	0.0034137		179965	0.0468136	0.420766
4624	0.0089302	0.013014	79836	0.0468136	
4676	0.0089302		167888	0.0468136	
4556	0.0089302		547366	0.1404407	0.113604
45398	0.1110915	0.006417	437867	0.1404407	
45810	0.1110915		512694	0.1404407	
197	0.0009444	0.173358	1667965	0.4681358	0.099799
175	0.0009444		1535132	0.4681358	
130	0.0009444		1349741	0.4681358	
	average				
	CV	0.041139	3932934	1.4044075	0.267053
			5083148	1.4044075	
			6339919	1.4044075	
			19613164	4.6813582	0.059136
			18166906	4.6813582	
			17415288	4.6813582	
				average	
				CV	0.206897
MIBK breath:			**MIBK blood:**		
MIBK 3/6/03			9/4/2002		
			MIBK 43		
area	umol/L	CV	RF	umol/L	CV
24916	0.071063	0.131057	0.0207454	0.0019846	0.254956
20298	0.071063		0.0298705	0.0019846	
26779	0.071063		0.029121	0.0198458	0.135523
30705	0.1151291	0.104345	0.0381261	0.0198458	
35236	0.1151291		0.0324092	0.0198458	
80347	0.2684152		0.1941405	0.1984577	0.23325
12229	0.0367261		0.1337822	0.1984577	
9411	0.0215768		0.2046489	0.1984577	
4072	0.0049628		0.1242589	1.9845771	1.07674
18981	0.071063		0.3995721	1.9845771	
10052	0.0215768		0.6882362	1.9845771	
951	0.0022819		4.445954	19.845771	0.180846
5874	0.0094799		6.0971884	19.845771	
	average				
	CV	0.117701	6.0971884	19.845771	
MIBK 9/4/02					0.348036
area	umol/L	CV			
4631	0.0414479	0.052067	3/6/2003		
			MIBK 43		
4972	0.0414479		RF	umol/L	CV

5421	0.0414479		0.2491431	0.1981407	0.339744
3536	0.0214207	0.041794	0.332414	0.1981407	
3745	0.0214207		0.4459493	0.1981407	
3290	0.0214207		1.7874837	0.7925627	0.082451
3264	0.0214207		1.8798479	0.7925627	
2531	0.009431	0.24278	2.0830148	0.7925627	
1662	0.009431		2.5910876	1.9814069	0.138133
	average CV	0.112214	3.3465934	1.9814069	
			2.6923589	1.9814069	
			7.7275107	7.9256275	0.144758
			9.4429322	7.9256275	
			7.027509	7.9256275	
			10.971419	19.814069	0.43792
			6.5137479	19.814069	
			14.134266	19.814069	
				average CV	0.228601
Acetone breath:			**Acetone blood:**		
Acetone 12/12/02			1/24/2003		
area	umol/L	CV	ace 43 RF	umol/L	CV
69399	0.9042873	0.013551	0.0866132	6.7662719	0.030899
70729	0.9042873		0.0829093	6.7662719	
38654	0.4202155	0.00825	0.1284477	27.065088	0.017178
38203	0.4202155		0.1253647	27.065088	
29116	0.288467	0.155043	0.1468099	67.662719	0.147424
26740	0.288467		0.1868955	67.662719	
20391	0.2076248		0.1421535	67.662719	
20195	0.2076248		0.3525588	270.65088	0.073866
18340	0.169476	0.076764	0.3042357	270.65088	
16349	0.169476		0.324665	270.65088	
13787	0.1270		0.0467023	676.62719	1.773146
5577	0.0518		0.0457589	676.62719	
3950	0.0390		0.1882106	676.62719	
2805	0.0295		5.9052073	2706.5088	0.146975
3826	0.0179232		6.0428775	2706.5088	
	average CV	0.063402	7.4901598	2706.5088	
Acetone 1/24/03				average CV	0.364915
area	umol/L	CV	12/12/2002		
46452	0.4490207	0.011128	ace 43 RF	umol/L	CV
47183	0.4490207		0.4184322	6.7662719	0.052746
23334	0.2320584	0.023982	0.4383736	6.7662719	
24339	0.2320584		0.463525	6.7662719	
24263	0.2320584		0.6790274	27.065088	0.034465
14517	0.1363356	0.01252	0.6448122	27.065088	
14715	0.1363356		0.6357791	27.065088	

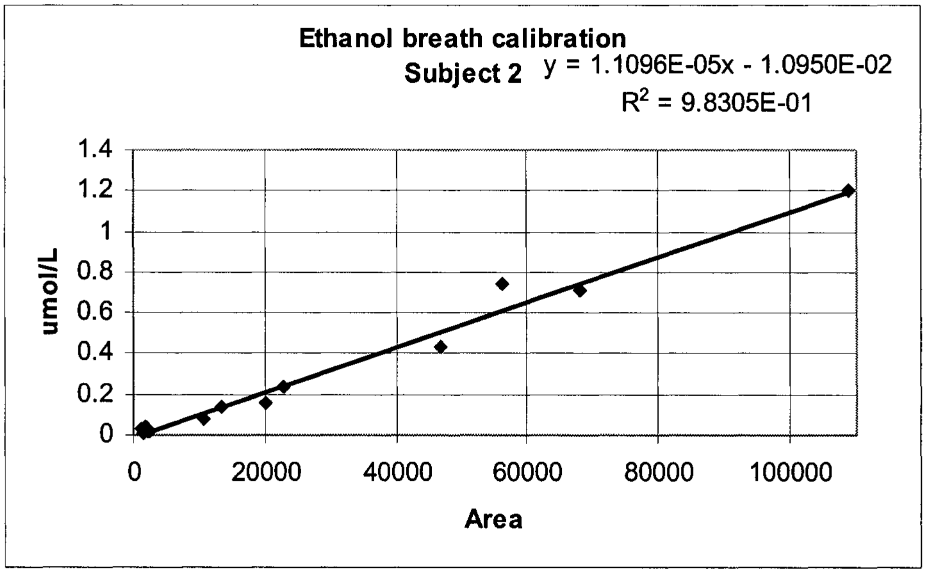
14352	0.1363356		1.6324714	67.662719	0.089689
3251	0.0313579	0.005873	1.3703203	67.662719	
3224	0.0313579		1.4479457	67.662719	
2284	0.0144184	0.179238	9.0113566	270.65088	0.180069
2379	0.0144184		9.5378704	270.65088	
2161	0.0144184		6.4181293	270.65088	
2366	0.0144184		10.658521	676.62719	0.087318
2487	0.0144184		11.693367	676.62719	
2610	0.0144184		9.742859	676.62719	
2180	0.0144184		2.1625206	2706.5088	0.166403
1921	0.0144184		1.5597301	2706.5088	
1118	0.0144184		1.7377645	2706.5088	
2218	0.0144184			average CV	0.101782
2529	0.0144184				
	average CV	0.046548			
Ethanol breath:			Ethanol blood:		
Ethanol 10/23/02			10/23/2003		
area	umol/L	CV	RF 45	umol/L	CV
31160	0.3706559	0.011149	97377	0.25	0.078792
31371	0.3706559		87099	0.25	
31701	0.3706559		1147219	25.598864	0.153454
31944	0.3706559		852363	25.598864	
11719	0.1378748	0.002475	926238	25.598864	
11747	0.1378748		15194806	255.98864	0.69219
11689	0.1378748		2765270	255.98864	
4180	0.0494457	0.032818	9184909	255.98864	
4374	0.0494457		50659824	767.96591	0.02304
2269	0.0258852	0.011967	50025833	767.96591	
2323	0.0258852		52275331	767.96591	
2291	0.0258852		104272744	2559.8864	0.065858
1108	0.011902	0.120697	102441234	2559.8864	
881	0.011902		91674295	2559.8864	
1117	0.011902		187052008	7679.6591	0.053679
	average CV	0.035821	201544925	7679.6591	
Ethanol 10/9/02			207290887	7679.6591	
area	umol/L	CV	236940071	25598.864	0.055414
181061	2.1750194	0.015026	213221983	25598.864	
185834	2.1750194		218388171	25598.864	
186600	2.1750194			average CV	0.160347
186862	2.1750194		10/7/2003		
95767	1.1240718	0.003449	RF 45	umol/L	CV
95104	1.1240718		266927	2.5571081	0.32047
95707	1.1240718		169923	2.5571081	
95247	1.1240718		131006	2.5571081	

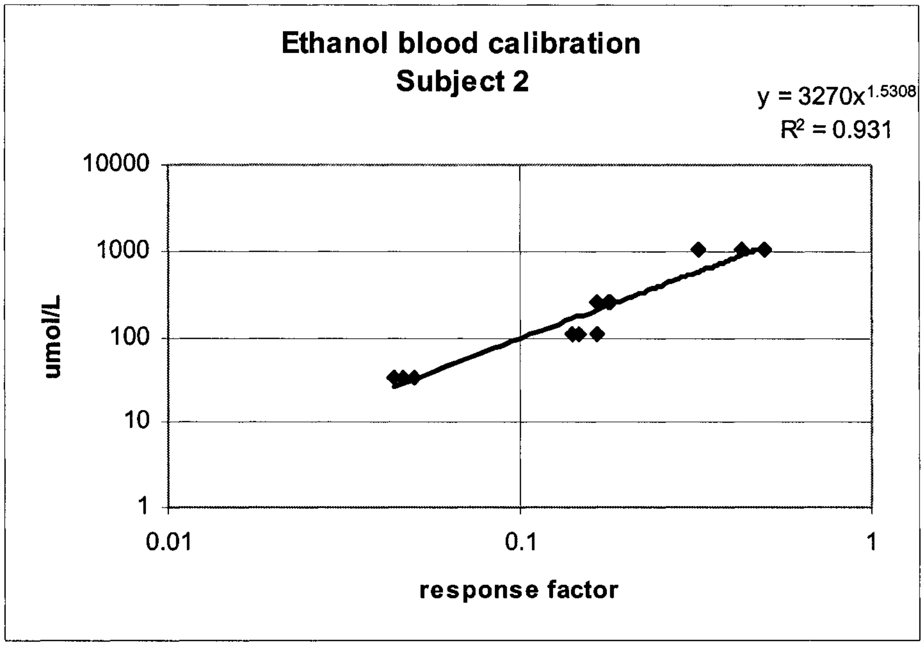
56274	0.6603986	0.004567	361316	25.571081	0.105399
56022	0.6603986		321250	25.571081	
56536	0.6603986		289536	25.571081	
17235	0.2017807	0.007362	5529153	255.71081	0.567125
17487	0.2017807		2085864	255.71081	
17387	0.2017807		1550081	255.71081	
5697	0.0698415	0.014961	62041362	2557.1081	0.043087
5496	0.0698415		57525916	2557.1081	
5607	0.0698415		57635570	2557.1081	
5555	0.0698415		11330568	25571.081	0.05693
2311	0.0257148	0.008873	12674162	25571.081	
2340	0.0257148		11786117	25571.081	
1093	0.0118237	0.030406		average CV	0.218602
1140	0.0118237				
	average CV	0.012092			

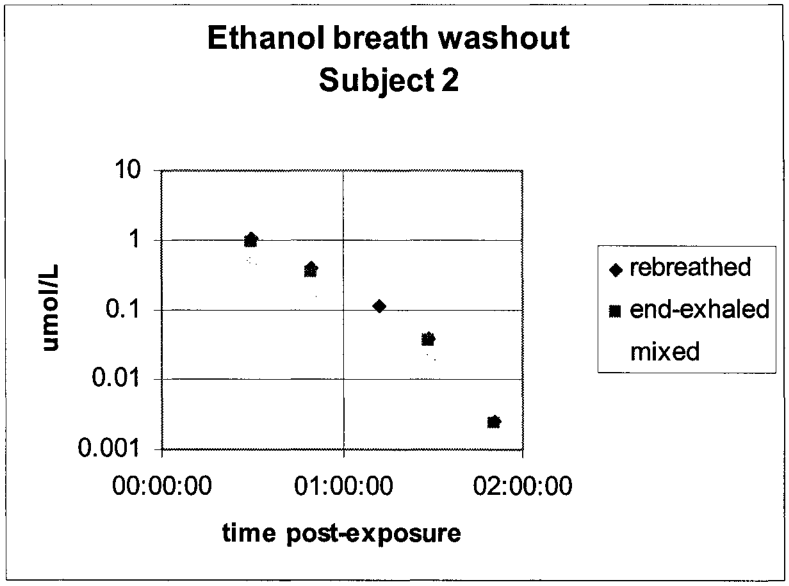
Appendix B: Graphical data display.

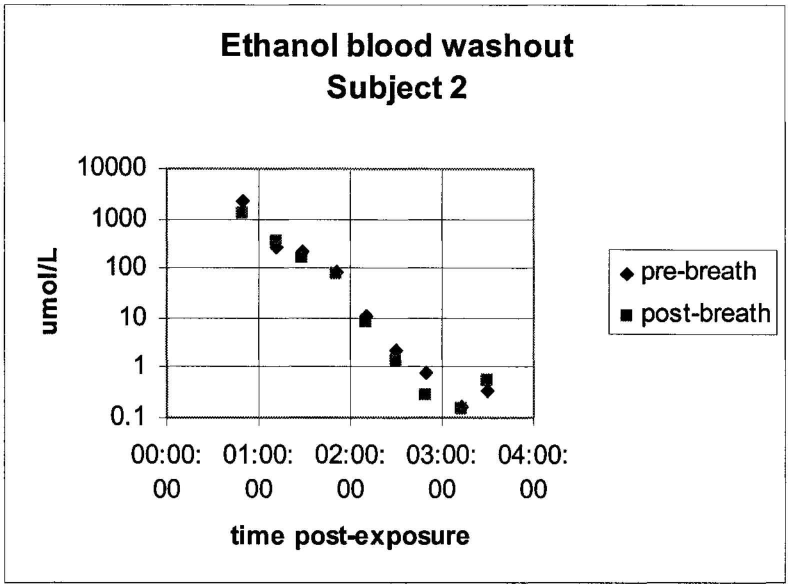
This is a set of graphs of calibration curves for both breath and blood, washout curves for both breath and blood, and correlations between blood and each of the four breath types considered here. Data are in chronological order within chemicals, and the chemicals are arranged in order from highest to lowest partition coefficient.

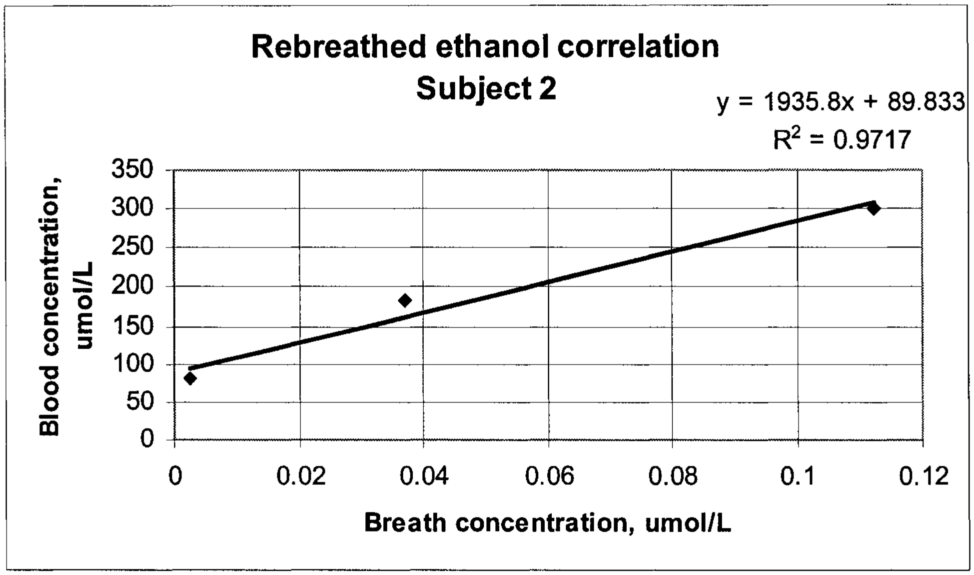
Ethanol
12/12/2002

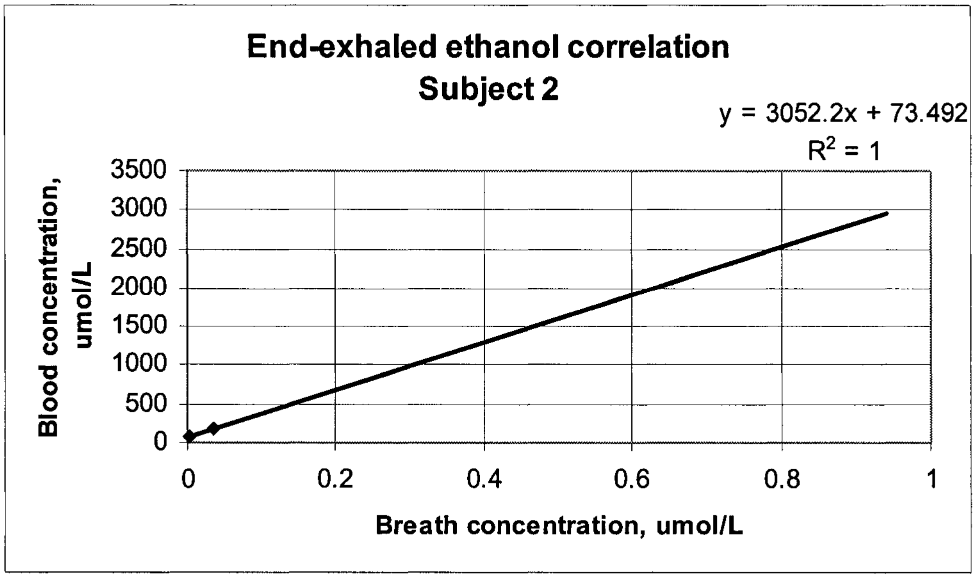


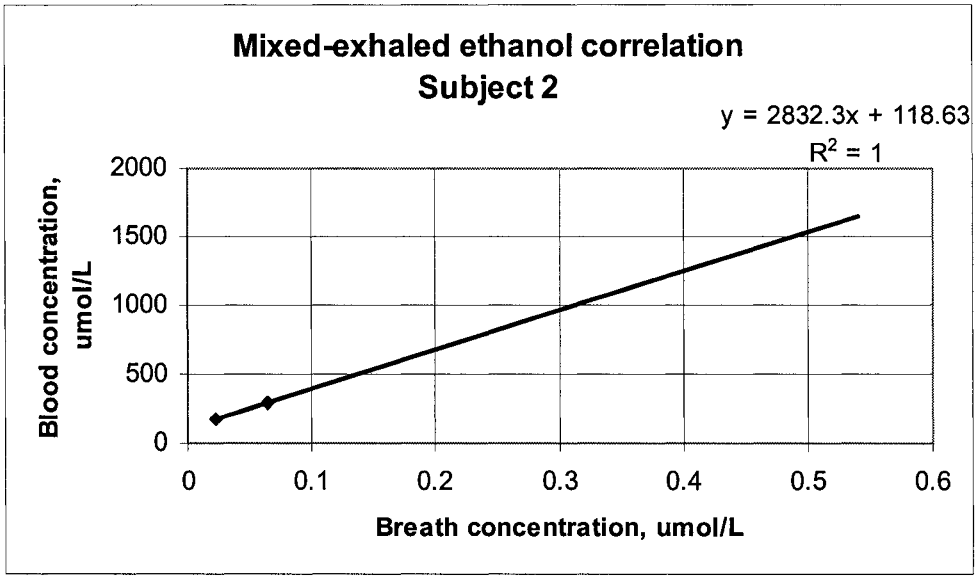


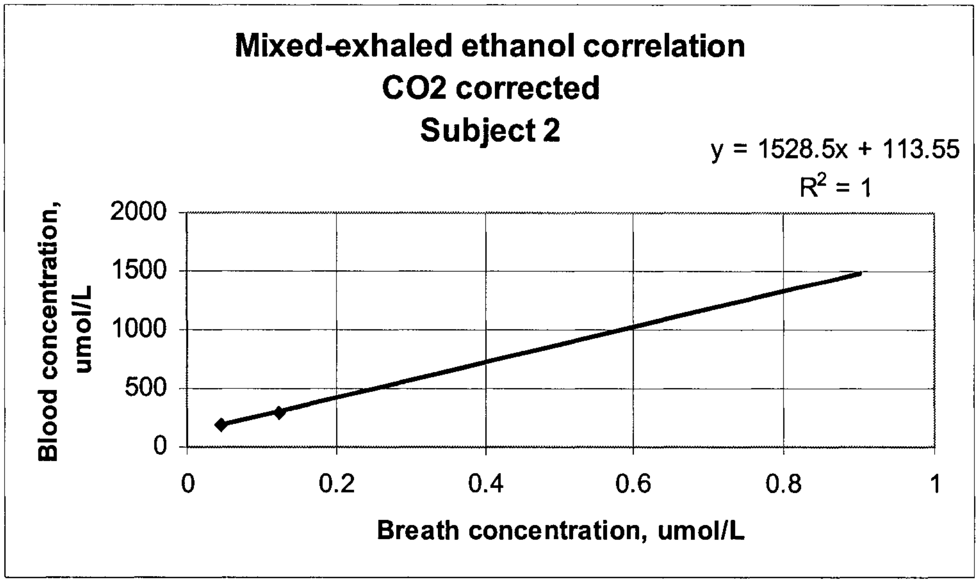

Ethanol breath washout
Subject 2
umol/L
10
1
0.1
0.01
0.001
00:00:00
01:00:00
02:00:00
time post-exposure
◆ rebreathed
■ end-exhaled
mixed


Ethanol blood washout
Subject 2
umol/L
10000
1000
100
10
1
0.1
00:00:00
01:00:00
02:00:00
03:00:00
04:00:00
time post-exposure
◆ pre-breath
■ post-breath

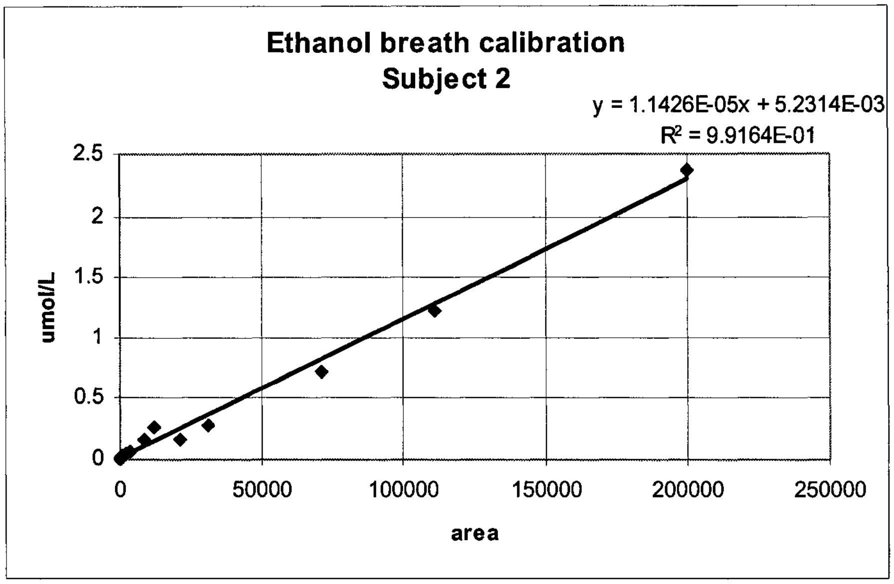

Rebreathed ethanol correlation
Subject 2
y = 1935.8x + 89.833
R² = 0.9717
Blood concentration, umol/L
350
300
250
200
150
100
50
0
0
0.02
0.04
0.06
0.08
0.1
0.12
Breath concentration, umol/L

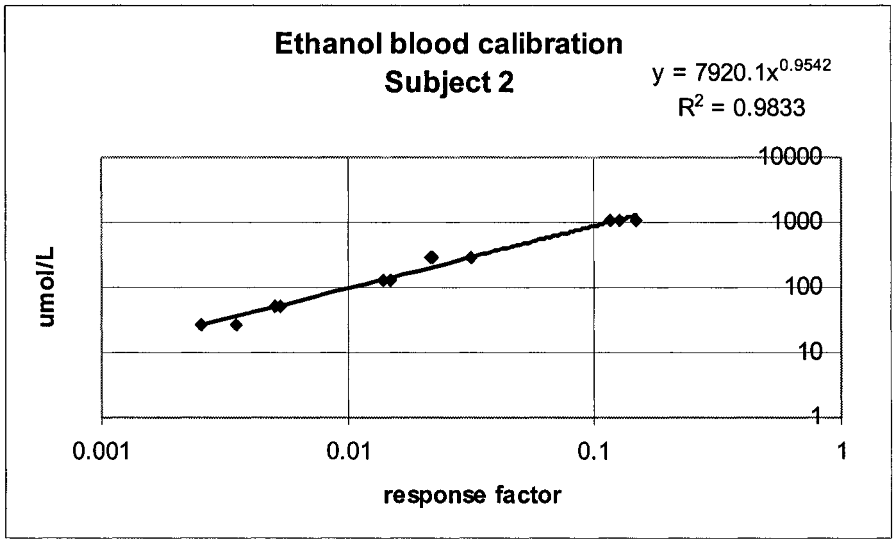

End-exhaled ethanol correlation
Subject 2
y = 3052.2x + 73.492
R² = 1
Blood concentration, umol/L
3500
3000
2500
2000
1500
1000
500
0
0
0.2
0.4
0.6
0.8
1
Breath concentration, umol/L

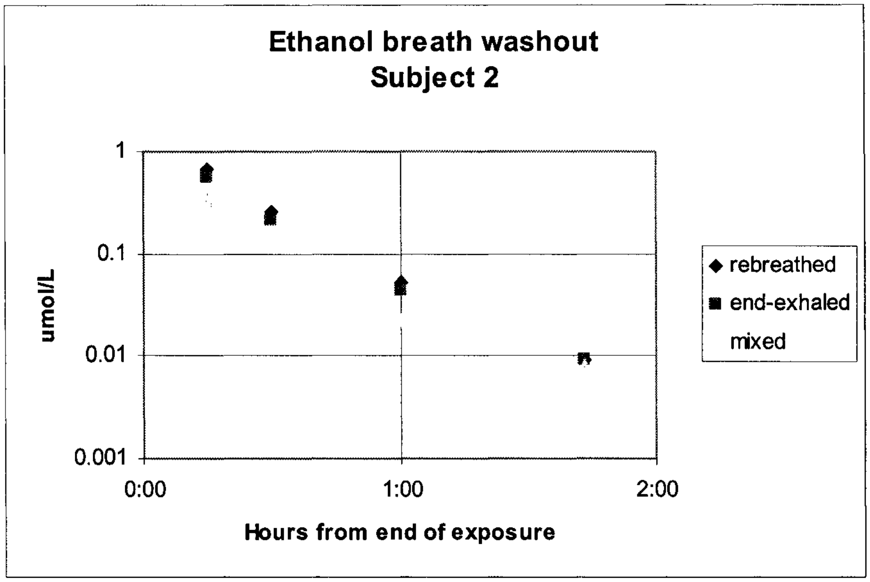

Mixed-exhaled ethanol correlation
Subject 2
y = 2832.3x + 118.63
R² = 1
Blood concentration, umol/L
2000
1500
1000
500
0
0
0.1
0.2
0.3
0.4
0.5
0.6
Breath concentration, umol/L

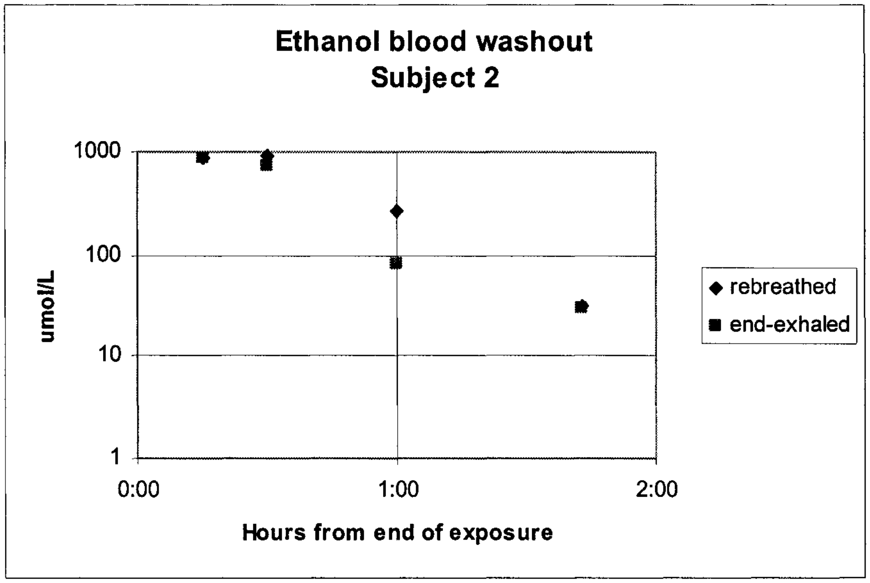

Mixed-exhaled ethanol correlation
CO2 corrected
Subject 2
y = 1528.5x + 113.55
R² = 1
Blood concentration, umol/L
2000
1500
1000
500
0
0
0.2
0.4
0.6
0.8
1
Breath concentration, umol/L

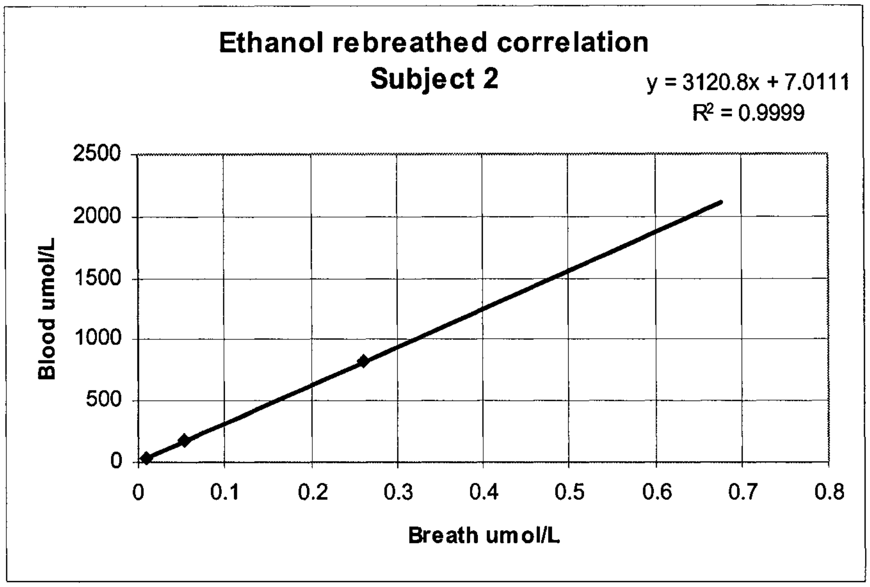
1/24/2003

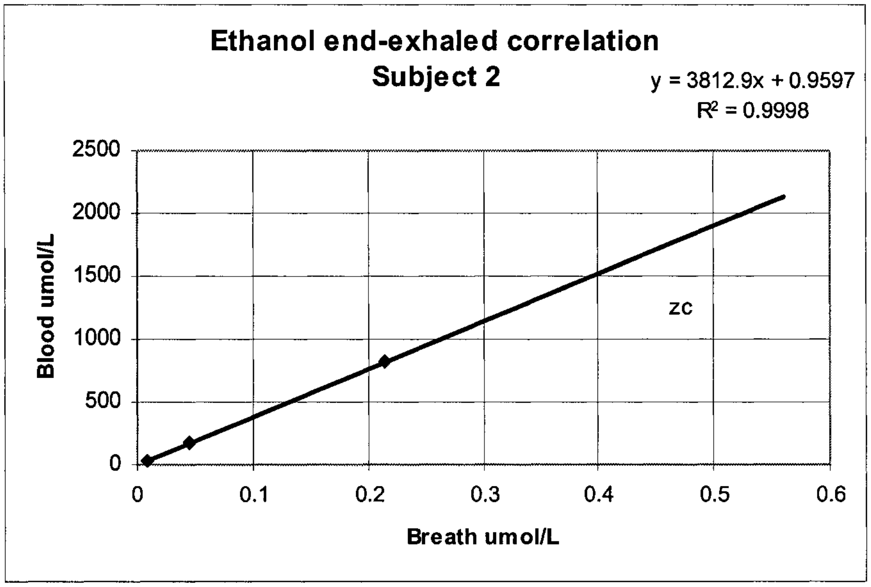

Ethanol breath calibration
Subject 2
y = 1.1426E-05x + 5.2314E-03
R² = 9.9164E-01
umol/L
2.5
2
1.5
1
0.5
0
0
50000
100000
150000
200000
250000
area

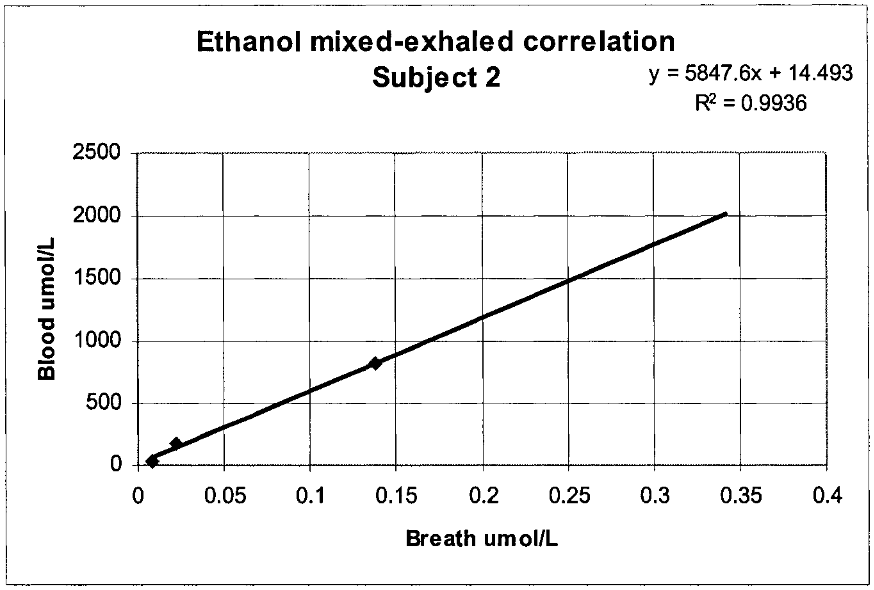

Ethanol blood calibration
Subject 2
y = 7920.1x^0.9542
R² = 0.9833
umol/L
10000
1000
100
10
1
0.001
0.01
0.1
1
response factor

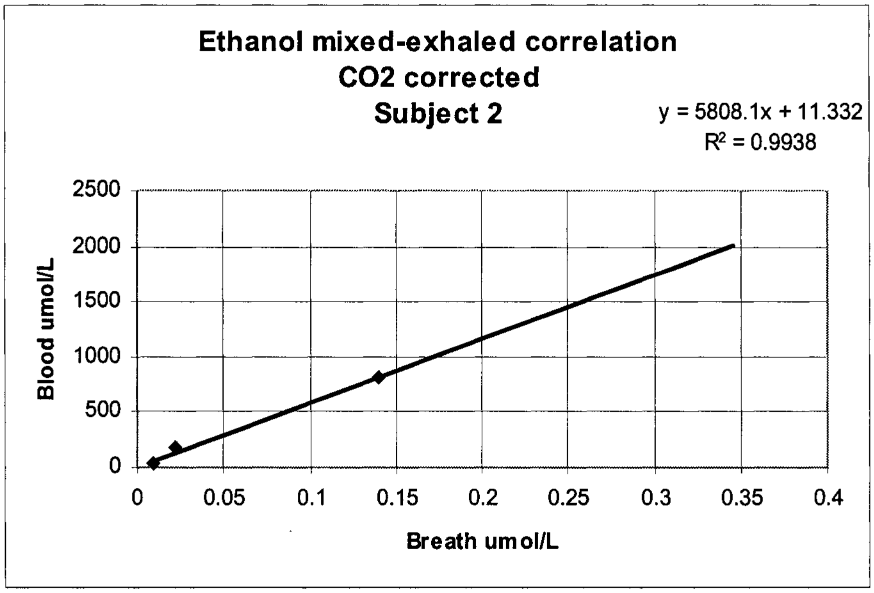

Ethanol breath washout
Subject 2
umol/L
1
0.1
0.01
0.001
0:00
1:00
2:00
Hours from end of exposure
◆ rebreathed
■ end-exhaled
mixed


Ethanol blood washout
Subject 2
umol/L
1000
100
10
1
0:00
1:00
2:00
Hours from end of exposure
◆ rebreathed
■ end-exhaled

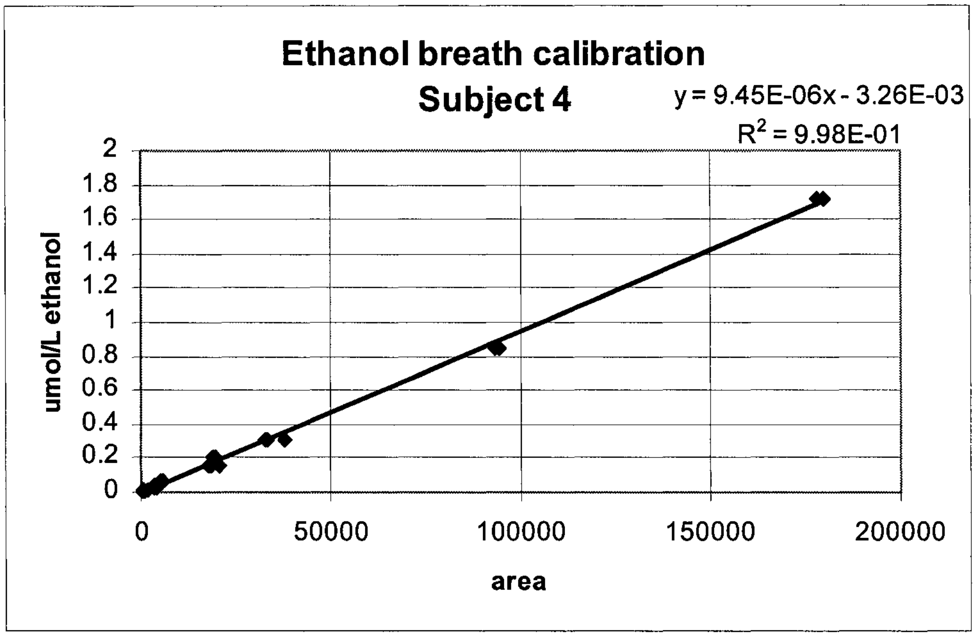

Ethanol rebreathed correlation
Subject 2
y = 3120.8x + 7.0111
R² = 0.9999
Blood umol/L
Breath umol/L
0
500
1000
1500
2000
2500
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8


Ethanol end-exhaled correlation
Subject 2
y = 3812.9x + 0.9597
R² = 0.9998
zc
Blood umol/L
Breath umol/L
0
500
1000
1500
2000
2500
0
0.1
0.2
0.3
0.4
0.5
0.6

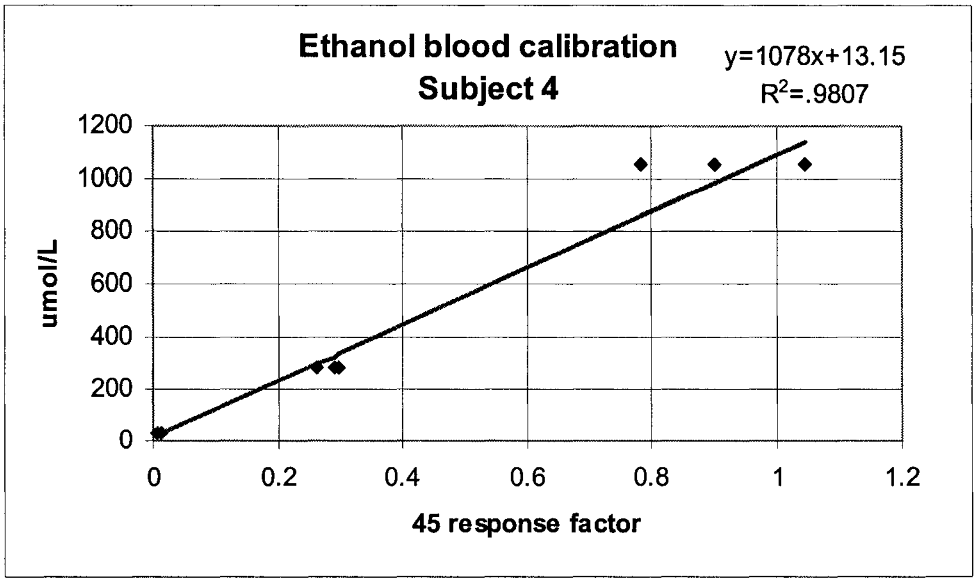

Ethanol mixed-exhaled correlation
Subject 2
y = 5847.6x + 14.493
R² = 0.9936
Blood umol/L
2500
2000
1500
1000
500
0
0
0.05
0.1
0.15
0.2
0.25
0.3
0.35
0.4
Breath umol/L


Ethanol mixed-exhaled correlation
CO2 corrected
Subject 2
y = 5808.1x + 11.332
R² = 0.9938
Blood umol/L
2500
2000
1500
1000
500
0
0
0.05
0.1
0.15
0.2
0.25
0.3
0.35
0.4
Breath umol/L

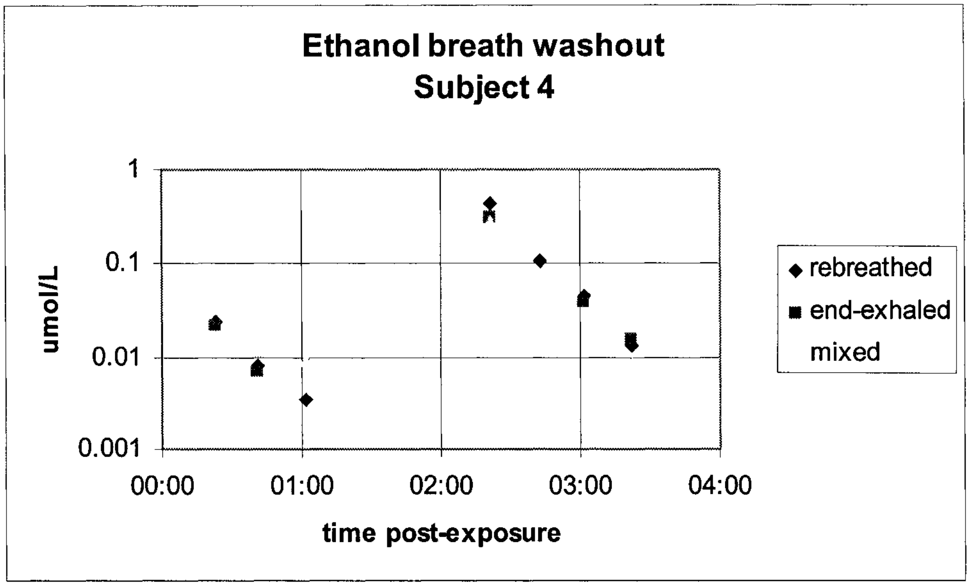
3/19/2003

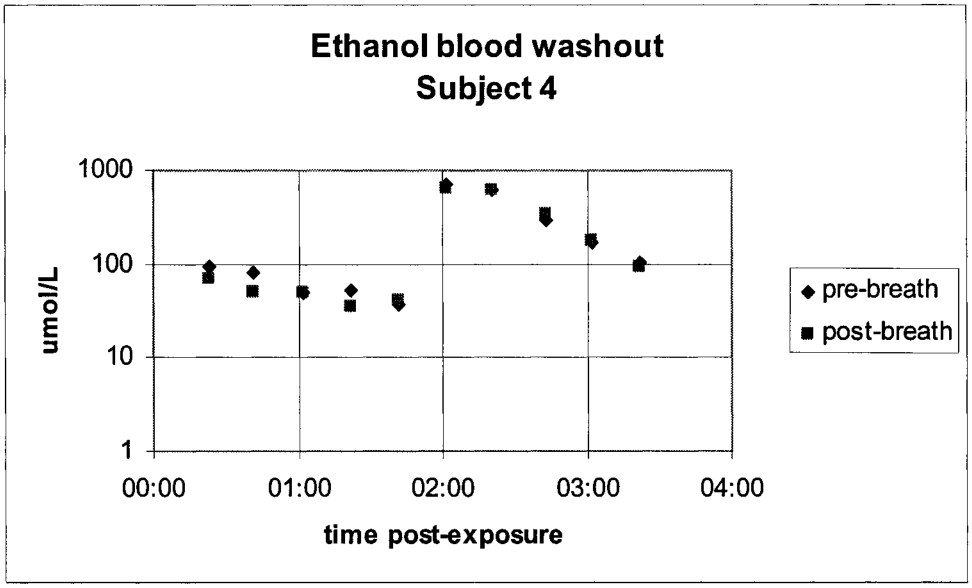


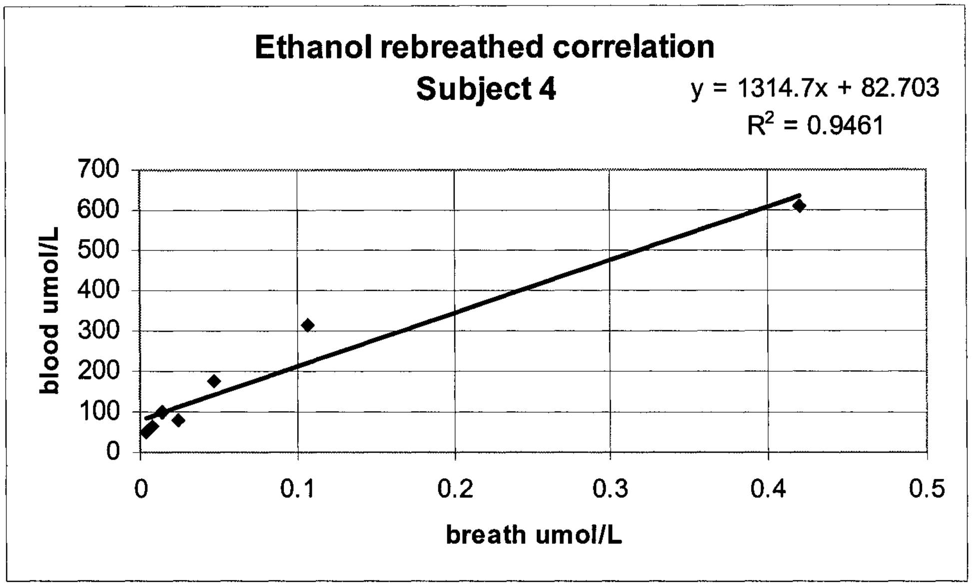
Ethanol breath calibration
Subject 4
y = 9.45E-06x - 3.26E-03
R^2 = 9.98E-01
umol/L ethanol
2
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
0
50000
100000
150000
200000
area

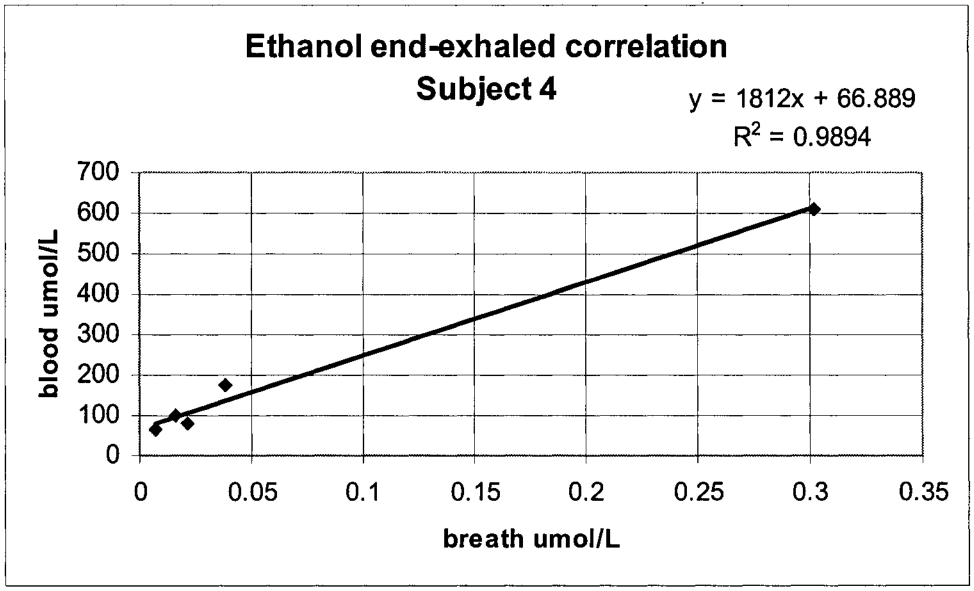


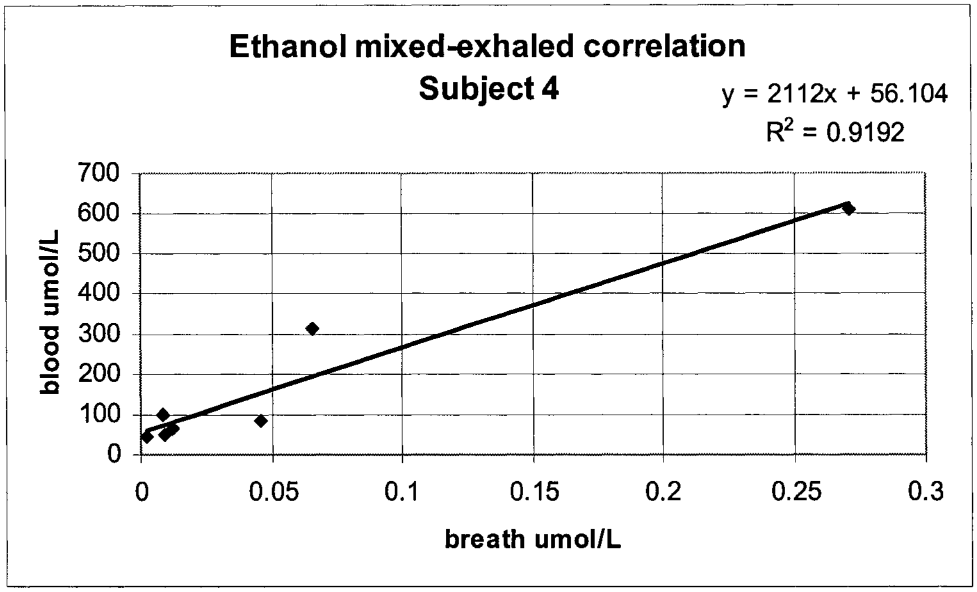
Ethanol blood calibration
Subject 4
y=1078x+13.15
R^2=.9807
umol/L
1200
1000
800
600
400
200
0
0
0.2
0.4
0.6
0.8
1
1.2
45 response factor

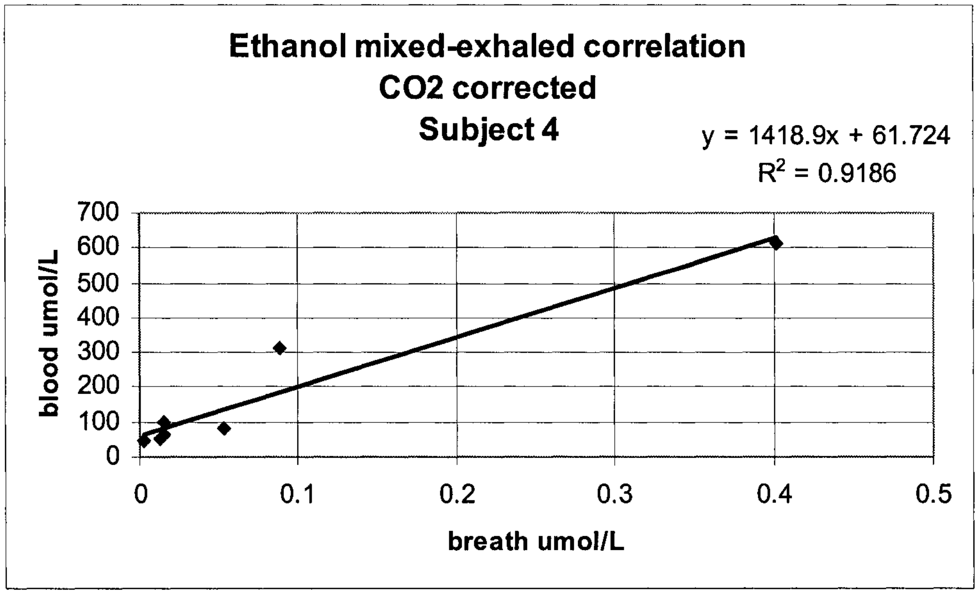

Ethanol breath washout
Subject 4
umol/L
1
0.1
0.01
0.001
00:00
01:00
02:00
03:00
04:00
time post-exposure
◆ rebreathed
■ end-exhaled
mixed


Ethanol blood washout
Subject 4
umol/L
1000
100
10
1
00:00
01:00
02:00
03:00
04:00
time post-exposure
◆ pre-breath
■ post-breath


Ethanol rebreathed correlation
Subject 4
y = 1314.7x + 82.703
R^2 = 0.9461
700
600
500
400
300
200
100
0
blood umol/L
0
0.1
0.2
0.3
0.4
0.5
breath umol/L


Ethanol end-exhaled correlation
Subject 4
y = 1812x + 66.889
R^2 = 0.9894
700
600
500
400
300
200
100
0
blood umol/L
0
0.05
0.1
0.15
0.2
0.25
0.3
0.35
breath umol/L


Ethanol mixed-exhaled correlation
Subject 4
y = 2112x + 56.104
R² = 0.9192
blood umol/L
700
600
500
400
300
200
100
0
0
0.05
0.1
0.15
0.2
0.25
0.3
breath umol/L


Ethanol mixed-exhaled correlation
CO2 corrected
Subject 4
y = 1418.9x + 61.724
R² = 0.9186
blood umol/L
700
600
500
400
300
200
100
0
0
0.1
0.2
0.3
0.4
0.5
breath umol/L

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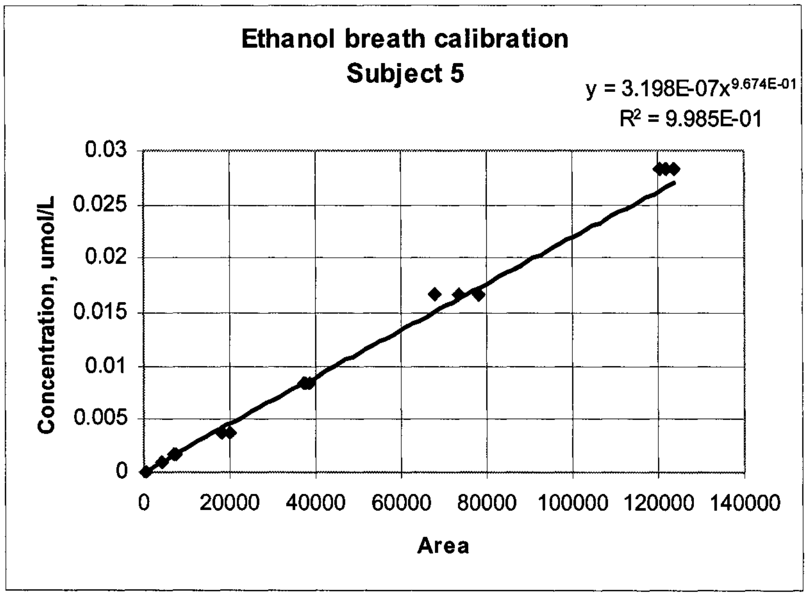
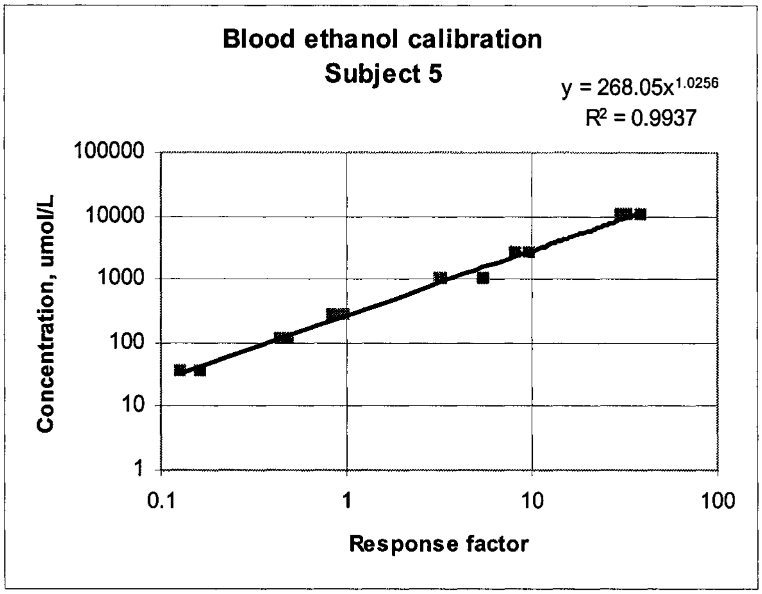
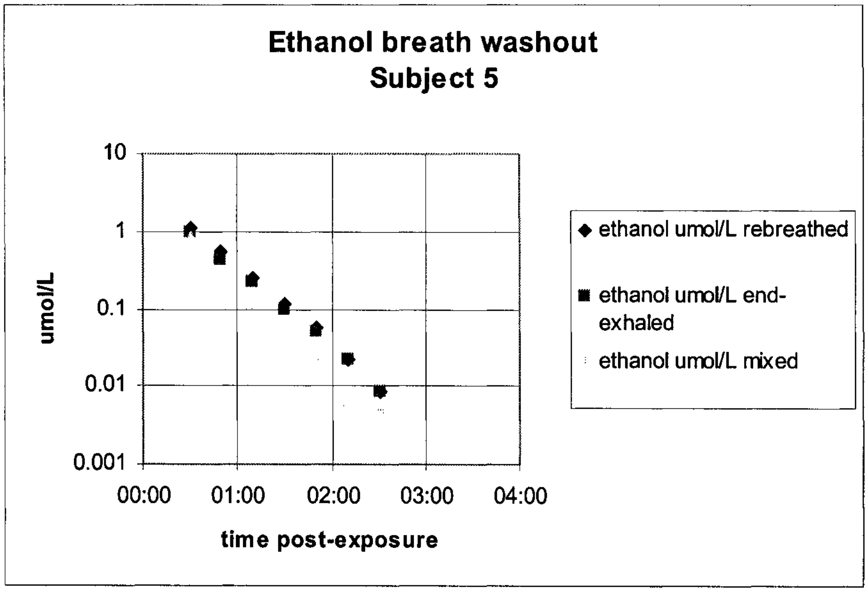
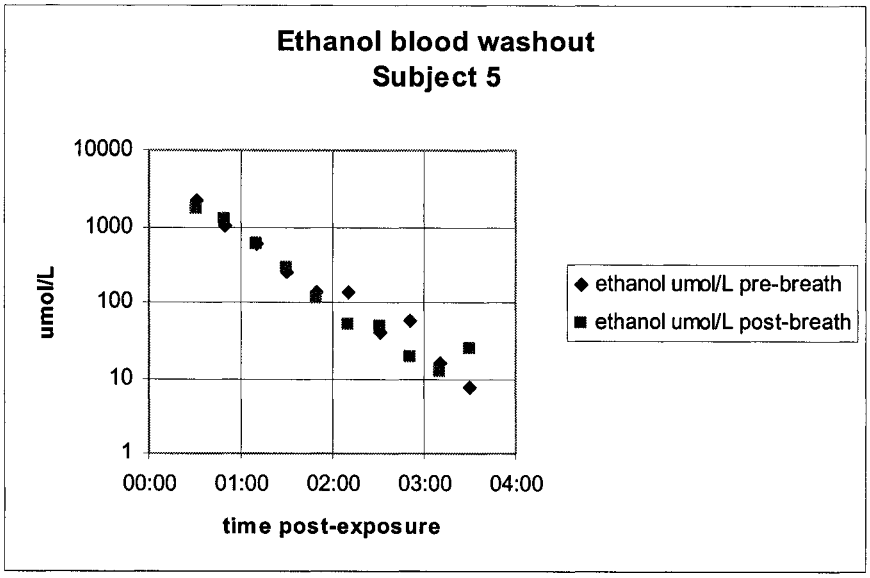
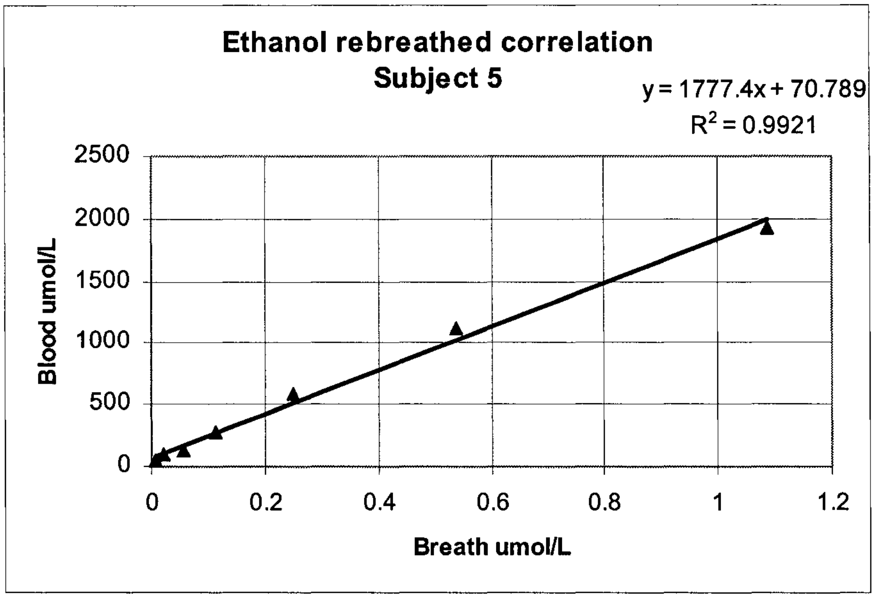
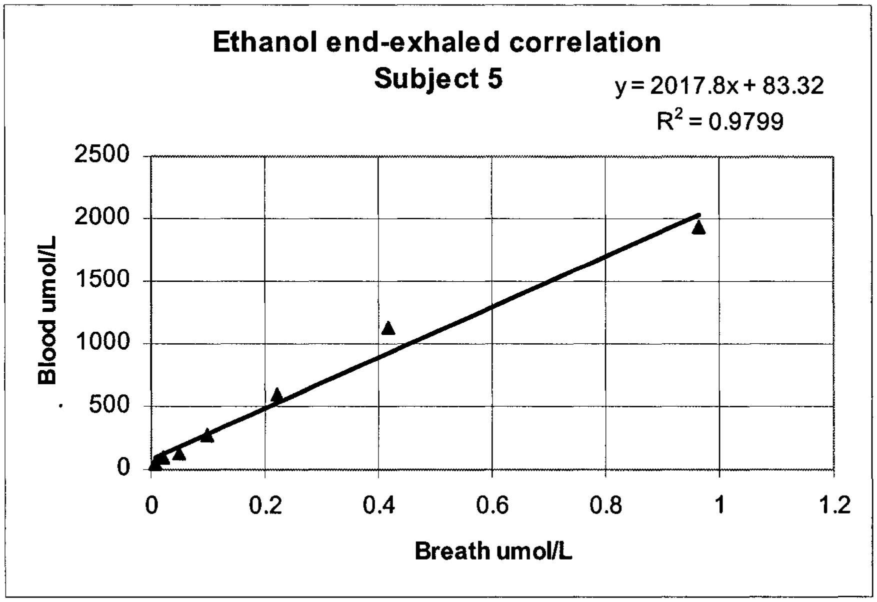

Ethanol breath calibration
Subject 5
y = 3.198E-07x9.674E-01
R2 = 9.985E-01
Concentration, umol/L
0.03
0.025
0.02
0.015
0.01
0.005
0
0
20000
40000
60000
80000
100000
120000
140000
Area

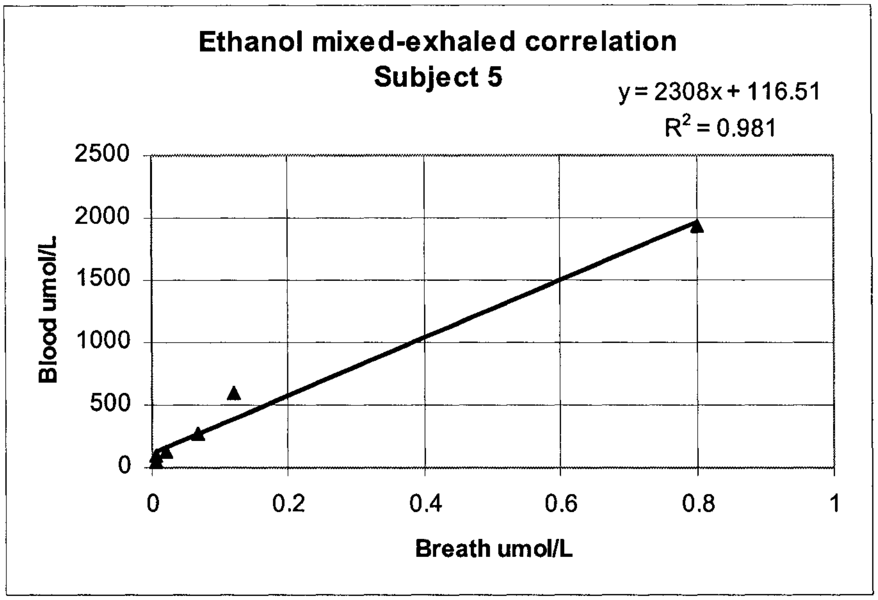

Blood ethanol calibration
Subject 5
y = 268.05x1.0256
R2 = 0.9937
Concentration, umol/L
100000
10000
1000
100
10
1
0.1
1
10
100
Response factor

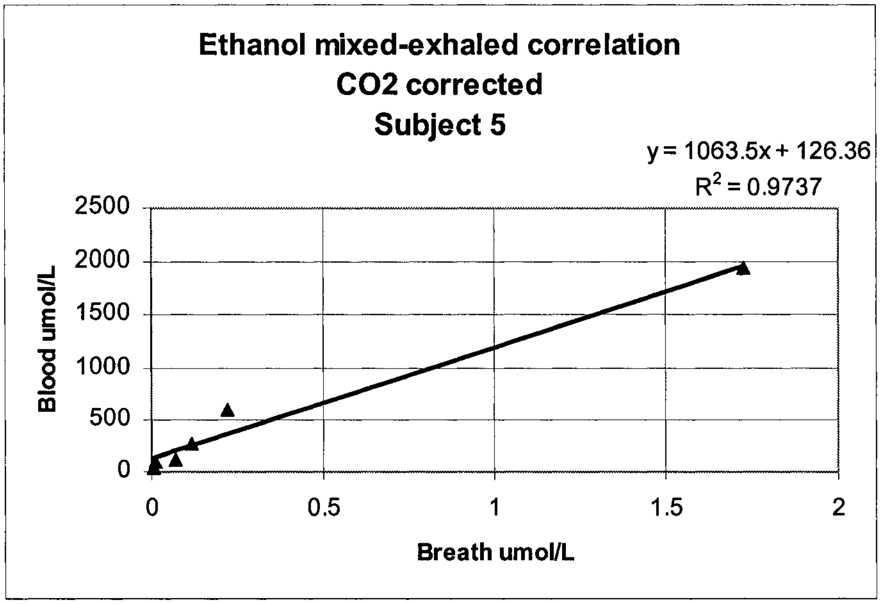

Ethanol breath washout
Subject 5
10
1
0.1
0.01
0.001
umol/L
00:00
01:00
02:00
03:00
04:00
time post-exposure
◆ ethanol umol/L rebreathed
■ ethanol umol/L end-exhaled
ethanol umol/L mixed

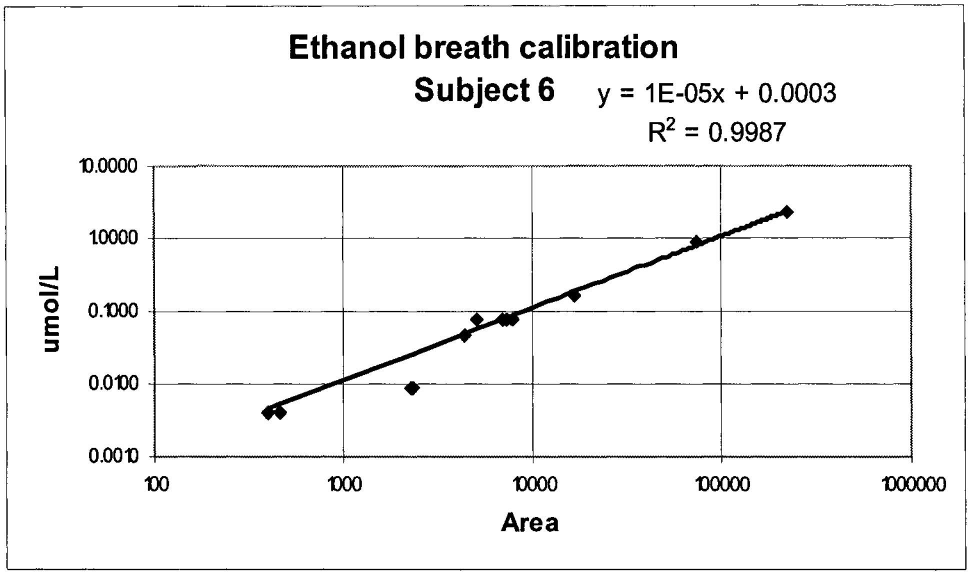

Ethanol blood washout
Subject 5
10000
1000
100
10
1
umol/L
00:00
01:00
02:00
03:00
04:00
time post-exposure
◆ ethanol umol/L pre-breath
■ ethanol umol/L post-breath


Ethanol rebreathed correlation
Subject 5
y = 1777.4x + 70.789
R² = 0.9921
Blood umol/L
2500
2000
1500
1000
500
0
0
0.2
0.4
0.6
0.8
1
1.2
Breath umol/L

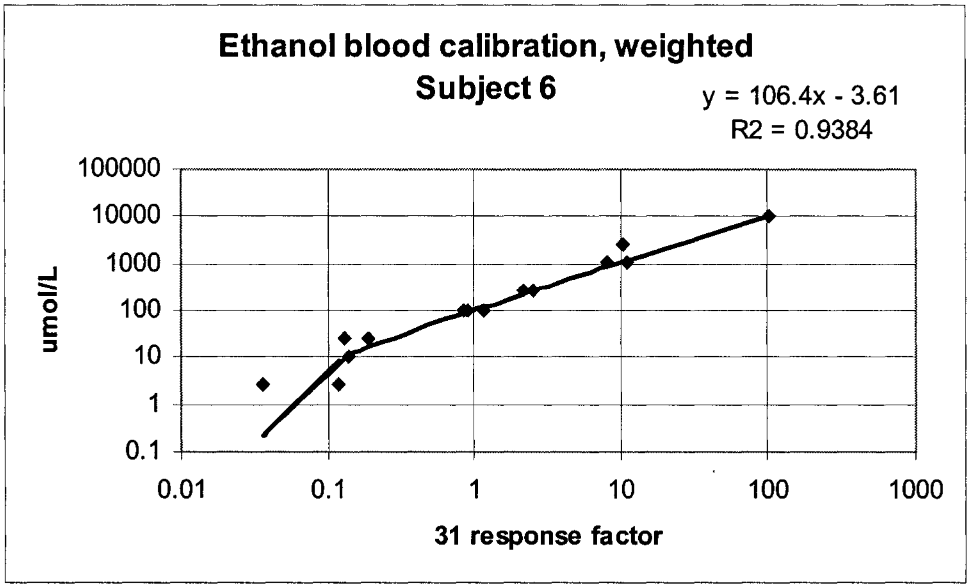

Ethanol end-exhaled correlation
Subject 5
y = 2017.8x + 83.32
R² = 0.9799
Blood umol/L
2500
2000
1500
1000
500
0
0
0.2
0.4
0.6
0.8
1
1.2
Breath umol/L

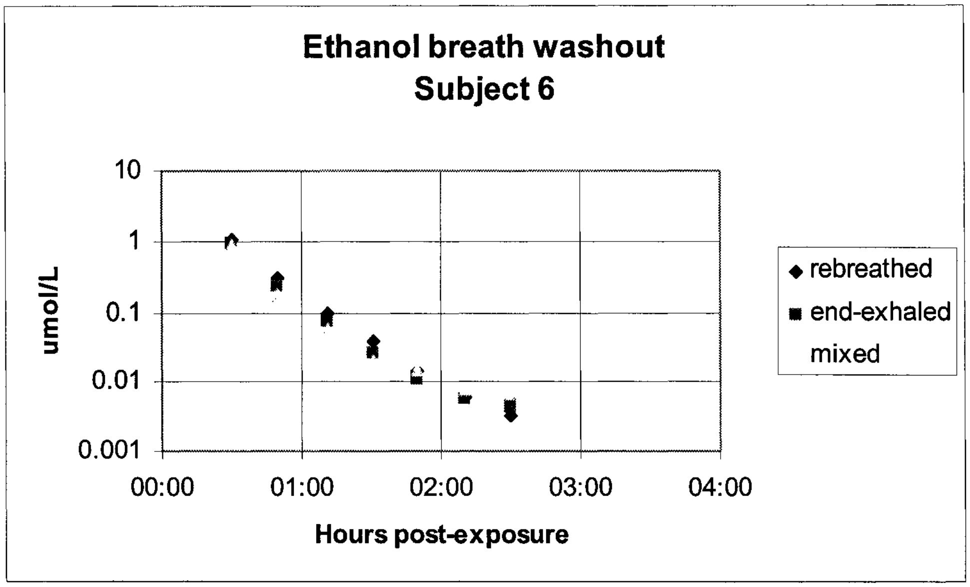

Ethanol mixed-exhaled correlation
Subject 5
y = 2308x + 116.51
R^2 = 0.981
Blood umol/L
2500
2000
1500
1000
500
0
0
0.2
0.4
0.6
0.8
1
Breath umol/L

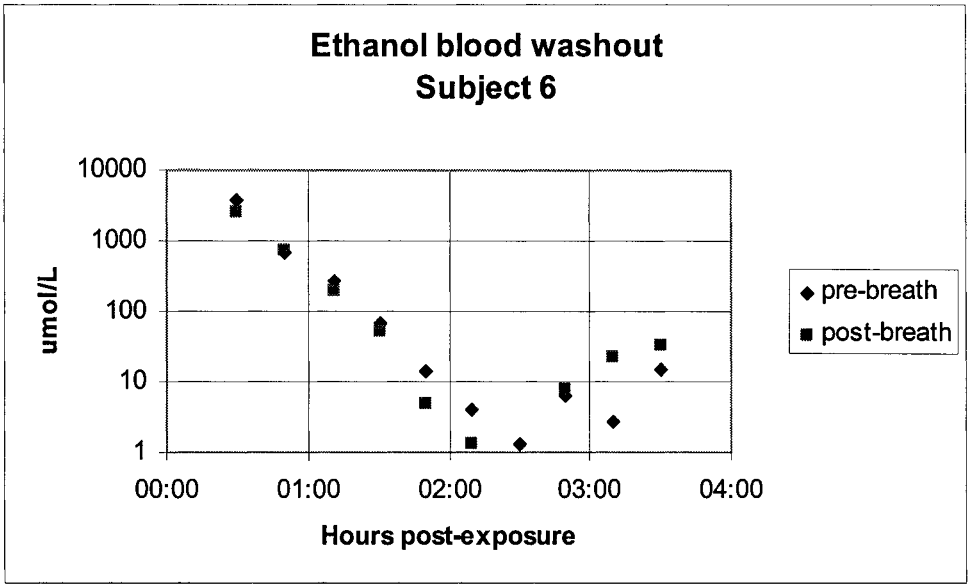

Ethanol mixed-exhaled correlation
CO2 corrected
Subject 5
y = 1063.5x + 126.36
R^2 = 0.9737
Blood umol/L
2500
2000
1500
1000
500
0
0
0.5
1
1.5
2
Breath umol/L

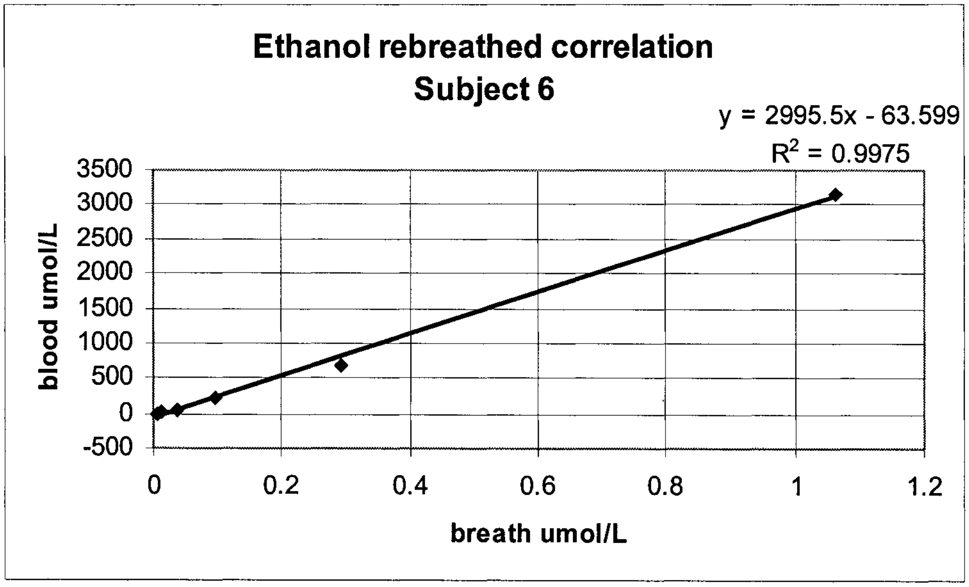

Ethanol breath calibration
Subject 6
y = 1E-05x + 0.0003
R² = 0.9987
umol/L
10.0000
1.0000
0.1000
0.0100
0.0010
100
1000
10000
100000
1000000
Area

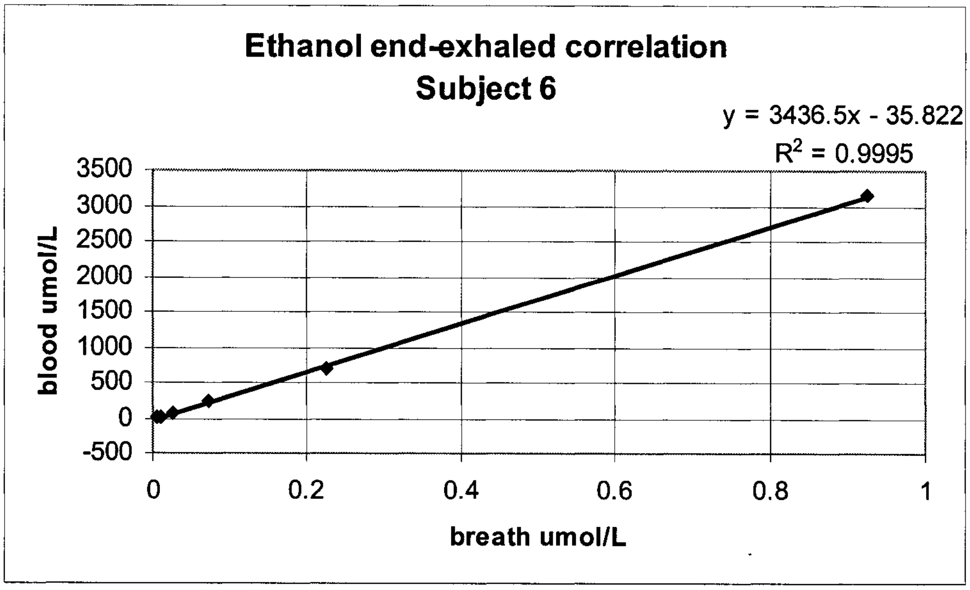
6/18/2003

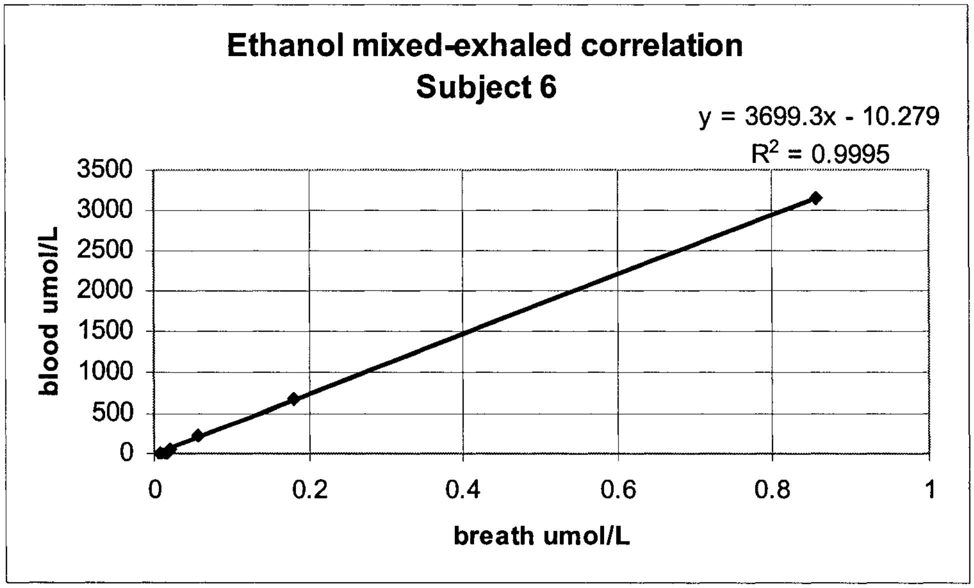

Ethanol blood calibration, weighted
Subject 6
y = 106.4x - 3.61
R2 = 0.9384
umol/L
100000
10000
1000
100
10
1
0.1
0.01
0.1
1
10
100
1000
31 response factor

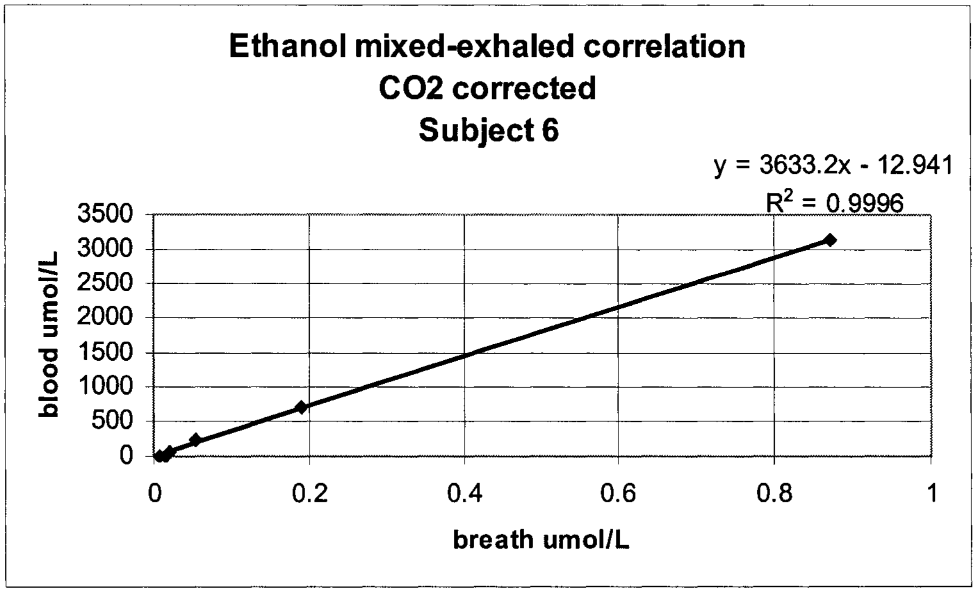

Ethanol breath washout
Subject 6
10
1
0.1
0.01
0.001
umol/L
00:00
01:00
02:00
03:00
04:00
Hours post-exposure
◆ rebreathed
■ end-exhaled
mixed


Ethanol blood washout
Subject 6
10000
1000
100
10
1
umol/L
00:00
01:00
02:00
03:00
04:00
Hours post-exposure
◆ pre-breath
■ post-breath

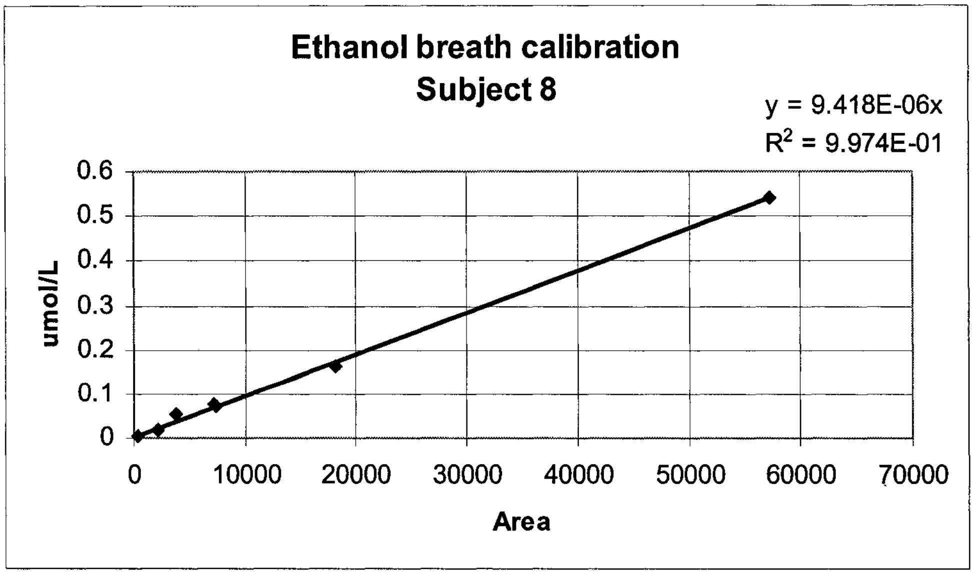

Ethanol rebreathed correlation
Subject 6
y = 2995.5x - 63.599
R2 = 0.9975
blood umol/L
3500
3000
2500
2000
1500
1000
500
0
-500
0
0.2
0.4
0.6
0.8
1
1.2
breath umol/L

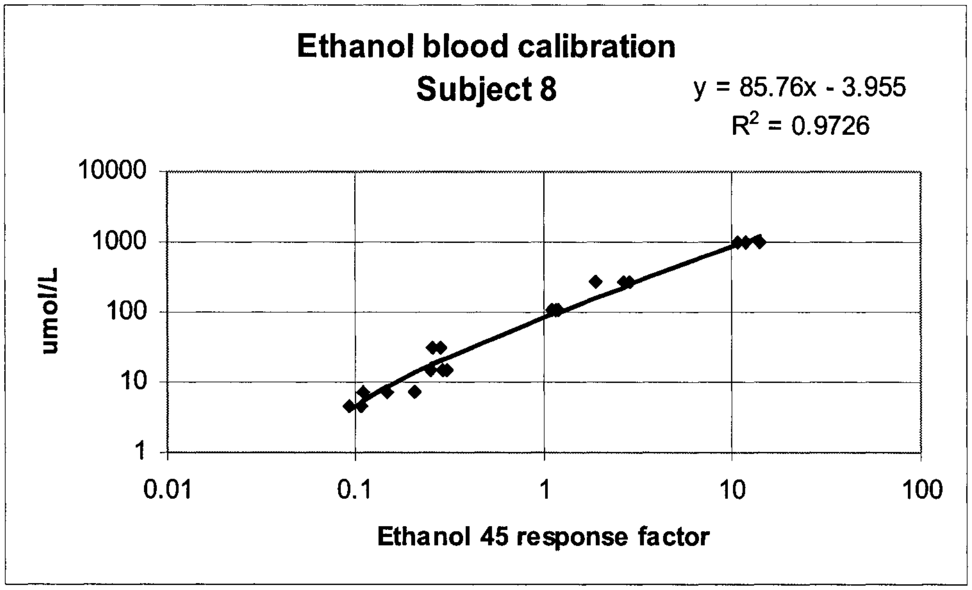

Ethanol end-exhaled correlation
Subject 6
y = 3436.5x - 35.822
R2 = 0.9995
blood umol/L
3500
3000
2500
2000
1500
1000
500
0
-500
0
0.2
0.4
0.6
0.8
1
breath umol/L

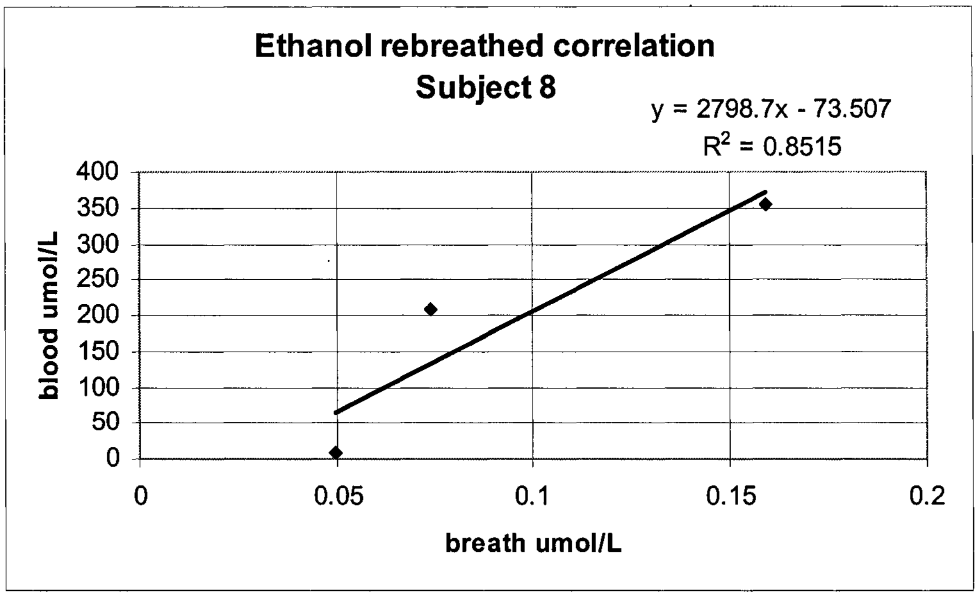

Ethanol mixed-exhaled correlation
Subject 6
y = 3699.3x - 10.279
R^2 = 0.9995
blood umol/L
3500
3000
2500
2000
1500
1000
500
0
0
0.2
0.4
0.6
0.8
1
breath umol/L

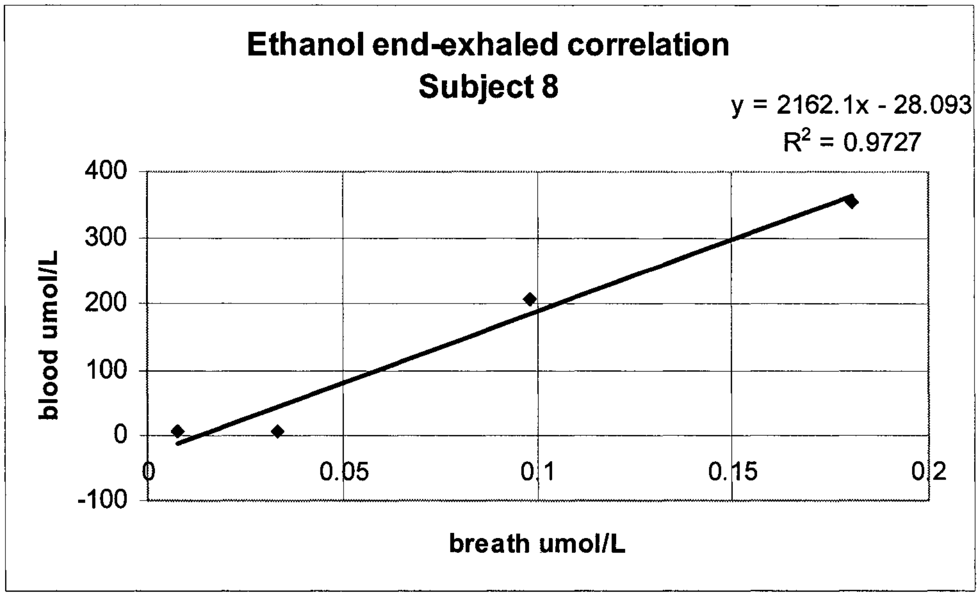

Ethanol mixed-exhaled correlation
CO2 corrected
Subject 6
y = 3633.2x - 12.941
R^2 = 0.9996
blood umol/L
3500
3000
2500
2000
1500
1000
500
0
0
0.2
0.4
0.6
0.8
1
breath umol/L

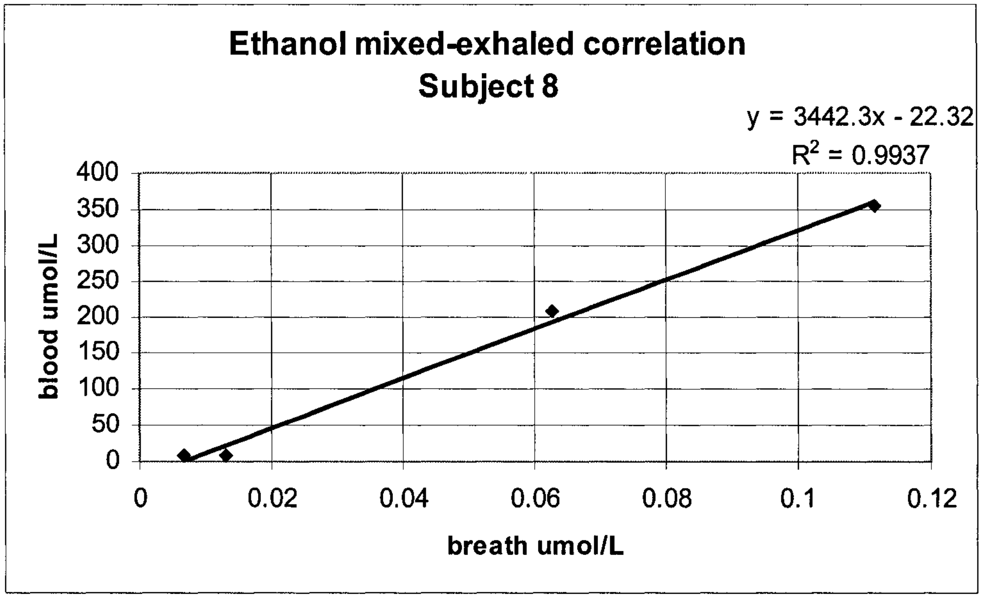
8/6/2003

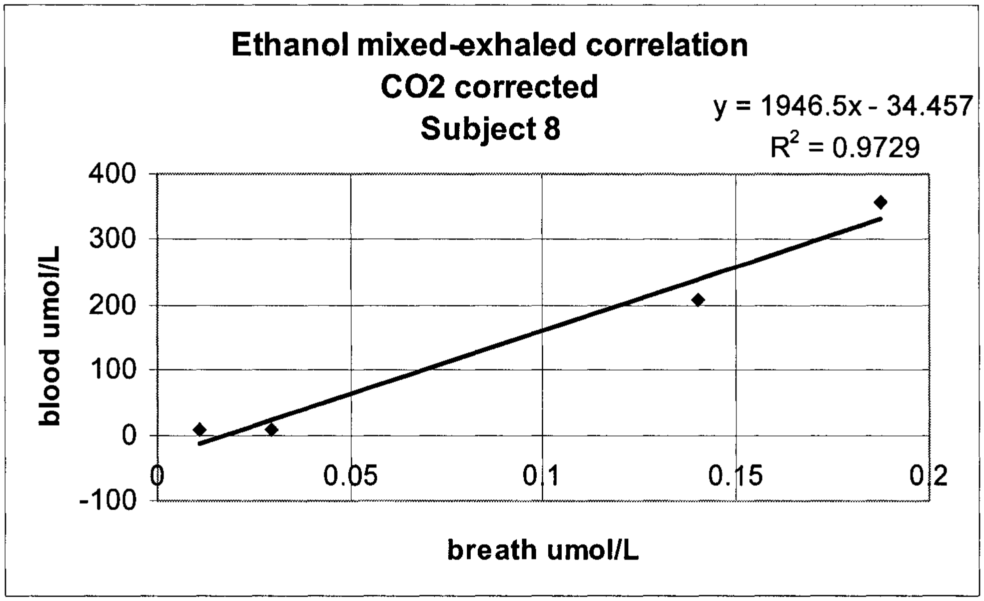

Ethanol breath calibration
Subject 8
y = 9.418E-06x
R² = 9.974E-01
0.6
0.5
0.4
0.3
0.2
0.1
0
umol/L
0
10000
20000
30000
40000
50000
60000
70000
Area


Ethanol blood calibration
Subject 8
y = 85.76x - 3.955
R² = 0.9726
10000
1000
100
10
1
umol/L
0.01
0.1
1
10
100
Ethanol 45 response factor

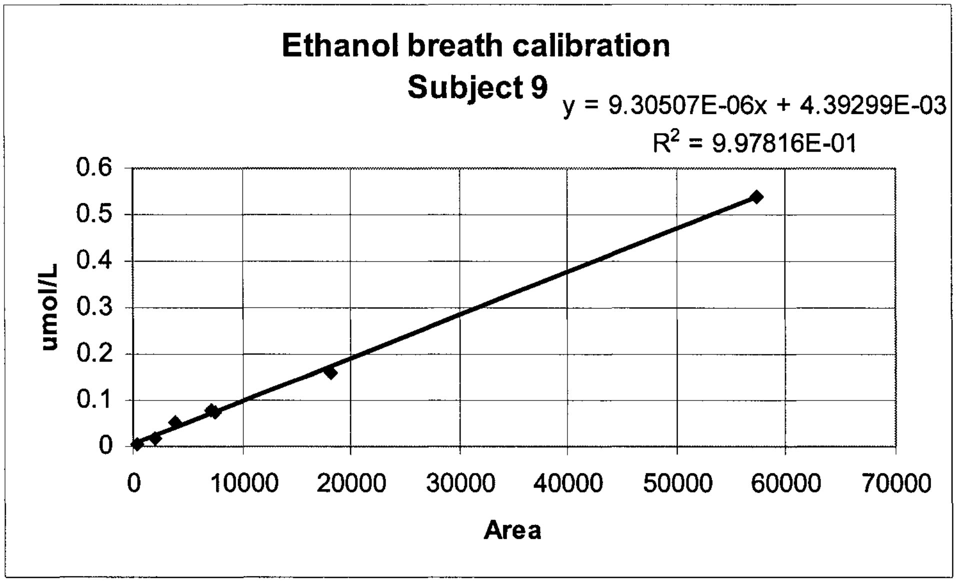

Ethanol rebreathed correlation
Subject 8
y = 2798.7x - 73.507
R^2 = 0.8515
blood umol/L
400
350
300
250
200
150
100
50
0
0
0.05
0.1
0.15
0.2
breath umol/L

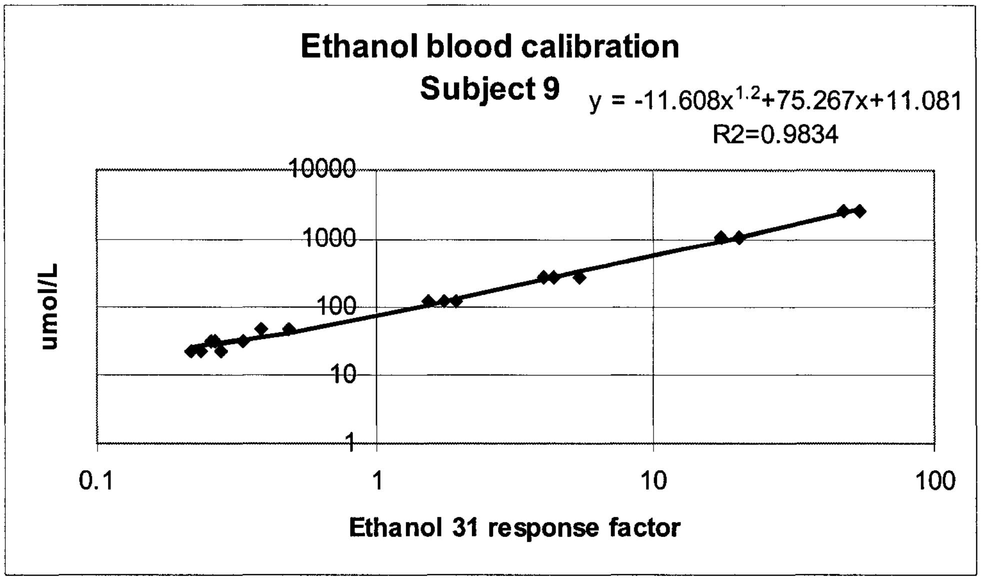

Ethanol end-exhaled correlation
Subject 8
y = 2162.1x - 28.093
R^2 = 0.9727
blood umol/L
400
300
200
100
0
-100
0
0.05
0.1
0.15
0.2
breath umol/L

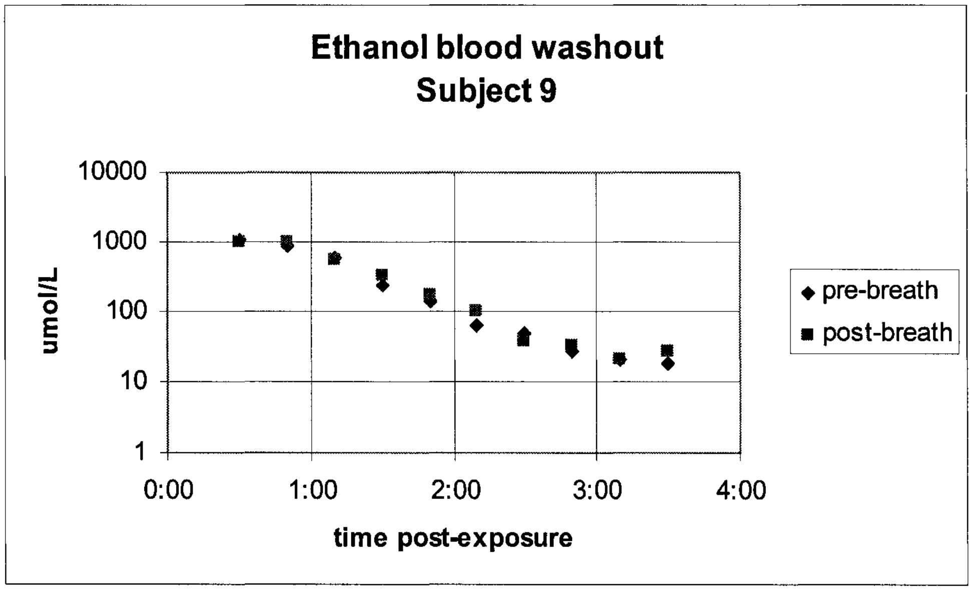

Ethanol mixed-exhaled correlation
Subject 8
y = 3442.3x - 22.32
R^2 = 0.9937
blood umol/L
400
350
300
250
200
150
100
50
0
0
0.02
0.04
0.06
0.08
0.1
0.12
breath umol/L

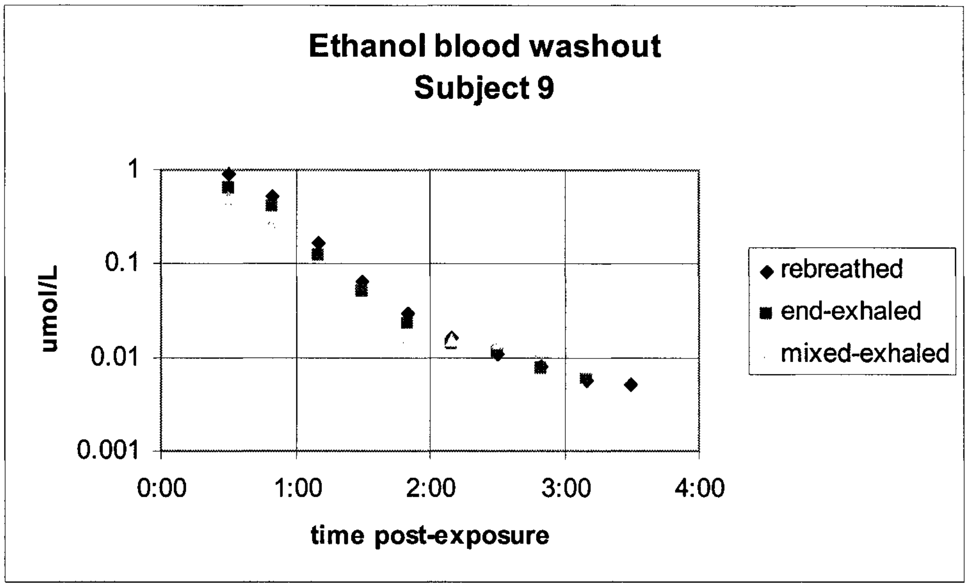

Ethanol mixed-exhaled correlation
CO2 corrected
Subject 8
y = 1946.5x - 34.457
R^2 = 0.9729
blood umol/L
400
300
200
100
0
-100
0
0.05
0.1
0.15
0.2
breath umol/L

8/11/2003

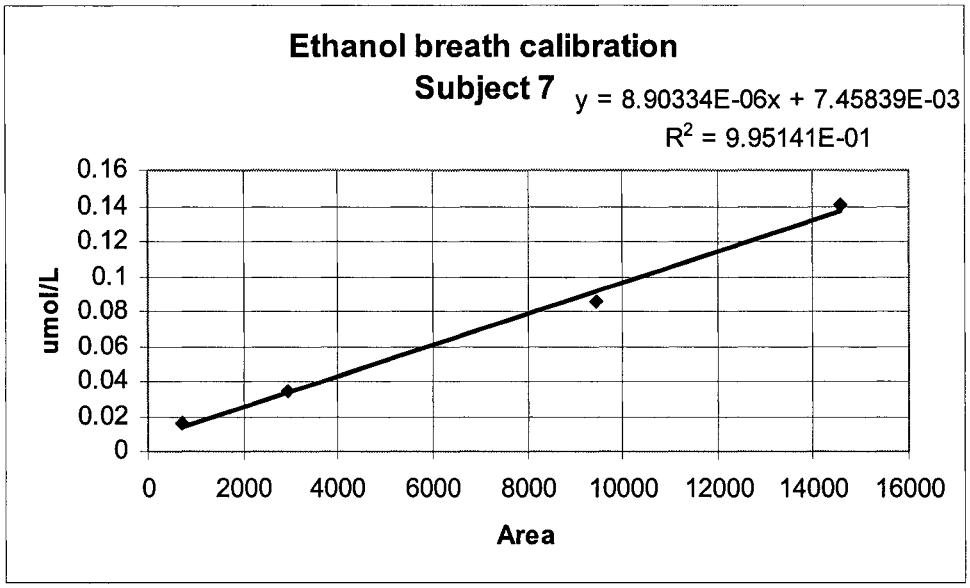

Ethanol breath calibration
Subject 9
y = 9.30507E-06x + 4.39299E-03
R2 = 9.97816E-01
umol/L
0.6
0.5
0.4
0.3
0.2
0.1
0
0
10000
20000
30000
40000
50000
60000
70000
Area

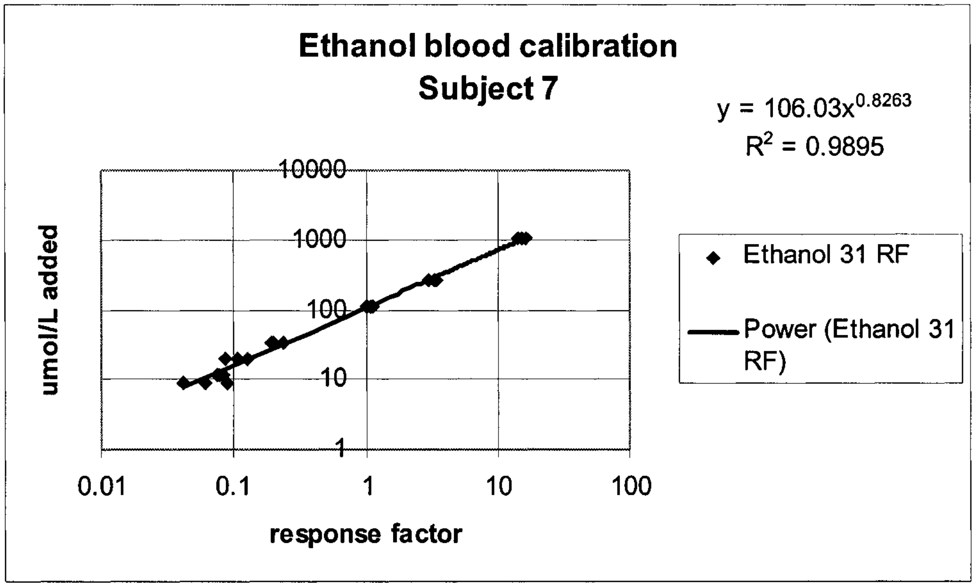

Ethanol blood calibration
Subject 9
y = -11.608x1.2+75.267x+11.081
R2=0.9834
umol/L
10000
1000
100
10
1
0.1
1
10
100
Ethanol 31 response factor

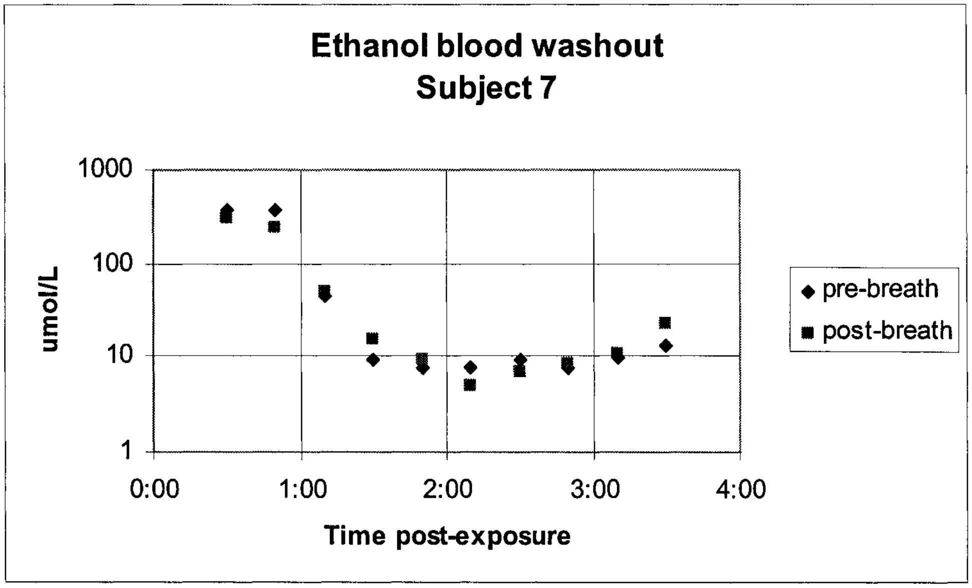

Ethanol blood washout
Subject 9
10000
1000
100
10
1
umol/L
0:00
1:00
2:00
3:00
4:00
time post-exposure
◆ pre-breath
■ post-breath

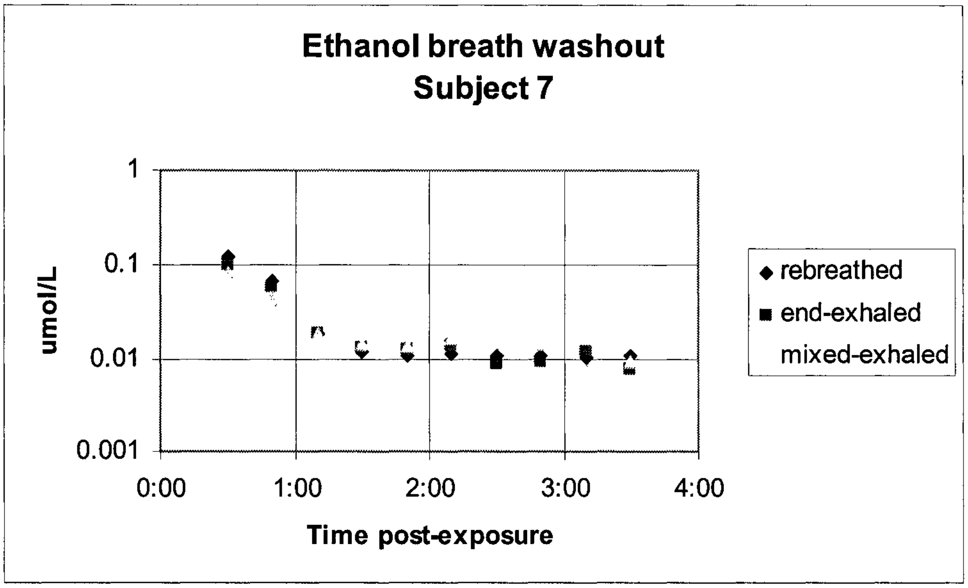

Ethanol blood washout
Subject 9
1
0.1
0.01
0.001
umol/L
0:00
1:00
2:00
3:00
4:00
time post-exposure
◆ rebreathed
■ end-exhaled
mixed-exhaled

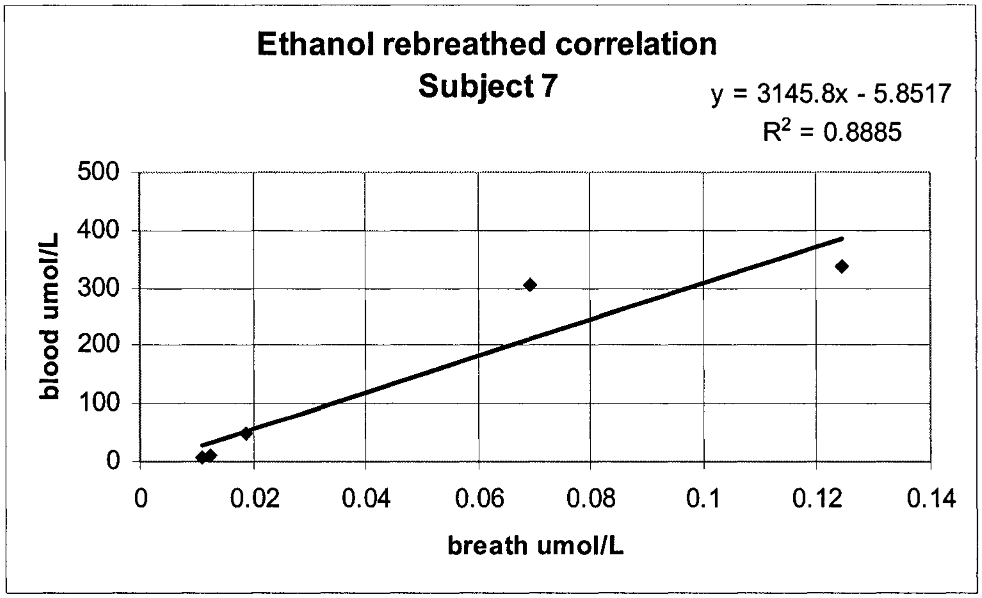
8/21/2003

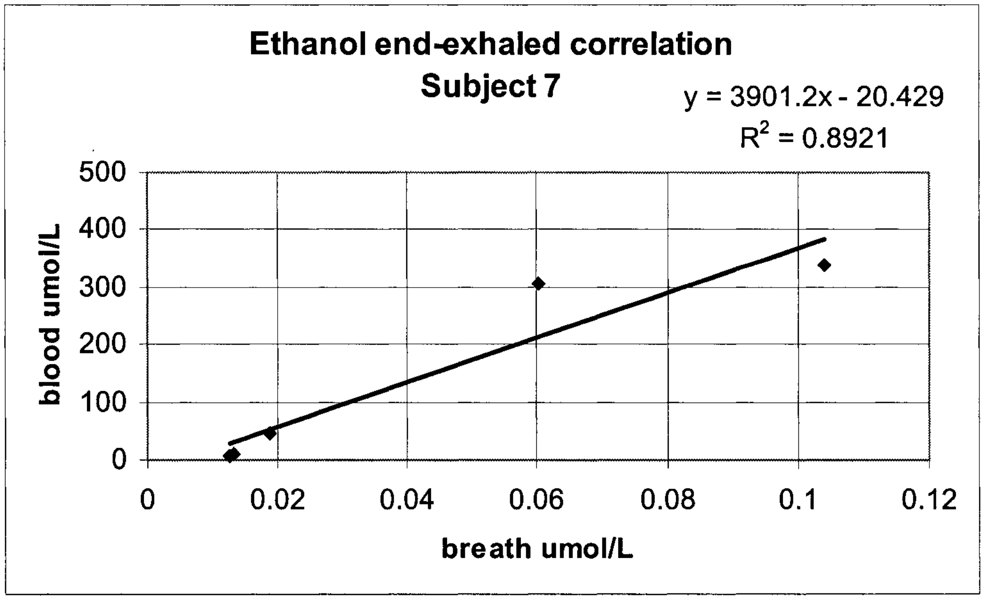

Ethanol breath calibration
Subject 7
y = 8.90334E-06x + 7.45839E-03
R² = 9.95141E-01
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
0
umol/L
0
2000
4000
6000
8000
10000
12000
14000
16000
Area

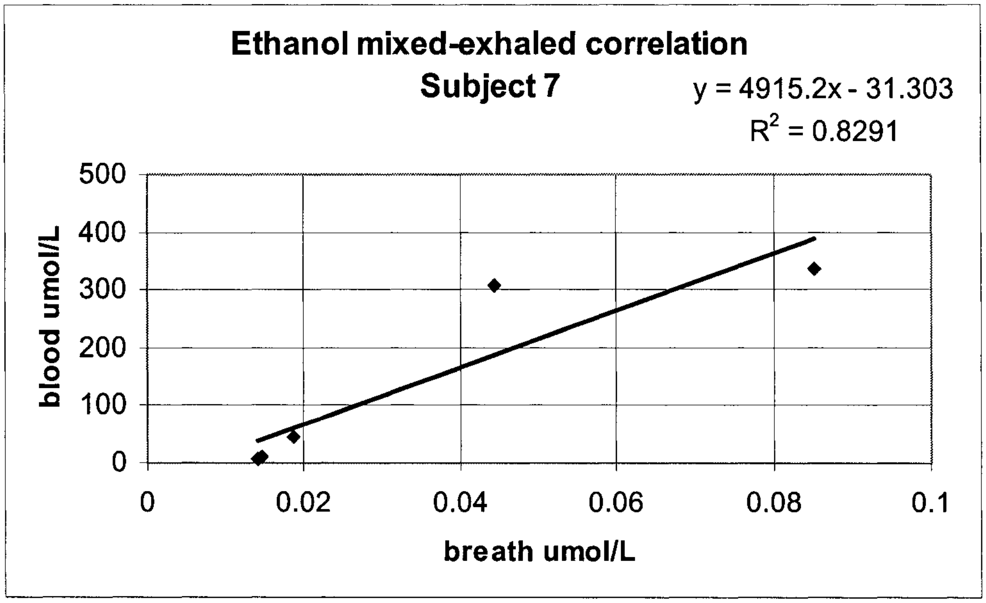

Ethanol blood calibration
Subject 7
y = 106.03x^0.8263
R² = 0.9895
10000
1000
100
10
1
umol/L added
0.01
0.1
1
10
100
response factor
Ethanol 31 RF
Power (Ethanol 31 RF)

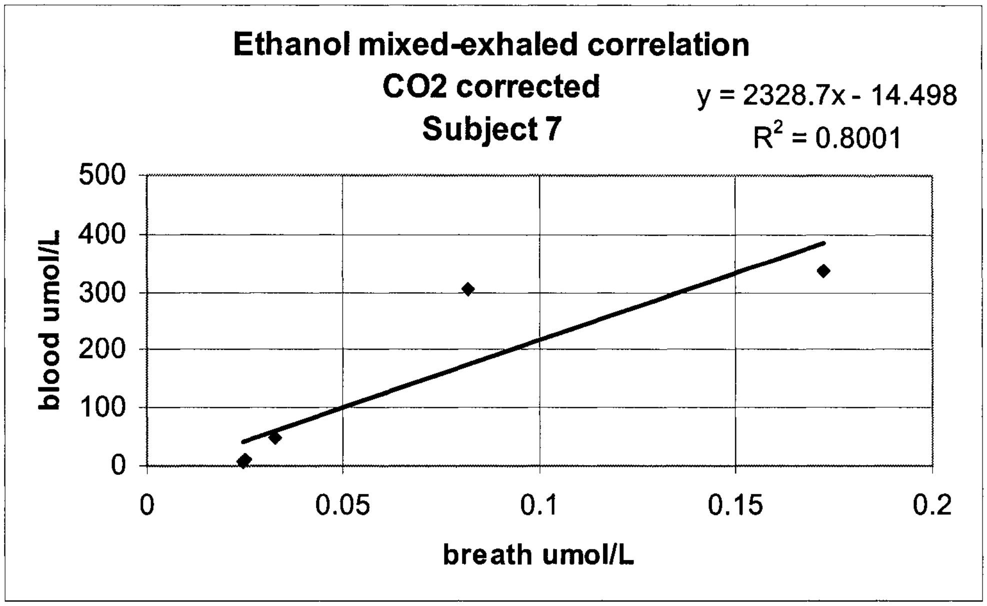

Ethanol blood washout
Subject 7
1000
100
10
1
umol/L
0:00
1:00
2:00
3:00
4:00
Time post-exposure
◆ pre-breath
■ post-breath


Ethanol breath washout
Subject 7
1
0.1
0.01
0.001
umol/L
0:00
1:00
2:00
3:00
4:00
Time post-exposure
◆ rebreathed
■ end-exhaled
mixed-exhaled

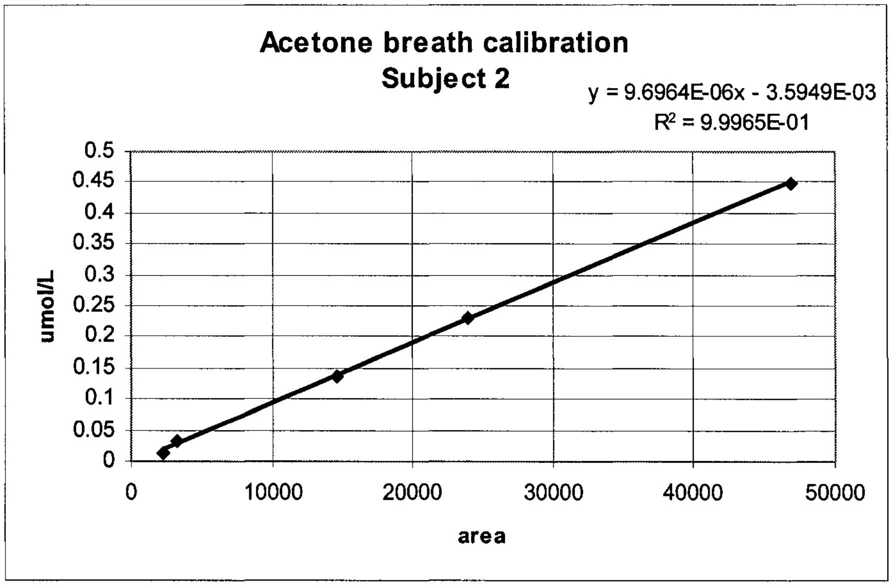

Ethanol rebreathed correlation
Subject 7
y = 3145.8x - 5.8517
R2 = 0.8885
blood umol/L
500
400
300
200
100
0
0
0.02
0.04
0.06
0.08
0.1
0.12
0.14
breath umol/L

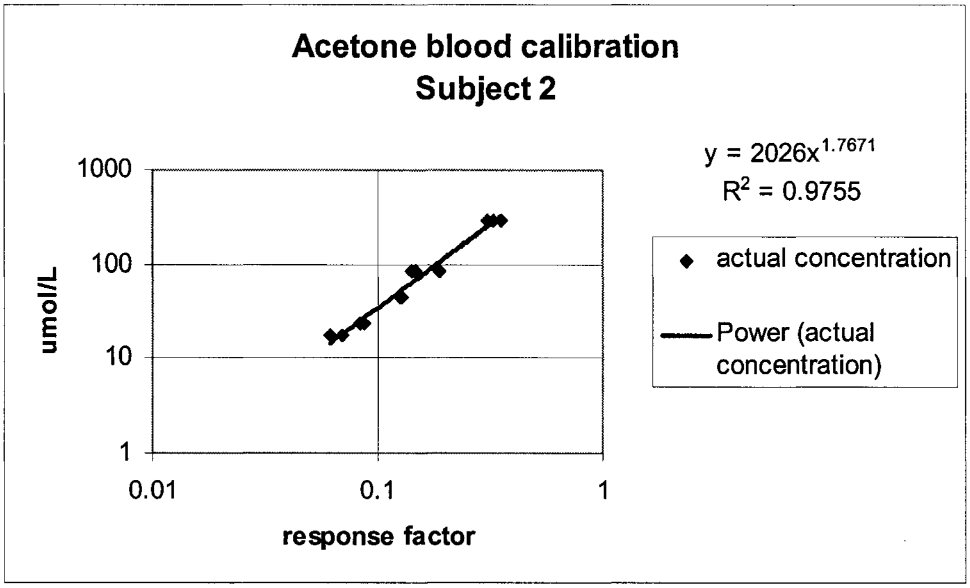

Ethanol end-exhaled correlation
Subject 7
y = 3901.2x - 20.429
R2 = 0.8921
blood umol/L
500
400
300
200
100
0
0
0.02
0.04
0.06
0.08
0.1
0.12
breath umol/L

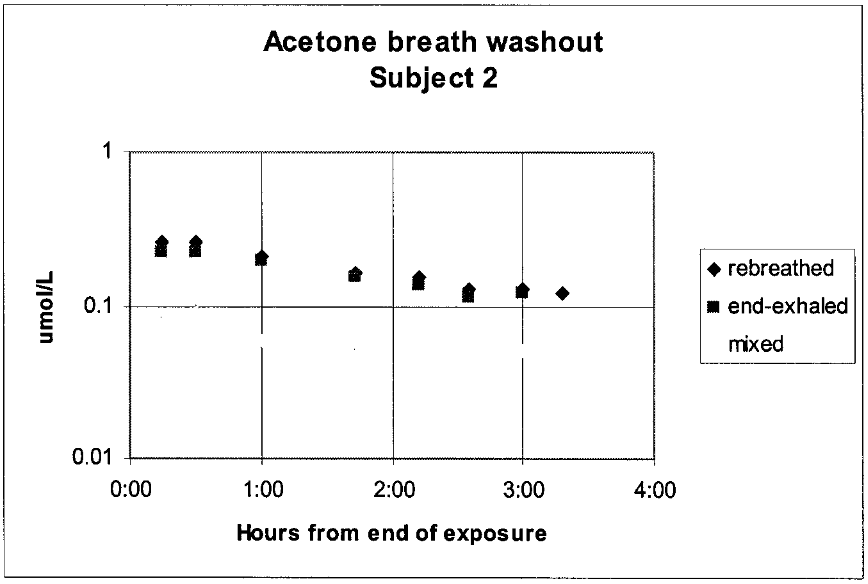


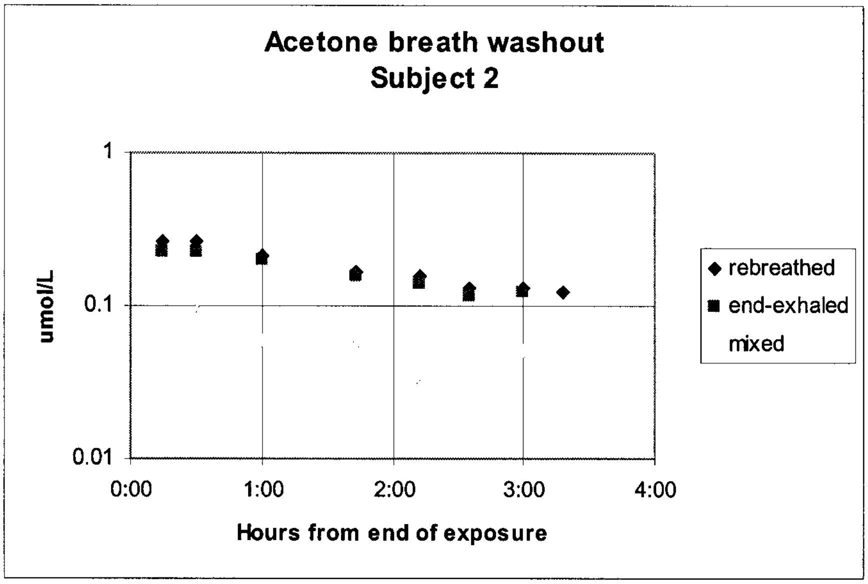


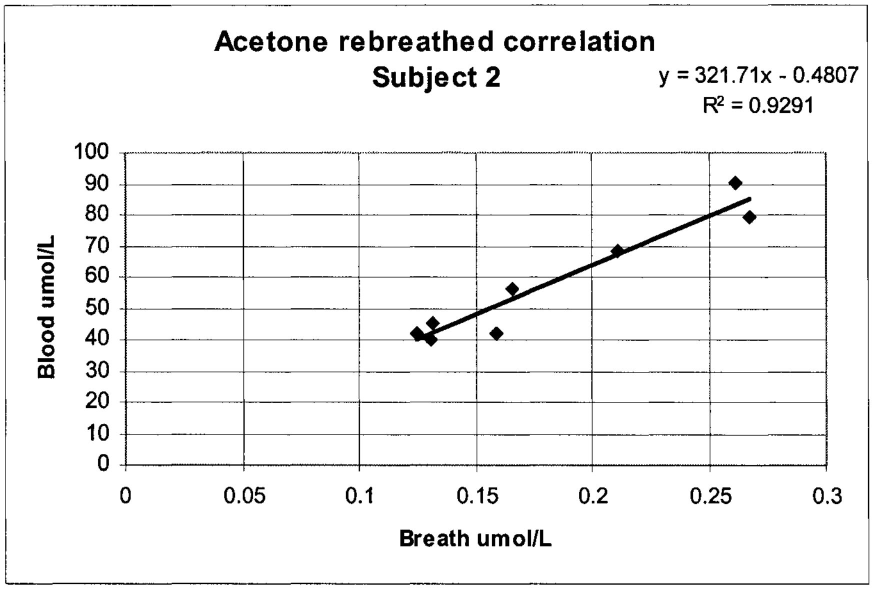
Acetone
1/24/03

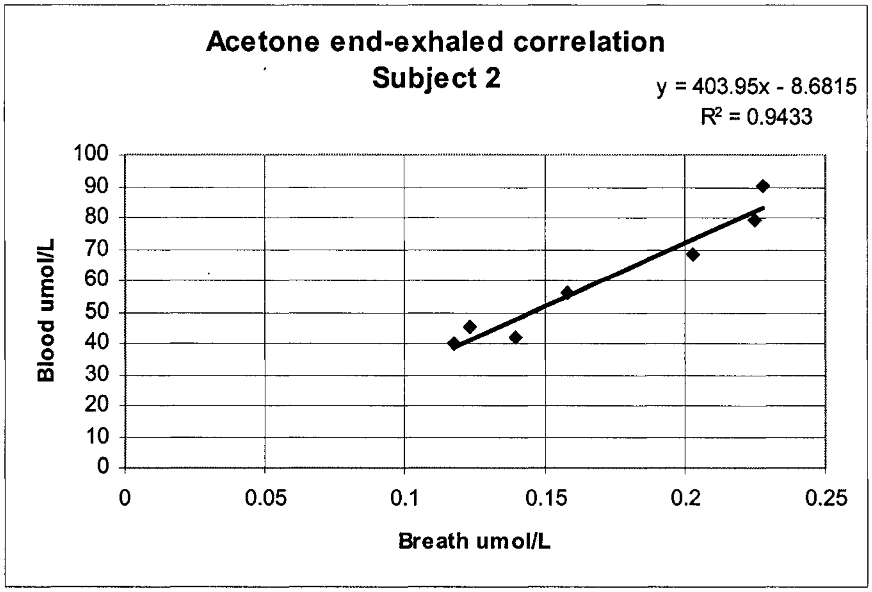

Acetone breath calibration
Subject 2
y = 9.6964E-06x - 3.5949E-03
R² = 9.9965E-01
umol/L
0.5
0.45
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
0
10000
20000
30000
40000
50000
area

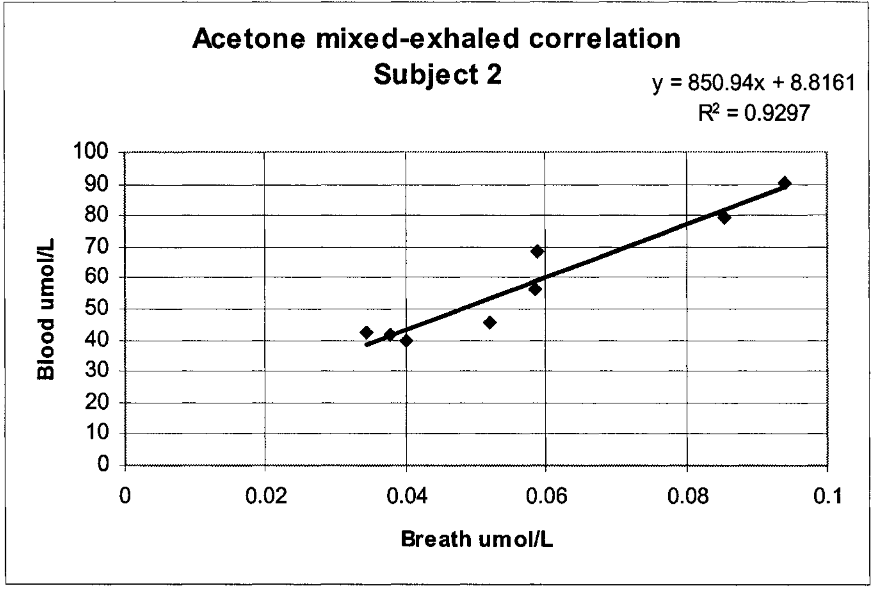

Acetone blood calibration
Subject 2
y = 2026x^1.7671
R² = 0.9755
◆ actual concentration
Power (actual concentration)
umol/L
1000
100
10
1
0.01
0.1
1
response factor

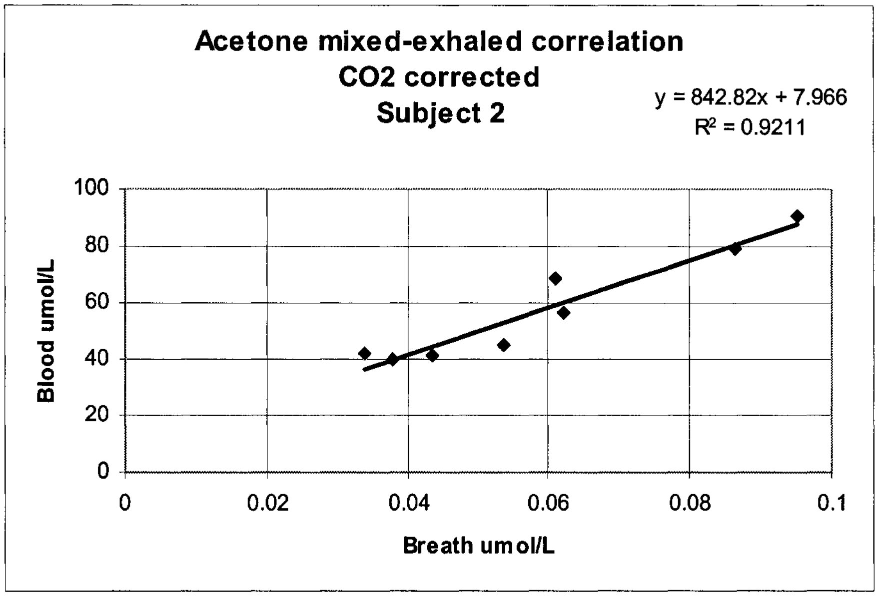

Acetone breath washout
Subject 2
1
0.1
0.01
umol/L
0:00
1:00
2:00
3:00
4:00
Hours from end of exposure
◆ rebreathed
■ end-exhaled
mixed

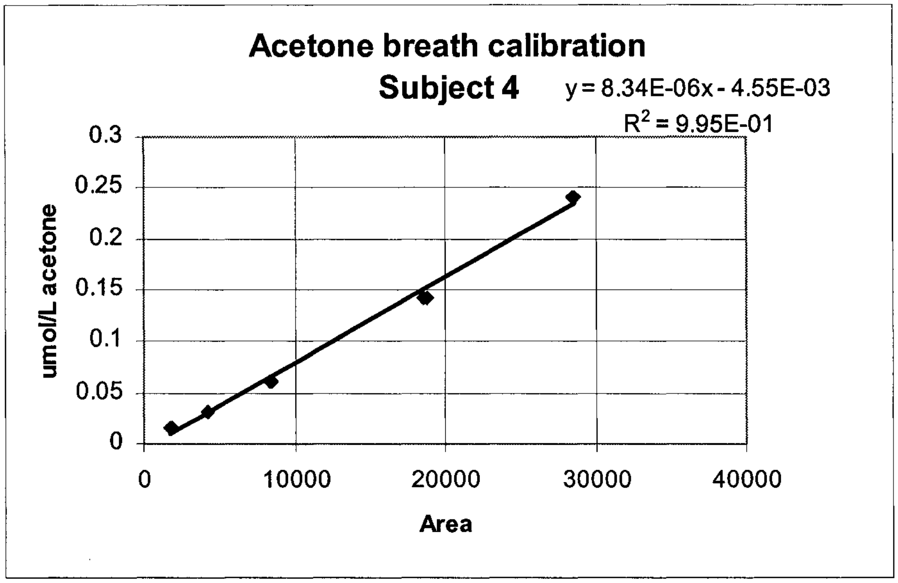

Acetone breath washout
Subject 2
1
0.1
0.01
umol/L
0:00
1:00
2:00
3:00
4:00
Hours from end of exposure
◆ rebreathed
■ end-exhaled
mixed

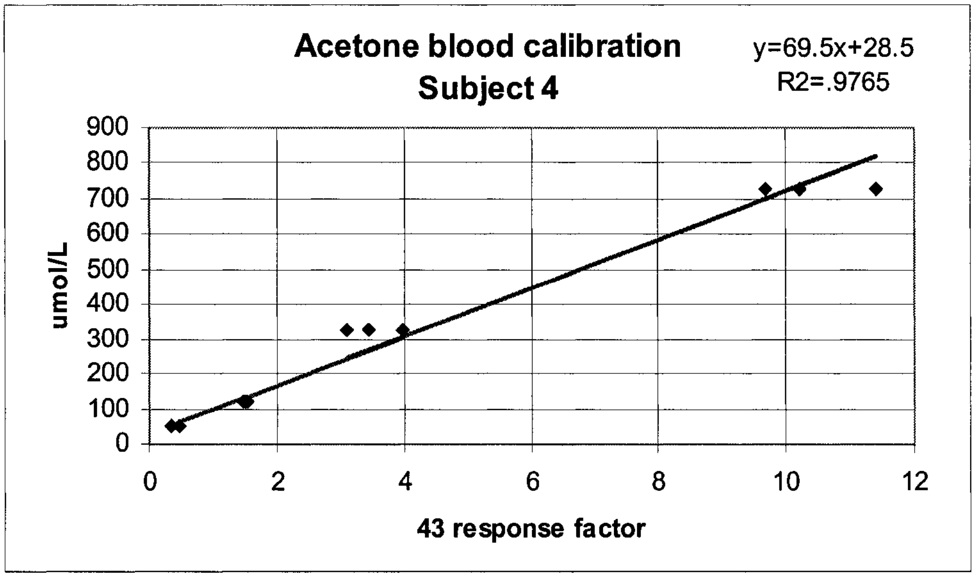

Acetone rebreathed correlation
Subject 2
y = 321.71x - 0.4807
R² = 0.9291
Blood umol/L
100
90
80
70
60
50
40
30
20
10
0
0
0.05
0.1
0.15
0.2
0.25
0.3
Breath umol/L

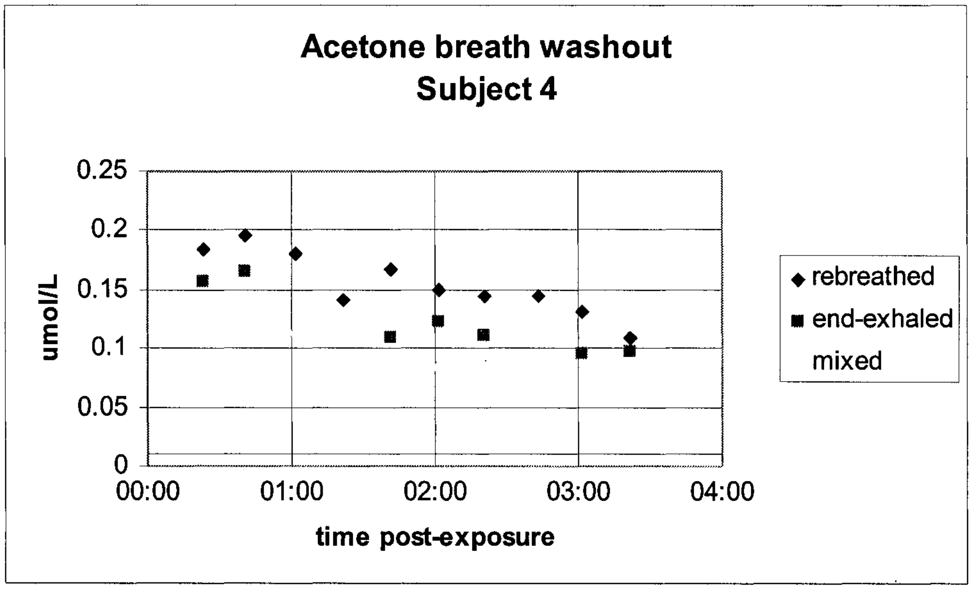

Acetone end-exhaled correlation
Subject 2
y = 403.95x - 8.6815
R² = 0.9433
Blood umol/L
100
90
80
70
60
50
40
30
20
10
0
0
0.05
0.1
0.15
0.2
0.25
Breath umol/L

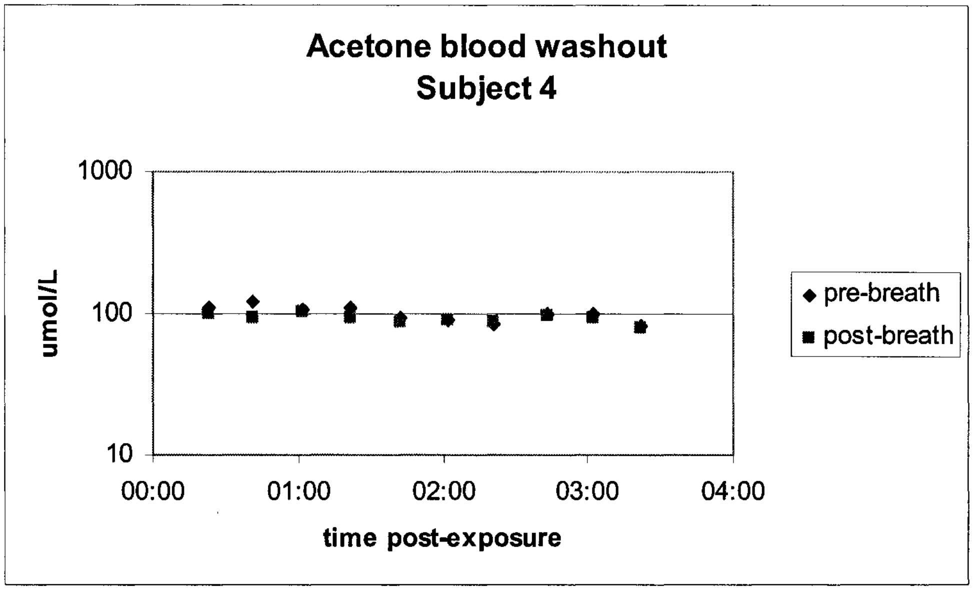

Acetone mixed-exhaled correlation
Subject 2
y = 850.94x + 8.8161
R² = 0.9297
Blood umol/L
100
90
80
70
60
50
40
30
20
10
0
0
0.02
0.04
0.06
0.08
0.1
Breath umol/L

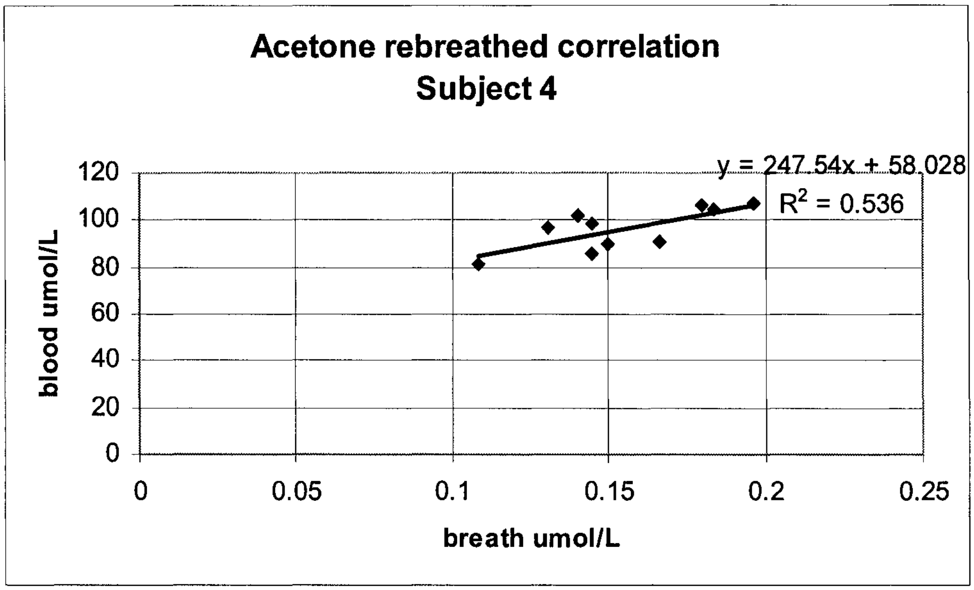

Acetone mixed-exhaled correlation
CO2 corrected
Subject 2
y = 842.82x + 7.966
R² = 0.9211
Blood umol/L
100
80
60
40
20
0
0
0.02
0.04
0.06
0.08
0.1
Breath umol/L

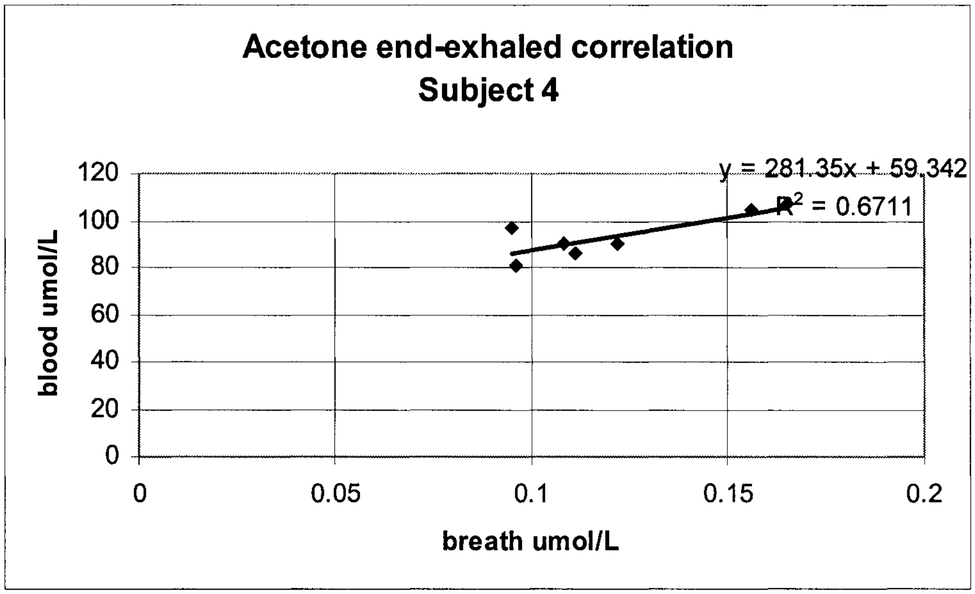

Acetone breath calibration
Subject 4
y = 8.34E-06x - 4.55E-03
R^2 = 9.95E-01
umol/L acetone
0.3
0.25
0.2
0.15
0.1
0.05
0
0
10000
20000
30000
40000
Area

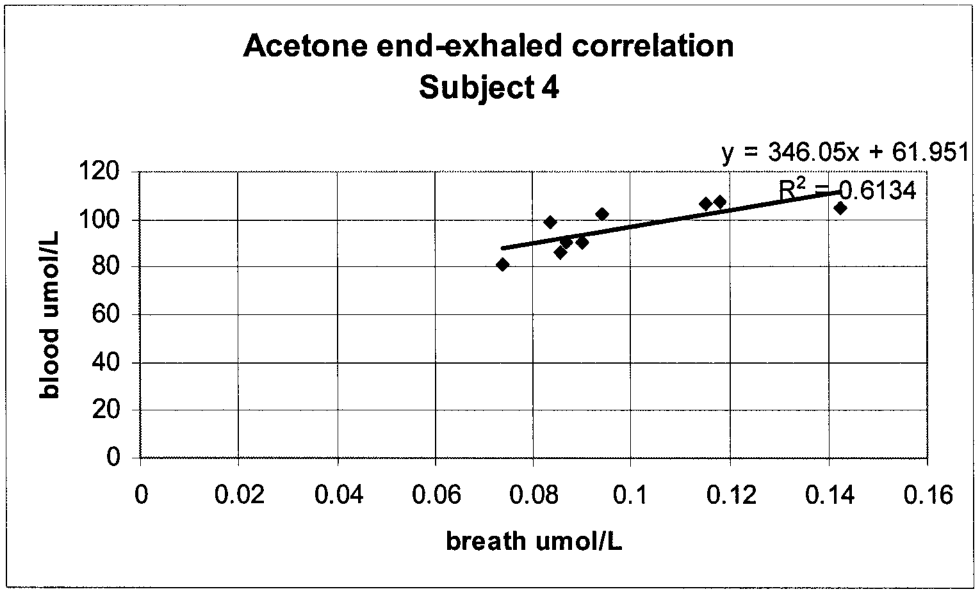

Acetone blood calibration
Subject 4
y=69.5x+28.5
R2=.9765
umol/L
900
800
700
600
500
400
300
200
100
0
0
2
4
6
8
10
12
43 response factor

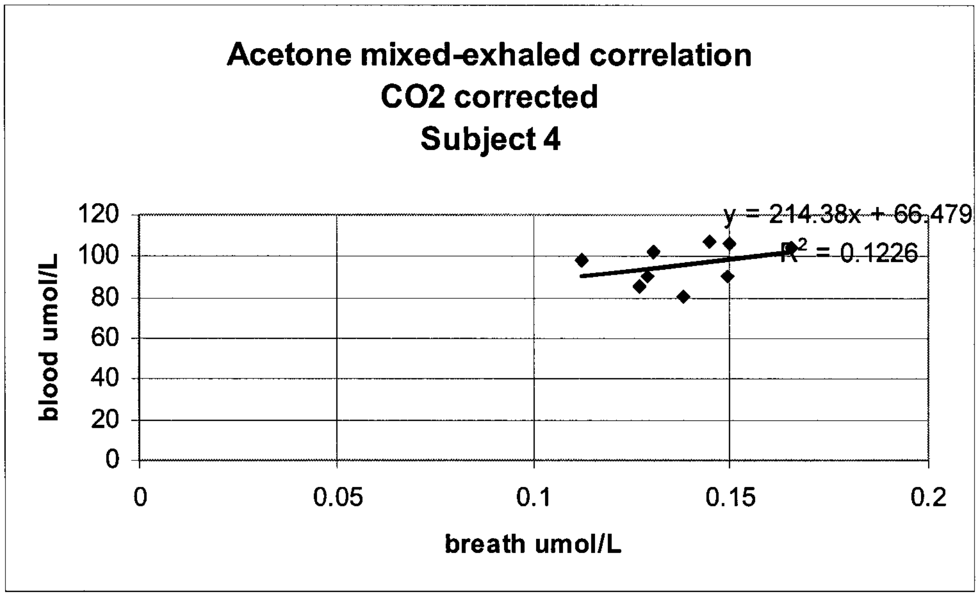

Acetone breath washout
Subject 4
0.25
0.2
0.15
0.1
0.05
0
umol/L
00:00
01:00
02:00
03:00
04:00
time post-exposure
◆ rebreathed
■ end-exhaled
mixed

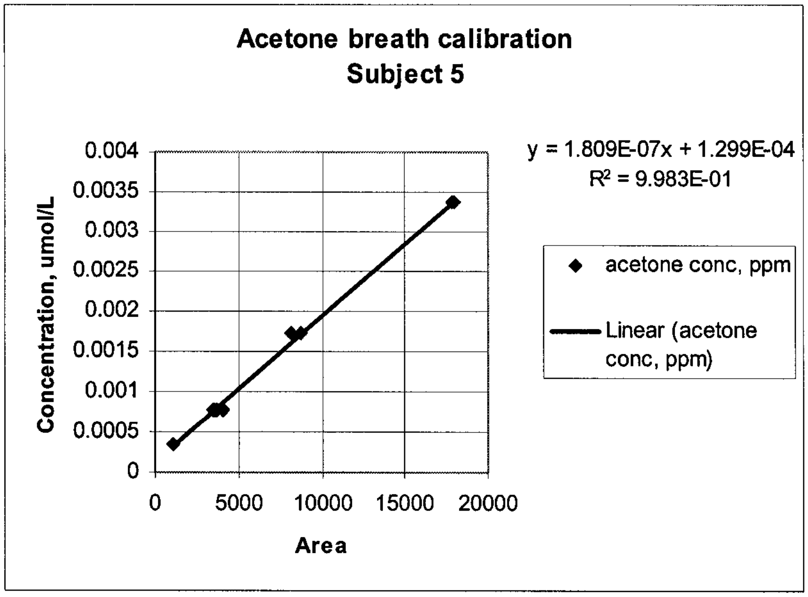

Acetone blood washout
Subject 4
1000
100
10
umol/L
00:00
01:00
02:00
03:00
04:00
time post-exposure
◆ pre-breath
■ post-breath

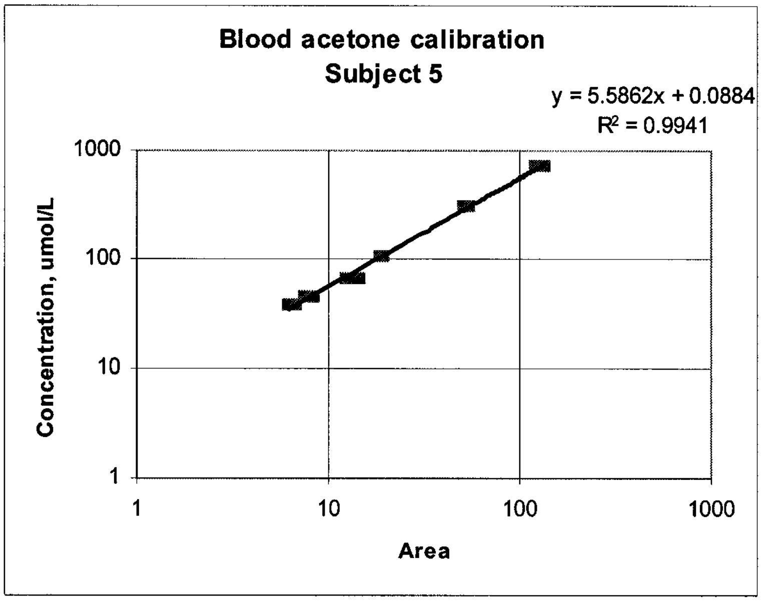

Acetone rebreathed correlation
Subject 4
y = 247.54x + 58.028
R2 = 0.536
blood umol/L
120
100
80
60
40
20
0
0
0.05
0.1
0.15
0.2
0.25
breath umol/L

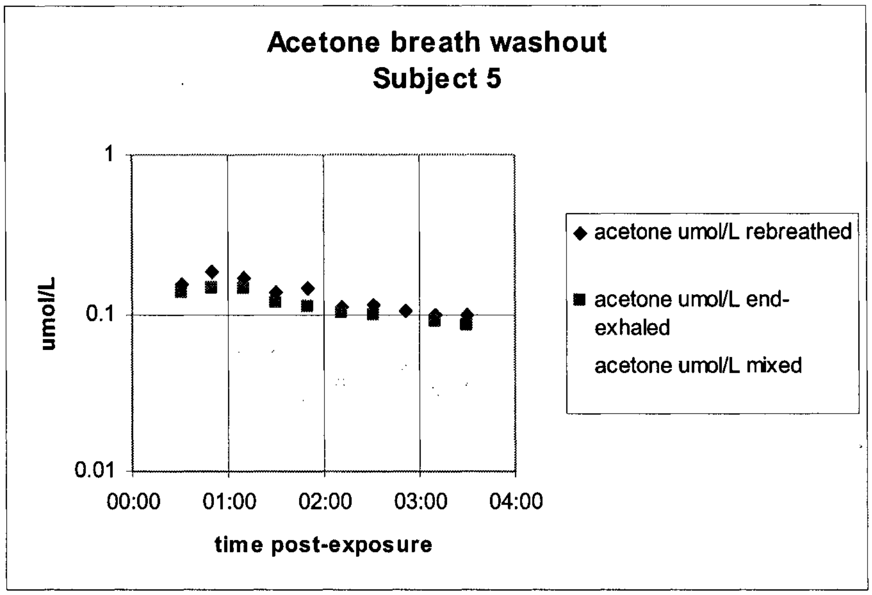

Acetone end-exhaled correlation
Subject 4
y = 281.35x + 59.342
R2 = 0.6711
blood umol/L
120
100
80
60
40
20
0
0
0.05
0.1
0.15
0.2
breath umol/L

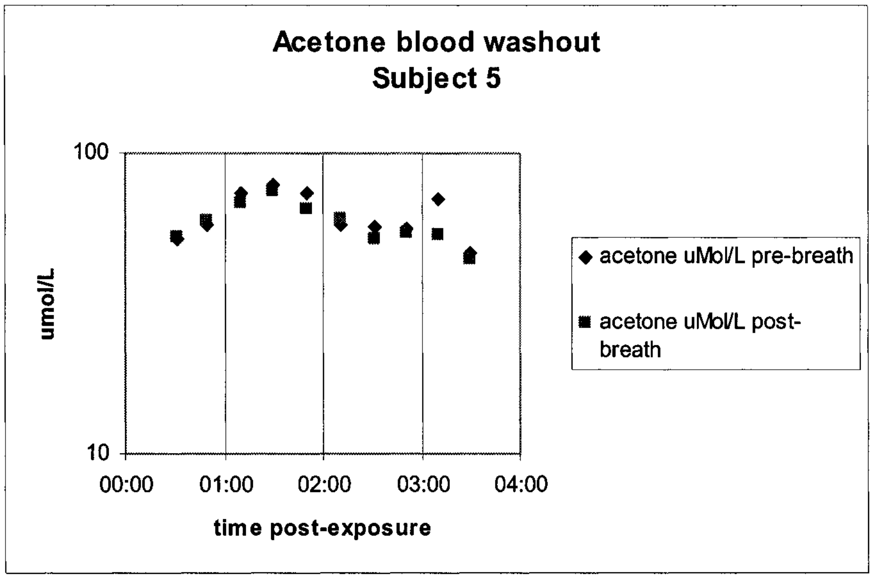

Acetone end-exhaled correlation
Subject 4
y = 346.05x + 61.951
R² = 0.6134
blood umol/L
120
100
80
60
40
20
0
0
0.02
0.04
0.06
0.08
0.1
0.12
0.14
0.16
breath umol/L

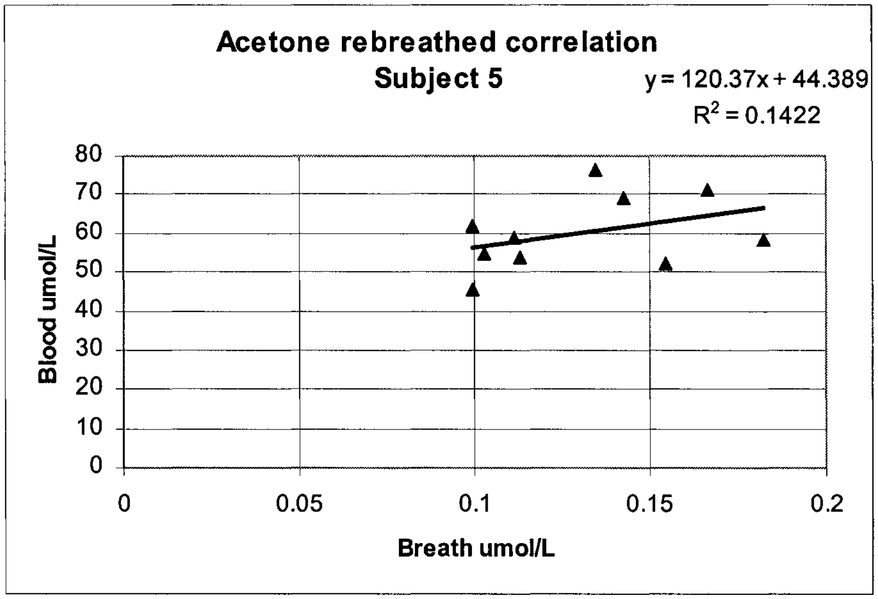

Acetone mixed-exhaled correlation
CO2 corrected
Subject 4
y = 214.38x + 66.479
R² = 0.1226
blood umol/L
120
100
80
60
40
20
0
0
0.05
0.1
0.15
0.2
breath umol/L

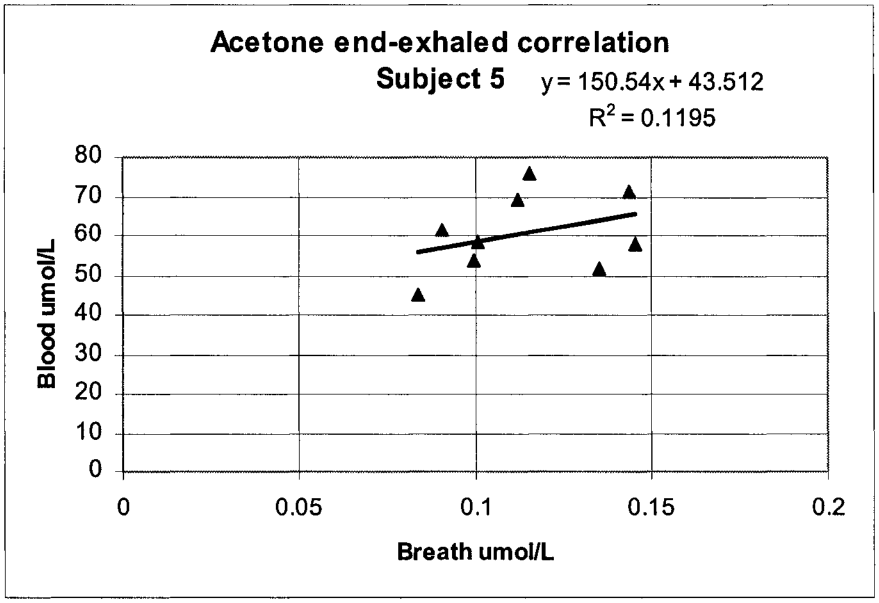

Acetone breath calibration
Subject 5
y = 1.809E-07x + 1.299E-04
R² = 9.983E-01
◆ acetone conc, ppm
Linear (acetone conc, ppm)
Concentration, umol/L
0.004
0.0035
0.003
0.0025
0.002
0.0015
0.001
0.0005
0
0
5000
10000
15000
20000
Area

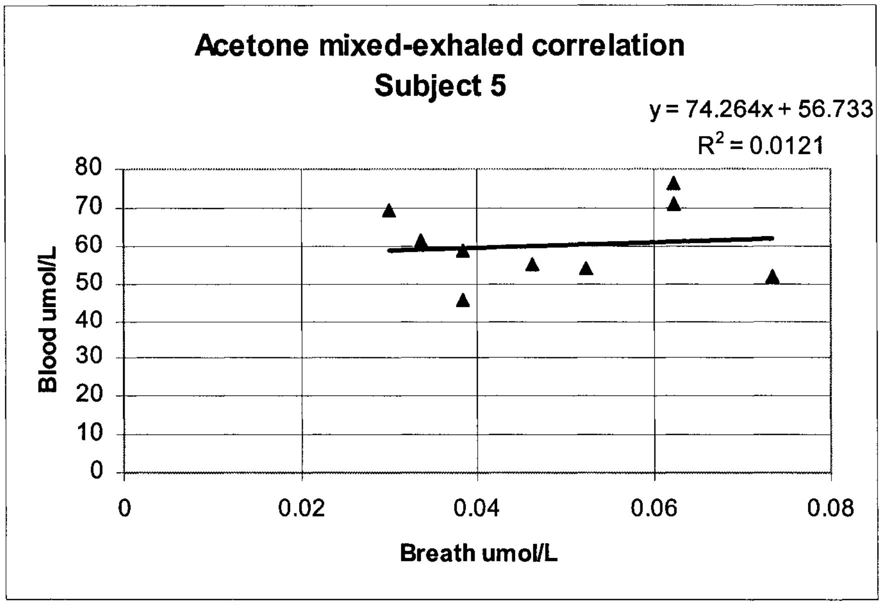

Blood acetone calibration
Subject 5
y = 5.5862x + 0.0884
R² = 0.9941
Concentration, umol/L
1000
100
10
1
1
10
100
1000
Area

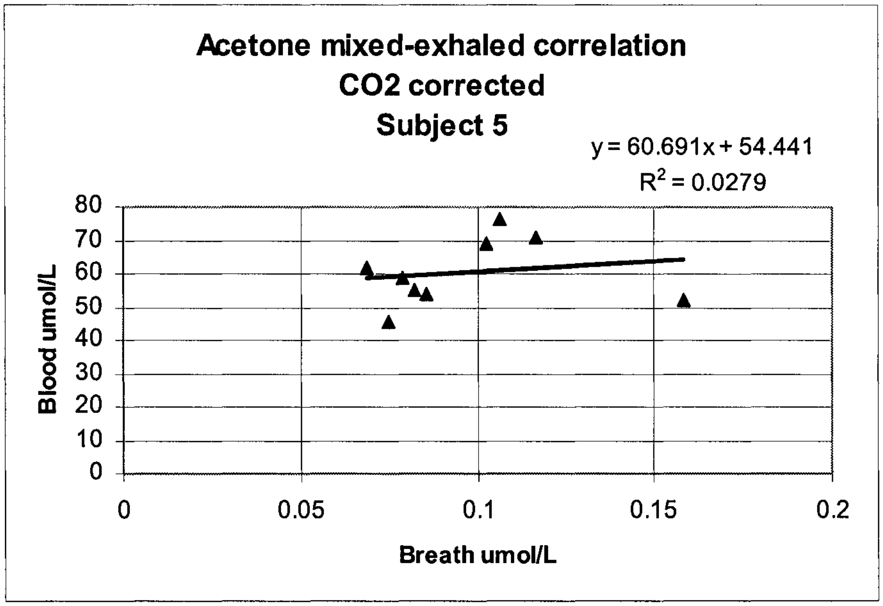

Acetone breath washout
Subject 5
1
0.1
0.01
umol/L
00:00
01:00
02:00
03:00
04:00
time post-exposure
◆ acetone umol/L rebreathed
■ acetone umol/L end-exhaled
acetone umol/L mixed

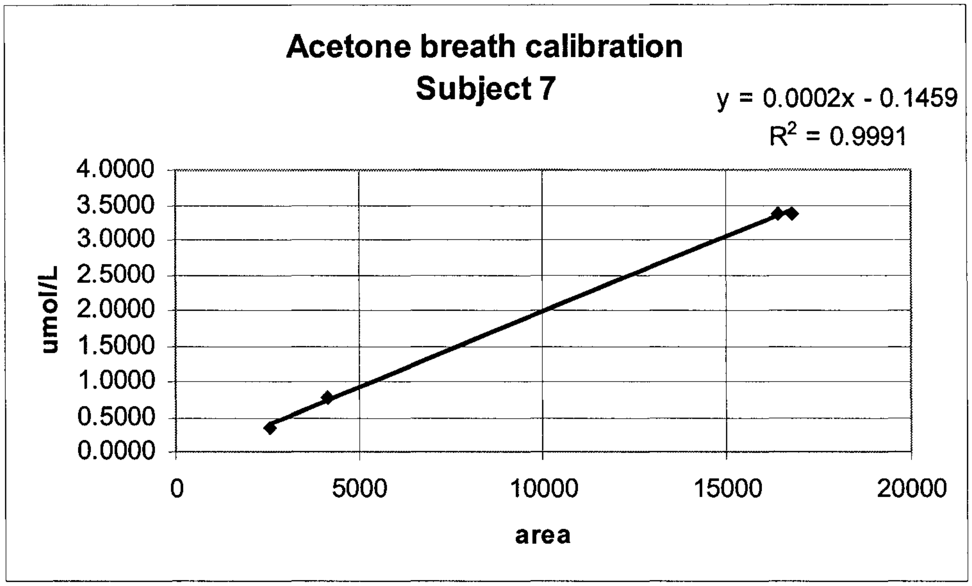

Acetone blood washout
Subject 5
100
10
umol/L
00:00
01:00
02:00
03:00
04:00
time post-exposure
◆ acetone uMol/L pre-breath
■ acetone uMol/L post-breath

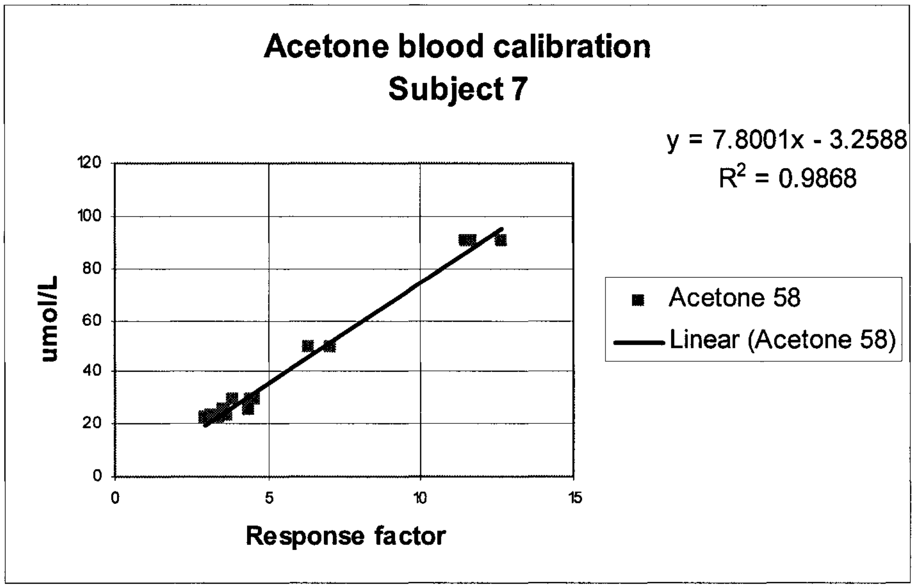

Acetone rebreathed correlation
Subject 5
y = 120.37x + 44.389
R² = 0.1422
Blood umol/L
80
70
60
50
40
30
20
10
0
0
0.05
0.1
0.15
0.2
Breath umol/L

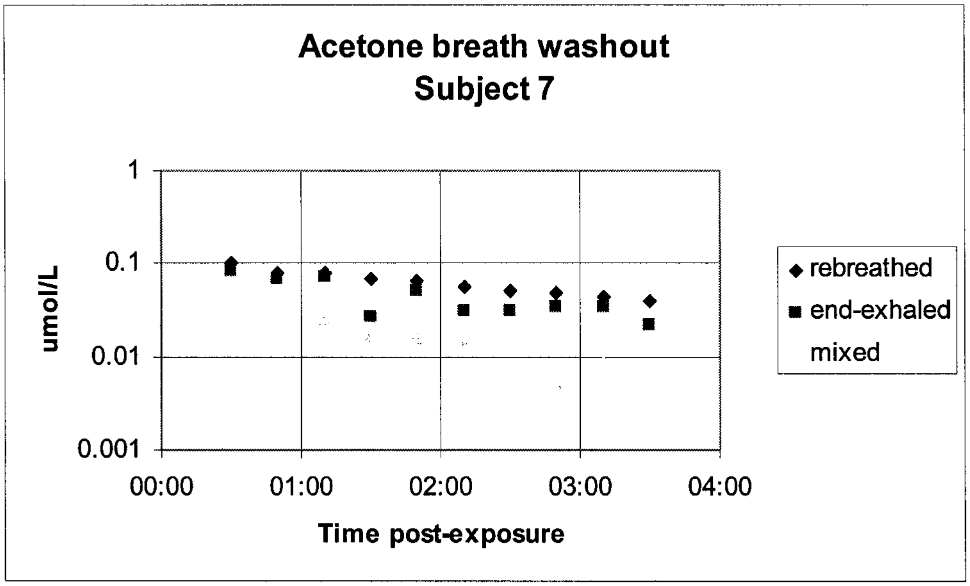

Acetone end-exhaled correlation
Subject 5
y = 150.54x + 43.512
R² = 0.1195
Blood umol/L
80
70
60
50
40
30
20
10
0
0
0.05
0.1
0.15
0.2
Breath umol/L

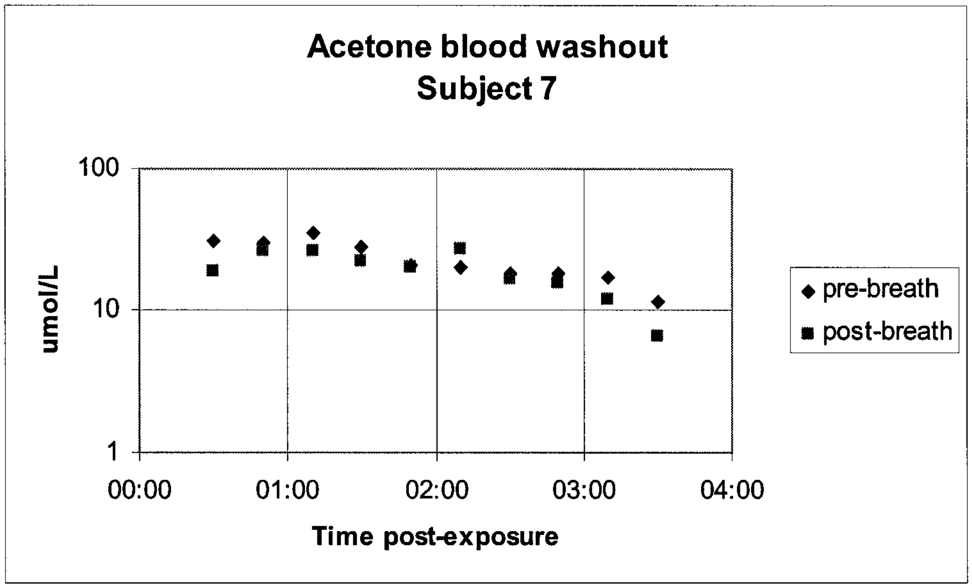

Acetone mixed-exhaled correlation
Subject 5
y = 74.264x + 56.733
R² = 0.0121
Blood umol/L
80
70
60
50
40
30
20
10
0
0
0.02
0.04
0.06
0.08
Breath umol/L

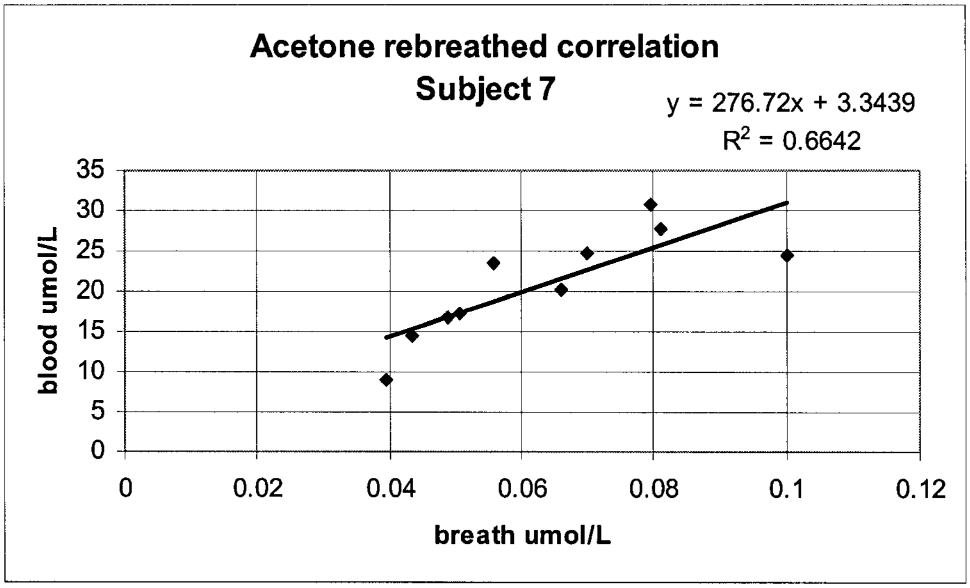

Acetone mixed-exhaled correlation
CO2 corrected
Subject 5
y = 60.691x + 54.441
R² = 0.0279
Blood umol/L
80
70
60
50
40
30
20
10
0
0
0.05
0.1
0.15
0.2
Breath umol/L

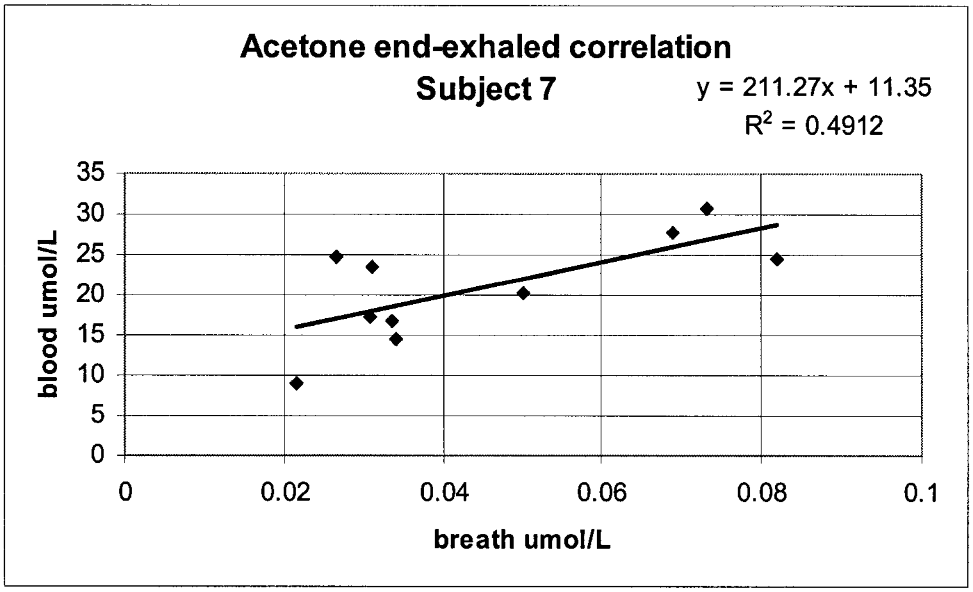

Acetone breath calibration
Subject 7
y = 0.0002x - 0.1459
R2 = 0.9991
4.0000
3.5000
3.0000
2.5000
2.0000
1.5000
1.0000
0.5000
0.0000
umol/L
0
5000
10000
15000
20000
area

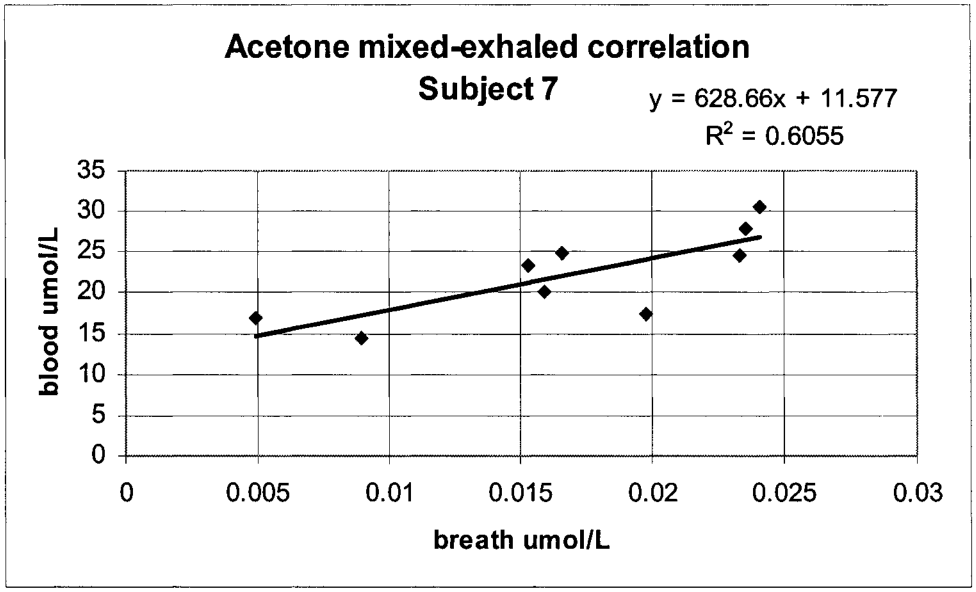

Acetone blood calibration
Subject 7
y = 7.8001x - 3.2588
R2 = 0.9868
120
100
80
60
40
20
0
umol/L
0
5
10
15
Response factor
Acetone 58
Linear (Acetone 58)

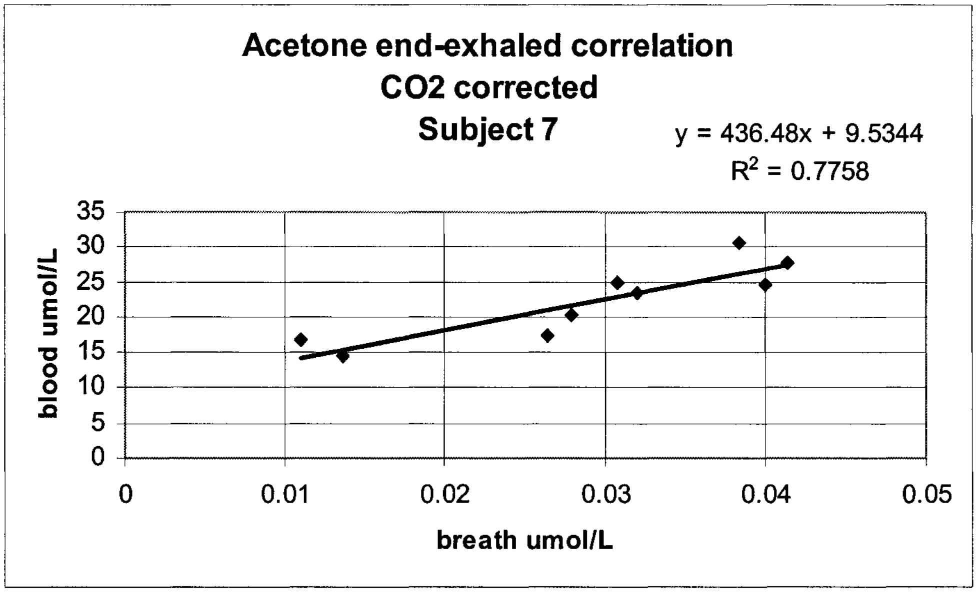

Acetone breath washout
Subject 7
1
0.1
0.01
0.001
umol/L
00:00
01:00
02:00
03:00
04:00
Time post-exposure
◆ rebreathed
■ end-exhaled
mixed


Acetone blood washout
Subject 7
100
10
1
umol/L
00:00
01:00
02:00
03:00
04:00
Time post-exposure
◆ pre-breath
■ post-breath

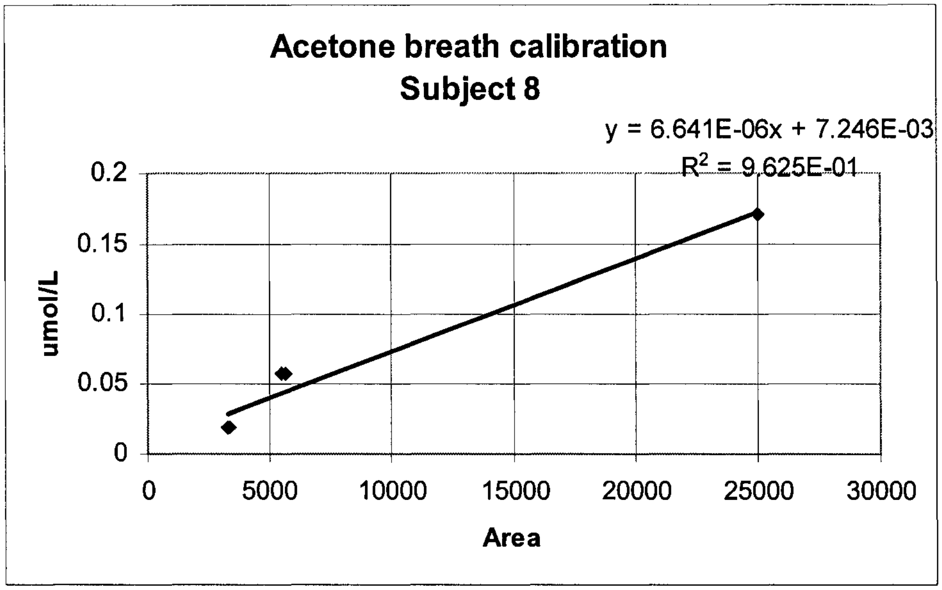

Acetone rebreathed correlation
Subject 7
y = 276.72x + 3.3439
$R^2 = 0.6642$
35
30
25
20
15
10
5
0
blood umol/L
0
0.02
0.04
0.06
0.08
0.1
0.12
breath umol/L

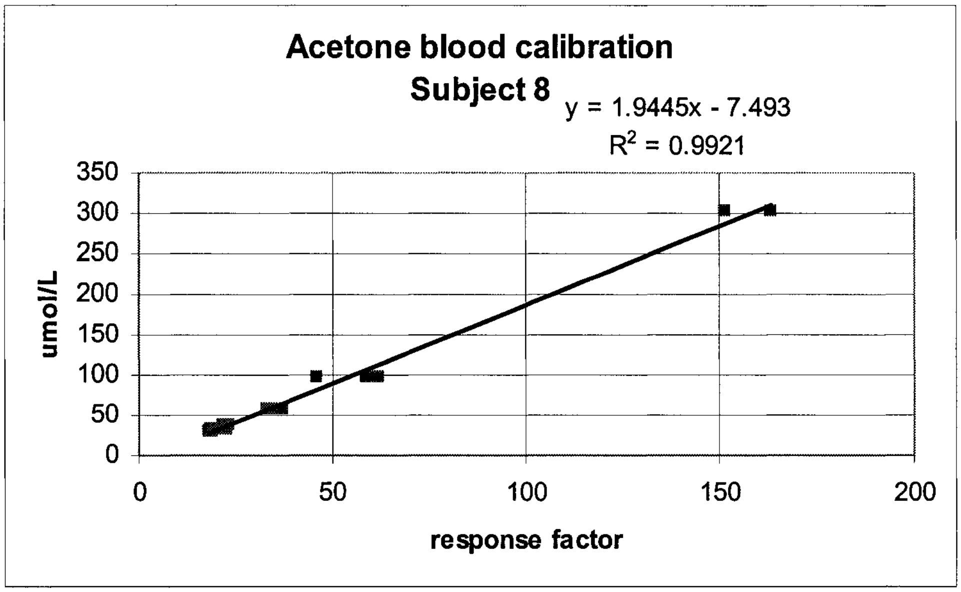

Acetone end-exhaled correlation
Subject 7
y = 211.27x + 11.35
$R^2 = 0.4912$
35
30
25
20
15
10
5
0
blood umol/L
0
0.02
0.04
0.06
0.08
0.1
breath umol/L

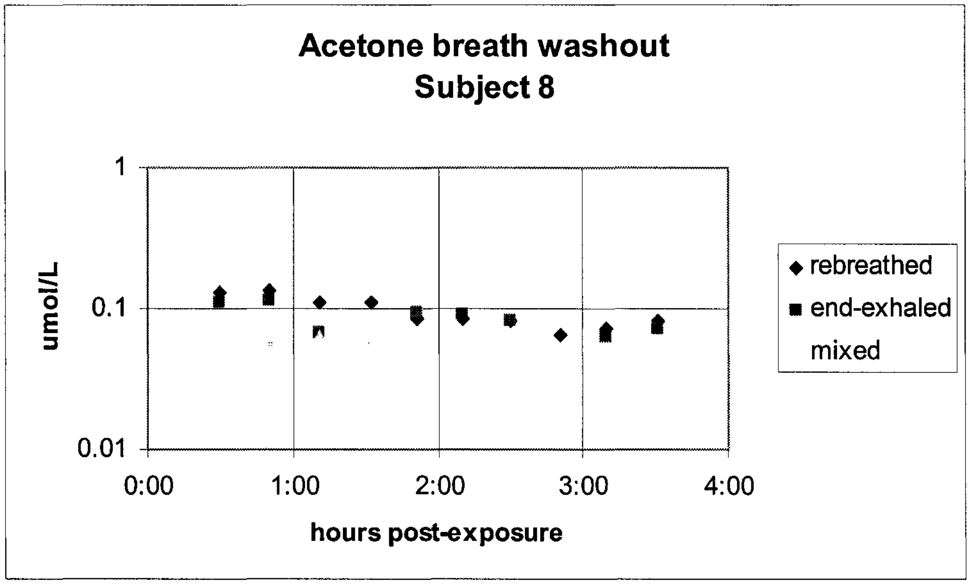

Acetone mixed-exhaled correlation
Subject 7
y = 628.66x + 11.577
R^2 = 0.6055
blood umol/L
35
30
25
20
15
10
5
0
0
0.005
0.01
0.015
0.02
0.025
0.03
breath umol/L

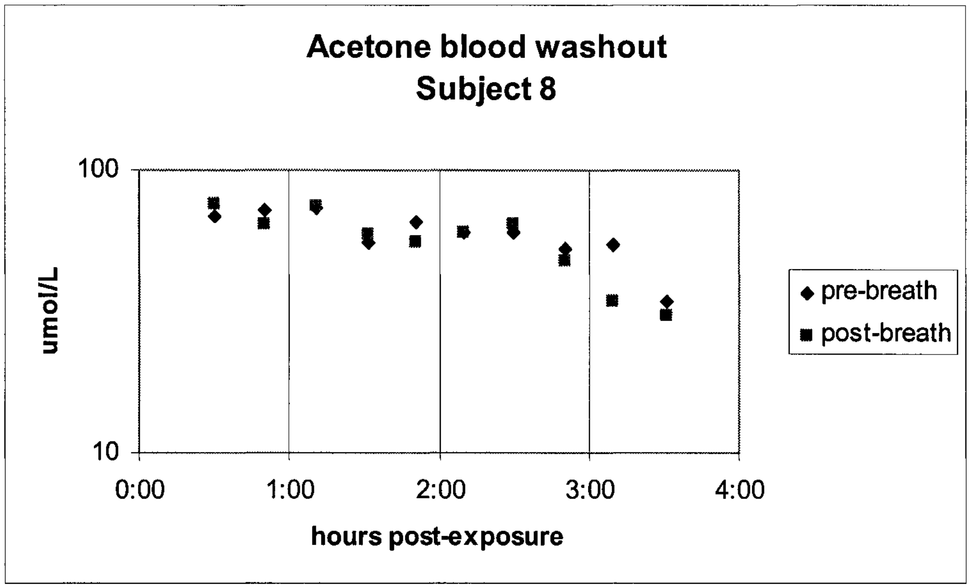

Acetone end-exhaled correlation
CO2 corrected
Subject 7
y = 436.48x + 9.5344
R^2 = 0.7758
blood umol/L
35
30
25
20
15
10
5
0
0
0.01
0.02
0.03
0.04
0.05
breath umol/L

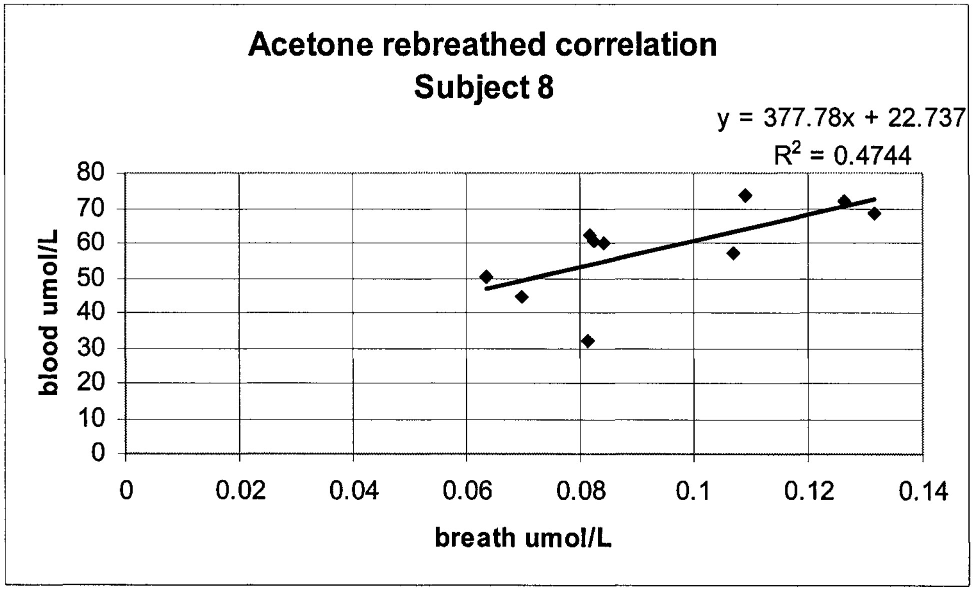
7/3/03

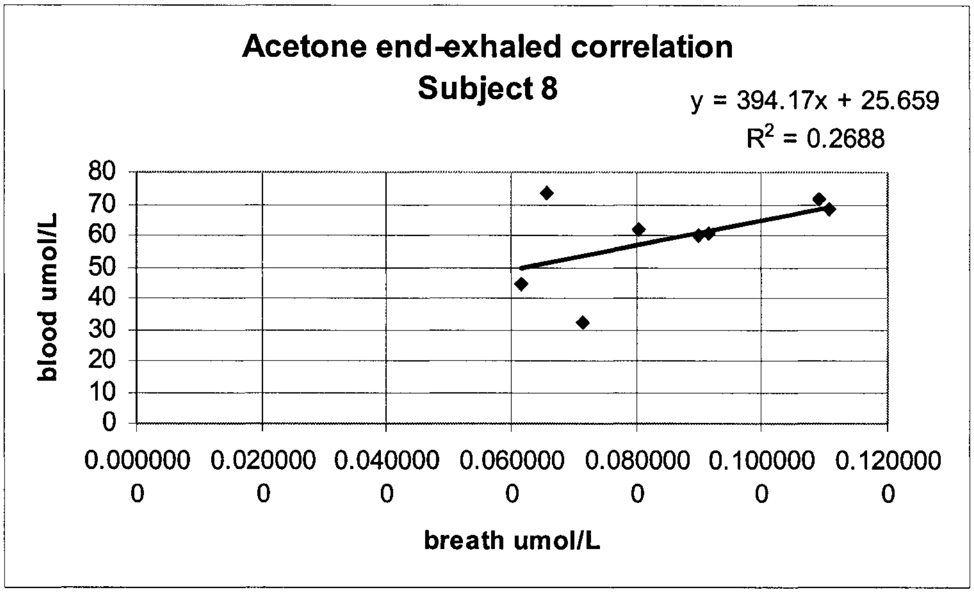

Acetone breath calibration
Subject 8
y = 6.641E-06x + 7.246E-03
R² = 9.625E-01
0.2
0.15
0.1
0.05
0
umol/L
0
5000
10000
15000
20000
25000
30000
Area

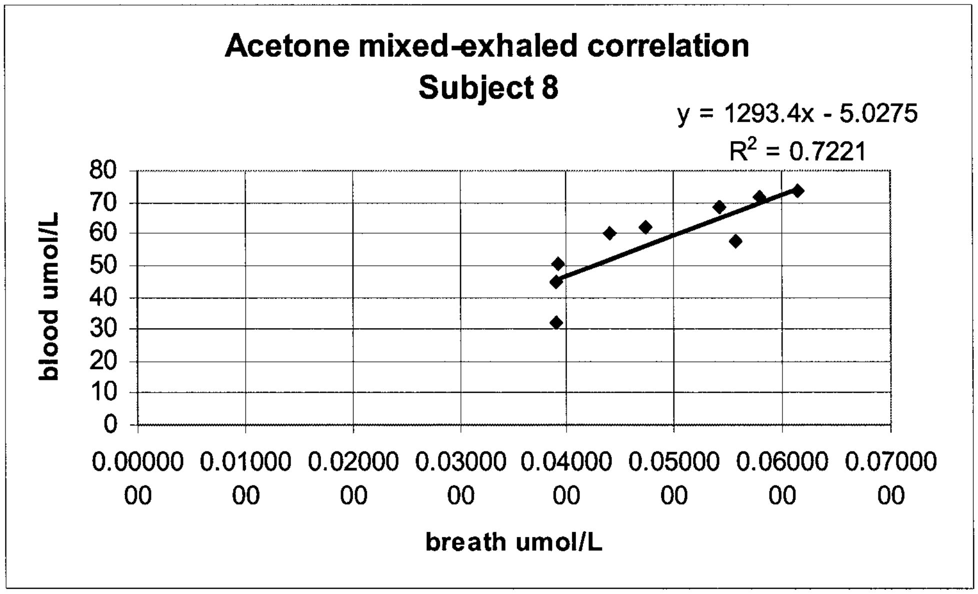

Acetone blood calibration
Subject 8
y = 1.9445x - 7.493
R² = 0.9921
350
300
250
200
150
100
50
0
umol/L
0
50
100
150
200
response factor

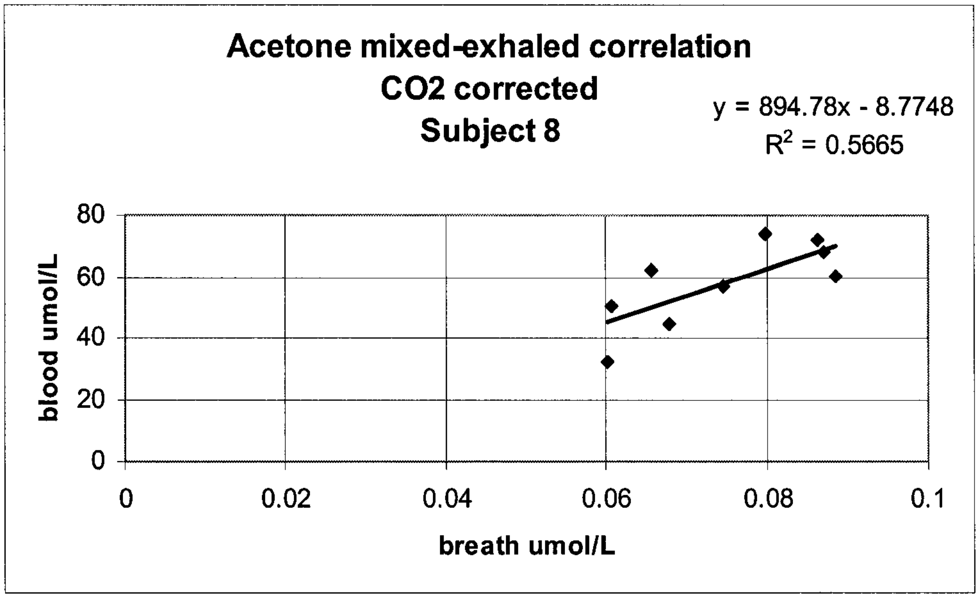

Acetone breath washout
Subject 8
umol/L
1
0.1
0.01
0:00
1:00
2:00
3:00
4:00
hours post-exposure
◆ rebreathed
■ end-exhaled
mixed

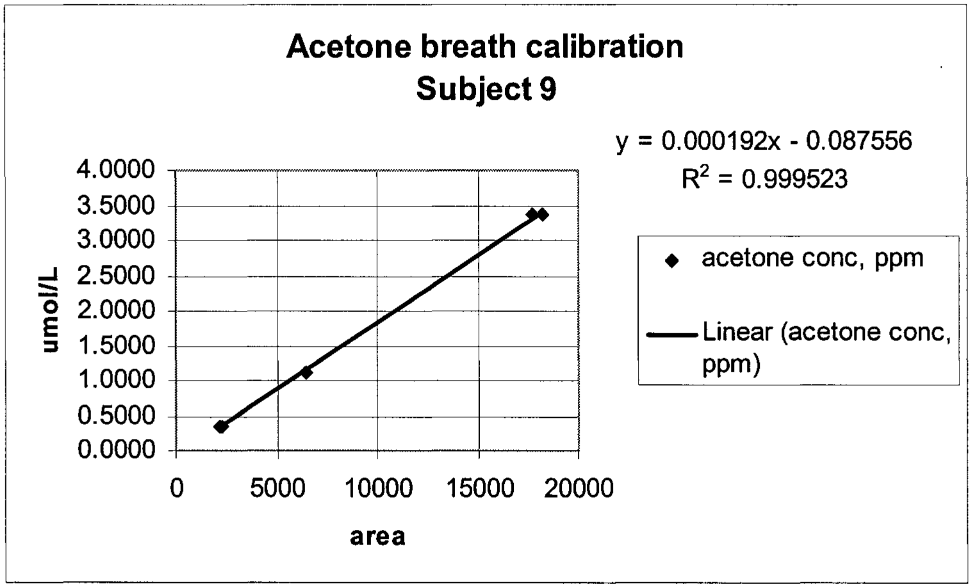

Acetone blood washout
Subject 8
umol/L
100
10
0:00
1:00
2:00
3:00
4:00
hours post-exposure
◆ pre-breath
■ post-breath

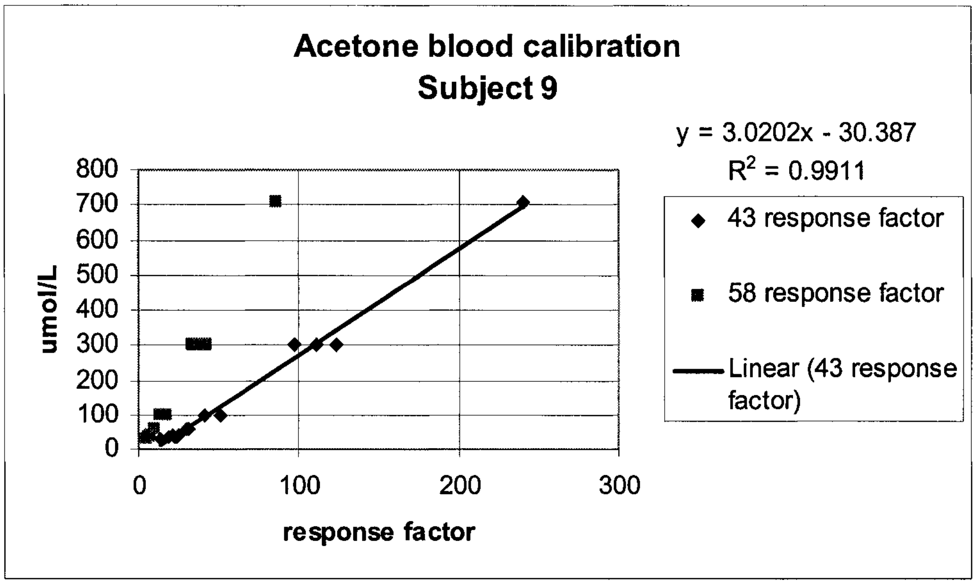

Acetone rebreathed correlation
Subject 8
y = 377.78x + 22.737
R² = 0.4744
80
70
60
50
40
30
20
10
0
blood umol/L
0
0.02
0.04
0.06
0.08
0.1
0.12
0.14
breath umol/L

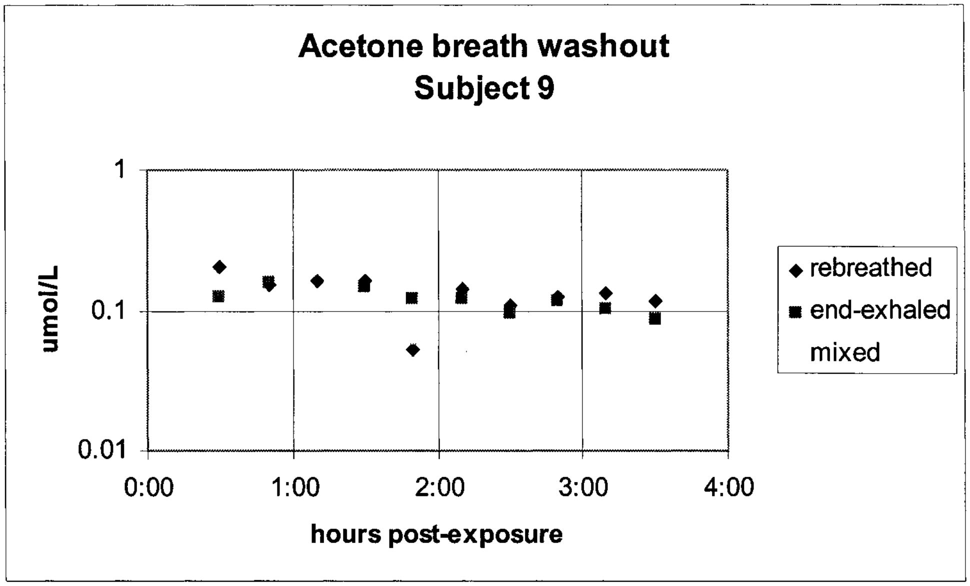

Acetone end-exhaled correlation
Subject 8
y = 394.17x + 25.659
R² = 0.2688
80
70
60
50
40
30
20
10
0
blood umol/L
0.0000000
0.0200000
0.0400000
0.0600000
0.0800000
0.1000000
0.1200000
breath umol/L

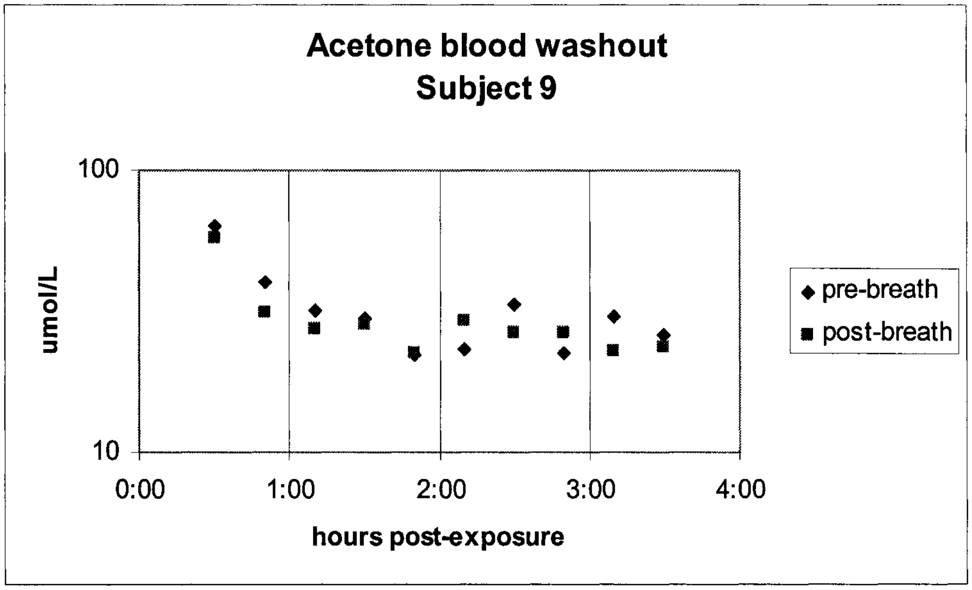

Acetone mixed-exhaled correlation
Subject 8
y = 1293.4x - 5.0275
R^2 = 0.7221
blood umol/L
80
70
60
50
40
30
20
10
0
0.0000000
0.0100000
0.0200000
0.0300000
0.0400000
0.0500000
0.0600000
0.0700000
breath umol/L

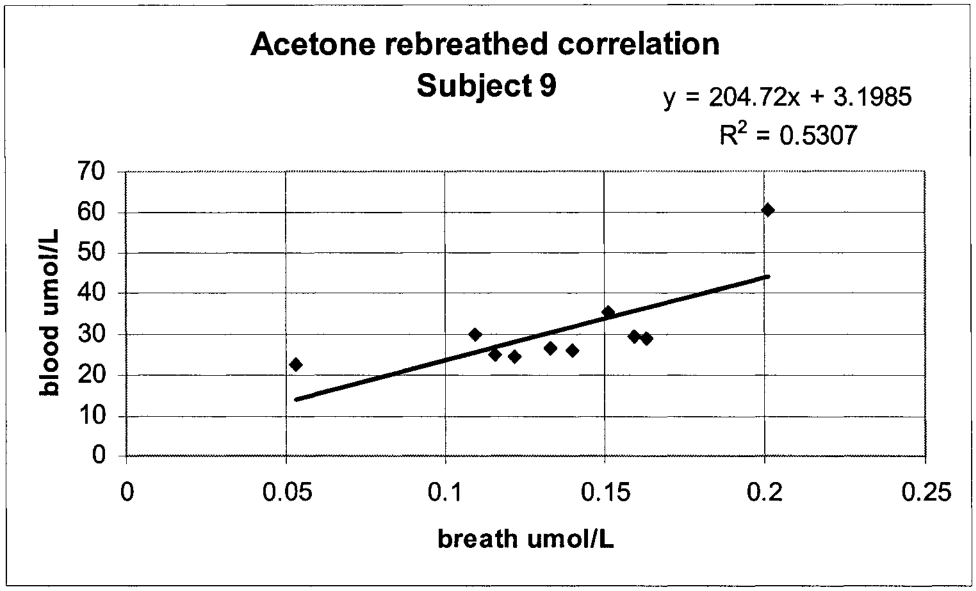

Acetone mixed-exhaled correlation
CO2 corrected
Subject 8
y = 894.78x - 8.7748
R^2 = 0.5665
blood umol/L
80
60
40
20
0
0
0.02
0.04
0.06
0.08
0.1
breath umol/L

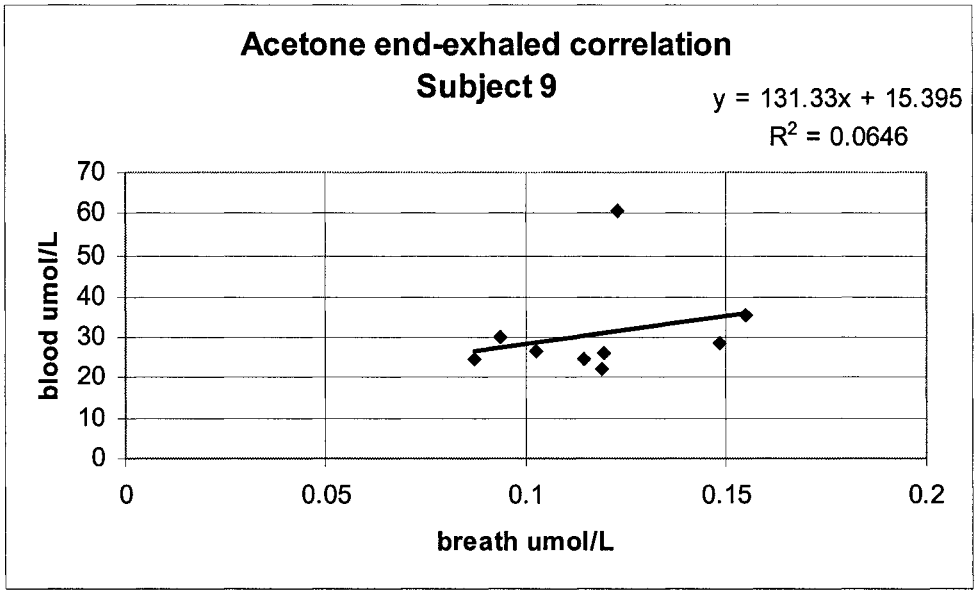

Acetone breath calibration
Subject 9
y = 0.000192x - 0.087556
R2 = 0.999523
umol/L
4.0000
3.5000
3.0000
2.5000
2.0000
1.5000
1.0000
0.5000
0.0000
0
5000
10000
15000
20000
area
◆ acetone conc, ppm
Linear (acetone conc, ppm)

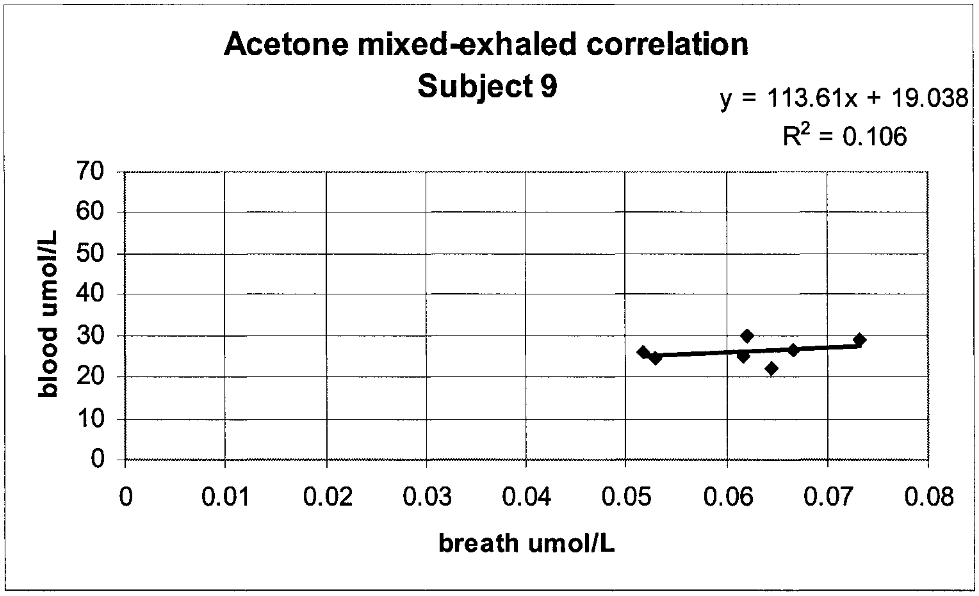

Acetone blood calibration
Subject 9
y = 3.0202x - 30.387
R2 = 0.9911
umol/L
800
700
600
500
400
300
200
100
0
0
100
200
300
response factor
◆ 43 response factor
■ 58 response factor
Linear (43 response factor)

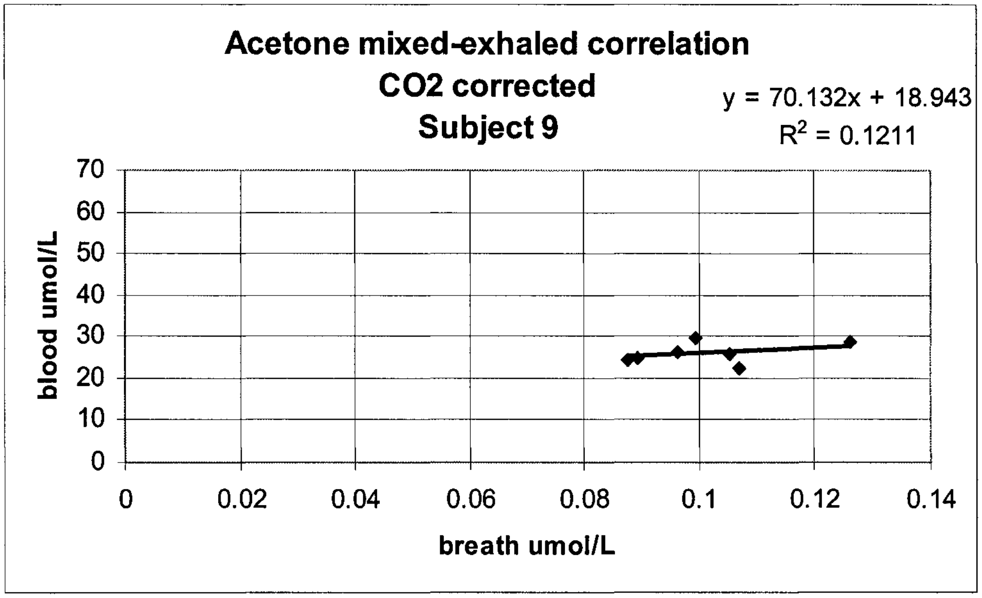

Acetone breath washout
Subject 9
umol/L
1
0.1
0.01
0:00
1:00
2:00
3:00
4:00
hours post-exposure
◆ rebreathed
■ end-exhaled
mixed


Acetone blood washout
Subject 9
umol/L
100
10
0:00
1:00
2:00
3:00
4:00
hours post-exposure
◆ pre-breath
■ post-breath

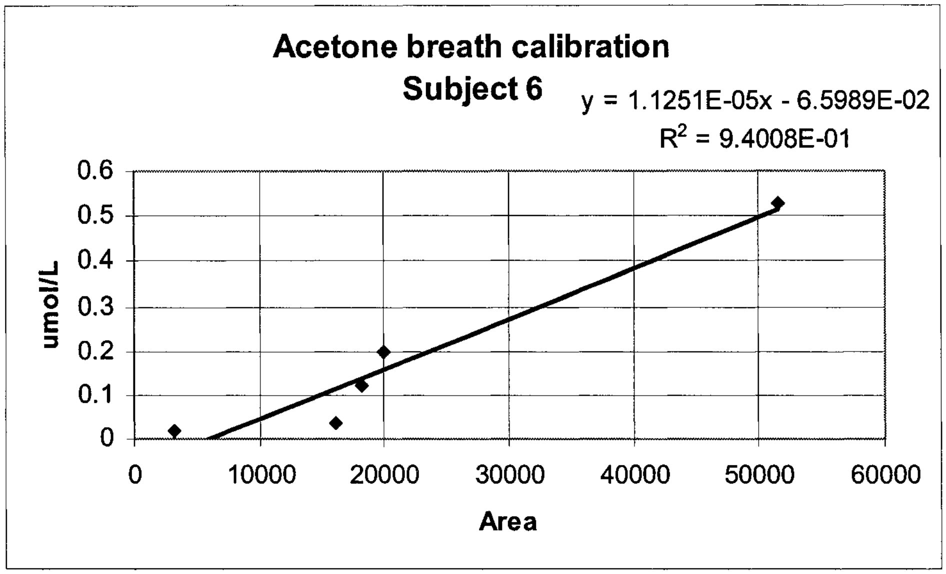

Acetone rebreathed correlation
Subject 9
y = 204.72x + 3.1985
R2 = 0.5307
blood umol/L
0
10
20
30
40
50
60
70
0
0.05
0.1
0.15
0.2
0.25
breath umol/L

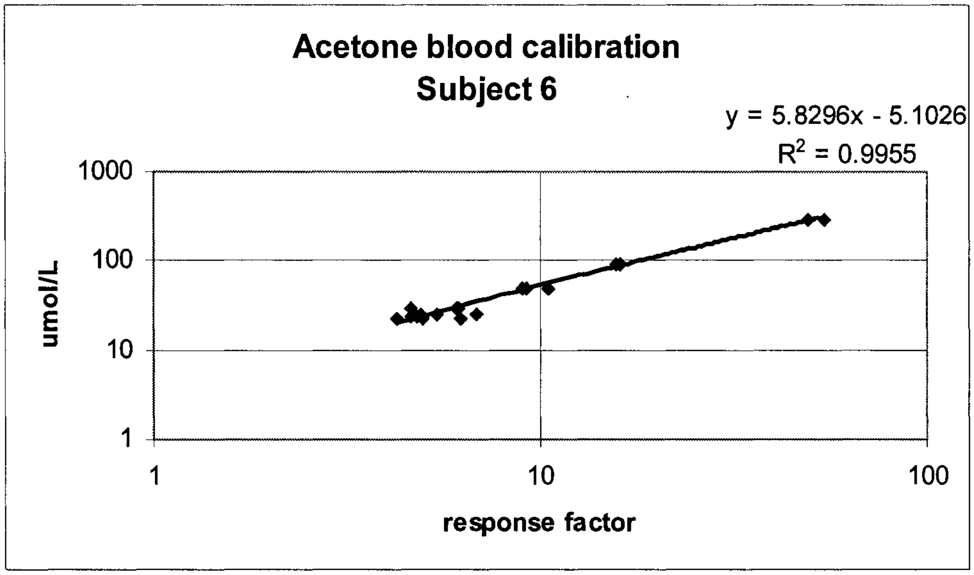

Acetone end-exhaled correlation
Subject 9
y = 131.33x + 15.395
R2 = 0.0646
blood umol/L
0
10
20
30
40
50
60
70
0
0.05
0.1
0.15
0.2
breath umol/L

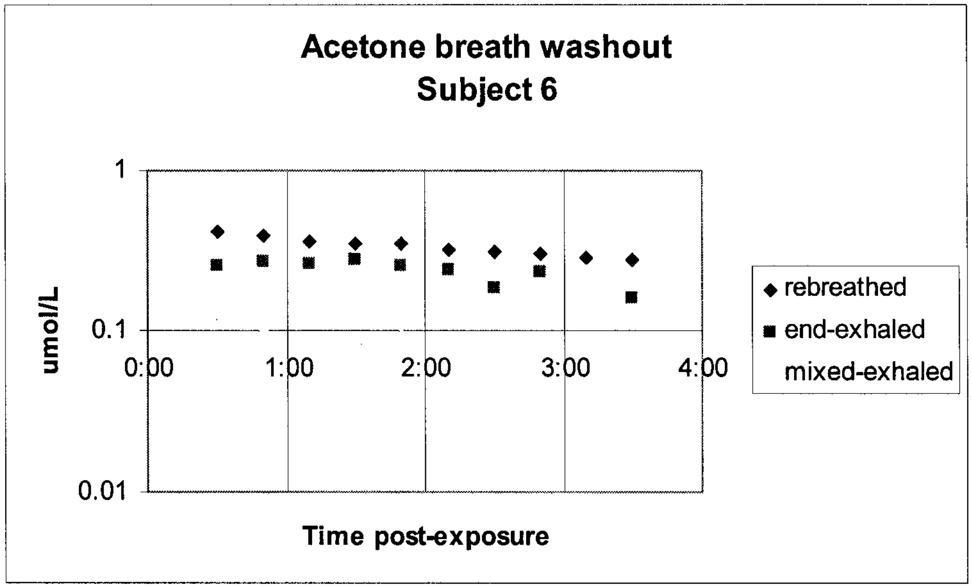

Acetone mixed-exhaled correlation
Subject 9
y = 113.61x + 19.038
R^2 = 0.106
blood umol/L
70
60
50
40
30
20
10
0
0
0.01
0.02
0.03
0.04
0.05
0.06
0.07
0.08
breath umol/L

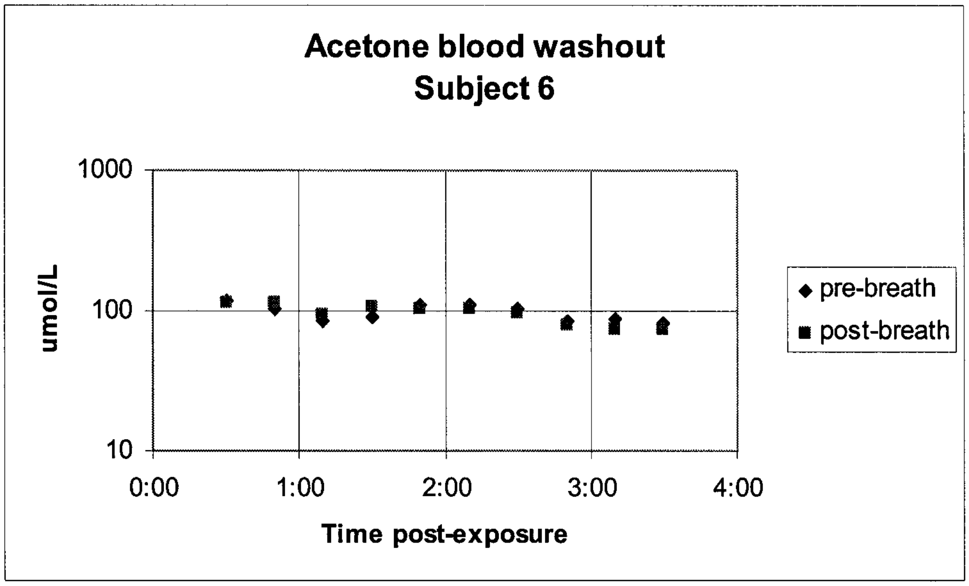

Acetone mixed-exhaled correlation
CO2 corrected
Subject 9
y = 70.132x + 18.943
R^2 = 0.1211
blood umol/L
70
60
50
40
30
20
10
0
0
0.02
0.04
0.06
0.08
0.1
0.12
0.14
breath umol/L

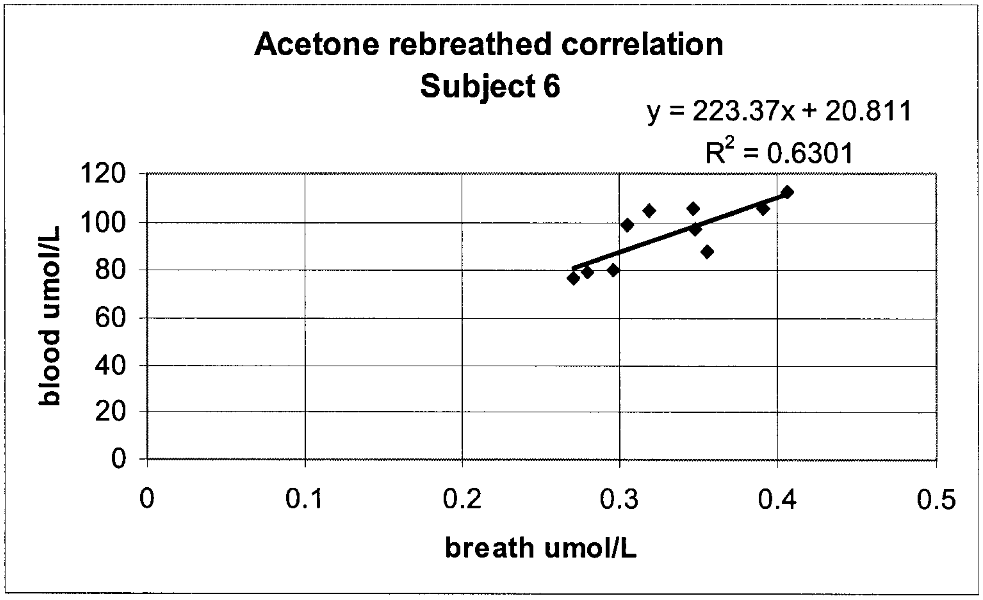
8/26/03

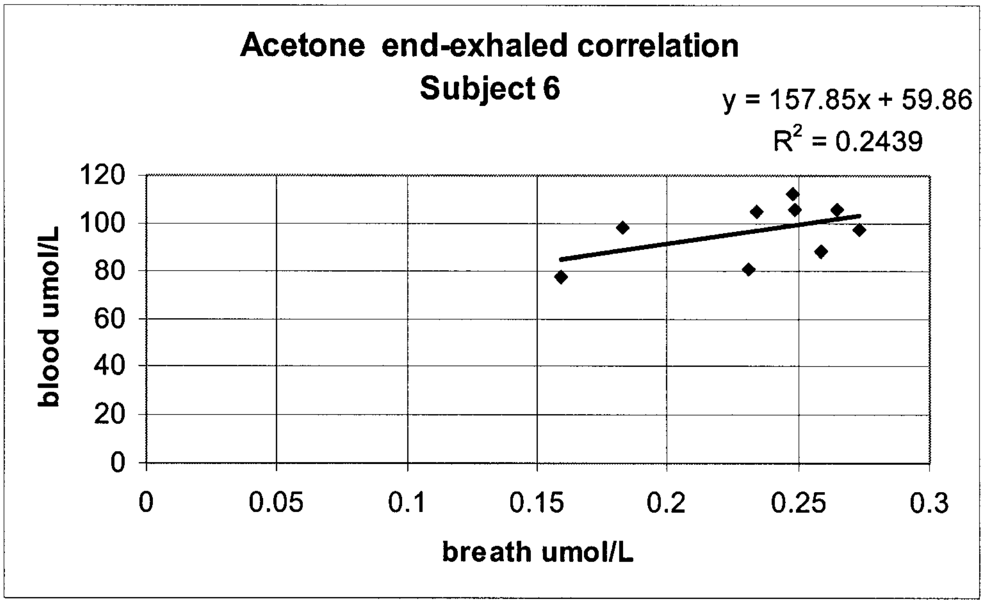

Acetone breath calibration
Subject 6
y = 1.1251E-05x - 6.5989E-02
R2 = 9.4008E-01
0.6
0.5
0.4
0.3
0.2
0.1
0
umol/L
0
10000
20000
30000
40000
50000
60000
Area

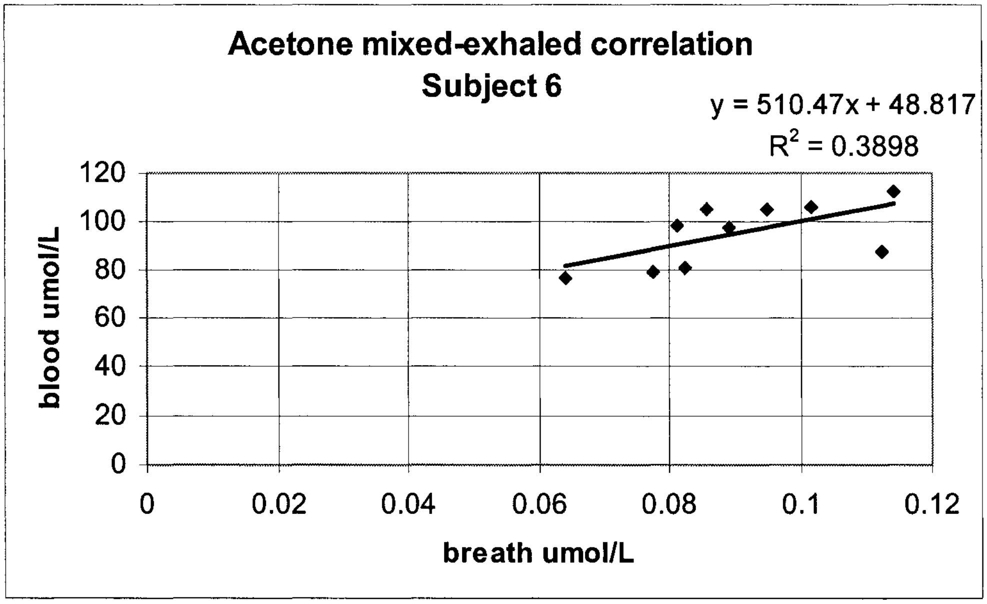

Acetone blood calibration
Subject 6
y = 5.8296x - 5.1026
R2 = 0.9955
1000
100
10
1
umol/L
1
10
100
response factor

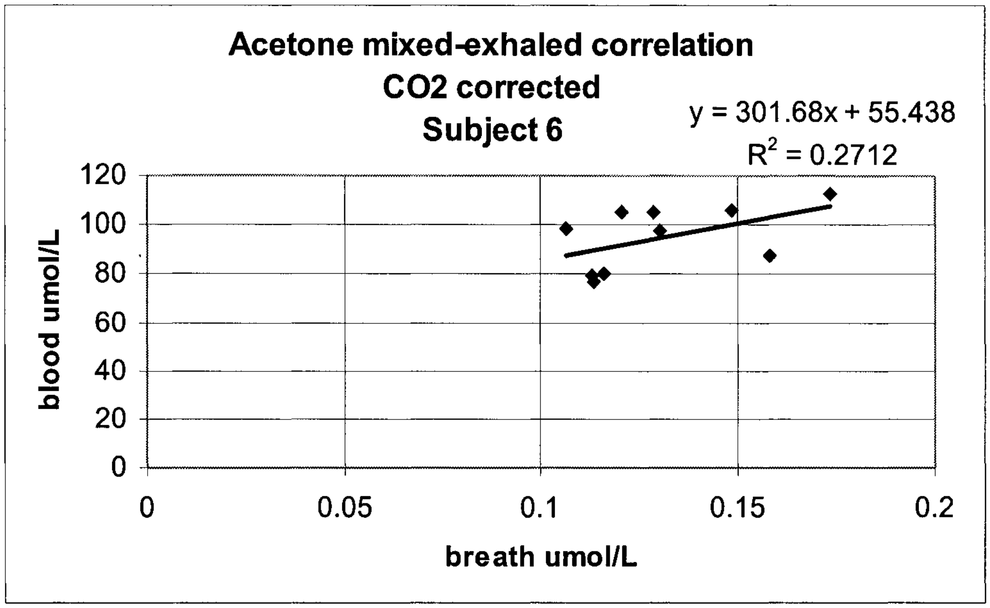

Acetone breath washout
Subject 6
1
0.1
0.01
umol/L
0:00
1:00
2:00
3:00
4:00
Time post-exposure
◆ rebreathed
■ end-exhaled
mixed-exhaled


Acetone blood washout
Subject 6
1000
100
10
umol/L
0:00
1:00
2:00
3:00
4:00
Time post-exposure
◆ pre-breath
■ post-breath

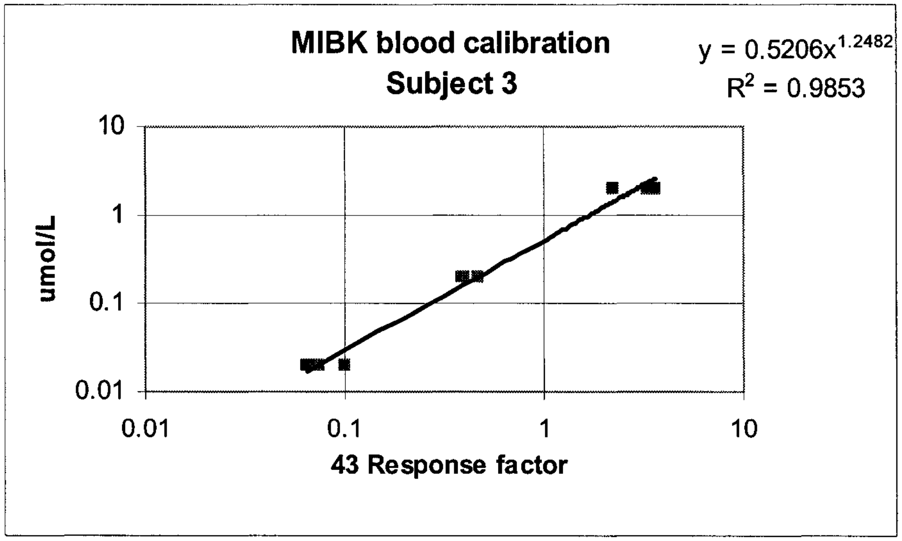

Acetone rebreathed correlation
Subject 6
y = 223.37x + 20.811
R^2 = 0.6301
120
100
80
60
40
20
0
blood umol/L
0
0.1
0.2
0.3
0.4
0.5
breath umol/L

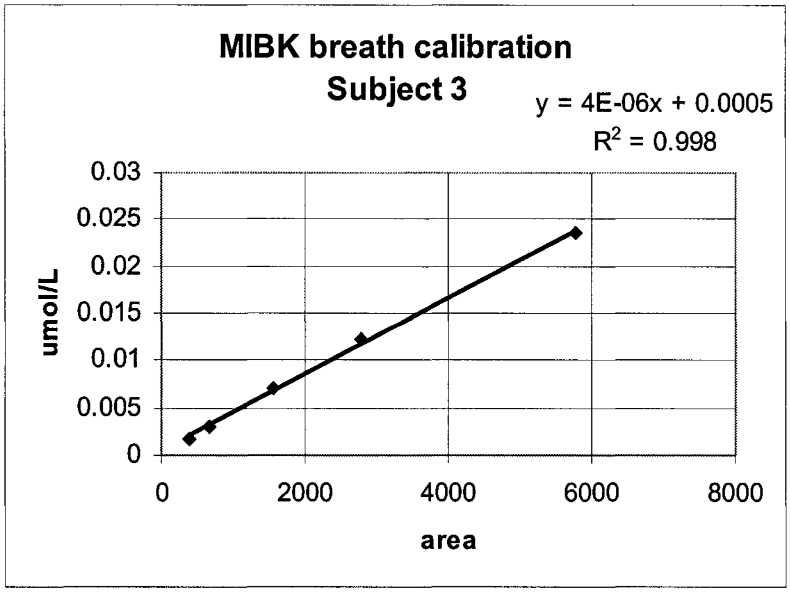

Acetone end-exhaled correlation
Subject 6
y = 157.85x + 59.86
R^2 = 0.2439
120
100
80
60
40
20
0
blood umol/L
0
0.05
0.1
0.15
0.2
0.25
0.3
breath umol/L

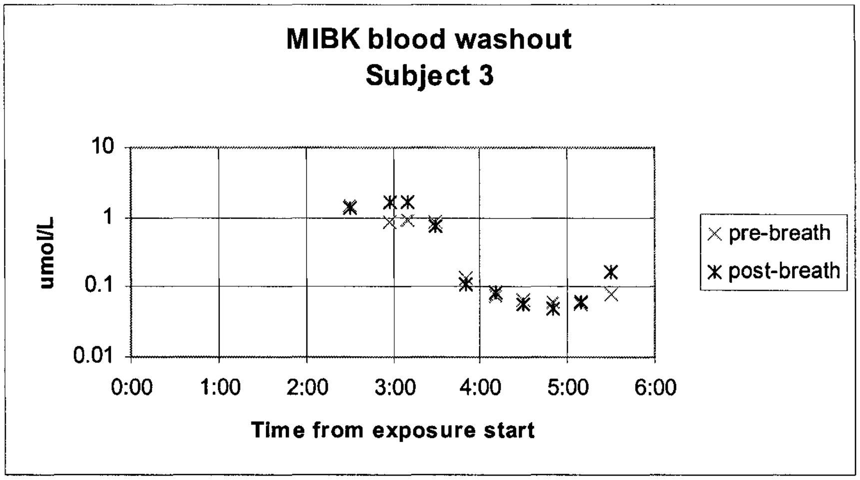

Acetone mixed-exhaled correlation
Subject 6
y = 510.47x + 48.817
R² = 0.3898
blood umol/L
120
100
80
60
40
20
0
0
0.02
0.04
0.06
0.08
0.1
0.12
breath umol/L

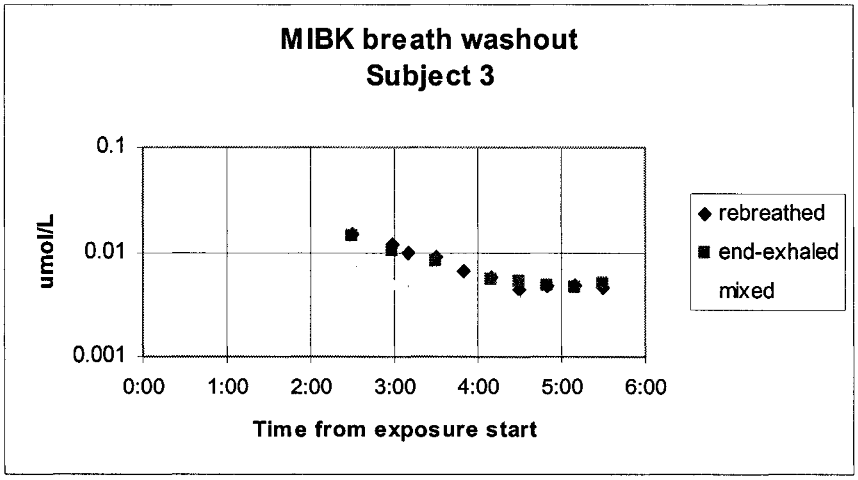

Acetone mixed-exhaled correlation
CO2 corrected
Subject 6
y = 301.68x + 55.438
R² = 0.2712
blood umol/L
120
100
80
60
40
20
0
0
0.05
0.1
0.15
0.2
breath umol/L

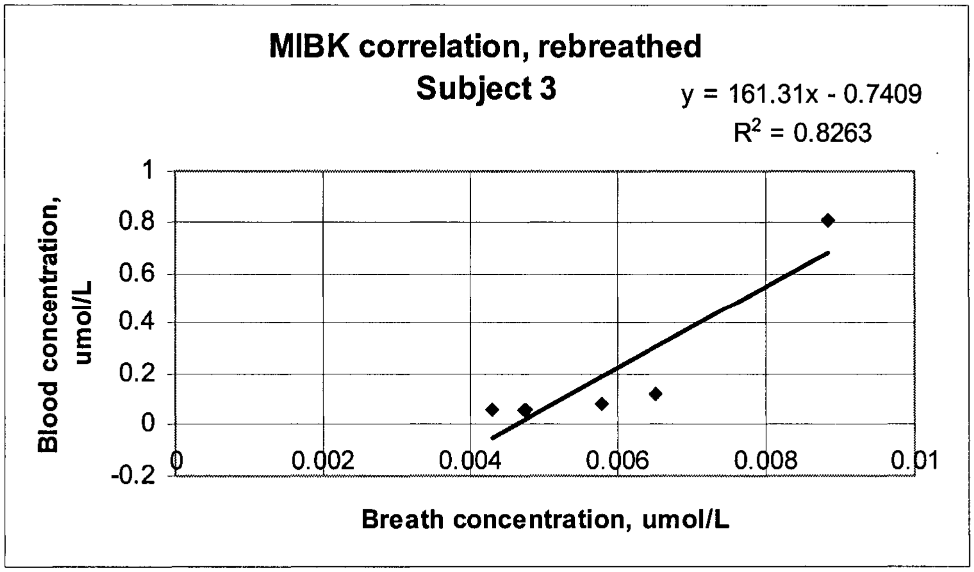
MIBK:
10/7/02:

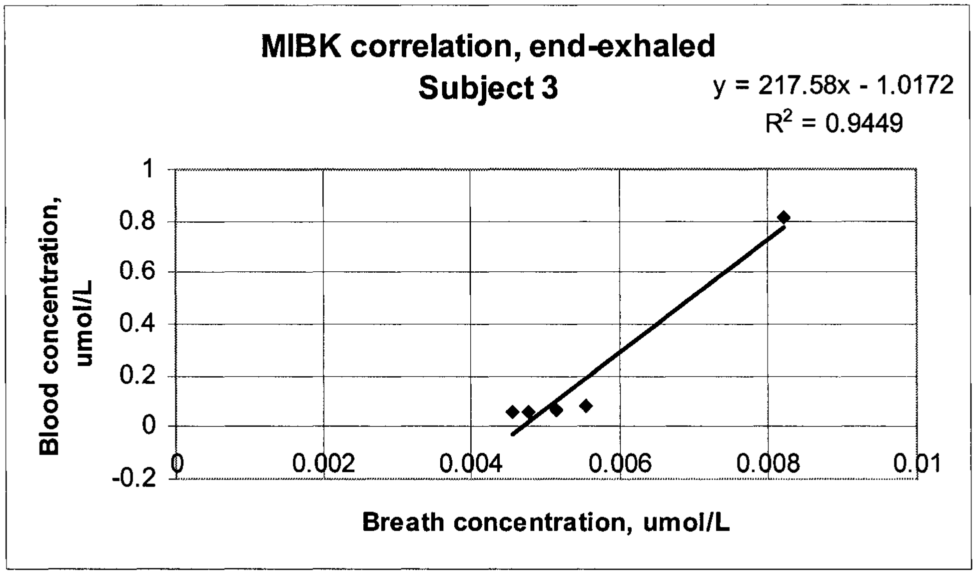

MIBK blood calibration
Subject 3
y = 0.5206x^1.2482
R^2 = 0.9853
umol/L
10
1
0.1
0.01
0.01
0.1
1
10
43 Response factor

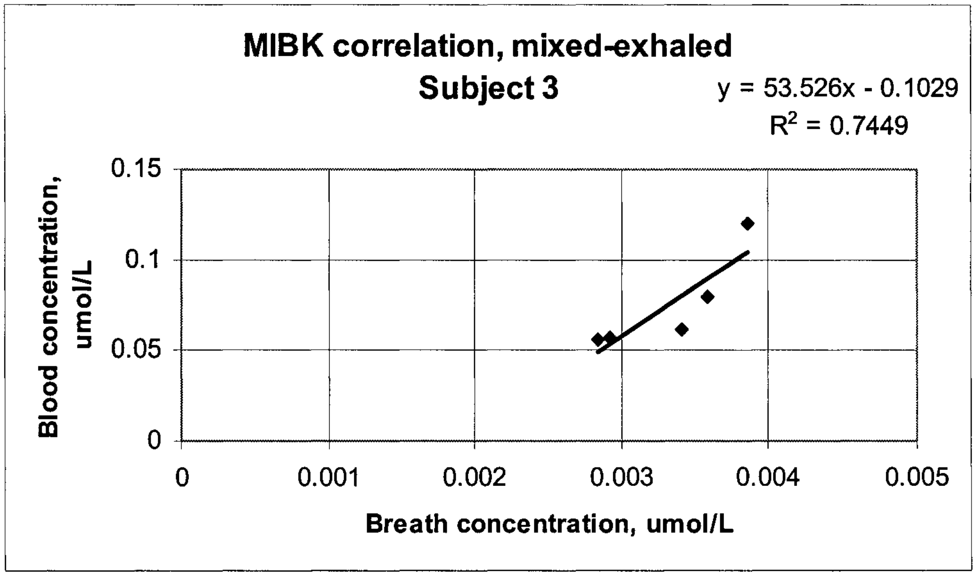

MIBK breath calibration
Subject 3
y = 4E-06x + 0.0005
R^2 = 0.998
umol/L
0.03
0.025
0.02
0.015
0.01
0.005
0
0
2000
4000
6000
8000
area

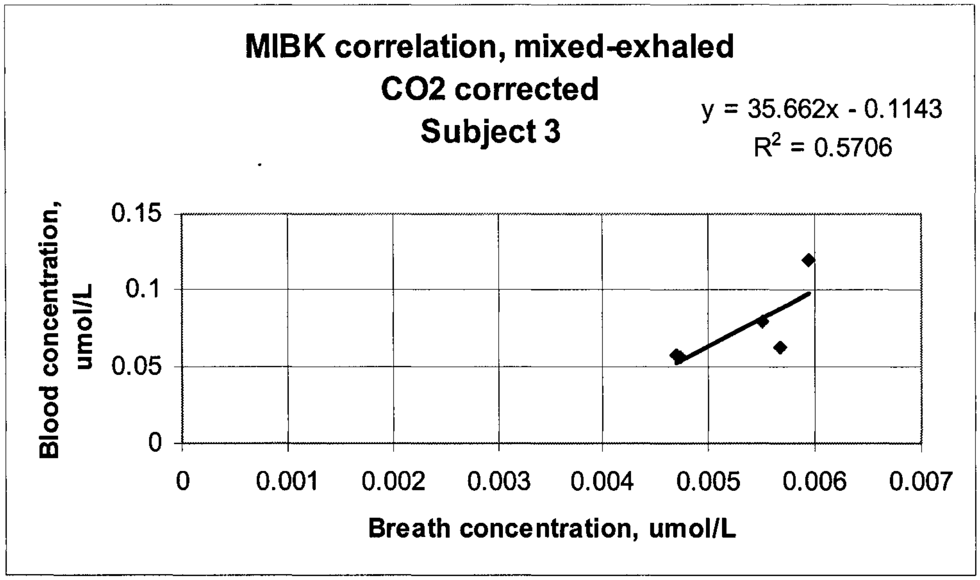

MIBK blood washout
Subject 3
umol/L
10
1
0.1
0.01
0:00
1:00
2:00
3:00
4:00
5:00
6:00
Time from exposure start
× pre-breath
⋇ post-breath


MIBK breath washout
Subject 3
umol/L
0.1
0.01
0.001
0:00
1:00
2:00
3:00
4:00
5:00
6:00
Time from exposure start
◆ rebreathed
■ end-exhaled
mixed

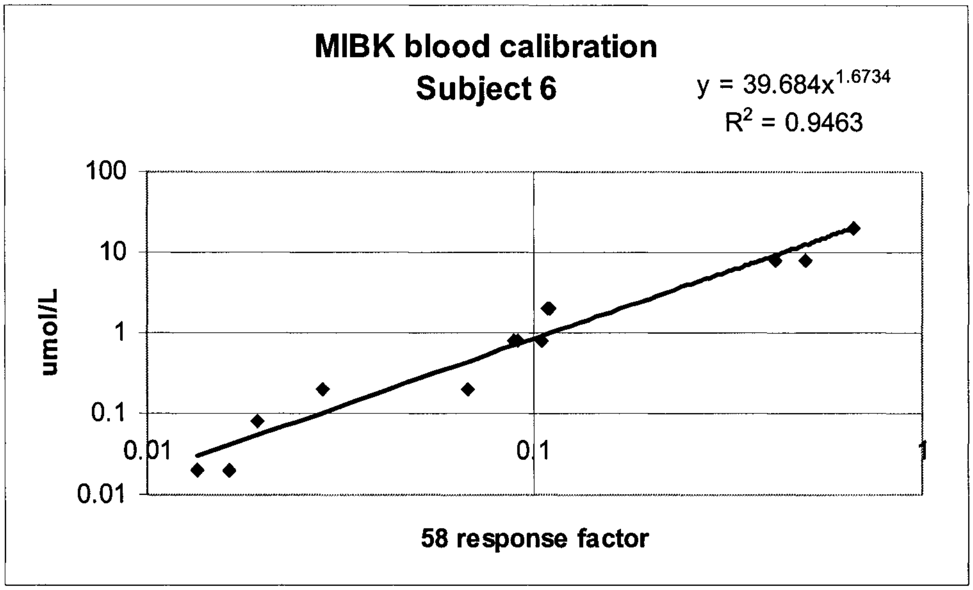

MIBK correlation, rebreathed
Subject 3
y = 161.31x - 0.7409
R2 = 0.8263
Blood concentration, umol/L
1
0.8
0.6
0.4
0.2
0
-0.2
0
0.002
0.004
0.006
0.008
0.01
Breath concentration, umol/L

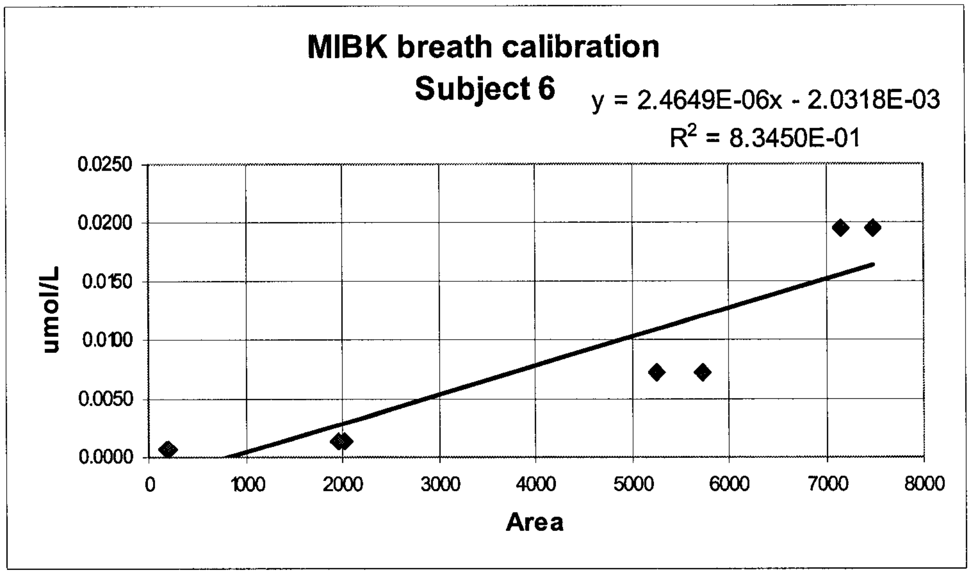

MIBK correlation, end-exhaled
Subject 3
y = 217.58x - 1.0172
R2 = 0.9449
Blood concentration, umol/L
Breath concentration, umol/L
1
0.8
0.6
0.4
0.2
0
-0.2
0
0.002
0.004
0.006
0.008
0.01

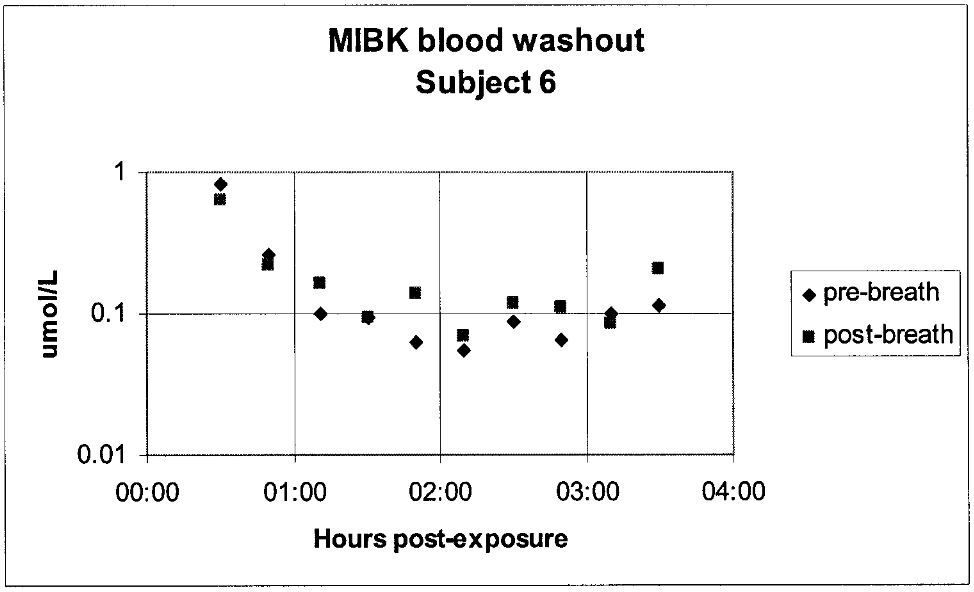

MIBK correlation, mixed-exhaled
Subject 3
y = 53.526x - 0.1029
R2 = 0.7449
Blood concentration, umol/L
Breath concentration, umol/L
0.15
0.1
0.05
0
0
0.001
0.002
0.003
0.004
0.005

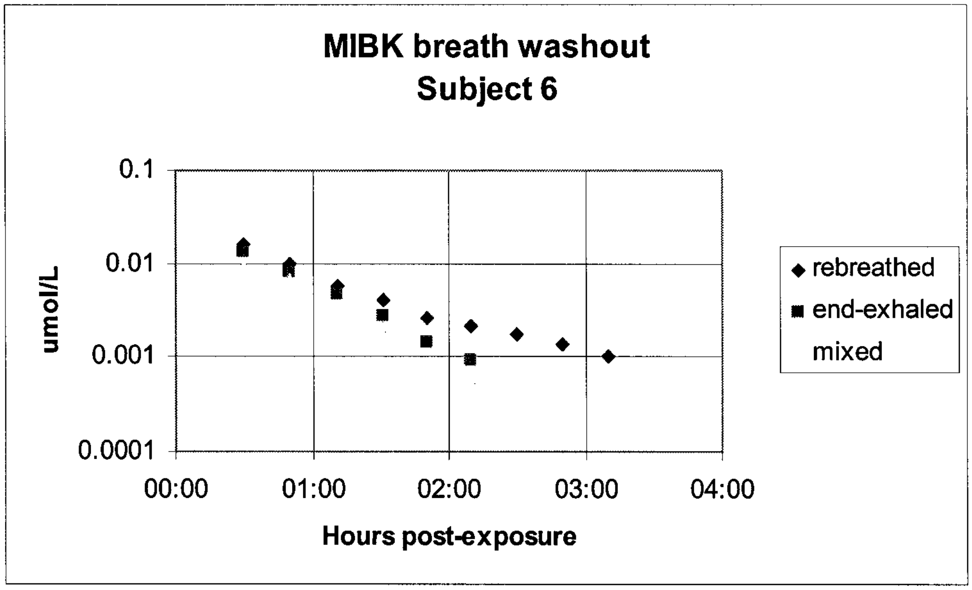

MIBK correlation, mixed-exhaled
CO2 corrected
Subject 3
y = 35.662x - 0.1143
R^2 = 0.5706
Blood concentration, umol/L
0.15
0.1
0.05
0
0
0.001
0.002
0.003
0.004
0.005
0.006
0.007
Breath concentration, umol/L

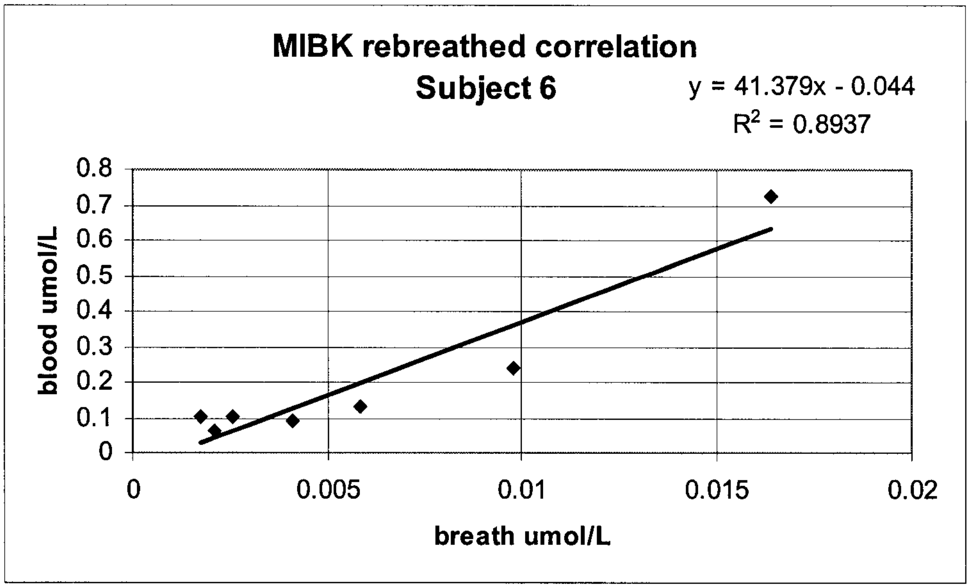
6/18/03

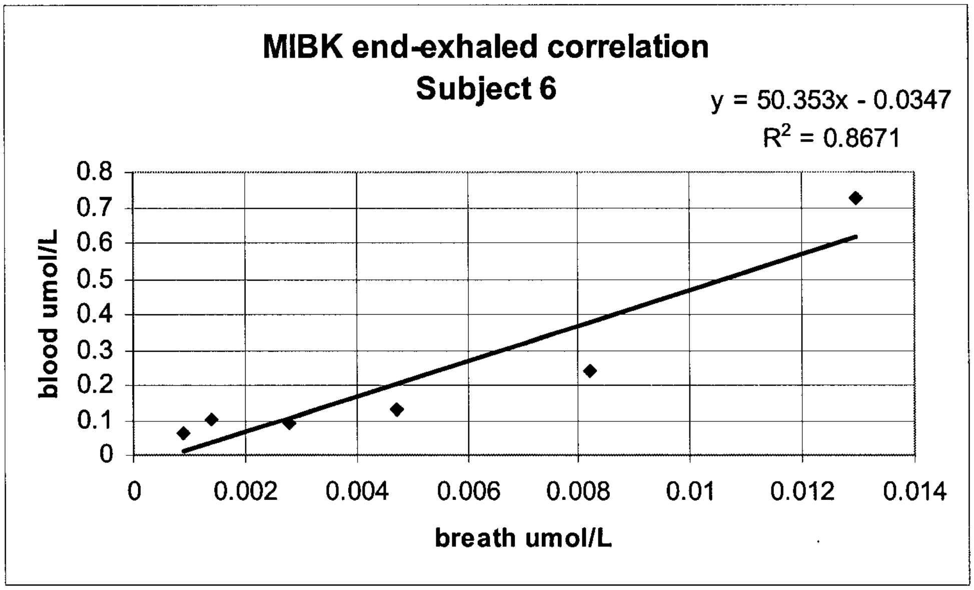

MIBK blood calibration
Subject 6
y = $39.684x^{1.6734}$
R^2 = 0.9463
100
10
1
0.1
0.01
umol/L
0.01
0.1
1
58 response factor

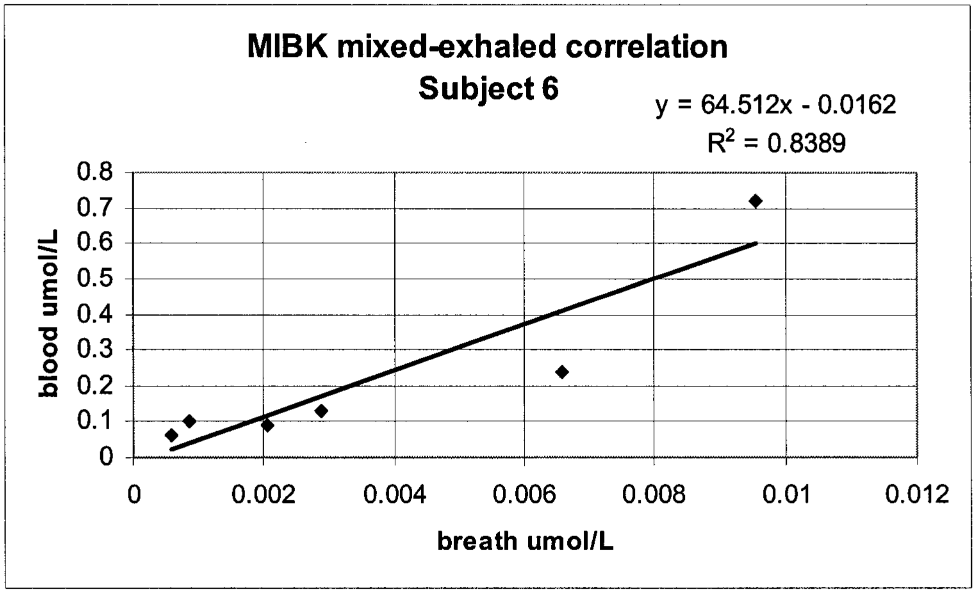

MIBK breath calibration
Subject 6
y = 2.4649E-06x - 2.0318E-03
R2 = 8.3450E-01
umol/L
0.0250
0.0200
0.0150
0.0100
0.0050
0.0000
0
1000
2000
3000
4000
5000
6000
7000
8000
Area

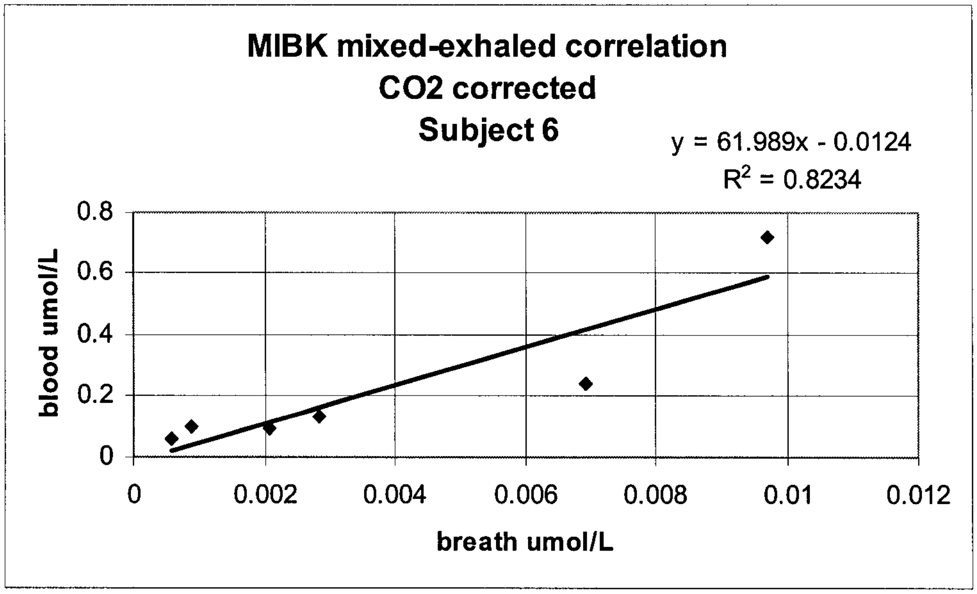

MIBK blood washout
Subject 6
umol/L
1
0.1
0.01
00:00
01:00
02:00
03:00
04:00
Hours post-exposure
◆ pre-breath
■ post-breath


MIBK breath washout
Subject 6
0.1
0.01
0.001
0.0001
umol/L
00:00
01:00
02:00
03:00
04:00
Hours post-exposure
◆ rebreathed
■ end-exhaled
mixed

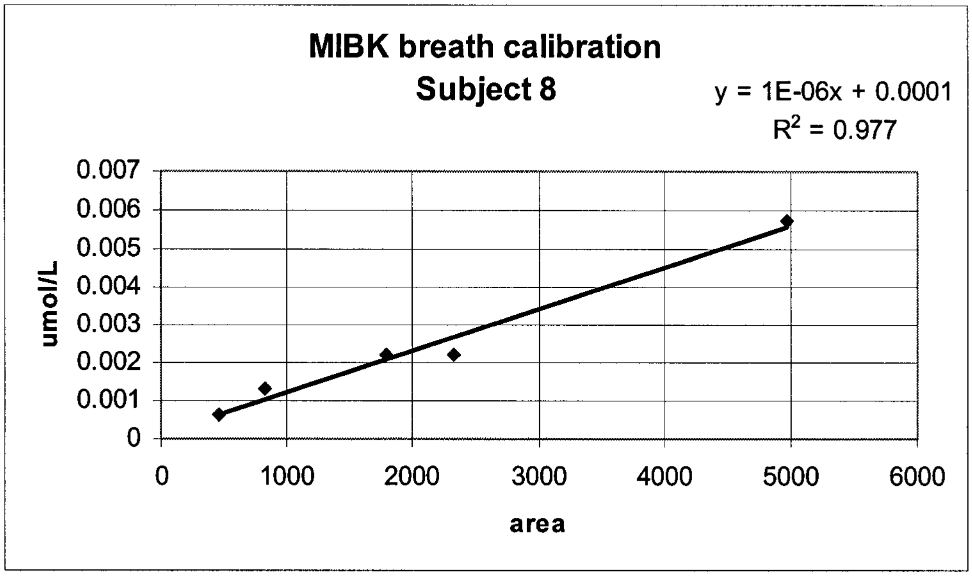

MIBK rebreathed correlation
Subject 6
y = 41.379x - 0.044
R² = 0.8937
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
blood umol/L
0
0.005
0.01
0.015
0.02
breath umol/L

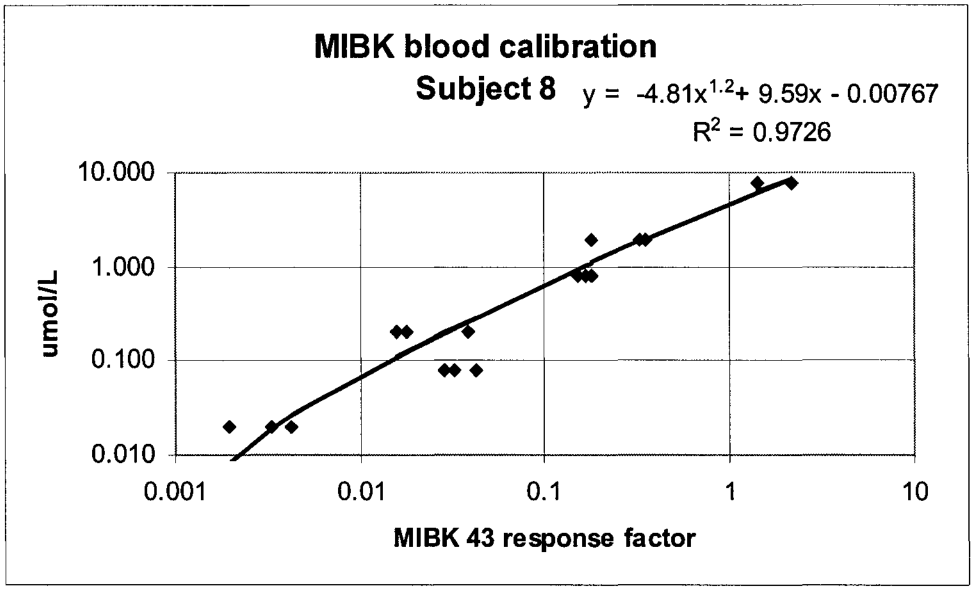

MIBK end-exhaled correlation
Subject 6
y = 50.353x - 0.0347
R2 = 0.8671
blood umol/L
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
0.002
0.004
0.006
0.008
0.01
0.012
0.014
breath umol/L

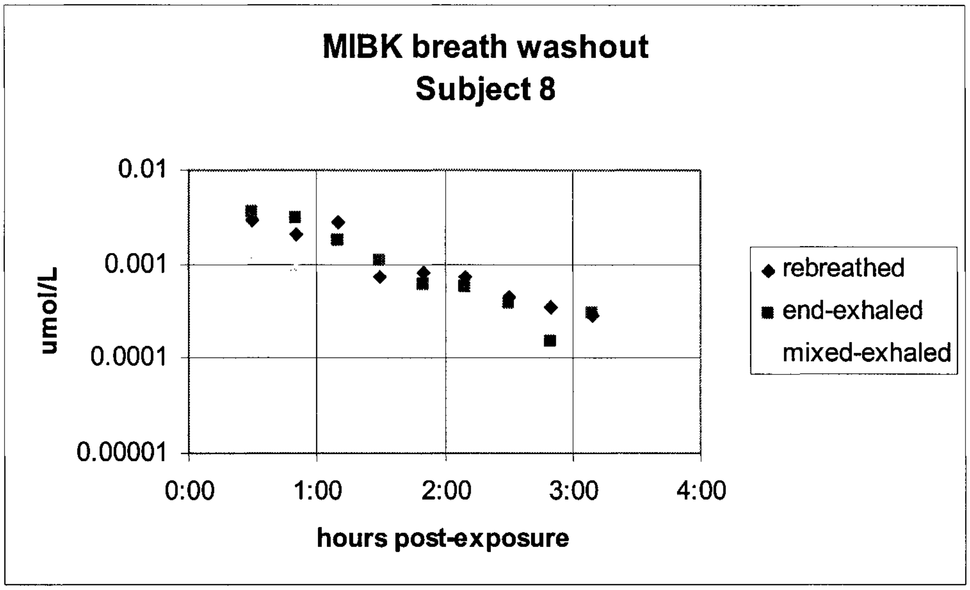

MIBK mixed-exhaled correlation
Subject 6
y = 64.512x - 0.0162
R2 = 0.8389
blood umol/L
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
0.002
0.004
0.006
0.008
0.01
0.012
breath umol/L

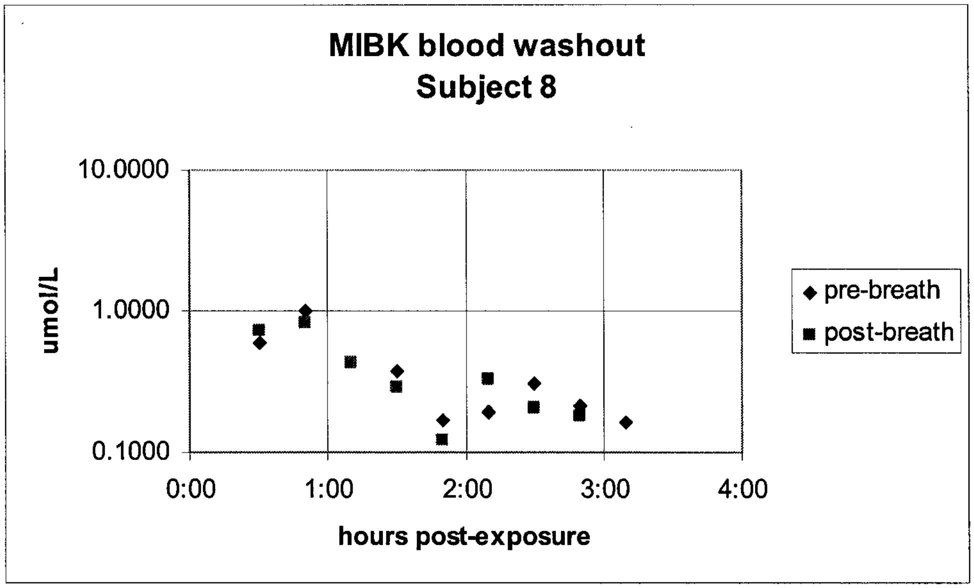

MIBK mixed-exhaled correlation
CO2 corrected
Subject 6
y = 61.989x - 0.0124
R2 = 0.8234
blood umol/L
0.8
0.6
0.4
0.2
0
0
0.002
0.004
0.006
0.008
0.01
0.012
breath umol/L

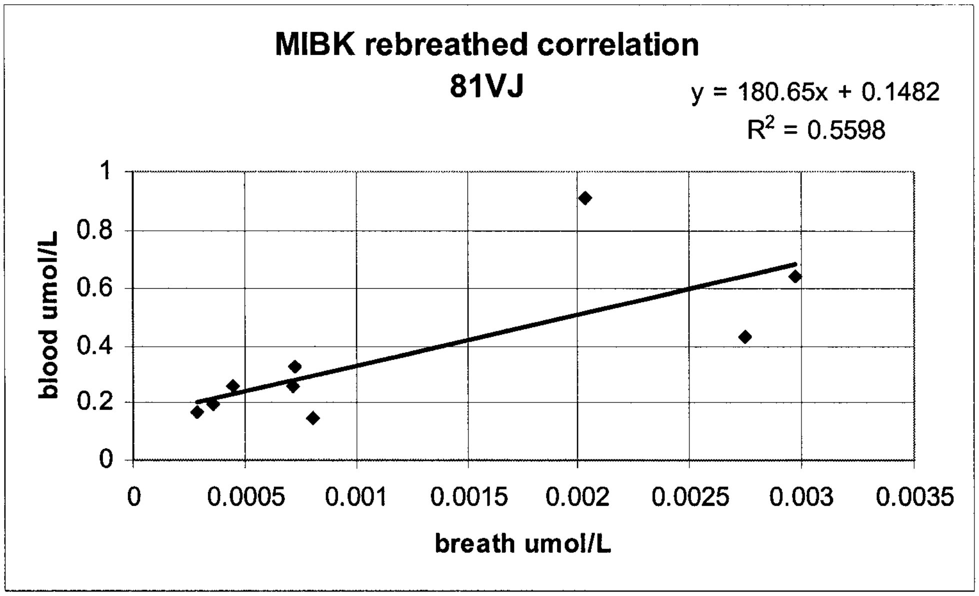
8/6/03

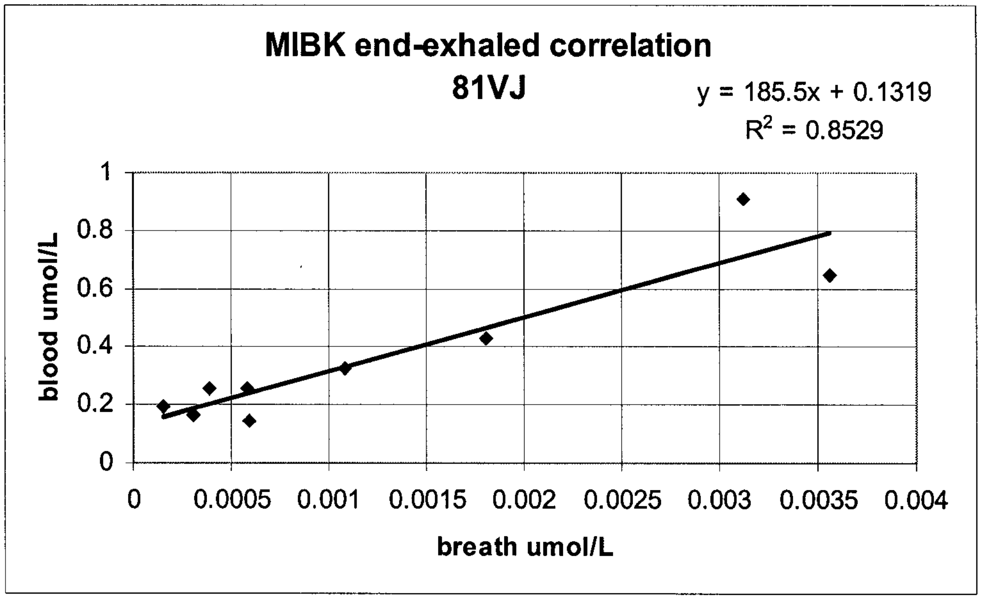

MIBK breath calibration
Subject 8
y = 1E-06x + 0.0001
R2 = 0.977
umol/L
0.007
0.006
0.005
0.004
0.003
0.002
0.001
0
0
1000
2000
3000
4000
5000
6000
area

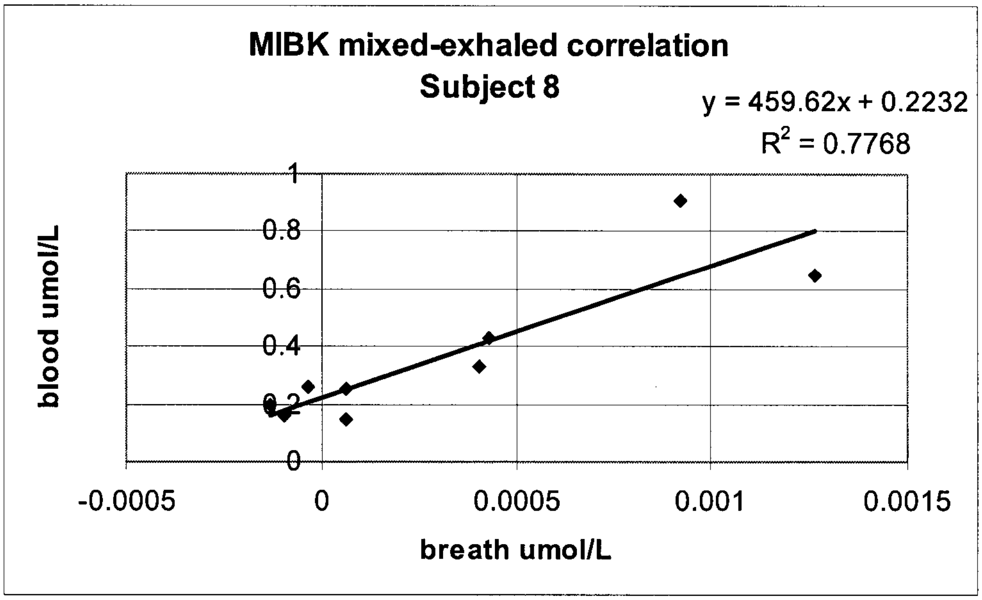

MIBK blood calibration
Subject 8
y = -4.81x^1.2 + 9.59x - 0.00767
R^2 = 0.9726
umol/L
10.000
1.000
0.100
0.010
0.001
0.01
0.1
1
10
MIBK 43 response factor

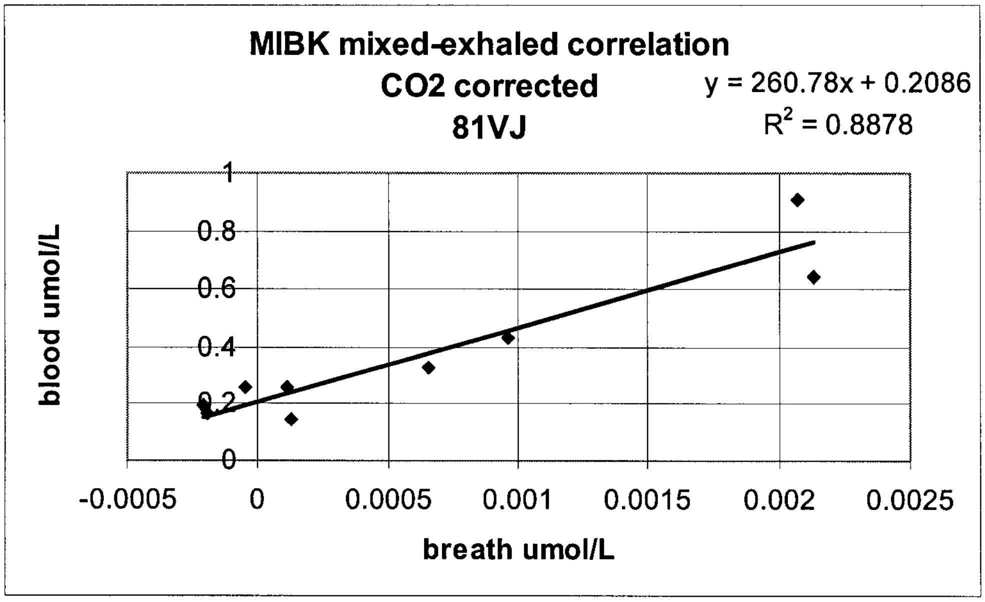

MIBK breath washout
Subject 8
umol/L
0.01
0.001
0.0001
0.00001
0:00
1:00
2:00
3:00
4:00
hours post-exposure
rebreathed
end-exhaled
mixed-exhaled


MIBK blood washout
Subject 8
10.0000
1.0000
0.1000
umol/L
0:00
1:00
2:00
3:00
4:00
hours post-exposure
◆ pre-breath
■ post-breath

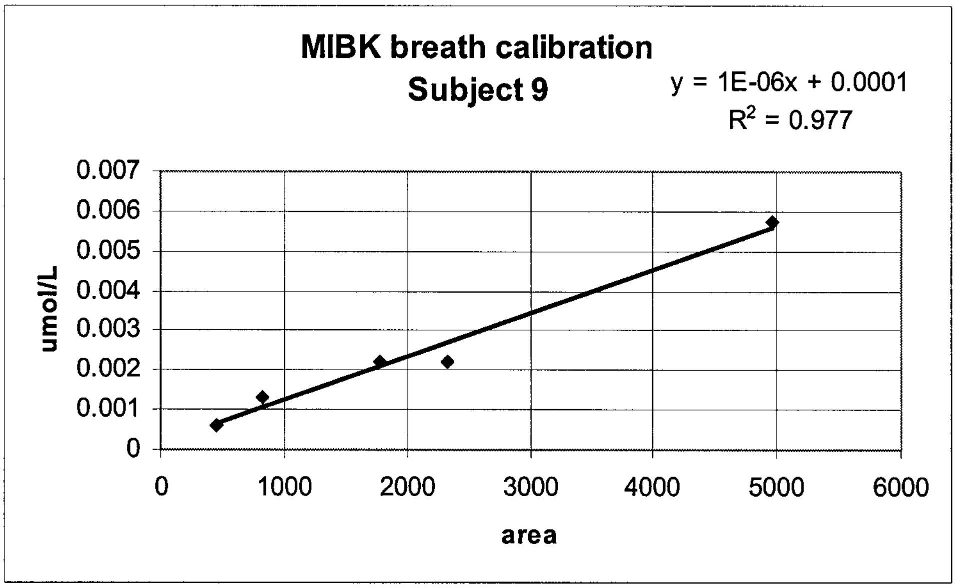

MIBK rebreathed correlation
81VJ
y = 180.65x + 0.1482
R^2 = 0.5598
1
0.8
0.6
0.4
0.2
0
blood umol/L
0
0.0005
0.001
0.0015
0.002
0.0025
0.003
0.0035
breath umol/L

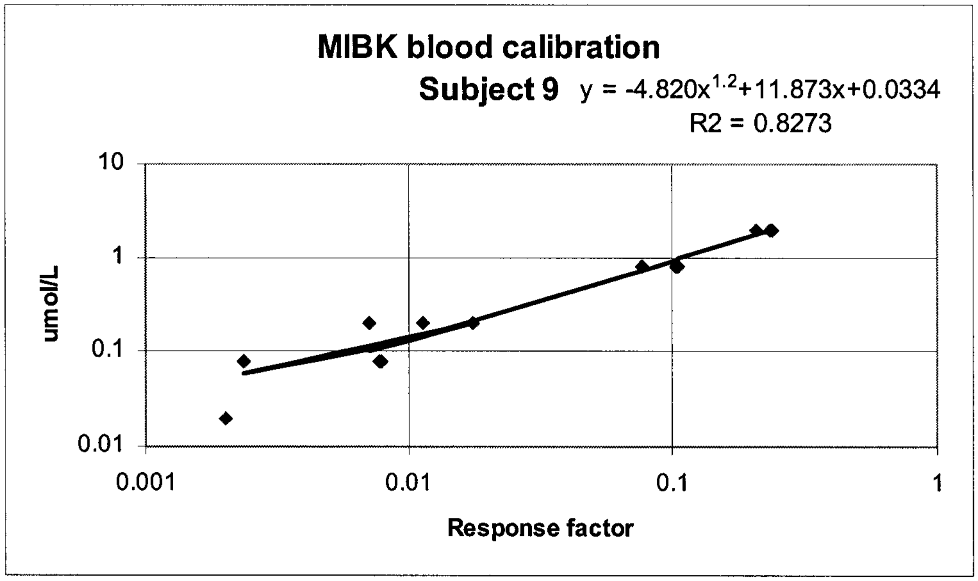

MIBK end-exhaled correlation
81VJ
y = 185.5x + 0.1319
R^2 = 0.8529
blood umol/L
1
0.8
0.6
0.4
0.2
0
0
0.0005
0.001
0.0015
0.002
0.0025
0.003
0.0035
0.004
breath umol/L

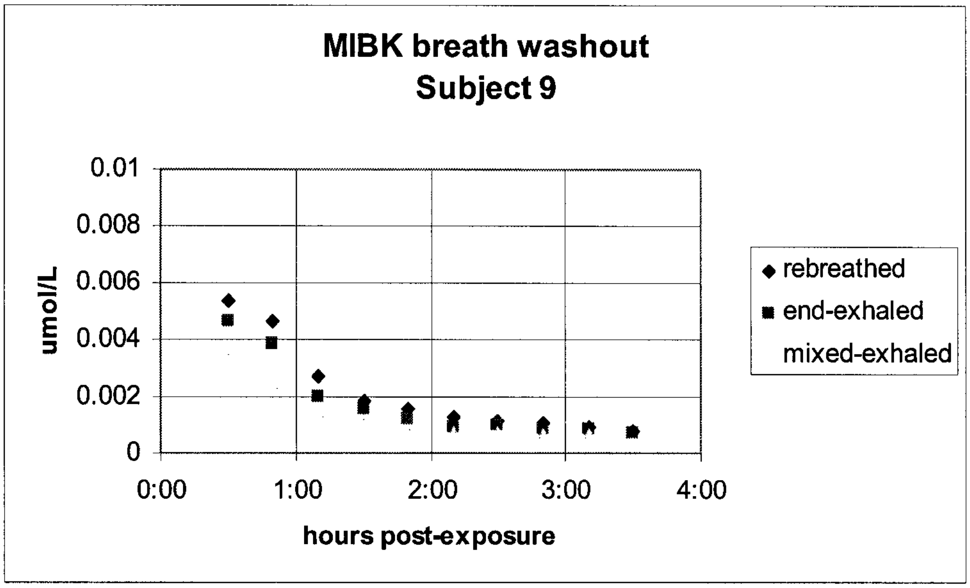

MIBK mixed-exhaled correlation
Subject 8
y = 459.62x + 0.2232
R^2 = 0.7768
blood umol/L
1
0.8
0.6
0.4
0.2
0
-0.0005
0
0.0005
0.001
0.0015
breath umol/L

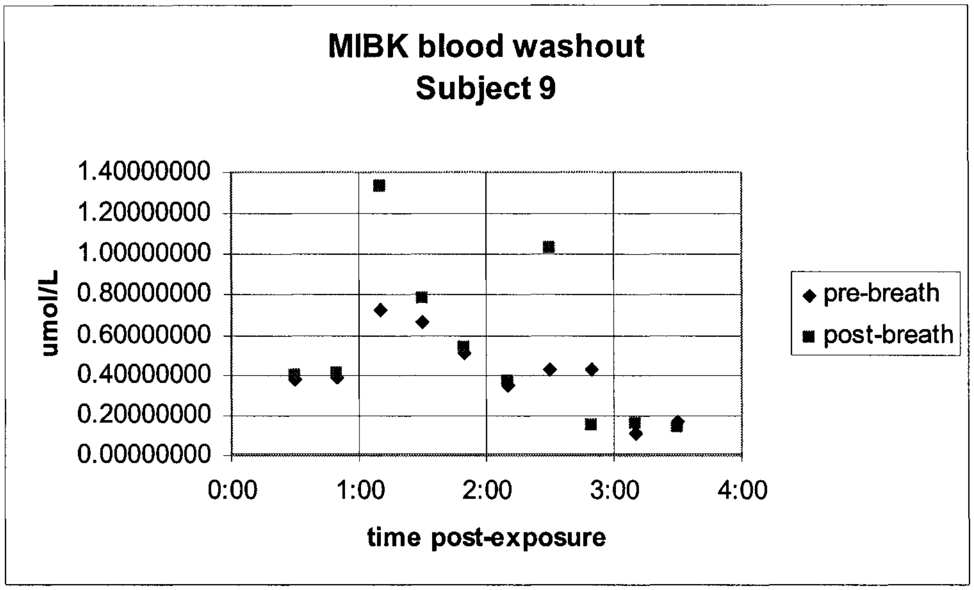

MIBK mixed-exhaled correlation
CO2 corrected
81VJ
y = 260.78x + 0.2086
R2 = 0.8878
blood umol/L
1
0.8
0.6
0.4
0.2
0
-0.0005
0
0.0005
0.001
0.0015
0.002
0.0025
breath umol/L

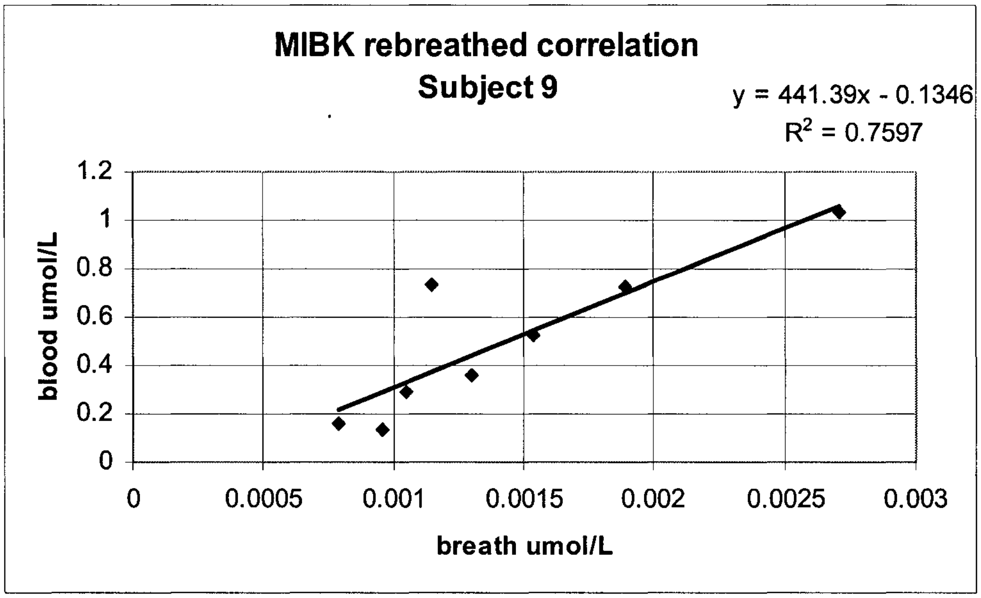
8/11/03

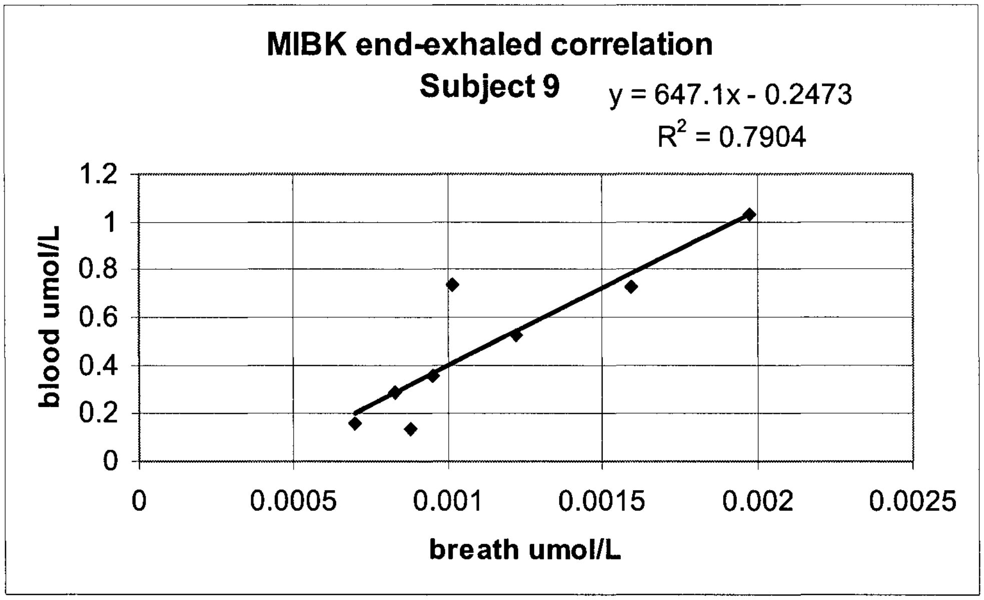

MIBK breath calibration
Subject 9
y = 1E-06x + 0.0001
R2 = 0.977
umol/L
0.007
0.006
0.005
0.004
0.003
0.002
0.001
0
0
1000
2000
3000
4000
5000
6000
area

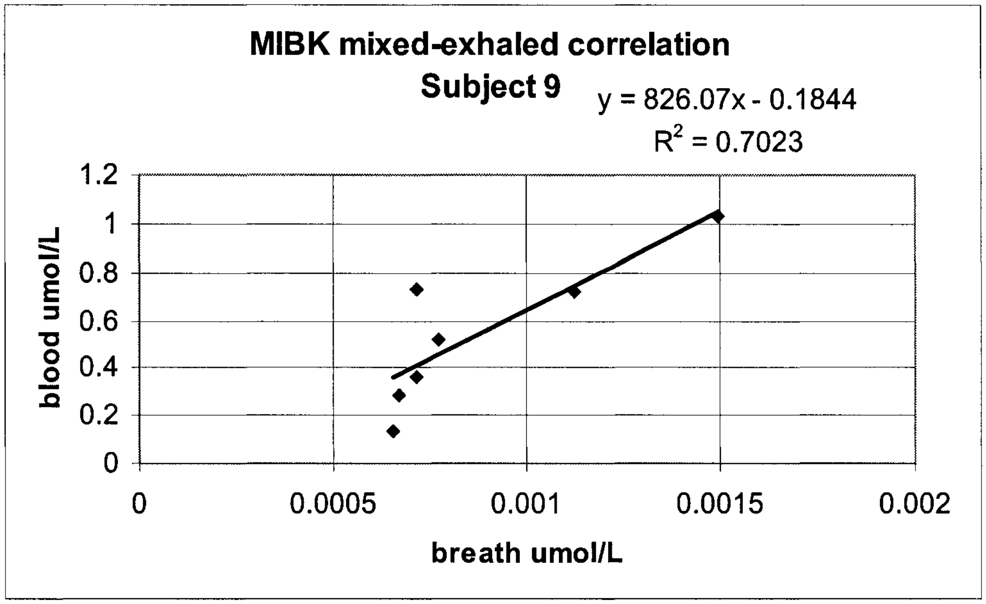

MIBK blood calibration
Subject 9
$y = -4.820x^{1.2}+11.873x+0.0334$
R2 = 0.8273
10
1
0.1
0.01
umol/L
0.001
0.01
0.1
1
Response factor

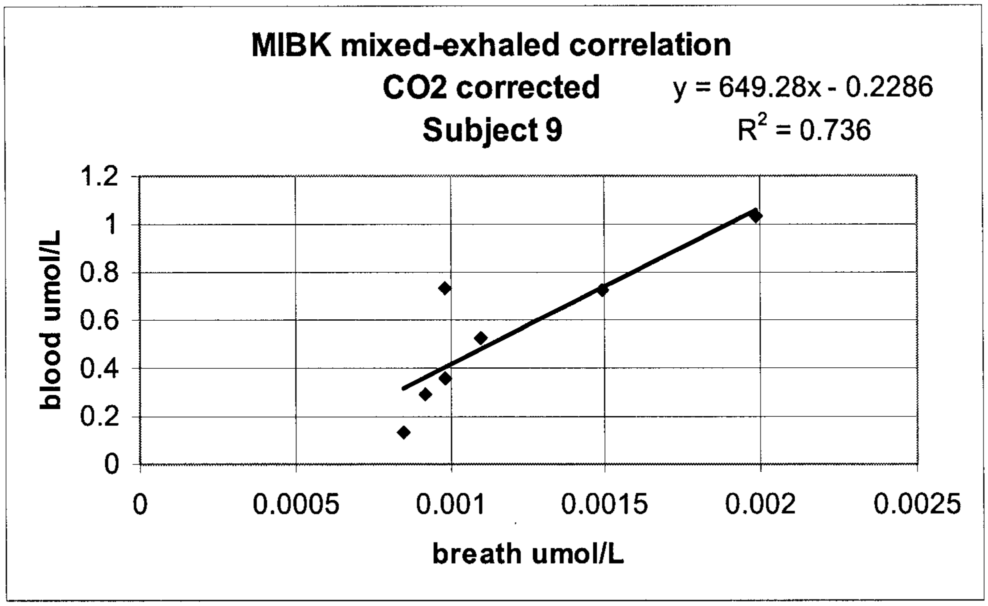

MIBK breath washout
Subject 9
0.01
0.008
0.006
0.004
0.002
0
umol/L
0:00
1:00
2:00
3:00
4:00
hours post-exposure
◆ rebreathed
■ end-exhaled
mixed-exhaled


MIBK blood washout
Subject 9
umol/L
1.40000000
1.20000000
1.00000000
0.80000000
0.60000000
0.40000000
0.20000000
0.00000000
0:00
1:00
2:00
3:00
4:00
time post-exposure
◆ pre-breath
■ post-breath

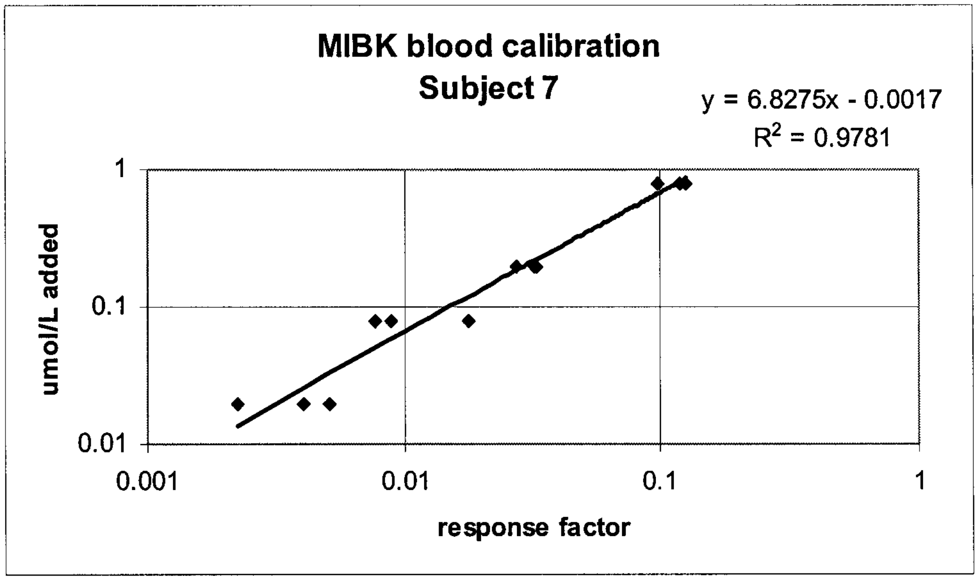

MIBK rebreathed correlation
Subject 9
y = 441.39x - 0.1346
R² = 0.7597
blood umol/L
1.2
1
0.8
0.6
0.4
0.2
0
0
0.0005
0.001
0.0015
0.002
0.0025
0.003
breath umol/L

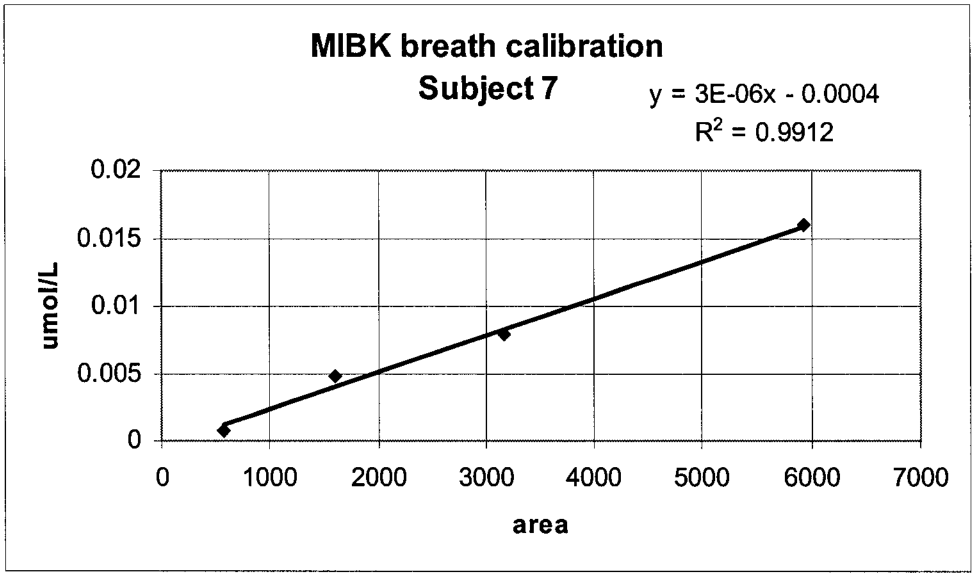

MIBK end-exhaled correlation
Subject 9
y = 647.1x - 0.2473
R2 = 0.7904
1.2
1
0.8
0.6
0.4
0.2
0
blood umol/L
0
0.0005
0.001
0.0015
0.002
0.0025
breath umol/L

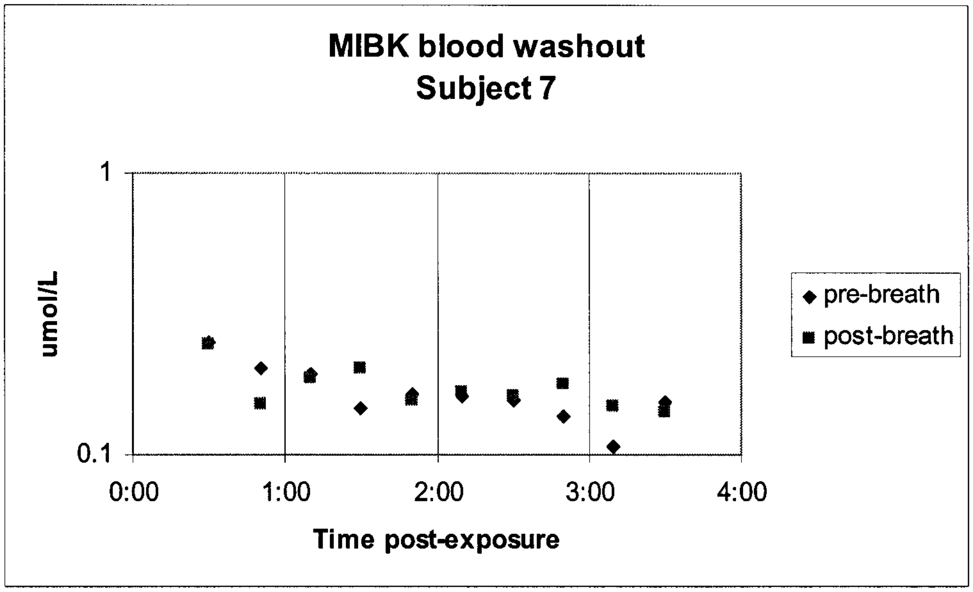

MIBK mixed-exhaled correlation
Subject 9
y = 826.07x - 0.1844
R2 = 0.7023
1.2
1
0.8
0.6
0.4
0.2
0
blood umol/L
0
0.0005
0.001
0.0015
0.002
breath umol/L

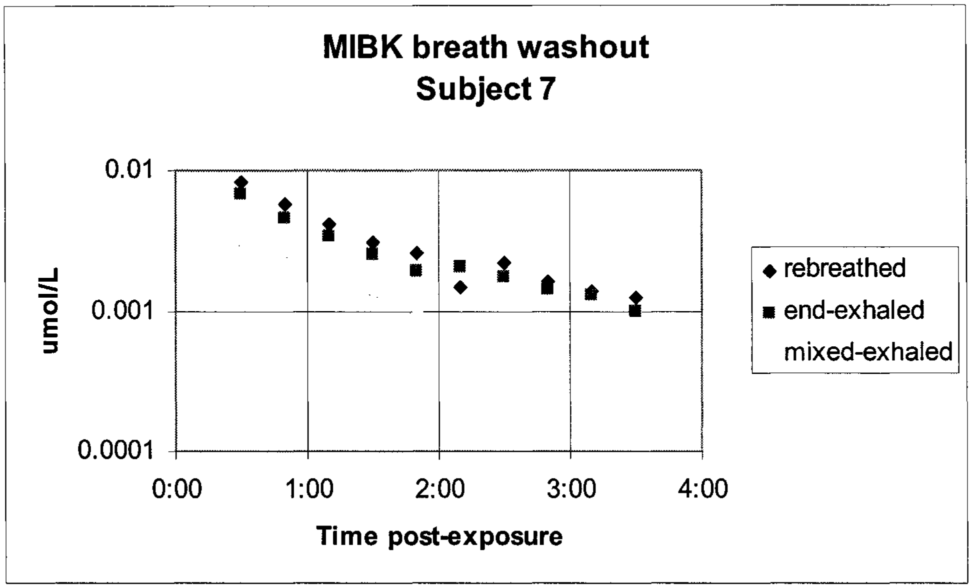

MIBK mixed-exhaled correlation
CO2 corrected
Subject 9
y = 649.28x - 0.2286
R2 = 0.736
1.2
1
0.8
0.6
0.4
0.2
0
blood umol/L
0
0.0005
0.001
0.0015
0.002
0.0025
breath umol/L

8/21/03

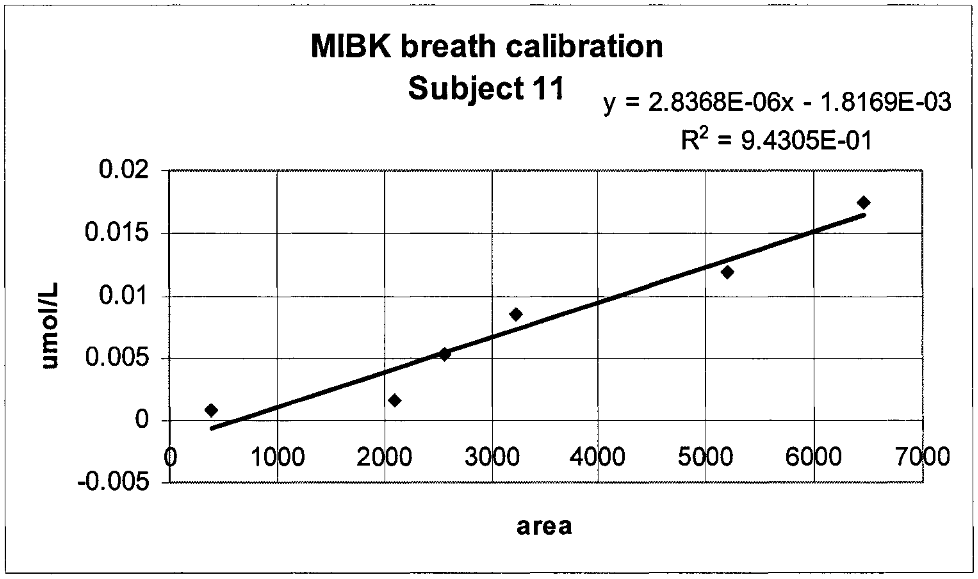

MIBK blood calibration
Subject 7
y = 6.8275x - 0.0017
R2 = 0.9781
1
0.1
0.01
umol/L added
0.001
0.01
0.1
1
response factor

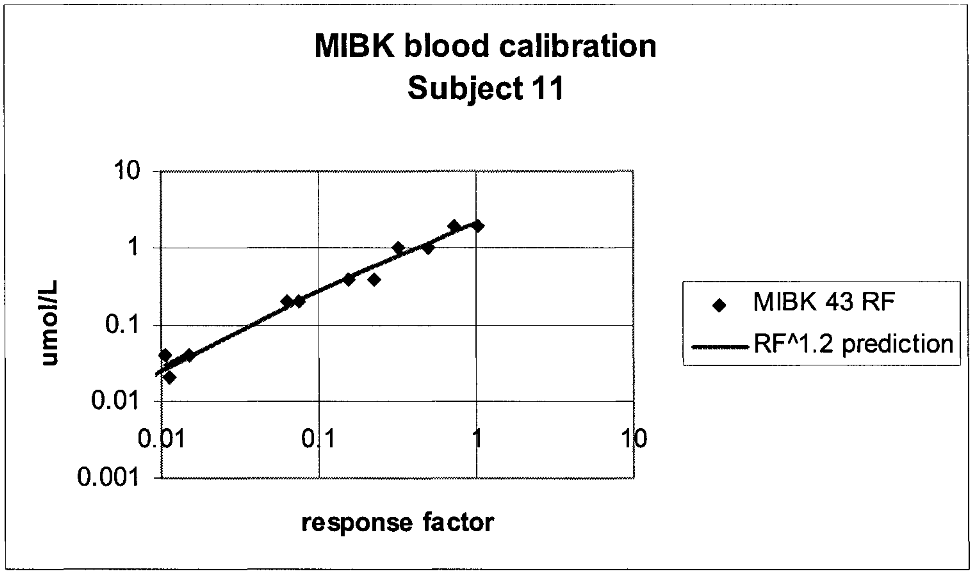

MIBK breath calibration
Subject 7
y = 3E-06x - 0.0004
R^2 = 0.9912
umol/L
0.02
0.015
0.01
0.005
0
0
1000
2000
3000
4000
5000
6000
7000
area


MIBK blood washout
Subject 7
umol/L
1
0.1
0:00
1:00
2:00
3:00
4:00
Time post-exposure
◆ pre-breath
■ post-breath

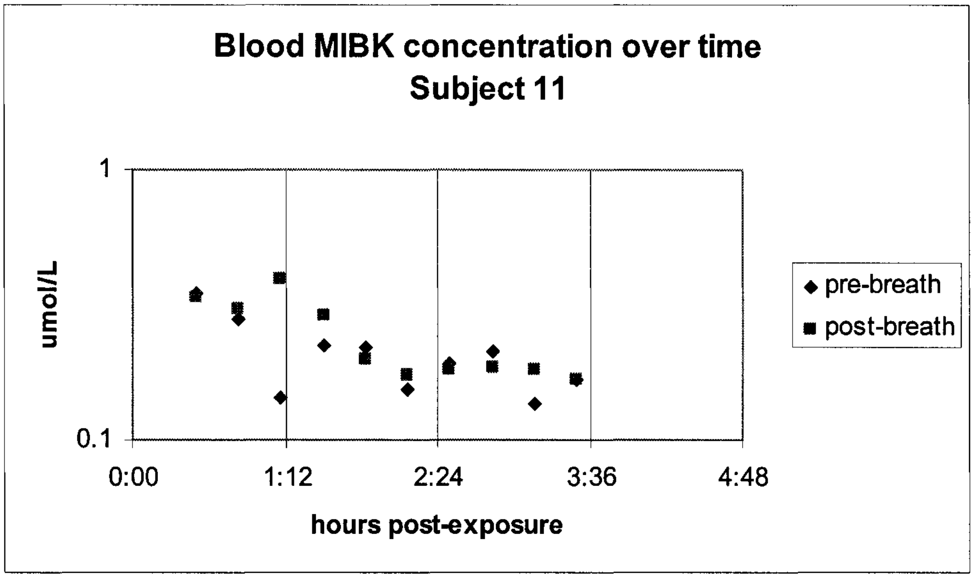

MIBK breath washout
Subject 7
0.01
0.001
0.0001
umol/L
0:00
1:00
2:00
3:00
4:00
Time post-exposure
◆ rebreathed
■ end-exhaled
mixed-exhaled

11/19/03

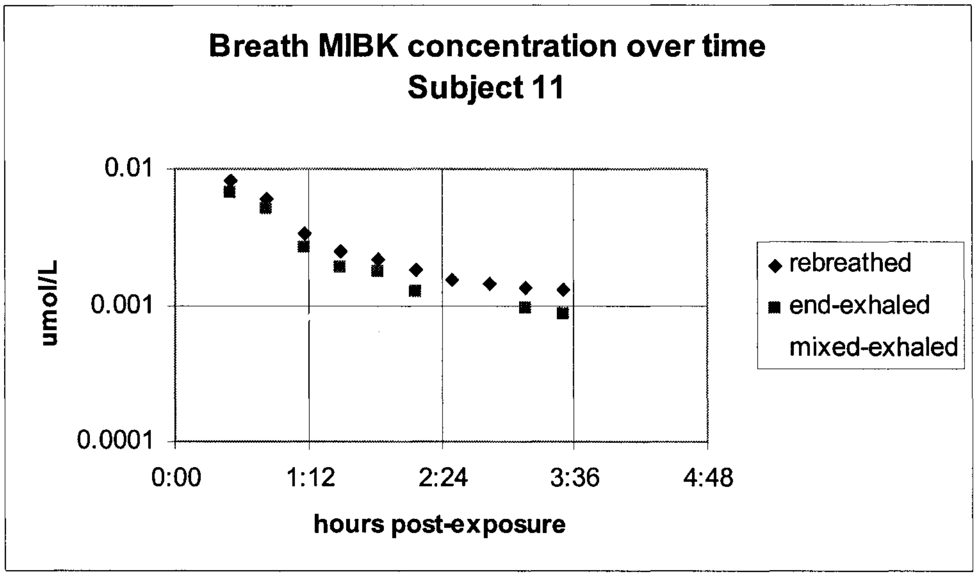

MIBK breath calibration
Subject 11
y = 2.8368E-06x - 1.8169E-03
R2 = 9.4305E-01
0.02
0.015
0.01
0.005
0
-0.005
umol/L
0
1000
2000
3000
4000
5000
6000
7000
area

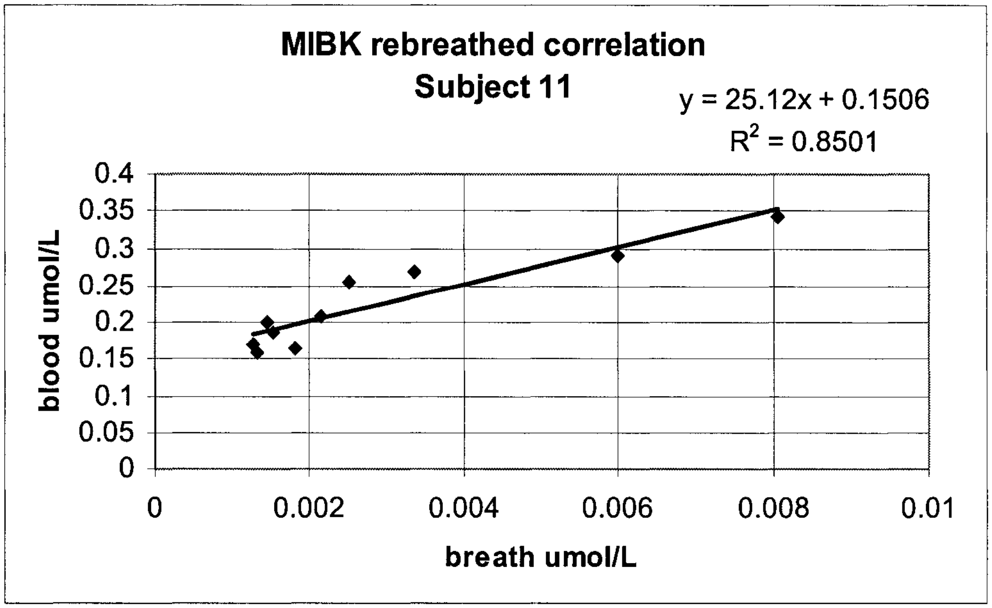


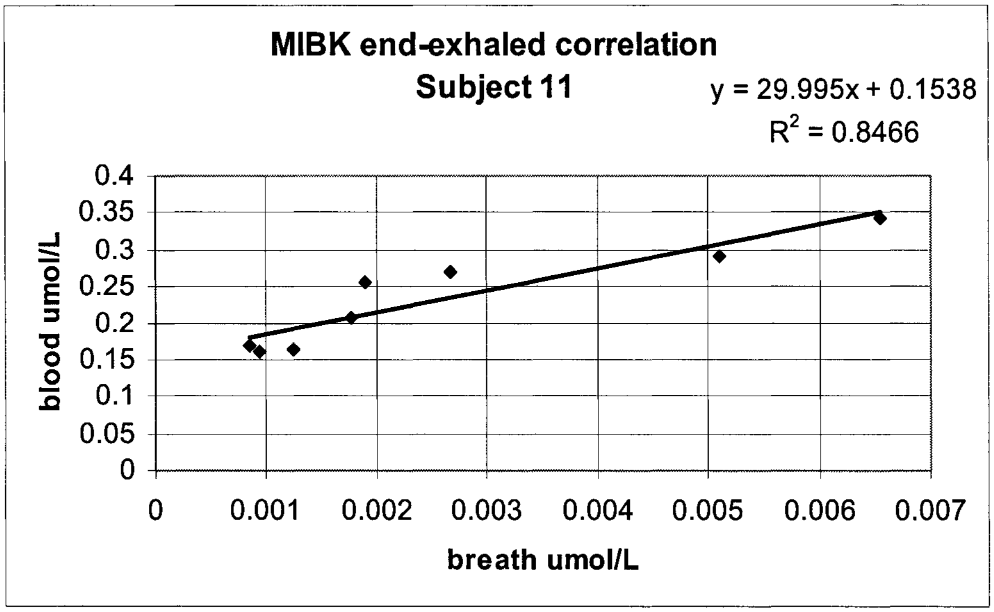
MIBK blood calibration
Subject 11

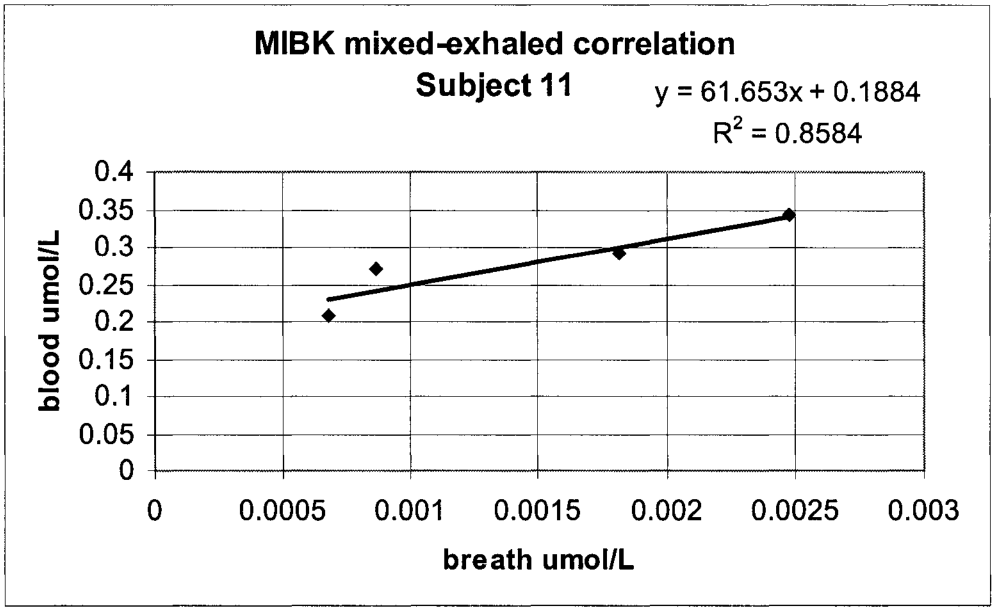


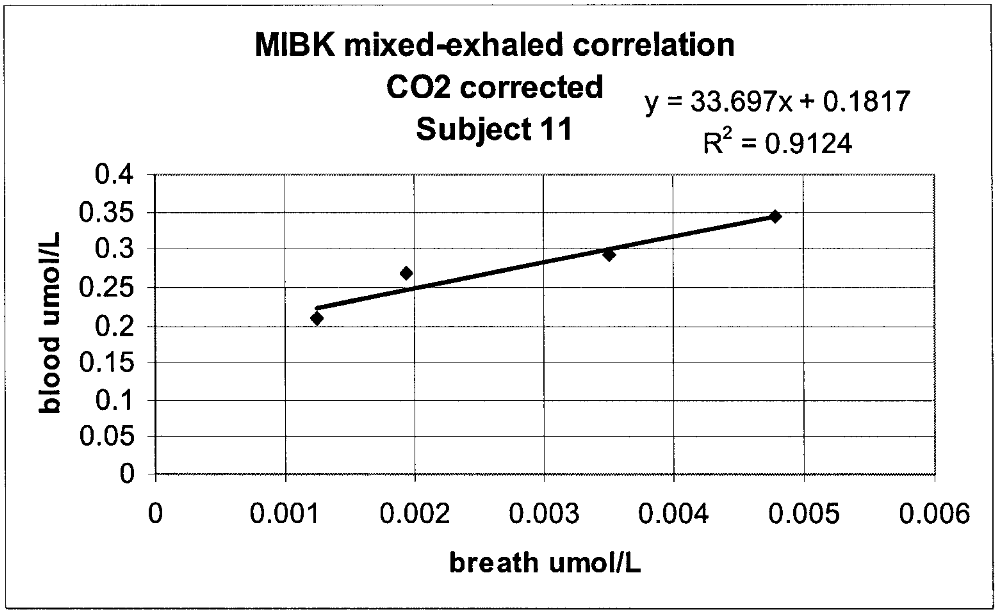
Blood MIBK concentration over time
Subject 11


Breath MIBK concentration over time
Subject 11
umol/L
0.01
0.001
0.0001
0:00
1:12
2:24
3:36
4:48
hours post-exposure
◆ rebreathed
■ end-exhaled
mixed-exhaled

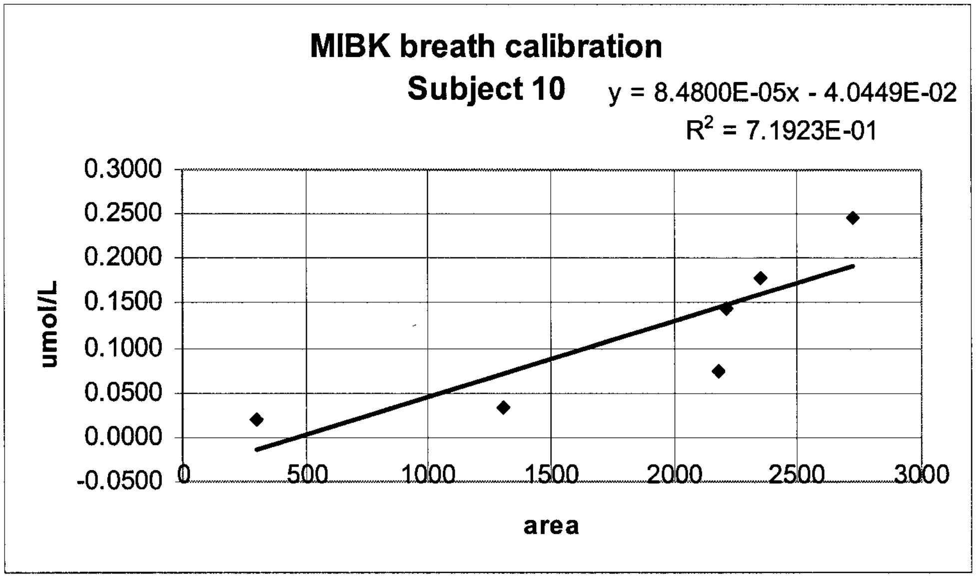

MIBK rebreathed correlation
Subject 11
y = 25.12x + 0.1506
R2 = 0.8501
blood umol/L
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
0
0.002
0.004
0.006
0.008
0.01
breath umol/L

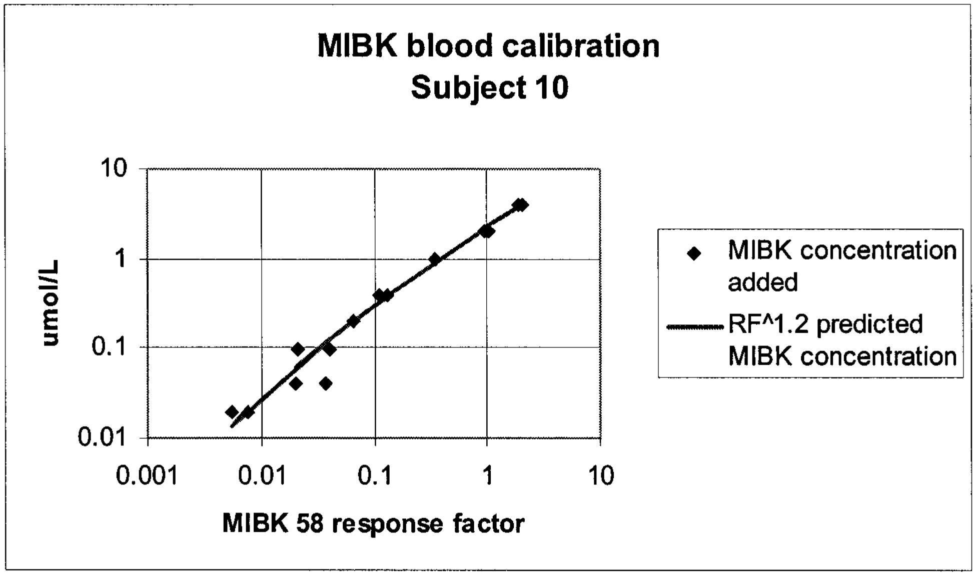

MIBK end-exhaled correlation
Subject 11
y = 29.995x + 0.1538
R2 = 0.8466
blood umol/L
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
0
0.001
0.002
0.003
0.004
0.005
0.006
0.007
breath umol/L

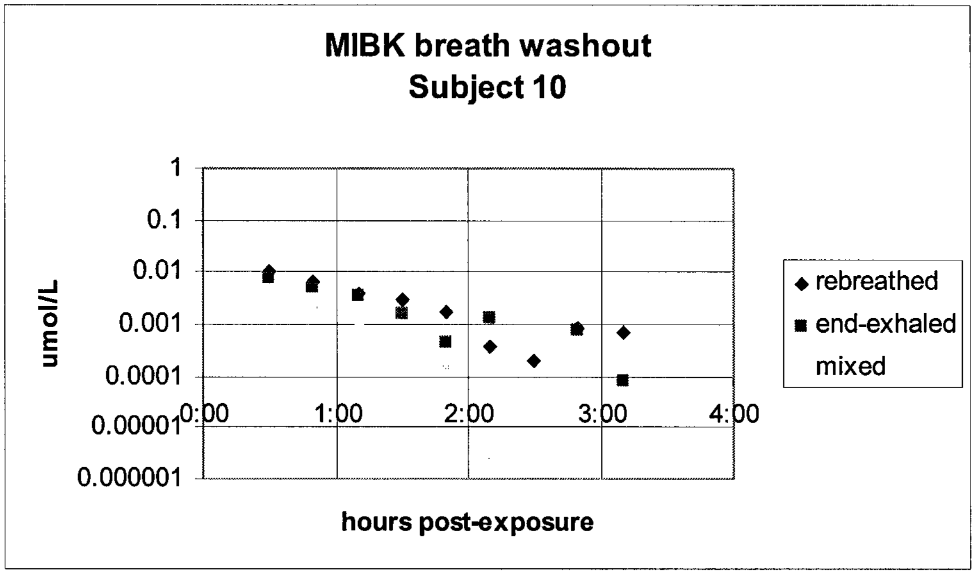

MIBK mixed-exhaled correlation
Subject 11
y = 61.653x + 0.1884
R2 = 0.8584
blood umol/L
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
0
0.0005
0.001
0.0015
0.002
0.0025
0.003
breath umol/L

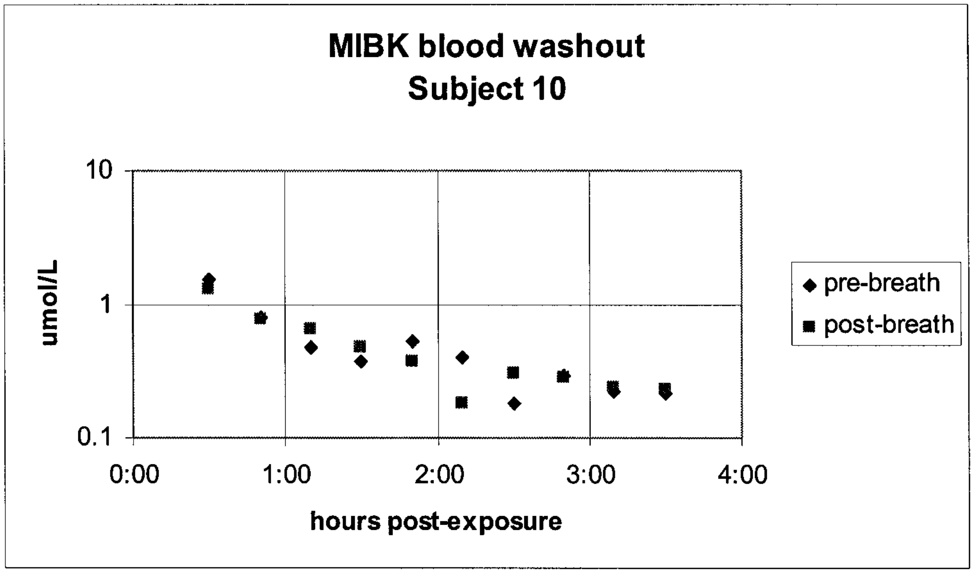

MIBK mixed-exhaled correlation
CO2 corrected
Subject 11
y = 33.697x + 0.1817
R2 = 0.9124
blood umol/L
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
0
0.001
0.002
0.003
0.004
0.005
0.006
breath umol/L

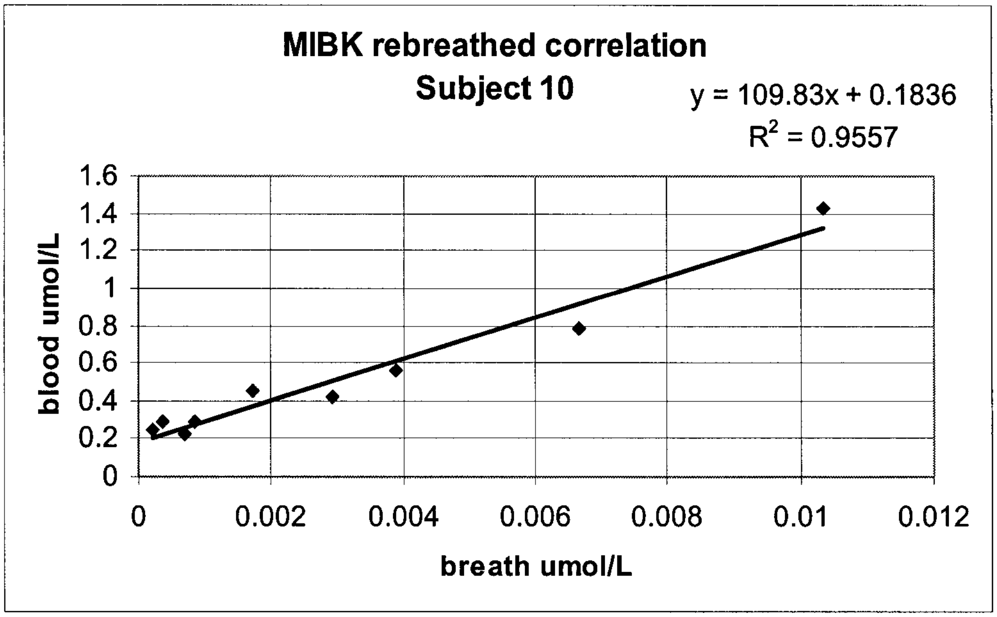
12/17/03

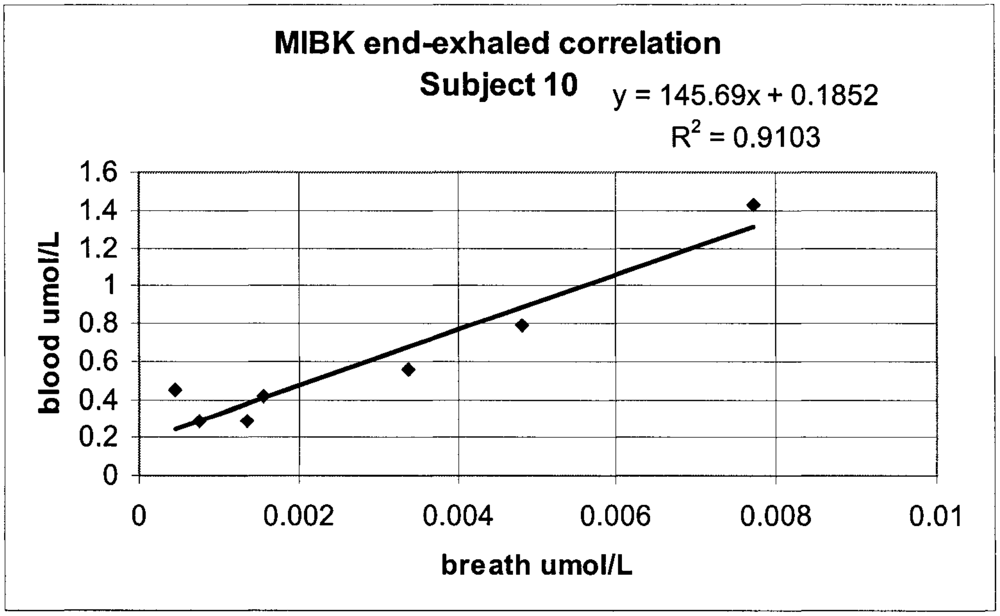

MIBK breath calibration
Subject 10
y = 8.4800E-05x - 4.0449E-02
R2 = 7.1923E-01
umol/L
0.3000
0.2500
0.2000
0.1500
0.1000
0.0500
0.0000
-0.0500
0
500
1000
1500
2000
2500
3000
area

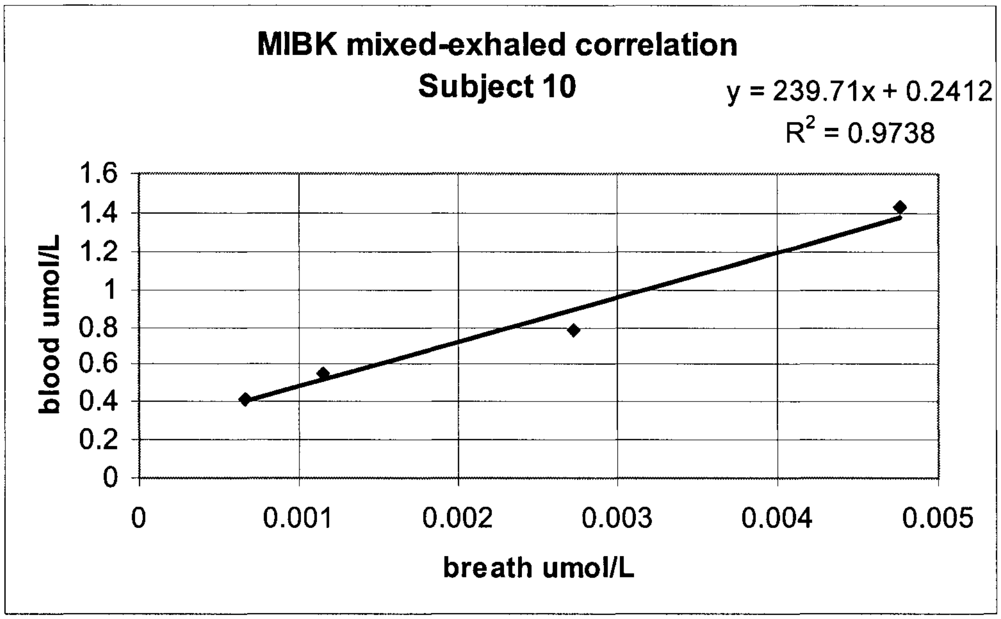

MIBK blood calibration
Subject 10
10
1
0.1
0.01
umol/L
0.001
0.01
0.1
1
10
MIBK 58 response factor
◆ MIBK concentration added
RF^1.2 predicted MIBK concentration

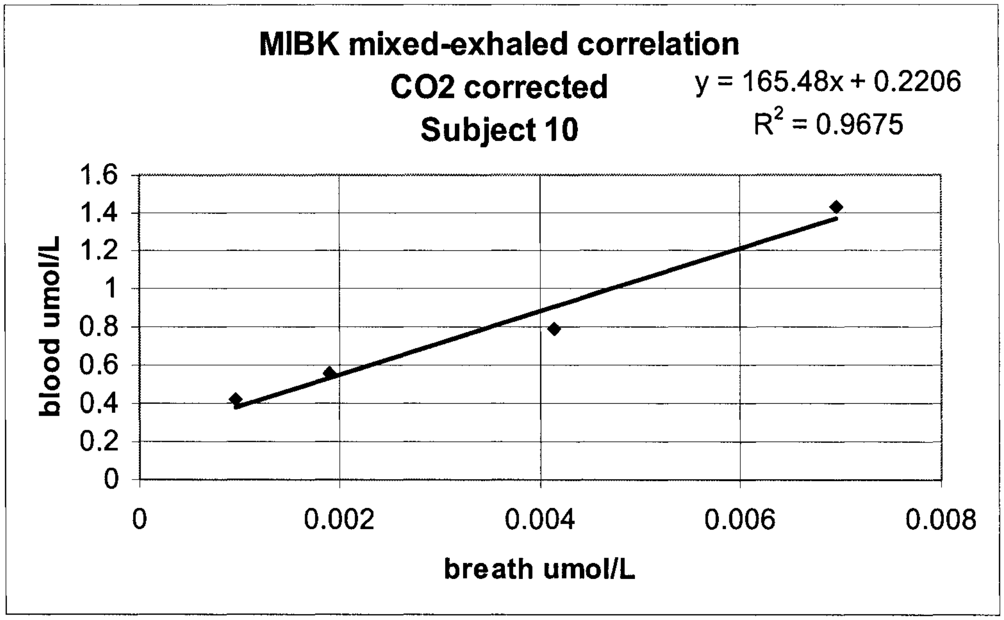

MIBK breath washout
Subject 10
1
0.1
0.01
0.001
0.0001
0.00001
0.000001
umol/L
0:00
1:00
2:00
3:00
4:00
hours post-exposure
◆ rebreathed
■ end-exhaled
mixed


MIBK blood washout
Subject 10
10
1
0.1
umol/L
0:00
1:00
2:00
3:00
4:00
hours post-exposure
◆ pre-breath
■ post-breath

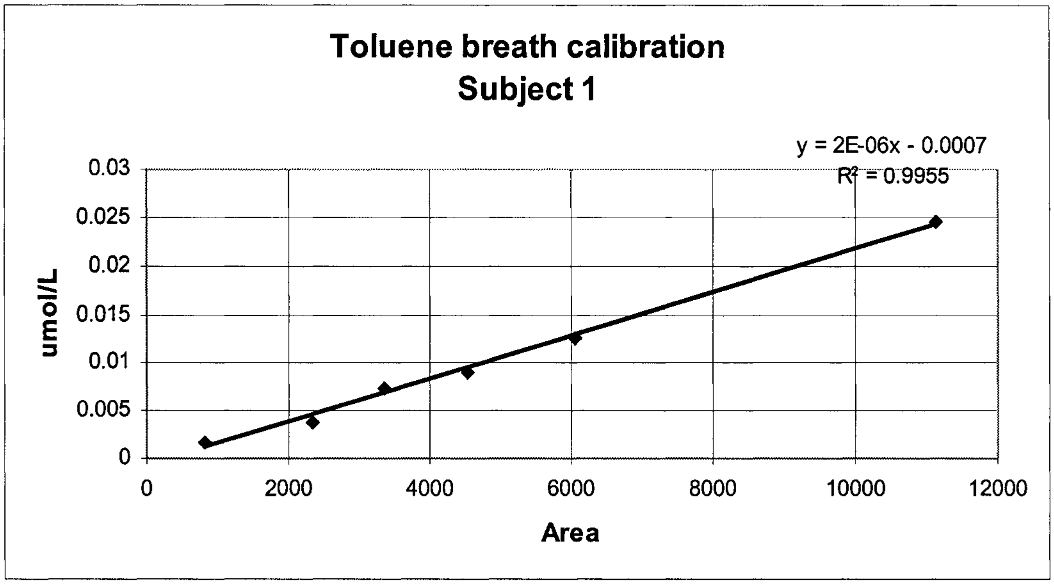

MIBK rebreathed correlation
Subject 10
y = 109.83x + 0.1836
R² = 0.9557
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
blood umol/L
0
0.002
0.004
0.006
0.008
0.01
0.012
breath umol/L

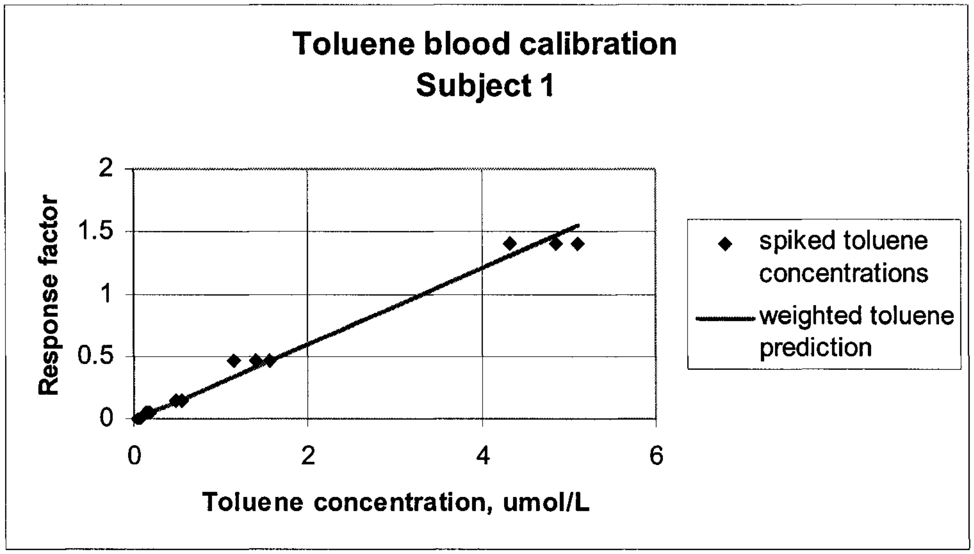

MIBK end-exhaled correlation
Subject 10
y = 145.69x + 0.1852
R2 = 0.9103
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
blood umol/L
0
0.002
0.004
0.006
0.008
0.01
breath umol/L

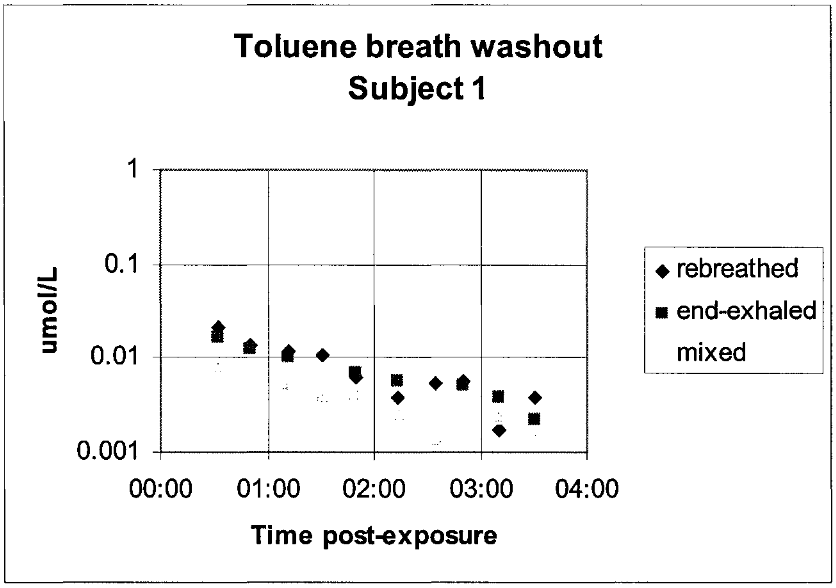

MIBK mixed-exhaled correlation
Subject 10
y = 239.71x + 0.2412
R2 = 0.9738
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
blood umol/L
0
0.001
0.002
0.003
0.004
0.005
breath umol/L

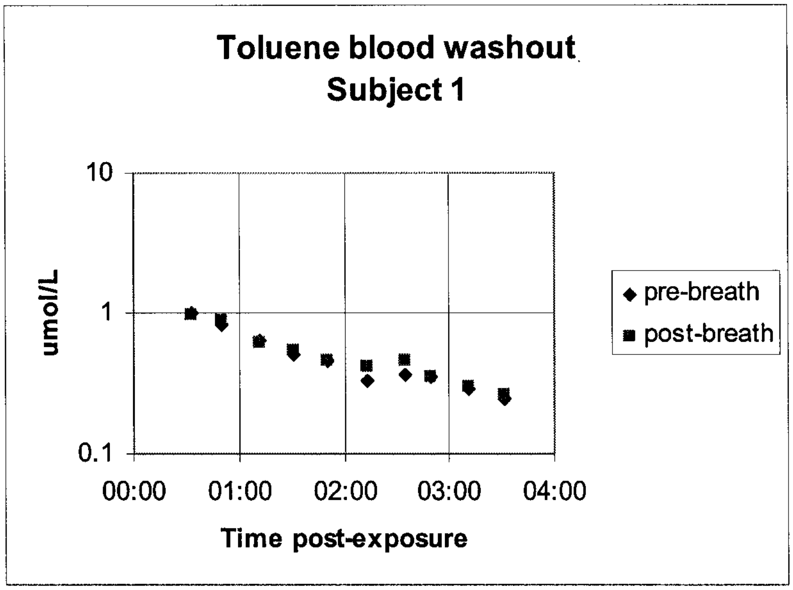


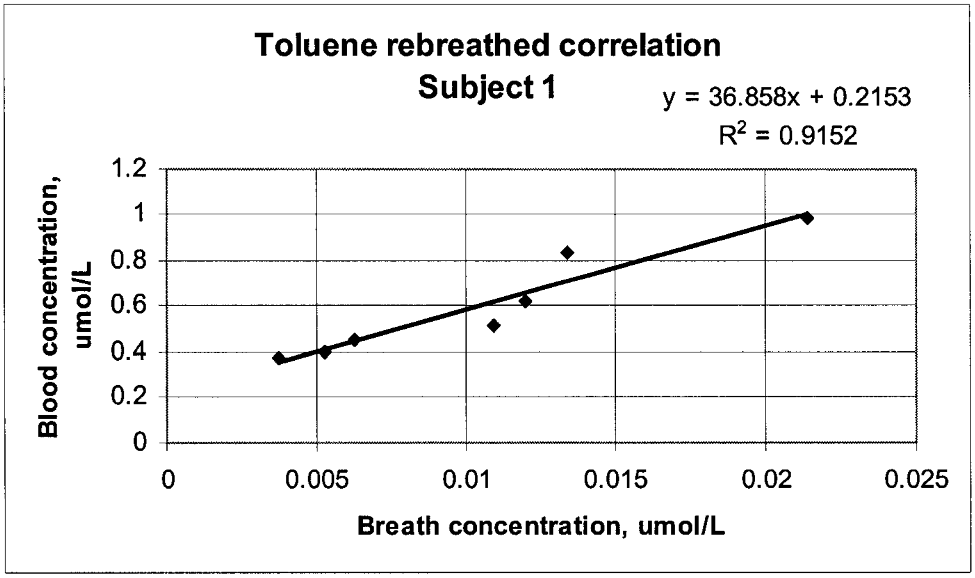
Toluene
10/23/02

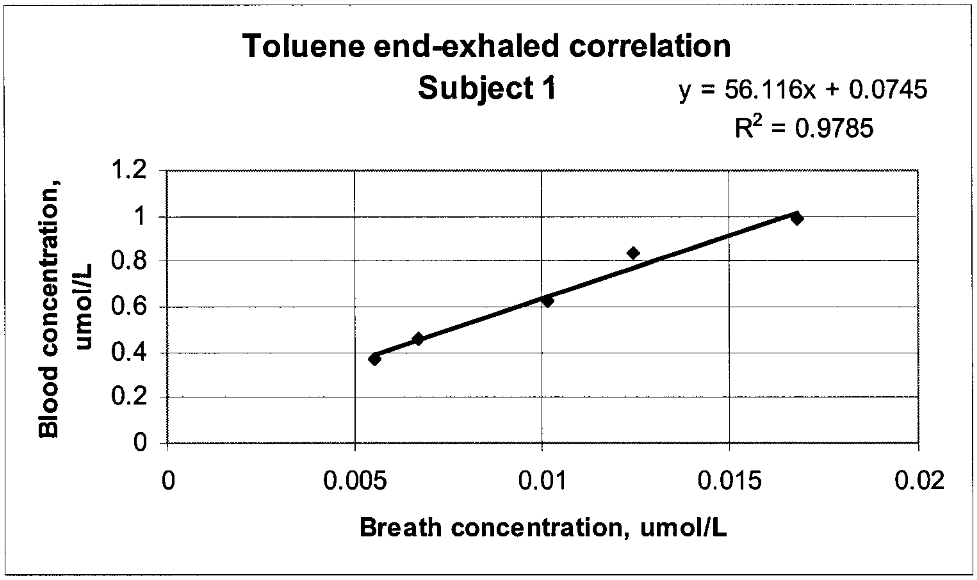


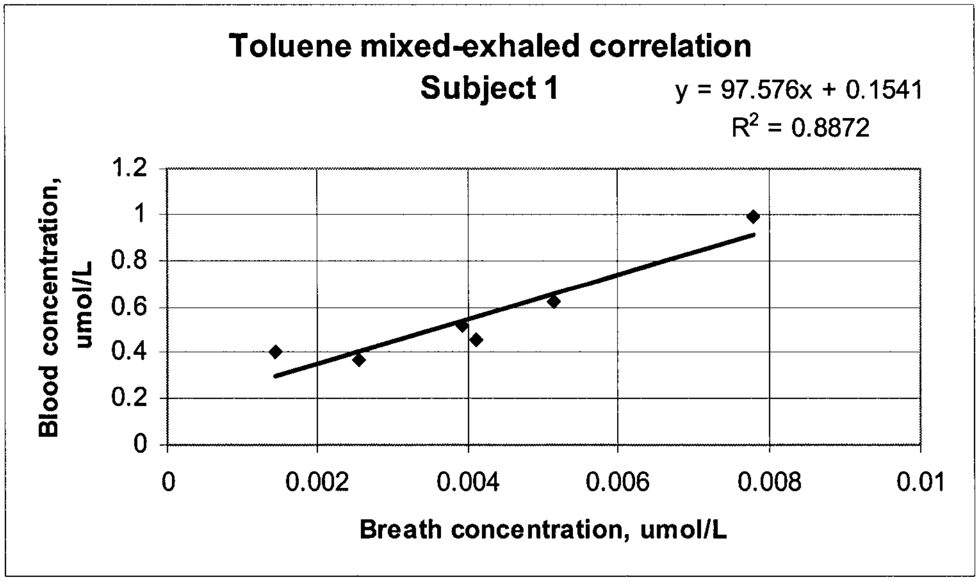

Toluene blood calibration
Subject 1
Response factor
2
1.5
1
0.5
0
0
2
4
6
Toluene concentration, umol/L
spiked toluene concentrations
weighted toluene prediction

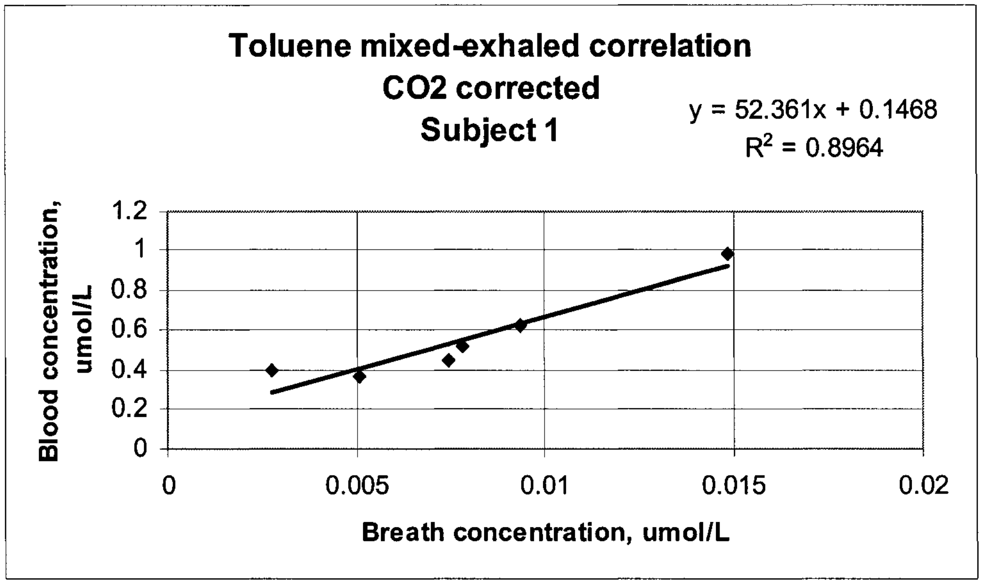

Toluene breath washout
Subject 1
umol/L
1
0.1
0.01
0.001
00:00
01:00
02:00
03:00
04:00
Time post-exposure
rebreathed
end-exhaled
mixed


Toluene blood washout
Subject 1
10
1
0.1
umol/L
00:00
01:00
02:00
03:00
04:00
Time post-exposure
◆ pre-breath
■ post-breath

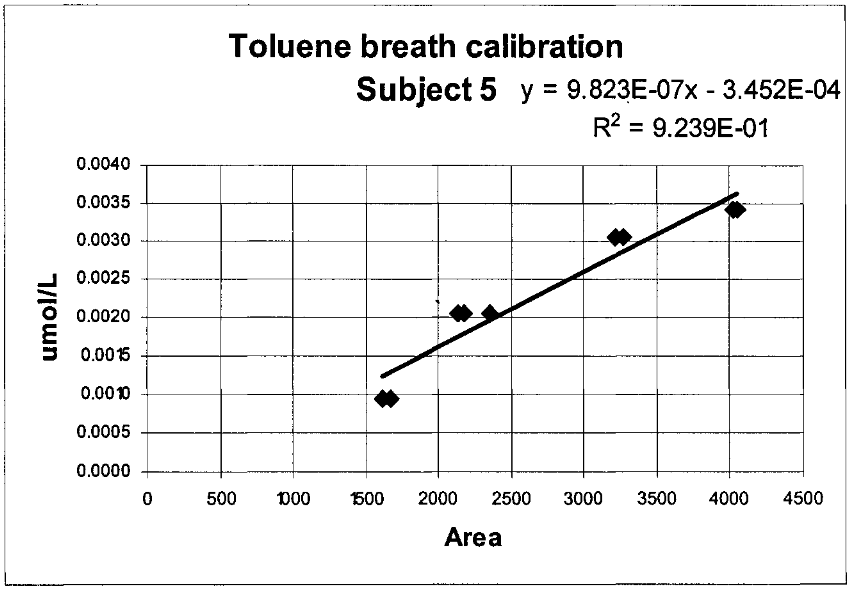

Toluene rebreathed correlation
Subject 1
y = 36.858x + 0.2153
R2 = 0.9152
1.2
1
0.8
0.6
0.4
0.2
0
Blood concentration, umol/L
0
0.005
0.01
0.015
0.02
0.025
Breath concentration, umol/L

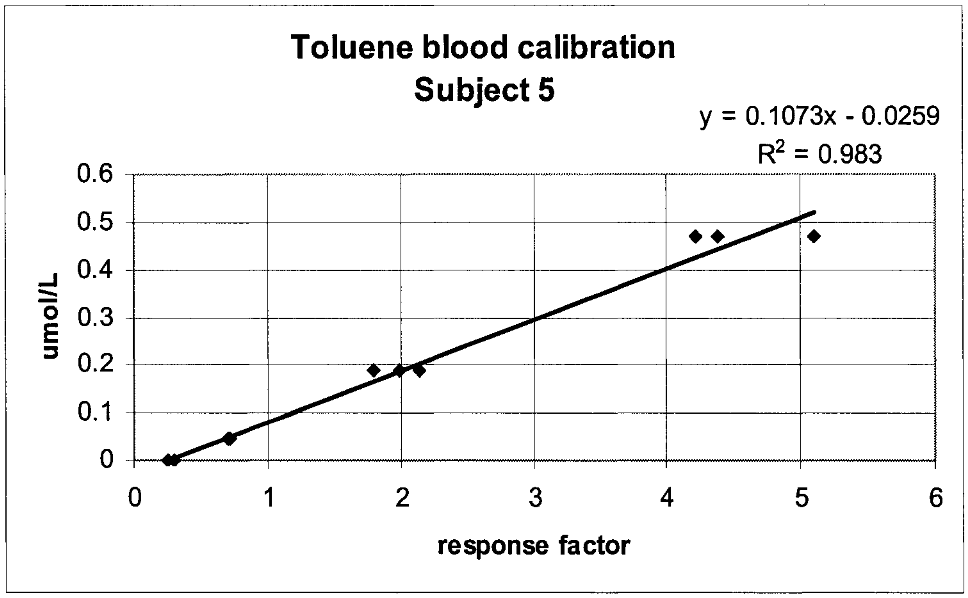

Toluene end-exhaled correlation
Subject 1
y = 56.116x + 0.0745
R^2 = 0.9785
Blood concentration, umol/L
1.2
1
0.8
0.6
0.4
0.2
0
0
0.005
0.01
0.015
0.02
Breath concentration, umol/L

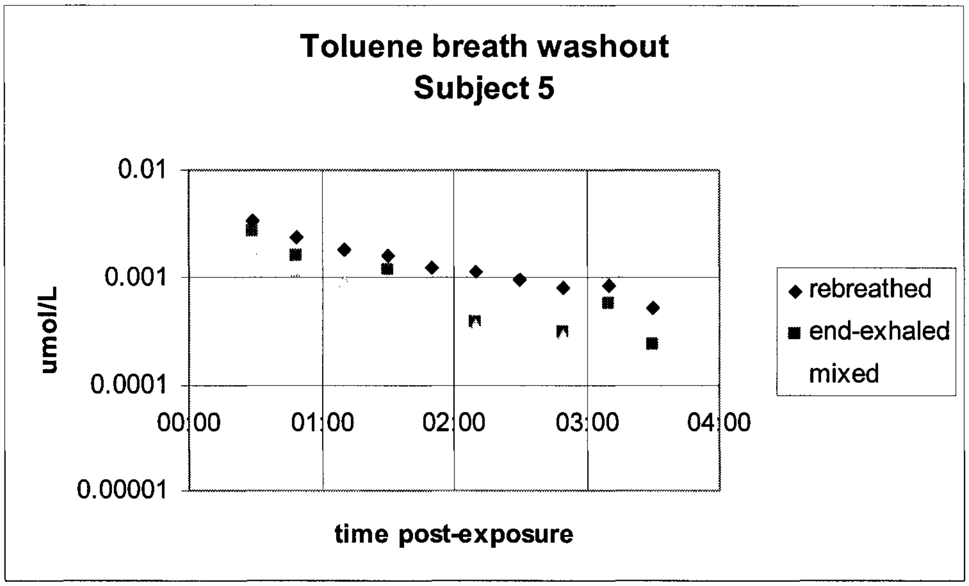

Toluene mixed-exhaled correlation
Subject 1
y = 97.576x + 0.1541
R^2 = 0.8872
Blood concentration, umol/L
1.2
1
0.8
0.6
0.4
0.2
0
0
0.002
0.004
0.006
0.008
0.01
Breath concentration, umol/L

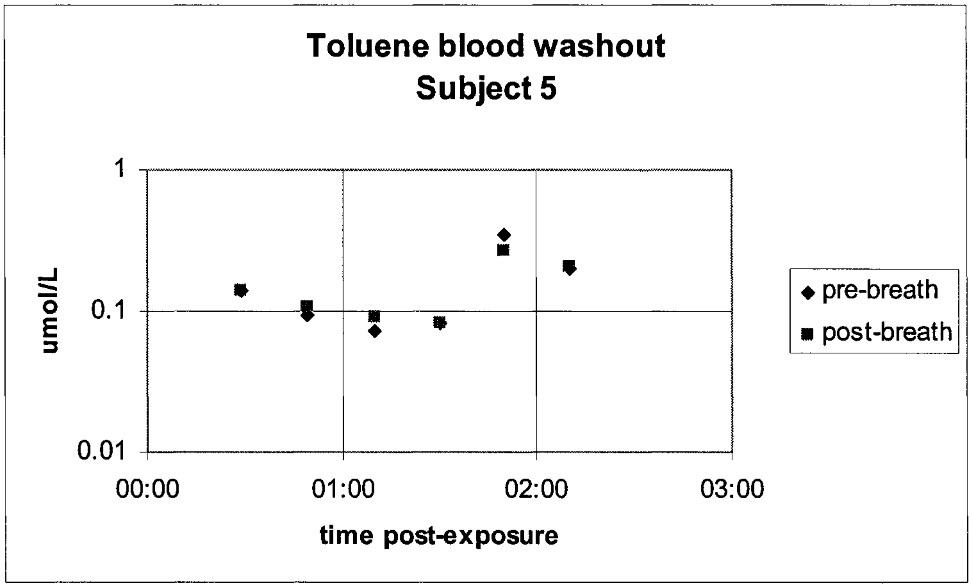

Toluene mixed-exhaled correlation
CO2 corrected
Subject 1
y = 52.361x + 0.1468
R² = 0.8964
Blood concentration, umol/L
1.2
1
0.8
0.6
0.4
0.2
0
0
0.005
0.01
0.015
0.02
Breath concentration, umol/L

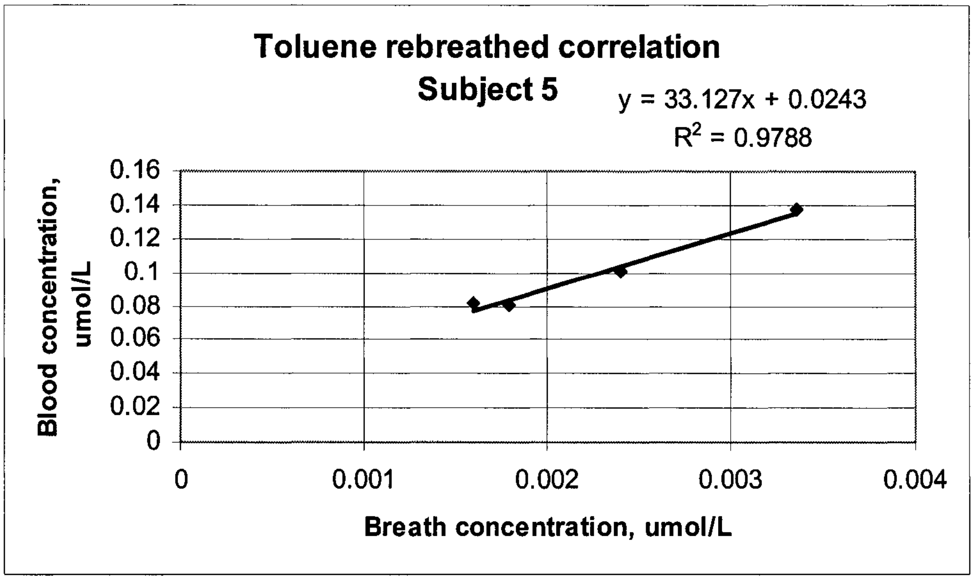
5/1/03:

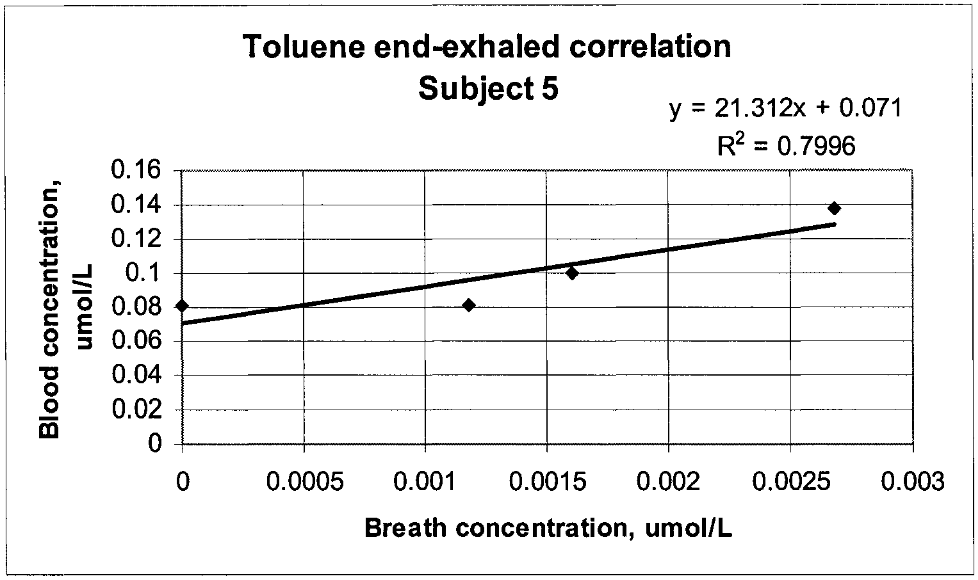

Toluene breath calibration
Subject 5
y = 9.823E-07x - 3.452E-04
R² = 9.239E-01
umol/L
0.0040
0.0035
0.0030
0.0025
0.0020
0.0015
0.0010
0.0005
0.0000
0
500
1000
1500
2000
2500
3000
3500
4000
4500
Area

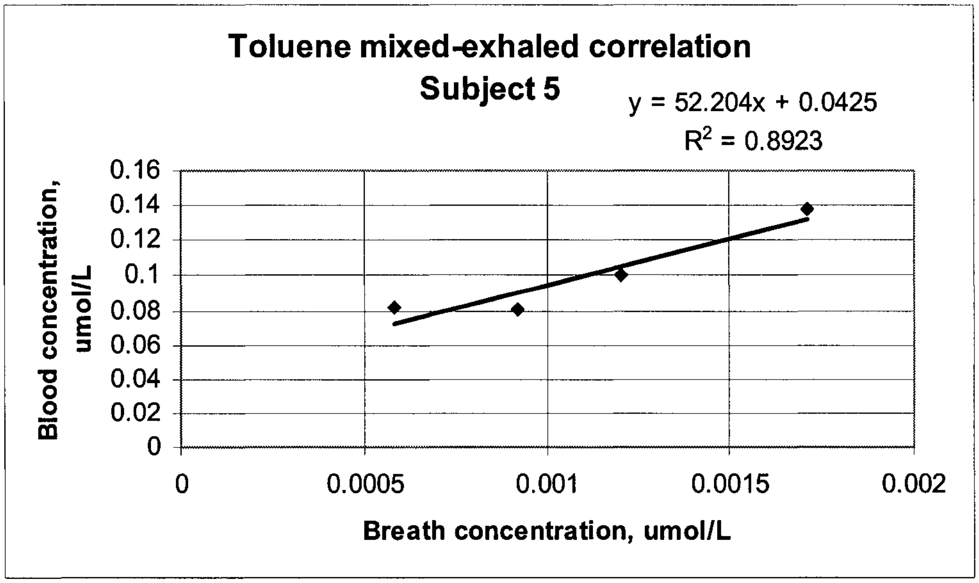

Toluene blood calibration
Subject 5
y = 0.1073x - 0.0259
R² = 0.983
umol/L
0.6
0.5
0.4
0.3
0.2
0.1
0
0
1
2
3
4
5
6
response factor

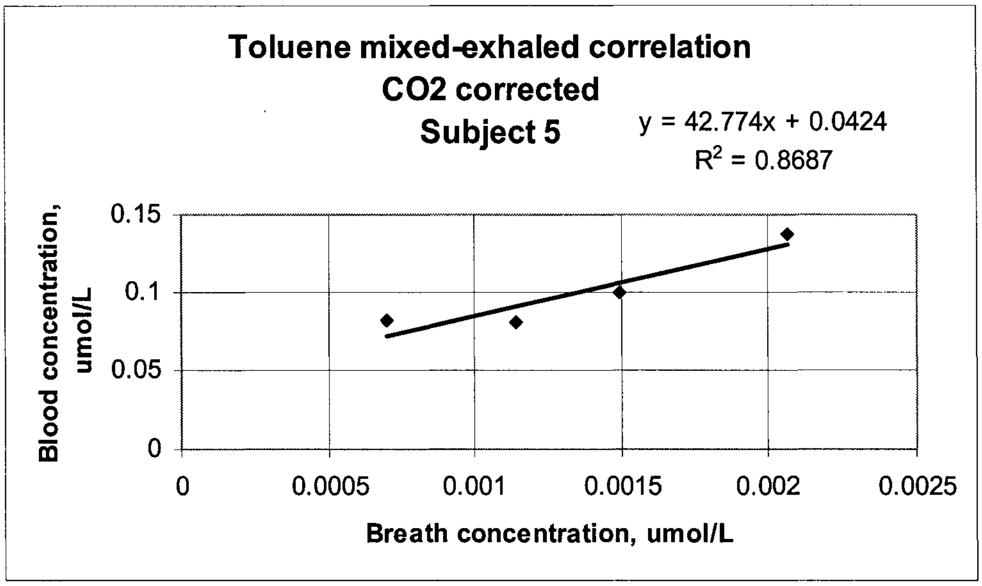

Toluene breath washout
Subject 5
umol/L
0.01
0.001
0.0001
0.00001
00:00
01:00
02:00
03:00
04:00
time post-exposure
rebreathed
end-exhaled
mixed


Toluene blood washout
Subject 5
umol/L
1
0.1
0.01
00:00
01:00
02:00
03:00
time post-exposure
◆ pre-breath
■ post-breath

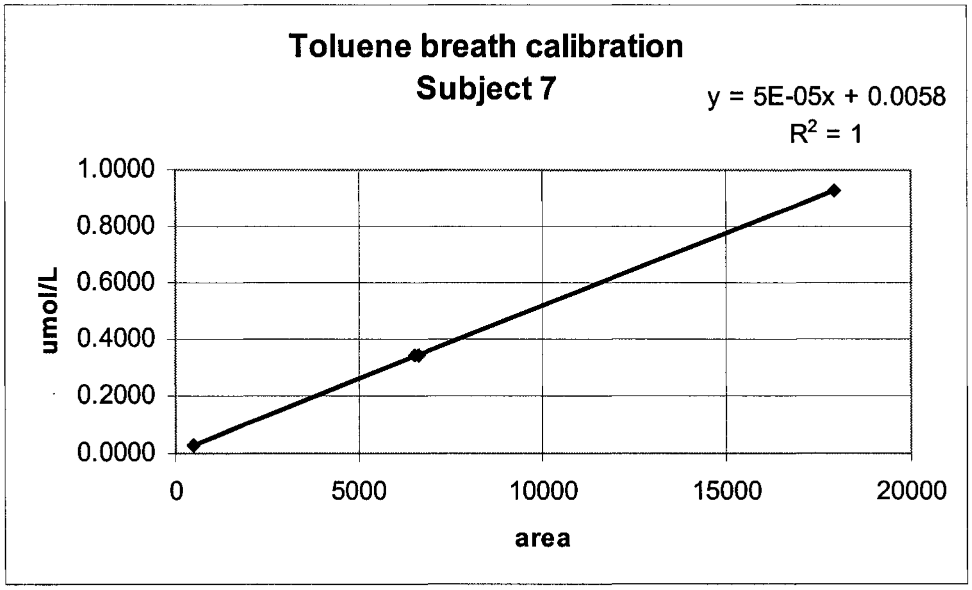

Toluene rebreathed correlation
Subject 5
y = 33.127x + 0.0243
R² = 0.9788
Blood concentration, umol/L
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
0
0
0.001
0.002
0.003
0.004
Breath concentration, umol/L

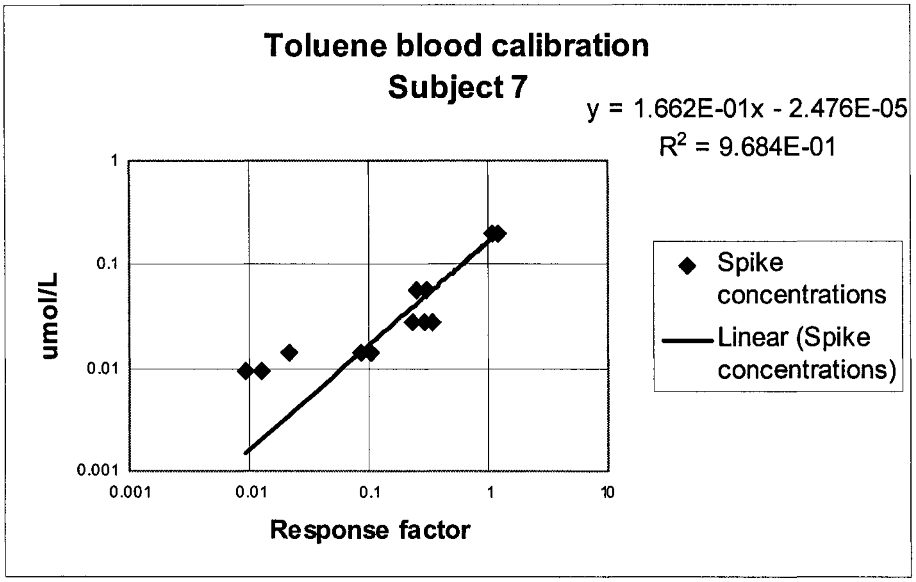

Toluene end-exhaled correlation
Subject 5
y = 21.312x + 0.071
R2 = 0.7996
Blood concentration, umol/L
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
0
0
0.0005
0.001
0.0015
0.002
0.0025
0.003
Breath concentration, umol/L

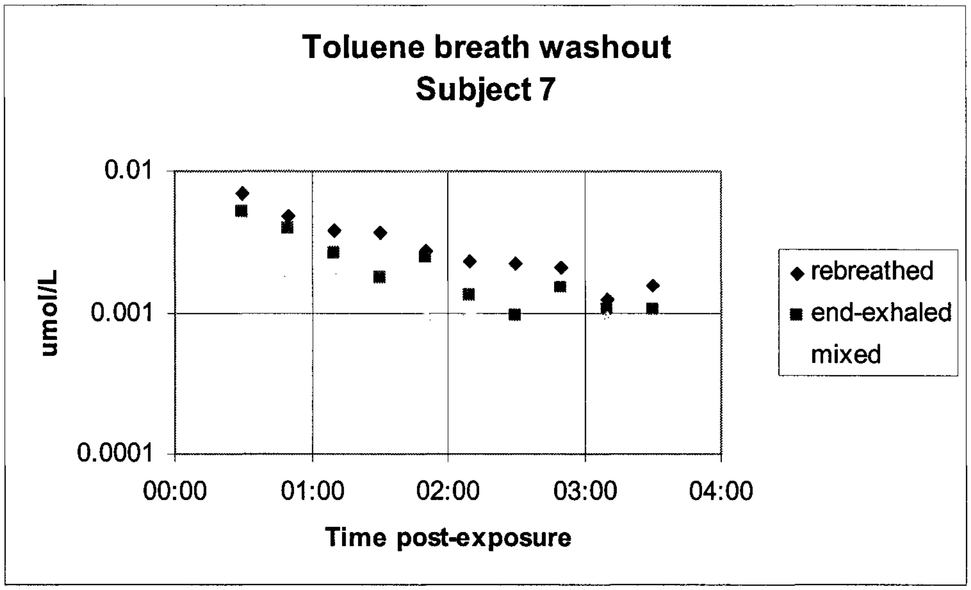

Toluene mixed-exhaled correlation
Subject 5
y = 52.204x + 0.0425
R2 = 0.8923
Blood concentration, umol/L
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
0
0
0.0005
0.001
0.0015
0.002
Breath concentration, umol/L

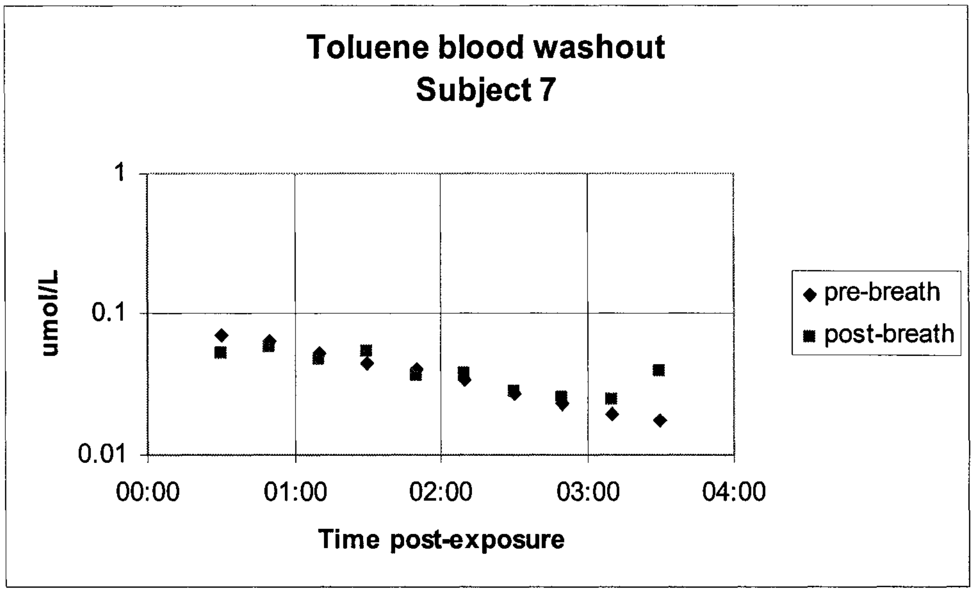

Toluene mixed-exhaled correlation
CO2 corrected
Subject 5
y = 42.774x + 0.0424
R2 = 0.8687
Blood concentration, umol/L
0.15
0.1
0.05
0
0
0.0005
0.001
0.0015
0.002
0.0025
Breath concentration, umol/L

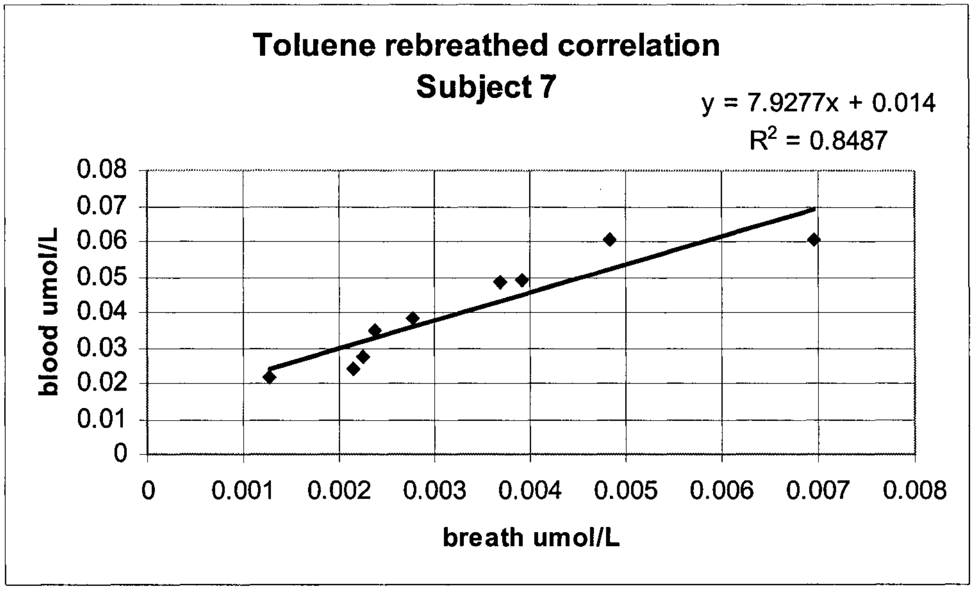
6/25/03

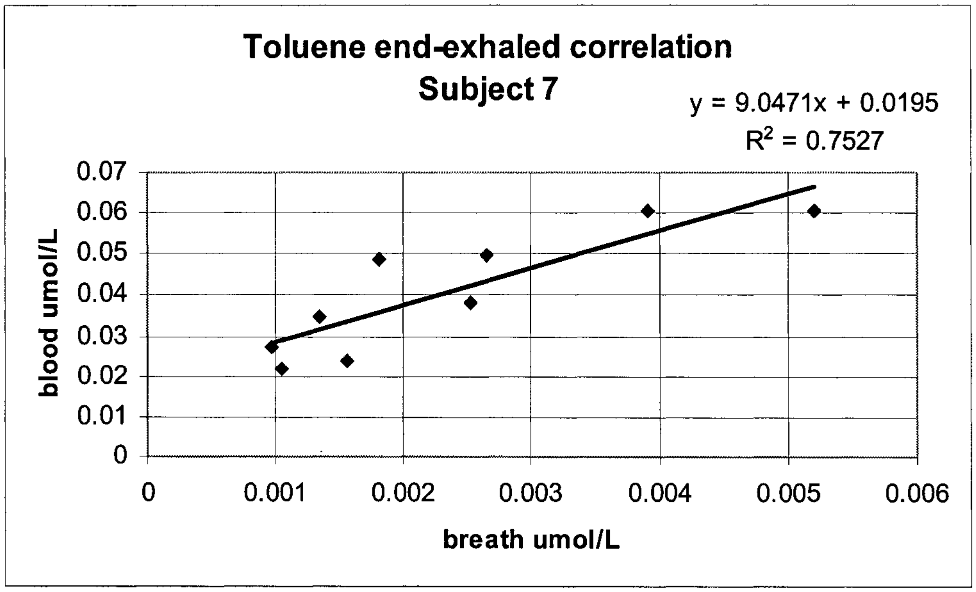

Toluene breath calibration
Subject 7
y = 5E-05x + 0.0058
R2 = 1
umol/L
1.0000
0.8000
0.6000
0.4000
0.2000
0.0000
0
5000
10000
15000
20000
area

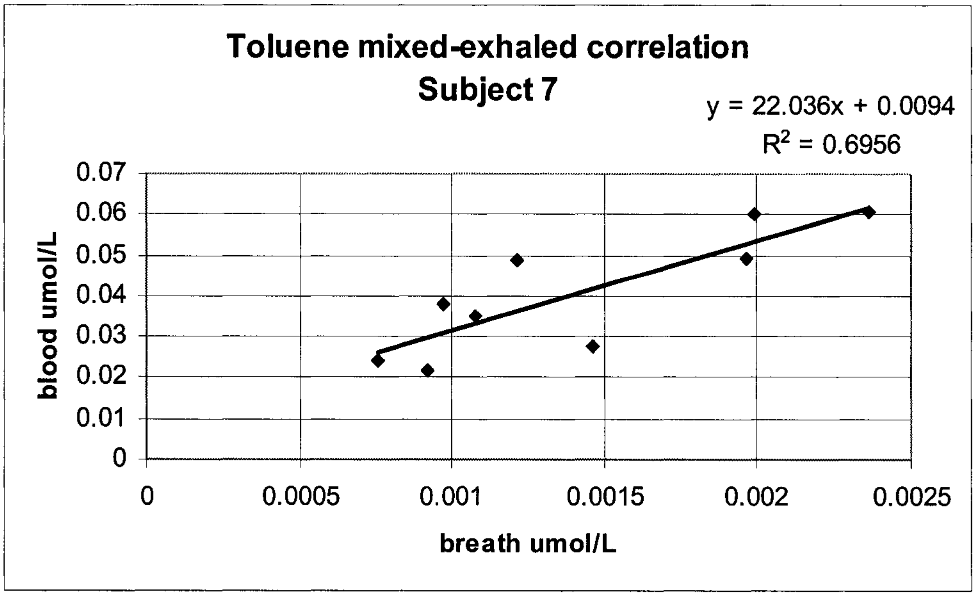

Toluene blood calibration
Subject 7
y = 1.662E-01x - 2.476E-05
R2 = 9.684E-01
umol/L
1
0.1
0.01
0.001
0.001
0.01
0.1
1
10
Response factor
◆ Spike concentrations
Linear (Spike concentrations)

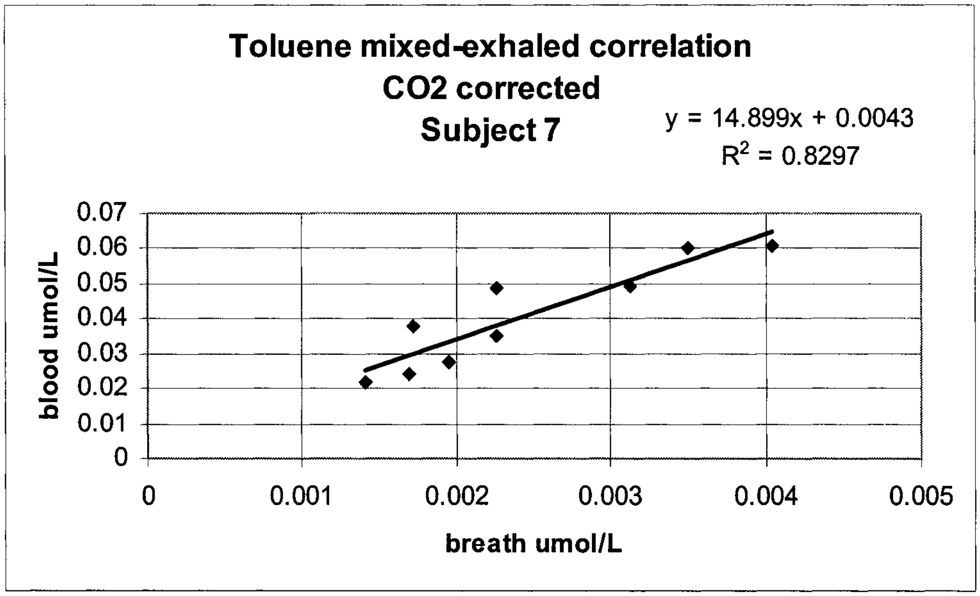

Toluene breath washout
Subject 7
umol/L
0.01
0.001
0.0001
00:00
01:00
02:00
03:00
04:00
Time post-exposure
◆ rebreathed
■ end-exhaled
mixed


Toluene blood washout
Subject 7
umol/L
1
0.1
0.01
00:00
01:00
02:00
03:00
04:00
Time post-exposure
◆ pre-breath
■ post-breath

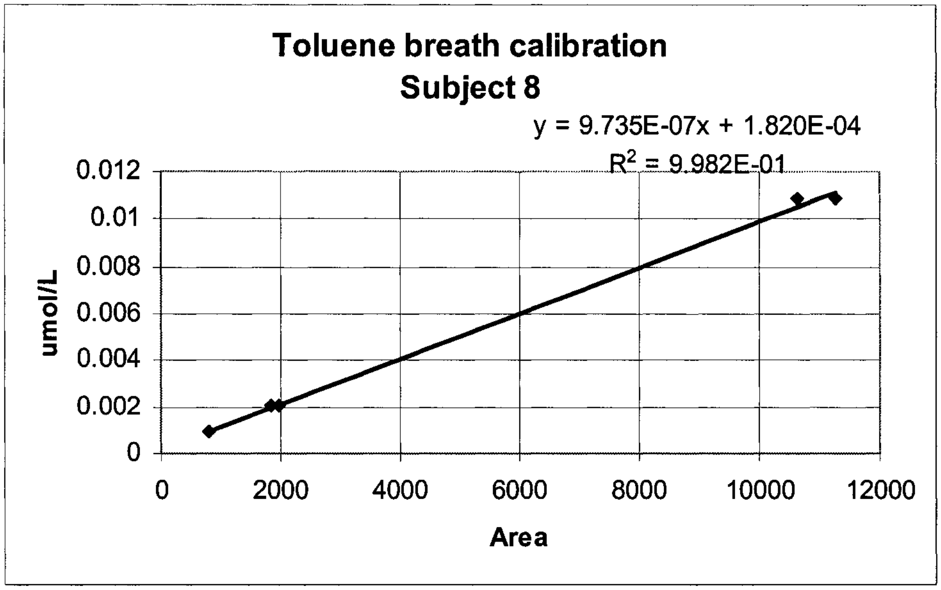

Toluene rebreathed correlation
Subject 7
y = 7.9277x + 0.014
R^2 = 0.8487
blood umol/L
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
0
0.001
0.002
0.003
0.004
0.005
0.006
0.007
0.008
breath umol/L

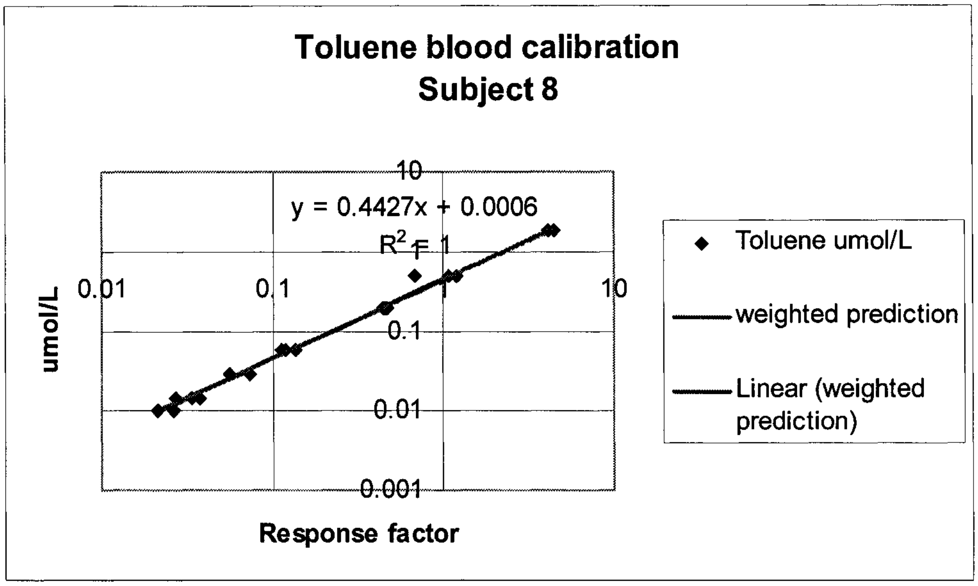

Toluene end-exhaled correlation
Subject 7
y = 9.0471x + 0.0195
R^2 = 0.7527
blood umol/L
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
0
0.001
0.002
0.003
0.004
0.005
0.006
breath umol/L

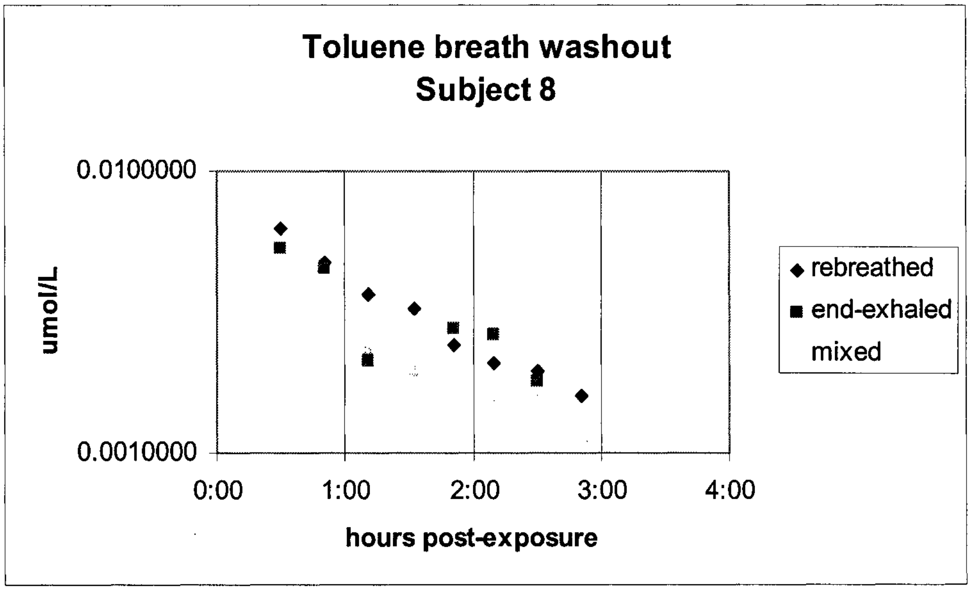

Toluene mixed-exhaled correlation
Subject 7
y = 22.036x + 0.0094
R^2 = 0.6956
blood umol/L
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
0
0.0005
0.001
0.0015
0.002
0.0025
breath umol/L

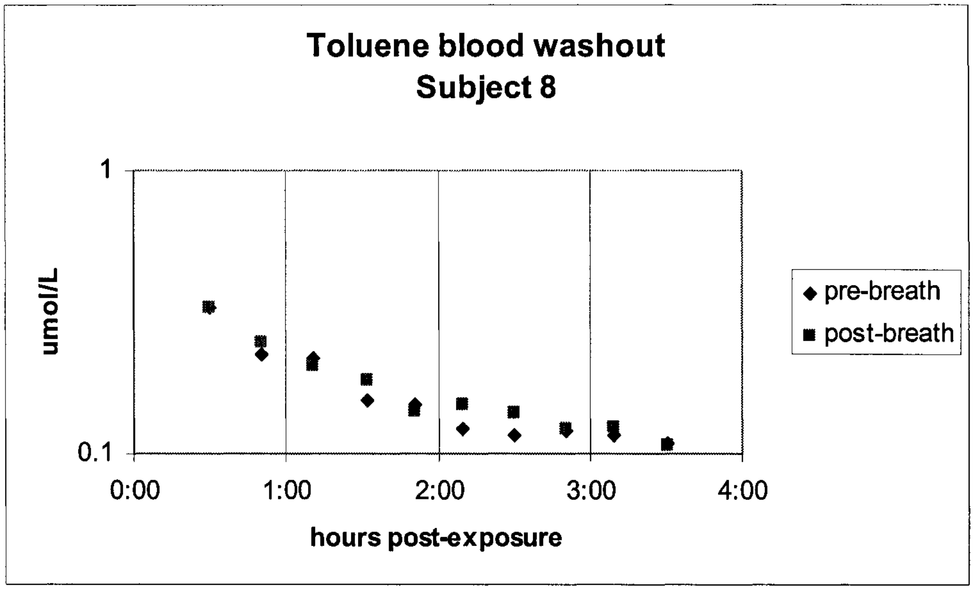

Toluene mixed-exhaled correlation
CO2 corrected
Subject 7
y = 14.899x + 0.0043
R2 = 0.8297
blood umol/L
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
0
0.001
0.002
0.003
0.004
0.005
breath umol/L

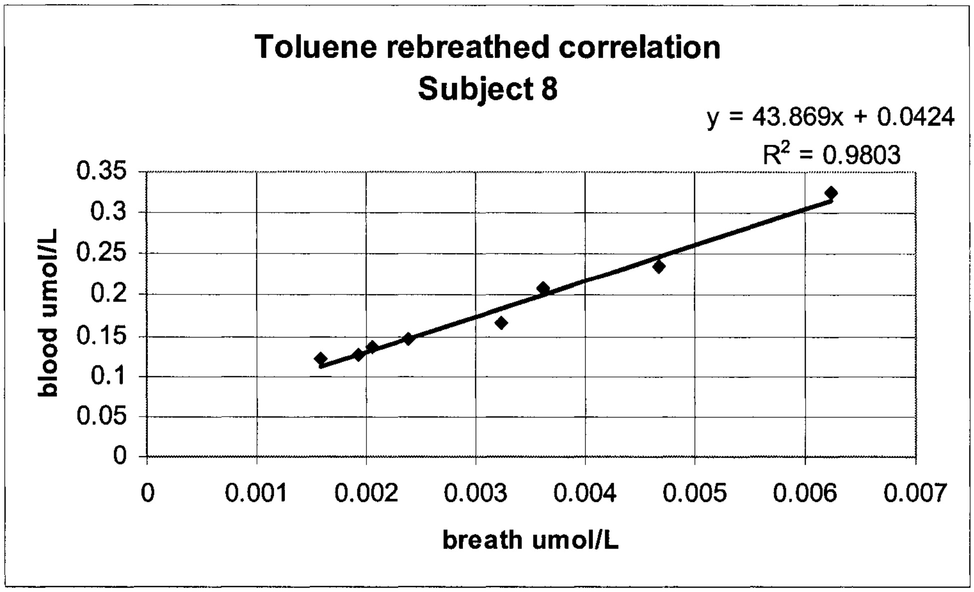
7/3/03

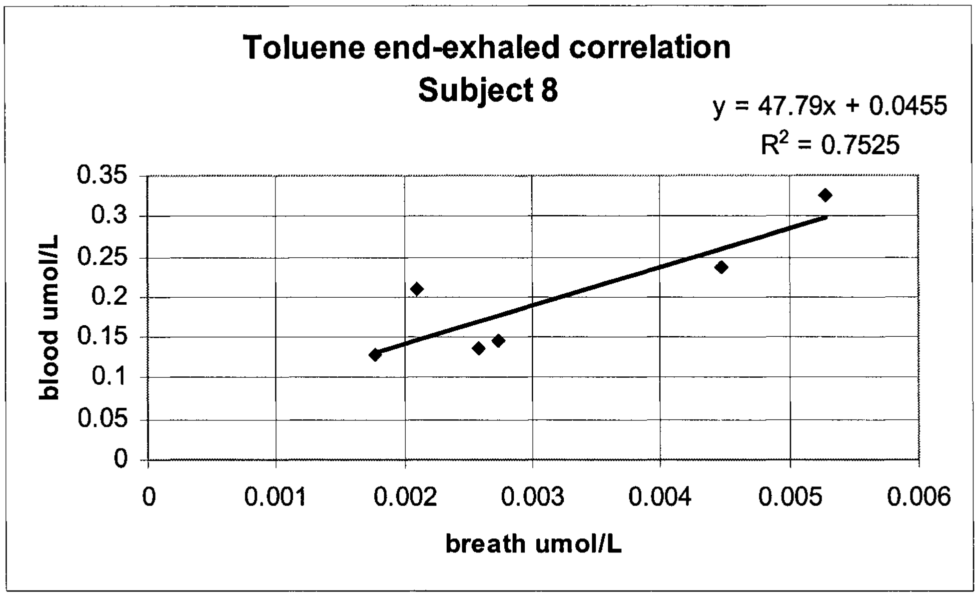

Toluene breath calibration
Subject 8
y = 9.735E-07x + 1.820E-04
R2 = 9.982E-01
umol/L
0.012
0.01
0.008
0.006
0.004
0.002
0
0
2000
4000
6000
8000
10000
12000
Area

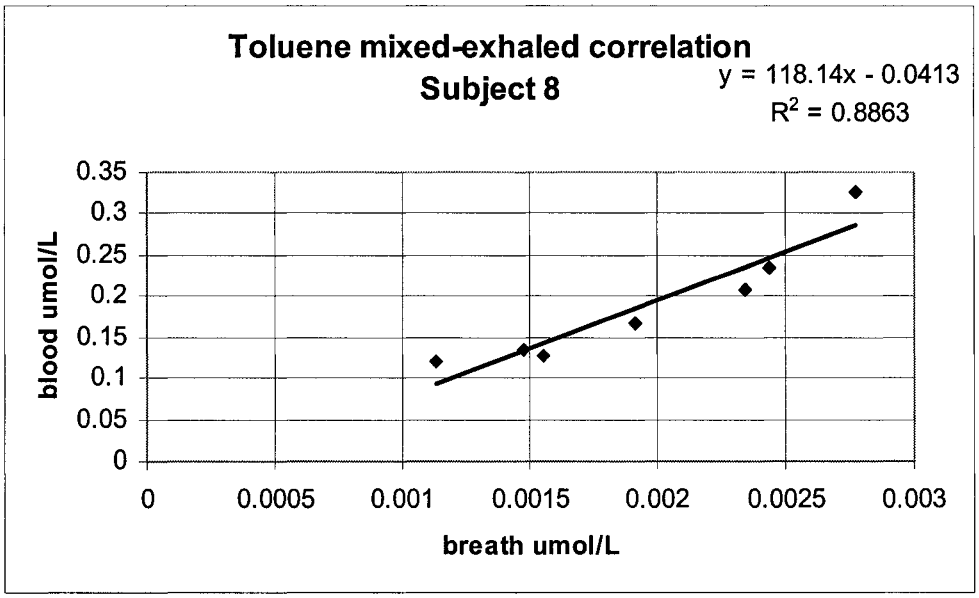

Toluene blood calibration
Subject 8
y = 0.4427x + 0.0006
R² = 1
10
0.01
0.1
1
10
0.1
0.01
0.001
umol/L
Response factor
◆ Toluene umol/L
weighted prediction
Linear (weighted prediction)

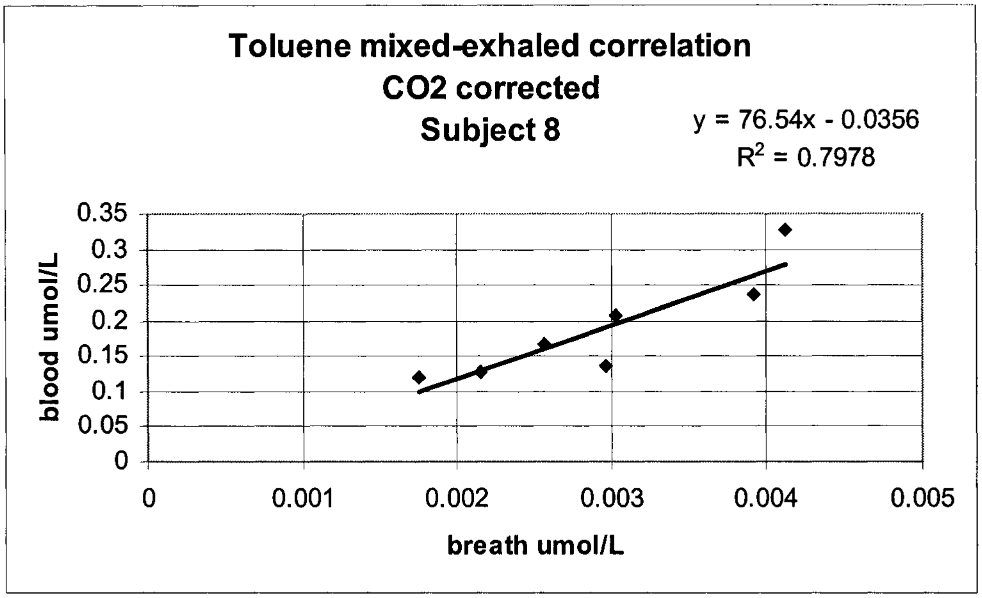

Toluene breath washout
Subject 8
0.0100000
0.0010000
umol/L
0:00
1:00
2:00
3:00
4:00
hours post-exposure
◆ rebreathed
■ end-exhaled
mixed


Toluene blood washout
Subject 8
1
0.1
umol/L
0:00
1:00
2:00
3:00
4:00
hours post-exposure
◆ pre-breath
■ post-breath

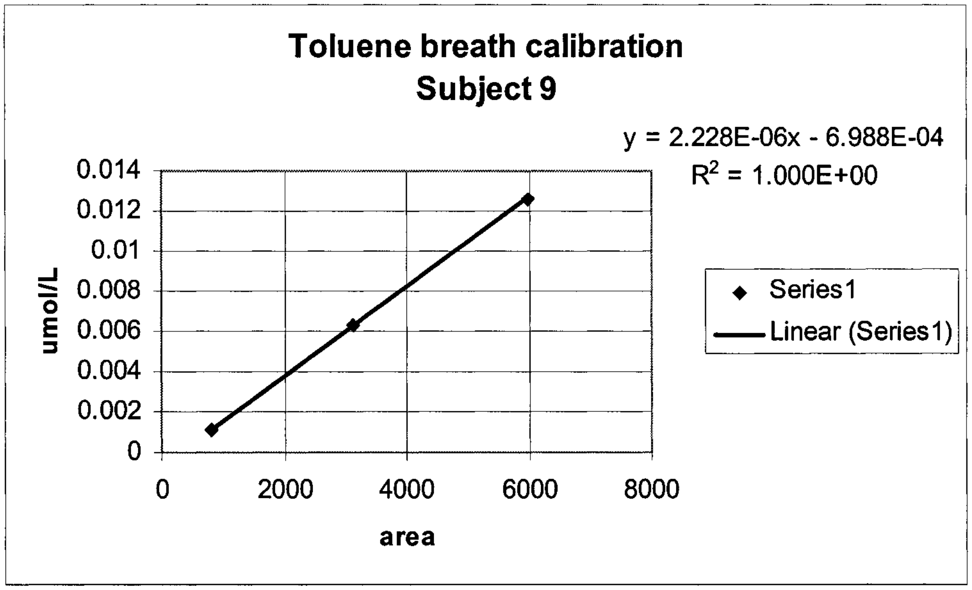

Toluene rebreathed correlation
Subject 8
y = 43.869x + 0.0424
R2 = 0.9803
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
blood umol/L
0
0.001
0.002
0.003
0.004
0.005
0.006
0.007
breath umol/L

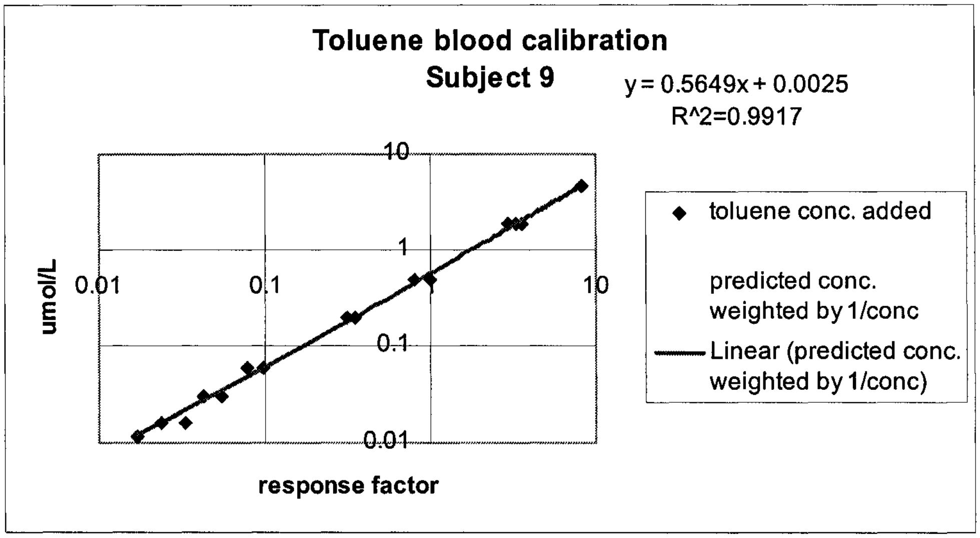

Toluene end-exhaled correlation
Subject 8
y = 47.79x + 0.0455
R² = 0.7525
blood umol/L
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
breath umol/L
0
0.001
0.002
0.003
0.004
0.005
0.006

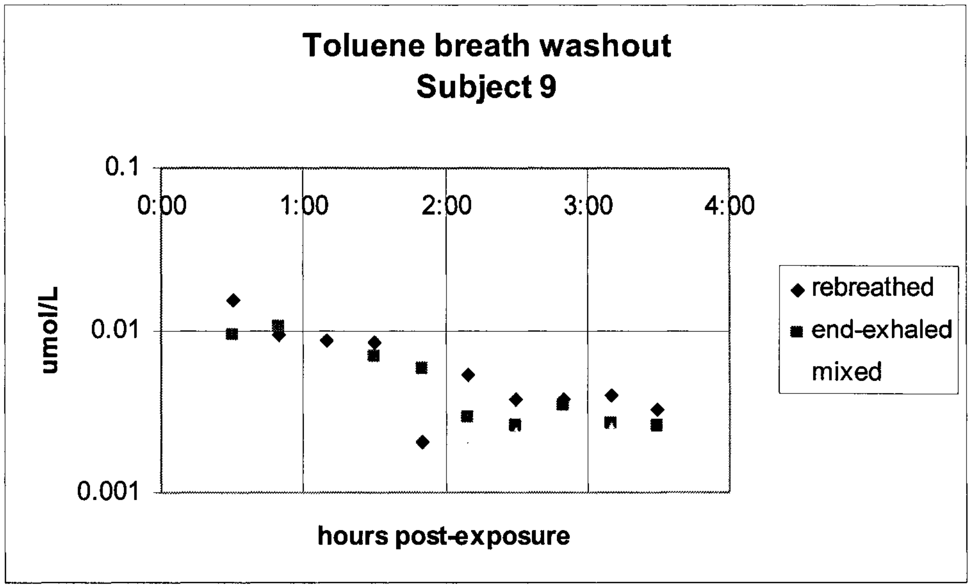

Toluene mixed-exhaled correlation
Subject 8
y = 118.14x - 0.0413
R² = 0.8863
blood umol/L
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
breath umol/L
0
0.0005
0.001
0.0015
0.002
0.0025
0.003

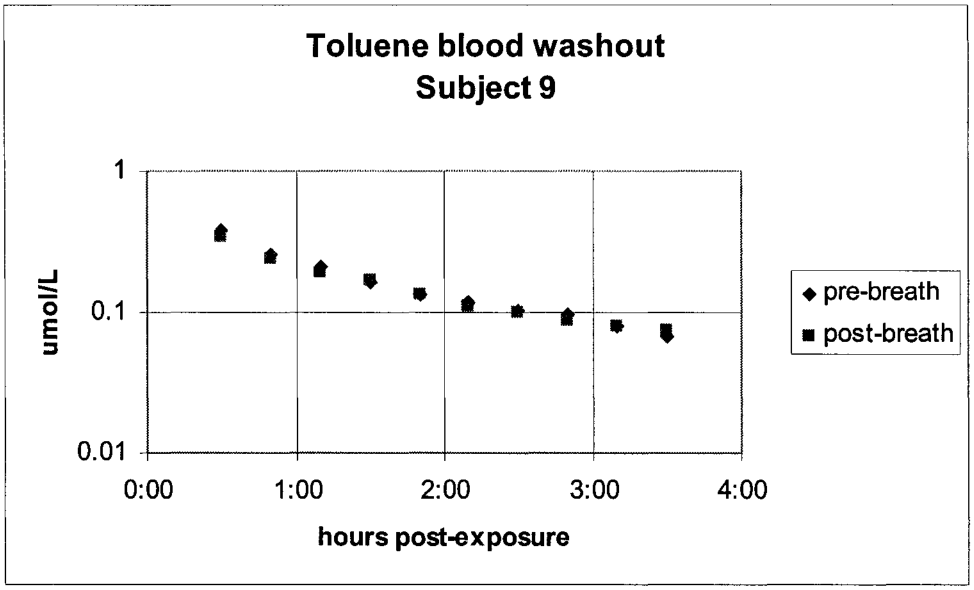

Toluene mixed-exhaled correlation
CO2 corrected
Subject 8
y = 76.54x - 0.0356
R2 = 0.7978
blood umol/L
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
0
0.001
0.002
0.003
0.004
0.005
breath umol/L

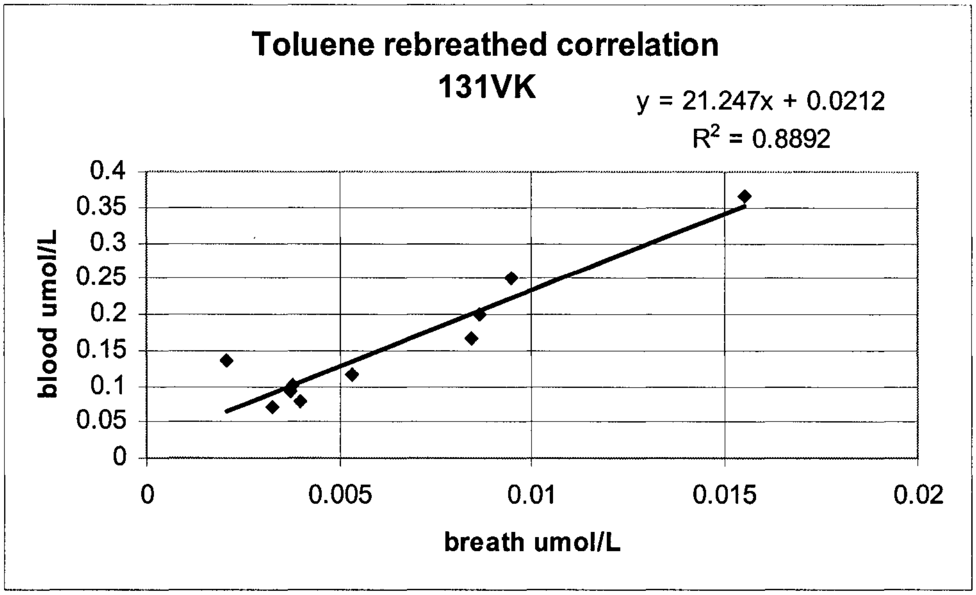
7/10/03

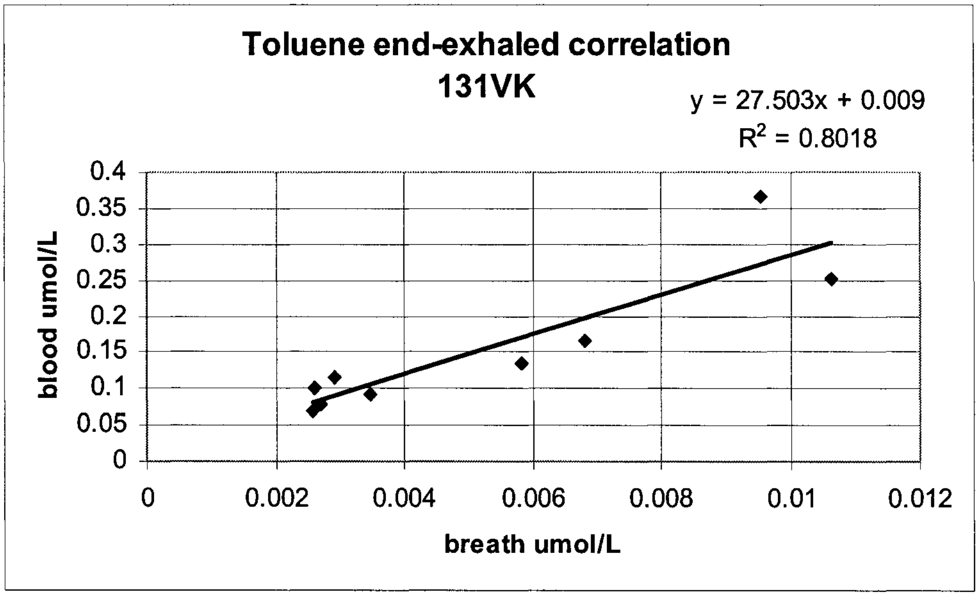

Toluene breath calibration
Subject 9
y = 2.228E-06x - 6.988E-04
R2 = 1.000E+00
umol/L
0.014
0.012
0.01
0.008
0.006
0.004
0.002
0
0
2000
4000
6000
8000
area
Series1
Linear (Series1)

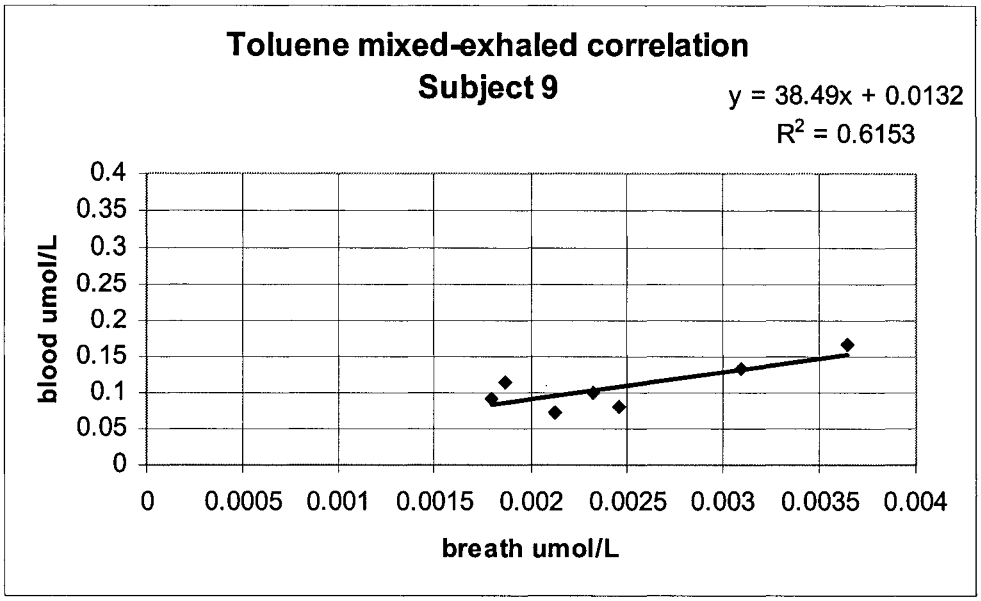

Toluene blood calibration
Subject 9
y = 0.5649x + 0.0025
R^2=0.9917
umol/L
10
1
0.1
0.01
0.01
0.1
1
10
response factor
◆ toluene conc. added
predicted conc. weighted by 1/conc
Linear (predicted conc. weighted by 1/conc)

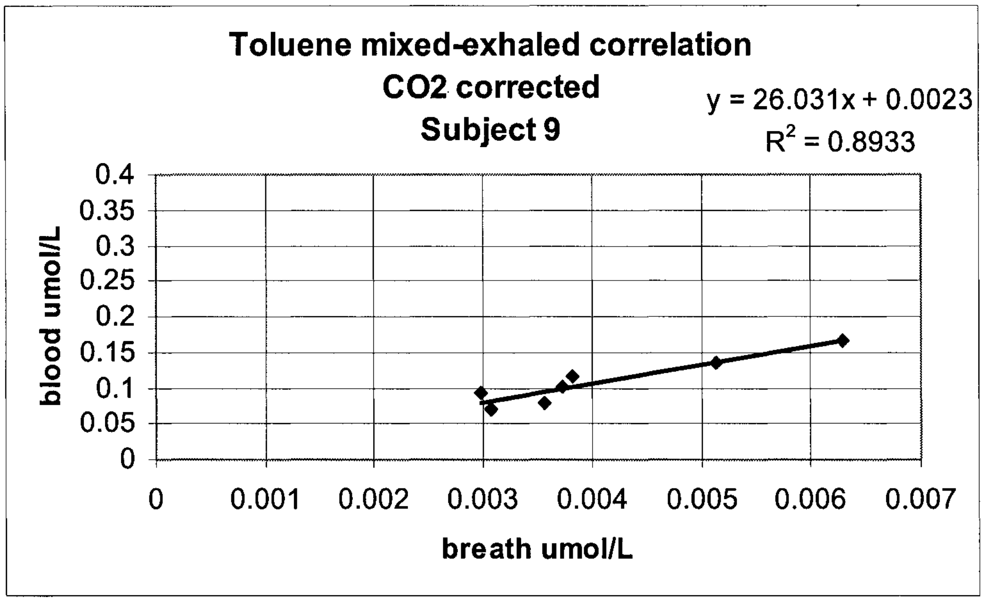

Toluene breath washout
Subject 9
umol/L
0.1
0.01
0.001
0:00
1:00
2:00
3:00
4:00
hours post-exposure
◆ rebreathed
■ end-exhaled
mixed


Toluene blood washout
Subject 9
umol/L
1
0.1
0.01
0:00
1:00
2:00
3:00
4:00
hours post-exposure
◆ pre-breath
■ post-breath

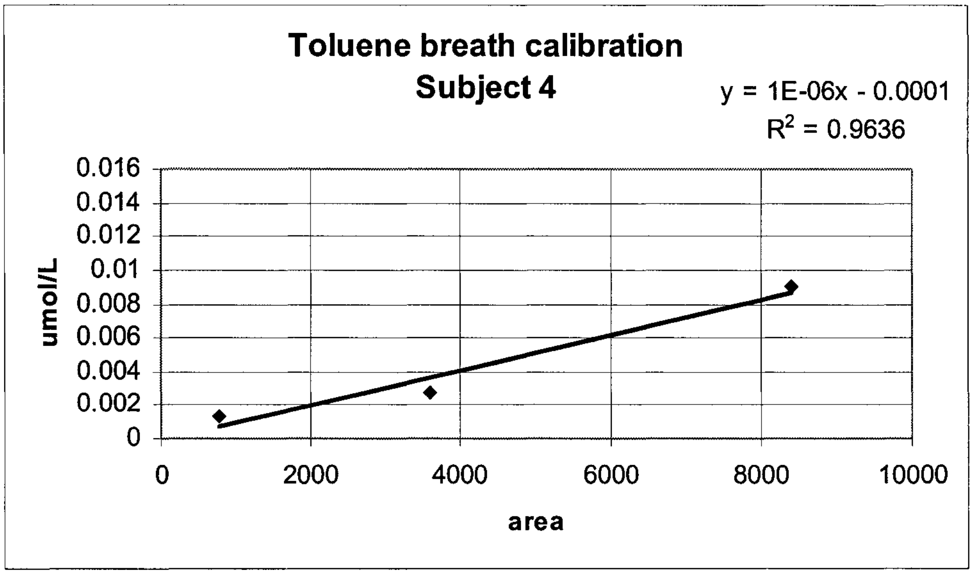

Toluene rebreathed correlation
131VK
y = 21.247x + 0.0212
R² = 0.8892
blood umol/L
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
0
0.005
0.01
0.015
0.02
breath umol/L

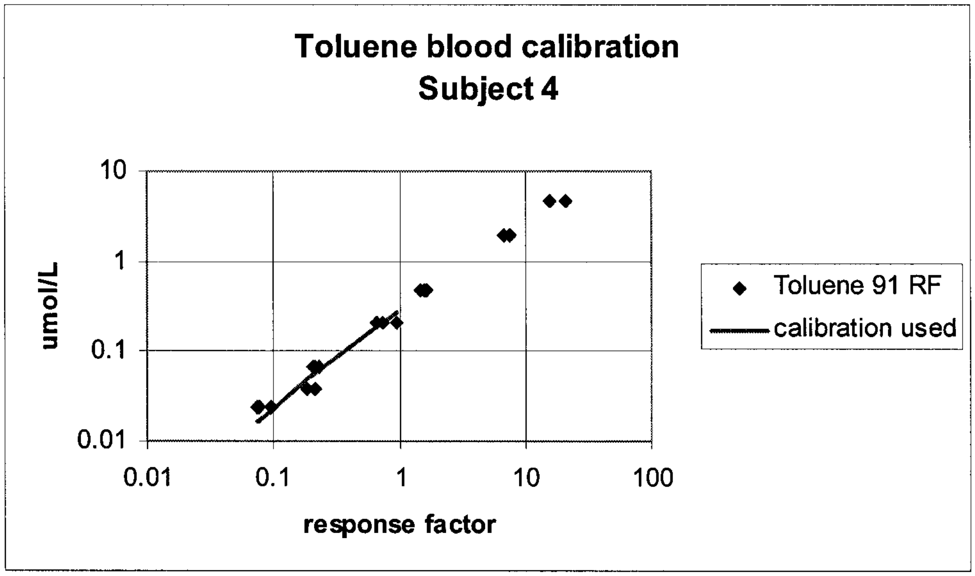

Toluene end-exhaled correlation
131VK
y = 27.503x + 0.009
R2 = 0.8018
blood umol/L
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
0
0.002
0.004
0.006
0.008
0.01
0.012
breath umol/L

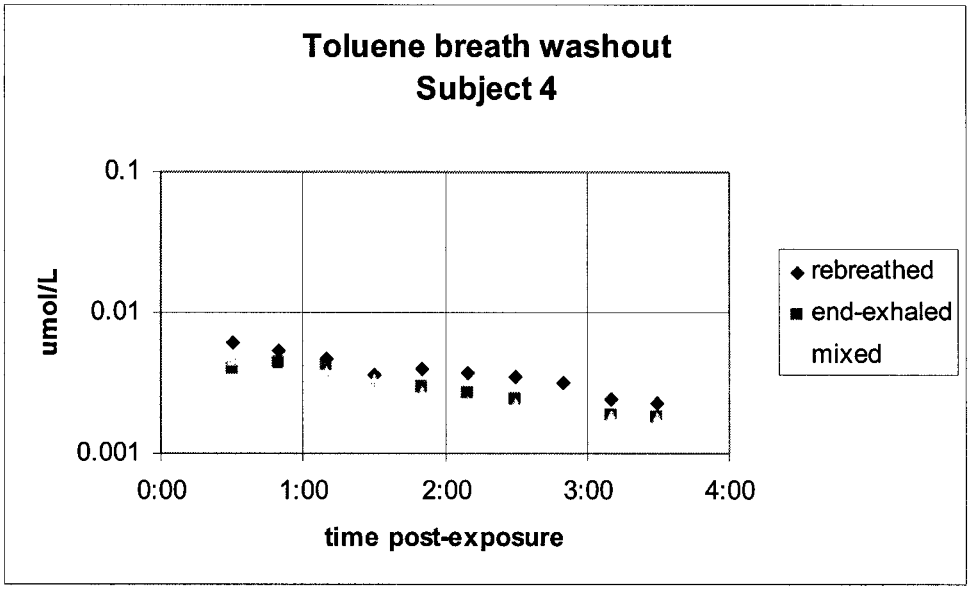

Toluene mixed-exhaled correlation
Subject 9
y = 38.49x + 0.0132
R2 = 0.6153
blood umol/L
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
0
0.0005
0.001
0.0015
0.002
0.0025
0.003
0.0035
0.004
breath umol/L

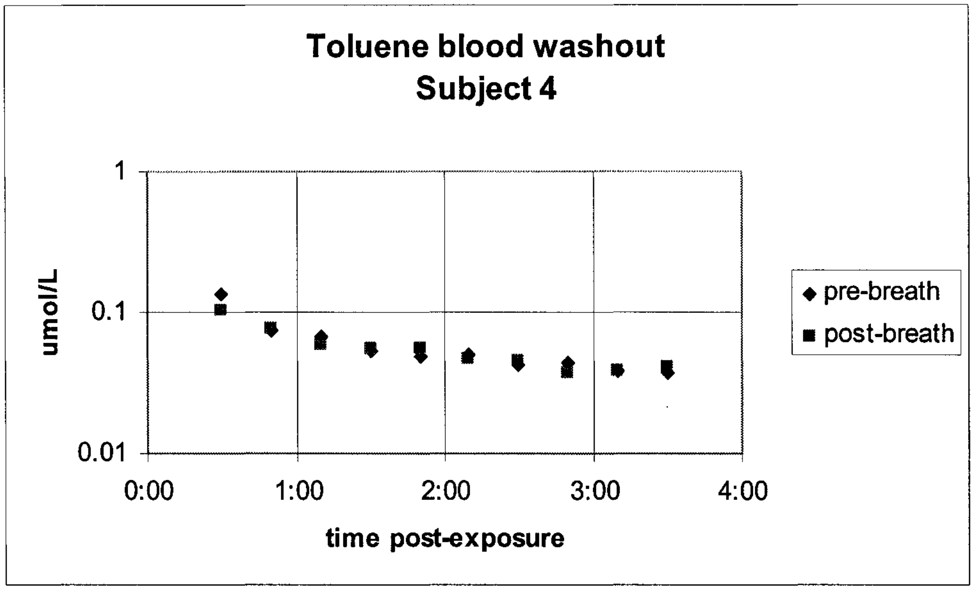

Toluene mixed-exhaled correlation
CO2 corrected
Subject 9
y = 26.031x + 0.0023
R^2 = 0.8933
blood umol/L
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
0
0.001
0.002
0.003
0.004
0.005
0.006
0.007
breath umol/L

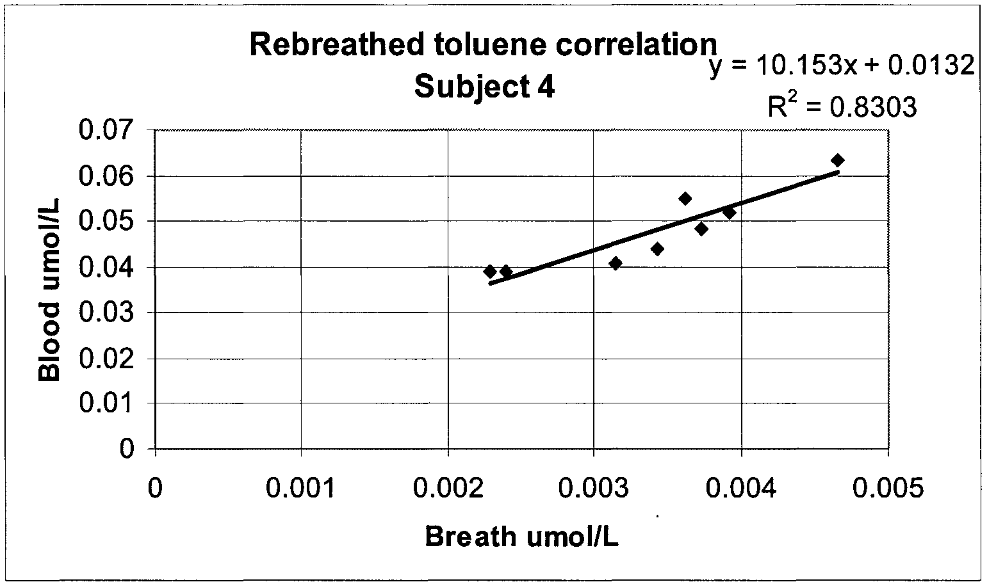
8/1/03

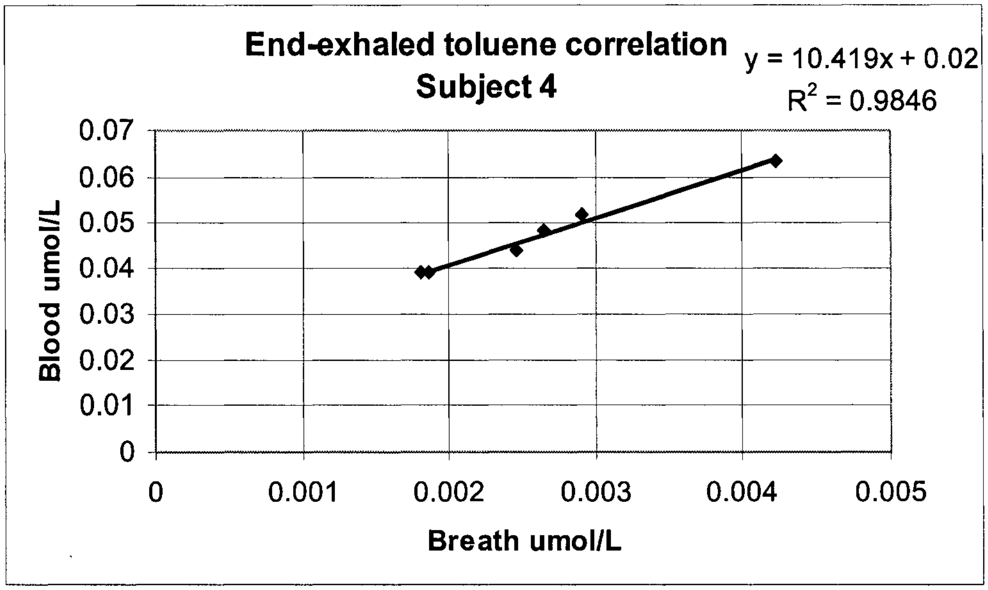

Toluene breath calibration
Subject 4
y = 1E-06x - 0.0001
R^2 = 0.9636
umol/L
0.016
0.014
0.012
0.01
0.008
0.006
0.004
0.002
0
0
2000
4000
6000
8000
10000
area

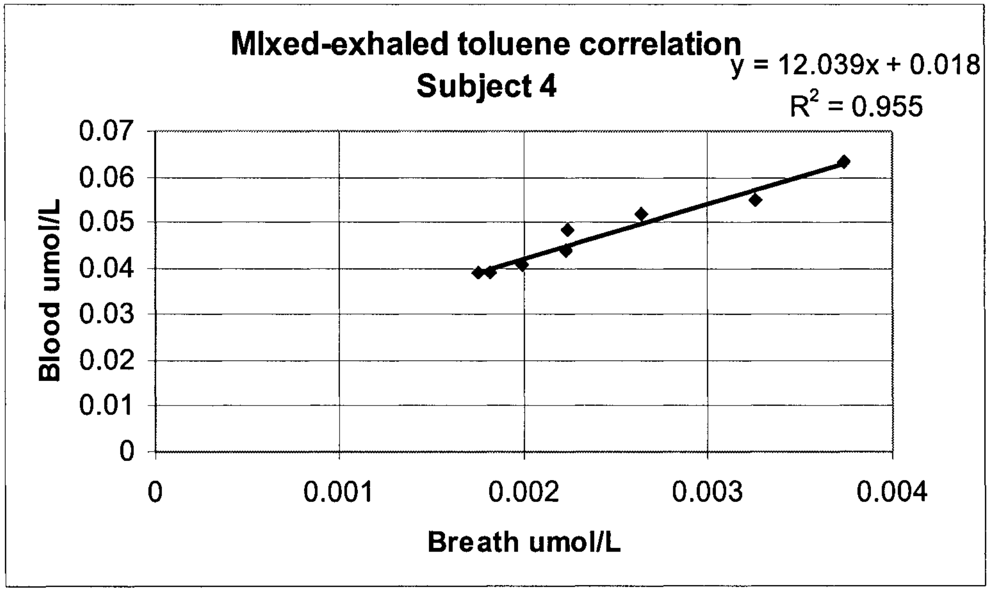

Toluene blood calibration
Subject 4
umol/L
10
1
0.1
0.01
0.01
0.1
1
10
100
response factor
◆ Toluene 91 RF
calibration used

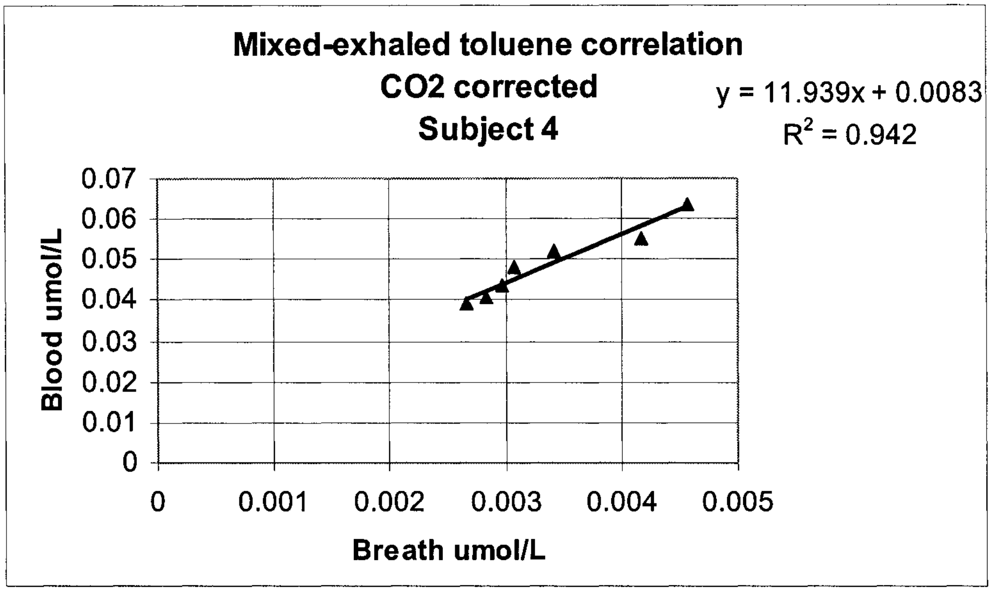

Toluene breath washout
Subject 4
umol/L
0.1
0.01
0.001
0:00
1:00
2:00
3:00
4:00
time post-exposure
◆ rebreathed
■ end-exhaled
mixed


Toluene blood washout
Subject 4
umol/L
1
0.1
0.01
0:00
1:00
2:00
3:00
4:00
time post-exposure
◆ pre-breath
■ post-breath

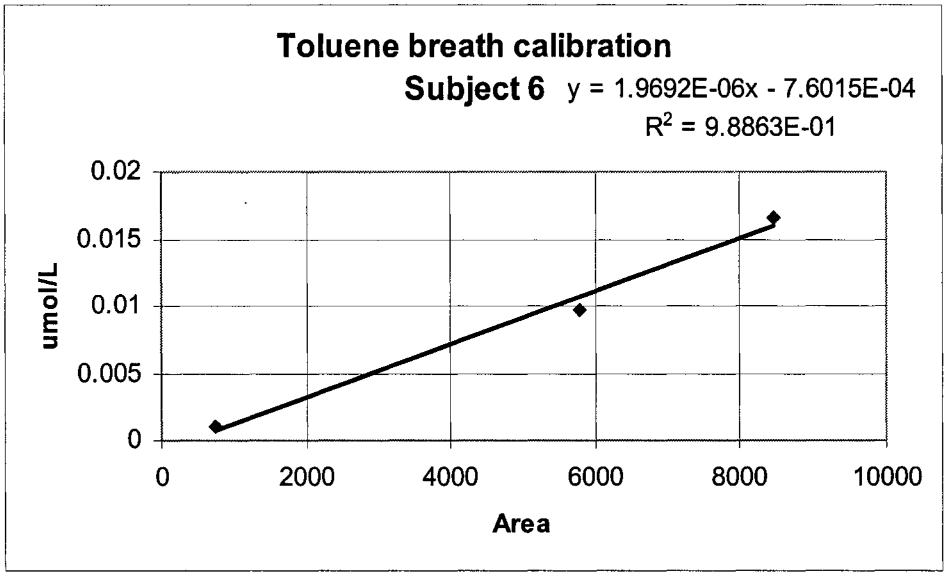

Rebreathed toluene correlation
Subject 4
y = 10.153x + 0.0132
R² = 0.8303
Blood umol/L
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
0
0.001
0.002
0.003
0.004
0.005
Breath umol/L

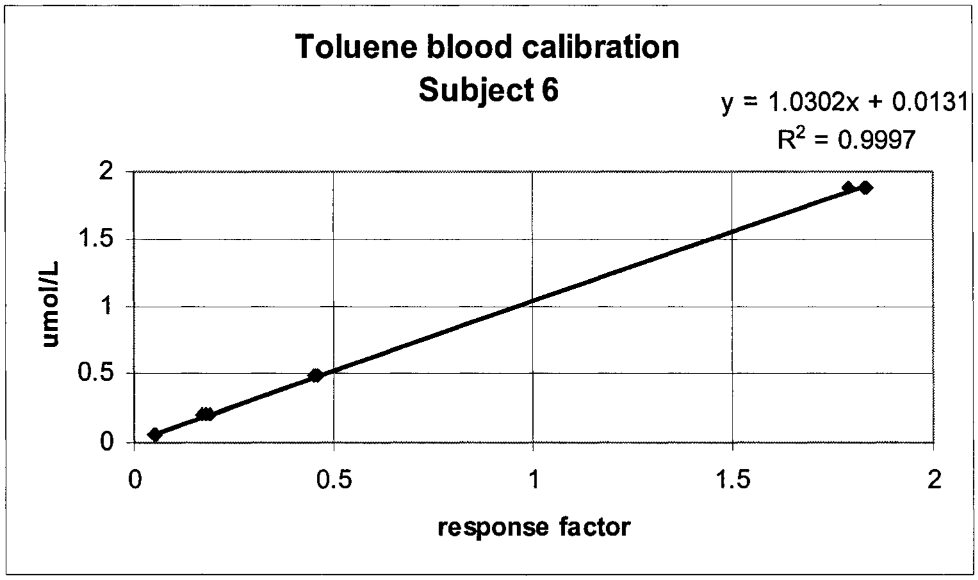

End-exhaled toluene correlation
Subject 4
y = 10.419x + 0.02
R² = 0.9846
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
Blood umol/L
0
0.001
0.002
0.003
0.004
0.005
Breath umol/L

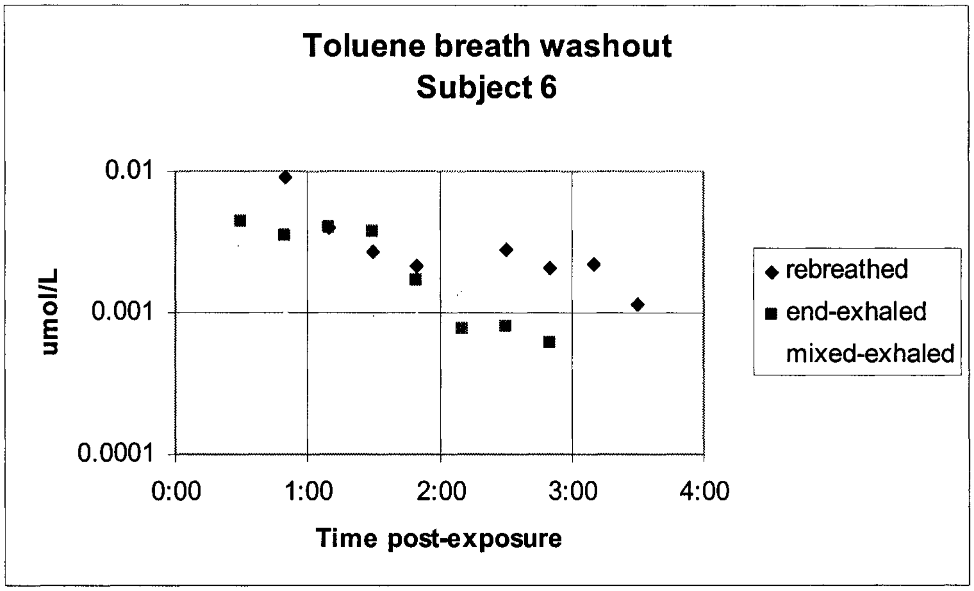

MIxed-exhaled toluene correlation
Subject 4
y = 12.039x + 0.018
R² = 0.955
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
Blood umol/L
0
0.001
0.002
0.003
0.004
Breath umol/L

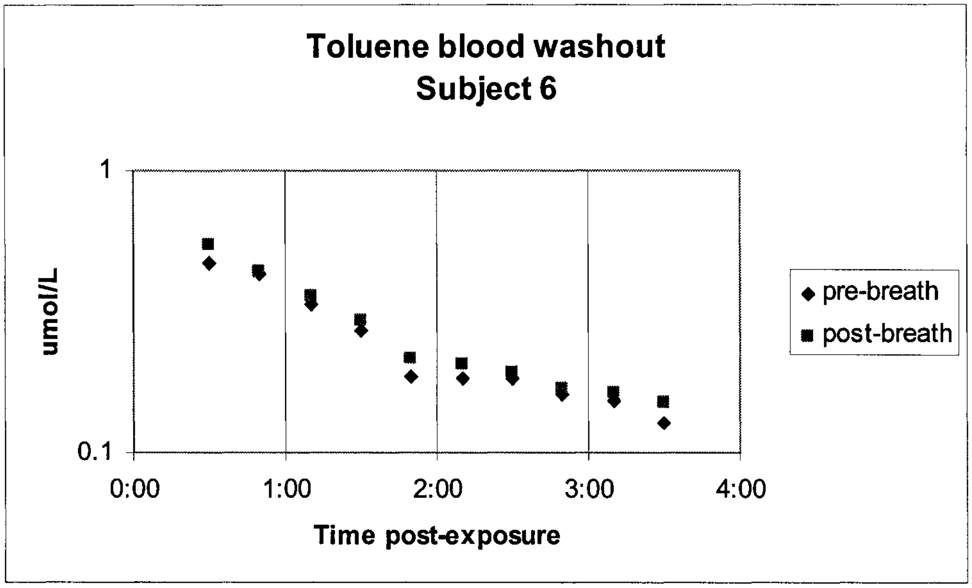

Mixed-exhaled toluene correlation
CO2 corrected
Subject 4
y = 11.939x + 0.0083
R2 = 0.942
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
Blood umol/L
0
0.001
0.002
0.003
0.004
0.005
Breath umol/L

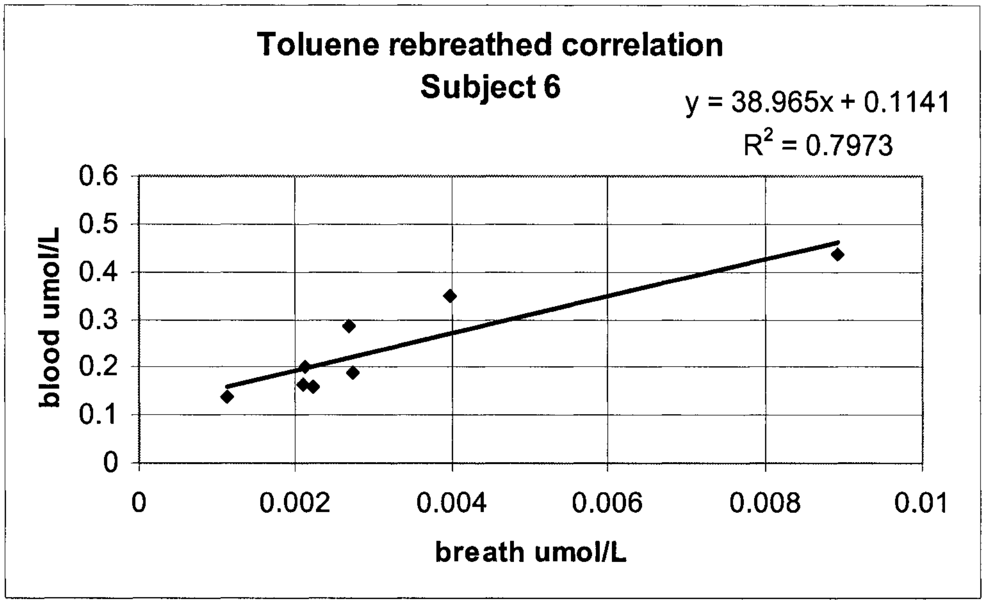
8/26/03

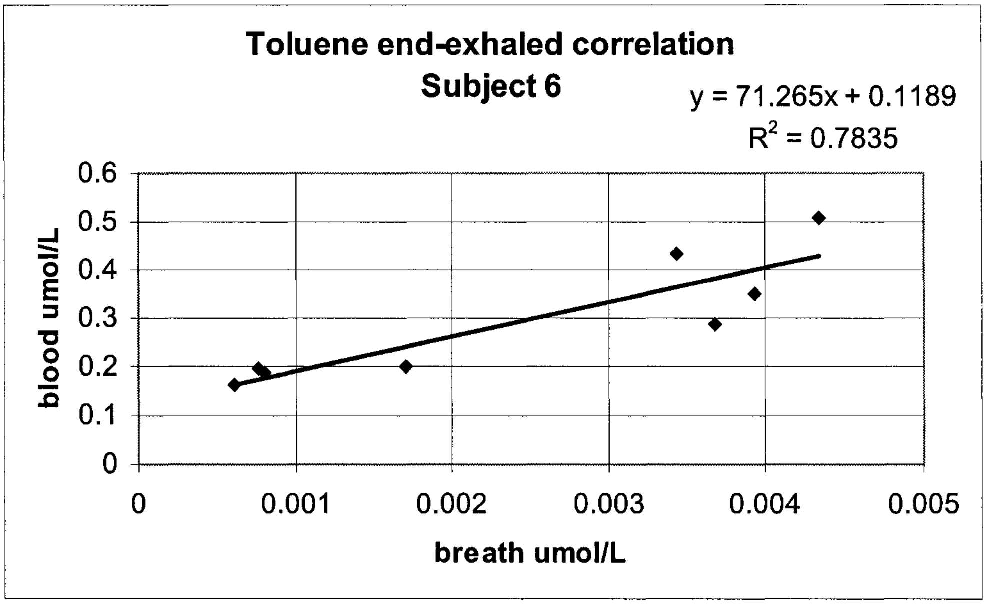

Toluene breath calibration
Subject 6
y = 1.9692E-06x - 7.6015E-04
R2 = 9.8863E-01
0.02
0.015
0.01
0.005
0
umol/L
0
2000
4000
6000
8000
10000
Area

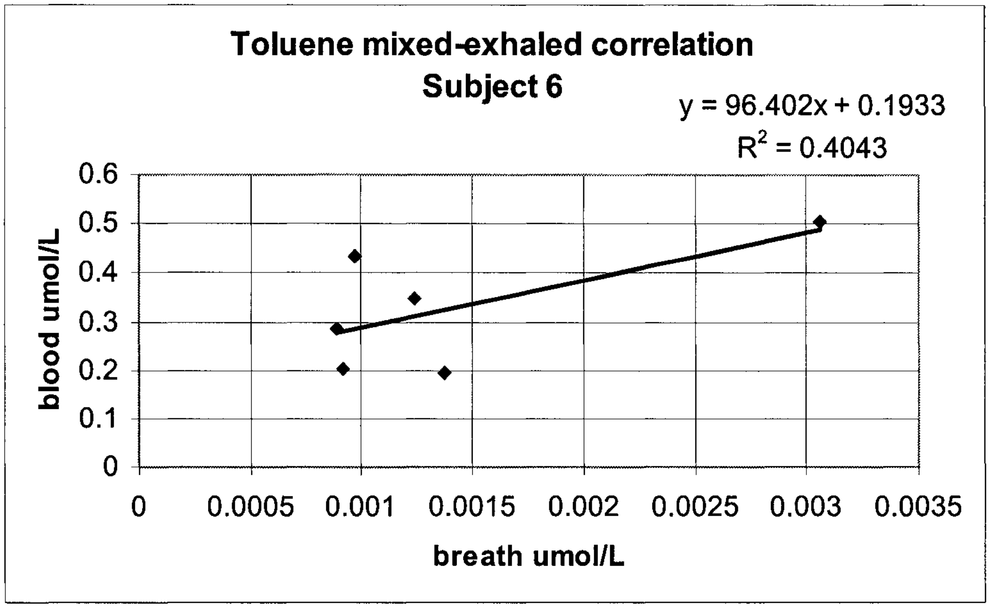

Toluene blood calibration
Subject 6
y = 1.0302x + 0.0131
R^2 = 0.9997
umol/L
2
1.5
1
0.5
0
0
0.5
1
1.5
2
response factor

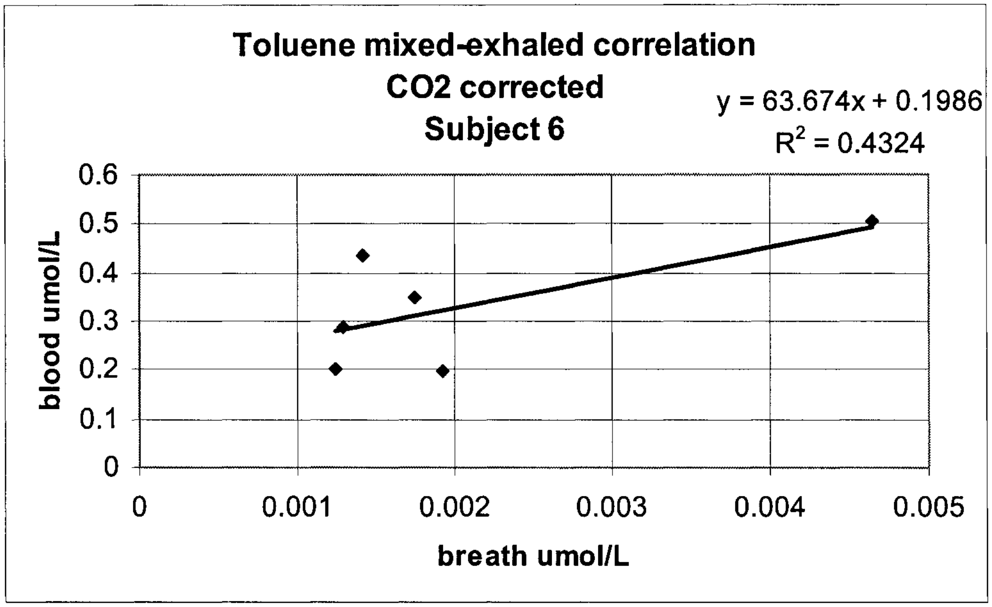

Toluene breath washout
Subject 6
umol/L
0.01
0.001
0.0001
0:00
1:00
2:00
3:00
4:00
Time post-exposure
◆ rebreathed
■ end-exhaled
mixed-exhaled


Toluene blood washout
Subject 6
umol/L
1
0.1
0:00
1:00
2:00
3:00
4:00
Time post-exposure
◆ pre-breath
■ post-breath

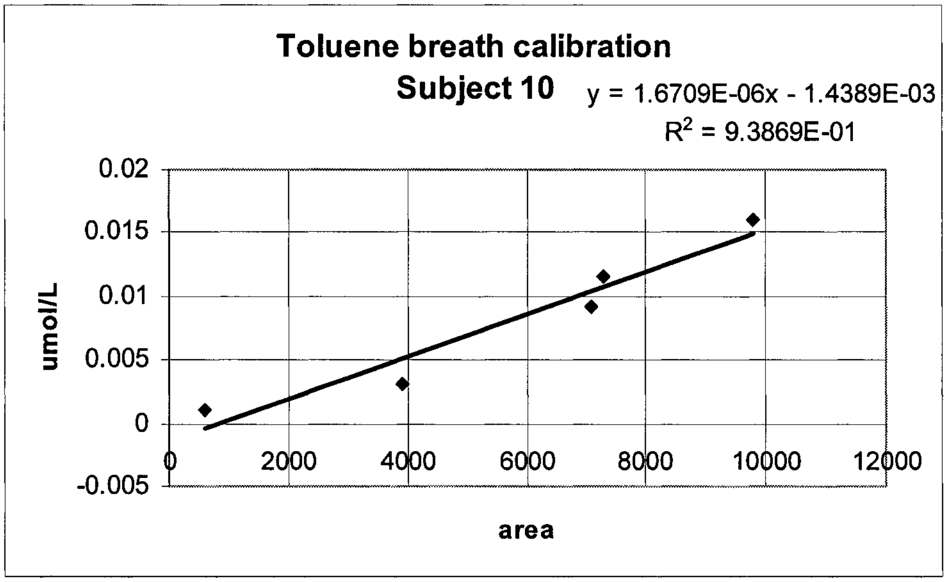

Toluene rebreathed correlation
Subject 6
y = 38.965x + 0.1141
R² = 0.7973
blood umol/L
0.6
0.5
0.4
0.3
0.2
0.1
0
0
0.002
0.004
0.006
0.008
0.01
breath umol/L

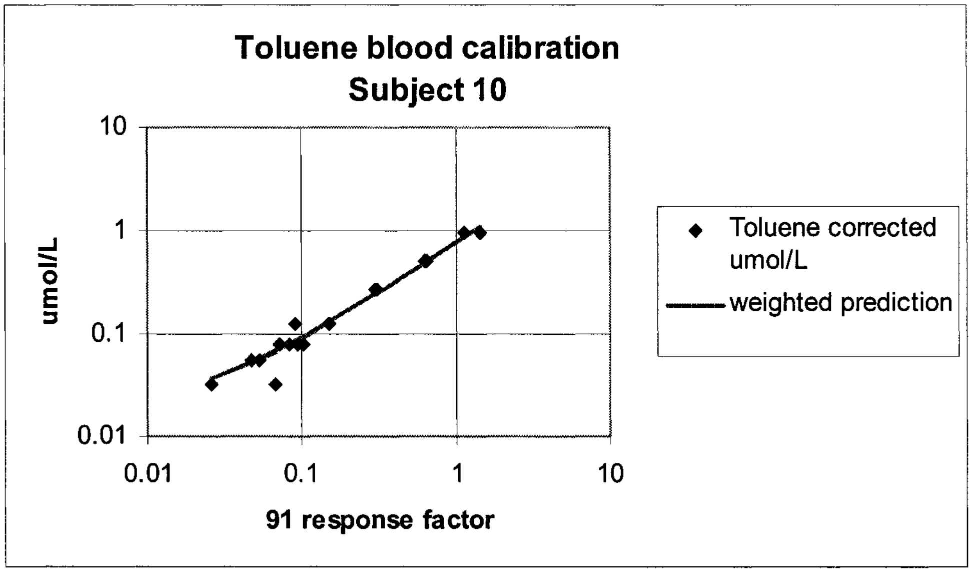

Toluene end-exhaled correlation
Subject 6
y = 71.265x + 0.1189
R2 = 0.7835
blood umol/L
0.6
0.5
0.4
0.3
0.2
0.1
0
0
0.001
0.002
0.003
0.004
0.005
breath umol/L

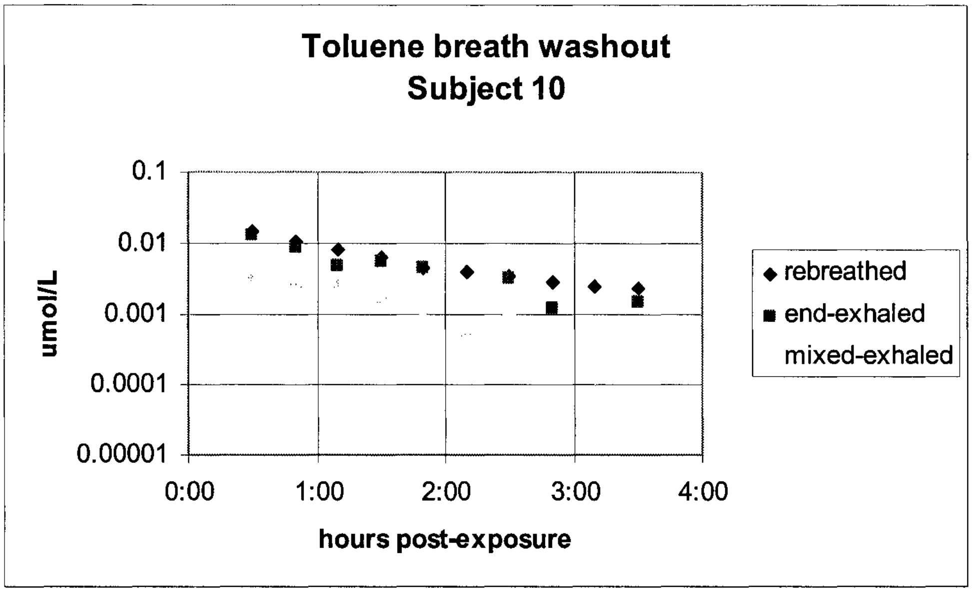

Toluene mixed-exhaled correlation
Subject 6
y = 96.402x + 0.1933
R2 = 0.4043
blood umol/L
0.6
0.5
0.4
0.3
0.2
0.1
0
0
0.0005
0.001
0.0015
0.002
0.0025
0.003
0.0035
breath umol/L

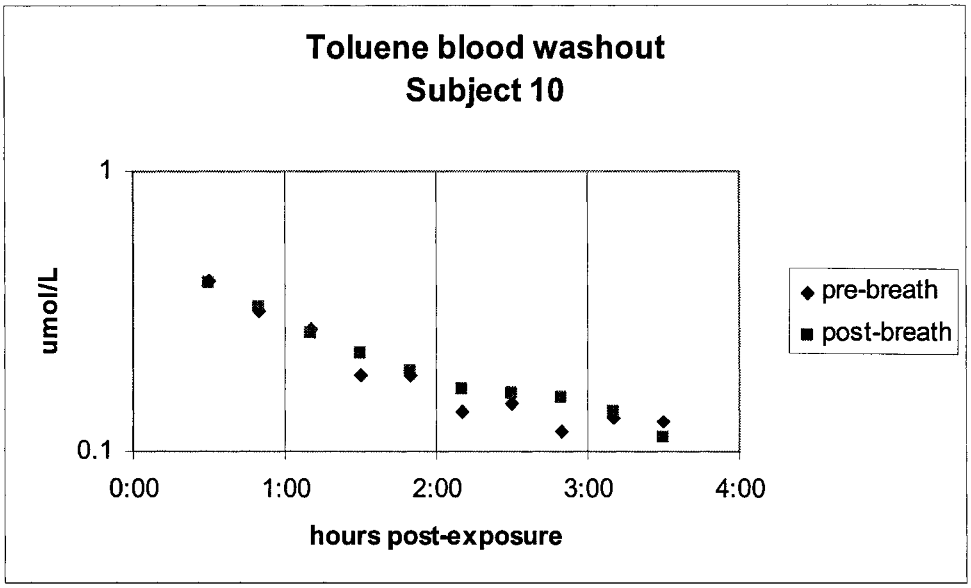

Toluene mixed-exhaled correlation
CO2 corrected
Subject 6
y = 63.674x + 0.1986
R² = 0.4324
0.6
0.5
0.4
0.3
0.2
0.1
0
blood umol/L
0
0.001
0.002
0.003
0.004
0.005
breath umol/L

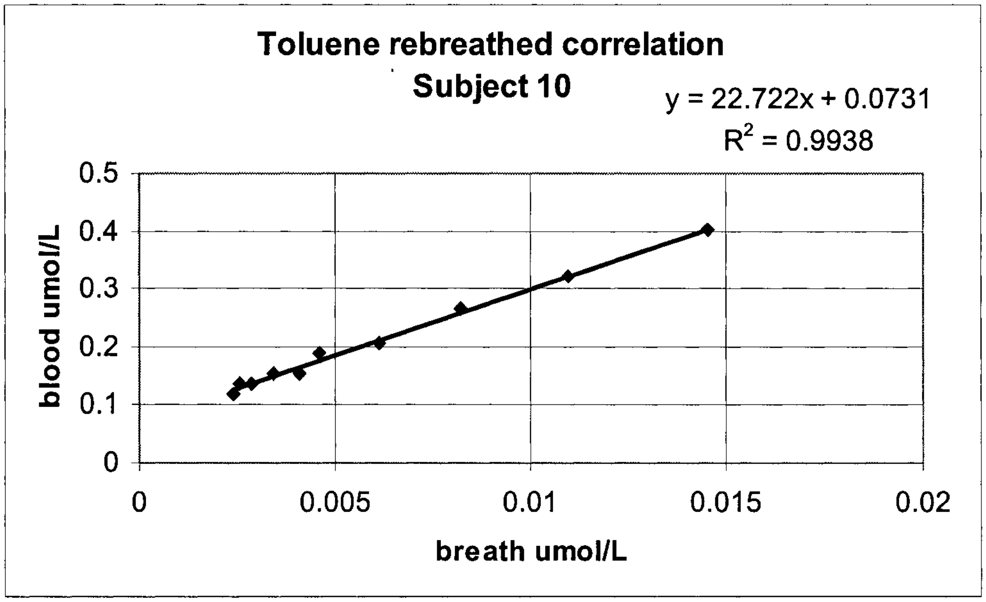
10/22/03

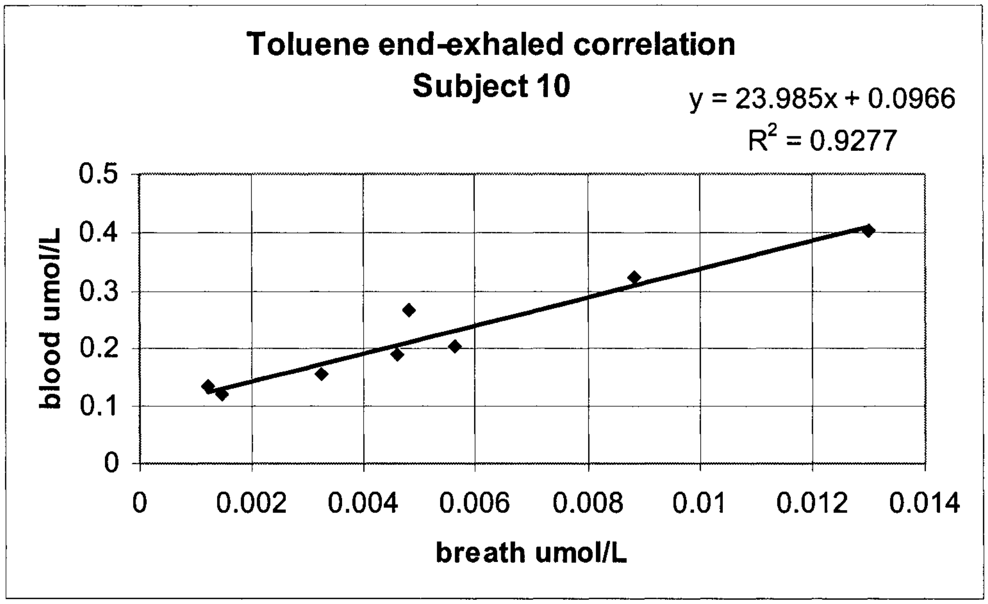

Toluene breath calibration
Subject 10
y = 1.6709E-06x - 1.4389E-03
R² = 9.3869E-01
0.02
0.015
0.01
0.005
0
-0.005
umol/L
0
2000
4000
6000
8000
10000
12000
area

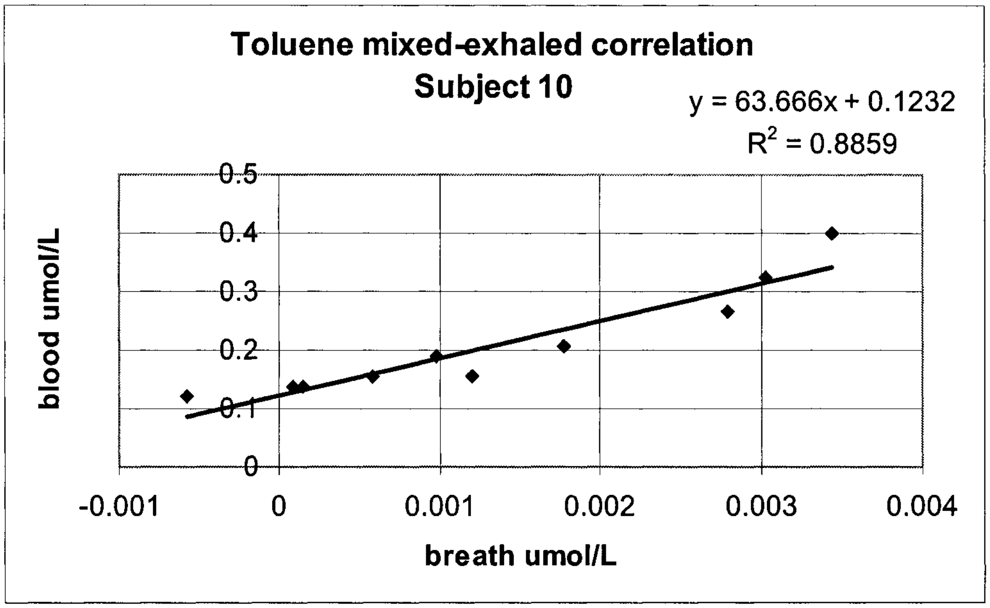

Toluene blood calibration
Subject 10
umol/L
10
1
0.1
0.01
0.01
0.1
1
10
91 response factor
Toluene corrected umol/L
weighted prediction

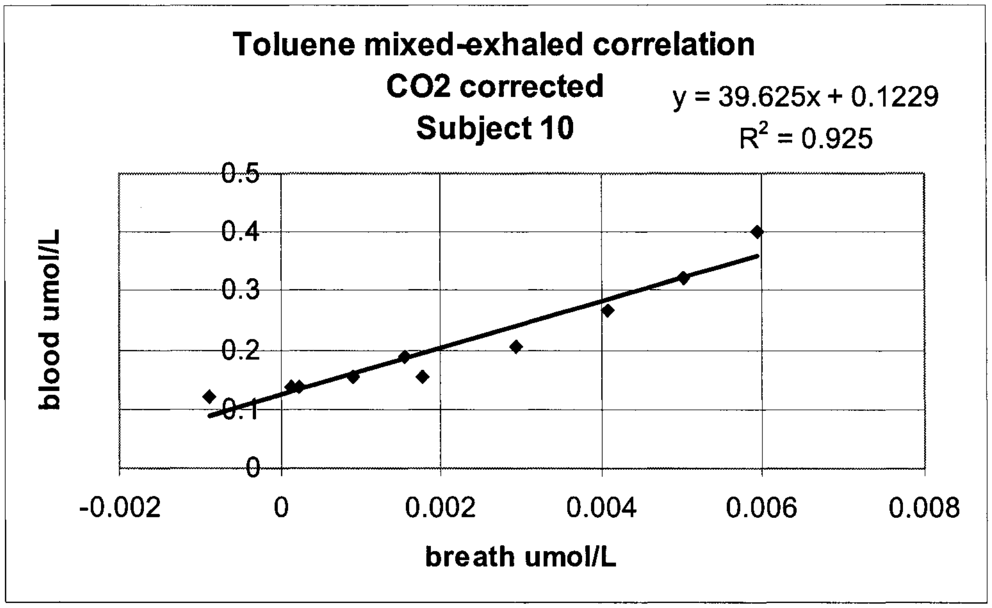

Toluene breath washout
Subject 10
umol/L
0.1
0.01
0.001
0.0001
0.00001
0:00
1:00
2:00
3:00
4:00
hours post-exposure
rebreathed
end-exhaled
mixed-exhaled


Toluene blood washout
Subject 10
1
0.1
umol/L
0:00
1:00
2:00
3:00
4:00
hours post-exposure
◆ pre-breath
■ post-breath

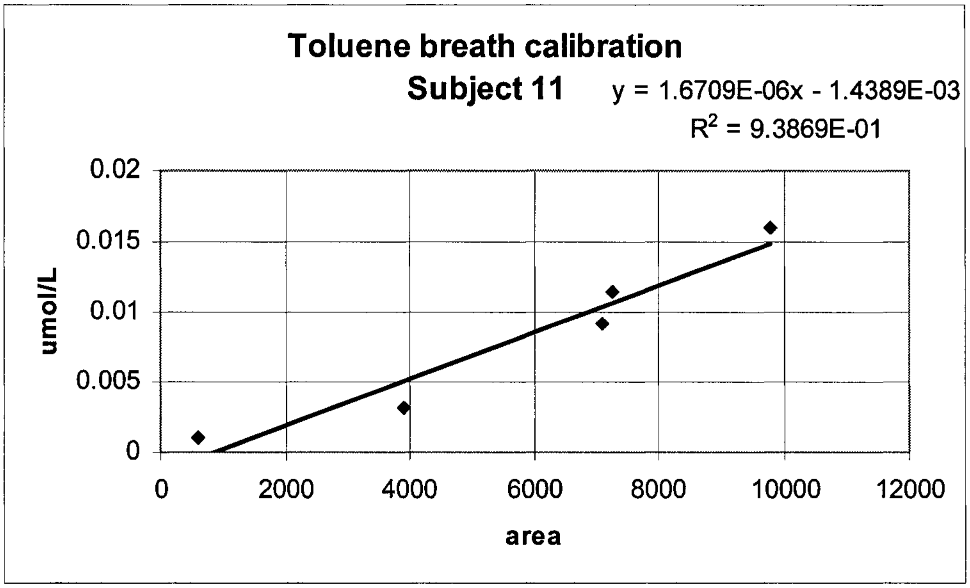

Toluene rebreathed correlation
Subject 10
y = 22.722x + 0.0731
R² = 0.9938
0.5
0.4
0.3
0.2
0.1
0
blood umol/L
0
0.005
0.01
0.015
0.02
breath umol/L

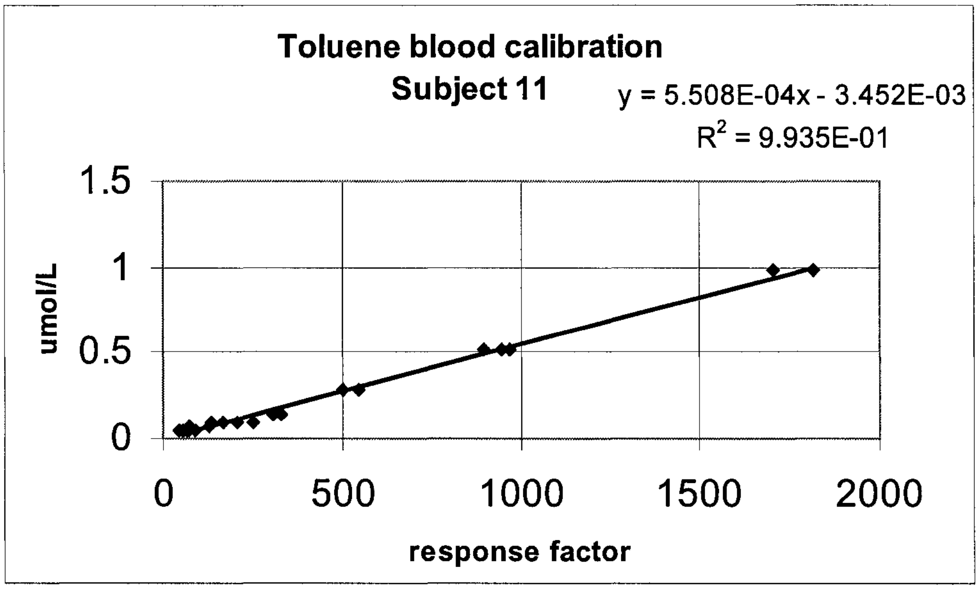

Toluene end-exhaled correlation
Subject 10
y = 23.985x + 0.0966
R^2 = 0.9277
blood umol/L
0.5
0.4
0.3
0.2
0.1
0
0
0.002
0.004
0.006
0.008
0.01
0.012
0.014
breath umol/L

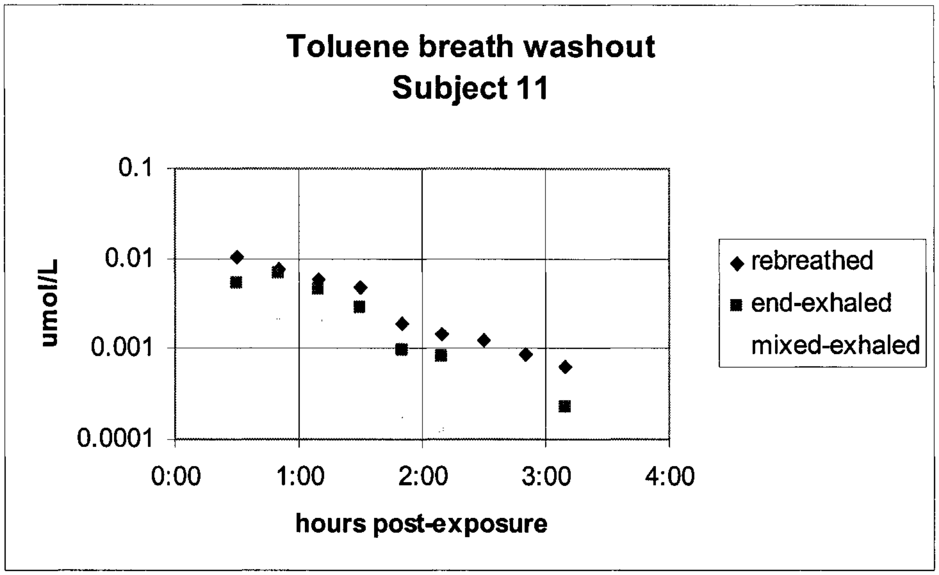

Toluene mixed-exhaled correlation
Subject 10
y = 63.666x + 0.1232
R^2 = 0.8859
blood umol/L
0.5
0.4
0.3
0.2
0.1
0
-0.001
0
0.001
0.002
0.003
0.004
breath umol/L

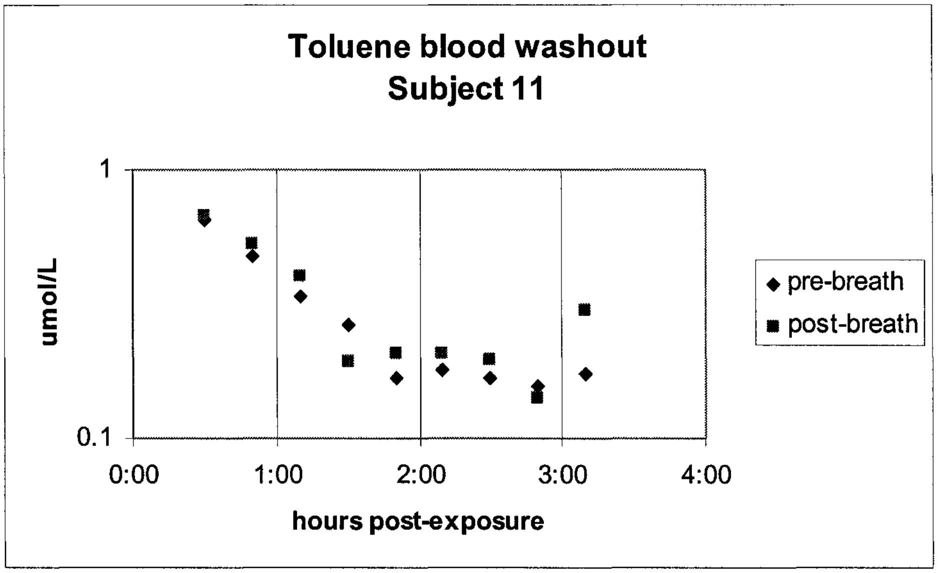

Toluene mixed-exhaled correlation
CO2 corrected
Subject 10
y = 39.625x + 0.1229
R2 = 0.925
blood umol/L
0.5
0.4
0.3
0.2
0.1
0
-0.002
0
0.002
0.004
0.006
0.008
breath umol/L

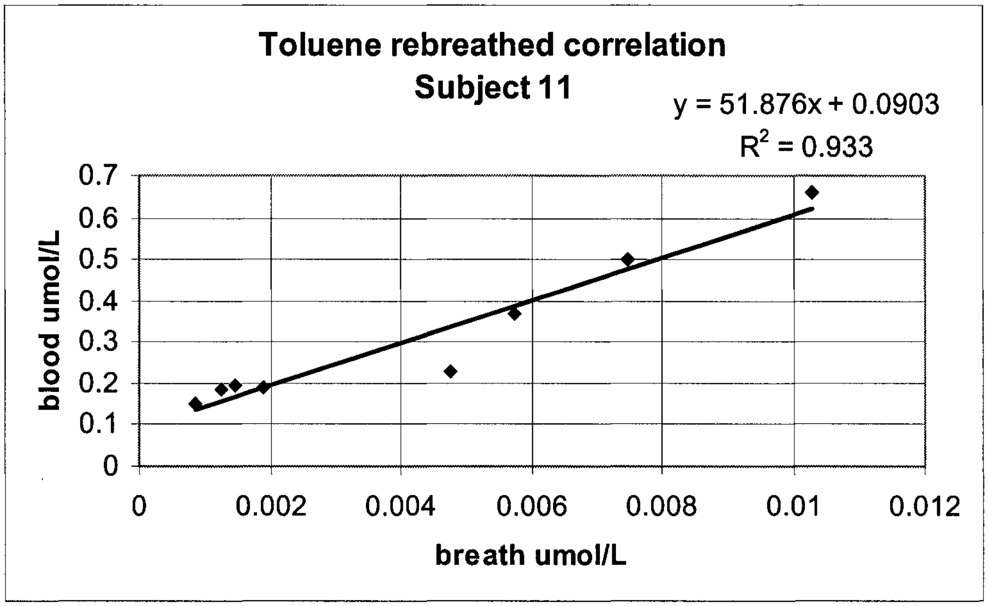
10/29/03

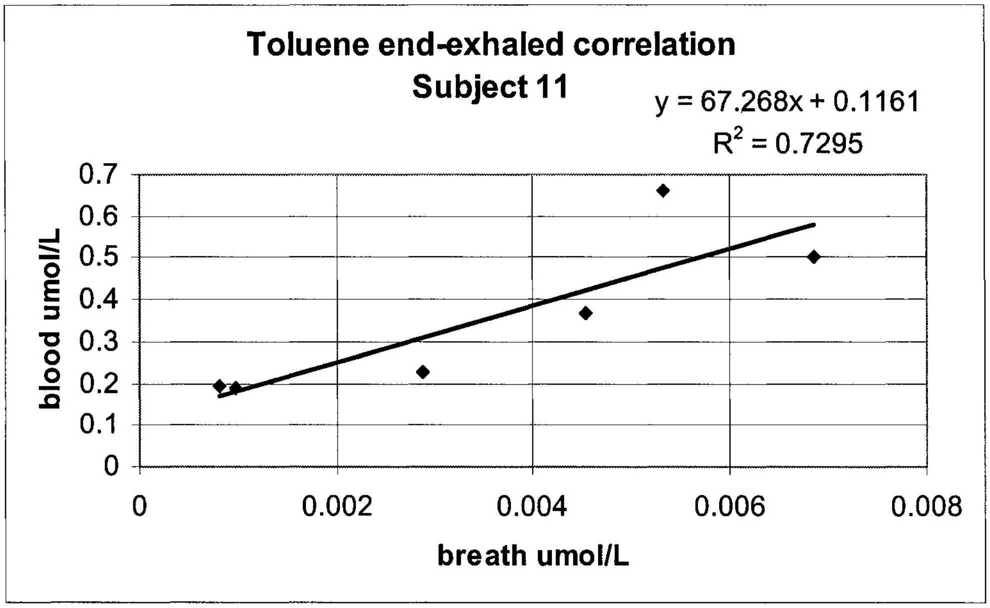

Toluene breath calibration
Subject 11
y = 1.6709E-06x - 1.4389E-03
R2 = 9.3869E-01
umol/L
0.02
0.015
0.01
0.005
0
0
2000
4000
6000
8000
10000
12000
area

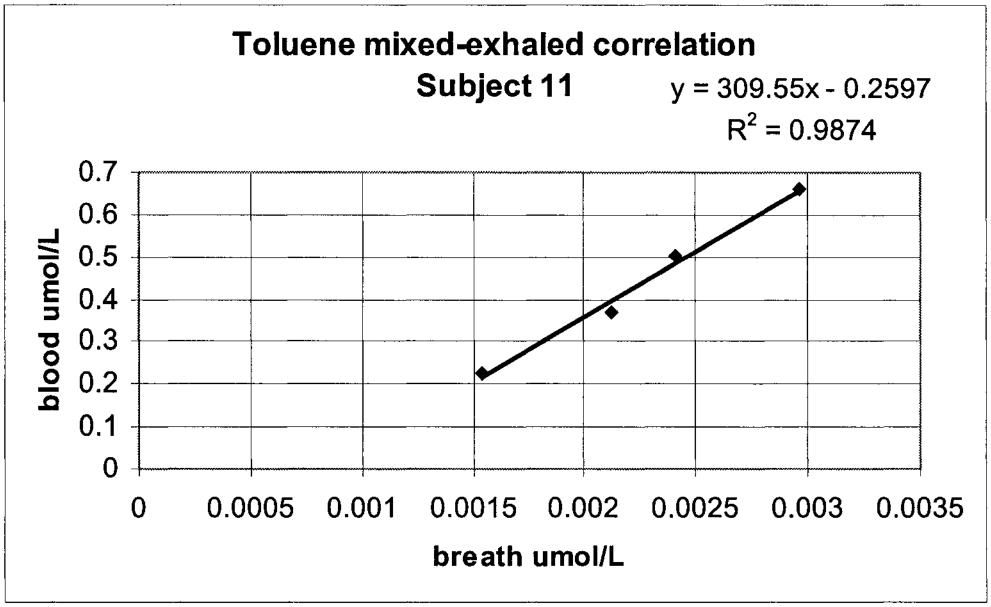

Toluene blood calibration
Subject 11
y = 5.508E-04x - 3.452E-03
R^2 = 9.935E-01
1.5
1
0.5
0
umol/L
0
500
1000
1500
2000
response factor

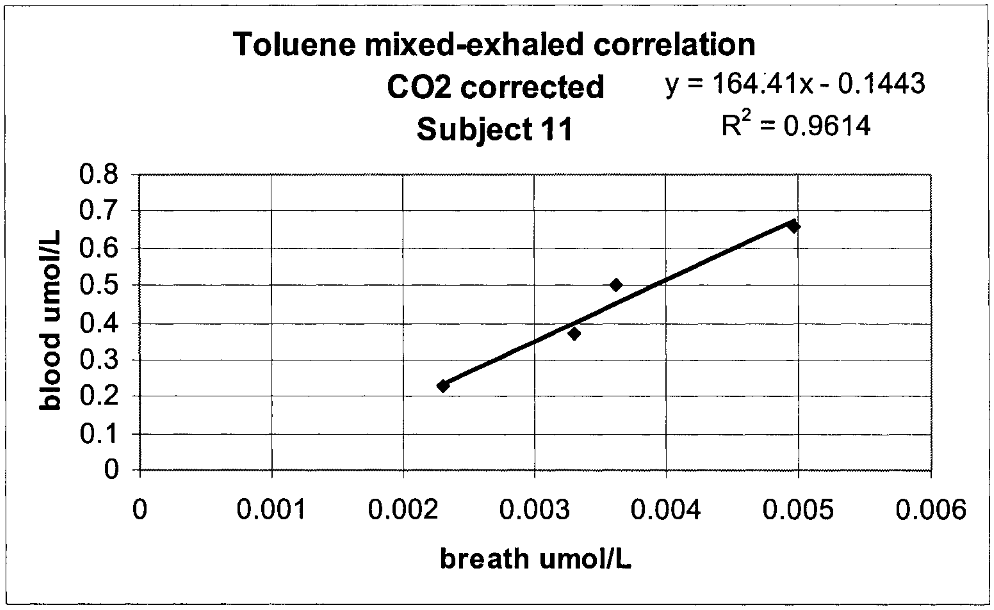

Toluene breath washout
Subject 11
0.1
0.01
0.001
0.0001
umol/L
0:00
1:00
2:00
3:00
4:00
hours post-exposure
◆ rebreathed
■ end-exhaled
mixed-exhaled


Toluene blood washout
Subject 11
umol/L
1
0.1
0:00
1:00
2:00
3:00
4:00
hours post-exposure
◆ pre-breath
■ post-breath

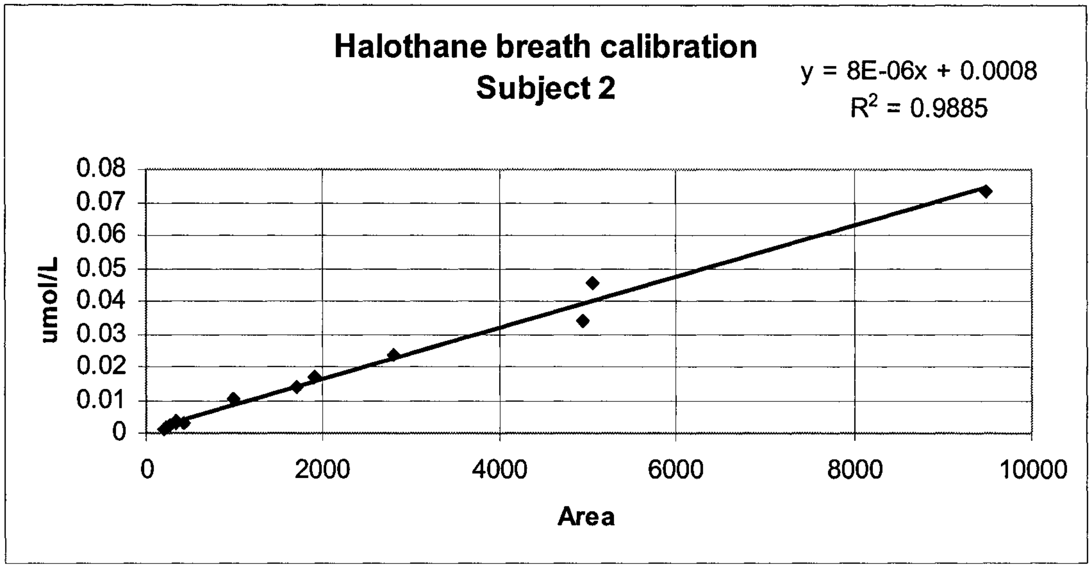

Toluene rebreathed correlation
Subject 11
y = 51.876x + 0.0903
$R^2 = 0.933$
blood umol/L
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
0.002
0.004
0.006
0.008
0.01
0.012
breath umol/L

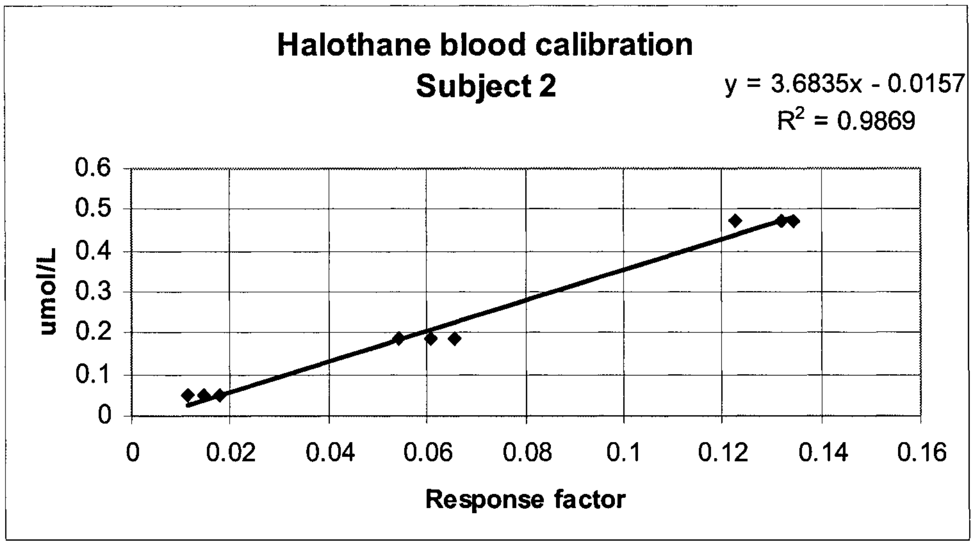

Toluene end-exhaled correlation
Subject 11
y = 67.268x + 0.1161
R2 = 0.7295
blood umol/L
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
0.002
0.004
0.006
0.008
breath umol/L

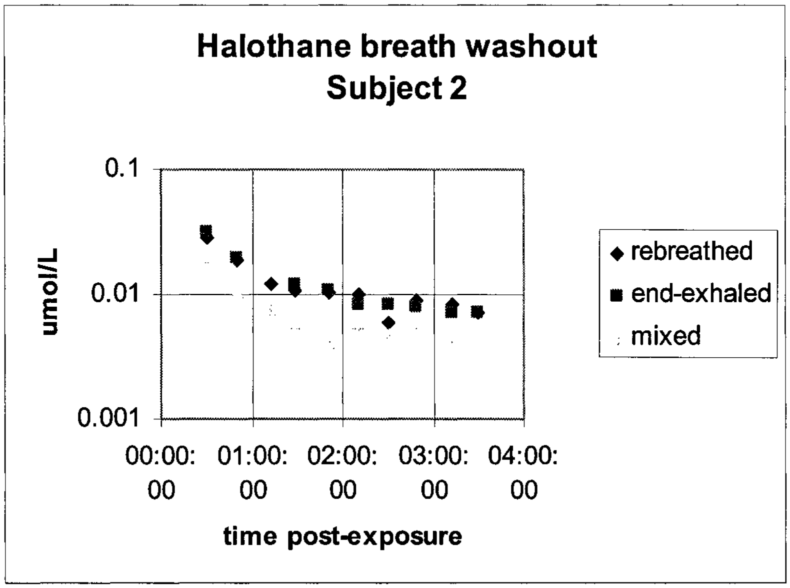

Toluene mixed-exhaled correlation
Subject 11
y = 309.55x - 0.2597
R2 = 0.9874
blood umol/L
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
0.0005
0.001
0.0015
0.002
0.0025
0.003
0.0035
breath umol/L

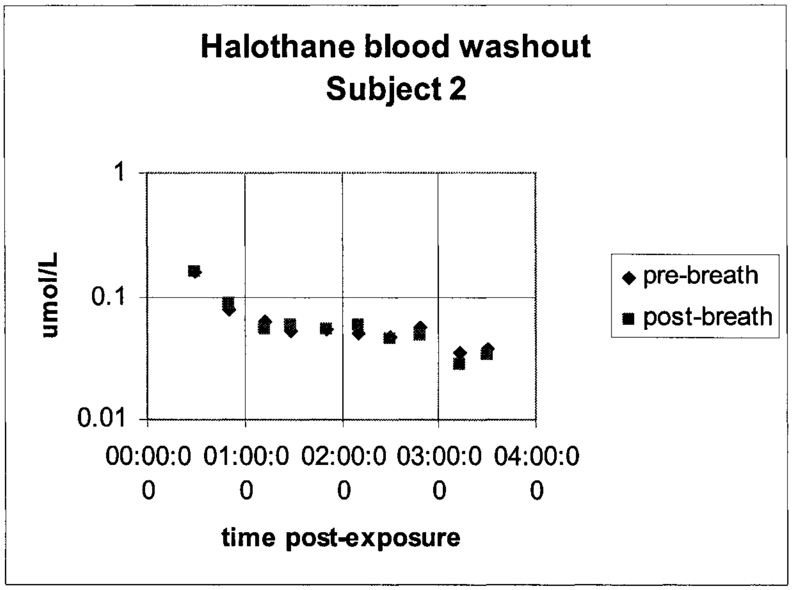


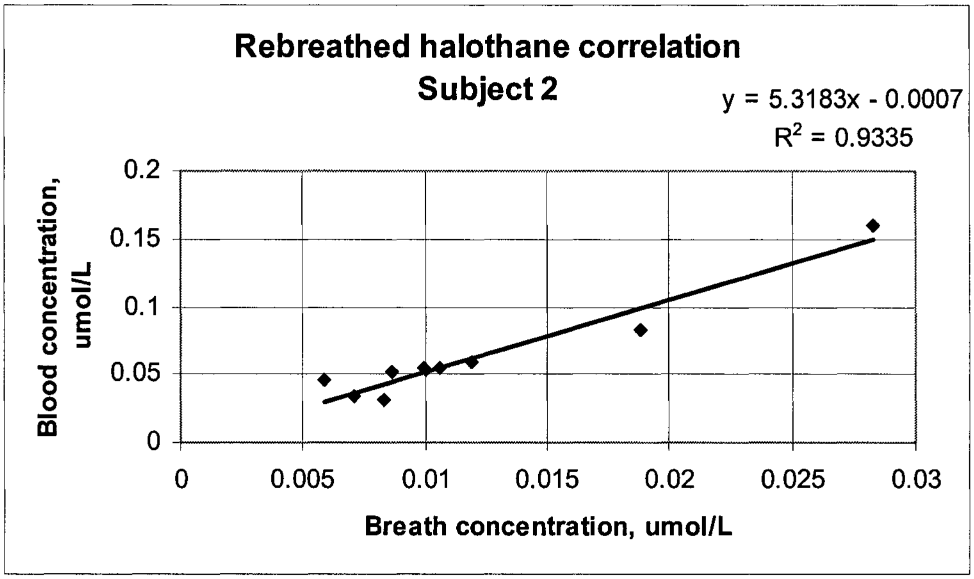
Halothane:
12/12/02

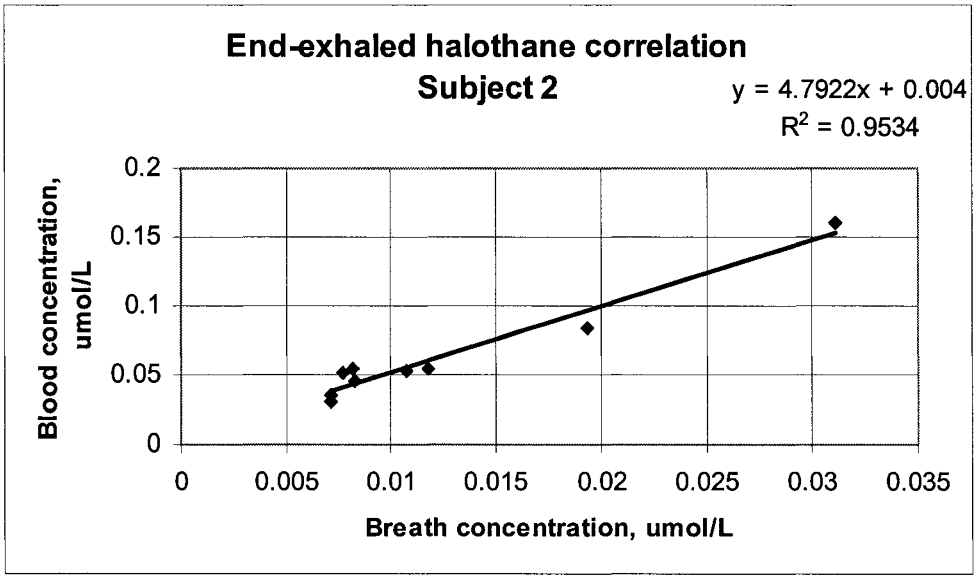


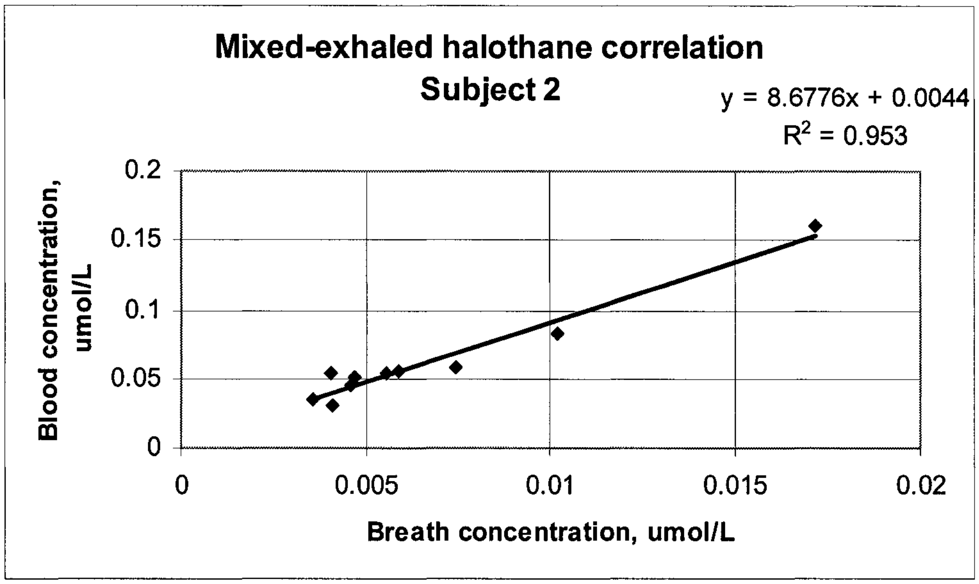

Halothane blood calibration
Subject 2
y = 3.6835x - 0.0157
R² = 0.9869
umol/L
0.6
0.5
0.4
0.3
0.2
0.1
0
0
0.02
0.04
0.06
0.08
0.1
0.12
0.14
0.16
Response factor

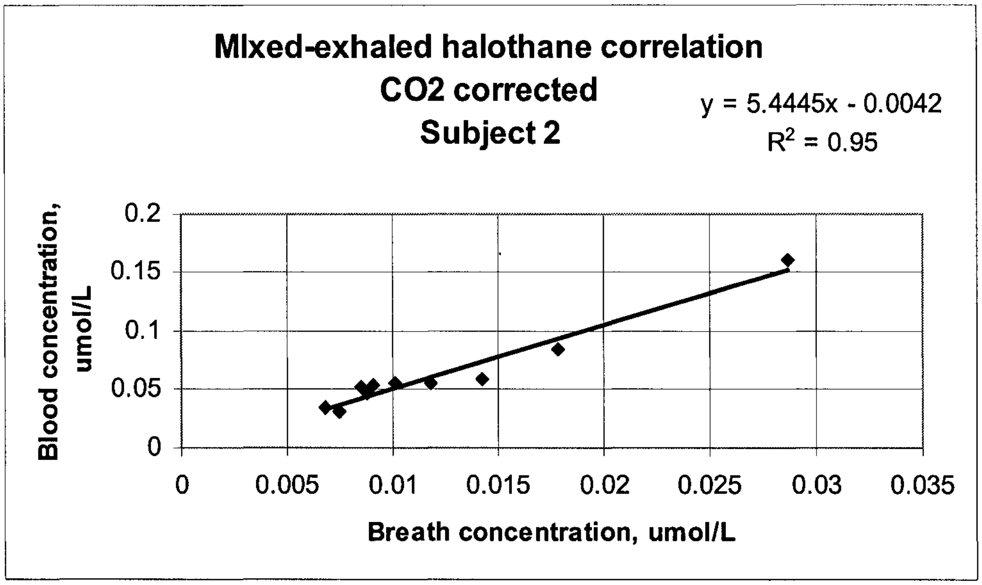

Halothane breath washout
Subject 2
umol/L
0.1
0.01
0.001
00:00:00
01:00:00
02:00:00
03:00:00
04:00:00
time post-exposure
◆ rebreathed
■ end-exhaled
mixed


Halothane blood washout
Subject 2
umol/L
1
0.1
0.01
00:00:00
01:00:00
02:00:00
03:00:00
04:00:00
time post-exposure
◆ pre-breath
■ post-breath

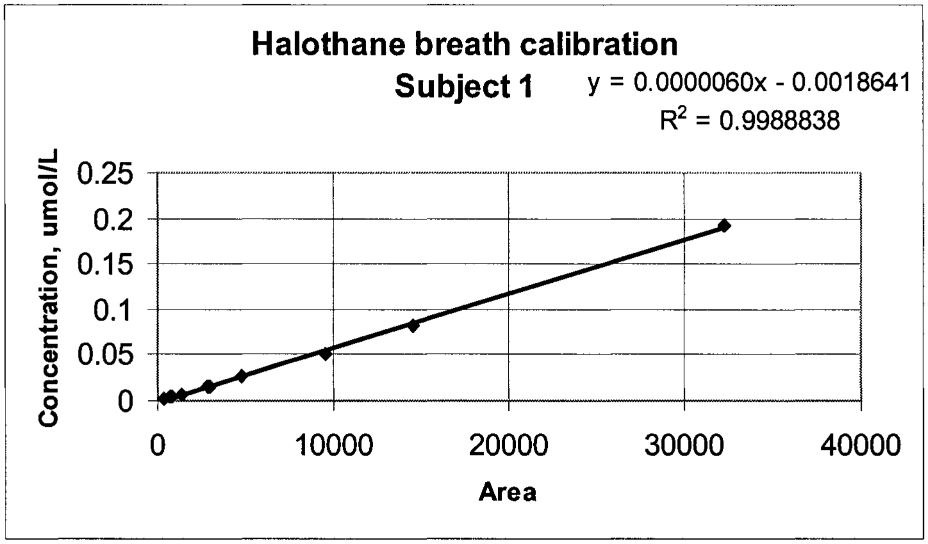

Rebreathed halothane correlation
Subject 2
y = 5.3183x - 0.0007
R² = 0.9335
Blood concentration, umol/L
0.2
0.15
0.1
0.05
0
0
0.005
0.01
0.015
0.02
0.025
0.03
Breath concentration, umol/L

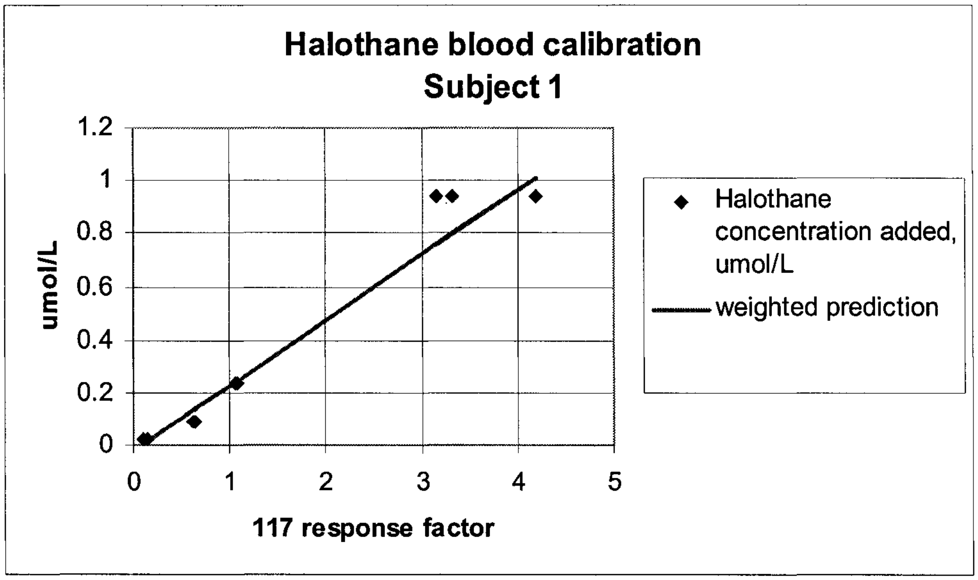

End-exhaled halothane correlation
Subject 2
y = 4.7922x + 0.004
R^2 = 0.9534
Blood concentration, umol/L
0.2
0.15
0.1
0.05
0
0
0.005
0.01
0.015
0.02
0.025
0.03
0.035
Breath concentration, umol/L

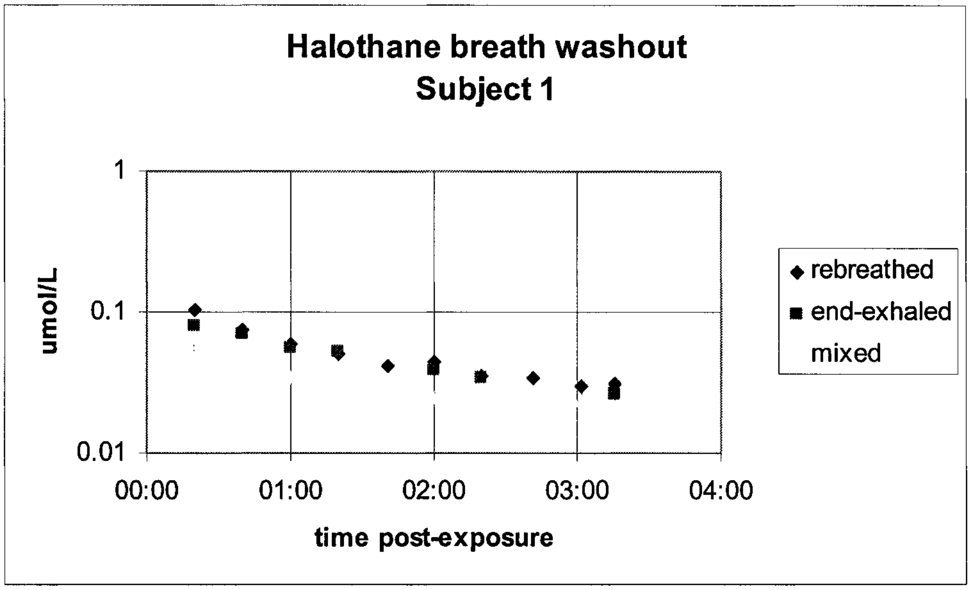

Mixed-exhaled halothane correlation
Subject 2
y = 8.6776x + 0.0044
R^2 = 0.953
Blood concentration, umol/L
0.2
0.15
0.1
0.05
0
0
0.005
0.01
0.015
0.02
Breath concentration, umol/L

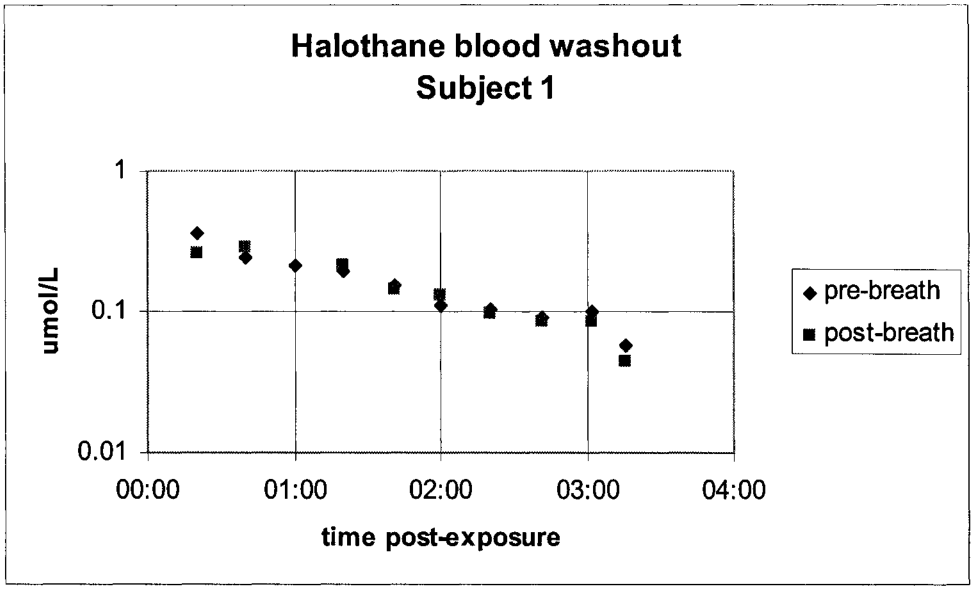

MIxed-exhaled halothane correlation
CO2 corrected
Subject 2
y = 5.4445x - 0.0042
R2 = 0.95
Blood concentration, umol/L
0.2
0.15
0.1
0.05
0
0
0.005
0.01
0.015
0.02
0.025
0.03
0.035
Breath concentration, umol/L

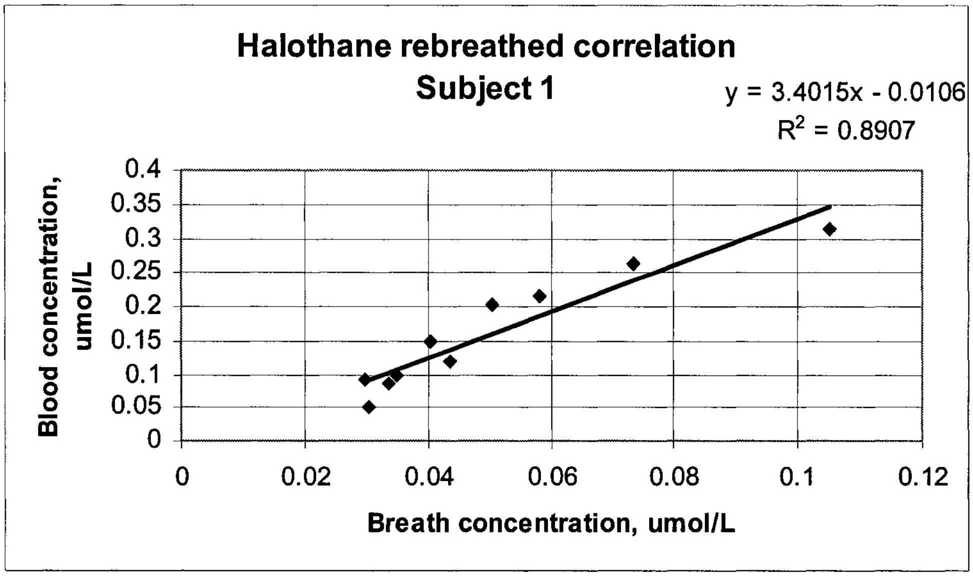
3//7/03

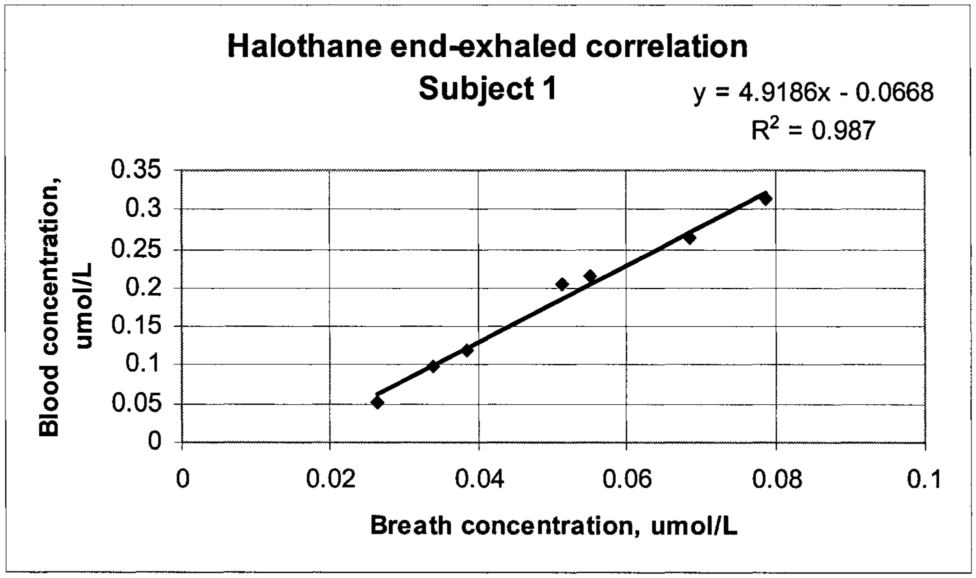

Halothane breath calibration
Subject 1
y = 0.0000060x - 0.0018641
R2 = 0.9988838
Concentration, umol/L
0.25
0.2
0.15
0.1
0.05
0
0
10000
20000
30000
40000
Area

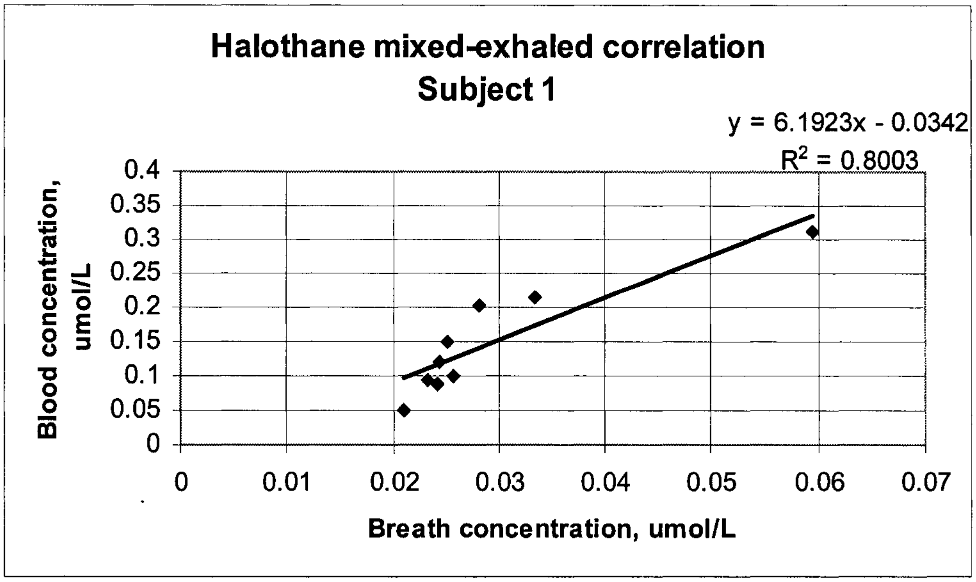

Halothane blood calibration
Subject 1
umol/L
1.2
1
0.8
0.6
0.4
0.2
0
0
1
2
3
4
5
117 response factor
◆ Halothane concentration added, umol/L
weighted prediction

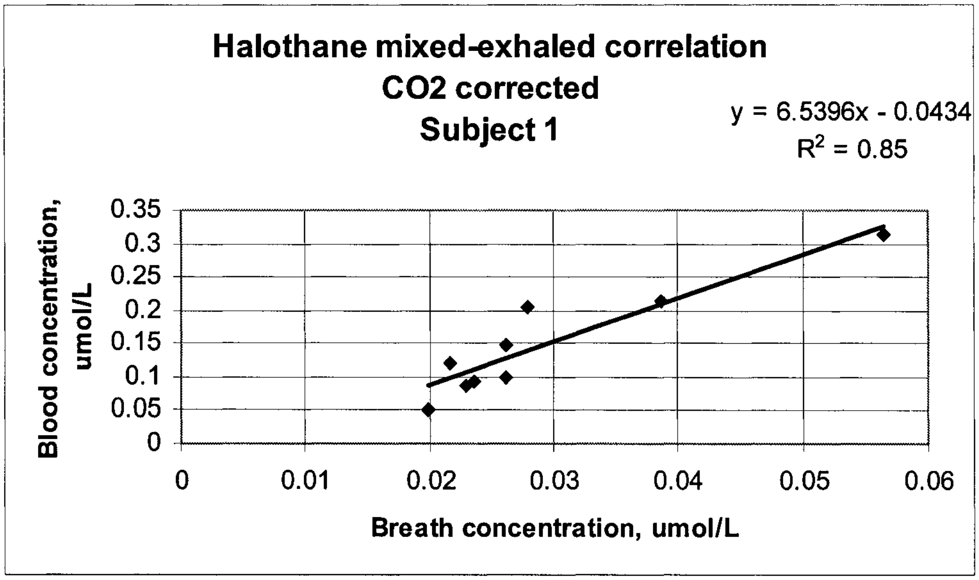

Halothane breath washout
Subject 1
umol/L
1
0.1
0.01
00:00
01:00
02:00
03:00
04:00
time post-exposure
◆ rebreathed
■ end-exhaled
mixed


Halothane blood washout
Subject 1
umol/L
1
0.1
0.01
00:00
01:00
02:00
03:00
04:00
time post-exposure
◆ pre-breath
■ post-breath

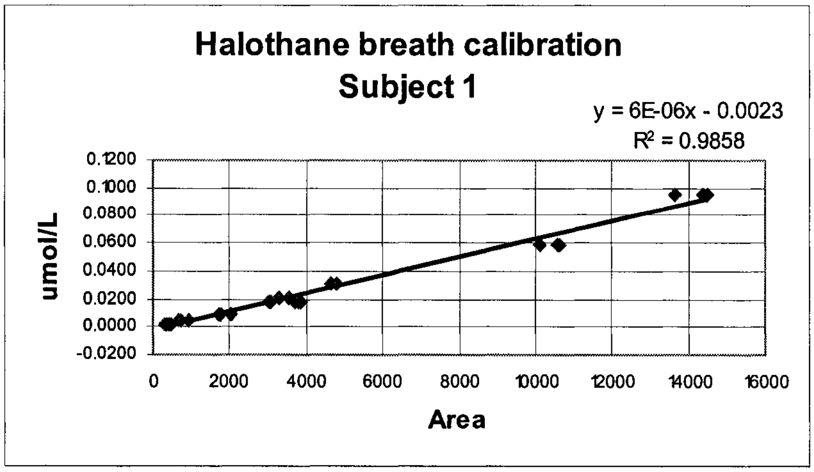

Halothane rebreathed correlation
Subject 1
y = 3.4015x - 0.0106
R2 = 0.8907
Blood concentration, umol/L
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
0
0.02
0.04
0.06
0.08
0.1
0.12
Breath concentration, umol/L

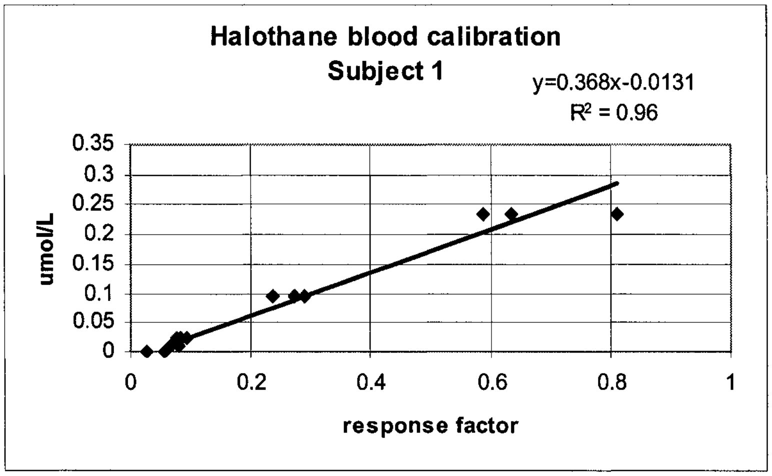

Halothane end-exhaled correlation
Subject 1
y = 4.9186x - 0.0668
R² = 0.987
Blood concentration, umol/L
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
0
0.02
0.04
0.06
0.08
0.1
Breath concentration, umol/L

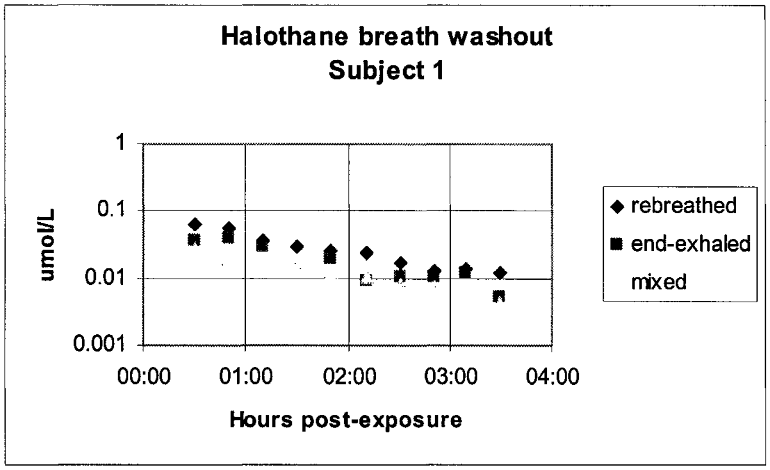

Halothane mixed-exhaled correlation
Subject 1
y = 6.1923x - 0.0342
R² = 0.8003
Blood concentration, umol/L
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
0
0.01
0.02
0.03
0.04
0.05
0.06
0.07
Breath concentration, umol/L

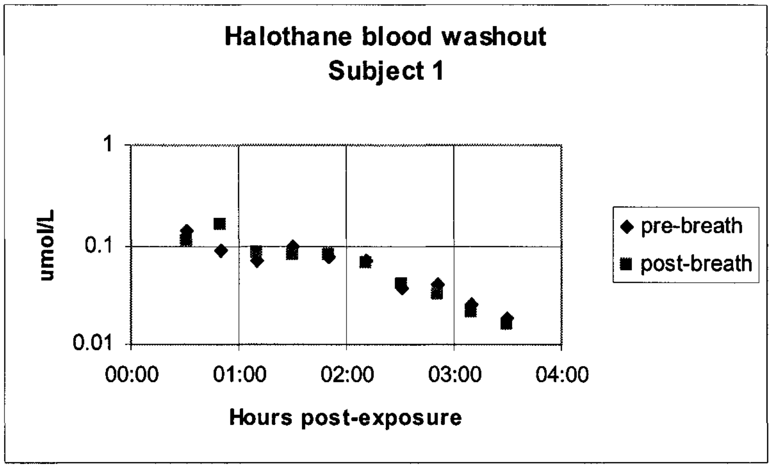

Halothane mixed-exhaled correlation
CO2 corrected
Subject 1
y = 6.5396x - 0.0434
R² = 0.85
Blood concentration, umol/L
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
0
0.01
0.02
0.03
0.04
0.05
0.06
Breath concentration, umol/L

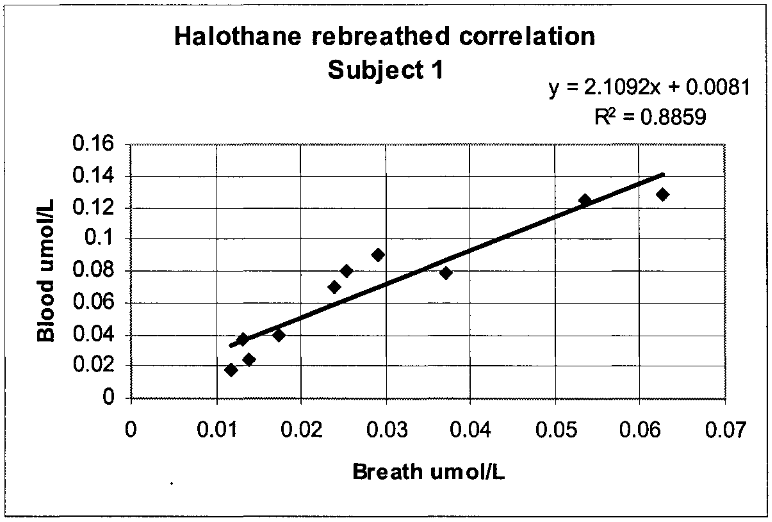
5/21/03:

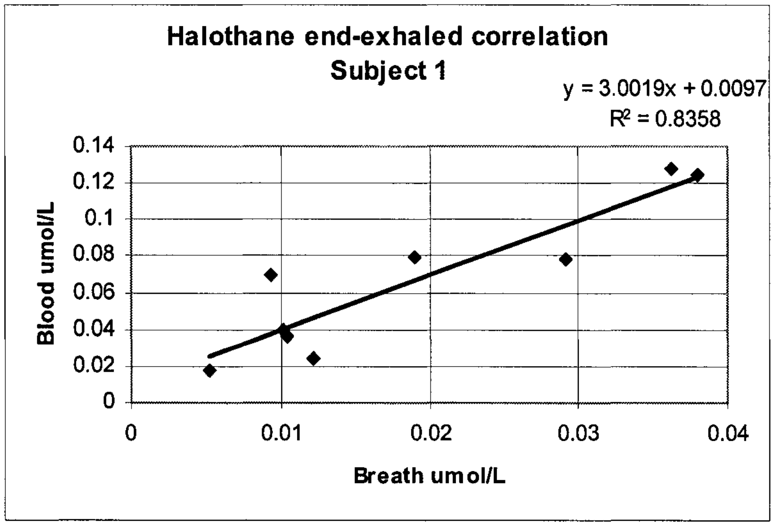

Halothane breath calibration
Subject 1
y = 6E-06x - 0.0023
R² = 0.9858
umol/L
0.1200
0.1000
0.0800
0.0600
0.0400
0.0200
0.0000
-0.0200
0
2000
4000
6000
8000
10000
12000
14000
16000
Area

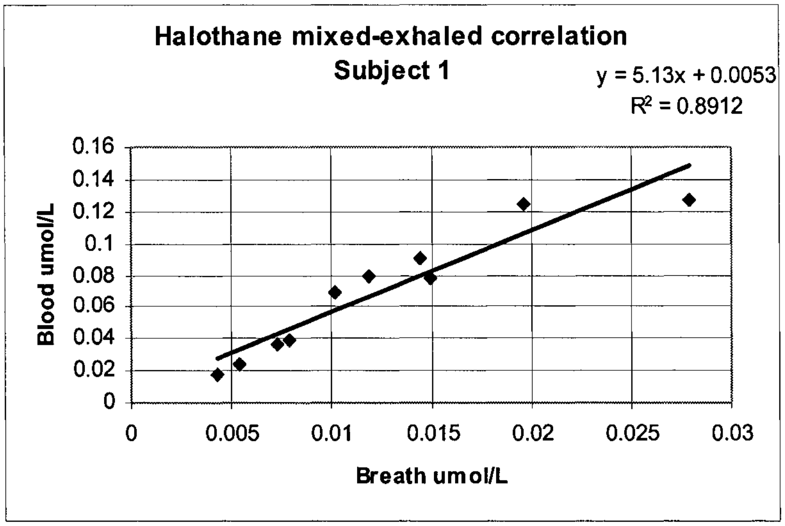

Halothane blood calibration
Subject 1
y=0.368x-0.0131
R² = 0.96
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
umol/L
0
0.2
0.4
0.6
0.8
1
response factor

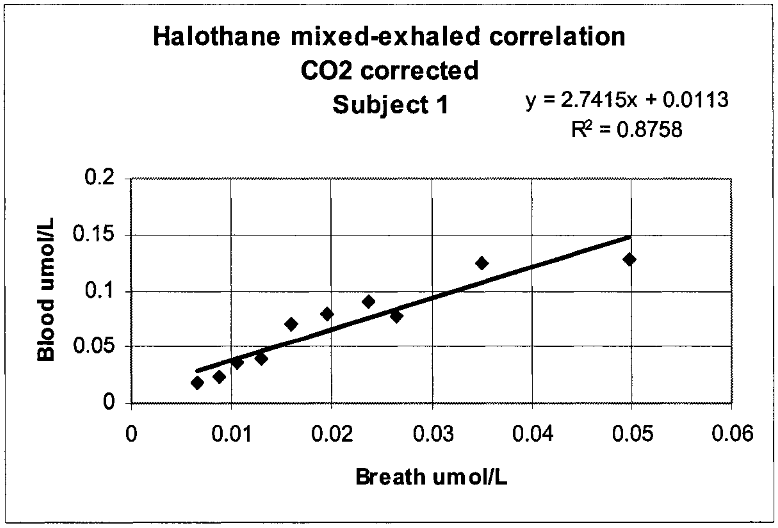

Halothane breath washout
Subject 1
1
0.1
0.01
0.001
umol/L
00:00
01:00
02:00
03:00
04:00
Hours post-exposure
rebreathed
end-exhaled
mixed

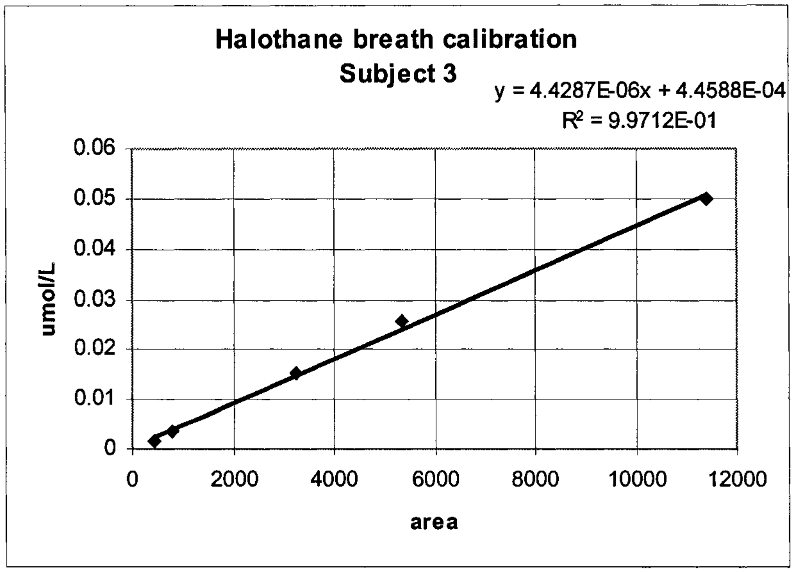

Halothane blood washout
Subject 1
1
0.1
0.01
umol/L
00:00
01:00
02:00
03:00
04:00
Hours post-exposure
pre-breath
post-breath

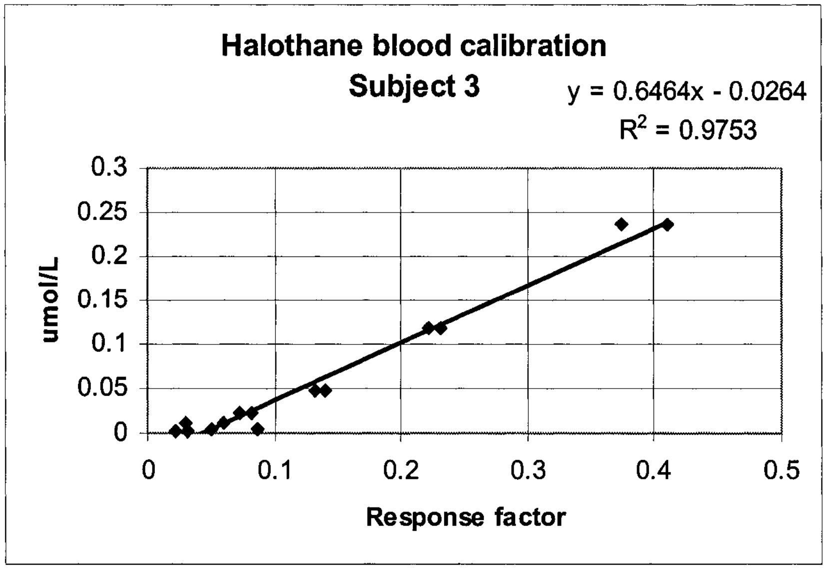

Halothane rebreathed correlation
Subject 1
y = 2.1092x + 0.0081
R² = 0.8859
Blood umol/L
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
0
0
0.01
0.02
0.03
0.04
0.05
0.06
0.07
Breath umol/L

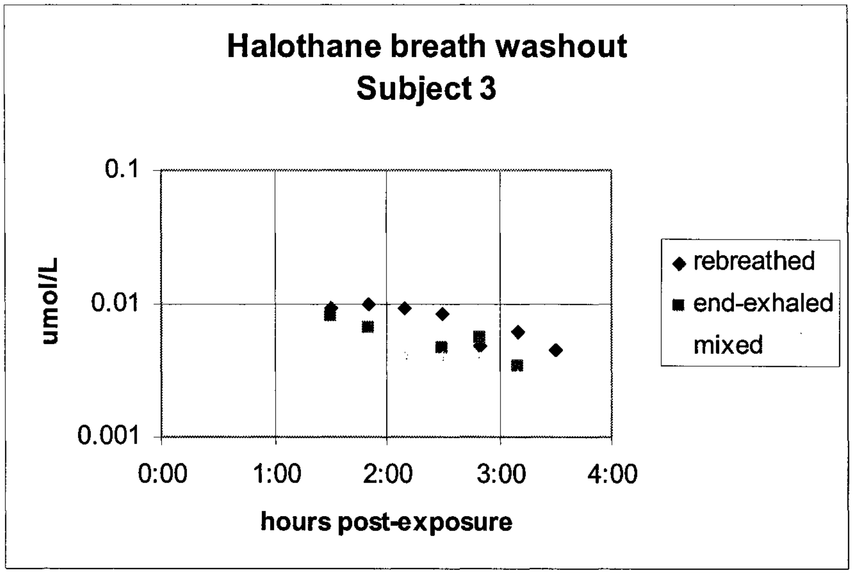

Halothane end-exhaled correlation
Subject 1
y = 3.0019x + 0.0097
R² = 0.8358
Blood umol/L
0.14
0.12
0.1
0.08
0.06
0.04
0.02
0
0
0.01
0.02
0.03
0.04
Breath umol/L


Halothane mixed-exhaled correlation
Subject 1
y = 5.13x + 0.0053
R² = 0.8912
Blood umol/L
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
0
0
0.005
0.01
0.015
0.02
0.025
0.03
Breath umol/L

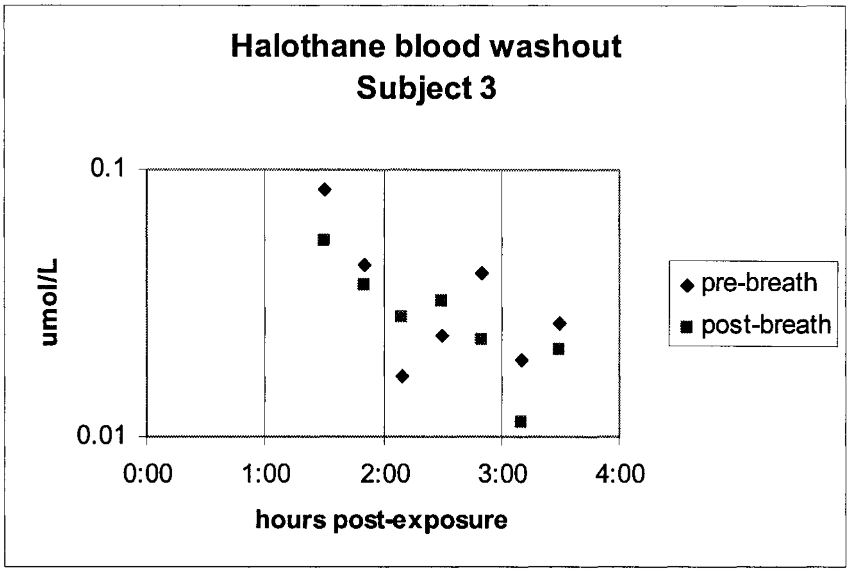

Halothane mixed-exhaled correlation
CO2 corrected
Subject 1
y = 2.7415x + 0.0113
R² = 0.8758
Blood umol/L
0.2
0.15
0.1
0.05
0
0
0.01
0.02
0.03
0.04
0.05
0.06
Breath umol/L


Halothane breath calibration
Subject 3
y = 4.4287E-06x + 4.4588E-04
R^2 = 9.9712E-01
0.06
0.05
0.04
0.03
0.02
0.01
0
umol/L
0
2000
4000
6000
8000
10000
12000
area

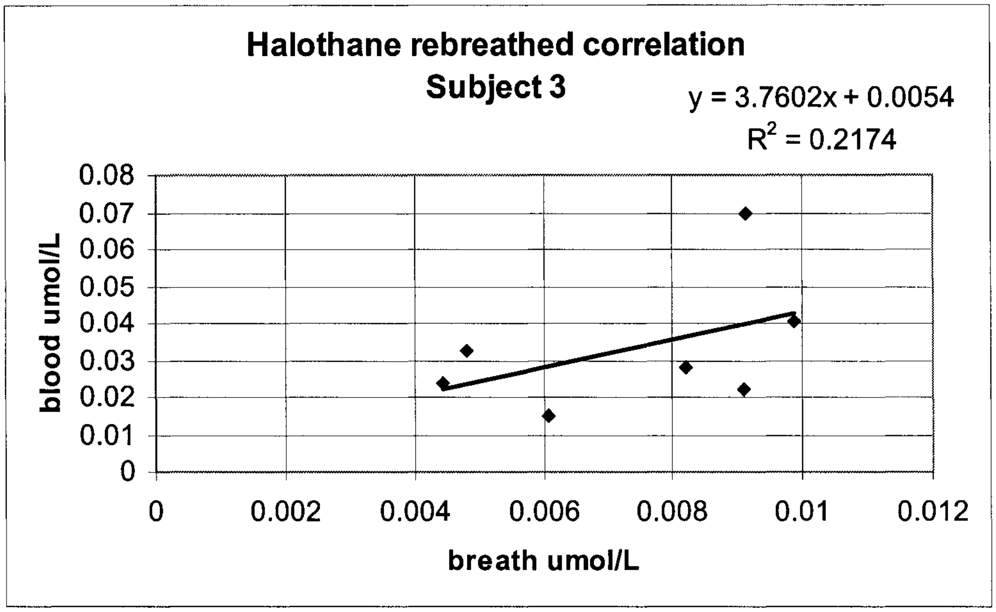

Halothane blood calibration
Subject 3
y = 0.6464x - 0.0264
R^2 = 0.9753
0.3
0.25
0.2
0.15
0.1
0.05
0
umol/L
0
0.1
0.2
0.3
0.4
0.5
Response factor

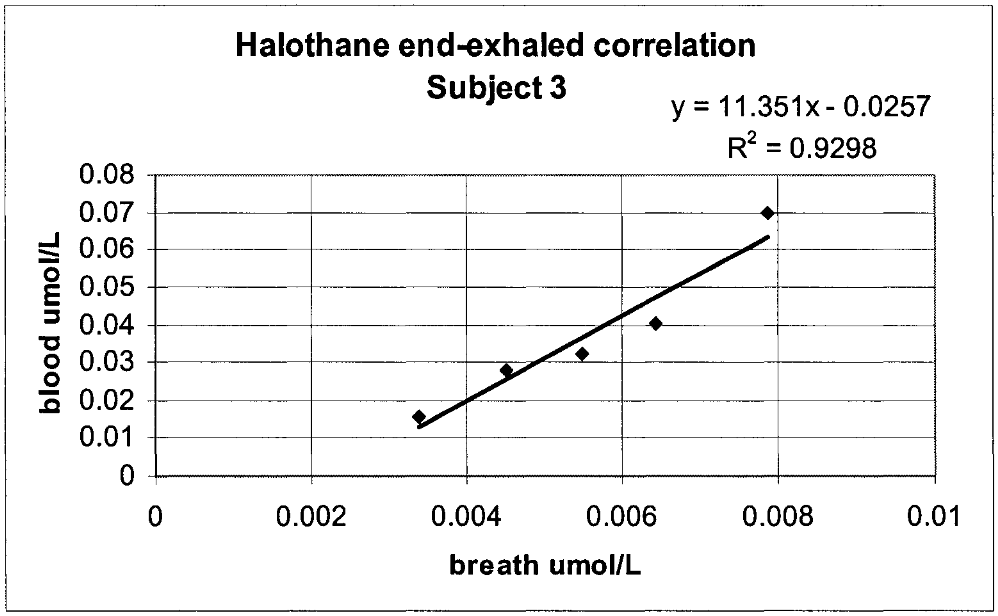


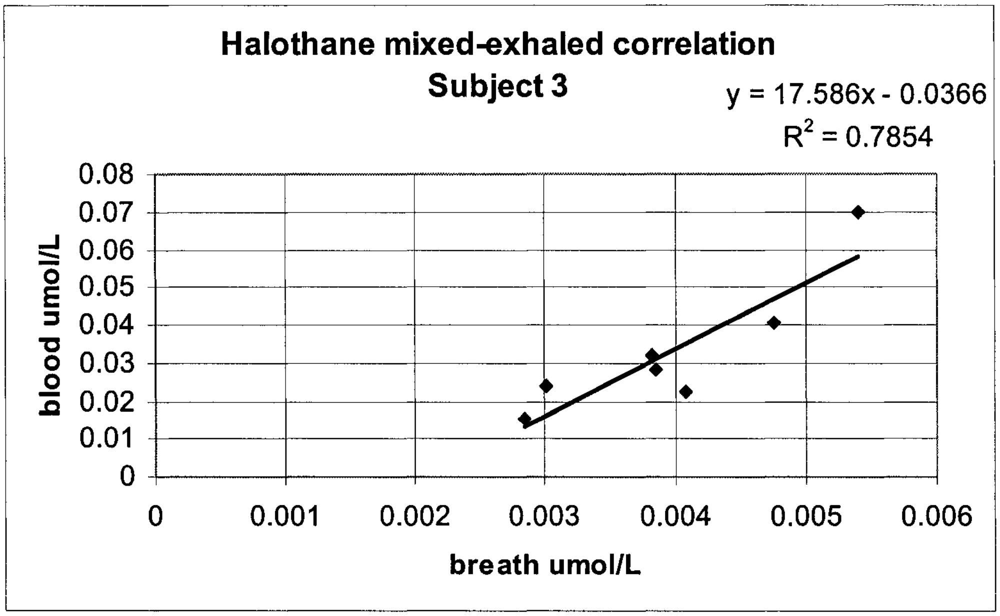
Halothane breath washout
Subject 3

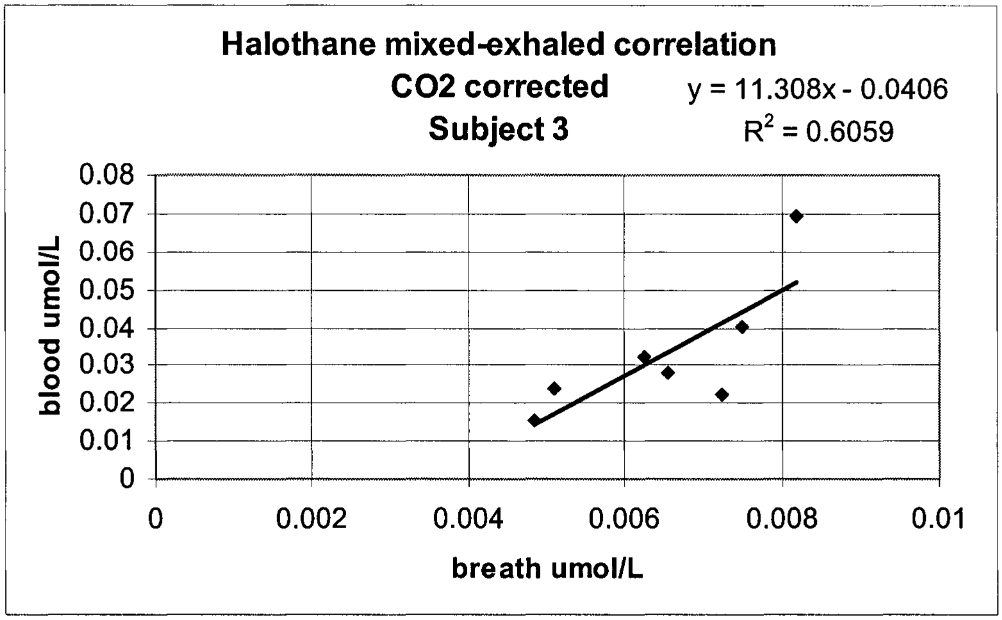


Halothane blood washout
Subject 3


Halothane rebreathed correlation
Subject 3
y = 3.7602x + 0.0054
R² = 0.2174
blood umol/L
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
0
0.002
0.004
0.006
0.008
0.01
0.012
breath umol/L


Halothane end-exhaled correlation
Subject 3
y = 11.351x - 0.0257
R² = 0.9298
blood umol/L
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
0
0.002
0.004
0.006
0.008
0.01
breath umol/L


Halothane mixed-exhaled correlation
Subject 3
y = 17.586x - 0.0366
R2 = 0.7854
blood umol/L
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
0
0.001
0.002
0.003
0.004
0.005
0.006
breath umol/L


Halothane mixed-exhaled correlation
CO2 corrected
Subject 3
y = 11.308x - 0.0406
R2 = 0.6059
blood umol/L
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
0
0.002
0.004
0.006
0.008
0.01
breath umol/L

Appendix C: Partition coefficients for individual regressions

These tables show calculated *in vivo* apparent partition coefficients for each of the four types of breath samples. The robust SE in this table is the standard error for the slope of the regression of blood concentrations on breath concentrations.

Rebreathed:		Ethanol			Acetone			MIBK			Toluene			Halothane		
	Subject	slope mean	robust SE	R^2	slope mean	robust SE	R^2	slope mean	robust SE	R^2	slope mean	robust SE	R^2	slope mean	robust SE	R^2
10/7/2002	3							161	37	0.826						
10/23/2002	1										36.9	2.36	0.915			
12/12/2002	2	1940	234	0.972										5.32	0.634	0.934
1/24/2003	2	3120	25.2	1	322	39.4	0.93									
3/7/2003	1													3.4	0.479	0.891
3/19/2003	4	1310	82	0.946	248	55.1	0.54									
5/1/2003	5										33.1	3.01	0.979			
5/21/2003	1													2.11	0.229	0.886
5/29/2003	5	1780	72.6	0.992	120	95.1	0.14									
6/18/2003	6	3000	43.7	0.998				42.2	8.81	0.845						
6/25/2003	7				277	95.4	0.66				7.93	1.66	0.849			
7/3/2003	8				378	93.1	0.47				43.9	2.5	0.98			
7/10/2003	9				205	103	0.53				21.2	2.64	0.889			
8/1/2003	4										18.6	4.69	0.818			
8/6/2003	8	2800	826	0.852				181	58.9	0.56						
8/11/2003	9	1810	168	0.93				441	57.6	0.76						
8/21/2003	7	3150	579	0.889				13.1	2.64	0.824						
8/26/2003	6				223	36.8	0.63				39	5.03	0.797			
10/22/2003	10										22.7	0.372	0.994			
10/29/2003	11										55	5.34	0.923			
11/19/2003	11							25.1	2.07	0.85						
12/10/2003	3													4.24	2.7	0.276
12/17/2003	10							110	11.7	0.956						
Average slopes:		2364			253.3			139			30.9			3.768		
Slope by random effects:		2239			251			55.7			31.1			3.16		

End-exhaled:		Ethanol			Acetone			MIBK			Toluene			Halothane		
		slope	robust	R^2	slope	robust	R^2	slope	robust	R^2	slope	robust	R^2	slope	robust	R^2
	Exposure	mean	SE		mean	SE		mean	SE		mean	SE		mean	SE	
10/7/2002	3							218	20.2	0.94						
10/23/2002	1										56.1	4.01	0.98			
12/12/2002	2	3050		1										4.79	0.41	0.95
1/24/2003	2	3810	39.4	1	404	46.7	0.94									
3/7/2003	1													4.92	0.22	0.99
3/19/2003	4	1810	47	0.99	281	82.6	0.67									
5/1/2003	5										36.6	1.27	1			
5/21/2003	1													3	0.4	0.84
5/29/2003	5	2020	127	0.98	151	141	0.12									
6/18/2003	6	3440	17.9	1				48	13	0.79						
6/25/2003	7				211	79.8	0.49				9.05	1.66	0.75			
7/3/2003	8				394	257	0.27				47.8	12.2	0.75			
7/10/2003	9				131	70.8	0.06				27.5	7.14	0.8			
8/1/2003	4										19.6	7.38	0.56			
8/6/2003	8	2160	189	0.97				186	44.3	0.85						
8/11/2003	9	2260	217	0.91				647	64.5	0.79						
8/21/2003	7	3900	712	0.89				17.2	3	0.85						
8/26/2003	6				158	87.3	0.24				71.3	14.7	0.78			
10/22/2003	10										24	1.2	0.93			
10/29/2003	11										67.3	17.4	0.73			
11/19/2003	11							30	3.02	0.85						
12/10/2003	3													9.81	2.55	0.86
12/17/2003	10						0.4	146	22.4	0.91						
Average slopes:		2806			247			185			39.9			5.63		
Slope by random effects:		2618			265			68.1			39.1			3.56		

Mixed-exhaled:		Ethanol			Acetone			MIBK			Toluene			Halothane		
	Exposure	slope mean	robust SE	R^2	slope mean	robust SE	R^2	slope mean	robust SE	R^2	slope mean	robust SE	R^2	slope mean	robust SE	R^2
10/7/2002	81VE							53.5	17.2	0.74						
10/23/2002	111ZA										97.6	20.2	0.89			
12/12/2002	91VD	2830		1										8.68	7.11	0.95
1/24/2003	101VD	5850	332	0.99	851	47.9	0.93									
3/7/2003	71ZA													6.19	3.43	0.8
3/19/2003	101VF	2110	91.8	0.92	346	115	0.61									
5/1/2003	111VG										52.2	12.5	0.89			
5/21/2003	62ZA													5.13	3.67	0.89
5/29/2003	101VG	2310	65	0.98	74.3	272	0.01									
6/18/2003	81VH	3700	22	1				62.1	18.9	0.78						
6/25/2003	131VI				629	158	0.61				22	3.31	0.7			
7/3/2003	131VJ				1290	284	0.72				118	23.7	0.89			
7/10/2003	131VK				114	79.1	0.11				38.5	38.5	0.62			
8/1/2003	141VF										23.3	5.81	0.84			
8/6/2003	81VJ	3440	155	0.99				496	181	0.72						
8/11/2003	81VK	3300	318	0.89				826	153	0.7						
8/21/2003	81VI	4920	990	0.83				32.2	8.97	0.77						
8/26/2003	131VH				510	241	0.39				96.4	29.2	0.4			
10/22/2003	131VL										78.3	13.3	0.89			
10/29/2003	131VM										310	12.9	0.99			
11/19/2003	81VM							61.7	16	0.86						
12/10/2003	91VE													17.3	6.15	0.76
12/17/2003	81VL							240	19.3	0.97						
Average slopes:		3558			544.9			253			92.9			9.33		
Slope by random effects:		3052			554			87.3			81.9			5.29		

Mixed-exhaled, CO2 corrected:		Ethanol			Acetone			MIBK			Toluene			Halothane		
	Exposure	slope mean	robust SE	R^2	slope mean	robust SE	R^2	slope mean	robust SE	R^2	slope mean	robust SE	R^2	slope mean	robust SE	R^2
10/7/2002	81VE							35.7	17.5	0.57						
10/23/2002	111ZA										52.4	10.6	0.9			
12/12/2002	91VD	1530		1										5.44	0.46	0.95
1/24/2003	101VD	5810	325	0.99	843	59.7	0.92									
3/7/2003	71ZA													6.54	0.6	0.85
3/19/2003	101VF	1420	70.3	0.92	214	161	0.12									
5/1/2003	111VG										42.8	11.6	0.87			
5/21/2003	62ZA													2.74	0.47	0.88
5/29/2003	101VG	1060	34.6	0.97	60.7	154	0.03									
6/18/2003	81VH	3630	19.9	1				59.8	19.4	0.77						
6/25/2003	131VI				436	82	0.78				14.9	2	0.83			
7/3/2003	131VJ				895	304	0.57				76.5	17.5	0.8			
7/10/2003	131VK				70.1	41.5	0.12				26	2.7	0.89			
8/1/2003	141VF										19	2.08	0.95			
8/6/2003	81VJ	1950	223	0.97				291	68.3	0.88						
8/11/2003	81VK	2490	240	0.89				649	115	0.74						
8/21/2003	81VI	2330	477	0.8				17.3	3.8	0.83						
8/26/2003	131VH				302	164	0.27				63.7	16.9	0.43			
10/22/2003	131VL										47.4	5.58	0.94			
10/29/2003	131VM										164	9.13	0.96			
11/19/2003	81VM							33.7	6.23	0.91						
12/10/2003	91VE													11.1	4.76	0.58
12/17/2003	81VL							165	16.2	0.97						
Average slopes:		2528			403			179			56.3			6.46		
Slope by random effects:		1598			361			74.3			49.9			4.49		

Appendix D: Linear regression with subject as a random effect

The statistical output from linear regressions of blood concentrations (average of pre-breath and post-breath samples) and breath concentrations of each type, for each chemical, treating subjects as a random variable, can be found below.

```
. xtreg  bloodethavg rebeth, re i(subjnum)

Random-effects GLS regression                   Number of obs      =        41
Group variable (i): subjnum                     Number of groups   =         6

R-sq:  within  = 0.9166                         Obs per group: min =         5
       between = 0.9146                                        avg =       6.8
       overall = 0.9155                                        max =        10

Random effects u_i ~ Gaussian                   Wald chi2(1)       =    423.69
corr(u_i, X)       = 0 (assumed)                Prob > chi2        =    0.0000

------------------------------------------------------------------------------
 bloodethavg |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      rebeth |   2239.002   108.7747    20.58   0.000     2025.807    2452.197
       _cons |   31.31793   33.42051     0.94   0.349    -34.18507    96.82093
-------------+----------------------------------------------------------------
     sigma_u |  29.855456
     sigma_e |  172.56818
         rho |  .02906148   (fraction of variance due to u_i)
------------------------------------------------------------------------------

. xtreg  bloodaceavg rebace, re i(subjnum)

Random-effects GLS regression                   Number of obs      =        68
Group variable (i): subjnum                     Number of groups   =         7

R-sq:  within  = 0.5846                         Obs per group: min =         8
       between = 0.4857                                        avg =       9.7
       overall = 0.5021                                        max =        10

Random effects u_i ~ Gaussian                   Wald chi2(1)       =     90.45
corr(u_i, X)       = 0 (assumed)                Prob > chi2        =    0.0000

------------------------------------------------------------------------------
 bloodaceavg |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      rebace |   251.2649   26.41988     9.51   0.000     199.4829     303.047
       _cons |   20.72725   9.396706     2.21   0.027     2.310049    39.14446
-------------+----------------------------------------------------------------
     sigma_u |  22.375362
     sigma_e |  7.7396798
         rho |  .89313776   (fraction of variance due to u_i)
------------------------------------------------------------------------------

. xtreg  bloodmibkavg rebmibk, re i(subjnum)

Random-effects GLS regression                   Number of obs      =        58
Group variable (i): subjnum                     Number of groups   =         6

R-sq:  within  = 0.4691                         Obs per group: min =         6
       between = 0.2682                                        avg =       9.7
```

```
      overall = 0.1136                                         max =         17

Random effects u_i ~ Gaussian                   Wald chi2(1)       =      31.09
corr(u_i, X)       = 0 (assumed)                Prob > chi2        =     0.0000

------------------------------------------------------------------------------
bloodmibkavg |      Coef.   Std. Err.       z     P>|z|      [95% Conf. Interval]
-------------+----------------------------------------------------------------
     rebmibk |   55.65026   9.980005      5.58   0.000      36.08981    75.21071
       _cons |   .0912665   .0711615      1.28   0.200     -.0482076    .2307405
-------------+----------------------------------------------------------------
     sigma_u |  .12244277
     sigma_e |  .18505885
         rho |  .30447874   (fraction of variance due to u_i)
------------------------------------------------------------------------------

. xtreg  bloodtolavg rebtol, re i(subjnum)

Random-effects GLS regression                   Number of obs      =         72
Group variable (i): subjnum                     Number of groups   =          9

R-sq:  within  = 0.8051                         Obs per group: min =          4
       between = 0.6619                                        avg =        8.0
       overall = 0.6193                                        max =         10

Random effects u_i ~ Gaussian                   Wald chi2(1)       =     260.08
corr(u_i, X)       = 0 (assumed)                Prob > chi2        =     0.0000

------------------------------------------------------------------------------
 bloodtolavg |      Coef.   Std. Err.       z     P>|z|      [95% Conf. Interval]
-------------+----------------------------------------------------------------
      rebtol |   31.05858   1.925864     16.13   0.000      27.28395     34.8332
       _cons |   .0637575    .037642      1.69   0.090     -.0100194    .1375345
-------------+----------------------------------------------------------------
     sigma_u |  .10635208
     sigma_e |  .04984594
         rho |  .81989495   (fraction of variance due to u_i)
------------------------------------------------------------------------------

. xtreg  bloodhalavg rebhal, re i(subjnum)

Random-effects GLS regression                   Number of obs      =         37
Group variable (i): subjnum                     Number of groups   =          3

R-sq:  within  = 0.8610                         Obs per group: min =          7
       between = 0.9444                                        avg =       12.3
       overall = 0.8522                                        max =         20

Random effects u_i ~ Gaussian                   Wald chi2(1)       =     206.15
corr(u_i, X)       = 0 (assumed)                Prob > chi2        =     0.0000

------------------------------------------------------------------------------
 bloodhalavg |      Coef.   Std. Err.       z     P>|z|      [95% Conf. Interval]
-------------+----------------------------------------------------------------
      rebhal |   3.160803   .2201414     14.36   0.000      2.729333    3.592272
       _cons |   .0070201   .0093222      0.75   0.451     -.0112511    .0252913
-------------+----------------------------------------------------------------
     sigma_u |  .01144436
     sigma_e |  .02387246
         rho |   .1868732   (fraction of variance due to u_i)
------------------------------------------------------------------------------

. xtreg  bloodethavg endeth, re i(subjnum)
```

```
Random-effects GLS regression                   Number of obs      =        39
Group variable (i): subjnum                     Number of groups   =         6

R-sq:  within  = 0.9197                         Obs per group: min =         5
       between = 0.9021                                        avg =       6.5
       overall = 0.9169                                        max =        11

Random effects u_i ~ Gaussian                   Wald chi2(1)       =    410.86
corr(u_i, X)       = 0 (assumed)                Prob > chi2        =    0.0000

------------------------------------------------------------------------------
 bloodethavg |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      endeth |    2618.01   129.1592    20.27   0.000     2364.863    2871.158
       _cons |   32.06859   35.42131     0.91   0.365     -37.3559    101.4931
-------------+----------------------------------------------------------------
     sigma_u |  35.406613
     sigma_e |   174.7624
         rho |  .03942782   (fraction of variance due to u_i)
------------------------------------------------------------------------------

. xtreg  bloodaceavg endace, re i(subjnum)

Random-effects GLS regression                   Number of obs      =        59
Group variable (i): subjnum                     Number of groups   =         7

R-sq:  within  = 0.3883                         Obs per group: min =         7
       between = 0.4904                                        avg =       8.4
       overall = 0.5197                                        max =        10

Random effects u_i ~ Gaussian                   Wald chi2(1)       =     37.54
corr(u_i, X)       = 0 (assumed)                Prob > chi2        =    0.0000

------------------------------------------------------------------------------
 bloodaceavg |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      endace |   265.0986   43.26942     6.13   0.000     180.2921    349.9051
       _cons |   26.64424   9.995194     2.67   0.008     7.054023    46.23446
-------------+----------------------------------------------------------------
     sigma_u |  21.996972
     sigma_e |  9.6692813
         rho |  .83806514   (fraction of variance due to u_i)
------------------------------------------------------------------------------

. xtreg  bloodmibkavg endmibk, re i(subjnum)

Random-effects GLS regression                   Number of obs      =        53
Group variable (i): subjnum                     Number of groups   =         6

R-sq:  within  = 0.4463                         Obs per group: min =         5
       between = 0.1877                                        avg =       8.8
       overall = 0.1064                                        max =        17

Random effects u_i ~ Gaussian                   Wald chi2(1)       =     28.27
corr(u_i, X)       = 0 (assumed)                Prob > chi2        =    0.0000

------------------------------------------------------------------------------
bloodmibkavg |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
     endmibk |   68.12721   12.81216     5.32   0.000     43.01583    93.23859
       _cons |   .0908543   .0840587     1.08   0.280    -.0738977    .2556063
-------------+----------------------------------------------------------------
     sigma_u |  .15449891
     sigma_e |   .1923059
```

```
         rho |  .39226516   (fraction of variance due to u_i)
------------------------------------------------------------------------------

. xtreg  bloodtolavg endtol, re i(subjnum)

Random-effects GLS regression                   Number of obs      =        62
Group variable (i): subjnum                     Number of groups   =         9

R-sq:  within  = 0.6921                         Obs per group: min =         3
       between = 0.6519                                        avg =       6.9
       overall = 0.5749                                        max =         9

Random effects u_i ~ Gaussian                   Wald chi2(1)       =    127.30
corr(u_i, X)       = 0 (assumed)                Prob > chi2        =    0.0000

------------------------------------------------------------------------------
 bloodtolavg |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      endtol |   39.14354   3.469296    11.28   0.000     32.34385    45.94324
       _cons |   .0688932   .0424901     1.62   0.105    -.0143859    .1521724
-------------+----------------------------------------------------------------
     sigma_u |  .11643421
     sigma_e |  .06650962
         rho |  .75398122   (fraction of variance due to u_i)
------------------------------------------------------------------------------

. xtreg  bloodhalavg endhal, re i(subjnum)

Random-effects GLS regression                   Number of obs      =        30
Group variable (i): subjnum                     Number of groups   =         3

R-sq:  within  = 0.9397                         Obs per group: min =         5
       between = 0.9954                                        avg =      10.0
       overall = 0.9261                                        max =        16

Random effects u_i ~ Gaussian                   Wald chi2(1)       =    350.81
corr(u_i, X)       = 0 (assumed)                Prob > chi2        =    0.0000

------------------------------------------------------------------------------
 bloodhalavg |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      endhal |   3.563465    .190254    18.73   0.000     3.190574    3.936356
       _cons |   .0090018   .0056436     1.60   0.111    -.0020595     .020063
-------------+----------------------------------------------------------------
     sigma_u |          0
     sigma_e |  .01747676
         rho |          0   (fraction of variance due to u_i)
------------------------------------------------------------------------------

. xtreg  bloodethavg mixeth, re i(subjnum)

Random-effects GLS regression                   Number of obs      =        40
Group variable (i): subjnum                     Number of groups   =         6

R-sq:  within  = 0.9273                         Obs per group: min =         5
       between = 0.9145                                        avg =       6.7
       overall = 0.9265                                        max =        11

Random effects u_i ~ Gaussian                   Wald chi2(1)       =    479.13
corr(u_i, X)       = 0 (assumed)                Prob > chi2        =    0.0000

------------------------------------------------------------------------------
 bloodethavg |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
```

```
      mixeth |   3052.466    139.452    21.89   0.000     2779.145    3325.786
       _cons |   56.43629   30.02416     1.88   0.060     -2.40999    115.2826
-------------+----------------------------------------------------------------
     sigma_u |  24.673861
     sigma_e |  161.66492
         rho |  .02276367   (fraction of variance due to u_i)
------------------------------------------------------------------------------

. xtreg  bloodaceavg mixace, re i(subjnum)

Random-effects GLS regression                   Number of obs      =        61
Group variable (i): subjnum                     Number of groups   =         7

R-sq:  within  = 0.4602                         Obs per group: min =         7
       between = 0.7076                                        avg =       8.7
       overall = 0.6861                                        max =        10

Random effects u_i ~ Gaussian                   Wald chi2(1)       =     54.59
corr(u_i, X)       = 0 (assumed)                Prob > chi2        =    0.0000

------------------------------------------------------------------------------
 bloodaceavg |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      mixace |   553.5125   74.91255     7.39   0.000     406.6866    700.3383
       _cons |   25.96319    7.99397     3.25   0.001      10.2953    41.63108
-------------+----------------------------------------------------------------
     sigma_u |   17.04605
     sigma_e |  8.6932684
         rho |    .793596   (fraction of variance due to u_i)
------------------------------------------------------------------------------

. xtreg  bloodmibkavg mixmibk, re i(subjnum)

Random-effects GLS regression                   Number of obs      =        42
Group variable (i): subjnum                     Number of groups   =         6

R-sq:  within  = 0.3817                         Obs per group: min =         4
       between = 0.0808                                        avg =       7.0
       overall = 0.0343                                        max =        13

Random effects u_i ~ Gaussian                   Wald chi2(1)       =     19.34
corr(u_i, X)       = 0 (assumed)                Prob > chi2        =    0.0000

------------------------------------------------------------------------------
bloodmibkavg |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
     mixmibk |   87.32016   19.85351     4.40   0.000     48.40798    126.2323
       _cons |   .1541602   .1248391     1.23   0.217    -.0905199    .3988403
-------------+----------------------------------------------------------------
     sigma_u |  .27351717
     sigma_e |  .18511963
         rho |   .6858362   (fraction of variance due to u_i)
------------------------------------------------------------------------------

. xtreg  bloodtolavg mixtol, re i(subjnum)

Random-effects GLS regression                   Number of obs      =        59
Group variable (i): subjnum                     Number of groups   =         9

R-sq:  within  = 0.6356                         Obs per group: min =         4
       between = 0.3238                                        avg =       6.6
       overall = 0.3654                                        max =         9

Random effects u_i ~ Gaussian                   Wald chi2(1)       =     89.72
```

```
corr(u_i, X)       = 0 (assumed)                Prob > chi2        =    0.0000

------------------------------------------------------------------------------
 bloodtolavg |      Coef.   Std. Err.       z     P>|z|      [95% Conf. Interval]
-------------+----------------------------------------------------------------
      mixtol |   81.87959   8.644189     9.47   0.000     64.93729    98.82189
       _cons |   .0517722   .0559009     0.93   0.354    -.0577916    .1613359
-------------+----------------------------------------------------------------
     sigma_u |  .15699554
     sigma_e |  .06356652
         rho |  .85915157   (fraction of variance due to u_i)
------------------------------------------------------------------------------

. xtreg  bloodhalavg mixhal, re i(subjnum)

Random-effects GLS regression                   Number of obs      =        36
Group variable (i): subjnum                     Number of groups   =         3

R-sq:  within  = 0.8464                         Obs per group: min =         7
       between = 0.9351                                        avg =      12.0
       overall = 0.8466                                        max =        19

Random effects u_i ~ Gaussian                   Wald chi2(1)       =    184.78
corr(u_i, X)       = 0 (assumed)                Prob > chi2        =    0.0000

------------------------------------------------------------------------------
 bloodhalavg |      Coef.   Std. Err.       z     P>|z|      [95% Conf. Interval]
-------------+----------------------------------------------------------------
      mixhal |   5.285165   .3888041    13.59   0.000     4.523123    6.047207
       _cons |   .0117589   .0088354     1.33   0.183    -.0055582    .0290759
-------------+----------------------------------------------------------------
     sigma_u |  .01107869
     sigma_e |  .02315618
         rho |  .18626299   (fraction of variance due to u_i)
------------------------------------------------------------------------------

. xtreg  bloodethavg mixceth, re i(subjnum)

Random-effects GLS regression                   Number of obs      =        40
Group variable (i): subjnum                     Number of groups   =         6

R-sq:  within  = 0.6954                         Obs per group: min =         5
       between = 0.4942                                        avg =       6.7
       overall = 0.6730                                        max =        11

Random effects u_i ~ Gaussian                   Wald chi2(1)       =     80.87
corr(u_i, X)       = 0 (assumed)                Prob > chi2        =    0.0000

------------------------------------------------------------------------------
 bloodethavg |      Coef.   Std. Err.       z     P>|z|      [95% Conf. Interval]
-------------+----------------------------------------------------------------
     mixceth |   1598.038   177.7006     8.99   0.000     1249.751    1946.325
       _cons |   113.9434    71.9011     1.58   0.113    -26.98019     254.867
-------------+----------------------------------------------------------------
     sigma_u |  104.31163
     sigma_e |  330.85225
         rho |  .09041501   (fraction of variance due to u_i)
------------------------------------------------------------------------------

. xtreg  bloodaceavg mixcace, re i(subjnum)

Random-effects GLS regression                   Number of obs      =        61
Group variable (i): subjnum                     Number of groups   =         7
```

```
R-sq:  within  = 0.2925                         Obs per group: min =         7
       between = 0.5801                                        avg =       8.7
       overall = 0.5762                                        max =        10

Random effects u_i ~ Gaussian                   Wald chi2(1)       =     27.79
corr(u_i, X)       = 0 (assumed)                Prob > chi2        =    0.0000

------------------------------------------------------------------------------
 bloodaceavg |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
     mixcace |   360.9231   68.46376     5.27   0.000     226.7366    495.1096
       _cons |   26.86584   9.977307     2.69   0.007      7.31068      46.421
-------------+----------------------------------------------------------------
     sigma_u |  20.452037
     sigma_e |  9.9522831
         rho |  .80854151   (fraction of variance due to u_i)
------------------------------------------------------------------------------

. xtreg  bloodmibkavg mixcmibk, re i(subjnum)

Random-effects GLS regression                   Number of obs      =        42
Group variable (i): subjnum                     Number of groups   =         6

R-sq:  within  = 0.4176                         Obs per group: min =         4
       between = 0.1300                                        avg =       7.0
       overall = 0.0265                                        max =        13

Random effects u_i ~ Gaussian                   Wald chi2(1)       =     22.00
corr(u_i, X)       = 0 (assumed)                Prob > chi2        =    0.0000

------------------------------------------------------------------------------
bloodmibkavg |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
    mixcmibk |   74.29939   15.83988     4.69   0.000     43.25381     105.345
       _cons |   .1062316   .1254958     0.85   0.397    -.1397356    .3521988
-------------+----------------------------------------------------------------
     sigma_u |  .26613761
     sigma_e |  .17966951
         rho |  .68692638   (fraction of variance due to u_i)
------------------------------------------------------------------------------

. xtreg  bloodtolavg mixctol, re i(subjnum)

Random-effects GLS regression                   Number of obs      =        59
Group variable (i): subjnum                     Number of groups   =         9

R-sq:  within  = 0.6931                         Obs per group: min =         4
       between = 0.4010                                        avg =       6.6
       overall = 0.4579                                        max =         9

Random effects u_i ~ Gaussian                   Wald chi2(1)       =    116.88
corr(u_i, X)       = 0 (assumed)                Prob > chi2        =    0.0000

------------------------------------------------------------------------------
 bloodtolavg |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
     mixctol |   49.87792   4.613575    10.81   0.000     40.83548    58.92036
       _cons |   .0562072   .0520557     1.08   0.280    -.0458202    .1582345
-------------+----------------------------------------------------------------
     sigma_u |  .14785672
     sigma_e |  .05833385
         rho |   .8653112   (fraction of variance due to u_i)
------------------------------------------------------------------------------
```

```
. xtreg  bloodhalavg mixchal, re i(subjnum)

Random-effects GLS regression                   Number of obs      =        36
Group variable (i): subjnum                     Number of groups   =         3

R-sq:  within  = 0.7397                         Obs per group: min =         7
       between = 0.9897                                        avg =      12.0
       overall = 0.7839                                        max =        19

Random effects u_i ~ Gaussian                   Wald chi2(1)       =    123.34
corr(u_i, X)       = 0 (assumed)                Prob > chi2        =    0.0000

------------------------------------------------------------------------------
 bloodhalavg |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
     mixchal |   4.489695   .4042611    11.11   0.000     3.697358    5.282032
       _cons |  -.0000331   .0087838    -0.00   0.997    -.0172491    .0171828
-------------+----------------------------------------------------------------
     sigma_u |          0
     sigma_e |  .03014333
         rho |          0   (fraction of variance due to u_i)
------------------------------------------------------------------------------
```

Appendix E: Effects of age and gender on slope, R2, and regressions between blood and breath.

```
. bysort solvent: regress rebslope age

______________________________________________________________________________

-> solvent = MIBK

      Source |       SS       df       MS              Number of obs =       7
-------------+------------------------------           F(  1,     5) =    0.25
       Model |  6349.10991     1  6349.10991           Prob > F      =  0.6372
    Residual |  126138.127     5  25227.6254           R-squared     =  0.0479
-------------+------------------------------           Adj R-squared = -0.1425
       Total |  132487.237     6  22081.2061           Root MSE      =  158.83

------------------------------------------------------------------------------
    rebslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         age |   1.715717   3.420011     0.50   0.637    -7.075701    10.50714
       _cons |   86.11501   121.4121     0.71   0.510    -225.9848    398.2148
------------------------------------------------------------------------------

______________________________________________________________________________

-> solvent = acetone

      Source |       SS       df       MS              Number of obs =       7
-------------+------------------------------           F(  1,     5) =    4.00
       Model |  18625.5333     1  18625.5333           Prob > F      =  0.1018
    Residual |  23253.8953     5  4650.77906           R-squared     =  0.4447
-------------+------------------------------           Adj R-squared =  0.3337
       Total |  41879.4286     6  6979.90476           Root MSE      =  68.197

------------------------------------------------------------------------------
    rebslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         age |  -7.097759   3.546743    -2.00   0.102    -16.21495    2.019435
       _cons |   463.1766   108.0032     4.29   0.008     185.5456    740.8076
------------------------------------------------------------------------------

______________________________________________________________________________

-> solvent = ethanol
```

```
      Source |       SS       df       MS              Number of obs =       8
-------------+------------------------------           F(  1,     6) =   12.78
       Model |  2532982.39     1  2532982.39           Prob > F      =  0.0117
    Residual |  1189605.11     6  198267.518           R-squared     =  0.6804
-------------+------------------------------           Adj R-squared =  0.6272
       Total |   3722587.5     7  531798.214           Root MSE      =  445.27

------------------------------------------------------------------------------
    rebslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         age |  -82.53109   23.09018    -3.57   0.012    -139.0307   -26.03146
       _cons |   4788.101   696.3039     6.88   0.000     3084.307    6491.895
------------------------------------------------------------------------------

_______________________________________________________________________________
-> solvent = halothane

      Source |       SS       df       MS              Number of obs =       4
-------------+------------------------------           F(  1,     2) =    0.83
       Model |  1.08945347     1  1.08945347           Prob > F      =  0.4592
    Residual |  2.63564675     2  1.31782337           R-squared     =  0.2925
-------------+------------------------------           Adj R-squared = -0.0613
       Total |  3.72510021     3  1.24170007           Root MSE      =   1.148

------------------------------------------------------------------------------
    rebslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         age |  -.0323232   .0355499    -0.91   0.459    -.1852821    .1206357
       _cons |    5.64621   1.978138     2.85   0.104    -2.865029    14.15745
------------------------------------------------------------------------------

_______________________________________________________________________________
-> solvent = toluene

      Source |       SS       df       MS              Number of obs =       9
-------------+------------------------------           F(  1,     7) =    0.18
       Model |  43.1429955     1  43.1429955           Prob > F      =  0.6819
    Residual |  1653.35205     7   236.19315           R-squared     =  0.0254
-------------+------------------------------           Adj R-squared = -0.1138
       Total |  1696.49504     8  212.061881           Root MSE      =  15.369

------------------------------------------------------------------------------
    rebslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
```

```
-------------+----------------------------------------------------------------
         age |  -.1953193   .4570079    -0.43   0.682    -1.275971    .8853326
       _cons |   36.95875   15.01727     2.46   0.043     1.448561    72.46894
------------------------------------------------------------------------------


. bysort solvent: regress endslope age

_______________________________________________________________________________

-> solvent = MIBK

      Source |       SS       df       MS              Number of obs =       7
-------------+------------------------------           F(  1,     5) =    0.28
       Model |  15276.8096     1  15276.8096           Prob > F      =  0.6187
    Residual |   271727.91     5   54345.582           R-squared     =  0.0532
-------------+------------------------------           Adj R-squared = -0.1361
       Total |   287004.72     6    47834.12           Root MSE      =  233.12

------------------------------------------------------------------------------
    endslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         age |   2.661372   5.019627     0.53   0.619    -10.24199    15.56473
       _cons |   102.4777   178.1993     0.58   0.590    -355.5982    560.5535
------------------------------------------------------------------------------


_______________________________________________________________________________

-> solvent = acetone

      Source |       SS       df       MS              Number of obs =       7
-------------+------------------------------           F(  1,     5) =    0.44
       Model |  6361.24006     1  6361.24006           Prob > F      =  0.5382
    Residual |  72941.6171     5  14588.3234           R-squared     =  0.0802
-------------+------------------------------           Adj R-squared = -0.1037
       Total |  79302.8571     6  13217.1429           Root MSE      =  120.78

------------------------------------------------------------------------------
    endslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         age |  -4.147991    6.28159    -0.66   0.538    -20.29533    11.99935
       _cons |   369.8049    191.283     1.93   0.111    -121.9037    861.5135
------------------------------------------------------------------------------


_______________________________________________________________________________
```

```
-> solvent = ethanol

      Source |       SS       df       MS              Number of obs =       8
-------------+------------------------------           F(  1,     6) =    3.46
       Model |  1824638.32     1  1824638.32           Prob > F      =  0.1123
    Residual |  3166949.18     6  527824.863           R-squared     =  0.3655
-------------+------------------------------           Adj R-squared =  0.2598
       Total |   4991587.5     7  713083.929           Root MSE      =  726.52

------------------------------------------------------------------------------
    endslope |      Coef.   Std. Err.      t     P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         age |  -70.04706   37.67441    -1.86   0.112     -162.233     22.1389
       _cons |   4863.882   1136.104     4.28   0.005     2083.937    7643.828
------------------------------------------------------------------------------

_______________________________________________________________________________
-> solvent = halothane

      Source |       SS       df       MS              Number of obs =       4
-------------+------------------------------           F(  1,     2) =    0.72
       Model |  8.14039726     1  8.14039726           Prob > F      =  0.4865
    Residual |  22.7340821     2   11.367041           R-squared     =  0.2637
-------------+------------------------------           Adj R-squared = -0.1045
       Total |  30.8744794     3  10.2914931           Root MSE      =  3.3715

------------------------------------------------------------------------------
    endslope |      Coef.   Std. Err.      t     P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         age |   .0883553    .104408     0.85   0.487    -.3608759    .5375865
       _cons |   .7025793   5.809672     0.12   0.915    -24.29442    25.69958
------------------------------------------------------------------------------

_______________________________________________________________________________
-> solvent = toluene

      Source |       SS       df       MS              Number of obs =       9
-------------+------------------------------           F(  1,     7) =    0.05
       Model |  25.9272944     1  25.9272944           Prob > F      =  0.8336
    Residual |  3816.91299     7  545.273284           R-squared     =  0.0067
-------------+------------------------------           Adj R-squared = -0.1351
       Total |  3842.84028     8  480.355035           Root MSE      =  23.351
```

```
------------------------------------------------------------------------------
    endslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         age |  -.1514149   .6943799    -0.22   0.834    -1.793362    1.490533
       _cons |   44.59371    22.8173     1.95   0.092    -9.360646    98.54806
------------------------------------------------------------------------------


. bysort solvent: regress mixslope age

_______________________________________________________________________________
-> solvent = MIBK

      Source |       SS       df       MS              Number of obs =       7
-------------+------------------------------           F(  1,     5) =    0.12
       Model |  13332.6923     1  13332.6923           Prob > F      =  0.7387
    Residual |  535805.662     5  107161.132           R-squared     =  0.0243
-------------+------------------------------           Adj R-squared = -0.1709
       Total |  549138.354     6   91523.059           Root MSE      =  327.35

------------------------------------------------------------------------------
    mixslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         age |   -2.48627   7.048683    -0.35   0.739    -20.60549    15.63295
       _cons |   329.7906   250.2318     1.32   0.245    -313.4507    973.0319
------------------------------------------------------------------------------

_______________________________________________________________________________
-> solvent = acetone

      Source |       SS       df       MS              Number of obs =       7
-------------+------------------------------           F(  1,     5) =    5.63
       Model |  584820.349     1  584820.349           Prob > F      =  0.0637
    Residual |  519042.068     5  103808.414           R-squared     =  0.5298
-------------+------------------------------           Adj R-squared =  0.4358
       Total |  1103862.42     6   183977.07           Root MSE      =  322.19

------------------------------------------------------------------------------
    mixslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         age |  -39.77206   16.75649    -2.37   0.064      -82.846    3.301876
       _cons |   1721.017   510.2581     3.37   0.020     409.3564    3032.677
------------------------------------------------------------------------------
```

```
-> solvent = ethanol

      Source |       SS       df       MS              Number of obs =       8
-------------+------------------------------           F(  1,     6) =    3.22
       Model |  3976053.13     1  3976053.13           Prob > F      =  0.1231
    Residual |  7417096.87     6  1236182.81           R-squared     =  0.3490
-------------+------------------------------           Adj R-squared =  0.2405
       Total |    11393150     7  1627592.86           Root MSE      =  1111.8

------------------------------------------------------------------------------
    mixslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         age |  -103.4017   57.65578    -1.79   0.123    -244.4803    37.67693
       _cons |   6594.924   1738.659     3.79   0.009      2340.58    10849.27
------------------------------------------------------------------------------
```

```
-> solvent = halothane

      Source |       SS       df       MS              Number of obs =       4
-------------+------------------------------           F(  1,     2) =    0.66
       Model |  22.6360167     1  22.6360167           Prob > F      =  0.5025
    Residual |  68.8068695     2  34.4034347           R-squared     =  0.2475
-------------+------------------------------           Adj R-squared = -0.1287
       Total |  91.4428861     3   30.480962           Root MSE      =  5.8654

------------------------------------------------------------------------------
    mixslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         age |   .1473363   .1816397     0.81   0.502    -.6341962    .9288689
       _cons |   1.479339   10.10715     0.15   0.897    -42.00823    44.96691
------------------------------------------------------------------------------
```

```
-> solvent = toluene

      Source |       SS       df       MS              Number of obs =       9
-------------+------------------------------           F(  1,     7) =    1.17
       Model |  8942.99274     1  8942.99274           Prob > F      =  0.3155
    Residual |  53553.7428     7  7650.53468           R-squared     =  0.1431
-------------+------------------------------           Adj R-squared =  0.0207
```

```
       Total |  62496.7355     8  7812.09194           Root MSE      =  87.467

------------------------------------------------------------------------------
    mixslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         age |  -2.812105   2.600973    -1.08   0.315     -8.96243     3.33822
       _cons |    179.785   85.46792     2.10   0.073     -22.3145    381.8845
------------------------------------------------------------------------------


. bysort solvent: regress mixcslope age

-------------------------------------------------------------------------------
-> solvent = MIBK

      Source |       SS       df       MS              Number of obs =       7
-------------+------------------------------           F(  1,     5) =    0.08
       Model |  4824.25666     1  4824.25666           Prob > F      =  0.7917
    Residual |  310817.932     5  62163.5864           R-squared     =  0.0153
-------------+------------------------------           Adj R-squared = -0.1817
       Total |  315642.189     6  52607.0314           Root MSE      =  249.33

------------------------------------------------------------------------------
   mixcslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         age |  -1.495562   5.368554    -0.28   0.792    -15.29587    12.30475
       _cons |   224.9345   190.5864     1.18   0.291    -264.9834    714.8524
------------------------------------------------------------------------------

-------------------------------------------------------------------------------
-> solvent = acetone

      Source |       SS       df       MS              Number of obs =       7
-------------+------------------------------           F(  1,     5) =    3.55
       Model |  295086.586     1  295086.586           Prob > F      =  0.1182
    Residual |  415580.109     5  83116.0217           R-squared     =  0.4152
-------------+------------------------------           Adj R-squared =  0.2983
       Total |  710666.695     6  118444.449           Root MSE      =   288.3

------------------------------------------------------------------------------
   mixcslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         age |  -28.25151   14.99372    -1.88   0.118    -66.79408    10.29107
```

```
       _cons |   1238.409   456.5791     2.71   0.042     64.73487    2412.083
------------------------------------------------------------------------------

_______________________________________________________________________________

-> solvent = ethanol

      Source |       SS       df       MS              Number of obs =       8
-------------+------------------------------           F(  1,     6) =    1.15
       Model |  2700946.71     1  2700946.71           Prob > F      =  0.3239
    Residual |  14038403.3     6  2339733.88           R-squared     =  0.1614
-------------+------------------------------           Adj R-squared =  0.0216
       Total |    16739350     7  2391335.71           Root MSE      =  1529.6

------------------------------------------------------------------------------
   mixcslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         age |  -85.22353   79.32037    -1.07   0.324    -279.3135    108.8664
       _cons |   5030.941   2391.973     2.10   0.080    -822.0055    10883.89
------------------------------------------------------------------------------

_______________________________________________________________________________

-> solvent = halothane

      Source |       SS       df       MS              Number of obs =       4
-------------+------------------------------           F(  1,     2) =    0.96
       Model |   11.206532     1   11.206532           Prob > F      =  0.4303
    Residual |  23.3270713     2  11.6635357           R-squared     =  0.3245
-------------+------------------------------           Adj R-squared = -0.0132
       Total |  34.5336034     3  11.5112011           Root MSE      =  3.4152

------------------------------------------------------------------------------
   mixcslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         age |   .1036682   .1057609     0.98   0.430    -.3513841    .5587205
       _cons |   .9996689   5.884953     0.17   0.881    -24.32124    26.32058
------------------------------------------------------------------------------

_______________________________________________________________________________

-> solvent = toluene

      Source |       SS       df       MS              Number of obs =       9
-------------+------------------------------           F(  1,     7) =    1.41
       Model |  2742.82063     1  2742.82063           Prob > F      =  0.2738
```

```
    Residual |  13619.2794     7  1945.61134           R-squared     =  0.1676
-------------+------------------------------           Adj R-squared =  0.0487
       Total |     16362.1     8   2045.2625           Root MSE      =  44.109

------------------------------------------------------------------------------
   mixcslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         age |  -1.557359    1.31165    -1.19   0.274    -4.658919    1.544201
       _cons |   104.4051   43.10079     2.42   0.046     2.487907    206.3223
------------------------------------------------------------------------------

. bysort solvent: regress rebrsquared age

_______________________________________________________________________________
-> solvent = MIBK

      Source |       SS       df       MS              Number of obs =       7
-------------+------------------------------           F(  1,     5) =    0.05
       Model |   .00096962     1   .00096962           Prob > F      =  0.8241
    Residual |  .088335059     5  .017667012           R-squared     =  0.0109
-------------+------------------------------           Adj R-squared = -0.1870
       Total |  .089304679     6  .014884113           Root MSE      =  .13292

------------------------------------------------------------------------------
 rebrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         age |   .0006705    .002862     0.23   0.824    -.0066865    .0080275
       _cons |   .7822536   .1016027     7.70   0.001     .5210754    1.043432
------------------------------------------------------------------------------

_______________________________________________________________________________
-> solvent = acetone

      Source |       SS       df       MS              Number of obs =       7
-------------+------------------------------           F(  1,     5) =    1.64
       Model |  .082915508     1  .082915508           Prob > F      =  0.2562
    Residual |  .252384359     5  .050476872           R-squared     =  0.2473
-------------+------------------------------           Adj R-squared =  0.0967
       Total |  .335299868     6  .055883311           Root MSE      =  .22467

------------------------------------------------------------------------------
 rebrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
```

```
         age |  -.0149756   .0116846    -1.28   0.256    -.0450118    .0150606
       _cons |    1.00095   .3558114     2.81   0.037     .0863081    1.915593
------------------------------------------------------------------------------


_______________________________________________________________________________

-> solvent = ethanol

      Source |       SS       df       MS              Number of obs =       8
-------------+------------------------------           F(  1,     6) =    1.18
       Model |  .003415247     1  .003415247           Prob > F      =  0.3198
    Residual |  .017423488     6  .002903915           R-squared     =  0.1639
-------------+------------------------------           Adj R-squared =  0.0245
       Total |  .020838736     7  .002976962           Root MSE      =  .05389

------------------------------------------------------------------------------
 rebrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         age |   .0030305   .0027944     1.08   0.320    -.0038072    .0098682
       _cons |   .8580919   .0842684    10.18   0.000     .6518945    1.064289
------------------------------------------------------------------------------


_______________________________________________________________________________

-> solvent = halothane

      Source |       SS       df       MS              Number of obs =       4
-------------+------------------------------           F(  1,     2) =    2.70
       Model |  .168770491     1  .168770491           Prob > F      =  0.2424
    Residual |  .125243124     2  .062621562           R-squared     =  0.5740
-------------+------------------------------           Adj R-squared =  0.3610
       Total |  .294013615     3  .098004538           Root MSE      =  .25024

------------------------------------------------------------------------------
 rebrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         age |  -.0127221   .0077495    -1.64   0.242    -.0460653    .0206212
       _cons |   1.421401    .431211     3.30   0.081    -.4339505    3.276752
------------------------------------------------------------------------------


_______________________________________________________________________________

-> solvent = toluene

      Source |       SS       df       MS              Number of obs =       9
-------------+------------------------------           F(  1,     7) =    0.00
```

```
       Model |  .000011837     1  .000011837           Prob > F      =  0.9658
    Residual |  .041977611     7  .005996802           R-squared     =  0.0003
-------------+------------------------------           Adj R-squared = -0.1425
       Total |  .041989449     8  .005248681           Root MSE      =  .07744

------------------------------------------------------------------------------
 rebrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         age |  -.0001023   .0023028    -0.04   0.966    -.0055475    .0053429
       _cons |   .9080602   .0756688    12.00   0.000     .7291318    1.086989
------------------------------------------------------------------------------


. bysort solvent: regress endrsquared age

_______________________________________________________________________________
-> solvent = MIBK

      Source |       SS       df       MS              Number of obs =       7
-------------+------------------------------           F(  1,     5) =    3.35
       Model |  .007948972     1  .007948972           Prob > F      =  0.1269
    Residual |  .011874939     5  .002374988           R-squared     =  0.4010
-------------+------------------------------           Adj R-squared =  0.2812
       Total |  .019823911     6  .003303985           Root MSE      =  .04873

------------------------------------------------------------------------------
 endrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         age |   .0019198   .0010493     1.83   0.127    -.0007777    .0046172
       _cons |   .7953906   .0372524    21.35   0.000     .6996302     .891151
------------------------------------------------------------------------------

_______________________________________________________________________________
-> solvent = acetone

      Source |       SS       df       MS              Number of obs =       7
-------------+------------------------------           F(  1,     5) =    0.00
       Model |  .000120796     1  .000120796           Prob > F      =  0.9761
    Residual |  .609620008     5  .121924002           R-squared     =  0.0002
-------------+------------------------------           Adj R-squared = -0.1998
       Total |  .609740803     6  .101623467           Root MSE      =  .34918

------------------------------------------------------------------------------
```

```
endrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
        age |   .0005716   .0181598     0.03   0.976    -.0461097    .0472529
      _cons |   .3834398   .5529913     0.69   0.519    -1.038069    1.804949
------------------------------------------------------------------------------

_______________________________________________________________________________

-> solvent = ethanol

     Source |       SS       df       MS              Number of obs =       8
-------------+------------------------------          F(  1,     6) =    0.16
      Model |  .00032337      1  .00032337            Prob > F      =  0.7010
   Residual | .011957752      6  .001992959           R-squared     =  0.0263
-------------+------------------------------          Adj R-squared = -0.1359
      Total | .012281122      7  .001754446           Root MSE      =  .04464

------------------------------------------------------------------------------
endrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
        age |   .0009325    .002315     0.40   0.701    -.0047321    .0065971
      _cons |   .9410826   .0698107    13.48   0.000      .770262    1.111903
------------------------------------------------------------------------------

_______________________________________________________________________________

-> solvent = halothane

     Source |       SS       df       MS              Number of obs =       4
-------------+------------------------------          F(  1,     2) =    1.09
      Model | .003734746      1  .003734746           Prob > F      =  0.4059
   Residual | .006846798      2  .003423399           R-squared     =  0.3529
-------------+------------------------------          Adj R-squared =  0.0294
      Total | .010581544      3  .003527181           Root MSE      =  .05851

------------------------------------------------------------------------------
endrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
        age |  -.0018925   .0018119    -1.04   0.406    -.0096886    .0059035
      _cons |   1.021902   .1008223    10.14   0.010     .5880983    1.455705
------------------------------------------------------------------------------

_______________________________________________________________________________

-> solvent = toluene
```

```
      Source |       SS       df       MS              Number of obs =       9
-------------+------------------------------           F(  1,     7) =    1.15
       Model |  .021583896     1  .021583896           Prob > F      =  0.3195
    Residual |  .131593345     7  .018799049           R-squared     =  0.1409
-------------+------------------------------           Adj R-squared =  0.0182
       Total |   .15317724     8  .019147155           Root MSE      =  .13711

------------------------------------------------------------------------------
 endrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         age |   .0043687   .0040772     1.07   0.319    -.0052722    .0140097
       _cons |   .6744993   .1339754     5.03   0.002     .3576978    .9913009
------------------------------------------------------------------------------


. bysort solvent: regress mixrsquared age

_______________________________________________________________________________
-> solvent = MIBK

      Source |       SS       df       MS              Number of obs =       7
-------------+------------------------------           F(  1,     5) =    0.39
       Model |  .003857432     1  .003857432           Prob > F      =  0.5601
    Residual |  .049553743     5  .009910749           R-squared     =  0.0722
-------------+------------------------------           Adj R-squared = -0.1133
       Total |  .053411175     6  .008901862           Root MSE      =  .09955

------------------------------------------------------------------------------
 mixrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         age |  -.0013373   .0021436    -0.62   0.560    -.0068476     .004173
       _cons |   .8337376   .0760987    10.96   0.000     .6381197    1.029355
------------------------------------------------------------------------------

_______________________________________________________________________________
-> solvent = acetone

      Source |       SS       df       MS              Number of obs =       7
-------------+------------------------------           F(  1,     5) =    1.21
       Model |  .129183374     1  .129183374           Prob > F      =  0.3207
    Residual |  .532097978     5  .106419596           R-squared     =  0.1954
-------------+------------------------------           Adj R-squared =  0.0344
       Total |  .661281352     6  .110213559           Root MSE      =  .32622
```

```
------------------------------------------------------------------------------
 mixrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         age |  -.0186926   .0169659    -1.10   0.321    -.0623049    .0249197
       _cons |   1.035425   .5166358     2.00   0.101    -.2926299    2.363479
------------------------------------------------------------------------------
```

```
-> solvent = ethanol

      Source |       SS       df       MS              Number of obs =       8
-------------+------------------------------           F(  1,     6) =    0.04
       Model |  .000181799     1  .000181799           Prob > F      =  0.8527
    Residual |  .029022781     6   .00483713           R-squared     =  0.0062
-------------+------------------------------           Adj R-squared = -0.1594
       Total |   .02920458     7  .004172083           Root MSE      =  .06955

------------------------------------------------------------------------------
 mixrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         age |  -.0006992   .0036066    -0.19   0.853    -.0095242    .0081258
       _cons |   .9709763   .1087594     8.93   0.000     .7048516    1.237101
------------------------------------------------------------------------------
```

```
-> solvent = halothane

      Source |       SS       df       MS              Number of obs =       4
-------------+------------------------------           F(  1,     2) =    8.62
       Model |  .018430246     1  .018430246           Prob > F      =  0.0991
    Residual |  .004277802     2  .002138901           R-squared     =  0.8116
-------------+------------------------------           Adj R-squared =  0.7174
       Total |  .022708048     3  .007569349           Root MSE      =  .04625

------------------------------------------------------------------------------
 mixrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         age |  -.0042041   .0014322    -2.94   0.099    -.0103664    .0019582
       _cons |    1.07522   .0796936    13.49   0.005     .7323258    1.418113
------------------------------------------------------------------------------
```

```
-> solvent = toluene

      Source |       SS       df       MS              Number of obs =       9
-------------+------------------------------           F(  1,     7) =    0.29
       Model |  .010764138     1  .010764138           Prob > F      =  0.6053
    Residual |  .257500559     7  .036785794           R-squared     =  0.0401
-------------+------------------------------           Adj R-squared = -0.0970
       Total |  .268264697     8  .033533087           Root MSE      =   .1918

------------------------------------------------------------------------------
 mixrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         age |   .0030852   .0057034     0.54   0.605    -.0104011    .0165715
       _cons |   .6928913    .187412     3.70   0.008     .2497324     1.13605
------------------------------------------------------------------------------


. bysort solvent: regress mixcrsquared age

_______________________________________________________________________________
-> solvent = MIBK

      Source |       SS       df       MS              Number of obs =       7
-------------+------------------------------           F(  1,     5) =   12.30
       Model |  .074857692     1  .074857692           Prob > F      =  0.0172
    Residual |  .030442085     5  .006088417           R-squared     =  0.7109
-------------+------------------------------           Adj R-squared =  0.6531
       Total |  .105299778     6  .017549963           Root MSE      =  .07803

------------------------------------------------------------------------------
mixcrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         age |  -.0058913   .0016801    -3.51   0.017    -.0102101   -.0015724
       _cons |   .9904015   .0596453    16.60   0.000     .8370784    1.143725
------------------------------------------------------------------------------

_______________________________________________________________________________
-> solvent = acetone

      Source |       SS       df       MS              Number of obs =       7
-------------+------------------------------           F(  1,     5) =    3.48
       Model |  .307657233     1  .307657233           Prob > F      =  0.1213
    Residual |  .442614213     5  .088522843           R-squared     =  0.4101
```

```
-------------+------------------------------           Adj R-squared =  0.2921
       Total |  .750271446     6  .125045241           Root MSE      =  .29753

------------------------------------------------------------------------------
mixcrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         age |   -.028847   .0154737    -1.86   0.121    -.0686234    .0109295
       _cons |   1.253932   .4711957     2.66   0.045     .0426851    2.465179
------------------------------------------------------------------------------

_______________________________________________________________________________

-> solvent = ethanol

      Source |       SS       df       MS              Number of obs =       8
-------------+------------------------------           F(  1,     6) =    0.00
       Model |  7.1006e-07     1  7.1006e-07           Prob > F      =  0.9916
    Residual |  .035076816     6  .005846136           R-squared     =  0.0000
-------------+------------------------------           Adj R-squared = -0.1666
       Total |  .035077526     7  .005011075           Root MSE      =  .07646

------------------------------------------------------------------------------
mixcrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         age |  -.0000437   .0039649    -0.01   0.992    -.0097455    .0096581
       _cons |   .9444336   .1195659     7.90   0.000     .6518663    1.237001
------------------------------------------------------------------------------

_______________________________________________________________________________

-> solvent = halothane

      Source |       SS       df       MS              Number of obs =       4
-------------+------------------------------           F(  1,     2) =    8.04
       Model |  .060038617     1  .060038617           Prob > F      =  0.1052
    Residual |  .014939398     2  .007469699           R-squared     =  0.8007
-------------+------------------------------           Adj R-squared =  0.7011
       Total |  .074978015     3  .024992672           Root MSE      =  .08643

------------------------------------------------------------------------------
mixcrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         age |   -.007588   .0026765    -2.84   0.105    -.0191039    .0039279
       _cons |   1.207809   .1489291     8.11   0.015      .567019    1.848599
------------------------------------------------------------------------------
```

```
-> solvent = toluene

      Source |       SS       df       MS              Number of obs =       9
-------------+------------------------------           F(  1,     7) =    0.58
       Model |  .016177634     1  .016177634           Prob > F      =  0.4706
    Residual |  .194755791     7  .027822256           R-squared     =  0.0767
-------------+------------------------------           Adj R-squared = -0.0552
       Total |  .210933426     8  .026366678           Root MSE      =   .1668

------------------------------------------------------------------------------
mixcrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         age |   .0037822   .0049601     0.76   0.471    -.0079464    .0155109
       _cons |    .723849   .1629872     4.44   0.003     .3384456    1.109252
------------------------------------------------------------------------------
```

Gender:

```
. bysort solvent: regress rebslope gennum

-> solvent = MIBK

      Source |       SS       df       MS              Number of obs =       7
-------------+------------------------------           F(  1,     5) =    0.09
       Model |    2247.503     1    2247.503           Prob > F      =  0.7808
    Residual |  130239.734     5  26047.9468           R-squared     =  0.0170
-------------+------------------------------           Adj R-squared = -0.1796
       Total |  132487.237     6  22081.2061           Root MSE      =  161.39

------------------------------------------------------------------------------
    rebslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      gennum |  -36.20833   123.2665    -0.29   0.781     -353.075    280.6584
       _cons |   190.7833   186.3615     1.02   0.353    -288.2741    669.8407
------------------------------------------------------------------------------

-> solvent = acetone
```

```
      Source |       SS       df       MS              Number of obs =       7
-------------+------------------------------           F(  1,     5) =    0.01
       Model |  56.6785714     1  56.6785714           Prob > F      =  0.9376
    Residual |    41822.75     5     8364.55           R-squared     =  0.0014
-------------+------------------------------           Adj R-squared = -0.1984
       Total |  41879.4286     6  6979.90476           Root MSE      =  91.458

------------------------------------------------------------------------------
    rebslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      gennum |       5.75   69.85214     0.08   0.938    -173.8106    185.3106
       _cons |     244.25    115.082     2.12   0.087    -51.57774    540.0777
------------------------------------------------------------------------------

_______________________________________________________________________________
-> solvent = ethanol

      Source |       SS       df       MS              Number of obs =       8
-------------+------------------------------           F(  1,     6) =    0.14
       Model |     86112.5     1     86112.5           Prob > F      =  0.7192
    Residual |     3636475     6  606079.167           R-squared     =  0.0231
-------------+------------------------------           Adj R-squared = -0.1397
       Total |   3722587.5     7  531798.214           Root MSE      =  778.51

------------------------------------------------------------------------------
    rebslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      gennum |     -207.5   550.4903    -0.38   0.719    -1554.501    1139.501
       _cons |       2675   870.4016     3.07   0.022      545.204    4804.796
------------------------------------------------------------------------------

_______________________________________________________________________________
-> solvent = halothane

      Source |       SS       df       MS              Number of obs =       4
-------------+------------------------------           F(  1,     2) =    4.59
       Model |  2.59470059     1  2.59470059           Prob > F      =  0.1654
    Residual |  1.13039962     2  .565199809           R-squared     =  0.6965
-------------+------------------------------           Adj R-squared =  0.5448
       Total |  3.72510021     3  1.24170007           Root MSE      =   .7518

------------------------------------------------------------------------------
    rebslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
```

```
-------------+----------------------------------------------------------------
      gennum |      -1.86   .8681012    -2.14   0.165    -5.595138    1.875138
       _cons |       7.18   1.564992     4.59   0.044     .4463844    13.91362
------------------------------------------------------------------------------

_______________________________________________________________________________
-> solvent = toluene

      Source |       SS       df       MS              Number of obs =       9
-------------+------------------------------           F(  1,     7) =    0.40
       Model |  90.7096032     1  90.7096032           Prob > F      =  0.5494
    Residual |  1605.78544     7   229.39792           R-squared     =  0.0535
-------------+------------------------------           Adj R-squared = -0.0817
       Total |  1696.49504     8  212.061881           Root MSE      =  15.146

------------------------------------------------------------------------------
    rebslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      gennum |     -6.389   10.16017    -0.63   0.549    -30.41399    17.63599
       _cons |     40.864   16.59149     2.46   0.043     1.631363    80.09664
------------------------------------------------------------------------------


. bysort solvent: regress endslope gennum

_______________________________________________________________________________
-> solvent = MIBK

      Source |       SS       df       MS              Number of obs =       7
-------------+------------------------------           F(  1,     5) =    0.19
       Model |  10256.6099     1  10256.6099           Prob > F      =  0.6848
    Residual |   276748.11     5   55349.622           R-squared     =  0.0357
-------------+------------------------------           Adj R-squared = -0.1571
       Total |   287004.72     6    47834.12           Root MSE      =  235.27

------------------------------------------------------------------------------
    endslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      gennum |     -77.35   179.6866    -0.43   0.685    -539.2491    384.5491
       _cons |      295.1   271.6606     1.09   0.327    -403.2259    993.4259
------------------------------------------------------------------------------

_______________________________________________________________________________
```

```
-> solvent = acetone

      Source |       SS       df       MS              Number of obs =       7
-------------+------------------------------           F(  1,     5) =    0.09
       Model |  1368.10714     1  1368.10714           Prob > F      =  0.7789
    Residual |    77934.75     5    15586.95           R-squared     =  0.0173
-------------+------------------------------           Adj R-squared = -0.1793
       Total |  79302.8571     6  13217.1429           Root MSE      =  124.85

------------------------------------------------------------------------------
    endslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      gennum |      28.25   95.35401     0.30   0.779    -216.8653    273.3653
       _cons |     202.75   157.0966     1.29   0.253    -201.0796    606.5796
------------------------------------------------------------------------------
```

```
-> solvent = ethanol

      Source |       SS       df       MS              Number of obs =       8
-------------+------------------------------           F(  1,     6) =    1.30
       Model |    891112.5     1    891112.5           Prob > F      =  0.2970
    Residual |     4100475     6    683412.5           R-squared     =  0.1785
-------------+------------------------------           Adj R-squared =  0.0416
       Total |   4991587.5     7  713083.929           Root MSE      =  826.69

------------------------------------------------------------------------------
    endslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      gennum |     -667.5   584.5565    -1.14   0.297    -2097.858    762.8581
       _cons |     3807.5   924.2649     4.12   0.006     1545.905    6069.095
------------------------------------------------------------------------------
```

```
-> solvent = halothane

      Source |       SS       df       MS              Number of obs =       4
-------------+------------------------------           F(  1,     2) =    0.03
       Model |  .508408541     1  .508408541           Prob > F      =  0.8717
    Residual |  30.3660708     2  15.1830354           R-squared     =  0.0165
-------------+------------------------------           Adj R-squared = -0.4753
       Total |  30.8744794     3  10.2914931           Root MSE      =  3.8965
```

```
------------------------------------------------------------------------------
    endslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      gennum |   .8233335   4.499339     0.18   0.872    -18.53576    20.18242
       _cons |   3.966666   8.111298     0.49   0.673    -30.93343    38.86676
------------------------------------------------------------------------------

_______________________________________________________________________________
-> solvent = toluene

      Source |       SS       df       MS              Number of obs =       9
-------------+------------------------------           F(  1,     7) =    0.85
       Model |  416.784632     1  416.784632           Prob > F      =  0.3868
    Residual |  3426.05565     7  489.436521           R-squared     =  0.1085
-------------+------------------------------           Adj R-squared = -0.0189
       Total |  3842.84028     8  480.355035           Root MSE      =  22.123

------------------------------------------------------------------------------
    endslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      gennum |    -13.695    14.8407    -0.92   0.387    -48.78769    21.39768
       _cons |      61.22   24.23476     2.53   0.039     3.913891    118.5261
------------------------------------------------------------------------------


. bysort solvent: regress mixslope gennum

_______________________________________________________________________________
-> solvent = MIBK

      Source |       SS       df       MS              Number of obs =       7
-------------+------------------------------           F(  1,     5) =    0.17
       Model |  18381.6041     1  18381.6041           Prob > F      =  0.6946
    Residual |   530756.75     5   106151.35           R-squared     =  0.0335
-------------+------------------------------           Adj R-squared = -0.1598
       Total |  549138.354     6   91523.059           Root MSE      =  325.81

------------------------------------------------------------------------------
    mixslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      gennum |    -103.55   248.8406    -0.42   0.695     -743.215     536.115
       _cons |        401   376.2116     1.07   0.335    -566.0826    1368.083
------------------------------------------------------------------------------
```

```
-> solvent = acetone

      Source |       SS       df       MS              Number of obs =       7
-------------+------------------------------           F(  1,     5) =    0.07
       Model |  14877.3861     1  14877.3861           Prob > F      =  0.8042
    Residual |  1088985.03     5  217797.006           R-squared     =  0.0135
-------------+------------------------------           Adj R-squared = -0.1838
       Total |  1103862.42     6   183977.07           Root MSE      =  466.69

------------------------------------------------------------------------------
    mixslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      gennum |   93.15833   356.4383     0.26   0.804    -823.0955    1009.412
       _cons |   398.5083   587.2353     0.68   0.528    -1111.028    1908.045
------------------------------------------------------------------------------
```

```
-> solvent = ethanol

      Source |       SS       df       MS              Number of obs =       8
-------------+------------------------------           F(  1,     6) =    0.61
       Model |     1051250     1     1051250           Prob > F      =  0.4645
    Residual |    10341900     6     1723650           R-squared     =  0.0923
-------------+------------------------------           Adj R-squared = -0.0590
       Total |    11393150     7  1627592.86           Root MSE      =  1312.9

------------------------------------------------------------------------------
    mixslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      gennum |       -725   928.3453    -0.78   0.465    -2996.579    1546.579
       _cons |       4645   1467.843     3.16   0.019     1053.318    8236.682
------------------------------------------------------------------------------
```

```
-> solvent = halothane

      Source |       SS       df       MS              Number of obs =       4
-------------+------------------------------           F(  1,     2) =    0.01
       Model |  .554699352     1  .554699352           Prob > F      =  0.9221
    Residual |  90.8881868     2  45.4440934           R-squared     =  0.0061
-------------+------------------------------           Adj R-squared = -0.4909
```

```
       Total |  91.4428861     3  30.480962           Root MSE      =  6.7412

------------------------------------------------------------------------------
    mixslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      gennum |   .8599995   7.784094     0.11   0.922    -32.63226    34.35225
       _cons |   7.820001   14.03298     0.56   0.633    -52.55902    68.19902
------------------------------------------------------------------------------

_______________________________________________________________________________
-> solvent = toluene

      Source |       SS       df       MS              Number of obs =       9
-------------+------------------------------           F(  1,     7) =    1.39
       Model |   10330.028     1   10330.028           Prob > F      =  0.2775
    Residual |  52166.7075     7  7452.38679           R-squared     =  0.1653
-------------+------------------------------           Adj R-squared =  0.0460
       Total |  62496.7355     8  7812.09194           Root MSE      =  86.327

------------------------------------------------------------------------------
    mixslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      gennum |     -68.18   57.91005    -1.18   0.278    -205.1155    68.75551
       _cons |     198.98   94.56672     2.10   0.073    -24.63475    422.5948
------------------------------------------------------------------------------


. bysort solvent: regress mixcslope gennum

_______________________________________________________________________________
-> solvent = MIBK

      Source |       SS       df       MS              Number of obs =       7
-------------+------------------------------           F(  1,     5) =    0.37
       Model |  21584.0744     1  21584.0744           Prob > F      =  0.5711
    Residual |  294058.114     5  58811.6228           R-squared     =  0.0684
-------------+------------------------------           Adj R-squared = -0.1179
       Total |  315642.189     6  52607.0314           Root MSE      =  242.51

------------------------------------------------------------------------------
   mixcslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      gennum |  -112.2083   185.2209    -0.61   0.571    -588.3338    363.9171
```

```
       _cons |   339.0833   280.0277     1.21   0.280    -380.7507    1058.917
------------------------------------------------------------------------------
```

```
-> solvent = acetone

      Source |       SS       df       MS              Number of obs =       7
-------------+------------------------------           F(  1,     5) =    0.00
       Model |  22.3201104     1  22.3201104           Prob > F      =  0.9905
    Residual |  710644.375     5  142128.875           R-squared     =  0.0000
-------------+------------------------------           Adj R-squared = -0.2000
       Total |  710666.695     6  118444.449           Root MSE      =     377

------------------------------------------------------------------------------
   mixcslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      gennum |  -3.608333   287.9384    -0.01   0.990    -743.7775    736.5608
       _cons |   408.6417   474.3811     0.86   0.428    -810.7937    1628.077
------------------------------------------------------------------------------
```

```
-> solvent = ethanol

      Source |       SS       df       MS              Number of obs =       8
-------------+------------------------------           F(  1,     6) =    3.03
       Model |    5611250     1     5611250           Prob > F      =  0.1326
    Residual |   11128100     6  1854683.33           R-squared     =  0.3352
-------------+------------------------------           Adj R-squared =  0.2244
       Total |   16739350     7  2391335.71           Root MSE      =  1361.9

------------------------------------------------------------------------------
   mixcslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      gennum |      -1675   962.9858    -1.74   0.133    -4031.341    681.3414
       _cons |       5040   1522.614     3.31   0.016     1314.297    8765.703
------------------------------------------------------------------------------
```

```
-> solvent = halothane

      Source |       SS       df       MS              Number of obs =       4
-------------+------------------------------           F(  1,     2) =    0.09
       Model |  1.55520012     1  1.55520012           Prob > F      =  0.7878
```

```
    Residual |  32.9784032     2  16.4892016           R-squared     =  0.0450
-------------+------------------------------           Adj R-squared = -0.4324
       Total |  34.5336034     3  11.5112011           Root MSE      =  4.0607

------------------------------------------------------------------------------
   mixcslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      gennum |       1.44   4.688881     0.31   0.788    -18.73463    21.61463
       _cons |          4      8.453     0.47   0.683    -32.37032    40.37032
------------------------------------------------------------------------------


-------------------------------------------------------------------------------
-> solvent = toluene

      Source |       SS       df       MS              Number of obs =       9
-------------+------------------------------           F(  1,     7) =    1.32
       Model |  2592.36458     1  2592.36458           Prob > F      =  0.2887
    Residual |  13769.7354     7  1967.10506           R-squared     =  0.1584
-------------+------------------------------           Adj R-squared =  0.0382
       Total |     16362.1     8   2045.2625           Root MSE      =  44.352

------------------------------------------------------------------------------
   mixcslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      gennum |    -34.155   29.75227    -1.15   0.289    -104.5079    36.19793
       _cons |     109.43   48.58525     2.25   0.059    -5.455849    224.3159
------------------------------------------------------------------------------


. bysort solvent: regress rebrsquared gennum


-------------------------------------------------------------------------------
-> solvent = MIBK

      Source |       SS       df       MS              Number of obs =       7
-------------+------------------------------           F(  1,     5) =    1.74
       Model |  .023037601     1  .023037601           Prob > F      =  0.2445
    Residual |  .066267077     5  .013253415           R-squared     =  0.2580
-------------+------------------------------           Adj R-squared =  0.1096
       Total |  .089304679     6  .014884113           Root MSE      =  .11512

------------------------------------------------------------------------------
 rebrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
```

```
-------------+----------------------------------------------------------------
      gennum |   -.115925    .087927    -1.32   0.245    -.3419486    .1100986
       _cons |     .96855   .1329331     7.29   0.001     .6268345    1.310266
------------------------------------------------------------------------------
```

```
-> solvent = acetone

      Source |       SS       df       MS              Number of obs =       7
-------------+------------------------------           F(  1,     5) =    2.15
       Model |  .100755292     1  .100755292           Prob > F      =  0.2027
    Residual |  .234544575     5  .046908915           R-squared     =  0.3005
-------------+------------------------------           Adj R-squared =  0.1606
       Total |  .335299868     6  .055883311           Root MSE      =  .21658

------------------------------------------------------------------------------
 rebrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      gennum |  -.2424333   .1654193    -1.47   0.203    -.6676571    .1827904
       _cons |   .9390667   .2725297     3.45   0.018     .2385067    1.639627
------------------------------------------------------------------------------
```

```
-> solvent = ethanol

      Source |       SS       df       MS              Number of obs =       8
-------------+------------------------------           F(  1,     6) =    2.47
       Model |  .006077534     1  .006077534           Prob > F      =  0.1671
    Residual |  .014761202     6    .0024602           R-squared     =  0.2916
-------------+------------------------------           Adj R-squared =  0.1736
       Total |  .020838736     7  .002976962           Root MSE      =   .0496

------------------------------------------------------------------------------
 rebrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      gennum |   -.055125   .0350728    -1.57   0.167     -.140945     .030695
       _cons |     1.0298   .0554549    18.57   0.000     .8941067    1.165493
------------------------------------------------------------------------------
```

```
-> solvent = halothane

      Source |       SS       df       MS              Number of obs =       4
```

```
-------------+------------------------------           F(  1,      2) =    0.39
       Model |  .047905602     1  .047905602           Prob > F      =  0.5963
    Residual |  .246108013     2  .123054007           R-squared     =  0.1629
-------------+------------------------------           Adj R-squared = -0.2556
       Total |  .294013615     3  .098004538           Root MSE      =  .35079

------------------------------------------------------------------------------
 rebrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      gennum |  -.2527333    .405058    -0.62   0.596    -1.995557    1.490091
       _cons |   1.186233   .7302288     1.62   0.246    -1.955687    4.328154
------------------------------------------------------------------------------

_______________________________________________________________________________
-> solvent = toluene

      Source |       SS       df       MS              Number of obs =       9
-------------+------------------------------           F(  1,      7) =    0.02
       Model |  .000124002     1  .000124002           Prob > F      =  0.8896
    Residual |  .041865446     7  .005980778           R-squared     =  0.0030
-------------+------------------------------           Adj R-squared = -0.1395
       Total |  .041989449     8  .005248681           Root MSE      =  .07734

------------------------------------------------------------------------------
 rebrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      gennum |     .00747   .0518782     0.14   0.890    -.1152025    .1301425
       _cons |     .89328   .0847168    10.54   0.000     .6929566    1.093603
------------------------------------------------------------------------------


. bysort solvent: regress endrsquared gennum

_______________________________________________________________________________
-> solvent = MIBK

      Source |       SS       df       MS              Number of obs =       7
-------------+------------------------------           F(  1,      5) =    1.25
       Model |  .003971685     1  .003971685           Prob > F      =  0.3139
    Residual |  .015852225     5  .003170445           R-squared     =  0.2003
-------------+------------------------------           Adj R-squared =  0.0404
       Total |  .019823911     6  .003303985           Root MSE      =  .05631
```

```
------------------------------------------------------------------------------
 endrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      gennum |   .0481333    .043005     1.12   0.314    -.0624144    .1586811
       _cons |   .7858667   .0650174    12.09   0.000     .6187342    .9529992
------------------------------------------------------------------------------

_______________________________________________________________________________
-> solvent = acetone

      Source |       SS       df       MS              Number of obs =       7
-------------+------------------------------           F(  1,     5) =    0.01
       Model |  .001503681     1  .001503681           Prob > F      =  0.9158
    Residual |  .608237123     5  .121647425           R-squared     =  0.0025
-------------+------------------------------           Adj R-squared = -0.1970
       Total |  .609740803     6  .101623467           Root MSE      =  .34878

------------------------------------------------------------------------------
 endrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      gennum |  -.0296167   .2663851    -0.11   0.916    -.7143813    .6551479
       _cons |   .4468833   .4388718     1.02   0.355    -.6812724    1.575039
------------------------------------------------------------------------------

_______________________________________________________________________________
-> solvent = ethanol

      Source |       SS       df       MS              Number of obs =       8
-------------+------------------------------           F(  1,     6) =    0.41
       Model |   .00079202     1   .00079202           Prob > F      =  0.5439
    Residual |  .011489103     6   .00191485           R-squared     =  0.0645
-------------+------------------------------           Adj R-squared = -0.0914
       Total |  .012281122     7  .001754446           Root MSE      =  .04376

------------------------------------------------------------------------------
 endrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      gennum |     -.0199   .0309423    -0.64   0.544     -.095613    .0558131
       _cons |    .998325   .0489241    20.41   0.000     .8786121    1.118038
------------------------------------------------------------------------------

_______________________________________________________________________________
-> solvent = halothane
```

```
      Source |       SS       df       MS              Number of obs =       4
-------------+------------------------------           F(  1,     2) =    0.30
       Model |  .001388901     1  .001388901           Prob > F      =  0.6377
    Residual |  .009192642     2  .004596321           R-squared     =  0.1313
-------------+------------------------------           Adj R-squared = -0.3031
       Total |  .010581544     3  .003527181           Root MSE      =   .0678

------------------------------------------------------------------------------
 endrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      gennum |  -.0430333   .0782843    -0.55   0.638    -.3798634    .2937967
       _cons |   .9964334    .141129     7.06   0.019     .3892043    1.603662
------------------------------------------------------------------------------


-------------------------------------------------------------------------------
-> solvent = toluene

      Source |       SS       df       MS              Number of obs =       9
-------------+------------------------------           F(  1,     7) =    0.00
       Model |  .000010035     1  .000010035           Prob > F      =  0.9835
    Residual |  .153167206     7  .021881029           R-squared     =  0.0001
-------------+------------------------------           Adj R-squared = -0.1428
       Total |   .15317724     8  .019147155           Root MSE      =  .14792

------------------------------------------------------------------------------
 endrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      gennum |   -.002125   .0992293    -0.02   0.984    -.2367651    .2325151
       _cons |     .81275   .1620408     5.02   0.002     .4295843    1.195916
------------------------------------------------------------------------------


. bysort solvent: regress mixrsquared gennum


-------------------------------------------------------------------------------
-> solvent = MIBK

      Source |       SS       df       MS              Number of obs =       7
-------------+------------------------------           F(  1,     5) =    1.43
       Model |  .011880969     1  .011880969           Prob > F      =  0.2853
    Residual |  .041530206     5  .008306041           R-squared     =  0.2224
-------------+------------------------------           Adj R-squared =  0.0669
```

```
       Total |  .053411175     6  .008901862           Root MSE      =  .09114

------------------------------------------------------------------------------
 mixrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      gennum |    -.08325   .0696074    -1.20   0.285    -.2621815    .0956815
       _cons |      .9114   .1052365     8.66   0.000      .640881    1.181919
------------------------------------------------------------------------------


_______________________________________________________________________________
-> solvent = acetone

      Source |       SS       df       MS              Number of obs =       7
-------------+------------------------------           F(  1,     5) =    0.00
       Model |  .000294562     1  .000294562           Prob > F      =  0.9642
    Residual |  .660986789     5  .132197358           R-squared     =  0.0004
-------------+------------------------------           Adj R-squared = -0.1995
       Total |  .661281352     6  .110213559           Root MSE      =  .36359

------------------------------------------------------------------------------
 mixrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      gennum |   .0131083   .2776961     0.05   0.964    -.7007322    .7269489
       _cons |   .4620584   .4575068     1.01   0.359    -.7140003    1.638117
------------------------------------------------------------------------------


_______________________________________________________________________________
-> solvent = ethanol

      Source |       SS       df       MS              Number of obs =       8
-------------+------------------------------           F(  1,     6) =    0.71
       Model |  .003100778     1  .003100778           Prob > F      =  0.4309
    Residual |  .026103803     6  .004350634           R-squared     =  0.1062
-------------+------------------------------           Adj R-squared = -0.0428
       Total |   .02920458     7  .004172083           Root MSE      =  .06596

------------------------------------------------------------------------------
 mixrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      gennum |   -.039375   .0466403    -0.84   0.431    -.1534997    .0747497
       _cons |     1.0095   .0737448    13.69   0.000      .829053    1.189947
------------------------------------------------------------------------------
```

```
------------------------------------------------------------------------------
-> solvent = halothane

      Source |       SS       df       MS              Number of obs =       4
-------------+------------------------------           F(  1,     2) =    3.09
       Model |  .013776963     1  .013776963           Prob > F      =  0.2211
    Residual |  .008931085     2  .004465543           R-squared     =  0.6067
-------------+------------------------------           Adj R-squared =  0.4100
       Total |  .022708048     3  .007569349           Root MSE      =  .06682

------------------------------------------------------------------------------
 mixrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      gennum |  -.1355333   .0771625    -1.76   0.221    -.4675369    .1964703
       _cons |   1.088533   .1391067     7.83   0.016     .4900054    1.687061
------------------------------------------------------------------------------


------------------------------------------------------------------------------
-> solvent = toluene

      Source |       SS       df       MS              Number of obs =       9
-------------+------------------------------           F(  1,     7) =    0.87
       Model |   .02966554     1   .02966554           Prob > F      =  0.3819
    Residual |  .238599157     7  .034085594           R-squared     =  0.1106
-------------+------------------------------           Adj R-squared = -0.0165
       Total |  .268264697     8  .033533087           Root MSE      =  .18462

------------------------------------------------------------------------------
 mixrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      gennum |     .11554   .1238488     0.93   0.382    -.1773158    .4083958
       _cons |     .60846   .2022442     3.01   0.020     .1302285    1.086692
------------------------------------------------------------------------------


. bysort solvent: regress mixcrsquared gennum

------------------------------------------------------------------------------
-> solvent = MIBK

      Source |       SS       df       MS              Number of obs =       7
-------------+------------------------------           F(  1,     5) =    0.69
       Model |  .012750212     1  .012750212           Prob > F      =  0.4444
```

```
    Residual |  .092549566     5  .018509913           R-squared     =  0.1211
-------------+------------------------------           Adj R-squared = -0.0547
       Total |  .105299778     6  .017549963           Root MSE      =  .13605

------------------------------------------------------------------------------
mixcrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      gennum |  -.0862417   .1039108    -0.83   0.444    -.3533528    .1808695
       _cons |   .9318166   .1570983     5.93   0.002     .5279825    1.335651
------------------------------------------------------------------------------

_______________________________________________________________________________
-> solvent = acetone

      Source |       SS       df       MS              Number of obs =       7
-------------+------------------------------           F(  1,     5) =    0.05
       Model |  .007153991     1  .007153991           Prob > F      =  0.8350
    Residual |  .743117456     5  .148623491           R-squared     =  0.0095
-------------+------------------------------           Adj R-squared = -0.1886
       Total |  .750271446     6  .125045241           Root MSE      =  .38552

------------------------------------------------------------------------------
mixcrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      gennum |     -.0646   .2944436    -0.22   0.835    -.8214914    .6922914
       _cons |      .5024   .4850985     1.04   0.348    -.7445853    1.749385
------------------------------------------------------------------------------

_______________________________________________________________________________
-> solvent = ethanol

      Source |       SS       df       MS              Number of obs =       8
-------------+------------------------------           F(  1,     6) =    1.18
       Model |  .005756643     1  .005756643           Prob > F      =  0.3194
    Residual |  .029320883     6  .004886814           R-squared     =  0.1641
-------------+------------------------------           Adj R-squared =  0.0248
       Total |  .035077526     7  .005011075           Root MSE      =  .06991

------------------------------------------------------------------------------
mixcrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      gennum |    -.05365   .0494308    -1.09   0.319    -.1746029    .0673029
       _cons |   1.023625    .078157    13.10   0.000     .8323817    1.214868
```

```
------------------------------------------------------------------------------

_____________________________________________________________________________

-> solvent = halothane

      Source |       SS       df       MS              Number of obs =       4
-------------+------------------------------           F(  1,     2) =    1.23
       Model |  .028518742     1  .028518742           Prob > F      =  0.3833
    Residual |  .046459273     2  .023229636           R-squared     =  0.3804
-------------+------------------------------           Adj R-squared =  0.0705
       Total |  .074978015     3  .024992672           Root MSE      =  .15241

------------------------------------------------------------------------------
mixcrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      gennum |     -.195    .175991    -1.11   0.383    -.9522283    .5622284
       _cons |     1.145   .3172724     3.61   0.069    -.2201129    2.510113
------------------------------------------------------------------------------

_____________________________________________________________________________

-> solvent = toluene

      Source |       SS       df       MS              Number of obs =       9
-------------+------------------------------           F(  1,     7) =    0.29
       Model |  .008349063     1  .008349063           Prob > F      =  0.6078
    Residual |  .202584363     7  .028940623           R-squared     =  0.0396
-------------+------------------------------           Adj R-squared = -0.0976
       Total |  .210933426     8  .026366678           Root MSE      =  .17012

------------------------------------------------------------------------------
mixcrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      gennum |   .061295   .1141196     0.54   0.608    -.2085549     .331145
       _cons |    .74533   .1863565     4.00   0.005     .3046669    1.185993
------------------------------------------------------------------------------
```

Regressions of blood concentration on breath concentration with subject as a random effect and age and gender included as predictors:

```
. xtreg bloodmibkavg rebmibk age male, re i(subjnum)

Random-effects GLS regression                   Number of obs      =        52
Group variable (i): subjnum                     Number of groups   =         5
```

```
R-sq:  within  = 0.4609                         Obs per group: min =         6
       between = 0.2791                                        avg =      10.4
       overall = 0.1582                                        max =        17

Random effects u_i ~ Gaussian                   Wald chi2(3)       =     33.90
corr(u_i, X)       = 0 (assumed)                Prob > chi2        =    0.0000

------------------------------------------------------------------------------
bloodmibkavg |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
     rebmibk |   57.91131   9.973787     5.81   0.000     38.36304    77.45957
         age |   .0028612   .0410722     0.07   0.944    -.0776388     .0833611
        male |   .0922618   .1811512     0.51   0.611    -.2627879     .4473116
       _cons |   .0162517   .9220462     0.02   0.986    -1.790926     1.823429
-------------+----------------------------------------------------------------
     sigma_u |  .18153302
     sigma_e |   .1823504
         rho |  .49775375   (fraction of variance due to u_i)
------------------------------------------------------------------------------

. xtreg bloodmibkavg endmibk age male, re i(subjnum)

Random-effects GLS regression                   Number of obs      =        48
Group variable (i): subjnum                     Number of groups   =         5

R-sq:  within  = 0.4314                         Obs per group: min =         6
       between = 0.0913                                        avg =       9.6
       overall = 0.1490                                        max =        17

Random effects u_i ~ Gaussian                   Wald chi2(3)       =     26.86
corr(u_i, X)       = 0 (assumed)                Prob > chi2        =    0.0000

------------------------------------------------------------------------------
bloodmibkavg |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
     endmibk |   67.34757   13.10847     5.14   0.000     41.65544    93.03971
         age |   .0110906   .0397439     0.28   0.780    -.0668059     .0889871
        male |   .0556428   .1741434     0.32   0.749    -.2856719     .3969576
       _cons |  -.1316029    .891762    -0.15   0.883    -1.879424     1.616218
-------------+----------------------------------------------------------------
     sigma_u |  .16992813
     sigma_e |  .18859174
         rho |  .44808329   (fraction of variance due to u_i)
------------------------------------------------------------------------------

. xtreg bloodmibkavg mixmibk age male, re i(subjnum)

Random-effects GLS regression                   Number of obs      =        37
Group variable (i): subjnum                     Number of groups   =         5

R-sq:  within  = 0.3818                         Obs per group: min =         4
       between = 0.0004                                        avg =       7.4
       overall = 0.0879                                        max =        13

Random effects u_i ~ Gaussian                   Wald chi2(3)       =     18.43
corr(u_i, X)       = 0 (assumed)                Prob > chi2        =    0.0004

------------------------------------------------------------------------------
bloodmibkavg |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
     mixmibk |   90.96954   21.36748     4.26   0.000     49.09006      132.849
         age |   .0169076   .0750965     0.23   0.822    -.1302789     .1640941
        male |   .0398794   .3276179     0.12   0.903    -.6022398     .6819987
```

```
       _cons |  -.1746951   1.688268    -0.10   0.918    -3.483639    3.134249
-------------+----------------------------------------------------------------
     sigma_u |  .34625785
     sigma_e |  .19654371
         rho |  .75631799   (fraction of variance due to u_i)
------------------------------------------------------------------------------

. xtreg bloodmibkavg mixcmibk age male, re i(subjnum)

Random-effects GLS regression                   Number of obs      =        37
Group variable (i): subjnum                     Number of groups   =         5

R-sq:  within  = 0.4187                         Obs per group: min =         4
       between = 0.3225                                        avg =       7.4
       overall = 0.1410                                        max =        13

Random effects u_i ~ Gaussian                   Wald chi2(3)       =      5.42
corr(u_i, X)       = 0 (assumed)                Prob > chi2        =    0.1437

------------------------------------------------------------------------------
bloodmibkavg |      Coef.   Std. Err.       z     P>|z|      [95% Conf. Interval]
-------------+----------------------------------------------------------------
    mixcmibk |   59.31973    26.0512     2.28   0.023     8.260323    110.3791
         age |   -.018313   .0274467    -0.67   0.505    -.0721075    .0354816
        male |   .0569978   .1115058     0.51   0.609    -.1615495    .2755452
       _cons |   .6096054   .6058827     1.01   0.314     -.577903    1.797114
-------------+----------------------------------------------------------------
     sigma_u |          0
     sigma_e |  .19059497
         rho |          0   (fraction of variance due to u_i)
------------------------------------------------------------------------------

. xtreg bloodethavg rebeth age male, re i(subjnum)

Random-effects GLS regression                   Number of obs      =        35
Group variable (i): subjnum                     Number of groups   =         5

R-sq:  within  = 0.9162                         Obs per group: min =         5
       between = 0.9950                                        avg =       7.0
       overall = 0.9245                                        max =        10

Random effects u_i ~ Gaussian                   Wald chi2(3)       =    379.60
corr(u_i, X)       = 0 (assumed)                Prob > chi2        =    0.0000

------------------------------------------------------------------------------
 bloodethavg |      Coef.   Std. Err.       z     P>|z|      [95% Conf. Interval]
-------------+----------------------------------------------------------------
      rebeth |   2217.253   118.0263    18.79   0.000     1985.925     2448.58
         age |  -2.828992   3.528661    -0.80   0.423     -9.74504    4.087055
        male |  -107.0924   87.32833    -1.23   0.220    -278.2528      64.068
       _cons |   197.1236   110.0533     1.79   0.073     -18.5769    412.8241
-------------+----------------------------------------------------------------
     sigma_u |          0
     sigma_e |  184.07992
         rho |          0   (fraction of variance due to u_i)
------------------------------------------------------------------------------

. xtreg bloodethavg endeth age male, re i(subjnum)

Random-effects GLS regression                   Number of obs      =        34
Group variable (i): subjnum                     Number of groups   =         5

R-sq:  within  = 0.9198                         Obs per group: min =         5
       between = 0.9937                                        avg =       6.8
```

```
       overall = 0.9276                                        max =         11

Random effects u_i ~ Gaussian                   Wald chi2(3)       =     384.40
corr(u_i, X)       = 0 (assumed)                Prob > chi2        =     0.0000

------------------------------------------------------------------------------
 bloodethavg |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      endeth |   2591.409   137.7499    18.81   0.000     2321.425    2861.394
         age |  -2.775813   3.654164    -0.76   0.447    -9.937842    4.386217
        male |  -123.8064   86.23513    -1.44   0.151    -292.8242    45.21133
       _cons |    206.375   111.0589     1.86   0.063    -11.29635    424.0464
-------------+----------------------------------------------------------------
     sigma_u |          0
     sigma_e |  183.46347
         rho |          0   (fraction of variance due to u_i)
------------------------------------------------------------------------------

. xtreg bloodethavg mixeth age male, re i(subjnum)

Random-effects GLS regression                   Number of obs      =         35
Group variable (i): subjnum                     Number of groups   =          5

R-sq:  within  = 0.9326                         Obs per group: min =          5
       between = 0.9982                                        avg =        7.0
       overall = 0.9396                                        max =         11

Random effects u_i ~ Gaussian                   Wald chi2(3)       =     482.16
corr(u_i, X)       = 0 (assumed)                Prob > chi2        =     0.0000

------------------------------------------------------------------------------
 bloodethavg |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      mixeth |   3026.423   143.6178    21.07   0.000     2744.937    3307.908
         age |  -3.162188    3.08771    -1.02   0.306    -9.213989    2.889612
        male |  -61.95323   77.01086    -0.80   0.421    -212.8917    88.98527
       _cons |    189.736   97.35843     1.95   0.051    -1.082989     380.555
-------------+----------------------------------------------------------------
     sigma_u |          0
     sigma_e |  163.44136
         rho |          0   (fraction of variance due to u_i)
------------------------------------------------------------------------------

. xtreg bloodethavg mixceth age male, re i(subjnum)

Random-effects GLS regression                   Number of obs      =         35
Group variable (i): subjnum                     Number of groups   =          5

R-sq:  within  = 0.7038                         Obs per group: min =          5
       between = 0.9701                                        avg =        7.0
       overall = 0.7310                                        max =         11

Random effects u_i ~ Gaussian                   Wald chi2(3)       =      84.26
corr(u_i, X)       = 0 (assumed)                Prob > chi2        =     0.0000

------------------------------------------------------------------------------
 bloodethavg |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
     mixceth |   1578.075    181.373     8.70   0.000      1222.59     1933.56
         age |  -4.402567   6.553099    -0.67   0.502     -17.2464    8.441271
        male |  -305.2974   158.5282    -1.93   0.054     -616.007    5.412227
       _cons |   485.6289   202.0286     2.40   0.016     89.66015    881.5976
-------------+----------------------------------------------------------------
     sigma_u |          0
```

```
     sigma_e |  342.52106
         rho |          0   (fraction of variance due to u_i)
------------------------------------------------------------------------------

. xtreg bloodethavg rebace age male, re i(subjnum)
independent variables are collinear with the panel variable subjnum
r(198);

. xtreg bloodaceavg rebace age male, re i(subjnum)

Random-effects GLS regression                   Number of obs      =        60
Group variable (i): subjnum                     Number of groups   =         6

R-sq:  within  = 0.4608                         Obs per group: min =        10
       between = 0.8180                                        avg =      10.0
       overall = 0.7659                                        max =        10

Random effects u_i ~ Gaussian                   Wald chi2(3)       =     54.37
corr(u_i, X)       = 0 (assumed)                Prob > chi2        =    0.0000

------------------------------------------------------------------------------
 bloodaceavg |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      rebace |   234.7189   32.26059     7.28   0.000     171.4893    297.9485
         age |   .9226417   .9844474     0.94   0.349     -1.00684    2.852123
        male |   20.41795   17.75396     1.15   0.250    -14.37918    55.21508
       _cons |  -16.81085   30.57129    -0.55   0.582    -76.72947    43.10778
-------------+----------------------------------------------------------------
     sigma_u |   18.91331
     sigma_e |  7.8273224
         rho |  .85377121   (fraction of variance due to u_i)
------------------------------------------------------------------------------

. xtreg bloodaceavg endace age male, re i(subjnum)

Random-effects GLS regression                   Number of obs      =        52
Group variable (i): subjnum                     Number of groups   =         6

R-sq:  within  = 0.2252                         Obs per group: min =         7
       between = 0.7652                                        avg =       8.7
       overall = 0.6728                                        max =        10

Random effects u_i ~ Gaussian                   Wald chi2(3)       =     21.60
corr(u_i, X)       = 0 (assumed)                Prob > chi2        =    0.0001

------------------------------------------------------------------------------
 bloodaceavg |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      endace |   243.9159   54.62811     4.47   0.000     136.8468    350.9851
         age |   .7469078   .8498538     0.88   0.379    -.918775    2.412591
        male |   11.70408   15.63918     0.75   0.454    -18.94815    42.35632
       _cons |   .7554238    26.8342     0.03   0.978    -51.83864    53.34949
-------------+----------------------------------------------------------------
     sigma_u |  15.234749
     sigma_e |  9.6982264
         rho |  .71162141   (fraction of variance due to u_i)
------------------------------------------------------------------------------

. xtreg bloodaceavg mixace age male, re i(subjnum)

Random-effects GLS regression                   Number of obs      =        53
Group variable (i): subjnum                     Number of groups   =         6

R-sq:  within  = 0.3065                         Obs per group: min =         7
```

```
       between = 0.7298                                         avg =        8.8
       overall = 0.6677                                         max =         10

Random effects u_i ~ Gaussian                   Wald chi2(3)       =     26.40
corr(u_i, X)       = 0 (assumed)                Prob > chi2        =    0.0000

------------------------------------------------------------------------------
 bloodaceavg |      Coef.   Std. Err.      z    P>|z|      [95% Conf. Interval]
-------------+----------------------------------------------------------------
      mixace |   449.0814   89.52686     5.02   0.000       273.612    624.5508
         age |   .3247119   .9931097     0.33   0.744     -1.621747    2.271171
        male |   7.227671   17.46322     0.41   0.679     -26.99962    41.45496
       _cons |   17.69759    29.8701     0.59   0.554     -40.84673    76.24191
-------------+----------------------------------------------------------------
     sigma_u |  18.212667
     sigma_e |   8.496262
         rho |  .82127095   (fraction of variance due to u_i)
------------------------------------------------------------------------------

. xtreg bloodaceavg mixcace age male, re i(subjnum)

Random-effects GLS regression                   Number of obs      =        53
Group variable (i): subjnum                     Number of groups   =         6

R-sq:  within  = 0.1685                         Obs per group: min =         7
       between = 0.6633                                        avg =       8.8
       overall = 0.5885                                        max =        10

Random effects u_i ~ Gaussian                   Wald chi2(3)       =     16.41
corr(u_i, X)       = 0 (assumed)                Prob > chi2        =    0.0009

------------------------------------------------------------------------------
 bloodaceavg |      Coef.   Std. Err.      z    P>|z|      [95% Conf. Interval]
-------------+----------------------------------------------------------------
     mixcace |   299.3836   78.16769     3.83   0.000      146.1777    452.5894
         age |   .2406392    .858722     0.28   0.779     -1.442425    1.923703
        male |   6.646515    15.0055     0.44   0.658     -22.76372    36.05675
       _cons |   19.47229   25.33177     0.77   0.442     -30.17706    69.12165
-------------+----------------------------------------------------------------
     sigma_u |  14.414534
     sigma_e |  9.3028381
         rho |  .70595838   (fraction of variance due to u_i)
------------------------------------------------------------------------------

. xtreg bloodtolavg rebtol age male, re i(subjnum)

Random-effects GLS regression                   Number of obs      =        72
Group variable (i): subjnum                     Number of groups   =         9

R-sq:  within  = 0.8051                         Obs per group: min =         4
       between = 0.5976                                        avg =       8.0
       overall = 0.6189                                        max =        10

Random effects u_i ~ Gaussian                   Wald chi2(3)       =    262.82
corr(u_i, X)       = 0 (assumed)                Prob > chi2        =    0.0000

------------------------------------------------------------------------------
 bloodtolavg |      Coef.   Std. Err.      z    P>|z|      [95% Conf. Interval]
-------------+----------------------------------------------------------------
      rebtol |   30.83392   1.917157    16.08   0.000      27.07636    34.59148
         age |    .003365   .0043472     0.77   0.439     -.0051555    .0118854
        male |   -.065895   .0995571    -0.66   0.508     -.2610234    .1292334
       _cons |  -.0031329   .1237691    -0.03   0.980     -.2457158      .23945
-------------+----------------------------------------------------------------
```

```
     sigma_u |  .12512803
     sigma_e |  .04984594
         rho |  .86304339   (fraction of variance due to u_i)
------------------------------------------------------------------------------

. xtreg bloodaceavg rebtol age male, re i(subjnum)

Random-effects GLS regression                   Number of obs      =        35
Group variable (i): subjnum                     Number of groups   =         4

R-sq:  within  = 0.5557                         Obs per group: min =         8
       between = 0.9667                                        avg =       8.8
       overall = 0.9267                                        max =        10

Random effects u_i ~ Gaussian                   Wald chi2(3)       =    392.13
corr(u_i, X)       = 0 (assumed)                Prob > chi2        =    0.0000

------------------------------------------------------------------------------
 bloodaceavg |      Coef.   Std. Err.       z     P>|z|      [95% Conf. Interval]
-------------+----------------------------------------------------------------
      rebtol |    2799.67   530.5879     5.28   0.000     1759.736    3839.603
         age |  -9.303943   .4950362   -18.79   0.000     -10.2742    -8.33369
        male |  -56.69321   3.555988   -15.94   0.000    -63.66282    -49.7236
       _cons |   299.0945   12.95081    23.09   0.000     273.7113    324.4776
-------------+----------------------------------------------------------------
     sigma_u |          0
     sigma_e |  6.3788641
         rho |          0   (fraction of variance due to u_i)
------------------------------------------------------------------------------

. xtreg bloodaceavg endtol age male, re i(subjnum)

Random-effects GLS regression                   Number of obs      =        32
Group variable (i): subjnum                     Number of groups   =         4

R-sq:  within  = 0.2855                         Obs per group: min =         6
       between = 0.9804                                        avg =       8.0
       overall = 0.9335                                        max =         9

Random effects u_i ~ Gaussian                   Wald chi2(3)       =    392.89
corr(u_i, X)       = 0 (assumed)                Prob > chi2        =    0.0000

------------------------------------------------------------------------------
 bloodaceavg |      Coef.   Std. Err.       z     P>|z|      [95% Conf. Interval]
-------------+----------------------------------------------------------------
      endtol |   2929.813     765.35     3.83   0.000     1429.755    4429.872
         age |  -10.01888   .5552358   -18.04   0.000    -11.10712   -8.930639
        male |  -64.06045   3.878235   -16.52   0.000    -71.66165   -56.45925
       _cons |   324.4674   14.37507    22.57   0.000     296.2928    352.6421
-------------+----------------------------------------------------------------
     sigma_u |          0
     sigma_e |  7.7894477
         rho |          0   (fraction of variance due to u_i)
------------------------------------------------------------------------------

. xtreg bloodtolavg endtol age male, re i(subjnum)

Random-effects GLS regression                   Number of obs      =        62
Group variable (i): subjnum                     Number of groups   =         9

R-sq:  within  = 0.6921                         Obs per group: min =         3
       between = 0.6342                                        avg =       6.9
       overall = 0.5833                                        max =         9
```

```
Random effects u_i ~ Gaussian                   Wald chi2(3)       =    126.29
corr(u_i, X)       = 0 (assumed)                Prob > chi2        =    0.0000

------------------------------------------------------------------------------
 bloodtolavg |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      endtol |   38.68685   3.501804    11.05   0.000     31.82344    45.55026
         age |   .0025431   .0047327     0.54   0.591    -.0067329    .0118191
        male |  -.0747446   .1076032    -0.69   0.487    -.2856429    .1361538
       _cons |   .0332801   .1338186     0.25   0.804    -.2289995    .2955597
-------------+----------------------------------------------------------------
     sigma_u |  .13464972
     sigma_e |  .06650962
         rho |  .80387006   (fraction of variance due to u_i)
------------------------------------------------------------------------------

. xtreg bloodtolavg mixtol age male, re i(subjnum)

Random-effects GLS regression                   Number of obs      =        59
Group variable (i): subjnum                     Number of groups   =         9

R-sq:  within  = 0.6356                         Obs per group: min =         4
       between = 0.4219                                        avg =       6.6
       overall = 0.4448                                        max =         9

Random effects u_i ~ Gaussian                   Wald chi2(3)       =     90.26
corr(u_i, X)       = 0 (assumed)                Prob > chi2        =    0.0000

------------------------------------------------------------------------------
 bloodtolavg |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      mixtol |   81.73761   8.696254     9.40   0.000     64.69327    98.78195
         age |   .0016117   .0058012     0.28   0.781    -.0097584    .0129819
        male |   -.129051   .1326379    -0.97   0.331    -.3890165    .1309145
       _cons |   .0737951   .1651174     0.45   0.655     -.249829    .3974193
-------------+----------------------------------------------------------------
     sigma_u |  .16828893
     sigma_e |  .06356652
         rho |  .87514001   (fraction of variance due to u_i)
------------------------------------------------------------------------------

. xtreg bloodtolavg mixctol age male, re i(subjnum)

Random-effects GLS regression                   Number of obs      =        59
Group variable (i): subjnum                     Number of groups   =         9

R-sq:  within  = 0.6931                         Obs per group: min =         4
       between = 0.5104                                        avg =       6.6
       overall = 0.5377                                        max =         9

Random effects u_i ~ Gaussian                   Wald chi2(3)       =    117.26
corr(u_i, X)       = 0 (assumed)                Prob > chi2        =    0.0000

------------------------------------------------------------------------------
 bloodtolavg |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
     mixctol |   49.89729   4.652907    10.72   0.000     40.77776    59.01682
         age |    .000573   .0053517     0.11   0.915    -.0099161    .0110622
        male |    -.11943   .1222222    -0.98   0.328    -.3589811    .1201211
       _cons |   .1047938   .1520609     0.69   0.491    -.1932402    .4028278
-------------+----------------------------------------------------------------
     sigma_u |  .15498416
     sigma_e |  .05833385
         rho |  .87591266   (fraction of variance due to u_i)
```

```
------------------------------------------------------------------------------

. xtreg bloodhalavg rebhal age male, re i(subjnum)
insufficient observations
r(2000);

. xtreg bloodhalavg rebhal age , re i(subjnum)
insufficient observations
r(2000);

. xtreg bloodhalavg rebhal age male, re i(subjnum)
insufficient observations
r(2000);

. xtreg bloodhalavg rebhal male , re i(subjnum)

Random-effects GLS regression                   Number of obs      =        37
Group variable (i): subjnum                     Number of groups   =         3

R-sq:  within  = 0.8610                         Obs per group: min =         7
       between = 0.9946                                        avg =      12.3
       overall = 0.8805                                        max =        20

Random effects u_i ~ Gaussian                   Wald chi2(2)       =    250.41
corr(u_i, X)       = 0 (assumed)                Prob > chi2        =    0.0000

------------------------------------------------------------------------------
 bloodhalavg |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      rebhal |   3.058979   .1976371    15.48   0.000     2.671617     3.44634
        male |  -.0282319   .0099573    -2.84   0.005     -.047748   -.0087159
       _cons |   .0262583   .0082145     3.20   0.001     .0101581    .0423585
-------------+----------------------------------------------------------------
     sigma_u |          0
     sigma_e |  .02387246
         rho |          0   (fraction of variance due to u_i)
------------------------------------------------------------------------------
```

Linear regressions of blood concentration on breath concentration, age, gender and lung clearance index:

```
. regress bloodethavg rebeth age male lci

      Source |       SS       df       MS              Number of obs =      15
-------------+------------------------------           F(  3,    11) =   16.75
       Model |  351000.549     3  117000.183           Prob > F      =  0.0002
    Residual |  76851.5044    11   6986.5004           R-squared     =  0.8204
-------------+------------------------------           Adj R-squared =  0.7714
       Total |  427852.053    14  30560.8609           Root MSE      =  83.585

------------------------------------------------------------------------------
 bloodethavg |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
```

```
      rebeth |    1496.85   214.2747     6.99   0.000     1025.235    1968.465
         age |  -2.179034   7.284922    -0.30   0.770    -18.21304    13.85497
        male |  (dropped)
         lci |   16.15109   45.71121     0.35   0.731    -84.45859    116.7608
       _cons |  -.2464654   179.4529    -0.00   0.999    -395.2196    394.7267
------------------------------------------------------------------------------

. regress bloodethavg endeth age male lci

      Source |       SS       df       MS              Number of obs =      14
-------------+------------------------------           F(  3,    10) =   29.89
       Model |  377479.885     3  125826.628           Prob > F      =  0.0000
    Residual |  42098.2184    10  4209.82184           R-squared     =  0.8997
-------------+------------------------------           Adj R-squared =  0.8696
       Total |  419578.104    13  32275.2387           Root MSE      =  64.883

------------------------------------------------------------------------------
 bloodethavg |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      endeth |   2034.575   218.5971     9.31   0.000      1547.51     2521.64
         age |   -6.59347   5.573675    -1.18   0.264    -19.01239    5.825452
        male |  (dropped)
         lci |   52.84904   33.17979     1.59   0.142    -21.08014    126.7782
       _cons |  -191.2481   125.2339    -1.53   0.158    -470.2865    87.79044
------------------------------------------------------------------------------

. regress bloodethavg mixeth age male lci

      Source |       SS       df       MS              Number of obs =      16
-------------+------------------------------           F(  3,    12) =   20.39
       Model |  392714.968     3  130904.989           Prob > F      =  0.0001
    Residual |  77034.9268    12  6419.57723           R-squared     =  0.8360
-------------+------------------------------           Adj R-squared =  0.7950
       Total |  469749.894    15  31316.6596           Root MSE      =  80.122

------------------------------------------------------------------------------
 bloodethavg |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      mixeth |   2414.129    310.848     7.77   0.000     1736.849    3091.409
         age |  -3.667645   6.642345    -0.55   0.591    -18.14007    10.80478
        male |  (dropped)
         lci |   22.49667   40.25067     0.56   0.586      -65.202    110.1953
       _cons |  -28.15288   150.2104    -0.19   0.854    -355.4332    299.1274
```

```
------------------------------------------------------------------------------

. regress bloodethavg mixceth age male lci

      Source |       SS       df       MS              Number of obs =      16
-------------+------------------------------           F(  3,    12) =   26.69
       Model |  408526.945     3  136175.648           Prob > F      =  0.0000
    Residual |  61222.9491    12  5101.91243           R-squared     =  0.8697
-------------+------------------------------           Adj R-squared =  0.8371
       Total |  469749.894    15  31316.6596           Root MSE      =  71.428

------------------------------------------------------------------------------
 bloodethavg |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
     mixceth |   1582.081   178.0075     8.89   0.000     1194.236    1969.926
         age |  -2.108389   5.900563    -0.36   0.727    -14.96461    10.74783
        male |  (dropped)
         lci |   23.90523   35.89147     0.67   0.518    -54.29556     102.106
       _cons |  -97.68504   135.0689    -0.72   0.483     -391.975    196.6049
------------------------------------------------------------------------------

. regress bloodaceavg rebace age male lci

      Source |       SS       df       MS              Number of obs =      30
-------------+------------------------------           F(  3,    26) =  182.70
       Model |  29937.7686     3  9979.2562            Prob > F      =  0.0000
    Residual |  1420.14204    26  54.6208479           R-squared     =  0.9547
-------------+------------------------------           Adj R-squared =  0.9495
       Total |  31357.9106    29  1081.30726           Root MSE      =  7.3906

------------------------------------------------------------------------------
 bloodaceavg |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      rebace |   220.6883   37.31387     5.91   0.000     143.9886    297.3881
         age |   3.369315   .2748261    12.26   0.000     2.804401    3.934228
        male |  (dropped)
         lci |   5.231986   .7492551     6.98   0.000      3.69187    6.772102
       _cons |  -130.6089   11.65106   -11.21   0.000     -154.558   -106.6598
------------------------------------------------------------------------------

. regress bloodaceavg endace age male lci

      Source |       SS       df       MS              Number of obs =      25
```

```
-------------+------------------------------           F(  3,    21) =   78.65
       Model |  24650.7309     3  8216.9103            Prob > F      =  0.0000
    Residual |  2194.09384    21  104.480659           R-squared     =  0.9183
-------------+------------------------------           Adj R-squared =  0.9066
       Total |  26844.8247    24  1118.53436           Root MSE      =  10.222

------------------------------------------------------------------------------
 bloodaceavg |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      endace |   180.7293   71.08529     2.54   0.019     32.89935    328.5593
         age |   2.615749   .3969426     6.59   0.000     1.790261    3.441236
        male |  (dropped)
         lci |    7.24081    .896526     8.08   0.000     5.376382    9.105238
       _cons |  -109.1887   18.45731    -5.92   0.000    -147.5728   -70.80459
------------------------------------------------------------------------------

. regress bloodaceavg mixace age male lci

      Source |       SS       df       MS              Number of obs =      26
-------------+------------------------------           F(  3,    22) =  145.60
       Model |  25677.3708     3  8559.12361           Prob > F      =  0.0000
    Residual |  1293.26764    22  58.7848928           R-squared     =  0.9520
-------------+------------------------------           Adj R-squared =  0.9455
       Total |  26970.6385    25  1078.82554           Root MSE      =  7.6671

------------------------------------------------------------------------------
 bloodaceavg |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      mixace |   391.0149   96.23285     4.06   0.001     191.4401    590.5896
         age |   1.756985   .2563119     6.85   0.000     1.225427    2.288544
        male |  (dropped)
         lci |   7.888339   .6377874    12.37   0.000     6.565649    9.211029
       _cons |  -93.59905   10.12473    -9.24   0.000    -114.5965   -72.60164
------------------------------------------------------------------------------

. regress bloodaceavg mixcace age male lci

      Source |       SS       df       MS              Number of obs =      26
-------------+------------------------------           F(  3,    22) =  101.75
       Model |  25157.4252     3  8385.80839           Prob > F      =  0.0000
    Residual |   1813.2133    22  82.4187864           R-squared     =  0.9328
-------------+------------------------------           Adj R-squared =  0.9236
       Total |  26970.6385    25  1078.82554           Root MSE      =  9.0785
```

```
------------------------------------------------------------------------------
 bloodaceavg |      Coef.   Std. Err.       t     P>|t|      [95% Conf. Interval]
-------------+----------------------------------------------------------------
     mixcace |     246.52   105.4341      2.34    0.029      27.86316    465.1769
         age |   1.982956   .2946273      6.73    0.000      1.371937    2.593976
        male |  (dropped)
         lci |   8.515163   .7352537     11.58    0.000       6.99034    10.03999
       _cons |  -104.7109   12.41994     -8.43    0.000     -130.4683   -78.95356
------------------------------------------------------------------------------

. regress bloodmibkavg rebmibk age male lci

      Source |       SS       df       MS              Number of obs =      28
-------------+------------------------------           F(  3,    24) =   19.83
       Model |  1.64516757     3  .548389189           Prob > F      =  0.0000
    Residual |  .663740049    24  .027655835           R-squared     =  0.7125
-------------+------------------------------           Adj R-squared =  0.6766
       Total |  2.30890762    27  .085515097           Root MSE      =   .1663

------------------------------------------------------------------------------
bloodmibkavg |      Coef.   Std. Err.       t     P>|t|      [95% Conf. Interval]
-------------+----------------------------------------------------------------
     rebmibk |     83.977   13.59805      6.18    0.000        55.912     112.042
         age |  -.3831754   .0710336     -5.39    0.000     -.5297815   -.2365693
        male |  (dropped)
         lci |   .4366799   .0834862      5.23    0.000      .2643728     .608987
       _cons |   5.737673   1.052723      5.45    0.000      3.564961    7.910386
------------------------------------------------------------------------------

. regress bloodmibkavg endmibk age male lci

      Source |       SS       df       MS              Number of obs =      26
-------------+------------------------------           F(  3,    22) =   24.13
       Model |  1.75055609     3  .583518696           Prob > F      =  0.0000
    Residual |  .531974014    22  .024180637           R-squared     =  0.7669
-------------+------------------------------           Adj R-squared =  0.7352
       Total |   2.2825301    25  .091301204           Root MSE      =   .1555

------------------------------------------------------------------------------
bloodmibkavg |      Coef.   Std. Err.       t     P>|t|      [95% Conf. Interval]
-------------+----------------------------------------------------------------
     endmibk |   108.8105   17.10104      6.36    0.000      73.34511    144.2759
```

```
         age |  -.4026614   .0675345    -5.96   0.000    -.5427193   -.2626036
        male |  (dropped)
         lci |   .4773443   .0816595     5.85   0.000     .3079929    .6466957
       _cons |   5.870301   .9893993     5.93   0.000     3.818412    7.922189
------------------------------------------------------------------------------

. regress bloodmibkavg mixmibk age male lci

      Source |       SS       df       MS              Number of obs =      20
-------------+------------------------------           F(  3,    16) =   21.39
       Model |  1.74616709     3  .582055698           Prob > F      =  0.0000
    Residual |  .435335217    16  .027208451           R-squared     =  0.8004
-------------+------------------------------           Adj R-squared =  0.7630
       Total |  2.18150231    19  .114815911           Root MSE      =  .16495

------------------------------------------------------------------------------
bloodmibkavg |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
     mixmibk |   176.2057   38.30566     4.60   0.000      95.0013      257.41
         age |  -.4554967   .0796096    -5.72   0.000    -.6242615   -.2867319
        male |  (dropped)
         lci |   .5286813   .1039457     5.09   0.000     .3083261    .7490364
       _cons |   6.806524   1.153571     5.90   0.000     4.361062    9.251985
------------------------------------------------------------------------------

. regress bloodmibkavg mixcmibk age male lci

      Source |       SS       df       MS              Number of obs =      20
-------------+------------------------------           F(  3,    16) =   18.32
       Model |  1.68961256     3  .563204187           Prob > F      =  0.0000
    Residual |   .49188975    16  .030743109           R-squared     =  0.7745
-------------+------------------------------           Adj R-squared =  0.7322
       Total |  2.18150231    19  .114815911           Root MSE      =  .17534

------------------------------------------------------------------------------
bloodmibkavg |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
    mixcmibk |     99.824   24.29139     4.11   0.001     48.32855    151.3195
         age |  -.4998974   .0843393    -5.93   0.000    -.6786887   -.3211061
        male |  (dropped)
         lci |   .5991259   .1073897     5.58   0.000     .3714698     .826782
       _cons |   7.315335   1.231914     5.94   0.000     4.703795    9.926876
------------------------------------------------------------------------------
```

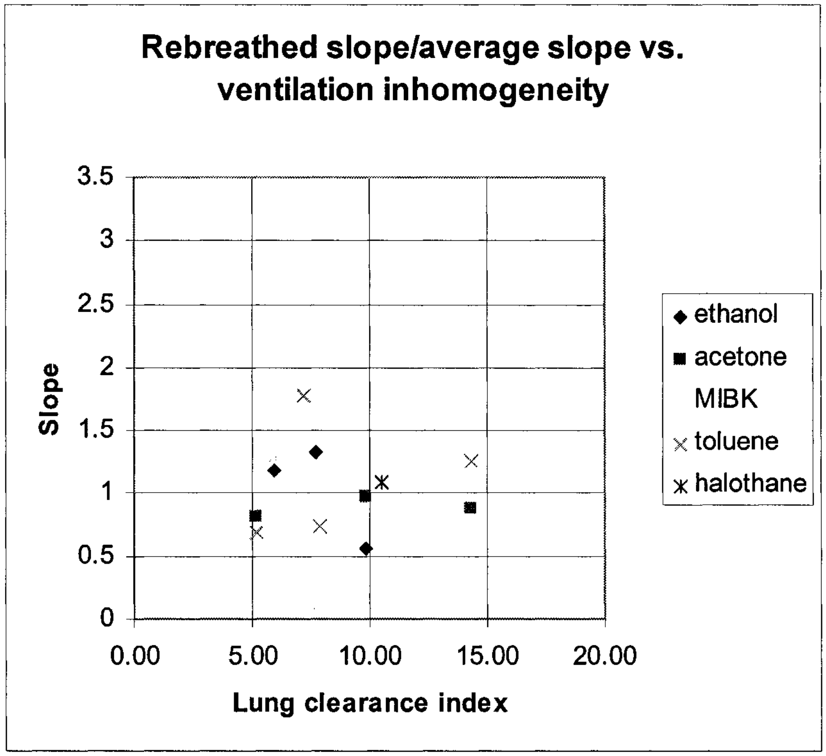
```
. regress bloodtolavg rebtol age male lci

      Source |       SS       df       MS              Number of obs =      34
-------------+------------------------------           F(  3,    30) =   38.56
       Model |  .454487857     3  .151495952           Prob > F      =  0.0000
    Residual |   .11787046    30  .003929015           R-squared     =  0.7941
-------------+------------------------------           Adj R-squared =  0.7735
       Total |  .572358317    33  .017344191           Root MSE      =  .06268

------------------------------------------------------------------------------
 bloodtolavg |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      rebtol |   27.76767   3.122889     8.89   0.000     21.38988    34.14546
         age |  -.0181533   .0029431    -6.17   0.000    -.0241639   -.0121428
        male |  (dropped)
         lci |   .0034792   .0037979     0.92   0.367    -.0042771    .0112355
       _cons |   .5076201   .0969606     5.24   0.000     .3096002    .7056401
------------------------------------------------------------------------------

. regress bloodtolavg endtol age male lci

      Source |       SS       df       MS              Number of obs =      31
-------------+------------------------------           F(  3,    27) =   18.85
       Model |  .415018723     3  .138339574           Prob > F      =  0.0000
    Residual |  .198145829    27  .007338734           R-squared     =  0.6768
-------------+------------------------------           Adj R-squared =  0.6409
       Total |  .613164552    30  .020438818           Root MSE      =  .08567

------------------------------------------------------------------------------
 bloodtolavg |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      endtol |   31.83871     5.4609     5.83   0.000     20.63387    43.04355
         age |   -.019505    .004117    -4.74   0.000    -.0279523   -.0110577
        male |  (dropped)
         lci |   .0087878    .005198     1.69   0.102    -.0018776    .0194532
       _cons |   .5253449   .1318856     3.98   0.000      .254738    .7959517
------------------------------------------------------------------------------

. regress bloodtolavg mixtol age male lci

      Source |       SS       df       MS              Number of obs =      24
-------------+------------------------------           F(  3,    20) =   25.22
```

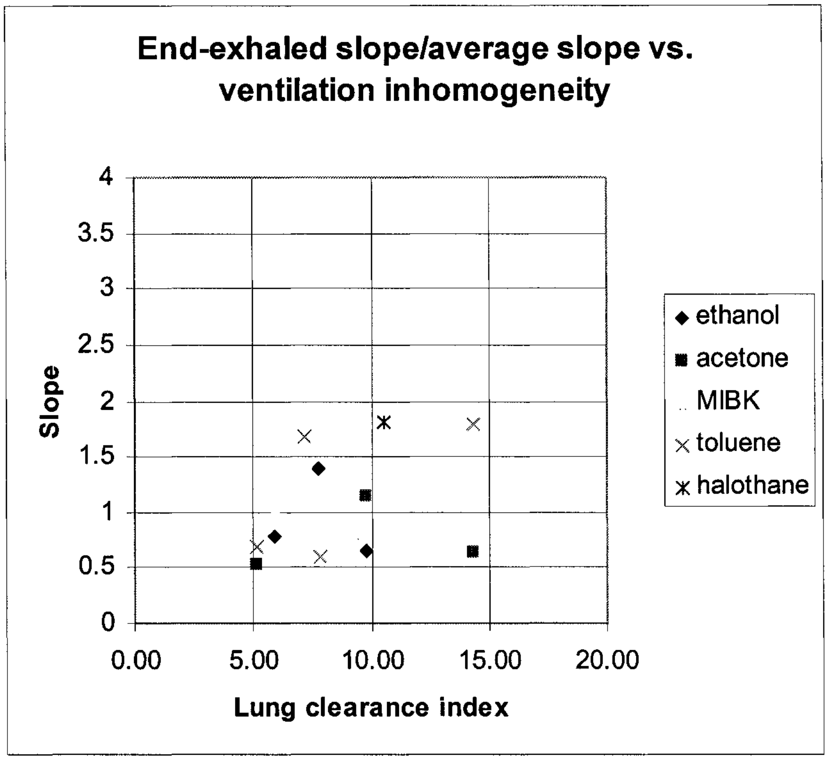
```
       Model |  .44302913     3  .147676377           Prob > F      =  0.0000
    Residual |  .11711204    20  .005855602           R-squared     =  0.7909
-------------+------------------------------           Adj R-squared =  0.7596
       Total |  .56014117    23  .024353964           Root MSE      =  .07652

------------------------------------------------------------------------------
 bloodtolavg |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      mixtol |   92.61108   19.80447     4.68   0.000     51.29967    133.9225
         age |  -.0272201   .0043555    -6.25   0.000    -.0363056   -.0181346
        male |  (dropped)
         lci |   .0113628   .0057228     1.99   0.061    -.0005748    .0233003
       _cons |   .6597461   .1514447     4.36   0.000     .3438381    .9756542
------------------------------------------------------------------------------

. regress bloodtolavg mixctol age male lci

      Source |       SS       df       MS              Number of obs =      24
-------------+------------------------------           F(  3,    20) =   28.28
       Model |  .453277289     3   .15109243           Prob > F      =  0.0000
    Residual |  .106863881    20  .005343194           R-squared     =  0.8092
-------------+------------------------------           Adj R-squared =  0.7806
       Total |  .56014117    23  .024353964           Root MSE      =   .0731

------------------------------------------------------------------------------
 bloodtolavg |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
     mixctol |   56.84291   11.17307     5.09   0.000     33.53629    80.14953
         age |   -.027798   .0041629    -6.68   0.000    -.0364816   -.0191145
        male |  (dropped)
         lci |   .0126974   .0055405     2.29   0.033       .00114    .0242548
       _cons |   .6675325   .1432872     4.66   0.000     .3686406    .9664243
------------------------------------------------------------------------------
```

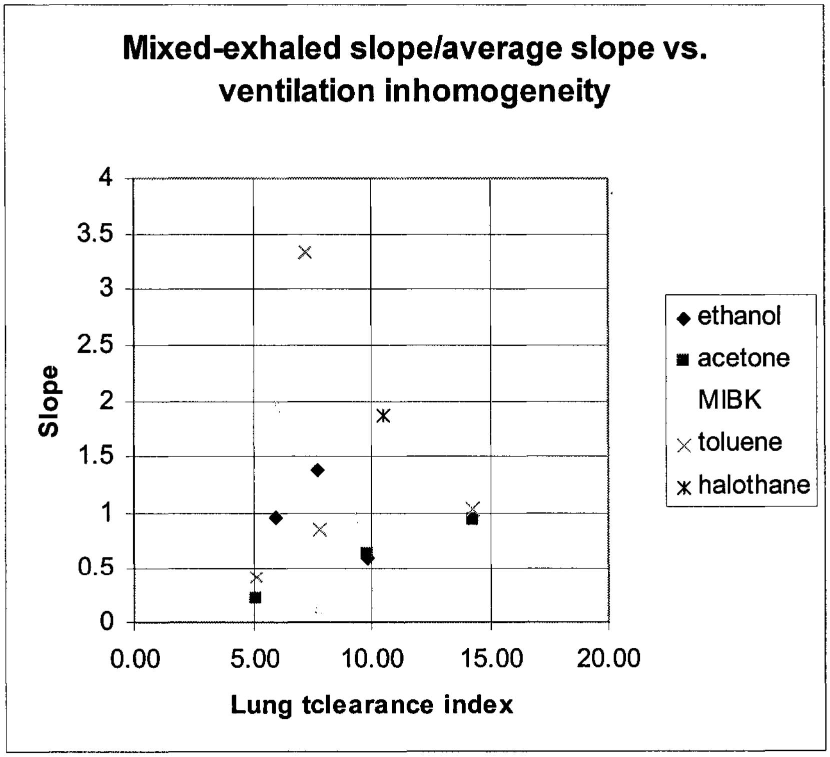
Appendix F: Inhomogeneity scatter plots and regressions

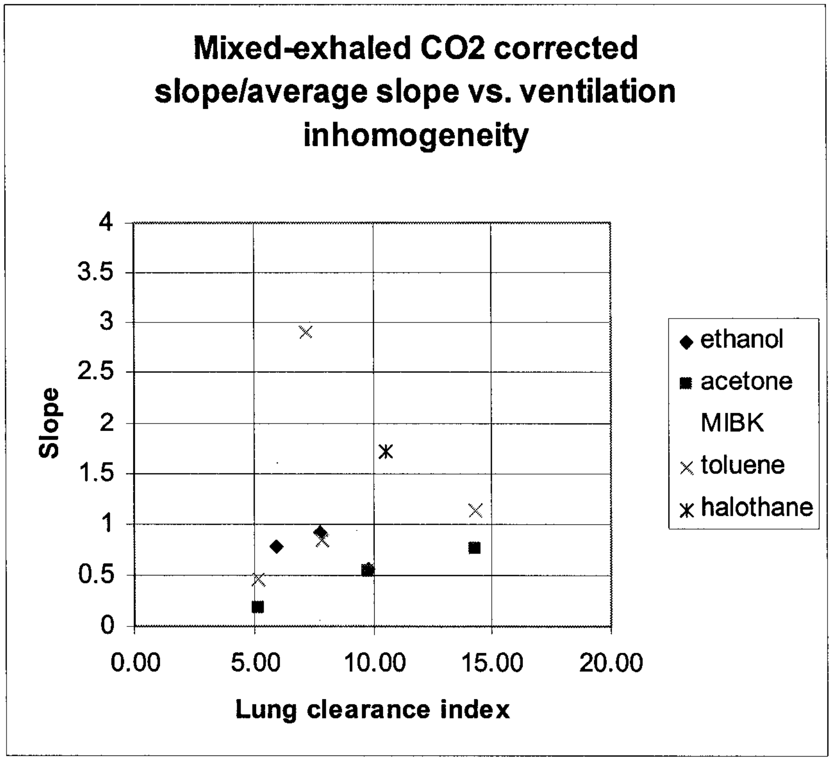
Scatter plots:

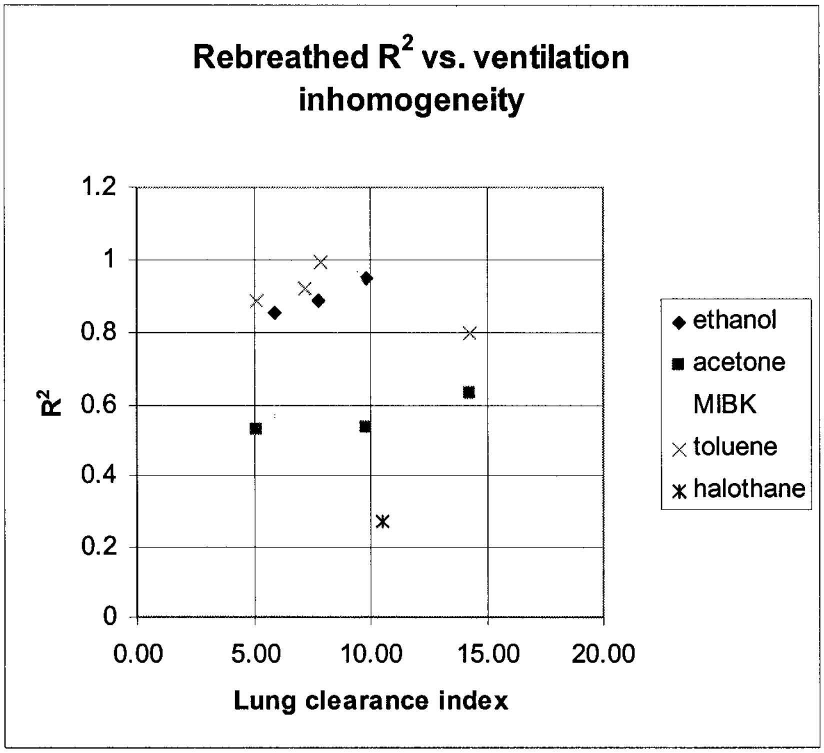
The following are scatter plots of individual blood/breath regression slope (personal partition coefficient) and correlation over inhomogeneity, measured as lung clearance index, which is the number of lung turnovers required for the subject to reach 2% of the initial end-tidal N_2 content.

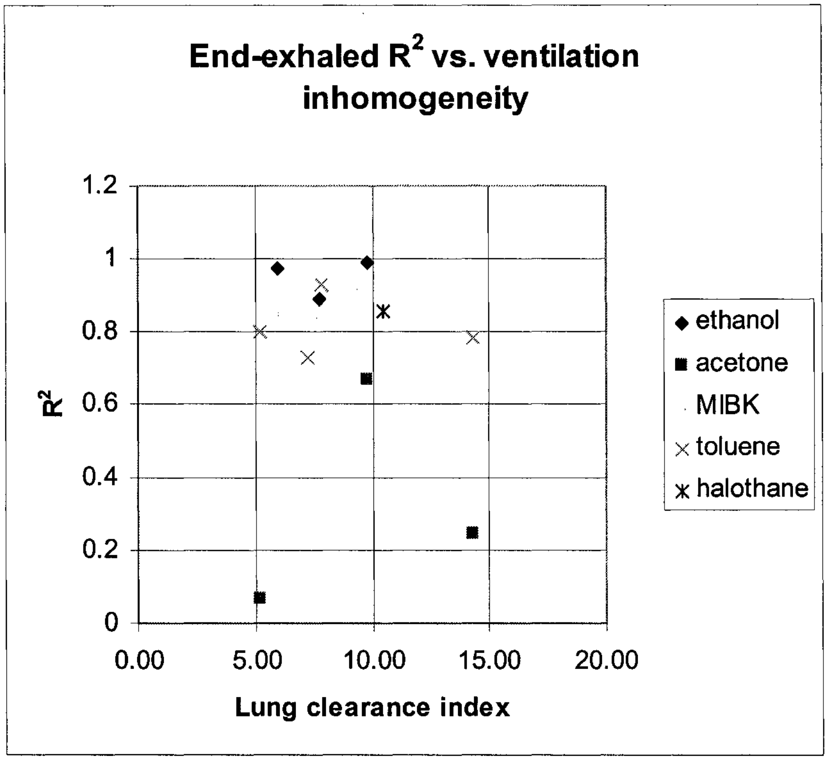


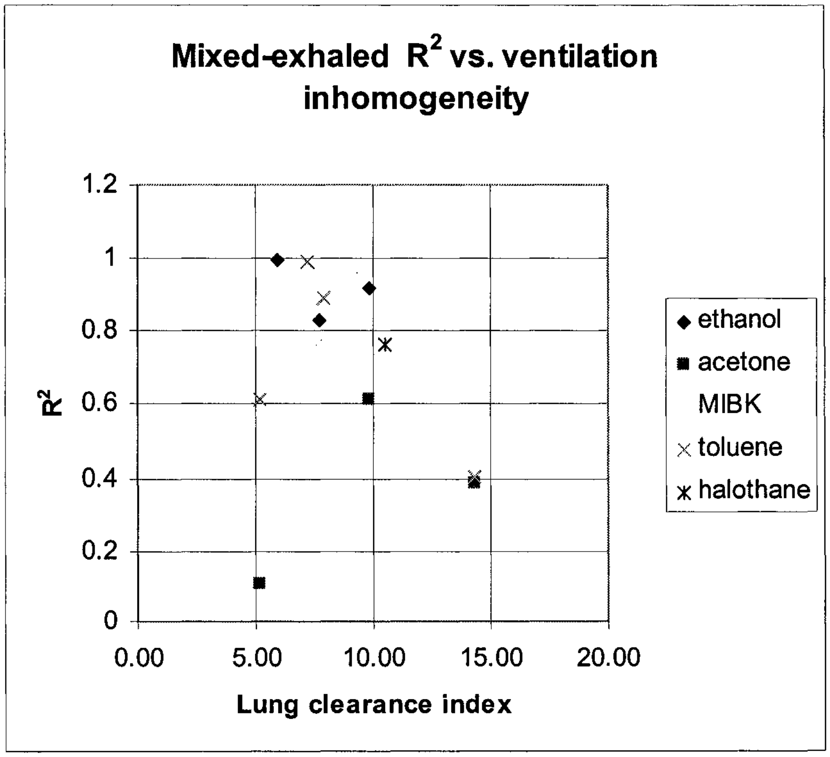

End-exhaled slope/average slope vs. ventilation inhomogeneity

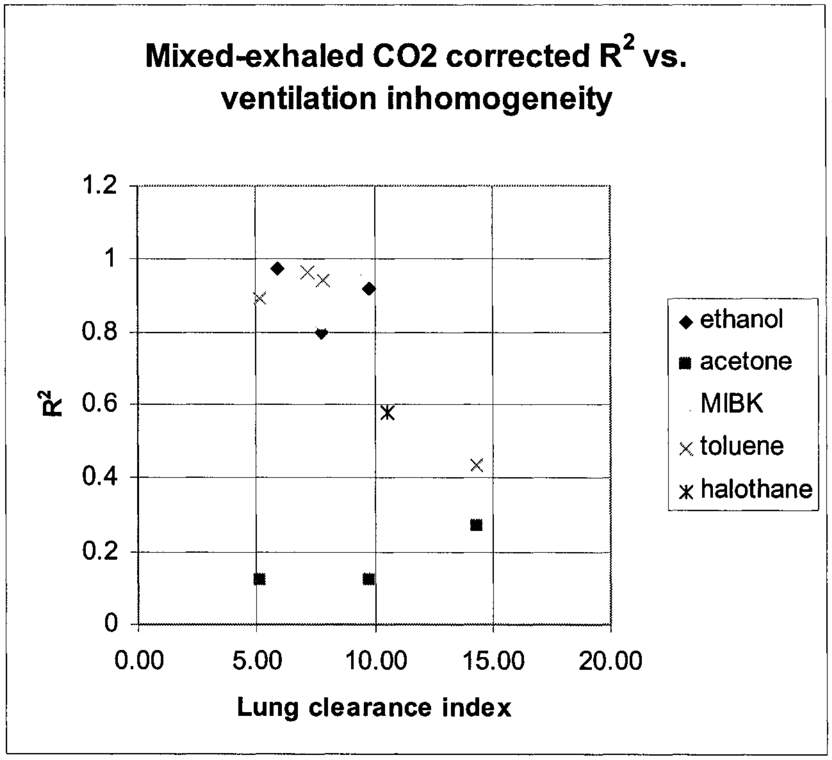

Mixed-exhaled slope/average slope vs. ventilation inhomogeneity


Mixed-exhaled CO2 corrected slope/average slope vs. ventilation inhomogeneity
Slope
4
3.5
3
2.5
2
1.5
1
0.5
0
0.00
5.00
10.00
15.00
20.00
Lung clearance index
◆ ethanol
■ acetone
MIBK
× toluene
⁎ halothane


Rebreathed R^2 vs. ventilation inhomogeneity
R^2
1.2
1
0.8
0.6
0.4
0.2
0
0.00
5.00
10.00
15.00
20.00
Lung clearance index
◆ ethanol
■ acetone
MIBK
× toluene
⁎ halothane


End-exhaled R^2 vs. ventilation inhomogeneity
1.2
1
0.8
0.6
0.4
0.2
0
R^2
0.00
5.00
10.00
15.00
20.00
Lung clearance index
ethanol
acetone
MIBK
toluene
halothane


Mixed-exhaled R^2 vs. ventilation inhomogeneity
1.2
1
0.8
0.6
0.4
0.2
0
R^2
0.00
5.00
10.00
15.00
20.00
Lung clearance index
ethanol
acetone
MIBK
toluene
halothane



Regressions of LCI on slope and correlation:

Linear regressions of the slope and correlation of individual regressions (one subject, one breath method, one chemical) on lung clearance index were performed. The output follows.

```
. bysort solvent: regress rebslope lci
```

```
-> solvent = MIBK

      Source |       SS       df       MS              Number of obs =       3
-------------+------------------------------           F(  1,      1) =    0.23
       Model |  2701.99985     1  2701.99985           Prob > F      =  0.7127
    Residual |  11505.0067     1  11505.0067           R-squared     =  0.1902
-------------+------------------------------           Adj R-squared = -0.6196
       Total |  14207.0066     2   7103.5033           Root MSE      =  107.26
```

```
------------------------------------------------------------------------------
    rebslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         lci |  -21.00055   43.33426    -0.48   0.713    -571.6145    529.6134
       _cons |   262.3709   337.9516     0.78   0.580    -4031.712    4556.454
------------------------------------------------------------------------------
```

```
-> solvent = acetone

      Source |       SS       df       MS              Number of obs =       3
-------------+------------------------------           F(  1,     1) =    0.22
       Model |  166.507853     1  166.507853           Prob > F      =  0.7223
    Residual |  766.158814     1  766.158814           R-squared     =  0.1785
-------------+------------------------------           Adj R-squared = -0.6429
       Total |  932.666667     2  466.333333           Root MSE      =   27.68

------------------------------------------------------------------------------
    rebslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         lci |   2.005313   4.301543     0.47   0.722    -52.65097     56.6616
       _cons |   205.7481   44.94855     4.58   0.137    -365.3774    776.8736
------------------------------------------------------------------------------
```

```
-> solvent = ethanol

      Source |       SS       df       MS              Number of obs =       3
-------------+------------------------------           F(  1,     1) =    1.67
       Model |  1192943.09     1  1192943.09           Prob > F      =  0.4197
    Residual |  716456.906     1  716456.906           R-squared     =  0.6248
-------------+------------------------------           Adj R-squared =  0.2495
       Total |     1909400     2      954700           Root MSE      =  846.44

------------------------------------------------------------------------------
    rebslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         lci |  -395.6693    306.632    -1.29   0.420    -4291.799     3500.46
       _cons |   5506.221   2441.145     2.26   0.266    -25511.47    36523.91
------------------------------------------------------------------------------
```

```
-> solvent = halothane
```

```
insufficient observations


------------------------------------------------------------------------------
-> solvent = toluene

      Source |       SS       df       MS              Number of obs =       4
-------------+------------------------------           F(  1,     2) =    0.16
       Model |  54.7147456     1  54.7147456           Prob > F      =  0.7311
    Residual |  701.912716     2  350.956358           R-squared     =  0.0723
-------------+------------------------------           Adj R-squared = -0.3915
       Total |  756.627462     3  252.209154           Root MSE      =  18.734

------------------------------------------------------------------------------
    rebslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         lci |   1.084857   2.747557     0.39   0.731    -10.73693    12.90664
       _cons |   25.09099   25.54564     0.98   0.430    -84.82301     135.005
------------------------------------------------------------------------------


. bysort solvent: regress endslope lci


------------------------------------------------------------------------------
-> solvent = MIBK

      Source |       SS       df       MS              Number of obs =       3
-------------+------------------------------           F(  1,     1) =    0.06
       Model |  917.138355     1  917.138355           Prob > F      =  0.8439
    Residual |  14643.8215     1  14643.8215           R-squared     =  0.0589
-------------+------------------------------           Adj R-squared = -0.8821
       Total |  15560.9598     2  7780.47992           Root MSE      =  121.01

------------------------------------------------------------------------------
    endslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         lci |  -12.23504   48.88945    -0.25   0.844    -633.4344    608.9643
       _cons |    210.202    381.275     0.55   0.679    -4634.356     5054.76
------------------------------------------------------------------------------


------------------------------------------------------------------------------
-> solvent = acetone

      Source |       SS       df       MS              Number of obs =       3
```

```
-------------+------------------------------           F(  1,      1) =    0.03
       Model |  391.984327     1  391.984327           Prob > F      =  0.8880
    Residual |  12394.0157     1  12394.0157           R-squared     =  0.0307
-------------+------------------------------           Adj R-squared = -0.9387
       Total |       12786     2        6393           Root MSE      =  111.33

------------------------------------------------------------------------------
    endslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         lci |     3.0768   17.30099     0.18   0.888    -216.7531    222.9067
       _cons |   159.9499    180.785     0.88   0.539    -2137.141    2457.041
------------------------------------------------------------------------------
```

```
-> solvent = ethanol

      Source |       SS       df       MS              Number of obs =       3
-------------+------------------------------           F(  1,      1) =    0.04
       Model |   100246.29     1   100246.29           Prob > F      =  0.8718
    Residual |  2405820.38     1  2405820.38           R-squared     =  0.0400
-------------+------------------------------           Adj R-squared = -0.9200
       Total |  2506066.67     2  1253033.33           Root MSE      =  1551.1

------------------------------------------------------------------------------
    endslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         lci |  -114.6982   561.8936    -0.20   0.872    -7254.234    7024.837
       _cons |   3517.979   4473.323     0.79   0.576    -53320.97    60356.93
------------------------------------------------------------------------------
```

```
-> solvent = halothane
insufficient observations
```

```
-> solvent = toluene

      Source |       SS       df       MS              Number of obs =       4
-------------+------------------------------           F(  1,      2) =    1.43
       Model |  796.128005     1  796.128005           Prob > F      =  0.3545
    Residual |  1114.59976     2   557.29988           R-squared     =  0.4167
-------------+------------------------------           Adj R-squared =  0.1250
       Total |  1910.72777     3  636.909255           Root MSE      =  23.607
```

```
------------------------------------------------------------------------------
    endslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         lci |   4.138202     3.4623     1.20   0.355    -10.75887    19.03528
       _cons |   11.72956   32.19101     0.36   0.750    -126.7772    150.2363
------------------------------------------------------------------------------


. bysort solvent: regress mixslope lci

_______________________________________________________________________________
-> solvent = MIBK

      Source |       SS       df       MS              Number of obs =       3
-------------+------------------------------           F(  1,     1) =    0.47
       Model |   34416.514     1   34416.514           Prob > F      =  0.6180
    Residual |  73525.9123     1  73525.9123           R-squared     =  0.3188
-------------+------------------------------           Adj R-squared = -0.3623
       Total |  107942.426     2  53971.2132           Root MSE      =  271.16

------------------------------------------------------------------------------
    mixslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         lci |  -74.94995   109.5489    -0.68   0.618    -1466.901    1317.001
       _cons |    830.683   854.3412     0.97   0.509    -10024.75    11686.12
------------------------------------------------------------------------------


_______________________________________________________________________________
-> solvent = acetone

      Source |       SS       df       MS              Number of obs =       3
-------------+------------------------------           F(  1,     1) =  116.27
       Model |  78503.5087     1  78503.5087           Prob > F      =  0.0589
    Residual |  675.157919     1  675.157919           R-squared     =  0.9915
-------------+------------------------------           Adj R-squared =  0.9829
       Total |  79178.6667     2  39589.3333           Root MSE      =  25.984

------------------------------------------------------------------------------
    mixslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         lci |    43.5421   4.038011    10.78   0.059    -7.765697     94.8499
       _cons |  -101.9279    42.1948    -2.42   0.250    -638.0637     434.208
```

```
------------------------------------------------------------------------------

-------------------------------------------------------------------------------
-> solvent = ethanol

      Source |       SS       df       MS              Number of obs =       3
-------------+------------------------------           F(  1,      1) =    0.35
       Model |  1034759.39     1  1034759.39           Prob > F      =  0.6580
    Residual |  2917040.61     1  2917040.61           R-squared     =  0.2618
-------------+------------------------------           Adj R-squared = -0.4763
       Total |     3951800     2     1975900           Root MSE      =  1707.9

------------------------------------------------------------------------------
    mixslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         lci |   -368.504   618.7194    -0.60   0.658    -8230.079    7493.071
       _cons |   6364.331   4925.722     1.29   0.419     -56222.9    68951.56
------------------------------------------------------------------------------


-------------------------------------------------------------------------------
-> solvent = halothane
insufficient observations


-------------------------------------------------------------------------------
-> solvent = toluene

      Source |       SS       df       MS              Number of obs =       4
-------------+------------------------------           F(  1,      2) =    0.01
       Model |  199.850194     1  199.850194           Prob > F      =  0.9330
    Residual |  44371.6894     2  22185.8447           R-squared     =  0.0045
-------------+------------------------------           Adj R-squared = -0.4933
       Total |  44571.5396     3  14857.1799           Root MSE      =  148.95

------------------------------------------------------------------------------
    mixslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         lci |  -2.073349   21.84531    -0.09   0.933    -96.06613    91.91943
       _cons |   148.7345   203.1085     0.73   0.540    -725.1709     1022.64
------------------------------------------------------------------------------


. bysort solvent: regress mixcslope lci
```

```
-> solvent = MIBK

      Source |       SS       df       MS              Number of obs =       3
-------------+------------------------------           F(  1,     1) =    0.29
       Model |  8449.43384     1  8449.43384           Prob > F      =  0.6853
    Residual |   29084.893     1   29084.893           R-squared     =  0.2251
-------------+------------------------------           Adj R-squared = -0.5498
       Total |  37534.3269     2  18767.1634           Root MSE      =  170.54

------------------------------------------------------------------------------
   mixcslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         lci |  -37.13657   68.90039    -0.54   0.685     -912.599    838.3259
       _cons |   442.4803   537.3347     0.82   0.561    -6385.004    7269.965
------------------------------------------------------------------------------
```

```
-> solvent = acetone

      Source |       SS       df       MS              Number of obs =       3
-------------+------------------------------           F(  1,     1) =   56.78
       Model |  26935.2266     1  26935.2266           Prob > F      =  0.0840
    Residual |  474.380491     1  474.380491           R-squared     =  0.9827
-------------+------------------------------           Adj R-squared =  0.9654
       Total |   27409.607     2  13704.8035           Root MSE      =   21.78

------------------------------------------------------------------------------
   mixcslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         lci |   25.50499   3.384763     7.54   0.084     -17.5025    68.51248
       _cons |  -53.73207   35.36875    -1.52   0.371    -503.1346    395.6705
------------------------------------------------------------------------------
```

```
-> solvent = ethanol

      Source |       SS       df       MS              Number of obs =       3
-------------+------------------------------           F(  1,     1) =    0.61
       Model |  158215.788     1  158215.788           Prob > F      =  0.5780
    Residual |  259584.212     1  259584.212           R-squared     =  0.3787
-------------+------------------------------           Adj R-squared = -0.2426
       Total |      417800     2      208900           Root MSE      =  509.49
```

```
------------------------------------------------------------------------------
   mixcslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         lci |  -144.0945   184.5702    -0.78   0.578    -2489.282    2201.093
       _cons |   3023.937   1469.392     2.06   0.288    -15646.46    21694.34
------------------------------------------------------------------------------

_______________________________________________________________________________
-> solvent = halothane
insufficient observations

_______________________________________________________________________________
-> solvent = toluene

      Source |       SS       df       MS              Number of obs =       4
-------------+------------------------------           F(  1,     2) =    0.00
       Model |  .212757199     1  .212757199           Prob > F      =  0.9956
    Residual |  11210.9346     2  5605.46732           R-squared     =  0.0000
-------------+------------------------------           Adj R-squared = -0.5000
       Total |  11211.1474     3  3737.04913           Root MSE      =   74.87

------------------------------------------------------------------------------
   mixcslope |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         lci |  -.0676491    10.9806    -0.01   0.996    -47.31336    47.17806
       _cons |   75.86017    102.093     0.74   0.535    -363.4107     515.131
------------------------------------------------------------------------------


. bysort solvent: regress rebrsquared lci

_______________________________________________________________________________
-> solvent = MIBK

      Source |       SS       df       MS              Number of obs =       3
-------------+------------------------------           F(  1,     1) =   32.22
       Model |  .078847315     1  .078847315           Prob > F      =  0.1110
    Residual |  .002447113     1  .002447113           R-squared     =  0.9699
-------------+------------------------------           Adj R-squared =  0.9398
       Total |  .081294427     2  .040647214           Root MSE      =  .04947

------------------------------------------------------------------------------
```

```
 rebrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         lci |    .113444   .0199855     5.68   0.111    -.1404958    .3673838
       _cons |  -.0899037   .1558612    -0.58   0.667    -2.070308    1.890501
------------------------------------------------------------------------------

______________________________________________________________________________
-> solvent = acetone

      Source |       SS       df       MS              Number of obs =       3
-------------+------------------------------           F(  1,     1) =    3.64
       Model |  .004907701     1  .004907701           Prob > F      =  0.3072
    Residual |  .001346717     1  .001346717           R-squared     =  0.7847
-------------+------------------------------           Adj R-squared =  0.5694
       Total |  .006254419     2  .003127209           Root MSE      =   .0367

------------------------------------------------------------------------------
 rebrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         lci |   .0108869    .005703     1.91   0.307    -.0615765    .0833503
       _cons |   .4592714   .0595929     7.71   0.082    -.2979282    1.216471
------------------------------------------------------------------------------

______________________________________________________________________________
-> solvent = ethanol

      Source |       SS       df       MS              Number of obs =       3
-------------+------------------------------           F(  1,     1) =  152.94
       Model |  .004515783     1  .004515783           Prob > F      =  0.0514
    Residual |  .000029526     1  .000029526           R-squared     =  0.9935
-------------+------------------------------           Adj R-squared =  0.9870
       Total |  .004545309     2  .002272654           Root MSE      =  .00543

------------------------------------------------------------------------------
 rebrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         lci |   .0243438   .0019684    12.37   0.051    -.0006676    .0493553
       _cons |   .7054847   .0156711    45.02   0.014     .5063644     .904605
------------------------------------------------------------------------------

______________________________________________________________________________
-> solvent = halothane
insufficient observations
```

```
------------------------------------------------------------------------------
-> solvent = toluene

      Source |       SS       df       MS              Number of obs =       4
-------------+------------------------------           F(  1,     2) =    1.63
       Model |  .008983694     1  .008983694           Prob > F      =  0.3294
    Residual |  .010991717     2  .005495858           R-squared     =  0.4497
-------------+------------------------------           Adj R-squared =  0.1746
       Total |  .019975411     3   .00665847           Root MSE      =  .07413

------------------------------------------------------------------------------
 rebrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         lci |  -.0139011   .0108727    -1.28   0.329    -.0606826    .0328805
       _cons |   1.020994   .1010899    10.10   0.010     .5860392    1.455949
------------------------------------------------------------------------------


. bysort solvent: regress endrsquared lci


------------------------------------------------------------------------------
-> solvent = MIBK

      Source |       SS       df       MS              Number of obs =       3
-------------+------------------------------           F(  1,     1) =    2.11
       Model |  .001611058     1  .001611058           Prob > F      =  0.3836
    Residual |  .000762323     1  .000762323           R-squared     =  0.6788
-------------+------------------------------           Adj R-squared =  0.3576
       Total |  .002373382     2  .001186691           Root MSE      =  .02761

------------------------------------------------------------------------------
 endrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         lci |    .016216   .0111547     1.45   0.384    -.1255178    .1579498
       _cons |   .7462774   .0869923     8.58   0.074    -.3590643    1.851619
------------------------------------------------------------------------------


------------------------------------------------------------------------------
-> solvent = acetone

      Source |       SS       df       MS              Number of obs =       3
-------------+------------------------------           F(  1,     1) =    0.09
```

```
       Model |  .016759652     1  .016759652           Prob > F      =  0.8102
    Residual |  .177403889     1  .177403889           R-squared     =  0.0863
-------------+------------------------------           Adj R-squared = -0.8274
       Total |  .194163541     2  .097081771           Root MSE      =  .42119

------------------------------------------------------------------------------
 endrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         lci |   .0201186   .0654555     0.31   0.810    -.8115729    .8518101
       _cons |   .1300419   .6839713     0.19   0.880    -8.560637    8.820721
------------------------------------------------------------------------------
```

```
-> solvent = ethanol

      Source |       SS       df       MS              Number of obs =       3
-------------+------------------------------           F(  1,     1) =    0.04
       Model |  .000225582     1  .000225582           Prob > F      =  0.8691
    Residual |  .005188603     1  .005188603           R-squared     =  0.0417
-------------+------------------------------           Adj R-squared = -0.9167
       Total |  .005414185     2  .002707092           Root MSE      =  .07203

------------------------------------------------------------------------------
 endrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         lci |    .005441   .0260944     0.21   0.869    -.3261201     .337002
       _cons |   .9089606   .2077418     4.38   0.143    -1.730649     3.54857
------------------------------------------------------------------------------
```

```
-> solvent = halothane
insufficient observations
```

```
-> solvent = toluene

      Source |       SS       df       MS              Number of obs =       4
-------------+------------------------------           F(  1,     2) =    0.02
       Model |   .00018598     1   .00018598           Prob > F      =  0.9061
    Residual |  .020915484     2  .010457742           R-squared     =  0.0088
-------------+------------------------------           Adj R-squared = -0.4868
       Total |  .021101463     3  .007033821           Root MSE      =  .10226
```

```
------------------------------------------------------------------------------
 endrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         lci |  -.0020001   .0149982    -0.13   0.906    -.0665322    .0625319
       _cons |   .8279259    .139447     5.94   0.027      .227934    1.427918
------------------------------------------------------------------------------


. bysort solvent: regress mixrsquared lci

________________________________________________________________________________
-> solvent = MIBK

      Source |       SS       df       MS              Number of obs =       3
-------------+------------------------------           F(  1,     1) =    6.74
       Model |  .031335835     1  .031335835           Prob > F      =  0.2341
    Residual |   .00465231     1   .00465231           R-squared     =  0.8707
-------------+------------------------------           Adj R-squared =  0.7415
       Total |  .035988145     2  .017994072           Root MSE      =  .06821

------------------------------------------------------------------------------
 mixrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         lci |   .0715169   .0275564     2.60   0.234    -.2786202     .421654
       _cons |   .2729039   .2149045     1.27   0.425    -2.457716    3.003524
------------------------------------------------------------------------------

________________________________________________________________________________
-> solvent = acetone

      Source |       SS       df       MS              Number of obs =       3
-------------+------------------------------           F(  1,     1) =    0.46
       Model |  .041033079     1  .041033079           Prob > F      =  0.6191
    Residual |  .088298301     1  .088298301           R-squared     =  0.3173
-------------+------------------------------           Adj R-squared = -0.3655
       Total |  .129331379     2   .06466569           Root MSE      =  .29715

------------------------------------------------------------------------------
 mixrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         lci |   .0314798   .0461786     0.68   0.619    -.5552753    .6182349
       _cons |   .0622807    .482539     0.13   0.918    -6.068959    6.193521
------------------------------------------------------------------------------
```

```
───────────────────────────────────────────────────────────────────────────────
-> solvent = ethanol

      Source |       SS       df       MS              Number of obs =       3
-------------+------------------------------           F(  1,     1) =    0.20
       Model |  .002305362     1  .002305362           Prob > F      =  0.7297
    Residual |   .01128178     1   .01128178           R-squared     =  0.1697
-------------+------------------------------           Adj R-squared = -0.6607
       Total |  .013587142     2  .006793571           Root MSE      =  .10622

------------------------------------------------------------------------------
 mixrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         lci |  -.0173937   .0384779    -0.45   0.730    -.5063017    .4715143
       _cons |   1.049671   .3063285     3.43   0.181    -2.842602    4.941944
------------------------------------------------------------------------------


───────────────────────────────────────────────────────────────────────────────
-> solvent = halothane
insufficient observations


───────────────────────────────────────────────────────────────────────────────
-> solvent = toluene

      Source |       SS       df       MS              Number of obs =       4
-------------+------------------------------           F(  1,     2) =    1.24
       Model |  .080702358     1  .080702358           Prob > F      =  0.3810
    Residual |  .129925976     2  .064962988           R-squared     =  0.3832
-------------+------------------------------           Adj R-squared =  0.0747
       Total |  .210628334     3  .070209445           Root MSE      =  .25488

------------------------------------------------------------------------------
 mixrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         lci |  -.0416642   .0373812    -1.11   0.381    -.2025025    .1191741
       _cons |   1.084396   .3475547     3.12   0.089    -.4110116    2.579803
------------------------------------------------------------------------------


. bysort solvent: regress mixcrsquared lci

───────────────────────────────────────────────────────────────────────────────
```

```
-> solvent = MIBK

      Source |       SS       df       MS              Number of obs =       3
-------------+------------------------------           F(  1,      1) =    0.54
       Model |  .003563279     1  .003563279           Prob > F      =  0.5962
    Residual |  .006582841     1  .006582841           R-squared     =  0.3512
-------------+------------------------------           Adj R-squared = -0.2976
       Total |  .010146121     2   .00507306           Root MSE      =  .08113

------------------------------------------------------------------------------
mixcrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         lci |   .0241164   .0327789     0.74   0.596    -.3923792    .4406121
       _cons |   .7067408   .2556335     2.76   0.221    -2.541391    3.954873
------------------------------------------------------------------------------


________________________________________________________________________________
-> solvent = acetone

      Source |       SS       df       MS              Number of obs =       3
-------------+------------------------------           F(  1,      1) =    3.03
       Model |  .011183822     1  .011183822           Prob > F      =  0.3318
    Residual |  .003687585     1  .003687585           R-squared     =  0.7520
-------------+------------------------------           Adj R-squared =  0.5041
       Total |  .014871407     2  .007435704           Root MSE      =  .06073

------------------------------------------------------------------------------
mixcrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         lci |   .0164346    .009437     1.74   0.332    -.1034744    .1363436
       _cons |   .0111218   .0986114     0.11   0.929    -1.241855    1.264099
------------------------------------------------------------------------------


________________________________________________________________________________
-> solvent = ethanol

      Source |       SS       df       MS              Number of obs =       3
-------------+------------------------------           F(  1,      1) =    0.08
       Model |  .001094399     1  .001094399           Prob > F      =  0.8294
    Residual |  .014522453     1  .014522453           R-squared     =  0.0701
-------------+------------------------------           Adj R-squared = -0.8598
       Total |  .015616851     2  .007808426           Root MSE      =  .12051
```

```
------------------------------------------------------------------------------
mixcrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         lci |  -.0119842   .0436559    -0.27   0.829    -.5666844     .542716
       _cons |    .990677    .347551     2.85   0.215    -3.425378    5.406732
------------------------------------------------------------------------------
```

```
-> solvent = halothane
insufficient observations
```

```
-> solvent = toluene

      Source |       SS       df       MS              Number of obs =       4
-------------+------------------------------           F(  1,     2) =   11.53
       Model |  .161182754     1  .161182754           Prob > F      =  0.0769
    Residual |  .027958658     2  .013979329           R-squared     =  0.8522
-------------+------------------------------           Adj R-squared =  0.7783
       Total |  .189141412     3  .063047137           Root MSE      =  .11823

------------------------------------------------------------------------------
mixcrsquared |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         lci |  -.0588816   .0173406    -3.40   0.077     -.133492    .0157289
       _cons |   1.315951   .1612253     8.16   0.015      .622254    2.009647
------------------------------------------------------------------------------
```

VITA

Marie Martin was born in Pomona, California and grew up in Fullerton, California and Huntsville, Alabama. She earned a Bachelor of Science in Environmental Science from Auburn University in 1995.

Marie now lives in Dallas, Texas and seeks to be a general practitioner and trainer of industrial hygiene and safety.