CRADA Final Report
for
CRADA Number ORNL99-0562

PERFLUORO(METHYLCYCLOHEXANE) TRACER
TAGGING TEST AND DEMONSTRATION

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J. A. Fraser
Tracer Detection Technology Corp.

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Abstract: On February 14 and 15, 2000, a demonstration of current perfluorocarbon tagging technology and the future potential of these methods was held at Oak Ridge National Laboratory (ORNL). The demonstration consisted of a brief technical discussion followed by a laboratory demonstration. The laboratory demonstrations included the detection of letters, parcels, briefcases and lockers containing perfluorocarbon-tagged papers. Discrimination between tagged and non-tagged items and between three perfluorocarbon tags was demonstrated along with the detection of perfluorocarbon in a background of non-fluorinated volatile organic solvent. All demonstrations involved real-time detection using a direct sampling ion trap mass spectrometer. The technical results obtained at ORNL during and in preparation for the demonstration are presented in Appendix 1 to assist Tracer Detection Technology Corp. in further evaluating their position on development and marketing of perfluorocarbon tracer technology.

Statement of Objectives: The objectives of this CRADA were to prepare and conduct a demonstration of perfluorocarbon tagging technology and to provide Tracer Detection Technology Corp. with an scientific evaluation of the technology.

Benefits to the Funding DOE Office's Mission: DOE can leverage the work performed under this CRADA in support of its on-going research and development efforts related to the protection of key DOE assets.

Technical Discussion of Work Performed by All Parties: ORNL performed experiments necessary to design and conduct a demonstration of current perfluorocarbon

tagging technology and to provide a scientific assessment of the that technology to Tracer Detection Technology Corp. The technology assessment prepared by ORNL is given in Appendix 1.

Tracer Detection Technology Corp. assisted in coordinating the technology demonstration held at ORNL and identified and extended invitations to appropriate federal, state and local law enforcement personnel, as well as representatives from federal funding agencies and the Office of Law Enforcement Technology Commercialization.

The technology demonstration was performed at ORNL on February 14 and 15, 2000. The demonstration was attended by representatives from the National Institute of Justice, Office of Law Enforcement Technology Commercialization, Federal Bureau of Investigation and other federal agencies, and the Knoxville Police Department. Mr. Jay Fraser, Tracer Detection Technology Corp., also attended the demonstration.

Inventions (Made or Reported): None

Commercialization Possibilities: Opportunities for commercialization of the technologies demonstrated under this program are viewed as existing within the private sector and government agencies. Addition fundamental research is required to produce commercial products. Issues for further study are discussed in Appendix 1.

Plans for Future Collaboration: No current plans.

Conclusions: The work under CRADA ORNL99-0562 with Tracer Detection

Technology Corp. has been completed. The technical demonstration was conducted on

February 14 and 15, 2000. The technical evaluation of perfluorocarbon tagging

technologies is attached to this CRADA Final Report as Appendix 1.

Appendix1: Perfluorocarbon Tagging Demonstration and Technology Evaluation

Perfluorocarbon Taggant Demonstration and Technology Evaluation

By

M. E. Sigman, M. B. Wise and M. R. Guerin

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(1) Executive Summary: On February 14 and 15, 2000, a demonstration of current perfluorocarbon tagging technology and the future potential of these methods was held at Oak Ridge National Laboratory (ORNL). The demonstration consisted of a brief technical discussion followed by a laboratory demonstration. The laboratory demonstrations included the detection of letters, parcels, briefcases and lockers containing perfluorocarbon-tagged papers. Discrimination between tagged and non-tagged items and between three perfluorocarbon tags was demonstrated along with the detection of perfluorocarbon in a background of non-fluorinated volatile organic solvent. All demonstrations involved real-time detection using a direct sampling ion trap mass spectrometer.   The demonstration was attended by representatives from the National Institute of Justice, Office of Law Enforcement, Technology Commercialization, Federal Bureau of Investigation and other federal agencies, as well as Mr. Jay Fraser, Tracer Detection Technology Corp. This report describes technical results obtained at ORNL in preparation for the demonstration. The data obtained on wax crayon perfluorocarbon emission rates and stabilities of cyclodextrin formulations were important in designing and optimizing demonstrations. The essential elements of our findings are presented here to assist Tracer Detection Technology Corp. in further evaluating their position on development and marketing of perfluorocarbon tracer technology.

(2) **Scientific Considerations/Data:** In preparation for a demonstration of perfluorocarbon tagging technology, several experiments were conducted to further characterize the taggants and detection systems. These tests were conducted to facilitate the preparation of the demonstrations described below.

2.1 <u>Perfluorocarbon physical data</u>: Four perfluorocarbons were utilized in these tests. They included perfluorocyclohexane (PFCH), perfluoro(methyl)cyclohexane (PFMCH), perfluoro-1,3-dimethylcyclohexane (PF-1,3-DMCH) and perfluoro(methyl)decalin (PFMD). These four representative perfluorocarbons vary dramatically in boiling point, as demonstrated in Table 1 along with the boiling point of perfluorodecalin (PFD). PFD was not utilized in this work. PFD, a mixture of cis and trans decalins, has found utility in various medical applications (vide infra). The chemical structrues for these compounds are shown in Figure 1.

Table 1: Perfluorocarbon Chemical Abstracts Number, formula weight (g/mol) and boiling point (°C).

Perfluorocarbon	CAS #	FW (g/mol)	bp (^{o}C)
PFCH	[355-68-0]	300	51(subl.)*
PFMCH	[355-02-2]	350	76
PF-1,3-DMCH	[335-27-3]	400	102
PFD	[306-94-5]	462	142
PFMD	[306-92-3]	512	160

* PFCH is a solid at room temperature and sublimes at 51°C.
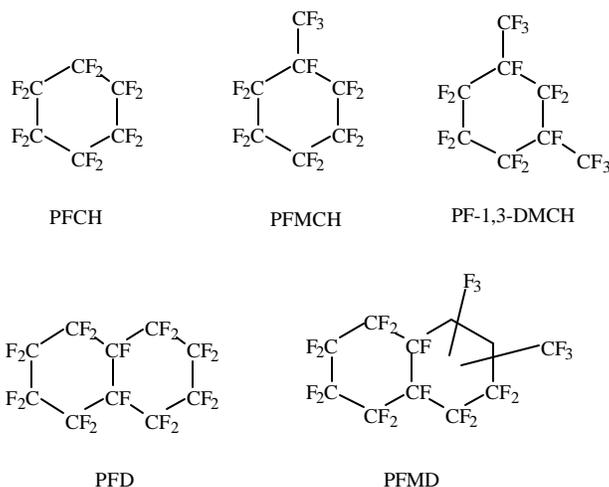
Figure 1: Chemical structrues of the perfluorocarbons listed in Table 1.

2.2 Perfluorocarbon formulations: Two formulations were utilized in this work, perfluorocarbon/wax crayons and perfluorocarbon/β-cyclodextrin host guest complexes. The formulations were characterized with regard to their perfluorocarbon release rates to allow for the development of simple models to guide the development of demonstrations and to illustrate important points relevant to real-world applications.

2.2.1 *Perfluoro(methyl)cyclohexane/**b**-Cyclodextrin complex:* Cyclodextrins (CD) are derived from enzymatic hydrolysis of starch. They are cyclic oligosaccharides consisting of six (α), seven (β) or eight (γ) interlinked [α-(1→4)]-D-glycocyl units. The cyclodextrins form a bowl-shaped structure with a hydrophobic interior that can readily complex non-polar organic compounds. In the case of a perfluorocarbon, the complexation is aided by a complementarity in charge, as shown in Figure 2A. The figure shows the electrostatic potential superimposed on the electron density for both β-CD and PFMCH. The colors

A   B
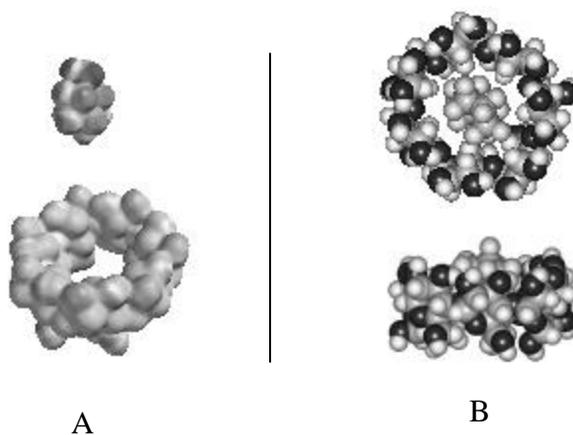
Figure 2: (A) Electrostatic potential superimposed on electron density maps for PFMCH and b-CD. (B) Space filling models of PFMCH inside the cavity of b-CD.

represent the response to a positive test charge and range from blue (repulsive) to red (attractive). The important feature is the complimentarity between the PFMCH (mostly red on fluorine) and the interior cavity of the cyclodextrin (mostly blue-green), implying a favorable electrostatic interaction, provided that PFMCH fits within the cyclodextrin cavity. The nature of the fit is shown in Figure 2B. The figure depicts a space filling model of PFMCH inside β-CD, as viewed from above and from the side.

In spite of the volatility of PFMCH (Table 1), the perfluorocarbon is quite stable when complexed with β-CD. Sample of PFMCH/β-CD prepared at ORNL and by Tracer Detection Technology Corp. have been shown to retain the perfluorocarbon in excess of one year. These complexes should therefore be considered as a long-term source of PFMCH. The material is produced as a crystalline solid, as shown in Figure 3. The
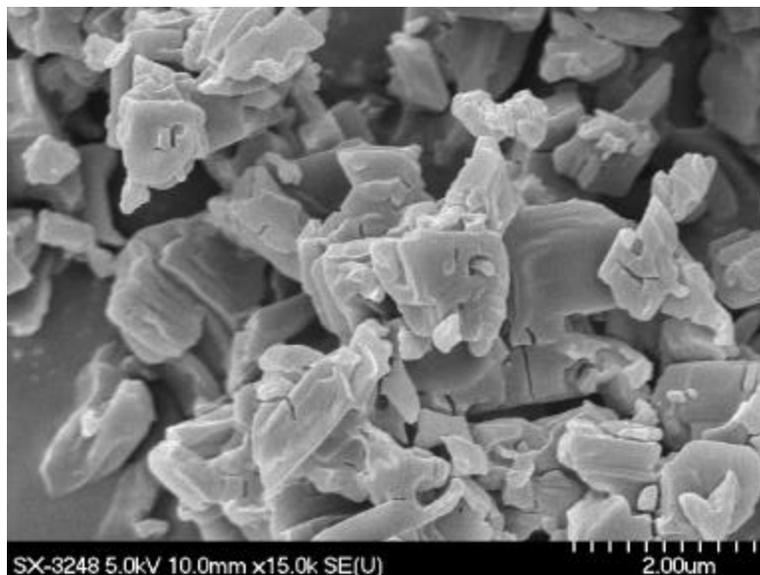
Figure 3: SEM image of PFMCH/b-CD complex crystals.

crystal dimensions are typically 1 mm and less. The material can be ground to produce finer powders.

2.2.2 *Perfluorocarbon/wax crayons:* Two types of wax, paraffin and bees wax, have been

used at ORNL to prepare perfluorocarbon/wax crayons. In these items, cyclodextrins are

not used. Without the cyclodextrin, the perfluorocarbon release is much faster. Paraffin

wax consists of an assortment of high molecular weight straight chain hydrocarbons,

whereas bees wax is composed of long chain fatty acid esters. Both waxes work well for

the preparation of perfluorocarbon-containing crayons. Crayons prepared at a 13% (w/w)

loading of perfluorocarbon show minimal to no weight loss on a mg scale (500 mg total

crayon weight) when stored open to the atmosphere over month periods of time.

However, when the crayons are used to mark a surface, the fluorocarbon escapes at fairly

rapid rate. The escape profile within a closed container generally contains two

exponential components. The minor component is typically quite fast ($t_{1/2} \sim 1.7$ min)

while the major component has a longer halflife. A typical perfluorocarbon escape profile

is shown in Figure 4. The data in Figure 4 shows the vapor concentration of PFMCH

reaching the 250-300 ppmv range within 100 minutes after marking a single piece of
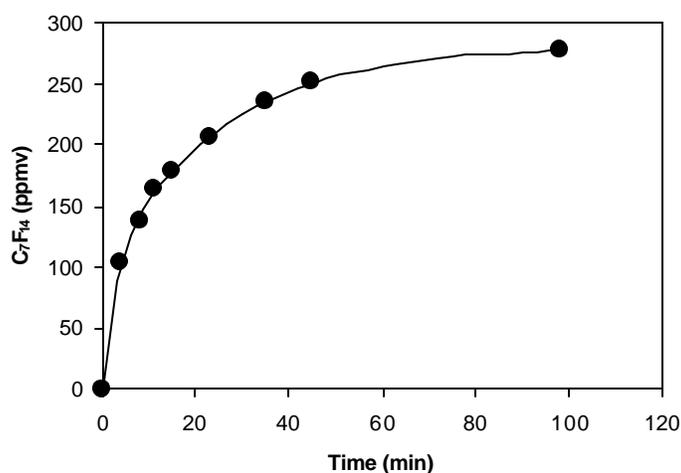
Figure 4: Vapor concentration of PFMCH release from a crayon-marked paper inside an IR cell.

paper (approximately 50 mg of bees wax crayon) and placing the paper inside of a static 160 ml volume IR cell. The fitted line through the data contains two exponential components, the first (33%) having a $t_{1/2}$ of 1.7 min and the second (66%) having a $t_{1/2}$ of 17.3 min. The fast component may correspond to rapid evaporation of liquid perfluorocarbon trapped as a droplet within the wax and the slower component may represent release of perfluorocarbon dissolved into
the wax matrix.

The $t_{1/2}$ values for PFMCH, PF-1,3-DMCH and PFMD in various wax crayons are given in Table 2. All release profiles have $t_{1/2}$ values of less than 1 h and any relationships between perfluorocarbon and wax structure is complex. Further study is required to determine these relationships. The short $t_{1/2}$ values make the wax crayon formulations ideal for a fast release of perfluorocarbon. Coupling the wax crayon technology with a stimulated release mechanism would enhance the utility of the material. Slower release formulations present detection challenges as discussed below.

Table 2: Perfluorocarbon release rates from wax crayons.

Perfluorocarbon/wax	$t_{1/2}$ (min)	Method
PFMCH/Bees Wax	17	IR
PFMCH/Paraffin Wax	13	IR
PF-1,3-DMCH/Bees Wax	46	IR
PF-1,3-DMCH/Bees Wax	13	IR
PFMD/Paraffin Wax	27	IR

2.3 <u>Perfluorocarbon detection</u>: The two methods of perfluorocarbon detection utilized in this work were IR absorbance and direct sampling ion trap mass spectrometry. Infrared (IR) absorption was used to measure release rates by perfluorocarbon/wax crayon

formulations, as discussed above. The limit of detection by IR absorption for the

perfluorocarbons studied here is in the low ppmv range. The direct sampling ion trap

mass spectrometer (DSITMS) technology was developed at ORNL. When operated in the

negative ion chemical ionization mode, the DSITMS gives real-time detection levels in

the low ppbv or upper pptv range for the perfluorocarbons employeed in this study. Field-

portable DSITMS instruments have been developed and deployed by ORNL staff;

however, the size of the instrument currently limits its use to portal or "chokepoint"

scenarios. Perfluorocarbons are also detectable by field-portable gas chromatographs with

electron capture detectors (GC/ECD), as previously employed by Tracer Detection

Technology Corp. in various field demonstrations. The detection limits for

perfluorocarbon detection by GC/ECD are expected to be in the upper pptv range. To our

knowledge, other promising detection technologies, such as ion mobility, have not been

tested for perfluorocarbon detection.

2.4 <u>Chokepoint model</u>: The data contained in this report allow us to make some simple

calculations concerning an idealized chokepoint and to consider the implications for

perfluorocarbon continuous release formulations.

The idealized chokepoint model is based on one of the scenarios used for the

demonstrations discussed below. The model, shown graphically in Figure 5, consists of a

chokepoint having dimensions of 12 x 12 x 18 inches, to give a total volume of 2.59×10^3

in^3 (4.24×10^{-2} m^3). These dimensions are not dramatically different from an airport

12" x 12" x 18"
$4.24 \times 10^{-2} \ m^3$
10 s residence time
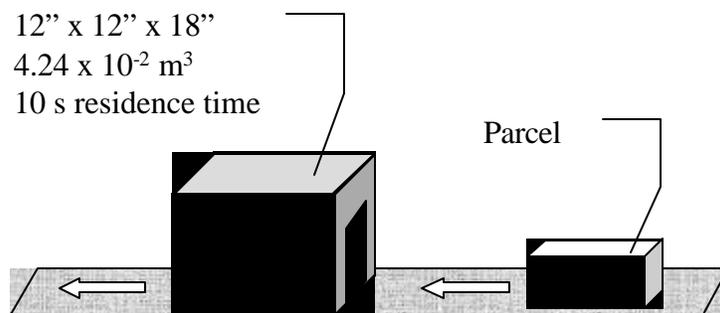
Parcel

Figure 5: Idealized chokepoint model.

security x-ray portal. The model further assumes that 50 mg of a 13% w/w crayon is used

to mark a parcel. The perfluorocarbon is assumed to penetrate the parcel container and

immediately fill the chokepoint. The parcel is allowed to remain resident in the

chokepoint for a period of 10 seconds, during which time it is off-gassing

perfluorocarbon into the total chokepoint volume.The vapor concentration of

perfluorocarbon that builds up inside the chokepoint is a function of the rate that the

marked paper emitts the tracer and the length of time between when the package is

marked and when it enters the chokepoint. This assumes an exponential emission of

perfluorocarbon into the vapor phase, as demonstrated for the wax crayons used in this

work. The graph in Figure 6 shows the vapor concentrations that would be obtained

under this model given realistic crayon emission rates for a parcel interrogated up to 3 h

after marking. It can be seen from Figure 6, that for crayons emitting with a short $t_{1/2}$ (i.e.

15 min), vapor concentrations exceeding 100 ppbv can be obtained immediately after the
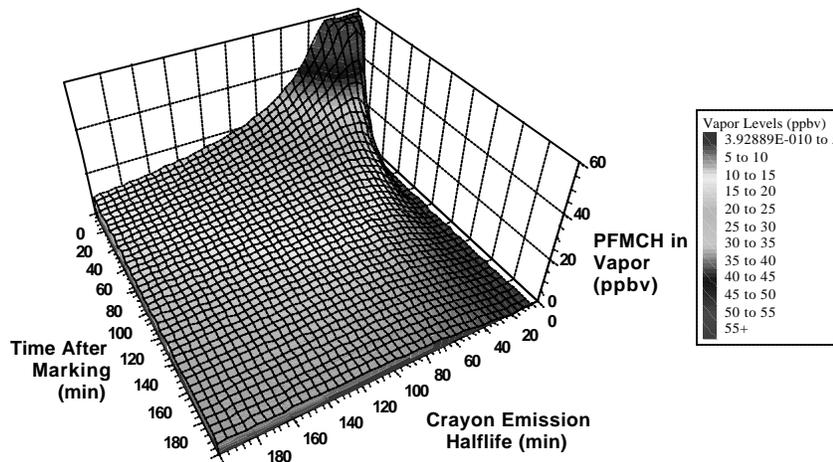
Figure 6: Vapor concentrations obtained under the model in Figure 5 calculated at a series of crayon emission rates.

parcel enters the chokepoint. However, the levels drop below 10 ppbv (the yellow band) within 1 hour. In the case of slower emitting crayons (i.e. $t_{1/2} = 80$ min), although the initial levels are lower, the vapor concentration remains above 10 ppbv for nearly 2 hours.

The implications of the data in Figure 6 are clear. Although it may be possible to design constantly emitting formulations with extended lifetimes, the emitted levels become so low that it becomes impossible to continuously detect the perfluorocarbon in real time. There are several methods to circumvent this limitation. The requirement of real time detection can be dropped, allowing large volumes of air to be sampled by methods that can remove and concentrate the perfluorocarbon. Using this methodology, it would be possible to lower the detection limits and retain near-real time detection. Alternatively, the sample could be allowed a longer residence time in the chokepoint; however, this may not be practical in all cases. New technologies with lower detection

limits and novel formulations providing timed release would also serve to obviate the limitations discussed above.

The demonstrations discussed below make use of perfluorocarbon/wax formulations that emit the fluorocarbon with halflives of approximately 15 min. In the simulated chokepoint demonstrations (those mimicing this simple model), the length of time that the perfluorocarbon could be detected was approximately 1 h. Longer detection times were possible in some instances. A complete understanding of all factors controlling the length of time that the perfluorocarbon can be detected is a topic for further research.

2.5 Health considerations: It is known that perfluorocarbons can be retained in the human body for extended periods of time. This is particularly obvious in the presence of technologies such as the DSITMS which provides very low detection levels in real-time. In the course of preparing for the demonstrations described below, it was noted that perfluorocarbon could be detected from one of the researchers at ORNL (breath, skin, urine) for three days after limited contact with a wax crayon formulation. In order to address any possible health considerations associated with long-term chronic exposure to perfluorocarbons, researchers in ORNL's Life Sciences Division were asked to review the appropriate literature and prepare a report on their findings. A copy of their report is attached as Attachment I to this document.

**(3)Demonstrations Performed:** On February 14 and 15, the following series of demonstrations were performed at ORNL.

3.1 Perfluorocarbon Detection by DSITMS: Detection of perfluorocarbons by DSITMS was demonstrated to highlight the real-time capabilities of the method, the low detection

limits and strong signal-to-noise. The computer display shown in Figure 7 demonstrates the detection both PFMCH and PF-1,3-DMCH at low ppbv levels by DSITMS.

3.2 Detection and Descrimination of Perfluorocarbon Taggants In Envelopes: Ten identical business envelopes, each containing a single folded 8.5 x 11 inch piece of paper, were numbered sequentially. A single mark was placed on an index card using a PFMCH/bees wax crayon and the card was placed inside one of the envelopes chosen at random by an independent observer. Likewise, a mark from a PF-1,3-DMCH crayon was placed on a second index card which was put into a randomly selected envelope. An independent operator of the DSITMS (M. B. Wise), who had no knowledge of which envelope contained the marked cards, was allowed to examine each envelope in turn, approximately 5 min after marking the cards. The two envelopes containing marked cards were easily distinguished from the envelopes that did not contain cards and the individual index cards were readily distinguished based on the molecular ions of their taggants. The length of time that PFDMCH could be detected emitting from an envelope was not determined. Fairly close proximity of the probe to the envelope is required for detection. Detection of a PFDMCH (m/z = 400) marked envelope by DSITMS is shown in Figure 8. This demonstration illustrates the use of perfluorocarbons to track marked items through, for example, the postal service.

3.3 Detection of Perfluorocarbons at a Simulated Chokepoint: Three numbered cardboard boxes (5" x 5" x 12") were used in this demonstration. A single mark was placed on an index card using a PFMCH/bees wax crayon and the card was placed inside one of the boxes chosen at random by an independent observer. A single mark from a PF-1,3-DMCH crayon was also placed on a second index card which was put into a randomly

selected box. The boxes were passed through a simulated chokepoint (12" x 12" x 18")

approximately 5 minutes after placing the marked cards inside the box, while allowing a

10 second residence time in the chokepoint. The chokepoint was static (no mechanical air

circulation) but not fully closed at the bottom. The air inside the chokepoint enclosure

was sampled by the DSITMS. M. B. Wise, functioning as an independent operator of the

DSITMS with no knowledge of which box contained a marked card, easily identified the

boxes containing marked cards. In this demonstration, it was also possible to readily

distinguish between the index cards. The boxes containing the marked cards were

detectable within the chokepoint for approximately 1 hour after the marked card was
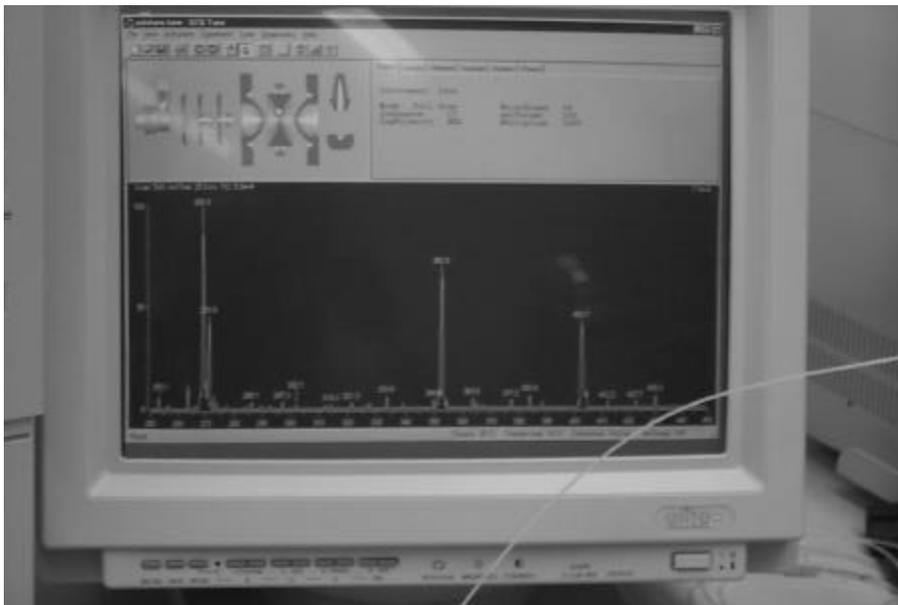
Figure 7: The DSITMS computer display demonstrates the detection both PFMCH and PF-1,3-DMCH at low ppbv levels.

Figure 8: Detection of a PFDMCH (m/z = 400) marked envelope by DSITMS.

Figure 9: A box enters the simulated chokepoint for DSITMS interrogation.
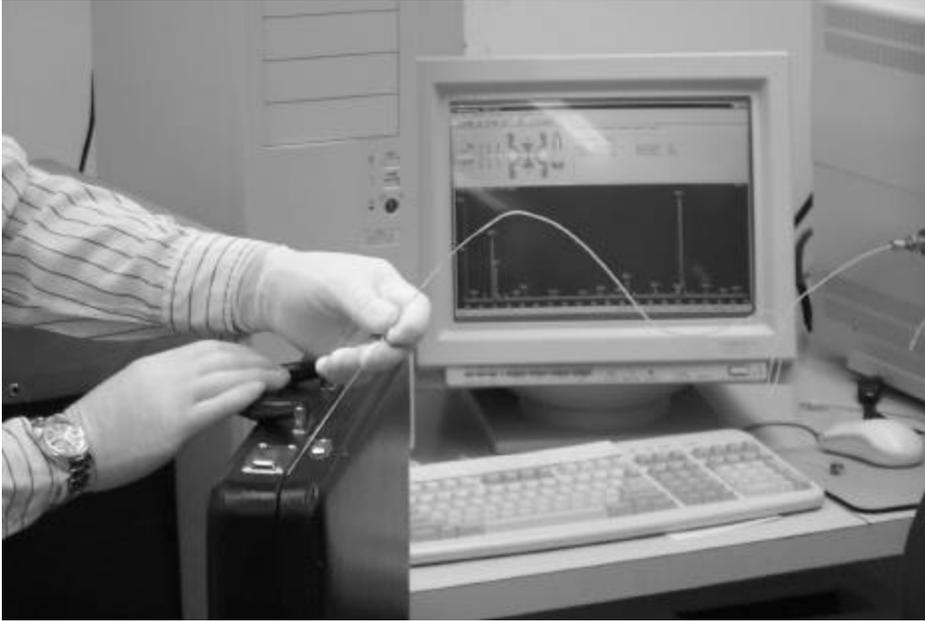
Figure 10: DSITMS detection of PF-1,3-DMCH from a marked item inside a briefcase.

placed inside the box. The detection period is in fair agreement with the model

chokepoint discussed above. Figure 9 shows a photograph taken as a box enters the

simulated chokepoint for DSITMS interrogation.

3.4 <u>Detection of Perfluorocarbon Taggants in "Lockers</u>:" A 3" x 5" note card was marked

with a PF-1,3-DMCH/bees wax crayon and placed inside a laboratory drawer

to simulate a marked item inside a locker. The drawer containing the perfluorocarbon-

marked item was readily detected outside of the drawer, allowing for identification of the

drawer holding the marked item. The perfluorocarbon could be detected in the drawer by

the DSITMS within minutes. The length of time that the marked item could be detected

was not determined. Detection for a period of approximately 1 hour is estimated based on

crayon off-gassing rates and detection limits

3.5 <u>Detection of Perfluorocarbon Taggants in a Briefcase</u>: A 3" x 5" note card was marked with a PF-1,3-DMCH/bees wax crayon and placed inside a standard briefcase. The perfluorocarbon was detected at the closure seam of the case for several hours after tagging. Figure 10 depicts this demonstration and clearly illustrates an additional chokepoint application.

3.6 <u>Detection of PFCH in Acetone</u>: A sample of acetone containing trace quantities of PFCH was placed inside a 10 ml vial. When the lid was loosened, the PFCH (m/z = 300) could easily be detected. This demonstration illustrates the detection of trace amounts of perfluorocarbon in the presence of extremely high levels of a secondary chemical such as acetone. Acetone, a commonly used drug-processing solvent, exhibits little response in the DSITMS operating in the NICI mode. Similarly, because of the mass resolution of the DSITMS, it would be very difficult to mask a perfluorocarbon signature with an odor (coffee) or chemical distractant. This demonstration also illustrates the possibility of using a volatile solvent delivery system as a method of applying a PFCH thin film residue to a surface.

3.7 <u>Detection of PFMCH/β-CD Marked Paper</u>: A one dollar bill was lightly dusted on one end with finely divided PFMCH/β-CD powder. It was demonstrated to those in attendance that PFMCH could be detected by DSITMS on the end of the dollar bill that had been dusted when the currency was physically probed with the DSITMS sampling tube. PFMCH vapor could not be detected immediately above the marked portion of the currency and none could be detected by physical probing on the unmarked end of the dollar bill. The PFMCH/β-CD powder was not detectable by visual inspection of the dollar bill. The PFMCH/β-CD complex can be detected months after being placed on the

paper. We anticipate that a lifetime of years is feasible for this material. This demonstration highlights the use of PFMCH/β-CD complex as a method for marking currency and documents. The PFMCH/β-CD powder can be transferred from the paper to the hand of a person handling the paper. The use of a physical probing method would be practical for tracking the movement of marked currency over a large area by conducting inspections at banks. Automation of the system would make the process less labor intensive.

3.8 Detection of PFMCH Enclosed Within Multiple Containers: A PFMCH/paraffin wax crayon was placed in a tightly closed 20 ml sample vial. The vial was placed inside of a one pint paint can that was closed by the standard pressure closure. The pint can was placed inside of a one-gallon paint can that was also closed. The PFMCH could be detected around the closure of the one-gallon can several hours after placing the vial inside, demonstrating the difficulty of confining perfluorocarbons by simple physical methods. Surface contamination is ruled out based on the length of time required to first observe the emitted perfluorocarbon.

3.9 Detection of PFMCH Tagged Ink: An ink-jet printer was used to print a multiple lines on a sheet of standard paper. A proprietary ink formulation containing PFMCH was used to print some words in red, while the remainder of the page was printed in black using a commercial ink-jet printer cartridge. The printing on the page was several months old at the time of the demonstration. The presence of PFMCH in the red ink was demonstrated by interrogating the ink through physical contact with the DSITMS sampling probe. A large $m/z = 350$ peak was observed for the red ink, whereas only background signal was

seen from the black ink. This demonstration was intended to establish the utility of perfluorocarbons for document verification and authentication.

(4) Issues Deserving Further Attention:

4.1 <u>Product Reproducibility and Shelf Life</u>: Crayon and cyclodextrin products need to be investigated for reproducibility of manufacture and shelf life under varying conditions of temperature, humidity, etc. Understanding and documenting these and related quality assurance issues is necessary for achieving court acceptance of evidence derived from this technology.

4.2 <u>Additional Formulations</u>: Current detection technologies provide opportunities for the use of perfluorocarbon taggants in various law enforcement applications. A wider selection of formulations would facilitate field trials of this technology. Suggested routes of study for further formulation development include;

♦ Additional perfluorocarbon/cyclodextrin formulations

♦ Stimulated release formulations (i.e. ultrasound, chemical, light….)

♦ Materials that degrade (erode) to give a large release of perfluorocarbon after a given period of time

4.3 <u>Environmental Stability/Transformations</u>: Initiation of field studies will require introducing perfluorocarbon formulations into the environment. It is important from an operational perspective to know the stability of the formulation under real conditions and to be aware of any chemical transformations. For example, cyclodextrins may be processed by microbes or insects possessing invertase enzymes, thereby releasing the perfluorocarbon.

4.4 <u>Combustion Products</u>: The products generated from perfluorocarbons in an internal combustion engine could prove useful for monitoring the movements of a vehicle. The combustion products may also have considerably greater toxicity. *These issues should be addressed in a laboratory prior to field tests.*

4.5 <u>Long-term Sampling Applications</u>: The focus of the demonstrations described in this document has been on applications requiring real-time detection. Sampling and analysis issues associated with applications that make use of long-term active or passive sampling (i.e. identifying a warehouse containing a marked package, unattended monitoring for stimulated release, etc.) have not been adequately addressed.

4.6 <u>Identification of User Needs</u>: Local, state and federal law enforcement agency representatives should be questioned for additional input on high priority applications. Those applications should be targeted for further development through appropriate funding sources.

4.7 <u>Influence of Container/Packaging Material on Detection Lifetime</u>: Certain packaging materials may adsorb and slow the release of perfluorocarbons and thus have a positive effect on the release rates. Other packaging materials may serve as barriers to the release of perfluorocarbons and thus have a negative effect on the detection of the tracer. Earlier studies, sponsored by the ATF found that most common packaging methods do not impose a significant barrier to the perfluorocarbon release. Nonetheless, this is an area deserving of some further consideration.

(5) Attachment I: Perfluorocarbon Toxicity Review.

Date: February 29, 2000

To: Mike Guerin

3:     P.Y. Lu

From: T. Borges, 1060 COM (574-6425) - NoRc

Subject: Perfluorocarbons

We were asked to review the toxicity perfluorocyclohexane (PFCH), perfluoromethylcyclohexane (PFMCH), perfluoror-1,3-dimethylcyclohexane (PF-1,3-DMCH), perfluorodecaline (PFD), and perfluoromethyldecaline (PFMD). To do this, we reviewed the MSDS sheets supplied with the request, did ChemID and TOXLINE literature searches for journal articles describing the environmental and health effects of these perfluorocarbons (a list of references used for the preparation of this report is provided in the attachment), and searched FedLaw and the Code of Federal Regulations for regulatory information. Presented is a synopsis of the review.

The MSDS sheets for the following perfluorocarbons were reviewed: Performance Fluid (3-M Corporation) 5070, 5862, 5060DL, 5052, 5040, and 5030 (compounds having 7, 6, 6, 5, 4, and 3 carbons, respectively); PFMCH; and PF-1,3-DMCH. All of the MSDS sheets stated the perfluorocarbons were volatile, water insoluble, extremely stable, and not fire or reactivity hazards. The health sections of the MSDS sheets show the compounds are slight health hazards; essentially the lowest rating a chemical can be given.   The precautions listed for the perfluorochemicals, such as eye cover and use of gloves, are standard precautions that should be followed with the use of any chemical. The recommended method of disposal was incineration suitable for halogens

Only a limited number of studies were found from literature searches for perfluoro-carbons. The only environmental studies described atmospheric experiments tracing a fluorocarbon plume from England over Europe (European Tracer Experiment) after its intentional release. No studies describing perfluorocarbon effects on the terrestrial or atomospheric environment were found.
Studies on health effects of perfluorocarbons are limited primarily to PFD. This per-fluorocarbon has been used intraoptically during retinal detachment repair and because of its oxygen and carbon dioxide carrying capabilities, as a blood expansion substitute. Animal studies of PFD and other perfluorocarbons, such as perfluoronated fatty acids, show them to be chemically stable,
inert, and nonmetabolizable.

During retinal attachment and other procedures involving intraocular repair, the vitreous humor of the eye is removed during the procedure to avoid clouding from blood and tissue. To maintain optical structure, the vitreous space is refilled with a fluid, often PFD. At the conclusion of the procedure, the PFD is removed and the chambers again

filled with vitreous fluid. Little toxicity from the use of PFD is experienced following the procedure, however, case reports do indicate that residual PFD left in the vitreous body can induce corneal clouding and edema. These effects are not the result of an interaction, but of the "physical" irritation of PFD to the cornea. Typically, it takes 4-13 weeks for the condition to develop, but is readily reversed with removal of PFD.

PFD in emulsion with perfluorotripropylamine has been used as a blood volume expander in the US, primarily in emergency situations and with patients who have religious convictions against receiving whole blood. These emulsions have seen more extensive use in Europe and Japan. Generally, emulsion use is typically limited to short durations of less one to two weeks. There have been reported instances of anaphylactic reactions during intravenous infusion of the emulsion that were traced to activation of the complement system. In addition, blood replacement emulsions have caused neutropenia with increased neutrophil adherence and cytotoxicity resulting in microvascular damage. The incidences of these reactions, however, are quite low.

As mentioned earlier, the perfluorocarbons are nonmetabolizable, however, they do induce hepatic metabolizing enzymes. PFD given to rats was shown to induce cytochrome P-450 in a manner similar to phenobarbital. As with phenobarbital induction, the activities of cytrochrome P-450 IIA1 and IIA2 (a.k.a. cytochrome P450$_b$ and cytochrome P450$_e$) were increased approximately two-fold following PFD treatment. Likewise, the activities of benzphetamine-N-demethylase and aldrin-epoxidase were increased. The activities of cytochrome P-450 IA1 and IA1 (induced by 3-methylcholanthrene-type inducers) and cytochrome P450 IV (induced by fatty acids and perfluoronated fatty acids) were unaffected. Although the perfluorocarbons are sequestered in the fat and later transferred to the liver, over time they are eliminated from the body via the lungs by exhalation.

No regulatory information on perfluorocarbons was located from searches made on FedLine and of the Code of Federal Regulations. Therefore, at the present time, no Federal regulations pertaining to perfluorocarbons have been made.

In summary, only limited information on the subject perfluorocarbons was located. The compounds are chemically and biological stable and pose limited health hazards. Standard precautions should be followed when using these chemicals. No Federal regulations were located concerning their use or disposal.

Attachment

References used for the preparation of this report.

Augustin AJ; Spitznas M; Koch FH; Boker T; Meller D; Lutz J; Systemic effects of different perfluorochemical agents, Graefes Arch Clin Exp Ophthalmol; 233, (1), 1995, P48-51.

Huang R; Levin SS; Schleyer H; Cooper DY; Mukherji B; Sloviter HA; Alteration by perfluorodecalin of hepatic metabolism and excretion of phenobarbital, Biochem Pharmacol; 37, ISS 19, 1988, P3761-4.

Kalinina E; Obraztsov V; Shekhtman D; Gudkova O, Kukushkin N; Saprin A, Effect of perfluorodecalin on activities of hepatic phase II xenobiotic biotransformation enzymes. Biochem Int; 24 (3). 1991. 543-548.

Lutz J; Krafft MP; Longitudinal studies on the interaction of perfluorochemicals with liver cytochromes P-450 by means of testing the rate of detoxification of pentobarbital, Adv Exp Med Biol; VOL 411, 1997, P391-4.

Malchiodi-Albedi F; Perilli R; Formisano G; Scorcia G; Caiazza S, Perfluorodecalin modifies the pattern of cell arrangement and induces loss of neurites in rat retinal cultures. J Biomed Mater Res; 41, (4), 1998, P608-13.

Meller D; Augustin AJ; Spitznas M; Lutz J; Meller K; Effects of different perfluorochemicals on dorsal root ganglion cells in vitro, Graefes Arch Clin Exp Ophthalmol; VOL 236, (3), 1998, P182-7.

Mishin VM; Obraztsov VV; Grishanova AY; Gutkina NI; Shekhtman DG; Khatsenko OG; Lyakhovich VV; The phenobarbital-type induction of rat liver microsomal monooxygenases by perfluorodecalin, Chem Biol Interact; 72, (1-2), 1989, P143-55.

Nodop K; Connolly R; Girardi F, The field campaigns of the European Tracer Experiment (ETEX): Overview and results, Atmospheric Environment; 32 (24). 1998. 4095-4108.

Obraztsov V; Sklifa A; Kukushkin N; Peculiarities of induction of the rabbit liver monooxygenase system following intravenous administration of fluorocarbon emulsion, Farmakol Toksikol (MOSC); 52 (5). 1989. 60-63.

Obraztsov V; Shekhtman D; Sklifas A; Uncoupling of the liver monooxygenase system by perfluorocarbons in vivo, Biokhimiya; 59 (8). 1994. 1175-1181.

Ramaesh K; Bhagat S; Wharton SB; Singh J; Corneal epithelial toxic effects and inflammatory response to perfluorocarbon liquid, Arch Ophthalmol; VOL 117, (10), 1999, P1411-3.

Straume A; Dietz R; Koffi E; Nodop K, Perfluorocarbon background concentrations in Europe.
Atmospheric Environment; 32 (24). 1998. 4109-4122.

Weinberger D; Goldenberg-Cohen N; Axer-Siegel R; Gaton DD; Yassur Y; Long-term follow-up of perfluorocarbon liquid in the anterior chamber, Retina; 18, (3), 1998, P233-7.

Wilbanks GA; Apel AJ; Jolly SS; Devenyi RG; Rootman DS; Perfluorodecalin corneal toxicity: five case reports, Cornea; 15, (3), 1996, P329-34

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