Thomas G. Grumbles

VISTA

To Kieth Fogg
Robert Martin

Date 4/21

XF: none

TGG: JEC: FBJ: AC: AJO: RF

Attached is an article evaluating the ability of 3 passive dosimeters to accurately measure short-term exposures to EtO.

<u>Bottom</u> <u>line</u> – only one, the 3M 3550/3551™ badge worked, and only with GC-ECD analysis.

TGG

Field Validation of Three Passive Dosimeters for Excursion Limit Monitoring of Ethylene Oxide

*Frank G. Szopinski**
Mark A. Puskar†
Lawrence H. Hecker

Corporate Industrial Hygiene Laboratory, Abbott Laboratories, D-38A, North Chicago, IL 60064

The Occupational Safety and Health Administration (OSHA) set a 5-ppm excursion limit (EL) for ethylene oxide (EtO) in April 1988. Both active and passive sampling methods have been proposed for monitoring workers against this new standard. Passive dosimetry has considerable advantages over active sampling for monitoring short-term exposures to EtO, including reduced sampling and analysis complexity, increased chemical stability, and reduced cost. The major disadvantage of these passive methods is their questionable ability to meet the OSHA requirement for the test result to fall within ±35% of the "true" result with 95% confidence at the EL over a 15-min sampling period. A field validation study was performed to estimate the accuracy of three EtO EL passive dosimeters: 3M 3550/3551™, Crystal Diagnostics AirScan®, and Assay Technology EO CHEM CHIP™. Area samples were taken at four unique concentration areas within a hospital products sterilization facility. A specially designed field exposure chamber was used to expose 12 dosimeters of each type concurrently at each sampling location while concurrently collecting six Tedlar® bag samples from locations surrounding the dosimeter array. The Tedlar bag samples were analyzed on-site by gas chromatography with flame ionization detection (GC-FID). To enhance the strength of this validation study, manufacturers of the dosimeters were requested to take part in the investigation. Their input was used during the design of the exposure chamber and study protocol and in the interpretation of the results. Two of the three dosimeter types were analyzed by the investigators. Dosimeters of the third type, 3M 3550/3551, were divided between an outside American Industrial Hygiene Association–accredited laboratory and 3M's laboratory for analysis. Using the Tedlar bag/GC-FID sample data to calculate the "actual concentration" during the exposure of the monitors, the precision, bias, and accuracy were calculated for each method at exposures bracketing the OSHA EL (ranging from 2.12 ppm to 15.8 ppm). The Assay Technology method did not meet the ±35% accuracy requirement at any concentration level studied. The Crystal Diagnostics method did not meet the ±35% accuracy requirement at EtO concentrations above 2.12 ppm. The 3M samples analyzed by the manufacturer met the ±35% accuracy requirement with a pooled accuracy of ±25%. The 3M samples analyzed by the outside laboratory did not meet the ±35% requirement at concentrations below 9.41 ppm.

In the hospital products manufacturing industry, ethylene oxide (EtO) is used for the sterilization of materials that cannot be subjected to high-temperature autoclaving. In hospitals, EtO is used for the sterilization of surgical instruments and supplies. Although the vast majority of EtO produced is used in the chemical production of glycols and related chemicals, it is estimated that the greatest number of occupational exposures to EtO occur during its use as a sterilization agent.[1]

The acute toxic effects of EtO, including skin, eye, and respiratory tract irritation and central nervous system depression, have long been recognized. Recently, major concern has focused on the carcinogenic and mutagenic effects of EtO.[2,3] For these reasons, in 1984, the Occupational Safety and Health Administration (OSHA) lowered the permissible exposure limit (PEL) to 1 ppm 8-hr time-weighted average (TWA) with a 0.5-ppm TWA action level. A short-term excursion limit (EL) of 5 ppm was added by OSHA in April 1988.

Methods for the determination of occupational exposures to EtO include the use of real-time area monitors, impingers, active adsorbents, and passive dosimeters. The advantages and disadvantages of each type have been discussed in detail elsewhere.[4] Basically, passive dosimetry has considerable advantages over active sampling for monitoring exposures to EtO, including reduced sampling and analysis complexity, increased chemical stability, and reduced cost. The major disadvantage of these passive methods is their questionable ability to meet the OSHA ±35% accuracy requirement at the 5-ppm excursion limit over a 15-min sampling period.

In this study, the method accuracy of three types of EtO passive dosimeters (3M 3550/3551™, Crystal Diagnostics AirScan®, and Assay Technology EO CHEM CHIP™) were estimated in a hospital products sterilization facility at con-

*Currently employed with The Raterman Group, Ltd., 154 West Hubbard, Suite 602, Chicago, IL 60610.

†Author to whom all correspondence should be addressed.

centrations bracketing the 5-ppm EL. A specially designed field exposure chamber was developed to allow all monitors to be exposed for the exact same time in the field. The validation of this exposure chamber and sampling protocol is detailed elsewhere.[5]

The 3M 3550/3551 dosimeter uses a derivatization technique that converts the EtO to 2-bromoethanol on the surface of the dosimeter during collection. The manufacturer recommends analysis by gas chromatography with electron capture detection (GC-ECD). Others have had better accuracy with analysis by gas chromatography with flame ionization detector (GC-FID).[6] The major disadvantage of this technique is that the monitors must be sent to an industrial hygiene laboratory for analysis.

The EO CHEM CHIP passive monitor utilizes a colorimetric reagent system immobilized on an adsorbent strip, which is encased within an EtO-selective membrane. EtO is chemically bonded as it enters the system and is held for later development. Concentration is proportional to surface reflectance of the absorbed strip.[7] On-site analysis of these monitors is possible immediately after sample collection. This is not, however, a direct-reading method. Specific corrections, including time, temperature, and blank, must be made to the raw data to generate accurate results. A description of this technique for 8-hr PEL monitoring, including a detailed discussion of the necessary corrections, is available.[8]

The Crystal Diagnostics AirScan utilizes the principle of nucleation and crystal growth to determine EtO concentrations. Basically, EtO causes a chemical reaction within the monitor forming an array of crystal seeds on sensitized film; a development solution, applied later to the dosimeter, causes rapid crystal growth directly proportional to the exposure level.[9] A major advantage of this method is that the sample can be developed and directly read on-site. One disadvantage is that a 2-hr waiting period is required following sampling and prior to development.

FIELD VALIDATION

Field validation of a new industrial hygiene method is necessary after laboratory validation of the method has been completed. The major problem with field validation studies is that the "actual concentration present" is generally not known in the field atmosphere; therefore, method accuracy cannot be determined. Tedlar bag sampling, followed by gas chromatography analysis has been used for monitoring the concentration of EtO in ambient air.[10] The problem with this method has been the lack of stability of the samples between collection in the field and analysis in the laboratory. The advent of the portable gas chromatograph offers the ability to take the instrument into the plant and concurrently generate near-real-time area data during field validation of EtO passive methods.[4,6] By estimating the actual concentration present during field validation, the actual method accuracy can be calculated from field validation data.

The OSHA standard for EtO EL method accuracy states that the absolute total error (sampling plus analysis) should be less than 35% in at least 95% of the samples analyzed at 5.0 ppm.[11]

With EtO PEL monitoring, OSHA accuracy requirements are also set at levels below and above the PEL of 1.0 ppm 8-hr TWA.[1] The standard states that method results should fall within 25% of the true value in at least 95% of the samples analyzed at 1.0 ppm and 2.0 ppm and that the total error should also be less than 35% in at least 95% of the samples analyzed at the action level (0.5 ppm). With EtO EL monitoring, however, accuracy requirements have not been set by OSHA at levels above and below the 5-ppm standard. The authors believe that to be useful in assessing worker exposure, any air-sampling method for short-term EtO monitoring must have at least ±35% accuracy over the range of 2.5 ppm to 20 ppm. Even if a sample's result is clearly over the standard (e.g., 15 ppm), if the result is known to be accurate, useful exposure information has been generated. The magnitude of the overexposure may help pinpoint the contaminant's release point or help in the identification of appropriate control strategies. From an OSHA compliance standpoint, there is little need for method accuracy requirements at 4× the standard, but for the practicing industrial hygienist who may want to use the method to collect area samples inside known high-concentration areas, the known accuracy of a method at concentrations above the standard is important.

The accuracy of an industrial hygiene sampling and analytical method is a function of both the precision and the bias.[12,13] Precision can be estimated by the total coefficient of variation (CV_t) for replicate determinations including both sampling and analysis steps. The bias (Bi) is estimated by using Equation 1, where the amount found is averaged over replicate determinations or the averaged bias is determined over a range of known amounts with single determinations.

$$B_i = \frac{\text{Amount Found} - \text{Amount Known}}{\text{Amount Known}} \quad (1)$$

Once both the precision and the bias of a method have be estimated, the accuracy can be estimated by using Equation 2.

$$\text{Accuracy } (\pm\%) = [2(CV_t) + |B_i|] \times 100 \quad (2)$$

METHODOLOGY

Passive dosimeters developed specifically for monitoring occupational exposure to EtO are marketed by numerous manufacturers. During this field validation study, 12 monitors from three manufacturers were simultaneously exposed at four different EtO concentrations bracketing the 5-ppm EL. Tedlar bag samples were also filled during the course of the sampling period and analyzed by portable GC-FID. Sample location parameters including temperature, air velocity, and humidity were recorded at each sampling location during sample collection. The Crystal Diagnostics and Assay Technology samples were analyzed by the investigators on-site. The 3M dosimeters, which must be sent to a laboratory for analysis, were divided between an outside American Industrial Hygiene Association (AIHA)–accredited lab and 3M for analysis. 3M analyzed the monitors they received by using GC-ECD, and the outside laboratory analyzed the 3M 3550/3551 they received by using a GC-FID method.

The precision, bias, and accuracy were calculated for each method at EtO-exposure levels bracketing the 5-ppm EL by using the Tedlar bag/GC-FID data as the actual concentration present. To enhance the strength of this study, the three manufacturers of the EtO passive dosimeters were requested to take

part in this investigation. Their input was requested during the design of the validation protocol, during the interpretation of the results, and in the preparation of this manuscript. The major role of each manufacturer during the study, however, was to advise the investigators on proper sampling, handling, preservation, analysis, and shipping procedures to ensure that the sampling and analysis techniques were not compromised.

Four sampling locations were selected inside a hospital products manufacturing sterilization facility, which was chosen because it had the highest temperatures and relative humidities of any of the authors' North American facilities. The assumption was made that if the dosimeters could operate in this environment, they would function at any facility. The goal of the sampling location selection process, inside the facility, was to find sampling locations that would average the following concentrations: 2.5 ppm, 5.0 ppm, 10 ppm, and 20 ppm, for 15 min. In actuality, the concentrations averaged 2.12 ppm, 5.28 ppm, 9.41 ppm, and 15.8 ppm as determined by the Tedlar bag/GC-FID data.

To ensure that each set of dosimeters was exposed to a homogeneous test atmosphere for exactly 15 min, a field exposure chamber and sampling protocol were developed. The field use of this protocol, along with the validation studies that were performed on the exposure chamber, sampling system, and calibration systems, are described elsewhere.[12]

Briefly, the chamber was designed as a 50- by 55-cm aluminum base with a 36- by 31- by 30-cm removable Plexiglas® cover. An adjustable aluminum grid allowed for all the dosimeter sampling ports to be held at the same level above the base. External sampling ports were installed at six locations across the base. Each of these ports was linked to an external personal sampling pump. The pumps were used to fill six separate Tedlar air-sampling bags during the course of the sampling period. Prior to and after the sample exposure period, the cover was placed on the base and the chamber was purged with EtO-free air. The purged chamber was removed from the contaminated area and the dosimeters were prepared for analysis or shipping. Blanks of each type of monitor and Tedlar bag/GC-FID samples were collected during the setup, exposure, and removal process inside the EtO-free setup location, where the monitors were handled, to document that no additional EtO contamination occurred during the preexposure and postexposure handling of the monitors.

CALIBRATION OF EQUIPMENT

Model HFS-513A Gilian high-flow sampling pumps (Gilian Instrument Corp., Wayne, N.J.) were used to draw air into the 4-mil thickness, 33-cm by 51-cm (10-L) Tedlar air-sampling bags (SKC-234-10) at a rate of 0.5 L/min. The pumps were calibrated prior to and after the 4 days of sampling.

The Tedlar bag samples were analyzed with an AID Model 511 portable gas chromatograph with a flame ionization detector (Analytical Instrument Development, Avondale, Pa.) equipped with a 3-mL gas-sampling loop. Air was continuously drawn through the loop at a rate of 50 mL/min with a Model XX55 vacuum/pressure pump (Millipore, Bedford, Mass.). Air samples were injected on-column by turning a two-way valve, which allowed the carrier (helium) to flow through the sampling loop and onto the column. The chromatograph was fitted with a 4-ft stainless steel column filled with 20% dinonyl phthalate on Chromosorb W (Supelco, Bellefonte, Pa.). The GC-FID was interfaced with a Hewlett Packard Model 3393A integrator equipped with a Model 9114B 3.5-in. disk drive for data storage. The detector's response was linear in the concentration range of interest. A linear least-squares fit typically yielded a correlation coefficient greater than 0.999. The GC-FID was calibrated over a range of standards bracketing the EtO concentrations of interest, prior to and after sampling at each location. Standards with concentrations at the suspected EtO level were also analyzed throughout the Tedlar bag analysis process. Known concentrations of EtO in air were generated by using a Model 450-57-D dynamic gas analyzer calibrator (Vici Metronics, Santa Clara, Calif.), as described elsewhere.[5] Air dilution flow rates were measured with a Model PN D-800268 Gilibrator (Gilian Instrument Corp., Wayne, N.J.) primary flow calibrator. With primary dilution, EtO standards were prepared in the range of 0.9 ppm to 32 ppm. With secondary dilution, standards were produced down to 0.1 ppm. The instrument's actual limit of detection is below 0.1 ppm but was not determined.

DETERMINATION OF ETO CONCENTRATION USING GC-FID

Each of the six bag samples collected during the 15-min sampling period were analyzed in quadruplicate. All bags were analyzed within 1 hr of collection. The mean concentration and standard deviation (SD) were calculated for each of the six bags. The mean value and SD were used to calculate a 95% confidence interval for the concentration found for each field evaluation performed.[14] This confidence interval, instead of the mean concentration value, was used to represent the actual concentration present for the calculation of the bias for each passive method. As an example, the mean concentration determined for Location 2 was 9.41 ppm. The 95% confidence interval was determined to be between 9.14 ppm and 9.68 ppm. Therefore, any passive method's mean concentration determined to be between those two values was stated as having no bias, and methods with means either below 9.14 or above 9.68 were stated to have bias. The bias was then calculated by using Equation 1.

ANALYSIS OF SAMPLES

Special precautions were taken to ensure accurate analysis with the 3M 3550/3551 device. To estimate analysis bias caused by laboratory error and to determine if accuracy was a function of the gas chromatography detector used to analyze the samples, the dosimeters were split and analyzed by two separate laboratories. Therefore, each laboratory received a total of 28 samples (6 samples plus 1 blank from each of the 4 sampling locations). 3M's Monitor Analysis Service performed the analysis on half of the 3550/3551 dosimeter samples collected by using the GC-ECD technique. An independent AIHA–accredited laboratory (National Loss Control [NATLSCO], Long Grove, IL) analyzed the second half of the samples by using a commonly used GC-FID technique. NATLSCO does not recommend using 3M

3550/3551 dosimeters with GC-FID analysis for EtO EL monitoring. The passive dosimeters were shipped to the designated laboratories for analysis following the manufacturer's recommendations on sample handling and preservation.

The two remaining types of dosimeters were analyzed by the investigators on-site. Half of each type were analyzed the day of collection, and the second half were stored and analyzed the next day. This was done to determine what effect letting exposed dosimeters sit overnight, prior to analysis, would have on the monitor's accuracy. Assay Technology's dosimeters were refrigerated according to the manufacturer's directions, and the Crystal Diagnostic devices were stored at room temperature as recommended by the manufacturer. The techniques and procedures recommended by the manufacturers were followed for developing and reading the dosimeters.

RESULTS AND DISCUSSION

All the blank monitors and Tedlar bag/GC-FID samples collected in the study setup location were below each method's limit of detection except for one AirScan monitor, which displayed full-scale readings (>22 ppm). The problem with this monitor is discussed later.

Table I lists the Tedlar bag/GC-FID sampling results and the sampling parameters obtained from the four sampling locations. The mean EtO concentration is presented along with the calculated 95% confidence intervals. Average location temperatures ranged from 28.5°C to 32.0°C, while average relative humidities ranged from 66% to 76%. The array of passive monitors was angled perpendicular to the room's airflow so that the room air could move freely between the array rows. Average location air velocities moving through the array of dosimeters were found to range from 8 to 28 ft/min when a hot wire anemometer was used.

A summary of the results of the three different passive dosimeters at the four sampling locations is presented as Table II. The first column lists the manufacturer and device name. The second column lists the analysis time or type of analysis. The third column lists the mean EtO concentration determined by the Tedlar bag/GC-FID technique at each of the four sampling locations. The fourth column lists the mean result obtained with each type of sampling device (n = 6) at each of the four sampling locations. The fifth column lists the calculated coefficient of variation. Column 6 lists the calculated bias. The final column lists the calculated method accuracy of each method at each sampling location if the bias as calculated by the mean GC-FID result was found to be statistically significant.

The Assay Technology EO CHEM CHIP dosimeters, analyzed the same day as they were collected, did not meet the ±3[illegible] accuracy requirement at any of the four concentrations studied. The ±35% accuracy was, however, met by dosimeters at the 5.28-ppm exposure level for the monitors that were stored and analyzed the next day. The authors feel that the problem with the EO CHEM CHIP monitors may be directly related to the variability in the blank's determination. When a series of blank monitors was analyzed, a CV of 0.15 was found. This variation affected the calculated precision and bias of the method when only one blank value was used to adjust the results for a whole box of samplers, as recommended by the manufacturer. In this study, accuracy was improved by using a mean blank correction derived from all blank values to adjust all sample values. Although this technique reduced the total error of all pooled samples by 50%, the total error of all pooled samples still did not meet the ±35% accuracy requirement. In response to these data, the manufacturer is revising instructions for use and examining unit-to-unit variation as a function of shelf life.

The Crystal Diagnostic AirScan dosimeters met the ±35% accuracy requirement at the 2.12-ppm concentration level for monitors analyzed both the same day and the next day. However, the dosimeters did not meet the ±35% accuracy requirement at any higher concentration level for either same-day or next-day analysis. This is a very unique situation; generally, methods are more accurate as concentration increases. In the case of the AirScan monitors, the most accurate data were obtained at the lowest concentration studied. A problem occurred with the [illegible] of these dosimeters. In approximately 10% of the AirScan [illegible] simeters handled, the capacity of the monitor was exceeded (>22 ppm for 15 min). This occurred even with a blank, as was discussed earlier. It is not known if this problem was caused by a manufacturing problem, repeatedly shipping the dosimeters, or improper activation of the monitors by the personnel performing the study. The possibility of EtO contamination during handling and/or storage can be ruled out based on all the other blank data available (other dosimeters and Tedlar bag/GC-FID data).

The 3M 3550/3551 dosimeters analyzed by 3M (GC-ECD) met the ±35% accuracy requirement at all four concentration levels. The 3M dosimeters analyzed by NATLSCO (GC-FID) met the ±35% accuracy requirements at and above 9.41 ppm but failed to meet ±35% below 9.41 ppm. This accuracy difference between laboratories was attributed to the sensitivity difference between the FID and ECD. An FID responds to carbon-based compounds and is less sensitive but more stable than an ECD detector. It is generally the detector of choice unless ultratrace analysis is required. The ECD responds specifically to compounds containing electronegative atoms, such as oxygen, sulfur, and halogen atoms. The detector can be overloaded very easily and m[illegible] be recalibrated often. When h[illegible] dled properly, however, it offers

TABLE I. Fifteen-Minute Average EtO Concentration, Temperature, Relative Humidity, and Air Velocity at the Four Sampling Locations

Location Number	EtO by GC-FID (ppm)		Temperature (°C)	Relative Humidity	Air Velocity	
	Mean[A]	95% CI			Mean[B]	SD
1	2.12	±0.12	30	66	8.0	2.7
2	5.28	±0.6	32	69	16.5	6.7
3	9.41	±0.27	31	69	NA[C]	
4	15.8	±0.5	29	76	10.5	2.8

[A]Mean of six Tedlar® bag samples, each analyzed in quadruplicate.

[B]16 measurements were collected and averaged.

[C]Data unavailable because of equipment malfunction.

TABLE II. Summary of Field Determination of Method Accuracy at the Four Sampling Locations

Manufacturer/ Device	Analysis Time or Type	EtO (ppm) GC Mean[A]	EtO (ppm) Method[B]	CV	Bias	Method Accuracy
Assay Technology EO CHEM CHIP™	Same day	2.12	0.83	0.87	−0.59	±233%
		5.28	3.6	0.27	−0.23	77
		9.41	3.1	0.36	−0.66	138
		15.8	8.9	0.11	−0.42	64
	Next day	2.12	1.0	0.98	−0.50	246
		5.28	5.3	0.09	0	18
		9.41	6.6	0.07	−0.27	41
		15.8	10	0.05	−0.35	45
Crystal Diagnostics AirScan®	Same day	2.12	1.9	0.09	−0.05	23
		5.28	7.5	0.16	+0.28	60
		9.41	>17.8[C]	0.14[D]	>+0.84	>112
		15.8	>20.7[C]	0.07[D]	>+0.27	>41
	Next day	2.12	1.9	0.06	−0.05	17
		5.28	7.2	0.15	+0.22	52
		9.41	>19.5[C]	0.13[D]	>+1.01	>127
		15.8	>21.4[C]	0.06[D]	>+0.32	>44
3M 3550/3551™	3M: GC-ECD	2.12	1.97	0.16	−0.02	34
		5.28	4.93	0.06	0	12
		9.41	7.73	0.04	−0.15	23
		15.8	13.1	0.06	−0.15	27
	NATLSCO: GC-FID	2.12	2.9	0.59	+0.29	147
		5.28	2.9	0.55	−0.38	148
		9.41	8.7	0.10	−0.05	25
		15.8	12.8	0.03	−0.17	23

[A]Mean of six Tedlar® bag samples, each analyzed in quadruplicate.

[B]Mean of six monitors.

[C]The capacity of one or more of the dosimeters was exceeded.

[D]Coefficient of variation calculated from less than six values.

greater sensitivity than does the FID for compounds containing electronegative atoms. For example, when analyzing 2-bromoethanol, the ECD is 55 times more sensitive than the FID.[15]

When the 3M 3550/3551 dosimeters were field validated for PEL monitoring in a previous study, significantly different results were again generated for GC-FID and GC-ECD methods.[6] A method accuracy of ±30% was observed when the GC-ECD method was used; ±7% method accuracy was estimated when the GC-FID method was used. A comparison of data from the two studies shows that the GC-ECD technique has similar accuracy for both PEL and EL monitoring; the GC-FID method is superior for PEL monitoring but is inappropriate for EL monitoring.

Additional information can be gained from the data in Table II. The data suggest that both the precision and bias of the EO CHEM CHIP monitors improve when the monitors are stored for 1 day prior to analysis. One-day storage appears to have slight to little effect on the overall accuracy of the AirScan monitors. The 3M 3550/3551 data suggest that the accuracy difference between the two methods used to analyze the monitors was more of a precision difference and not a bias difference. This again points to the sensitivity of the detectors used.

The results of this study suggest a significant bias error can be expected with both the EO CHEM CHIP and AirScan monitors. EO CHEM CHIP results were, on the average, approximately 38% low; AirScan results were, on the average, >36% high. On the average, a −8% bias error was determined for the 3M 3550/3551 monitors when analyzed by either GC-ECD or GC-FID.

CONCLUSIONS

The results of this field validation study suggest that the Assay Technology EO CHEM CHIP and the Crystal Diagnostics AirScan EtO dosimeters will not meet ±35% accuracy requirements over the concentration range of 2.12 ppm to 15.8 ppm over the specific temperature, humidity, and location parameters studied. The results also suggest that the 3M 3550/3551 monitors analyzed by GC-ECD will meet the accuracy requirement over the 2.12 ppm to 15.8 ppm concentration range. The average bias over this range for the 3M 3550/3551 GC-ECD method was −8% with a pooled CV_t of 9%, yielding an accuracy of ±25%. The 3M 3550/3551 monitors analyzed by GC-FID will not meet the accuracy requirement over the 2.12 ppm to 15.8 ppm concentration range. The reason for this difference was attributed to the sensitivity difference between the two different detectors.

It is strongly recommended that field validation be performed by using at least two independent methods prior to selecting a method for routine monitoring of employee exposures to EtO. Also, annual dual monitoring that uses two independent methods to document that the selected monitoring method is working properly is recommended.

The strength of this validation study and subsequent conclusions may have been enhanced by the inclusion of a previously validated active pump method.[4] Unfortunately, the complexity of the study, demands of many carefully timed steps, and size limitations of the field exposure chamber made the inclusion of the active pump method infeasible.

ACKNOWLEDGMENT

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Ed. Note: A prepublication copy of this manuscript, "Field Validation of Three Passive Dosimeters for Excursion Limit Monitoring of Ethylene Oxide," was forwarded to the manufacturers for review and comment. Their responses follow.

Dear Sir:

Thank you for the opportunity to comment on "Field Validation of Three Passive Dosimeters for Excursion Limit Monitoring of Ethylene Oxide" by F. Szopinski, M. Puskar, and L. Hecker.

The study was well-designed, well-executed, and well-presented. The authors' conclusions appear valid for this study.

Sincerely,

Donald J. Larsen, CIH
3M Occupational Health and Environmental Safety Division

Dear Sir:

Re: Comment on "Field Evaluation of Three Passive Dosimeters for Excursion Limit Monitoring of Ethylene Oxide"

The authors did an excellent job in controlling many variables in their extensive field validation. They even acknowledged that the *erroneous* off-scale AirScan® readings may have been related to circumstances unknown to the manufacturer. However, I am not entirely in agreement with their treatment of the data; absolute biases for test methods should not be estimated when the "true" concentration, as determined by only one reference method, is not verified.

According to Ms. Mary Ann Cassinelli et al., authors of the National Institute for Occupational Safety and Health (NIOSH) "Protocol for the Evaluation of Passive Monitors," and Dr. Richard Brown et al., authors of the Health and Safety Executive "A Proposal for a Harmonized Approach to the Evaluation of Diffusive Samplers for Occupational Hygiene Measurement," at least two independent sampling/analytical methods should be used in a field method validation to accurately determine true concentrations. A match of 10% or less between the results of two independent methods indicates that the two methods are accurately measuring the true concentration.

Calculation of test method biases assume that the true concentration is known. As described in the paper, the confidence intervals for the gas chromatography estimates of true concentrations take into account *random* sampling/analytical error. Since the authors did not use a second independent method, such as a validated active pump method, to verify that systematic error was not a factor, there is a possibility that the confidence intervals do not include the true concentration. If so, some or all test method biases estimated by the authors may be artifacts of the study design.

The contamination-related off-scale readings, noted by the authors, were caused by the hydrating solution contacting the lower pad in the diffusion port of the AirScan Monitor. As the authors suggest, the contact was probably caused by vigorous shaking during hydration and shipping the AirScan from place to place. Shortly after the authors reported the erroneous off-scale readings to the manufacturer, Crystal Diagnostics redesigned the diffusion port to prevent erroneous off-scale readings.

I appreciate the authors' acknowledgment that a second independent method may have improved the study design. However, I am surprised that they evaluated the data as if the