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Short Communication

An Integrated Air Monitoring Approach for Assessment of Formaldehyde in the Workplace

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ABSTRACT

The aim of this study is to validate an integrated air monitoring approach for assessing airborne formaldehyde (FA) in the workplace. An active sampling by silica gel impregnated with 2,4-dinitrophenylhydrazine, a passive solid phase microextraction technique using O-(2,3,4,5,6-pentafluorobenzyl)hydroxylamine as on-fiber derivatization reagent, an electrochemical direct-reading monitor, and an enzyme-based badge were evaluated and tested over a range of 0.020–5.12 ppm, using dynamically generated FA air concentrations. Simple linear regression analysis showed the four methods were suitable for evaluating airborne FA. Personal and area samplings in 12 anatomy pathology departments showed that the international occupational exposure limits in the GESTIS database were frequently exceeded. This monitoring approach would allow a fast, easy-to-use, and economical evaluation of both current work practices and eventual changes made to reduce FA vapor concentrations.

1. Introduction

Formaldehyde (FA) is an ubiquitous environmental chemical classified as a human carcinogen [1]. The revenue from world consumption of industrial-grade FA is forecast to grow 3.77% annually over the 2017–2022 period [2], with world production expected to exceed 52 million tons in 2017 [3]. Global FA detector production revenue is estimated to reach US$86.29 million by 2017 and $103.81 million by 2022 [2]. Urea-, phenol-, and melamine-FA resins, found in such everyday items such as plywood, carpets, facial tissues, and insulation, accounted for approximately 70% of world demand for FA in 2015 [4].

The number of North American employees directly involved in sectors where FA is used is estimated at 700,000 [5]. In the European Union, instead, the number of workers exposed to FA above the background level is calculated to be 1.7 million, 175,380 of them in Italy [5,6]. Although most exposed workers are foreseeably engaged in chemical and plastics factories, the highest mean levels of exposure were actually recorded in the health-care sector [6–9].

Currently, there are substantial differences among associations' guidelines concerning FA occupational exposure, not only in terms of parts per million (ppm) limits but also regarding which values to assess [10]. For example, the American National Institute for Occupational Safety and Health (NIOSH) proposes recommended exposure limits as an 8-h time-weighted average (TWA) (0.016 ppm) and a 15-min short-term exposure limit (STEL) (0.1 ppm), which are significantly lower than the workplace exposure limits indicated by the UK's Health and Safety Executive (2 ppm for both the TWA and a 10-min STEL). In contrast, the People's Republic of China, New Zealand, Finland, Israel, Canada–Quebec and Canada–Ontario indicate FA occupational exposure limits in terms of a ceiling (C). Similarly, the American Conference of Governmental Industrial Hygienists for many years adopted a threshold limit value ceiling (TLV-C) (0.3 ppm): in 2016, however, they began requiring additional information: TLV-TWA (0.1 ppm) and TLV-STEL (0.3 ppm) [11]. Likewise, the European Scientific Committee on Occupational Exposure Limits recently proposed an FA-related TWA of 0.3 ppm, but a STEL of 0.6 ppm [12]. NIOSH's Immediately Dangerous to Life or Health is 20 ppm for FA.

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A huge number of analytical methods for determining airborne FA values have been developed. The current, validated methods for detecting gaseous FA are based on either active or passive sampling: the former using 2,4-dinitrophenylhydrazine (DNPH) as reagent on a filter and the latter using O-(2,3,4,5,6-pentafluorobenzyl) hydroxylamine (PFBHA) as reagent on solid sorbent. The samples are subsequently analyzed by liquid chromatography (LC) or gas chromatography (GC) [12−14]. The electrochemical sensors for FA vapor detection are convenient, real time, and portable instruments that may be useful as screening tools [15].

In our study, two laboratory-based methods were then correlated with the results from commercially available direct-reading instruments, specifically the Formaldemeter htV and the Dräger colorimetric badge. The aim of this industrial hygiene (IH) work was to assess four analytical methods for measuring long- and short-term exposure to airborne FA in the workplace. Our new, integrated monitoring approach is described here to provide a validated strategy for evaluating FA risk in workplace activities. In addition to laboratory testing, this article also outlines the validation protocol used to assess FA monitoring in anatomy pathology departments.

2. Materials and methods

2.1. Measurement devices

Four methods for FA monitoring were compared. First, active air sampling was performed by Sep-Pak XpoSure Aldehyde Sampler Plus Short DNPH-coated cartridges on a silica sorbent (Cat. No. WAT047205, Waters, Milford, MA, USA) attached to GilAir Plus pumps equipped with Gilian CONNECT software (Sensidyne, St. Petersburg, FL, USA) at 0.3 (8 h) and 1.2 L/min (15-min) for personal sampling; for area sampling (0.5 L/min), a 16-position automatic collector box (Bravo M Plus, TCR Tecora, Milan, Italy) was utilized [16]. Second, for passive sampling, solid phase microextraction (SPME) was used [14,17]. A 65-μm SPME fiber Fast Fit Assembly (FFA) polydimethylsiloxane/divinylbenzene (Cat. No. FFA57293-U, Supelco, Bellefonte, PA, USA) was doped with 1 mL PFBHA water solution (17 mg/mL water) for 60 s in the headspace of a 20 mL vial previously equilibrated for 5 min at 60°C. Personal and area samplings were performed both by rapid FFA−SPME [14] (for 1 min: experimental sampling rate = 18.3±0.8 mL/min) using an SPME Automatic Fiber Sampler (Chromline, Prato, Italy) with a Wi-Fi module and by TWA−FFA−SPME [13] [for 8 h; experimental sampling rate for Z distance (the retraction of the SPME fiber into the needle) = 3 mm was 0.03±0.0025 mL/min] with a Diffusive Sampling Fiber Holder for FFA−SPME (Cat. No. 57584-U, Supelco, Bellefonte, PA, USA). All the active and diffusive samples were then analyzed by a Varian CP-3800 GC with two injection ports set in splitless mode and equipped with Merlin Microseal Septa (Merlin Instrument Co., Newark, NJ, USA). To analyze the FA-2,4-dinitrophenylhydrazone, the method by Dugheri et al [16] was adopted, with modifications; in this case, we use a nitrogen−phosphorus thermionic specific detector (TSD), a diphenylamine (Cat. No. 24,258-6, Aldrich, Sigma−Aldrich, Saint Louis, MO, USA) as internal standard, and a MEGA-35 column (30 m × 0.25 mm × 0.25 μm film thickness) (Mega, Milan, Italy). The initial column temperature was set to 70°C (1 min) and then increased by 10°C/min to 310°C. Instead, FA-pentafluorobenzyl-oxime was measured by a flame ionization detector fitted with an Agilent J&W VF-5 ms column (60 m × 0.25 mm × 1.00 μm film thickness). The initial column temperature was set to 45°C (1 min) and then increased by 7°C/min to 300°C. Helium, flowing at rates of 2.0 and 1.0 mL/min, served as the carrier for both TSD and flame ionization detector, respectively.

Full automation of these GC procedures was achieved using a Flex GC autosampler (EST Analytical, Fairfield, CT, USA) equipped with a 45-position Multi Cartridge/Multi Fiber eXchange (Chromline, Prato, Italy) that allowed the desorption of the Plus Short cartridge and the FFA−SPME fiber in automated mode. For the two chromatographic techniques, a signal-to-noise ratio of 3:1 and 10:1, estimated by injection of the FA-2,4-dinitrophenylhydrazone solution (Cat. No. 56677, Fluka, Sigma−Aldrich, Saint Louis, MO, USA) and FA-pentafluorobenzyl-oxime (Cat. No. 41558, Sigma−Aldrich, Saint Louis, MO, USA), were used to calculate the limit of detection and limit of quantification (LOQ), respectively.

The third method used the Formaldemeter htV (PPM Technology, Norfolk, UK), an active sampler (a 10-mL snatch-sample of air taken in by internal pump) with an electrochemical sensor with a resolution of 0.01 ppm, and a mean response time of 60 s. Alcohols, aldehydes, and phenols are all positive interferences for the Formaldemeter htV which as well, as noted by the manufacturer, is sensitive to high temperature (>40°C) and relative humidity (>70%).

The fourth method was the Dräger-Bio-Check F badge (Cat. No. 6400235, Drägerwerk AG & Co. KgaA, Lübeck, Germany); this colorimetric badge is based on an enzymatic reaction that turns different shades of pink within categorical values (<0.05 ppm, 0.05 to 0.1 ppm, 0.1 to 0.2 ppm, 0.2 to 0.3 ppm, and >0.3 ppm) after 2 hours of exposure. It allows, as well as the Formaldemeter htV, for conducting measurements of both area and personal FA sampling without any additional accessories. Furthermore, the instrumental LOQs of the enzyme-based badge and of the electrochemical sensor were provided by the manufacturer.

2.2. Dynamic calibration system

The FA atmospheres were generated by a Harvard Plus 11 syringe-pump, set to 2 μL/min connected to an Adsorbent Tube Injector System (Supelco, Bellefonte, PA, USA) (Fig. 1). The sampling methods were trialed using FA set as follow (0.020, 0.040, 0.080, 0.160, 0.320, 0.640, 1.280, 2.560, and 5.120 ppm). All four samplers were exposed at the same time for each FA air concentration, and for each one, five determinations were performed. The FA air concentration ($C_{FA\ air}$) was calculated according to the following formula:

$$C_{FA\ air} = C_{Sol}F_{syringe}/F_{air}$$

where, $C_{FA\ air}$ is the concentration of analyte in air (μg/L), C_{Sol} is the concentration of the solution (μg/μL), $F_{syringe}$ is the syringe-pump flow (μL/min), and F_{air} is the air flow (L/min). The concentration of water vapor produced by the impinger was determined by measuring the dew point temperature with a photoacoustic infrared Innova type 1312 Multigas Monitor (LumaSense Technologies, Santa Clara, CA, USA). Atmospheric pressure was determined with a GE Druck DPI 705 digital pressure indicator (General Electric, Boston, MA, USA).

2.3. Sampling sites

These methods were then evaluated in 12 hospitals of Italy: in operating theaters during the immersion of biopsies in plastic containers filled with FA and in pathology laboratories during the registration and the slicing of previously fixed surgical pathology specimens. The operating theaters and the pathology laboratories were provided with aspirating hoods Zefiro (Diapath, Bergamo, Italy). In the four hospitals where Tissue-SAFE under-vacuum sealing (UVS) (Milestone, Bergamo, Italy) was adopted for large biopsies (>2 cm in size), the specimens were vacuum sealed in
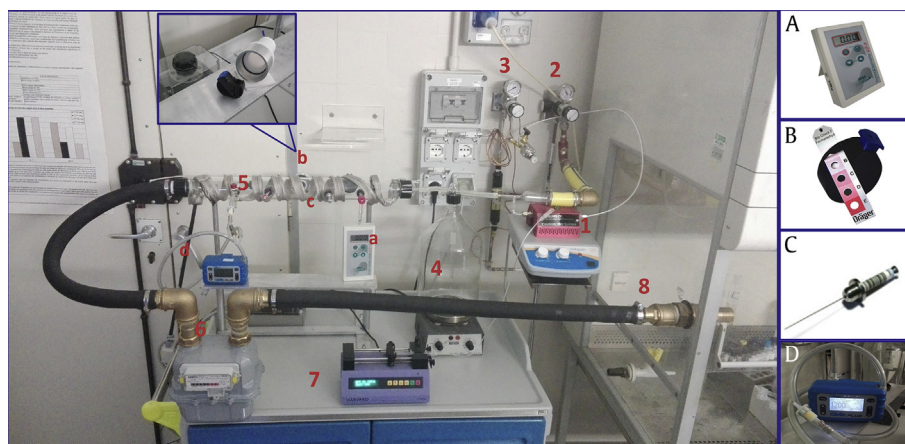
Fig. 1. Dynamic calibration system. 1. ATIS Injector System. 2. Manometer for auxiliary inlet gas. 3. Inlet-gas. 4. Mixing chamber. 5. Measurement chamber: A. Formaldemeter-htV, B. Dräger-Bio-Check F (in detail: adapter), C. FFA-SPME-fiber, D. DNPH-cartridges and GilAir Plus. 6. Rotameter. 7. Syringe-pump. 8. Extractor-hood.

plastic bags and labeled immediately after air removal. Next, the samples were refrigerated at 4°C inside the premises of the surgical theater until they were transferred to pathology where the tissue was fixed in 4% FA. UVS procedures eliminate FA usage upstream, confining its use to the anatomic pathology laboratory.

2.4. Statistical analysis

In Table 1, mean and standard deviation of the collected values are reported for each method. Moreover, we report the mean squared error (MSE) computed between the observed and the theoretical values. We implemented simple regression models to assess the calibration of each method, and we evaluate the significance of the regression coefficients β by testing the hypothesis of perfect calibration (H_0: β = 1) and linear association (H_0: β = 0). We report for each method, the estimates of β, standard error (se), and p values for both the tests obtained by performing a Wald test on the coefficient estimates. In addition, we report the residual MSE and, for the sake of completeness, also the estimated Pearson's correlation coefficients ρ and the p value of the *t* test for correlations for the hypothesis H_0: ρ = 0. Moreover, the FA enzyme-based badge system, whose results depend on people correctly identifying the shade of pink found on the sorbent, was tested for inter-rater reliability via a concordance correlation analysis (Cohen's kappa). Pearson correlation analysis was used also to examine the correlations between electrochemical sensor, the DNPH-cartridge, and PFBHA—SPME methods in the hospital FA monitoring campaign.

3. Results

3.1. Performance of the four methods

The statistic analysis applied on the experimental data demonstrated that all three methods are suitable for FA vapor monitoring (Table 1). Notably, the DNPH-cartridge technique showed the lowest LOQ value (0.001 μg/mL), and the smallest variability (MSE of 0.008) resulted without statistical significance, testing the theoretical FA atmospheres values and the calibration curve (H_0: β = 1). The PFBHA—SPME method, instead showed the best calibration LOQ values for rapid FFA—SPME and TWA—FFA—SPME of 0.03 ppm (1-min sampling) and 5.00 ppm/min (8-h sampling), respectively. Furthermore, the correlation analysis on the visual enzyme-based badge method showed an impressive level of concordance (0.8—1.00 for Cohen's Kappa) (Fig. 2).

3.2. Monitoring campaigns

The four analytical methods resulted all significantly correlated (p value < 0.05) by Pearson test analysis as shown in Table 2. The highest DNPH active-sampling 8-h TWA values were measured in operating theaters during the immersion of large biopsies in plastic containers filled with 4% FA ranging in size from 1000 to 5000 mL (0.512 ppm) and of small biopsies (<2 cm in diameter) using the 20, 60, and 120 mL container with 4% FA (0.086 ppm), during the registration of small biopsies (0.726 ppm), and in the pathology laboratories during the slicing of previously fixed large (0.897 ppm) and small surgical pathology specimens (0.501 ppm). The rapid FFA—SPME 1-min sampling—supported by the Formaldemeter—enabled us to attribute these levels: in operating theaters, the turning off of the aspirating hood between one large biopsy and another (4.55 ppm) and using prefilled containers with 4% FA not capsuled in the lid (0.22 ppm); the nonperfect seal of prefilled containers (3.94 ppm) in secretariat; and the exhaust vapors of FA-impregnated gauze in the waste bin (5.09 ppm). Using the UVS, the highest 8-h TWA value found was 0.23 ppm (1.84 ppm for a 1-min SPME sampling) during the filling of the bag with 4% FA, when the vacuum apparatus was not set in a fume hood.

The results of the personal samplings, presented in Table 2, show that 54% of the total measurements were between 0.1 and 0.3 ppm and that 19% ranged from 0.31 to 2.00 ppm, while only 4% were greater than 2.01 ppm.

4. Discussion

The aim of our work was to create an innovative monitoring approach for measuring airborne FA in the workplace that is simple, fast, and sensitive. To come up with a successful protocol, two fundamental requisites had to be met. First of all, we had to develop two indirect monitoring methods, which are able to sample at differing time intervals and are highly sensitive, simple to use, and cheap. We used chemisorption based on substrate impregnated with derivatizing agents, the most commonly used reaction in IH for determining airborne FA quantities, but derivatization necessarily involves many steps: taking into consideration the reagent's blank value, removing the unreacted agent, and confirming the derivative via mass spectrometry (MS). For example, the sampling carried out in an XAD-2 solid sorbent tube doped with 2-(hydroxymethyl) piperidine (2-HMP), as proposed by the NIOSH 2539 (0.24 ppm per 10-L of air) and under-vacuum sealing Occupational Safety and Health Administration (OSHA) 52 (0.016 ppm

Table 1
Performance comparison of the four methods performed in the lab settings.

Theoretical FA atmospheres (ppm)	Active-sampling DNPH cartridge Mean ± standard deviation (ppm)	Passive-sampling TWA PFBHA—SPME Mean ± standard deviation (ppm)	Passive-sampling Rapid PFBHA—SPME Mean ± standard deviation (ppm)	Electrochemical direct-reading Formaldemeter htV Mean ± standard deviation (ppm)
0.020	0.021 ± 0.003	0.018 ± 0.004	0.004 ± 0.005	0.004 ± 0.005
0.040	0.042 ± 0.004	0.032 ± 0.016	0.040 ± 0.016	0.024 ± 0.021
0.080	0.079 ± 0.003	0.056 ± 0.017	0.054 ± 0.017	0.064 ± 0.021
0.160	0.163 ± 0.011	0.178 ± 0.052	0.120 ± 0.042	0.216 ± 0.066
0.320	0.313 ± 0.016	0.332 ± 0.090	0.368 ± 0.095	0.302 ± 0.094
0.640	0.642 ± 0.034	0.644 ± 0.086	0.602 ± 0.091	0.638 ± 0.097
1.280	1.298 ± 0.093	1.322 ± 0.243	1.442 ± 0.288	1.284 ± 0.291
2.560	2.541 ± 0.072	2.776 ± 0.312	2.318 ± 0.421	2.556 ± 0.277
5.120	5.124 ± 0.272	5.424 ± 0.437	5.082 ± 0.372	5.456 ± 0.444
MSE	0.008	0.045	0.048	0.047
$\beta \pm se$	0.997 ± 0.008	0.923 ± 0.015	0.999 ± 0.021	0.933 ± 0.016
p value test, H0: $\beta = 0$	<0.001	<0.001	<0.001	<0.001
p value test, H0: $\beta = 1$	0.812	<0.001	0.976	<0.001
Residual MSE	0.008	0.030	0.047	0.033
Correlation	0.998	0.994	0.991	0.994
p value test, H0: $\rho = 0$	<0.001	<0.001	<0.001	<0.001

DNPH, 2,4-dinitrophenylhydrazine, FA, formaldehyde; PFBHA, O-(2,3,4,5,6-pentafluorobenzyl) hydroxylamine; MSE, mean squared error; SPME, solid phase microextraction; TWA, time-weighted average.

per 24-L) methods, had poor detection limits. With the 2-HMP method, large blank subtractions had to be performed: 0.67±0.19 and 0.56±0.23 μg/cartridge for ORBO 24 2-HMP on Amberlite XAD-2 (Cat. No. 20231, Supelco, USA) and Sorbent Tubes XAD-2 2-HMP (Cat. No. 226-118, SKC, USA), respectively. Instead, the low FA blank concentration (0.007±0.05 μg/cartridge) in Sep-Pak XpoSure Aldehyde Sampler Plus Short DNPH allowed higher sensitivity. Next, we observed that by removing the excess of DNPH reagent using a polymeric Oasis mixed-mode cation-exchange sorbent (MCX Plus, Cat. No. 186003516, Waters, USA) not only did the LOQ drop by one order of magnitude but also LC and GC analyses could be coupled with single- and triple-quadrupole MS, as well.

Fig. 2. Cohen's kappa (Y axis) vs FA concentrations (X axis) scatterplot of FA enzyme-based badge visual testing. Lowest, highest and mean results from eleven selected subjects are shown vertically on the graph. Kappa = 0 is approximately equivalent to an accuracy = 0.5.
FA, formaldehyde.

Confirming findings by previous authors [18,19], we found, however, that the coefficient of variation in the DNPH-LC/ultraviolet FA method is approximately 23% for low levels of FA (0.012 μg/cartridge). Moreover, the purchase and maintenance costs for the LC system are much higher than that of the GC. Consequently, we suggest a GC column with a 35% phenyl, 65% methyl polysiloxane stationary phase, since it permitted the chromatographic separation of the DNPH degradation product (2,4-dinitroaniline) from the FA-2,4-dinitrophenylhydrazone using the cheaper and easier GC-TSD, rather than the MS one.

The OSHA 1007 method recommends three passive samplers: the DSD-DNPH Diffusive Sampling Device (Supelco, USA), the UMEx 100 Passive Sampler (SKC Inc., USA), and the ChemDisk 571 Aldehyde Monitor (Assay Technology Inc., USA) with manufacturer's specifications, respectively, of 71.9 (uptake rate: 0.00530 μg/(ppb*h)), 28.6 (reporting limit: 0.040 ppm/h), and 16.2 mL/min (reporting limit: 0.080 ppm/h). We believe these systems are not suitable for C or STEL comparison or for low FA air concentrations because of their poor captation capability compared to active sampling.

Unlike the PFBHA passive method which involves thermal desorption, the DNPH active sampling requires chemical extraction before injection into the chromatographic unit. This problem is easily overcome by using SPME, a solvent-free technique that incorporates sampling, isolation, and enrichment in one step. The derivatization kinetics showed that the reaction of PFBHA with FA was instantaneous during the sampling and also the SPME's fiber retraction inside the needle allowed excellent evaluation of TWA occupational exposure limits.

The second requirement for a new air monitoring approach was to improve the management of data from the indirect and direct reading methods. All four samplers were employed remotely by FA Data Storing System (Chromline, Italy) as much as possible to avoid operator variability or mistakes. The sampling data and their analytical results were then integrated into a laboratory information management system (LIMS, Bika Lab System, South Africa) which generate reports and analyze historical data (Fig. 3).

Combining the rapid FFA—SPME's 1-min and the Formaldemeter's IH monitorings enabled us to identify when peaks in emissions occurred. Specifically, comparing the repeated
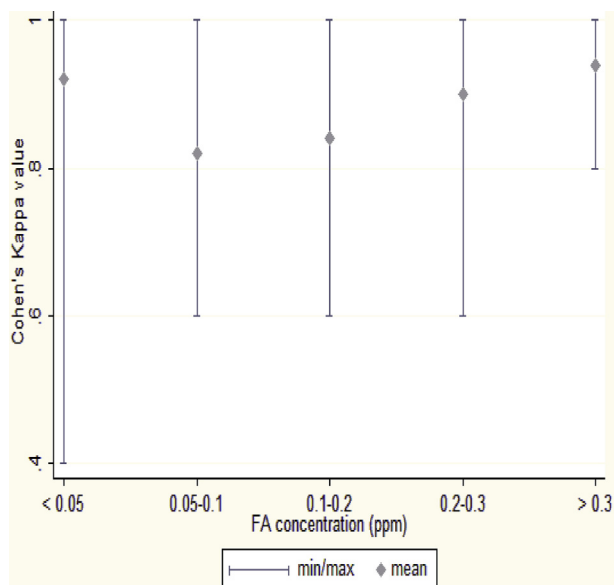
Table 2
Summary of FA personal sampling results determined in 12 hospitals by the four evaluated methods.

Hospital wards	Operations	Number of operations/8 h (mean)	15-min STEL/8-h TWA (Number of samplings)	Active-sampling DNPH-cartridge method		Passive-sampling PFBHA-SPME method		Formaldemeter *htV* electrochemical sensor		Dräger-Bio-check F enzyme-based badge
				15-min exposure[*] Sampling 15 min Mean (min−max) (*ppm*)	**8-h exposure** Sampling 8 h Mean (min−max) (*ppm*)	**15-min exposure**[*] Sampling 1 min Rapid-FFA-SPME Mean (min−max) (*ppm*)	**8-h exposure** Sampling 8 h TWA-FFA-SPME Mean (min−max) (*ppm*)	**15-min exposure**[*] Sampling 10 sec Mean (*ppm*)	**8-h exposure** Sampling 10 sec Mean (min−max) (*ppm*)	**8-h exposure** Sampling 2 h Mean (min−max) (*ppm*)
Operating theater[†]	Immersion of the biopsy in 4% FA container [1]SecurBiop 60 mL (Trace, Italy) [2]MGM 20-, 60-, 220-mL (Meccanica G.M., Italy) [3]BiopSafe 20-mL (Axlab Innovation, Denmark) [4]Kaltek 10-,30-,60-mL (Kaltek, Italy) [5]Kaltek 1-, 5-L (Kaltek, Italy)									
	Background[§]	−	4/7	0.02 (0.01−0.04)	0.011 (0.006−0.026)	<0.03 (<0.03−0.03)	0.013 (<0.01−0.029)	0.03 (0.01−0.05)	0.01	up to 0.05 (up to 0.05)
	Immersion of small biopsies in pre-filled 4% FA containers[1,2,3,4]	41	16/25	0.05 (0.01−0.10)	0.016 (0.012−0.086)	0.04 (<0.03−0.22)	0.019 (0.011−0.101)	0.05 (0.01−0.31)	0.03	up to 0.05 (up to 0.05−>0.3)
	Immersion of large biopsies in 1 or 5 L 4% FA containers[5]	22	16/14	0.419 (0.01−1.36)	0.101 (0.036−0.512)	0.59 (<0.03−4.55)	0.089 (<0.01−0.473)	0.65 (0.02−4.02)	0.09	0.1 to 0.2 (up to 0.05−>0.3)
Segretariat[‡]	Registration and labeling of the 4% FA containers coming from operating theater Background[§]	−	7/10	0.04 (0.03−0.08)	0.021 (0.018−0.036)	0.05 (<0.03−0.09)	0.029 (0.015−0.048)	0.06 (0.01−0.06)	0.04	up to 0.05 (0.05−0.1)
	Registration and labeling of biopsies in pre-filled 4% FA containers[1,2,3,4]	78	44/42	0.29 (0.02−1.29)	0.084 (0.01−0.726)	0.21 (<0.03−3.94)	0.077 (0.02−0.673)	0.32 (0.0−3.52)	0.09	up to 0.05 (up to 0.05−>0.3)
	Registration and labeling of biopsies in 1 or 5 L 4% FA containers[5]	97	26/47	0.19 (0.02−0.99)	0.071 (0.01−0.349)	0.18 (<0.03−3.78)	0.055 (0.02−0.301)	0.21 (0.03−3.66)	0.06	up to 0.05 (up to 0.05−>0.3)
Pathology laboratory[‡]	Cut up of previously fixed surgical pathology specimens Background[§]	−	8/5	0.04 (0.02−0.07)	0.032 (0.019−0.041)	0.05 (0.04−0.10)	0.038 (0.018−0.051)	0.05 (0.01−0.06)	0.03	up to 0.05 (0.05−0.1)
	Cut up of previously fixed small biopsies	61	31/76	0.201 (0.08−1.17)	0.083 (0.046−0.501)	0.175 (0.07−3.06)	0.067 (0.032−0.436)	0.229 (0.03−3.48)	0.08	up to 0.05 (up to 0.05−>0.3)
	Cut up of previously fixed large biopsies	82	36/30	0.385 (0.11−1.76)	0.196 (0.066−0.897)	0.431 (0.13−5.09)	0.215 (0.087−1.126)	0.311 (0.19−4.77)	0.431	0.1 to 0.2 (up to 0.05−>0.3)
	Sealed by UVS of the labeled bags after the reduction	23	13/15	0.29 (0.07−0.57)	0.099 (0.048−0.23)	0.33 (0.05−1.84)	0.108 (0.035−0.17)	0.32 (0.04−1.01)	0.39	up to 0.05 (up to 0.05−>0.3)
Pearson correlation factor (p value) (number of determinations = 471)				Active-sampling DNPH-cartridge method *vs* passive-sampling PFBHA−SPME method = 0.82 (p < 0.05) Passive-sampling PFBHA−SPME method *vs* Formaldemeter *htV* electrochemical sensor = 0.81 (p < 0.05) Formaldemeter *htV* electrochemical sensor *vs* active-sampling DNPH-cartridge method = 0.77 (p < 0.05)						

DNPH, 2,4-dinitrophenylhydrazine; FA, formaldehyde; FFA, fast fit assembly; PFBHA, O-(2,3,4,5,6-pentafluorobenzyl) hydroxylamine; SPME, solid phase microextraction; STEL, short-term exposure limit; TWA, time-weighted average; UVS, under-vacuum sealing.

[*] The 15 min measurements were performed during the most critical activity for the occupational exposure.

[†] Surgery department with a mean of eight operating theaters.

[‡] Segretariats and pathology laboratories receive specimens also from several ambulatories and regional peripheral hospitals.
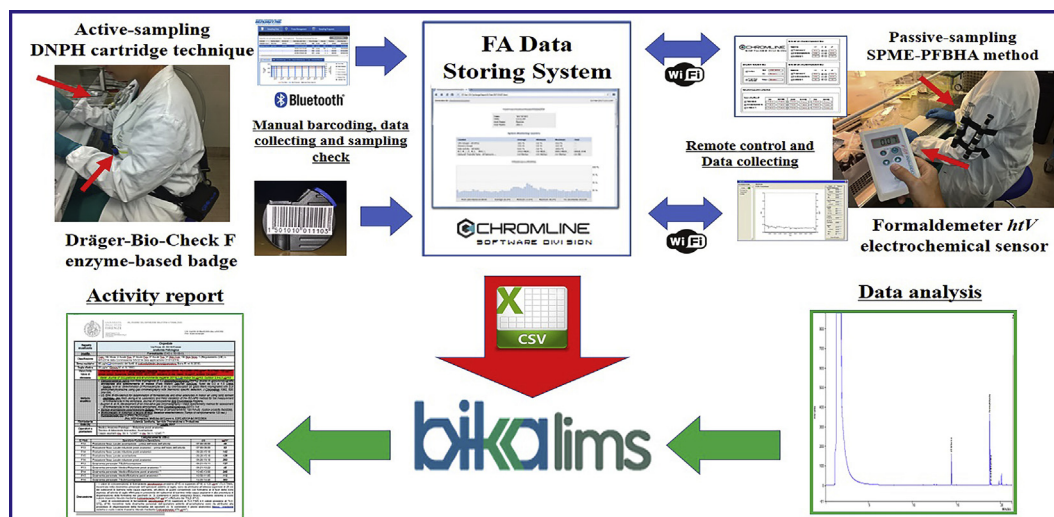
[§] Area sampling before starting work.

Fig. 3. FA Data Storing System: the connection of the four analytical methods and the linking output to Bika LIMS.
DNPH, 2,4-dinitrophenylhydrazine; FA, formaldehyde; PFBHA, O-(2,3,4,5,6-pentafluorobenzyl) hydroxylamine; SPME, solid phase microextraction.

continuous monitoring data with the C and STEL limit values gives us a picture of workplace exposure. On the downside, the rapid FFA−SPME requires a large number of fibers for sampling while the Formaldemeter may have low specificity in certain conditions, but the SPME makes up for the latter's shortcomings. TWA limit values could be evaluated easily in terms of feasibility for operators by DNPH active sampling and TWA−FFA−SPME, being the analytical methods both validated. Although active sampling is more sensible and useful to compare with indoor/outdoor in living environment, the passive sampling avoids the difficulties of pumps and wet chemistry. The miniaturized structure of the Draeger-Bio-Check F allowed real-time measure also as leak detector, inspections, and to verify any breakthrough of charcoal-impregnated face masks.

We have already started to expand the application of this methodology and to create a framework by carrying out inter-laboratory exercises as other research group [18−20].

5. Conclusion

In conclusion, given the continuous updating of occupational exposure limits for FA in recent years, with significant differences between countries, we propose an integrated air monitoring approach for assessing FA in the workplace which allows for measuring concurrently multiple parameters: personal/ambient, direct/indirect, TWA/STEL/C, elevated sensitivity. Furthermore, the high number of analyses necessary to evaluate FA occupational exposure, as it is now considered carcinogenic, requires economical and simple-to-use samplers, whose work should be, as far as possible, automated so as to avoid errors and be faster.

Monitoring airborne FA is especially important because of FA's lack of biological indicators and its low odor threshold. Our experimental and field comparisons demonstrate that these four FA vapor measuring methods agree and are all easily sustainable, either individually or combined, in an IH plan to prevent significant exposure to this chemical. This integrated monitoring is suitable for the quick assessment of airborne FA exposure; moreover, it may assist in improving the safety and air quality in the workplaces where FA is used. The campaign carried out in 12 hospitals of Italy revealed that the occupational exposure limits were frequently exceeded in normal use, but the subsequent introduction of UVS sealing for large biopsies, restricted the use of FA to appropriately ventilated areas in the pathology lab.

Conflicts of interest

The authors have no conflicts of interest to declare.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.shaw.2018.05.002.

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