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STRATEGY TO EVALUATE THE IMPACT OF FORMALDEHYDE IN ANATOMICAL PATHOLOGY LABORATORY PART III: EQUIVALENCE TEST PROCEDURE FOR AIR MONITORING METHODS

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SUMMARY: To date, formaldehyde (FA) is one of the more common chemicals and its use is widespread around the world in different sectors, especially in chemical facilities and health care. FA is widely used in working activities owing to its chemical and physical properties. However, it also represents a concerning hazard for the workers' health due to its toxicity and recognized carcinogenicity. The FA exposure evaluation in occupational setting has arisen interest in the scientific community that leads to the development of several analytical instruments in order to assess both long term and short-term exposure. The paper presents and discusses an equivalence tests procedure via the 2.4-dinitrophenylhydrazine (DNPH)-active air sampling formaldehyde (FA) reference method and two non-reference instruments based on continuous, direct reading monitoring, namely ProCeas® (AP2E) and NEMo XT (Ethera). The FA standard atmosphere calibration system was used to check the reference method by Pearson's test. Subsequently, the Passing-Bablok test was carried out between the non-reference methods and the DNPH method for potential systematic or proportional errors, and finally the Bland-Altman plot was applied to determine the mean bias and the variances of the recorded values by the reference and non-reference methods in on-field sampling. The results showed a good correlation between the non-references method and the DNPH ones, suggesting their possible applications in heterogeneous occupational scenarios.

Key words: *formaldehyde, equivalence procedure, occupational monitoring*

INTRODUCTION

Formaldehyde (FA) is the one of the most important carcinogen in outdoor air among the 187 hazardous air pollutants (HAPs) identified by the United States (US) Environmental Protection Agency (EPA). It is by far the FA is the most important HAP in terms of health risk, accounting for over 50% of the total HAPs-related cancer risks in the US *(Strum et al., 2016)*. In occupational setting in the European Union, the number of workers exposed to FA above the background level is calculated to be 1.7 million *(Scarselli et al., 2017)*. Although most exposed workers are foreseeably engaged in chemical and plastics factories, the highest mean levels of exposure were recorded in the health-care sector, especially in Anatomical Pathology Laboratories *(Higashikubo et al., 2017, D'Ettore et al., 2017)*.

The protection of the air against pollutants is one of the most important elements of European

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Union (EU) policy both in the environmental and occupational fields. In 2008 the Directive of European Parliament and European Council 2008/50/EC establishes the need to reduce pollution to levels which minimise harmful effects on human health, and the environment, to improve the monitoring and assessment of air quality including the deposition of pollutants and to provide information to the public. Since 2019, the scientific evaluation of the relationship between the health effects of hazardous chemical agents and the level of occupational exposure was conducted by European Chemicals Agency (ECHA) and its Committee for Risk Assessment (RAC).

As a pollutant, formaldehyde (FA) can be released into the environment by both natural and human activities. In the urban environment, the FA air concentrations ranging from 1.2 to 36 μg/m^3 *(Rodrigues et al., 2017, Salthammer, 2019)*. The European Commission instituted, in November 2014, an outdoor air limit for FA of 0.9 μg/m^3 *(Dugheri et al., 2019)*. In 2015, the EU e Scientific Committee on Occupational Exposure Limits (SCOEL) proposed the FA OELs of 0.36 mg/m^3 for 8-hour exposure and 0.72 mg/m^3 for 15-minute exposure. Besides, the expert panel endorsed Directive 2019/983 of June 5, 2019, which introduced a transitional period of 5 years for the healthcare sector, during which the FA limit value of 0.6 mg/m^3 for 8-hour exposure would apply.

These restrictive limit and reference values for airborne FA can only be simultaneously detected with a few analytical methods, therefore a monitoring strategy is necessary which allows the assessments of both occupational hygiene and air quality. The reference methods to detect gaseous FA are based on active or passive sampling using 2,4-dinitrophenylhydrazine (DNPH), as reagent, whether on filters or solid sorbent and later analysed by liquid- (L) or gas-chromatography (GC) *(Dugheri et al., 2017, 2021)*. These indirect methods provide FA concentration averaged 8 hours at high sensitivity, however the results are not in real time mode.

Results obtained *(Dugheri et al., 2022)* suggest that occupational monitoring, which comprises long- and short-term evaluation, must be recommended to obtain a complete exposure assessment, especially, for FA with chronic and acute toxicity and related occupational limits. To simplify the sampling process and analytic operations, portable direct-reading, in-continuous FA monitors are of increased interest, laying the bases for on-site analyses as confirmation-level methods, with high specificity, like conventional monitoring methods *(Dugheri et al., 2021)*. The experimental and field comparisons showed that direct-reading instruments are consistent *(Hack et al., 2005, Wisthaler et al., 2008, Chevallier et al., 2012)*. Furthermore, they can be easily integrated into an occupational hygiene plan to prevent significant acute toxicity resulting from FA air monitoring in the workflow connected to the anatomical pathology laboratory *(Dugheri et al., 2018)*.

In EU, a methodology for the demonstration of equivalence of non-reference methods for gases and vapors in the occupational hygiene field has not been regulated yet. The UNI EN 482:2021 and ISO 20581, as basic performance requirements, as well as UNI EN 14412:2005 and ISO 22065:2020, allowed the validation of the method but not the comparison between reference and non-reference methods.

Differently, concerning the ambient air quality and cleaner air in Europe *(Directive of European Parliament and European Council 2008/50/EC)*, in the methodology of equivalence determination, the member countries are allowed to apply another measurement methods provided that they are able to demonstrate its equivalence with the reference method. The Directive established a group of laboratories that shall be involved in the wide quality assurance programmes and shall also coordinate the appropriate realisation of reference methods and the demonstration of equivalence of non-reference methods. Likewise, in a non-standard guide *(EC Working Group on Guidance for the Demonstration of Equivalence, 2010)*, the EU recommends a procedure based on estimation of uncertainty of the results obtained using a candidate sampler by laboratory and field tests. The criteria for acceptance of the candidate monitoring, as equivalent to the reference method, are as follows: n. 4 campaigns a year (each with n. 40 'side by side' measurements), orthogonal regression applied to each set of measurements separately and then again to one global measurement set, inclination coefficient of the straight 'b' does not

differ significantly from unity, coefficient of axis interception 'a' does not differ significantly from zero, elimination of gross errors using Grubbs test, difference in expanded relative uncertainty between results for the candidate sampler and the reference sampler less than 25%.

The paper present and discuss a new methodology of equivalence determination - for occupational hygiene - via laboratory and on-field tests comparing the DNPH-active air sampling FA reference indirect method versus two non-reference instruments based in-continuous, direct reading monitoring, namely ProCeas® Formaldehyde analyzer (AP2E, Aix-en-Provence, France) and NEMo IAQ Monitor XT (Ethera, Crolles, France).

MATERIALS AND METHODS

Air monitoring system

This work introduced an airborne FA monitoring system that improved measurements in terms of specificity, sensitivity, and robustness. The three methods of monitoring FA airborne described here are still in use, and available on the market. Specifically, the reference method is indicated below:

- DNPH-coated cartridges on a silica sorbent (Sep-Pak XpoSure Sampler Plus Short, Cat. No. WAT047205, Waters, Milford, MA, US) were used in active sampling by a 6-position GasCheck Basic automatic collector box (AMS Analitica, Pesaro, Italy) set to 0.3 and 1.2 L/min flow rate for 8-h and 15-min, respectively. The capillary GC analysis of FA-2,4-DNP-hydrazone was performed as described in previous work *(Dugheri et al., 2020, 2018, 2017)*. Briefly, a 35% phenyl-65% polydimethylsiloxane (PDMS) stationary phase column (Cat. No. 122-3832UI, DB-35MS UI, Agilent J&W GC Column, Santa Clara, CA, US) was connected to large-volume injection (LVI)/ programmed temperature vaporisation (PTV) injector (SCION Instruments, Amundsenweg, The Netherlands), and a nitrogen-phosphorus thermionic specific detector (TSD) within a GC Varian CP3800. Certified Reference Material (CRM) - produced following International Organization for Standardization (ISO) 17034 and ISO/International Electrotechnical Commission (IEC) 17025 guidelines - were used for GC calibrations. Fully automation of the elution of DNPH-coated cartridges and the subsequent analysis was performed using a *xyx* robotic system called Multi-Purpose autoSampler (GERSTEL GmbH & Co.KG, Mülheim an der Ruhr, Germany), on-line with the GC and equipped with the DNPH-option (GERSTEL GmbH & Co.KG) controlled using the MAESTRO software (GERSTEL GmbH & Co.KG).

We compared the reference method with two in-continuous, direct reading, pre-calibrated (from the manufacturers) instruments:

- Next Environmental Monitoring (NEMo, Cat. No. NE-KIT440) XT (Ethera) passive sampler with a nanoporous FA sensor (Cat. No. NE-FOR01x), which uses a sol-gel process based on colour variation with an optical reader every 2-hours and and Limit of Detection (LoD) of 8 mg/m^3,
- ProCeas® Formaldehyde analyzer (AP2E) a laser infrared spectrometer for instantaneous (response time up to 2 seconds) monitoring (LoD of 1.2 mg/m^3).

Data management

Collection of the air samples for FA was conducted based on UNI EN 1540:2022 e ISO 18158:2016. The two Machine to Machine (M2M) solutions - NEMo XT by Sigfox and GasCheck Basic via conventional Mobile Communications (GSM) together with ProCeas® by Virtual Private Network (VPN) - have successfully allowed remote monitoring systems. A Database Management System (DBMS) has provided a central data repository that be accessed by multiple users in a controlled manner. The centralized storage and management of data within the DBMS has provided: data abstraction and independence, data security and uniform data administration procedures. Its interface with open-source Bika LIMS (Cape Town, South Africa) has allowed to implement instrument interfaces, quality control

and ISO 17025 accreditation, eliminating human errors and reducing administration costs.

Equivalence tests procedure

The proposed equivalence procedure between the reference and non-reference methods is articulated in three steps, indicated below.

i) Linear regression model with Pearson coefficient (r) to verify the correlation of the dynamic atmosphere standards with reference method. DNPH reference method was verified with the dynamic FA atmosphere standard (0.024-12.28 mg/m^3), obtained by permeation tube, using a linear regression model with Pearson coefficient (r). This test aims to evaluate statistical significance of the correlation between the DNPH method, used as reference method in the subsequent steps of the equivalence procedure, and the standard vapors, used as calibrators: 10 gaseous standards at different concentration (ranging from 0.013 to 14.652 mg/m^3) were tested in triplicated with the DNPH method in the test chamber at 25°C. The average values, resulted by the DNPH method, were plotted against the expected value, equal to the FA gaseous standard concentrations.

ii) Passing-Bablock regression for pairwise compared reference and non-reference methods in test chamber. NEMo XT, ProCeas® and the reference DNPH method were used in the test chamber at 25°C to analyze 17 FA concentration calibration levels (ranging from 0.010 to 2.560 mg/m^3). The results of the two direct reading instruments were compared pairwise with the one obtained by DNPH reference method, using Passing-Bablock regression plot. This regression analysis allows us to evaluate the constant (intercept) and proportional (slope) systematic error. It is always necessary to report not only these two parameters, precise estimates of the true intercept and the true slope, but also the corresponding intervals of 95% confidence, that are the intervals in which with a certain confidence (95%) the true intercept and the true slope can be found. In particular, the relevant intervals of confidence must include 0 (zero) for the intercept and 1 (one) for the slope in order to demonstrate the absence of constant and proportional systematic error.

iii) Bland-Altman regression for pairwise compared reference and non-reference methods on-field measurements. Reference and non-reference methods were compared pairwise by Bland-Altman plot with Confidence Intervals (CIs) calculation from the results obtained by on-field measurements. The average of the two methods (x-axis) can be graphed toward the differences of the two methods expressed as a percent from the mean, i.e., method1- method2/mean * 100 (y-axis).

We proceed by assessing the possible presence of systematic error by calculating the "bias," obtained as the mean of all differences and the associated confidence interval of 95%: there is a systematic error significant ("bias" significant) when the value 0 (zero) will not be within the relevant 95% confidence interval. In the absence of systematic error, the points corresponding to the differences between the two methods should accumulate randomly around the zero line. In addition to the mean difference (and the corresponding 95% confidence interval), it is also necessary to calculate the interval encompassing 95% of these differences using the mean±1.96SD, where the mean and SD are the mean ("bias") and SD of the differences found, respectively. This interval has considerable importance in the experiment of comparison, because it makes it possible to identify the magnitude of most (95 percent) of the differences found *(Vidali et al., 2016)*.

The statistical analysis was performed with Excel (Microsoft Office 365, Microsoft, Redmond, US) and a new interactive website (available at https://bahar.shinyapps.io/method_compare/) developed by Bahar et al. *(Bahar et al, 2017)* for method comparison and bias estimation studies, based on free and open-source tools using R programming language *(R Core Team, 2021)*.

Laboratory measurement for the test for equivalence: dynamic FA atmosphere standard by permeation tube

Calibration of the air monitoring devices was verified with a dynamic calibration system. To carry out FA dynamic atmosphere standard,

permeation tube devices filled with paraformaldehyde were purchased from Fine Metrology (Spadafora, Messina, Italy). Each tube was calibrated according to Environmental Protection Agency (EPA) and certified (±5%) for the permeation rate (48, 92, 143, and 176 ng/min) at the calibration temperature (60 °C).

The calibration gas generator with temperature controlling system (Sonimix 6000C1, LNI Swissgas, Versoix, Switzerland) was employed to generate FA atmosphere at constant concentrations from one or more permeation tubes. The temperature of the chamber which directly affects the permeation rate of the FA gas was controlled digitally at 60 °C. According to the manufacturer, the desired volumetric concentration is established or changed by simply varying the inert carrier gas flow (which sweeps the calibration gas from the chamber) from 0.5 to 5 L/min.

The gas concentration generated from permeation tubes with different dilution gas flows can be represented by

$$[FA_{air}] = (W/T) \times F_{air}^{-1}$$

where $[FA_{air}]$ is the concentration of the FA in the air (µg/L), F_{air} is the airflow (L/min), W/T, the permeation rate (PR) (ng/min) given by W, the FA weight loss (ng) and T, the measurement interval (min); *(Dugheri et al., 2022)*.

On-field measurements for the test for equivalence

This study was carried for n.4 months between 2021 and 2022 in the anatomical pathology laboratory, at the General Hospital of Macerata (Macerata, Italy). Environmental air monitoring was carried out in the Pathology Lab gross room, where tissue specimens were examined and dissected by residents, pathologists, and trained technicians. All three monitoring devices (GasCheck Basic automatic collector box, NEMo XT, and ProCeas®); (Figure 1) were placed on a tripod, positioned near the operation area at 40 cm from the operator's breathing zone and connected wirelessly to the Chromline FA Data Storing System *(Dugheri et al., 2018)*.

Figure 1. Monitoring devices: Proceas® (a), GasCheck (b) and NEMo XT (c)

Slika 1. Uređaji za nadzor: Proceas® (a), GasCheck (b) i NEMo XT (c)

RESULTS AND DISCUSSION

Linear regression model with Pearson coefficient (r) to verify the correlation of the dynamic atmosphere standard with reference method.

This step was carried out to verify the significance of correlation between the reference method using DNPH with the FA standard vapors, obtained by permeation tube, used as standard calibrators. The results were shown in Figure 2.

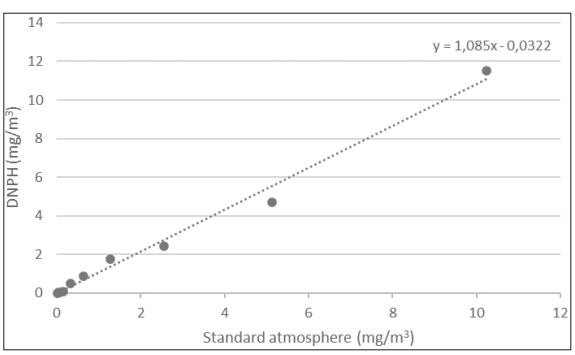

Figure 2. Graphical representation of the linear regression model of DNPH method paired with standard atmospheres

Slika 2. Grafički prikaz modela linearne regresije DNPH metode sparen sa standardnim atmosferama

The data obtained by the DNPH method plotted on the respective expected values of the FA gaseous standard showed a *r* equal to 0.98. In sight of this, the DNPH method presents a strong positive correlation with the generated standard atmospheres of FA, and it can be assumed as reference method for the subsequent evaluations of the equivalence procedure.

The uses of permeation tubes have grown to such an extent that they are now produced commercially for more than 400 compounds *(Tumbiolo et al., 2005)*. Permeation methods use a sealed container divided into two sections by a permeable membrane made of polymers, that is selected according to the application. In the permeation tube, the analyte migrates through the permeable membrane at a defined temperature and the permeation rate is obtained by gravimetric determination *(Dugheri et al., 2022)*. Concerning the FA, this reference method for standard gaseous dynamic generation involves the depolymerization of paraformaldehyde or polyoxymethylene in a permeation tube *(Brewer et al., 2013)*. The permeation tube technology presents fewer issues compare to the other FA generation systems technologies: *i)* the motor-driven syringe pump system is affected by the formation of FA oligomers, water condensation, and time limits of generation *(Andrawes, 1984)*, *ii)* the nebulizers require further tests to optimize their geometry and guarantee sufficient robustness *(Dugheri et al., 2022)*, *iii)* the catalytic conversion of methanol is not commercially available, and it is set for research-specific applications *(Dugheri et al., 2022)*.

Thus, in this context, the FA vapor standards generated by permeation are used to test the method based on DNPH derivatization. This method is considered the reference method to determine the derivatized FA concentrated on a solid sorbent, and this well-defined procedure can be also certified using FA-DNPH-hydrazone standards, such as in most Proficiency Testing programs (such the IFA - Institut fur Auslandsbeziehungen der Deutschen Gesetzlichen Unfallversicherung-proficiency testing for aldehydes). The analysis of FA DNPH-derivatives was carried out with GC coupled with specific detector. In consideration of the user-friendliness, the portability, and the contained costs, as well as its "green line" - hydrogen, nitrogen, or air as a carrier gas *(Margolin et al., 2022)*, and introduction of MicroElectroMechanical Systems (MEMS) technology *(Immadeddine and Khaladoun, 2018)* - GC is considered a mature technique for high performance, robustness, and wide applicability in a routine and industrial environment. Particularly, Capillary GC (CGC), introduced about 60 years ago, has evolved through many developmental milestones into an indispensable instrument in many analytical laboratories *(David and Sandra, 2022)*. The analytical separation by GC was used considering that previous Authors *(Huynh et al., 2002, Hafkenscheid and van Oosten, 2002, Dugheri et al., 2018)* found that the coefficient of variation in the DNPH-LC/ultraviolet FA method was approximately 23% for low levels of FA (0.012 mg/cartridge). Moreover, the LC technique - more expensive in terms of purchase and maintenance than GC - is limited in terms of co-elution and specificity, given that the detection and quantification limits exceed the indoor air quality legal requirements, especially during short sampling times.

The GC analysis of DNPH-derivatives suffers from one major problem that is the excess of the derivatizing agent, that must be removed from the sample prior to analysis. To overcome this issue, according to previously proposed procedure *(Dugheri et al., 2017)* a clean-up of the sample by cation exchange solid phase extraction, using a polymeric MCX Plus Oasis mixed-mode cation-exchange cartridge (Cat. No. 186003516, Waters, Milford, US), was carried out. This step drop the LOD by one order of magnitude. Consequently, we selected the cheaper and easier-to-operate system consisting of a GC/TSD apparatus that permitted the separation of the major DNPH degradation product (2,4-dinitroaniline) from the FA-2,4-dinitrophenylhydrazone.

Passing-Bablock regression for pairwise compared reference and non-reference methods in test chamber.

In this step, the two in-continuous direct reading instruments are tested and paired with the reference method with DNPH, analysing FA standard vapors in a test chamber at 25°C.

The great ferment for in-continuous, direct reading instruments for both short- and long-term

airborne FA monitoring is due to their ease of use and possibility of remote management, as well as defined calibration by the manufacturing company. Immediate measurement methods are simplified procedures for the assessment of the target substances concentration on the spot. Compared to indirect collecting methods, instantaneous ones provide results in a shorter time. Thanks to the simplification of sampling and determination, FA in-continuous, direct reading monitors are increasingly attractive. Spectroscopic techniques present specificity and thanks to their sensitivity and high sampling frequency, can be chosen as reference methods. Between these kind of instruments, the ProCeas® (AP2E) Formaldehyde is a new complete pre-calibrated instrument based on enhanced laser infrared (IR) spectrometer for measurement of FA in ambient air. Optical Feedback Cavity Enhanced Absorption Spectroscopy (OFCEAS) is a direct intensity measurement scanning spectroscopy technique, relying on hyper-reflective measurement gas cells and laser source purity enhancement technique. This instrumental setting allow to achieve extremely low-level detection of trace gases in very short times. OFCEAS technology associated with Low Pressure Sampling (LPS) - a novel sampling technique under reduced pressure (50 mbar absolute at flow rate of 3 to 9 Liters/hour at atmospheric pressure) - enables direct FA airborne measurement providing selectivity and simultaneous multi-component measurement without interferences, regardless of the matrix. LPS in the sampling system removes any risk for chemicals adsorption/desorption and condensation in the line. The NEMo incorporates an innovative measurement technology developed by ETHERA under CEA/CNRS license based on nano-porous materials and direct optical reading. The measuring is ranged from 7 to 2000 ppb according to exposure time (from 15 to 120 minutes). The sampling is of the diffusive type by consumable Formaldehyde sensor (ETHERA ref. NE-FOR01x) to be replaced every 7-15 days according to exposure concentrations. In another commercial version - Profil'Air® measuring kit - ETHERA allows to perform both active and passive sampling for short- and long-term exposures with the consumable Formaldehyde sensor by a subsequent manual spectrophotometric analysis.

The results of the statistical analysis of Proceas® and NEMo XT paired with DNPH method were showed in Figure 3 and 4 respectively.

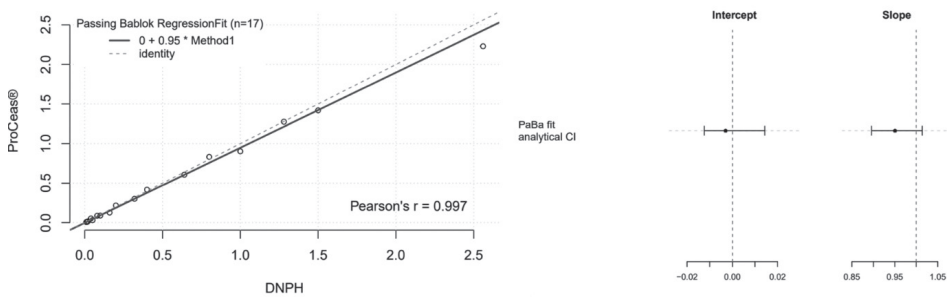

Figure 3. Graphical representation of Passing-Bablock regression between Proceas® and DNPH
Slika 3. Grafički prikaz Passing-Bablock regresije između Proceas® i DNPH

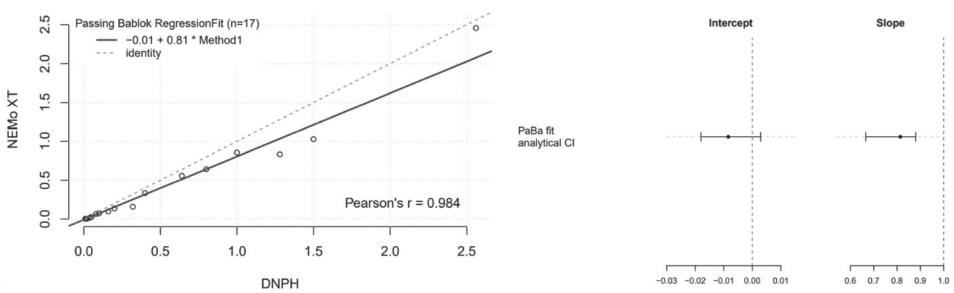

Figure 4. Graphical representation of Passing-Bablock regression between NEMo XT and DNPH
Slika 4. Grafički prikaz Passing-Bablock regresije između NEMo XT i DNPH

The data showed that the Proceas® does not present both constant and proportional systematic error, since its intervals of confidence for slope and intercept include 0 and 1, respectively (Table 1 and Figure 3); concerning the NEMo XT, it shows instead the presence of proportional systematic error since the respective relevant interval of confidence does not include 1 (Table 2 and Figure 4). This errors can lead either to a mathematical correction, or to an examination of the causes of error with consequent elimination. In this case, the proportional systematic error observed for the NEMo XT could be attributed to a non-perfect interface between the direct reading instruments and the test chamber.

Table 1. Estimate (EST), and upper-lower confidence interval (UCI-LCI) for intercept and slope

Tablica 1. Procjena (EST) i gornji-donji interval pouzdanosti (UCI-LCI) za odsječak i nagib

Pair		EST	UCI	LCI
Proceas® vs DNPH	Intercept	-0.003009	-0.01239	0.01434
	Slope	0.9505	0.8958	1.014
NEMo XT vs DNPH	Intercept	-0.008415	-0.01794	0.0029
	Slope	0.8141	0.6655	0.8799

Bland-Altman regression for pairwise compared reference and non-reference methods on-field measurements.

The three methods, DNPH, NEMo and Proceas®, were tested for pairwise in an anatomical pathology laboratory in order to observe their closeness agreement during on field measurements.

The paired results, DNPH vs Proceas® - DNPH vs NEMoXT - Proceas® vs NEMo XT, were graphed in Figure 5.

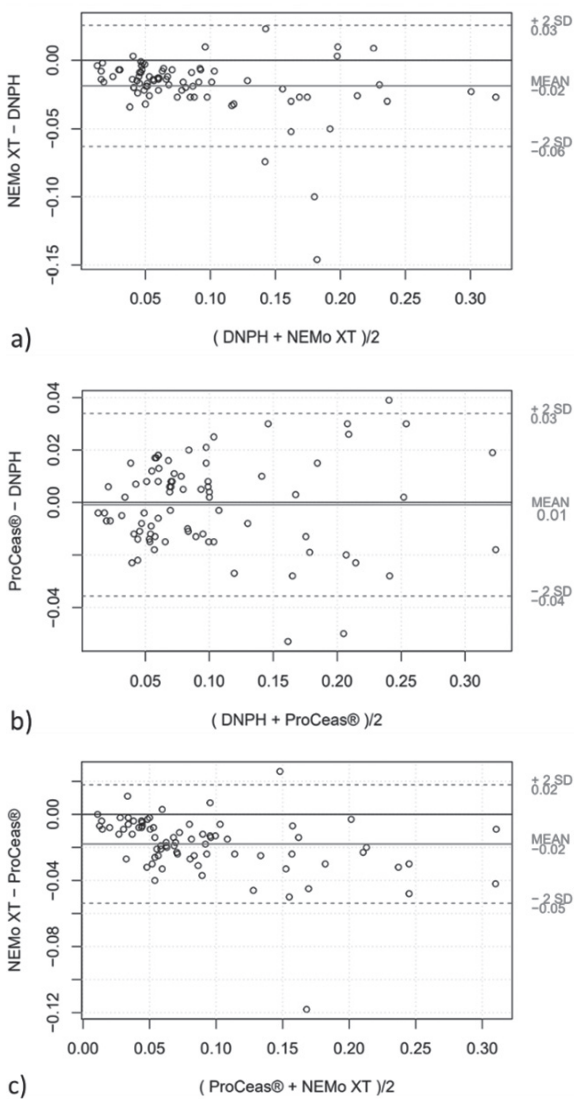

Figure 5. Bland-Altman regressions for pairwise FA monitoring methods: a) DNPH vs NEMo XT, b) DNPH vs Proceas®, c)Proceas® vs NEMo XT

Slika 5. Bland-Altmanove regresije za parne metode praćenja FA: a) DNPH prema NEMo XT, b) DNPH prema Proceas®, c) Proceas® prema NEMo XT

The two direct reading instruments showed a small bias paired both with the reference DNPH method and between each other: 0.02 for DNPH vs NEMo XT, 0.01 for DNPH vs Proceas® and 0.02 for Proceas® vs NEMo XT. The biases observed are not systematic significant error in all the three tests carried out, since the value 0 is included in each 95% confidence interval. There are some outliers measures that could be due to the heterogeneity of the sampled environment and the monitored tasks.

The grossing activities could be the main target for reducing pollution by formalin vapours. Pathologists spend long hours in front of the aspirating chemical fume hood and, therefore easy monitoring of the airborne FA with multipoint configured instruments or lower priced instruments are recommended. The 8-h TWA levels are not always appropriate assessing the occupational exposure because they are influenced not only by the proportion of large vs small specimens grossed during the work shift, but also heavily by the intraday workload variation. For these reasons, the introduction of in-continuous monitoring systems should be adopted to make a fair assessment of FA exposure and, at the same time, to evaluate the goodness of high-tech tools and FA mitigation solutions adopted. In this sight, for short-term sampling we used a ProCeas® with multichannel monitoring; weight (20 kg) and size (standard 19″, 4U rack, 550 mm depth), as well as high cost (around 50,000 euros), requires centralization of monitoring, managed with a multipoint sampler. Conversely, the small size (190x135x70 mm) and weight (520 grams), as well as the battery power (lithium battery 3.6V, 17Ah-D type with connector, lifetime up to one year), and the lowest cost (around 5,000 euros) compared to ProCeas®, make the NEMo XT wearable near the breathing area. In this study, the direct reading instruments are mounted on a tripod, located near the chemical fume hood. In order to assess the occupational exposure, the EN 689:2018 encourages the use of personal sampling devices within the breathing zone of the worker. EN 1540:2011 and ISO 18158:2016 specify that the breathing zone corresponds to a hemisphere (circa 30 cm in radius) extending out in front of the face, centered on the midpoint of a line running from ear to ear, with a plane connecting this line, the top of the head and the larynx. However, some Authors *(Vimercati et al., 2010, Lee et al., 2017, Dugheri et al., 2019)* revealed similar FA median concentrations of the personal and area exposures, indicating that they were comparable - with an approximate ratio of 1.0 - when work processing no-requires continuous movement around the work area.

CONCLUSION

For the first time, the Authors present an equivalence test procedure for FA air monitoring methods in work environments. The test carried out on two direct reading, in-continuous monitoring systems showed that both instruments could guarantee performance equal to the assumed reference method, DNPH sampling system and subsequent GC-TSD analysis. The possibility to introduce these kind of instruments in heterogenous occupational scenario, maintaining similar performances of reference method, both in term of sensitivity and specificity, could allow a complete environmental and personal occupational monitoring.

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STRATEGIJA ZA OCJENJIVANJE UČINKA FORMALDEHIDA U ANATOMSKOM PATOLOŠKOM LABORATORIJU TREĆI DIO: PROVOĐENJE TESTA EKVIVALENCIJE ZA METODE PRAĆENJA ZRAKA

SAŽETAK: Sve do danas formaldehid (FA) često je korištena kemikalija a njegova je uporaba raširena diljem svijeta u različitim sektorima a naročito u kemijskim pogonima i zdravstvu. FA se mnogo koristi u raznim radnim postupcima zbog svojih kemijskih i fizikalnih svojstava. Međutim, njegova toksičnost i karcinogeničnost predstavljaju opasnost za zdravlje radnika. Istraživanje izlaganja FA-u u radnom okružju predmet je zanimanja znanstvene zajednice i rezultira razvojem više analitičkih instrumenata kojima se utvrđuje njegov učinak na zdravlje nakon duljeg i kraćeg izlaganja. U radu je predstavljen i opisan postupak za test ekvivalencije pomoću FA referentne metode 2.4 dinitrofenilhidrazin (DNPH) -aktivnim uzimanjem uzoraka i dva nereferentna instrumenta temeljena na kontinuiranom izravnom praćenju očitanja, ProCeas® (AP2E) i NEMo XT (Ethera). Korištena je sustav za FA standardnu kalibraciju kako bi se referentna metoda provjerila pomoću Pearsonovog testa. Zatim je napravljen Passing-Bablok test između nereferentnih metoda i DNPH metode za otkrivanje mogućih sistemskih i proporcionalnih pogrešaka, a na kraju je izrađen Bland-Altman grafikon za određivanje srednjeg odstupanja i varijacija u vrijednostima dobivenima referentnim i nereferentnim metodama uzorkovanja na terenu. Rezultati su pokazali dobru korelaciju između nereferentne metode i DNPH metoda, naznačujući moguće primjene u raznorodnim radnim uvjetima.

Ključne riječi: *formaldehid, postupak ekvivalencije, praćenje radnog okružja*

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