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Air sampling methods evaluation to measure the formaldehyde occupational exposure at the laboratory

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ABSTRACT An exhaustive risk analysis of potential exposition to formaldehyde in the laboratories has been made due to its dangerous characteristics: CMR substance, very reactive, with a great solubility in water and that deposit in respiratory tract level, nose and rhino-pharynx. The present paper aims to determine which is the most adequate air sampling methodology for ensuring the best evaluation method of the potential exposition risk to formaldehyde in the laboratories. With this goal, the recommendations over the exposition of workers to formaldehyde made by different Health and Safety institutes all over the world have been collected and analysed. In order to choose the best technology for evaluating the risk of exposition to formaldehyde, a study comparing different samplers has been conducted. These samplers belong to two main families: Active samplers and Passive Samplers. The advantages and disadvantages of these two families have been compared, and their performances have been tested within 6 experiments conducted in SANOFI and in the Institut Pasteur (three in each). The article finalizes with a comparison of the different samplers, giving a summary chart that allows choosing the most adequate technology taking into account the restrictions of the laboratory and the sampling time where we have to evaluate the potential risk of exposition.

Key Words: air sampling, formaldehyde, CMR (Carcinogenic, mutagenic, reprotoxic substances)

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1. INTRODUCTION

At room temperature, formaldehyde, also known as methanal or formic aldehyde, is a colourless gas with a pungent, irritating odour. It is highly reactive, hygroscopic, and

Molecular Weight	30,03 g/mol
Melting Point	*- 92 °C ; - 118 °C*
Boiling Point	*- 20 à - 19 °C*
Density	*0,816 g/cm to - 20 °C*
Vapour Density (air = 1)	*1,04-1,06*
Vapour Pressure	*517-519 kPa to 25 °C*
Auto-Ignition	*424 °C*
Odor Threshold	*0,05-1 ppm*

readily undergoes to polymerization. The gas of formaldehyde is easily soluble in water and in polar solvents like ethanol, acetone and oxide de diethyl. Pure gas formaldehyde is not available commercially: it is sold as 30-55% by weight aqueous solutions. This commercial solution, called formalin, includes 0, 5-15% of methanol as an inhibitor of the polymerisation. Formaldehyde has a diverse and extensive utilization due to its physical and chemical properties. For example, due to its conservation and antibacterial properties, it is used as a raw material for the manufacture of formaldehyde-based resins, which are widely used in a variety of industries, predominately the wood industry. Formalin is also used directly or in blends, typically in hospital and laboratories.

Occupational exposure to formaldehyde at the laboratory occurs mainly in pathologic and histologic areas where the formaldehyde is used like disinfectant and like fixative agent. (3)

Like disinfectant, formaldehyde is effective for most of virus and bacteria. Presently due to its toxicities properties most of the product disinfectants contain a solution of formaldehyde inferior to 2, 5% (4). Like fixative agent, the aldehydes are the fixators most used at the industry in the histologic or pathologic sampling with the aim of preserve the form and the structure of the biological tissues.

Formaldehyde is easily absorbed for the respiratory tract (5) as it is the simplest aldehyde and it readily react with proteins and nucleic acids. Indeed, when formaldehyde is inhaled the most of it is retained on nose area, oral mucous and trachea (6).

1.1. REGULATORY FRAME

Presently, formaldehyde is classed as a substance CMR of category C1B and M2 by the **6th Adaptation to Technical Progress (ATP) to the CLP Regulation** of 17th June 2014. Concerning CIRC classification formaldehyde was classed as a carcinogen of category 1, eight years ago.

This affected its use, as the regulatory frame in Europe includes “the Directive on the protection of workers from the risks related to exposure to carcinogens or mutagens at work”: Directive 2004/37/EC of European Parliament and of the Council of 29 April 2004. (7). The following paragraphs have been extracted from the directive:

In all work situations workers must be protected in respect of preparations containing

one or more carcinogens or mutagens and from carcinogenic or mutagenic compounds arising at work. Occupational exposure limit values must be regarded as an important component of the general arrangements for the protection of workers.
Wherever a carcinogen or mutagen is used, the employer must make use of existing appropriate procedures for the measurement of carcinogens or mutagens, in particular for the early detection of abnormal exposures resulting from an unforeseeable event or an accident. (8)

1.2. SAMPLING METHODS

The agencies for occupational safety and health in Europe and USA (NIOSH, OSHA, and INRS in France) have concluded that chemical risk evaluation is currently carried out by sampling the air in the breathing area of the operator. Thus, these methods are prioritised. It is important to take into account that the formaldehyde TWA (Time Weighted Averages for 8h) in Europe is between 0, 3-0, 75 ppm. Therefore, accuracy is an important factor as these limits are so low.
Air sampling methods can be classified into active (or dynamic) and passive (diffusional monitoring), depending on the technique. While some institutes for Safety and Health or administrations, like OSHA, have specified active sampling as the standard technique for evaluating gases and vapours in the work place, passive system has been developed in recent years and has gained acceptance as an alternative technique.

1.2.1. ACTIVE SYSTEMS

With **active systems**, the pollutant is collected by forcing air through collecting devices where the sample is concentrated. The collecting device may be in glass or plastic. Air is forced through the device and the contaminant, or the products of its reaction, are analysed. The requirements for the analysis of air sampled with active systems are a fixative, a pump (to move the air) and a system to measure the volume of sampled air, either directly or by using flow and duration data. The flow and the volume of sampled air are specified in the reference manuals, besides other characteristics as humidity or temperature. The efficacy of the collection increases by reducing the rate of intake or by increasing the amount of fixative used.
The main advantages are:
The possibilities in terms of pollutant nature, range of concentrations and sampling durations are larger.
They may be used for personal and ambiance sampling
Some of the disadvantages are:
They are heavy to implement and more expensive due to the utilization of extra material.

Figure 1: flowmeter, pump, tubes supporting and pipe
They cause an important discomfort for the operator

1.2.2. PASSIVE SYSTEMS

Passive systems capture pollutants by diffusion onto a base with a solid adsorbent, either alone or impregnated with a specific reactant.
The quantity of pollutant captured depends on the diffusion coefficient of the gas or vapour and also of the geometric form of the device.

Advantages:

It is not necessary the utilization of a pump: for this reason they are easily and more comfortable to the operator
Extra materiel is not necessary
More economic
Easier to use : formation not necessary

Disadvantages:

The may be use just for personal evaluation. It is not recommended to use it for sampling times inferior to 30 min except if the sampler has been validated.

Figure 2. *Samplers Fixation to the operator's blouse*

2. EXPERIMENTAL AND METHODS

In order to know the best technique for sampling formaldehyde, a comparative study between the different samplers have been executed. The samplers to evaluate have been selected taking into account their cost and availability.
In order to compare the different sampling supports, they all have been placed at the same time attached to the operator's blouse (at breathing zone level) as showed in Figure 2:
The activities evaluated for every operator have been carried out at the same conditions

In all the activities have been used the appropriate collective or individual protection equipment.

Five samplers have been compared (Table 2): Two actives (Waters and Silica Gel tubes) and three passives (UMEx100, PEL and STEL).

At SANOFI laboratories, occupational exposure to formaldehyde have been sampled in three activities. The product used have been the same for all this activities: the commercial name is «aldehyde formique 4% tamponné RS » it is a mixture between: distilled water (50-100%) -Formaldehyde (2, 5-10%) and Methanol (≤2, 5%).At INSTITUT PASTEUR laboratories, occupational exposure at formaldehyde have been also sampled at three activities. However, the products used for each activity are different with mixtures adapted to each utilisation. The activities sampled are described in Table 3.

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Techno	Sampler	Manufacturer's description	Validation methods based on	Application	Analysis
Active	***Waters Cartridge***	***Samplers contain acidified 2, 4-Dinitrophenylhydrazine (DNPH)-coated silica, packed in Waters Sep-Pak Plus cartridges.*** ***The samplers are constructed from high-purity and high-density polyethylene components, triaxially-compressed packed beds and Luer fittings equipped with end caps and plugs.***	***EPA TO-11A*** ***NIOSH 2016*** ***Métropol 001 pour Aldéhydes***	***Flow rates of up to 1.5 l/min*** ***0,012 á 2ppm***	***HPLC-UV operated at 365 nm following extraction with acetonitrile***
	Tubes Cat. Nos. 226-119	***Sorbent sample are two-section tubes containing 300 and 150 mg of DNPH-coated silica gel, respectively. The second section acts as a backup section to detect sample breakthrough.***	***EPA TO-11A*** ***NIOSH 2016*** ***Métropol 001 pour Aldéhydes***	***Flows rates of up to 0,5 l/min*** ***0,012 á 2ppm***	***HPLC-UV operated at 365 nm following extraction with acetonitrile***
Passive	***Badge SKC UMEx100***	***Silica gel filter paper treated with 2, 4-dinitrophenylhydrazine (DNPH) placed in a polypropylene housing containing a number of inlet holes. The sampler is opened by sliding a cover to expose the holes to the air and is closed by replacing the sliding cover.***	***OSHA 1007***	***0.06 to 3.0 ppm***	***HPLC-UV operated at 365 nm following extraction with acetonitrile***
	Badge SKC PEL /STEL	***permeable plastic membrane allows for controlled diffusion of air onto a chemically impregnated paper; no liquid reagents are necessary for sampling. Formaldehyde combines with the reactive media (sodium hydrogen sulphite) on the paper and forms the stable compound formaldehyde bisulphite.***	***NIOSH 3500***	***The Personal Formaldehyde Passive Sampler is available in two configurations: the PEL Sampler for full-shift (eight hours) sampling and the STEL sampler for 15-minute sampling.*** ***PEL 0.2 to 2 ppm*** ***STEL 0.5 to 6 ppm***	***Chromotropic acid analysis***

Table 2: *Characteristics of the samplers evaluated*

Activity	Activity description	Duration (min)	Product	Sampled at laboratories :
1	*Tissue fixation*	15	*« aldéhyde formique 4% tamponné »*	*SANOFI*
2	*Flask preparation to the organs preservation*	15	*« aldéhyde formique 4% tamponné »*	*SANOFI*
3	*Organs recovery and substitution of formaldehyde by sucrose*	15	*« aldéhyde formique 4% tamponné »*	*SANOFI*
4	*Material disinfestation*	15	*« ASEPTANIOS TERMINAL HPH »: Formaldehyde (0 à 2, 5%) Alcohol ethylic (2, 5 à 10%), Alcohol methylic (<1%), Propan-2-ol (<1%)*	*INSTITUT PASTEUR*
5	*Introduction of the organs in the pots with formaldehyde*	15	*« Q Path Formol tamponné à 4% »: Formaldehyde (4-5%) and Methanol (< 3%)*	*INSTITUT PASTEUR*
6	*Perfusion, dissection and Introduction of the organs in the pots with formaldehyde*	45	*Developed by the Institut Pasteur and content the paraformaldehyde*	*INSTITUT PASTEUR*

Table 2: *Characteristics of the samplers evaluated*

3. RESULTS AND DISCUSSION

The results obtained in the sampling campaign (ppm) are showed in the following graphics for the six activities carried out by the six operators who wore the samplers. Each data series indicates the sampler used. The duration of all the activities was about 15 minutes. However if the operator stayed at the laboratory , the PEL 8h support was used during more time: for this reason just for this sampler the results are referred to 8h, so this results are no comparable to the rest.

A code was established for every sampler:

S – Activities carried out at SANOFI laboratories

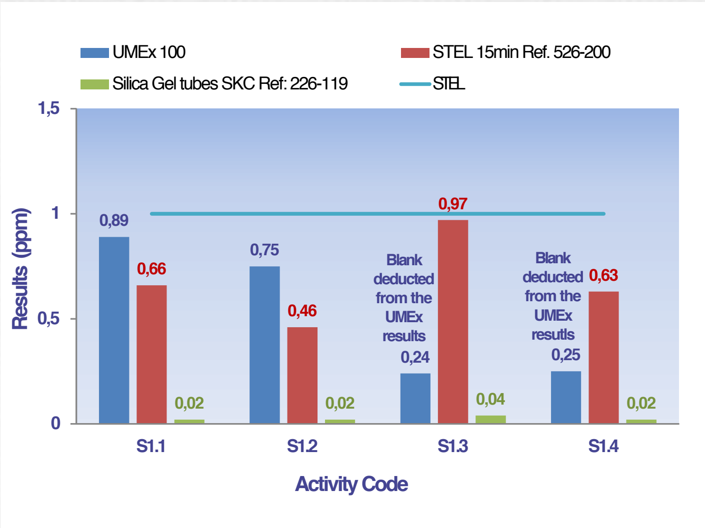
IP – Activities carried out at PASTEUR laboratories

First number **- (1, 2, 3 or 4**) – number of the activity

Second number **- (1, 2, 3 or 4)** – number of repetition of the activity

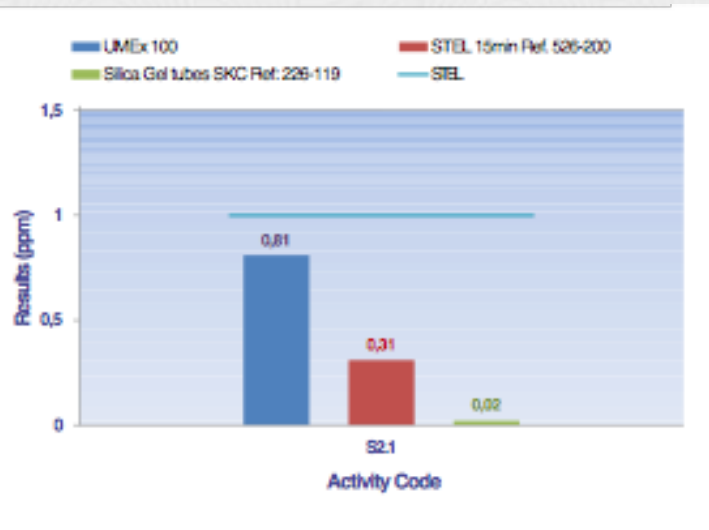
B – Blank sampler

Regarding the potential risk evaluation, as can be seen in the figures below the STEL (short-term exposure limit of 1ppm) and the TWA (Time Weighted Averages for 8h) have never been exceeded.



For the activity 1 (Figure 3) three samplers of short duration have been used: UMEx100, STEL 15 and the tubes. The activity was repeated four times.

One repetition was carried out for the activity 2 (Figure 4) and two for the activity 3, (Figure 4) where the PEL sampler was also used.



As can be noted in activities carried out at SANOFI (Figure 3 to 5) the tendency is similar: actives samplers' results (Silica gel tubes) are inferior to diffusional samplers' results (STEL 15 and UMEx100). Results obtained with the tubes show a great repetitively. Regarding the UMEx sampler it is necessary to take into account that two types of blanks were used:

Opened blanks that were not exposed to formaldehyde: that means that the sampler was extracted from the bag and was put in "on" position

Blanks not opened : the sampler was not extracted from the bag

Blanks opened have given a positive value: according to the laboratory analysis the reason of this incoherence is the utilization period of the sampler was not enough, so

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for the two first experiences the blank value was not used.
Regarding **UMEx 100** samplers; Figure 3 shows the difference between the results of repetition one and two (S1.1 and S1.2) and the two last ones (S1.3 and S1.4). This difference is due to the blank deduction. It can be therefore concluded that the send of a no opened blank is indispensable.
Regarding the **STEL 15** samplers, as can be seen in Figure 3 the dispersion date is more important in this case. This means that we have an inferior precision. This can be due to the type of analyse used, that apparently offer the resultants less rigorous.
For the sampling campaigned carried out at PASTEUR laboratories like in the campaigns of SANOFI every data series indicate the sampler used, all the activities have been carried out four times in the same conditions. In this case two samplers of active technology: tubes SKC tubes and WATERS cartridges have been used.
All the activities have had a duration of around 15 minutes, except the activity 6 which had a duration of around 50 minutes. In this case the sampler PEL 8h has been used and the results are referred to 8h so these results are no comparable to the rest.

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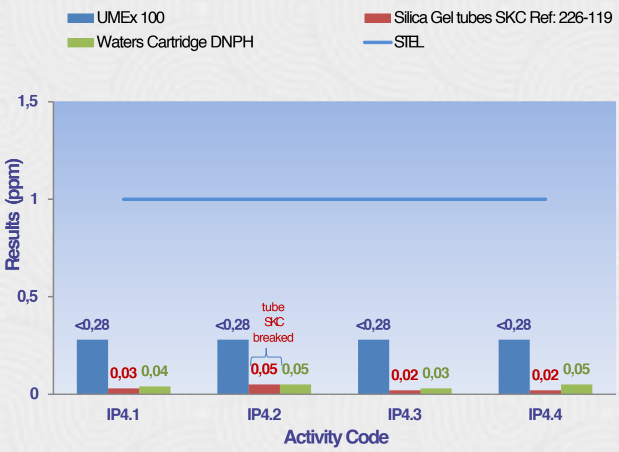
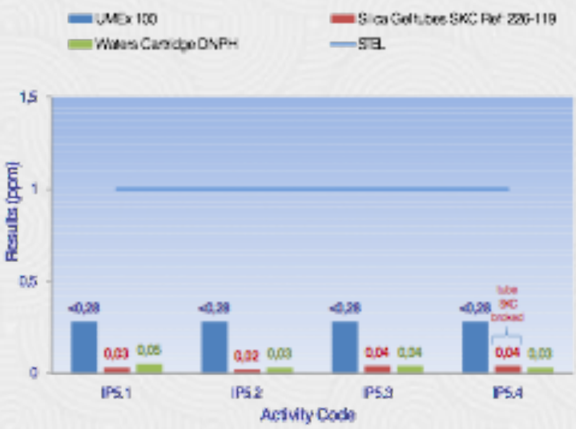
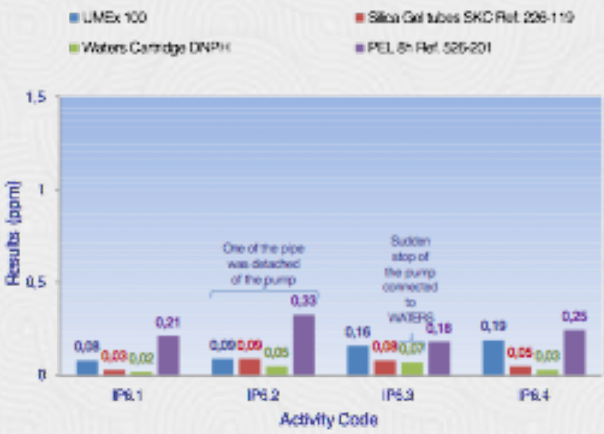


The same trend can be seen for the three activities carried out in Institut Pasteur's Laboratories and similar to SANOFI campaign: results of active technologies are always inferior to the passive technologies.
It is remarkable that this time the batch expiration date was superior to the SANOFI's batch. This confirms the necessity of minimizing the time of storage before using the sampler.





UMEX 100

As shown in figure 6, 7 and 8, the results are more similar to the active technologies. They are the minimum results detectable for 15 minutes.

In the activity 6 (figure 8) we can see that the passive technology results are similar to the active technology results. The reason is that, when the diffusion time is considerable, the passive technology shows better results. This happens because diffusion takes an amount of time to reach to the stationary regime.

In the activity IP6.2, one of the pipes was accidentally unplugged from the peristaltic pump, and consequently a higher quantity of formaldehyde was detected by the supports. We can remark that, in this case, the UMEx badge was also close to the active technology results.

TUBES SKC AND WATERS CARTRIDGES

The results obtained with the different active technologies (tube and cartridge) show a great reproducibility. In the three cases studied (Figures 6-8) the results are similar (excepting the measure where the tube was unplugged). The tube SKC (made in glass) was broken twice (IP4.2 and IP5.4) what shows a big disadvantage compared to the plastic Waters cartridge.

PEL 8H

As for the activities performed in SANOFI, the PEL 8h results have been extrapolated to 8h. The repetitiveness seen for the activity 6 has been considered as acceptable.

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4. CONCLUSION

The aim of this paper is to evaluate the most appropriate samplers available to evaluate the formaldehyde occupational exposure risk in the laboratories. Using the different techniques recommended by the agencies for occupational safety and health in Europe and USA, a comparison study of the different formaldehyde samplers has been made. The performances of five different samplers have been tested within 6 experiments conducted in SANOFI and in the Institut Pasteur laboratories. (Three in each).

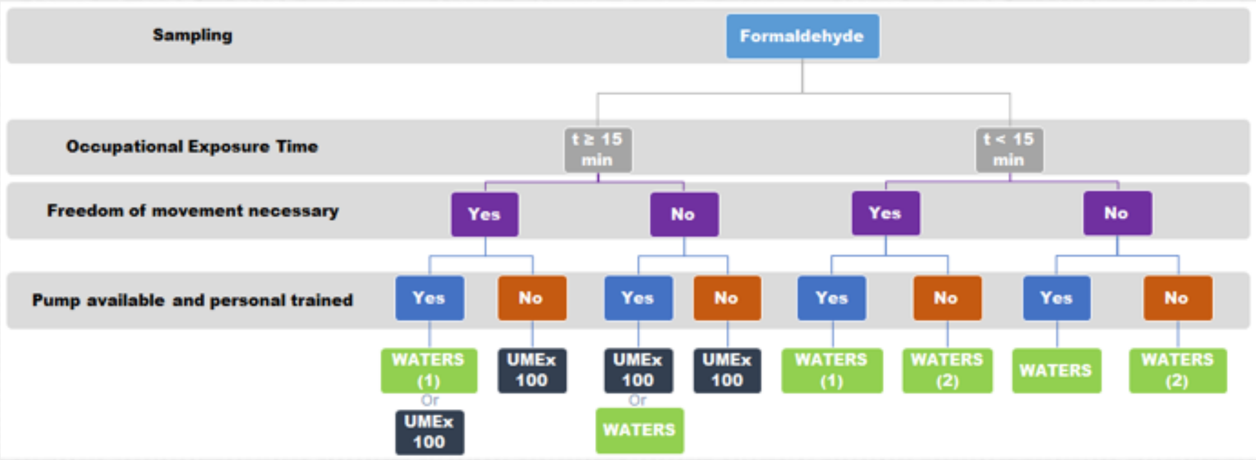
	Sensibility	Easiness of use	High expiration dates	No need of a cold chain
UMEx 100	***Yes , for a t>15min and send of a blank***			
STEL / PEL				
Waters				
Tube SKC				

As we have been able to see from the experiences described, we recommend performing the measures of formaldehyde with the following two technologies: UMEX-100 (passive technology) or WATERS (active technology). In the table hereunder, the most remarkable characteristics of each support have been used: The sensibility and the precision of the measure, the easiness of use, the expiration dates for the technologies, the need of a cold chain in order to not to damage the product. The colours hereunder indicate that the characteristic is well respected (green), respected enough (orange) or not enough respected (red):

Down below a summary chart that allows to choose the most adequate technology is showed

(1) When water samplers are used in these conditions, the cartridge and the pump have to be watched in order to protect them from breakage or inadvertent shutdown. Ensure that the tubing is not twisted during operations. It recommended stick the tubing in the back of manipulator.

(2) In these conditions it is recommended do the rental or purchase of a pump and staff training



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