Toxicological assessment method for evaluating the occupational risk of workers involved in dynamic olfactometry

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The paper aims to propose a new method to evaluate the occupational exposure risk for examiners involved in dynamic olfactometry. Indeed, during olfactometric analysis, human examiners are possibly exposed, at increasing concentration, to hazardous pollutants potentially present in odorous samples. A standardized method to evaluate the examiners' occupational safety is not yet available and the literature model existing present some critical aspect if applied to real odorous samples, mainly related to selection of the reference concentration to be applied and to the presence in the samples of compounds for which toxicity threshold is available. Due to these critical aspects, a deepening of assessment procedure to evaluate the occupation exposure risk for panellists involved in dynamic olfactometry is necessary.Therefore, this paper aimes to propose a standardized approach for risk assessment in dynamic olfactometry. The proposed approach allows the quantification synthetic and conservative risk indices, which in turn can be used to calculate the minimum dilution factor useful for protecting the health of exposed subjects.In this model, the use of the hazard index (HI) for the mixture of compounds that make up the odour sample was proposed to assess the non-carcinogenic risk; the calculation of the inhalation risk (IR) was applied to estimate the carcinogenic risk. The methodology proposed in this paper uses different databases to retrieve proper occupational exposure limits, according to a hierarchical basis. These implementations allow obtaining the complete characterization of real mixtures and an accurate toxicological evaluation. From this elaboration, a more precise and conservative minimum dilution value can be evaluated and applied to protect the panellists' health.

Keywords: occupational health; odorous emissions, olfactometric analysis, olfactometric assessors, occupational risk assessment

1 Introduction

Concerns related to odorous emissions from different industrial plants have increased in recent years, even related to their potential health impact [1]–[4]. Indeed, the statement that unpleasant odour may lead a health hazard persists, leading to complaints from exposed citizens [5]–[7]. For these reasons, the monitoring of odorous emissions emitted by industrial plants has become increasingly important and increasingly required to companies by local control agencies and several countries currently have specific regulations on this topic[8]–[12]. Among the various analytical techniques available, the most diffuse and the only currently regulated at the European level to quantify odour is dynamic olfactometry [13]. Dynamic olfactometry provides the sample odour concentration, expressed in European odour units per cubic meter (ou_E/m^3). The odour concentration represents the number of dilutions with neutral air that are necessary to reach the odour threshold value. This technique is standardized by EN 13725:2003 and directly involves humans examiners, called panellists [14]. Dynamic olfactometry uses the nose as a sensor, due to the human nose's ability to perceive and distinguish the presence of an odour. During the analysis, odorous samples are diluted with neutral air by specific equipment, called olfactometer, and presented to human examiners at increasing concentration. Therefore, even at more diluted level, panellists are directly exposed to odorous and hazardous compounds potentially contained in the emission' sample. For

this reason, by conducting olfactometric analysis, an undefined occupational exposure risk exists for panellists involved. The exposure assessment for human health risk is therefore fundamental to define appropriate measures to protect the health of the panellists and thus to safely conduct olfactometric analyses. The specific occupational exposure of panellists and the regulations on sample handling impose strict limits on the possible protective measures to be taken to ensure the safety of the involved personnel: (i) Chemical transformations of odour samples or removal of hazardous pollutants are not allowed to avoid alteration of the sample; (ii) personal protective equipment (i.e., respiratory protective equipment) to protect the panellists against inhalation of hazardous substances cannot be adopted, for the same principles underlying the method as described above. In addition, exposure monitoring of panellist is not practicable in this exposure scenario. As the panellists are exposed to increasing concentrations of odorous emissions, a valuable protection measure that can be taken is the definition of a minimum dilution value, not to be overcome during analyses. The necessity to estimate the exposure risk for panellists involved in olfactometric analysis is a requirement already present in the EN 13725:2003 and additional remarks on this topic have been made in the current revision of the standard (prEN 13725:2019). Currently, the standard, solely prescribes to control and minimise the potential toxicological exposure risk and to inform exposed workers of the potential risk related to the olfactometric analysis. For these reasons, the standard revision should introduce guidance on risk assessment for panel members, prescribing the use of current relevant exposure limits. However, at the current state, a standardized method for estimating employment risk is not yet described. The absence of a standardized method to evaluate the exposure risk for panellist during olfactometric analysis can lead to several critical problems in the toxicological assessment. In particular, the absence of a reference concentrations may lead to non-comparable and even incorrect assessment of the panellists' exposure risk. Indeed, for workers exposure, different occupational exposure limits coexist: they can vary according to the exposure time and the exposure route considered. In addition, the occupational exposure limits can varied in accordance with the risk assessment approach applied [15]–[17]. In the literature, only two articles have proposed a methodology to assess occupational risk for workers involved in dynamic olfactometry. In these two studies, a methodology to estimate the minimum dilution value to be applied has been proposed. The first article [18], based on chemical data available in the literature, establishes the minimum dilution value to be used during the analysis of odour samples collected from different categories of industrial plants. The second study conducts a toxicological evaluation for odour emissions from an Italian municipal solid waste (MSW) incinerator, based on the authorised concentrations at stack emission for chemicals of potential concern (COPs) [19]. Both articles calculate the minimum dilution value to be applied by estimating the non-carcinogenic and carcinogenic risk for panellists' activity. However, in the absence of specific and detailed method in the standards about dynamic olfactometry, the assessment can be conducted using different reference databases. In addition, the two papers do not describe how to consider, in the toxicological evaluation of real samples, the compounds observed for which there is no exposure limit in the proposed databases. This problem can be crucial in presence of a high number of undefined compounds in an odorous sample. For all these reasons, there is a clear need to discuss an assessment method that considers these critical issues and that can be easily implemented and used to assess minimum dilution levels for real samples, in which compounds may be present for which an exposure threshold is not readily available. Therefore, this article aims to present a robust method for assessing occupational risk for dynamic olfactometry panellists. The proposed method has been constructed to be easily usable by olfactometric operators and considering the criticalities observed in the literature in this field.

2 Method development

2.1 Occupational exposure of panel involved in dynamic olfactometry

To conduct a toxicological assessment for olfactometric examiners and determinate the minimum dilution values useful to guarantee their safety, preliminary observations about their exposure should be conducted. Firstly, it is essential to assess the type of exposure. Panellists have to be considered as workers and therefore occupational exposure limits have to be used within the toxicological

assessment. However, the work exposure of these employees involved in olfactometric analysis is unusual. Indeed, panellists usually work in daily sessions of 1 or 2 hours and the examiner is called for a maximum of one analysis session per day in order to avoid nose fatigue. In addition, each odour presentation lasts for a maximum of 15 seconds, according to standard requirements [14]. Therefore, an olfactometric examiner will never be exposed for the same length of time as a common worker, who is generally exposed for a conventional 8-hour workday and a 40-hour workweek, for the entire working lifetime [20][21].

Nevertheless, it is necessary to investigate the salubriousness of the panel because of the specific concentration to which they may be exposed during analysis. According to the sampling requirements of EN 13725:2003, odour emissions to which examiners are exposed during the analysis have to be collected directly at the odour source [14]. Therefore, the odour emissions analysed are not diluted by atmospheric dispersion, but only by the olfactometer during analysis session. As described previously, odour samples are diluted by this instrument with neutral air and presented to panellists at increasing concentration, until the examiners can distinguish the presence of an odour different from neutral air. Consequently, examiners may potentially be exposed to not negligible concentrations of hazardous pollutants. This exposure concentration is potentially higher than the exposure concentration of employees working directly inside the plant, precisely because the emission is not diluted in ambient air. For all these reasons, it remains necessary to assess the toxicological risk for examiners involved in dynamic olfactometry, using a precautionary approach but considering all the aspects associated with such a peculiar exposure scenario.

2.2 Method description

For what has been described above, in the considered scenario the source of exposure for panellists is the sample itself (which is diluted with neutral air) and the exposure pathway is limited to inhalation of chemicals in air through the olfactometer. This should be considered as a combined exposure scenario (i.e., a scenario in which exposure to multiple chemicals occurs by a single route, from one source of release). The odour samples could also be generally classified as a discharge mixture (i.e., a substance combination that are emitted by a single industrial site) which is typically complex and variable in composition [22]. Then, a method was defined with the aim of characterising the health risk posed by the odour samples with a general and simplified, but robust approach. As a function of the exposure modes, a non-carcinogenic risk assessment was calculated, based on short-term exposure.

Further, for carcinogenic health effects, an excess lifetime cancer risk was calculated considering a “non-threshold” toxicity and assuming a linear dose-response relationship, as described in 2.2.2. For this study, it was assumed that no chemical transformations or abatements are induced during the dilution steps.

2.2.1 Risk Assessment (Non-carcinogenic health effects)

The potential non-carcinogenic chronic risk was evaluated using the hazard index (HI) (Equation 1). The HI is equal to the sum of each chemical component’s Hazard Quotient (HQ = Exposure ÷ Safe Dose = Chemical concentration in odour sample ÷ Exposure reference value), as reported in Equation 2 [22].

$$HI = \sum_{i}^{N} HQ_i \qquad \text{Equation 1}$$

$$HQ = \frac{Exposure}{Occupational\ Limit\ Value} \qquad \text{Equation 2}$$

HI is one of the more straightforward ways to assess combined exposures to multiple chemicals and this approach is widely adopted for occupational chemical risk assessment. For example, ECHA suggests the use of risk characterization ratios (RCRs), calculated as the ratio between the exposure to a chemical and the corresponding derived no-effect level (DNEL) for that chemical [23]. A recent

EU standard [21] also suggests a similar approach (Appendix C.2 - Exposure Index) as “Tier 1” method for the risk assessment of simultaneous workplace exposure to several chemical agents. Another example of application of a similar method is also provided by ACGIH (American Conference of Governmental Industrial Hygienists), which applies a similar method for applying its own Threshold Limit Values for Mixtures [20]. Overall, HI represents a simple and flexible approach that can be quickly applied to different samples in the same scenario. The HI approach provides a transparent index of acceptable risk (i.e., HI ≤ 1: risk acceptable; HI > 1: potential concern). Further, it does not require an in-depth analysis of the toxicokinetic and toxicodynamic characteristics (or an evaluation of the specific toxicological endpoints) of each chemical in the mixture. For this reason, applying HI, it is possible to consider at the same time chemicals belonging to different groups and easily quantifying the percent contribution of each substance, which in turn permit the identification of target chemicals for risk management [22].

This approach also has some drawbacks: HI could be potentially over-conservative, which at the same time can be seen as an advantage, especially in the case in which the mixture under investigation is complex and poorly characterized from a toxicological point of view. Further, HI is a rather simplified approach, that does not consider chemical interactions ad toxicokinetic or toxicodynamic differences. More complex approaches are available, but they require different assumptions and deeper toxicological characterizations and are difficult to apply for the purpose of this study [22], [24]–[28]. Finally, to apply the HI method, reference values for all chemicals need to be available these values are often not available.

This last issue could be one of the most critical aspects regarding the applicability of the HI method because very often reference values for occupational human exposure are not available to derive the single HQ. On the contrary, for some chemicals, several different reference concentration values are available. More in general, different occupational exposure limit values for chemicals exist at European and International level and were developed within different legislative frameworks. This is particularly critical for the case study under consideration, the panel's occupational exposure risk assessment, for which at the regulatory level (EN 13725:2003 and prEN 13725:2019) no toxicological parameter is specified to be adopted in the evaluation. Concerning this selection, the type of reference values used within a single HI calculation should be consistent, because each value is derived using slightly different assumptions, or since different critical effects may have driven the derivation of the reference values for the components. For example, OELs are developed for occupational safety and health purposes while DNELs were initially intended to play a role within risk management processes and prevention scheme in a regulatory framework. This could result in difficulty for the selection of the most appropriate limit value by experts and for the application of such limit values in the risk characterization in real exposure scenarios [12].

To overcome these problems and to allow the application of the HI method in this context, in this study a method has been proposed for the searching and for selecting the most appropriate reference value for the different chemicals that can be identified in the mixture of chemical agents present in odour samples. Furthermore, considering that chemical-specific reference values may not be found for all components of the mixture, two different approaches for using appropriate generic reference values have been proposed. Thus, for the purpose of the risk assessment of odorous samples, the assessor must apply a precise and careful evaluation procedure, divided into the following points [12]:

- Search among the proper occupational exposure limit values (i.e., short-term, inhalation exposure route) available for each component.
- Ensure that the selected value is equivalent or more conservative than the binding value, if this is available.
- Evaluate the derivation procedure of the limit value and the starting points in order to select the most robust limit values for the specific purpose of the assessment, always in a path that is documented as much as possible to ensure consistency, transparency and professional correctness.

The role and competence of the assessor remains crucial for a proper choice. However, considering that the purpose of this work is to suggest a method to be implemented and used by any olfactometric laboratory to assess panel safety, it was decided to construct and propose a toxicological assessment approach widely usable and more flexible. In addition, the decision-making process

described in this paper has been structured to solve the main criticalities observed in the state of the art, in particular, the unavailability of a specific reference threshold to be adopted in the evaluation and the presence of compounds for which no toxicity threshold is provided.

To conduct the toxicological assessment, it is essential to investigate the chemical nature of real samples to be analysed by dynamic olfactometry. The most applied analytical technique to obtain qualitative and quantitative information about compounds present in gaseous environmental matrices, such as odour samples, is the Gas Chromatography coupled with Mass Spectrometry (GC-MS). Indeed, GC-MS is the widely used analytical technique to achieve the resolution of complex mixtures and the identification and quantification of unknown molecules [13], [29], [30].

Thus, to evaluate the HI value for a specific odour sample, once its chemical composition has been defined, in terms of nature and concentration of pollutants present, the following scheme has been constructed with basic elements for selecting the most relevant limit values to be used within the risk assessment process. For each component of the mixture identified by GC-MS analysis, the assessor should:

1. Check among the occupational limit values (OELs) for short-term exposure (15-minute) that have the force of law at the international level. In this case the following OELs have been identified as those of interest:
   - *Indicative occupational exposure limit values (IOELV)*: health-based, non-binding values, derived from the most recent scientific data available and taking into account the availability of reliable measurement techniques [12]. The last update of list of the available IOELV was performed with the publication of Directive 2019/1831 (former European Directives reporting IOELVs are Directives 91/322/CEE, 2000/39/EC, 2006/15/Ec, 2009/161/EU, 2017/164/EU);
   - *Binding occupational exposure limit values (BOELV)*: these are to be understood as binding threshold limit values, specially developed for the protection of the health of workers exposed to substances with genotoxic, carcinogenic or respiratory sensitization effects for which it is not possible to define a No Observed Adverse Effect Level (NOAEL) or a Lowest Observed Adverse Effect Level (LOAEL) [12]. BOELV are reported in European Directives 98/24/CE, 2003/18/CE, 2004/37/CE, (UE) 2017/2398, (UE) 2019/130, (UE) 2019/983. The methodology to be adopted to define a IOELVs and BOELVs is reported in a specific guideline [31].

2. Check among Derived No Effect Levels (DNELs) for workers' short-term exposure and to prevent systematic effects. DNELs are levels of exposure above which humans should not be exposed. DNELs must be declared by the registrants in the framework of REACH Regulation (Regulation (EC) 1907/2006)). The methodology to be adopted to develop a DNEL is reported in a specific guideline [32]. Several DNEL types may be established for the same chemical. For the purpose of this study, Acute – inhalation, systemic effects DNELs for workers should be considered. DNELs for registered substances are publicly available on ECHA website [33].

3. Check for other short-term occupational limit values without mandatory value, defined at national level, choosing the most conservative value among those available at international level.

The updated international OELs are available in GESTIS database - International limit values for chemical agents [34]. This database contains a collection of occupational limit values from 32 lists from 27 countries: various European states, Australia, Canada (Ontario and Québec), Israel, Japan, New Zealand, Singapore, South Korea, The People's Republic of China, Turkey, and the United States. IOELVs and BOELVs are also collected in this database. Limit values of more than 2,000 substances are listed. ACGIH Threshold limit Values are not included in this database, but given their use is widely diffused, this source has also been consulted [20]. It should be noted that limit values defined by the various expert bodies and authorities differ in the criteria for their derivation, the level of protection which they offer, and their legal relevance.

After consulting the various sources mentioned above, in search of the respective exposure limit values, the assessor will be able to define, based on those available, which limit value to use.
The proposed hierarchical order to follow is: (1) short-term OEL with legal value at international level; (2) DNEL (for workers' acute - inhalation, to prevent systemic effects); (3) Short term OEL without force of law, defined at national level. The assessor should ensure that the selected threshold value should be equivalent or more conservative than the binding value, anyway.
The application of this procedure makes it possible to provide a toxicity value useful for calculating the HQ of a wide range of compounds present in a real odour sample.
However, even consulting different sources according to the above scheme, it is possible that for some of the components of a mixture of an odour sample it may not be possible to establish a specific threshold value and that a non-negligible percentage of the mixture may not be characterized in terms of risk. In order to resolve this critical issue and complete the HI calculation, an approach is proposed.
Indeed, for each compound for which a toxicity threshold is not available in the above databases,the assessor could use an occupational limit value defined for a family or group of chemical agents, if available (e.g., Hydrocarbons, aliphatic, C6-C8; Hydrocarbons, aliphatic, C9-C14; Hydrocarbons, aromatic, C9-C14; etc.) instead of the specified limit value for a single chemical. Discussing hydrocarbon molecules, another methods for defining a limit value for a family or group of chemical agents can be considered, such as the reciprocal calculation procedure (RCP) for deriving exposure limits, as described in [20].
In any case, with the application of this approximation, it is considered possible to be able to characterize the HI of the entire mixture of chemicals that make up the odour sample, thus helping to complete its risk characterization. An acceptable non-carcinogenic risk level is obtained for HI lower than 1. It is however possible that even applying these two approaches, for a minor component of the odour sample it could not be possible to identify an exposure limit value and therefore that this component may not be characterized in terms of risk (i.e., HQ could not be calculated for some components). This aspect possibly introduces an element of uncertainty in the risk assessment, which must be considered.

2.2.2 Risk Assessment (Carcinogenic risk)

A method was also defined and applied to characterise the health risk posed by the odour sample. Carcinogenic excess lifetime risk was calculated based on Equation 3, as reported in existing guideline [35].

$$Inhalation\ Risk = CDI\ \times IUR \qquad \text{Equation 3}$$

where IUR is the Inhalation Unit Risk and CDI was the chronic daily intake, expressed in μg/m^3. IUR values were retrieved by the Risk Assessment Information System [36], while CDI has to be calculated in accordance with the working exposure time of the examiners involved in the olfactometric analysis. Indeed, CDI can be calculated as follow (Equation 4):

$$CDI = \frac{C_{air}\ \times EF_{iw} \times ED_{iw}\ \times ET_{iw}}{AT_{iw}\ \times LT} \qquad \text{Equation 4}$$

where C_{air} is concentration observed of pollutant [μg/m^3], EF_{iw} is the exposure frequency [day/year], ED_{iw} is the exposure duration [year], ET is exposure time [hours/day], AT_{ir} is averaging time [days/years] LT_{iw} is lifetime [years].
Therefore, to calculate CDI, it will be necessary to define these parameters for each olfactometric laboratory, with reference to the exposure of the panels involved in the analyses. Indeed, exposure parameters are closely correlated to the duration and frequency of panellists' exposure to pollutants in odour samples. Therefore, to assess a realistic specific risk, it will be necessary for each

olfactometric laboratory responsible to record in detail the representative work activity (i.e., the "worst-case scenario") of the examiners involved.
Observing the scientific literature about panellists' exposure, the parameters used to calculate the CDI are reported in In the model proposed in this paper, the inhalation risk was calculated for each component classified as carcinogenic or potential carcinogenic, according to the definition supplied in Part 3 of Annex VI to Regulation (EC) No 1272/2008:

- Carcinogen if the compound is classified as carcinogens of category 1A or 1B.
- Suspected to have cancerogenic potential for human if the compound is classified as carcinogens of category 2.

Inhalation Risk factor for each carcinogen and suspected carcinogen pollutants was calculated and were summed to obtain the total Inhalation Risk of the sample. An acceptable carcinogenic risk level is defined for an Inhalation Risk lower than< 10^{-6} for a single compound and lower than 10^{-5} in the case of mixtures.

Table *1* as an example. In a previous study [19], two hypothetical exposure scenario are described, in which panellists were considered to be exposed in the performance of their tasks, but with a different workload. The references for the parametrization of these two scenarios were derived from two different olfactometric laboratories: a "commercial" laboratory (owned by a private company) and an "institutional" laboratory (owned by an environmental inspection authority). As shown in In the model proposed in this paper, the inhalation risk was calculated for each component classified as carcinogenic or potential carcinogenic, according to the definition supplied in Part 3 of Annex VI to Regulation (EC) No 1272/2008:

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Table *1*, the exposure parameters vary considerably depending on the exposure scenario, modifying the resulting CDI.
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Table 1. Parameter for inhalation Risk calculation (derived from [19])

Parameter [unit]	"Commercial Lab" Scenario	"Institutional Lab" scenario
Inhalation Unit Risk -IUR $[\mu g/m^3]^{-1}$	Retrieved by the Risk Assessment Information System (https://rais.ornl.gov/) for carcinogen chemical in the odour sample (Carcinogen cat. 1A, 1b, 2)	
Exposure concentration - C_{air} $[\mu g/m^3]$	Chemical's concentration in the odour sample (Carcinogen cat. 1A, 1B, 2)	
Exposue Frequency - EF_{iw} [day/year]	90	10
Exposure Duration - ED_{iw} [year]	10	7

Expsoure Time - ET_{iw} [hours/day]	0,073	0,17
Averaging time - ATiw [days/years]	365	365
Life-time of the exposed individuals - LT [years]	70	70

2.2.3 Minimum dilution of the odour sample

As previously described, during olfactometric analysis odorous samples are presented to examiners at increasing concentration.Due to this, for every odour sample analysed by dynamic olfactometry, a minimum dilution level can be defined to avoid any health impact for the involved panellists. As stated above, no preventive or protective measures other than sample dilution can be applied, due to the requirements and specifications of the analysis. The minimum dilution level is defined as the dilution step not to be exceeded in order not to expose examiners to dangerous concentrations of pollutants within an odour sample. The determination of the minimum dilution value is defined on the results of the characterization of the non-cancerogenic risk (HI calculation) and of the carcinogenic risk (Inhalation Risk calculation). Indeed, by comparing the results obtained using the method described above with the acceptable safety criteria for carcinogenic and non-carcinogenic risk, it is possible to define the minimum dilution level for an odour sample. In Table 2 the acceptability criteria for non-carcinogenic and carcinogenic risk were reported: if HI o IR are higher than these parameters, a minimum dilution value must be set to protect panellist's health.

Table 2. Risk acceptability criteria adopted in this method

Risk type	Acceptance parameters
Non-carcinogenic (NC)	HI < 1
Carcinogenic (C)	IR < 10^{-6} for single substance
	IR < 10^{-5} for gaseous mixture

First of all, it is necessary to evaluate if an odour sample, according to the elaboration performed, exceeds the acceptability criteria (Table 2) for either or both criteria. As described above, in dynamic olfactometry, the odour concentration of an odorous gas sample is determined by presenting the sample to a panel of selected and screened human examiners, varying the concentration by diluting with neutral air. The dilution factor needed to reach the panel detection threshold determines the quantity value for the odour concentration of the undiluted odour sample. Concerning the minimum dilution, as mentioned, the goal is to protect the panellists' health. For this purpose, if both HI and IR respect the acceptability values shown in Table 2, it is not necessary to define a minimum level of dilution as regards the potential impact on health. Contrariwise, if calculated HI and/or IR values exceed the acceptability parameters for the sample as-it-is (i.e., for the undiluted sample), it is necessary to determine the minimum dilution value, which allows the above thresholds to be respected. For this purpose, knowing a priori the different dilution steps applied by the olfactometer, it is easy to evaluate the minimum level of dilution to be applied to avoid incurring an unacceptable carcinogenic or non-carcinogenic risk. It should be noted that the dynamic olfactometry method still uses a minimum dilution for technical and procedural reasons, in particular this dilution is typically fixed at a 4. This implies that the definition of a minimum diluition value can be considered conservative, even with respect to any elements of uncertainty that can be introduced with some simplifications and assumptions that become necessary. For the conduction of olfactometric analysis, it is necessary to calculate HI and IR on the as-it-is sample, and then apply this parameter to define, on the dilution scale applicable by the olfactometer, the minimum dilution step. The entire decision-making process is reported in **Errore. L'origine riferimento non è stata trovata.**.

2.2.4 Limitations and Strengths of the method

Some assumptions and limitations must be considered in the interpretation of the results of this procedure as the study design limits the general applicability of the findings. Major limitations of the present method (which should be considered in the interpretation of the results and the general applicability of the findings) are summarized hereafter. (i) As mentioned in paragraph 2.2.1, HI is a simplified approach, that does not consider chemical interactions ad toxicokinetic or toxicodynamic differences. Our aim was to define simple and flexible approach, anyway. This need to be rather simple - but conservative enough - to be quickly applied to different samples in the same scenario, to allow the performance of dynamic olfactometry tests while protecting the health of the panellists. The application of the HI method should be seen a “firsttier method” for risk assessment in a wider tiered approach. This Tier-1 method, to be effective, must be simple (i.e., data poor) and conservative (protective). However, it is an implicit limit of the method which can lead to a certain degree of uncertainty. Therefore, it is advisable to suggest the application of "higher tier" risk assessment methods if further, specific in-depth toxicological assessments prove to be necessary, or if decidedly non-negligible risks are highlighted by means of the tier 1 assessment phase. As reported above, more complex approaches are available, requiring different assumptions and deeper toxicological characterizations [22], [24]–[28]. In any case, it is good to remember that skills and expertise in the field of toxicology and health impact assessment must not be taken for granted, therefore in case of doubt in the application of the above method, it is good to refer to experts in the field. (ii) Further, difficulties may arise for the selection of the most appropriate occupational limit value for HQ and calculation. The proposed method respects some general principles of caution and invites to refer to reliable sources for the choice of the limit values. It should be remembered that various exposure limit values are available, which are derived according to different principles and methods. In this regard, differences could be observed by comparing exposure with different exposure levels and this could result, for the same sample, in defining different probabilities of risk [15], [17], [37], [38]. The proposed hierarchical criteria should make it possible to take a choice in compliance with the binding exposure limit values and in general following a principle of conservatism. The selection of limit values from different sources could have introduced a bias in the risk assessment process, thus the assessor should have sufficient knowledge on this topic and should ensure that the selected threshold value should be appropriate.

Despite these limitations, this study has several strengths, as it provides important insights into the risk assessment procedure for panellists exposed to odours sample in dynamic olfactometry, an unusual occupational exposure scenario characterized by the impossibility of applying the classic hierarchy of risk management and mitigation measures (i.e., elimination / replacement of the risk agent, confinement of the risk agent, use of collective protection devices and use of personal protection equipment).

In summary, (i) to the best of our knowledge, this is one of the first studies aimed to propose a standardized approach for risk assessment in dynamic olfactometry. Further, (ii) the proposed approach allows the quantification synthetic and conservative risk indices, which in turn can be used to calculate the minimum dilution factor useful for protecting the health of exposed subjects.

The method proposed in this study may need to update in the future, according to the evolution of knowledge on the topic and results obtained in real exposure scenario. However, at the current state, this study could represent an advancement of the knowledge about the risk related to occupational exposure in dynamic olfactometry.

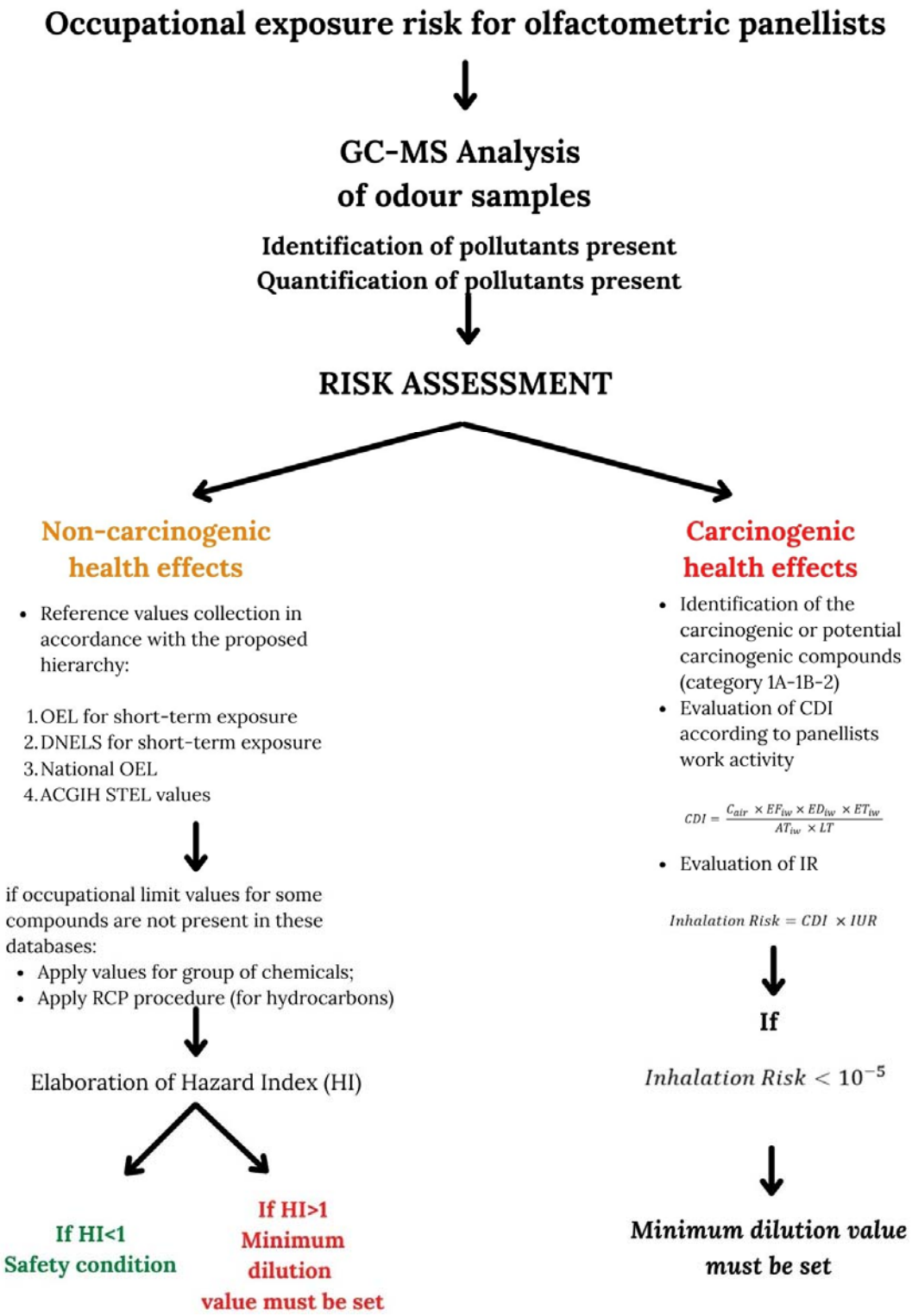

Fig. 1 Process of decision-making proposed

3 Conclusions

Dynamic olfactometry is one of the most widely applied techniques to quantify odour concentration. The analysis is conducted directly involving human examiners. During the analysis of odorous samples, these panellists are directly exposed, at increasing concentration, to odour and the

pollutants potentially toxic it contains. Therefore, the evaluation of the occupational exposure risk of these workers is fundamental to conduct dynamic olfactometry under safe conditions. Despite the importance of this problem, nowadays a standardized method is not described in the standards available about dynamic olfactometry (EN 13725:2003 and prEN 13725:2019). In addition, in the scientific literature, only two papers have deepened this argument, proposing two models for conducting this evaluation. However, the proposed models do not consider some critical aspects that may be observed during the analysis of real odour samples. In particular, the models suggest using different toxicological databases and don't describe how to consider compounds for which there is no toxicity threshold. Therefore, the aim of this work has been to propose a general and simplified, but robust method for the assessment of occupational exposure risk for panellists involved in dynamic olfactometry. The method proposed in this article is based on the assessment of carcinogenic and non-carcinogenic risks using values established by international regulations and commonly applied reference standards in the field of toxicology. Appling common and easily available assessment methods based on properly selected occupational limit values, this assessment method can be applied by different olfactometric laboratories to assess the occupational risk of their examiners, achieving uniformity of results. In addition, several reference databases were proposed for the assessment of non-carcinogenic effects, with a hierarchy between them, based on the adequacy of available limits, to obtain toxicological information for the largest number of compounds present in a real odour sample. By minimising the number of compounds for which no hazard information is available, it is possible not to underestimate the potential exposure risk. To assess the minimum level of dilution to be adopted, the proposed model uses the calculation of HI and IR. Although simplified, the HI calculation appers, in according to the particular exposure of examiners to pollutants during testing activities, conservative and can be easily applied to the case of occupational exposure of examiners involved in dynamic olfactometry. Therefore, the model proposed in this paper appears to be a practical solution, combining a robust occupational risk assessment procedure and an easily implementable approach. This is particularly important considering the need to have, regarding this issue, a procedure that can be used by variousoperators.

Declaration of intererest

The authors declare no conflict of interest.

Author Contribution

Elisa Polvara: Investigation, Visualitation, Writing – Original draft preparation; Andrea Spinazzè: Methodology, Visualitation, Writing – Original draft preparation; Marzio Invernizzi: Writing - Review & Editing; Andrea Cattaneo: Writing - Review & Editing; Selena Sironi: Writing - Review & Editing, Supervision, Project administration; Domenico Cavallo: Writing - Review & Editing, Supervision.

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