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Prevention of silica health effects in Italy: current challenges for the occupational health and safety Unit of the Italian National Health Service

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Summary
Background: *Since its foundation in 2002, the Italian Silica Network (NIS), a collaborative network of professionals and public authorities, has been engaged in several aspects of research, control, and prevention of silica exposure and effects, and also in support for compensation claims for silica-related occupational health effects in Italy.* **Methods:** *We start with a report on the NIS point of view concerning the recent scientific results (from epidemiology and laboratory studies), including those carried out by NIS in cooperation with Italian universities and other public agencies. This is followed by a description of the data on silica exposure in different Italian workplaces and guidelines for the management of occupational exposure to silica, as developed by two model regional programmes for the ceramics industry, metal foundries and tunnel excavation.* **Results:** *The NIS initiatives highlighted the persistence of workplace conditions posing a significant risk for silica-related health effects, particularly in small industries and workshops. Experimental work has also shown that a number of physical and chemical factors affect the bioreactivity of silica particles.* **Conclusion:** *Based on NIS experience, it appears clear that currently conditions exist in Italy so as to positively contribute to the WHO Programme for the eradication of silicosis and the other diseases related to silica exposure. In order to achieve this goal, a coordinated and wide-ranging effort is required to reduce the wide gap in specific prevention activities, particularly in small industries and workshops, where high levels of silica exposure sometimes occur.*

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Riassunto

«Prevenzione degli effetti sulla salute della silice in Italia: le sfide attuali per i servizi di medicina e sicurezza sul lavoro del Servizio Sanitario Nazionale». *Il NIS, costituito nel 2002, è una rete collaborativa di operatori ed Enti pubblici (della sanità e della ricerca italiana, e di altri Enti incaricati dell'applicazione del controllo delle norme), che in questi anni ha affrontato il tema della prevenzione del rischio da esposizione a silice libera cristallina in Italia. In questo articolo viene inizialmente presentata la posizione del NIS in merito alle attualità epidemiologiche e della ricerca di laboratorio, e successivamente vengono presentate sinteticamente due esperienze regionali "modello", quella della Toscana e quella dell'Emilia Romagna, riguardanti la valutazione delle esposizioni in alcuni comparti lavorativi italiani e gli interventi di controllo dei rischi messi in atto, con particolare riferimento ai risultati ottenuti nei comparti ceramica per piastrelle, fonderie e gallerie. Da quanto descritto, emerge che esistono oggi in Italia le condizioni per poter rispondere positivamente agli obiettivi del Programma globale dell'OMS per l'eliminazione delle malattie silice-correlate, ma, perché ciò effettivamente avvenga, è necessario che si affronti in modo coordinato e diffuso la grave lacuna rappresentata dalle carenze nella organizzazione della prevenzione del rischio silice nelle piccole e piccolissime imprese.*

Introduction

Recent scientific evidence regarding the carcinogenicity of inhaled crystalline silica (hereafter called simply silica), and the results of surveys on occupational silica exposure in Italy pose new challenges related to undetected conditions of occupational exposure to silica and the consequent lack of appropriate preventive action and compensation of occupational diseases (silicosis and lung cancer) deriving from such exposures.

There are three main challenges: the first concerns silicosis. In 2008, WHO launched the "*Global program for the elimination of silicosis*" which also covered developed countries, such as Italy. To comply with the initiative, a necessary step was to verify the number of silicosis claims compensated by the National Institute for the Insurance of Workplace Accidents and Occupational Diseases (INAIL), the methods used to identify the cases, and the specific surveillance activities implemented by the occupational safety and health (OSH) services of the National Health Service. However, by applying the risk estimates developed by the Scientific Committee on Occupational Exposure Limits (SCOEL), reported in table 1, the number of cases appeared substantially underestimated: to generate annually about 300 new silicosis cases, the same average number reported annually to INAIL in 2004-2008, half of which were compensated (53, 54), only 5 percent of the 250,000 exposed Italian workers (58) should have been exposed for 15 years to the lowest SCOEL cumulative silica level, 3 mg/m^3. Besides, the number of Italian workers exposed to silica is believed to be underestimated, especially in the building trade, where more than 100,000 workers might be exposed. The disappearance of silicosis in Italy has been postulated. However, underreporting to INAIL because of misdiagnosis is possible, as it is indeed well known that only a minority of cases are diagnosed using established ILO criteria (52).

In 2009, following years of discussion, IARC confirmed the classification of silica in Group 1, among the known human carcinogens (85), providing a second serious challenge. It should be emphasized that, as occurred in 1997, the IARC conclusions left some scientific questions open related to silica carcinogenesis, and specifically those con-

Table 1 - Relationship between silica exposure (respirable fraction) and risk of silicosis

Annual exposure to silica (mg/m^3)	Cumulative exposure to silica over 15 years (mg/m^3)	Risk of silicosis (ILO category 2/1) 15 years after exposure
0.02	0.3	0.25%
0.04	0.6	0.5%
0.1	1.5	2.5%
0.3	4.5	20%

cerning occupational exposure to different silica polymorphs.

A third challenge emerged in 2010 with the results of the monitoring survey of occupational exposure to silica in several Italian areas, promoted by the Italian Silica Network (NIS). These activities, carried out in several occupational sectors, revealed a significant under-evaluation of occupational exposure to silica, especially in small industries and workshops, and particularly in the construction industry.

Since its foundation in 2002, the NIS, a collaborative network of professionals and public authorities, has been engaged in occupational health prevention, control, research and insurance coverage of silica-related health effects (8, 61). Thanks to the expertise of NIS members, several aspects related to silica exposure and effects have been assessed, sometimes by applying original methods. The results and comments regarding these activities are briefly reported.

THE NIS OPINION ON SILICA CARCINOGENICITY

The evaluation process regarding silica carcinogenicity has been highly controversial and time-consuming. As Steenland wrote: *"it took over 20 years of studies to convince IARC and other agencies that silica should be considered a known carcinogen"* (82). On March 2009 the new IARC revision was announced (85), which confirmed the previous classification in Group 1 among the 107 agents classified as human carcinogens.

In 1987, IARC first classified silica among the agents "probably carcinogenic to humans" (Group 2A) (50). Ten years later, in 1997, reviewing further papers published on this issue, the IARC Working Group judged the new scientific evidence as *"sufficient in humans for the carcinogenicity of inhaled crystalline silica in the form of quartz or cristobalite from occupational sources"*. Silica was therefore classified in Group 1 (51). In the succeeding years, following the impact of the IARC classification on OSH activities, discussion spread and was sometimes fierce, within the scientific community and numerous studies and reviews were carried out to assess and overcome the methodological limitations of the studies considered by IARC (9, 27, 44, 49, 56, 62, 66, 80, 81, 90). Debate and new studies were also generated from the IARC Working Group conclusions themselves, which noted that silica carcinogenicity was not detected in all industrial environments and this phenomenon might have been *"dependent on inherent characteristics of the crystalline silica or on external factors… affecting its biological activity or distribution of its polymorphs"* (51). This aspect was the motivation to call for further inquiry into the causal role played by silica in lung carcinogenicity before defining and applying measures to reduce and control occupational exposure to silica, in addition to those already in place. In this respect, the economic implications of implementing the necessary additional control measures had a heavy impact.

Silica carcinogenicity

The were essentially four main problems in interpreting epidemiological findings on silica carcinogenicity in humans: (i) the possible confounding role played by smoking; (ii) the possible confounding role played by other occupational carcinogens, in particular radon and arsenic in miners, and PAH in foundry and pottery workers; (iii) the evaluation of the dose-response relationship and the possible identification of a threshold level of exposure; (iv) the role played by silicosis.

Several studies published after 1997 took smoking into consideration in the analysis of lung cancer risk related to silica exposure (9, 14, 58, 68, 69): as expected, the confounding effect of this important lung cancer risk factor was generally modest; in fact, in the last 15 years, it seems very unlikely that smoking habits among silica exposed workers would differ compared to the reference populations (3, 48, 71, 79).

Possible confounding by other occupational lung carcinogens was expectedly of greater significance and for this reason several studies on working populations exposed almost exclusively to silica were carried out (2, 4, 40, 58, 70) and other studies collected information on other possible occupational exposures and adjusted silica risk estimates for the effect of these possible confounders (9, 14, 69).

On the question of the dose-response relationship, three independent studies consistently showed an increasing risk of lung cancer in relation to increasing cumulative exposure to silica (9, 55, 83). Nevertheless, a tendency of a levelling out of risk at exposure levels higher than 5 mg/m^3/year was observed. A question that is still open regards the role played by silicosis (13). Association with lung cancer risk has always been found to be stronger among silicotics (49, 78, 84), but it is not yet clear whether this is due to silicosis *per se*, or to the very high level of silica exposure experienced by silicotics (4, 26, 55, 62).

Despite the continuing scientific debate to clarify the previously mentioned scientific questions that are still open, NIS believes that the IARC programme assessing and weighing the evidence of cancer risk related to specific agents and work processes by means of interdisciplinary working groups of expert scientists reviewing the published reports, will constitute an authoritative reference for occupational and public health prevention activities that cannot be delayed any longer.

Mechanisms of inflammation, fibrogenicity and carcinogenicity

Several *in vitro* experimental studies on the toxicity of crystalline silica(s) showed a remarkable variability between the various silica sources in several biological responses. This led to the well known statement on the "variability of quartz hazard" (20, 21, 31). A variability was also found in animal tests, concerning both fibrosis and cancer. Sometimes, the variability within a set of samples of the same polymorph, e.g. quartz, exceeded even the variability between different polymorphs (5, 6, 33, 76). This has led most scientists to discard the idea of a toxic response related to a specific polymorph, but has convinced the scientific community that each silica source should be examined as far as its toxic potential is concerned. In the meantime, new experimental studies are required, with well defined crystalline silica specimens, to establish the set of chemical and morphological properties that render silica particles pathogenic.

In this regard, the *'inherent characteristics'* of silica particles, mentioned in the previously cited preamble to the Group 1 classification of some silica polymorphs in the previous IARC monograph (51), are accounted for by the state of the external surface (defects, chemical functionalities, etc.) determined by the origin of the sample, while the *'external factors'* suggest that contact, association or contamination by substances other than silica might activate (or blunt) silica carcinogenicity. Both inherent characteristics and external factors may act at different stages of the development of the disease. Different surface functionalities may be implicated in each step. Various biological responses elicited by a series of different silica dusts have shown that some cellular responses, e.g. cytotoxicity, inflammation, transforming power, and DNA damage, are not related to the same property of the silica particle (14, 23, 25). The carcinogenic power of a given dust is the result of how and to what extent each of the particle characteristics plays a role in one (or more) of the subsequent cellular and molecular events taking place in the carcinogenic mechanism. One point is confirmed by several studies, i.e., the greater power of freshly ground dusts, e.g., as in sandblasting (87). In fact, immediately after cleavage, a large number of surface active radicals are formed which rapidly decay (16, 31). Metal contamination may influence toxicity in different directions. The association with clay or other aluminium-containing compounds inhibits most adverse effects (22, 72). Iron in traces (isolated iron ions) may enhance the effects, e.g., by increasing surface reactivity towards free radical generation (30). Conversely, an extended iron coverage may reduce some adverse cellular effects, e.g. cytotoxicity and cell transformation (34, 37).

Experimental evidence ascribes an important role to the production of reactive oxygen (ROS) and nitrogen (RNS) species. ROS and RNS are likely to be mediators of silica-induced responses including inflammation, lipid peroxidation, protein oxidation, fibrosis and cell proliferation (10, 21, 47). Silica particles can induce ROS generation directly and/or by stimulation of cells (19, 43). In the former case, both silicon-based surface radicals and traces of iron ions (located in a particular redox and

coordinate position on the surface) are active centres for free radical release in solution (36). In the latter case, the silica particle, engulfed by alveolar macrophages (AM), may induce AM activation. Macrophages release ROS and RNS, chemotactic factors, hydrolases, cytokines, and growth factors, but subsequently die, releasing the particle free in the alveolar space. Subsequent ingestion-release cycles, accompanied by a continuous recruitment of AM, neutrophils and lymphocytes, are the cause of the chronic inflammation elicited by silica dusts. Bronchiolar and alveolar epithelial cells are also affected by both AM products and the extracellular particle itself, again resulting in cell activation and/or death (11, 17, 36, 46).

ROS can directly induce DNA damage (39, 47, 73). Morphological transformation observed in Syrian hamster embryo (SHE) cells correlates well with the amount of hydroxyl radicals generated (24, 34). In contrast, ROS generation does not correlate with cytotoxicity, which is not affected by antioxidants. Similarly, cytotoxicity does not correlate with transforming effects (23).

Crystalline silica may also deplete the antioxidant defense in the lung lining layer by simple surface reactions, thereby enhancing the extent of oxidative damage. A substantial consumption of ascorbic acid (29) and glutathione (GSH) by quartz (28) was observed in cell free tests. Quartz also inhibits G6PD, but not other oxidoreductases, and this inhibition is prevented by GSH, suggesting that silica contributes to oxidative stress also by inhibiting the pentose phosphate pathway, which is critical for regeneration of reduced GSH (67).

Studies supported by NIS

To face the challenges posed by the IARC classification to prevention of silica-related occupational diseases in the workplaces and to understand the pathogenicity of a silica-containing dust, it is crucial to differentiate the various sources of occupational exposure to silica and detect the critical workplaces where the most hazardous exposures are generated, in order to undertake appropriate preventive measures. NIS addressed these issues by supporting two laboratory studies and surveillance programmes of workplace exposure to silica in several Italian regions.

In 2006, the Italian Ministry of Health issued a ministerial decree launching a national initiative called the "Coordinated Oncology Programme". Within the framework of this programme, research on the variability of crystalline silica hazard in various workplaces and identification of the chemical and physical properties involved in silica toxicity was assigned to the NIS. This project covered several Italian Regions and was carried out by the "G. Scansetti" Interdepartmental Centre for Studies on Asbestos and other Toxic Particulates of the University of Turin. The aim of the project was to monitor possible adverse health reactions induced by various industrial samples containing free crystalline silica. It should be noted that silica toxicity and carcinogenicity varies according to the source of crystalline silica, so that identifying the level of hazard posed by specific work environments is extremely useful in any risk management approach. The main goals of the project were: (i) to gain new knowledge on silica health hazard management in the various workplaces considered; (ii) and to increase knowledge of the effects of the "external factors", i.e., other airborne contaminants, and of "inherent characteristics", i.e., the effects of the process of grinding the powder to micro- or nano-size particles, on the biological activity of silica. Severe exposure to crystalline silica occurs in cement and brick manufacturing, ceramics manufacturing and steel and foundry industries (89). On the basis of the knowledge acquired in the past (20, 31) indicating that crystalline status, morphology and contaminants on the particle surface play a pivotal role in silica toxicity, a large number of samples from such industrial sectors were analyzed. A systematic analysis of the chemical and physical properties possibly related to adverse effects on cells and tissues (32) was carried out on samples of the raw materials collected at critical steps of processing and finished products.

The chemical and physical properties considered in this project included:

- morphology (presence of irregular surfaces, shape edges and spikes);
- granulometry (fraction of inhalable and respirable particles and surface area);

- bulk composition (presence of aluminium and metal transition ions, identification of silica polymorphs);
- surface properties.

We examined the presence of surface radicals (35), the potential to catalyze free radical generation in solution (36) and the amount of bio-available iron (iron that may be mobilized by chelants) on sample surfaces (30, 78), which are among the most significant surface properties involved in silica toxicity.

Samples with higher surface reactivity were also tested in cell cultures. Cytotoxicity, measured as leakage of lactate dehydrogenase (67), and ROS and RNS generation, implicated in cytotoxic and mutagenic effects, were investigated using alveolar macrophages (MH-S) (38). As expected, a high variability in terms of surface reactivity and cellular responses was observed for the different samples depending on their origin and their contact with other materials during the manufacturing process. ROS and RNS generation are highly sensitive properties. Most samples tested were capable of catalyzing hydroxyl radical generation and of increasing the intracellular level of nitric oxide, but only a few samples, such as quartz and waste products from ceramic tile manufacture, which contain several transition metal ions as contaminants, were able to stimulate ROS generation and manifest cytotoxicity.

Particle size and the extent of the exposed surface played an important role in the cellular responses elicited as previously described (45). It should be pointed out that the ability of the quartz samples used in ceramics (tiles and sanitaryware) manufacture to catalyze free radical generation and induce adverse cellular responses was greater for the fine than for the coarse fraction, even when compared by surface unit. However, whereas cytotoxicity and ROS generation did not vary across samples when compared by surface unit, iron-rich quartz samples showed a greater capacity of generating nitric oxide. Iron is the most common and the most abundant transition metal ion in nature, in the human body and also in the materials studied. However, the amount of bioavailable iron on the sample surface was generally very low, and it did not correlate with free radical release or ROS generation.

Another ongoing study supported by NIS aims to assess whether exposure to silica is reflected by the formation of malonaldehyde-deoxy guanosine (M1dG) adduct, a biomarker of exposure and cancer risk, in the nasal mucosa of silica-exposed workers in different types of industries. *In vitro* experiments confirmed the validity of the M1dG adduct as a marker of inflammation via macrophage activation and release of hypochlorite (41, 42). Recent studies showed that an increasing level of M1dG reflects exposure to environmental carcinogens able to induce the production of free radicals (65). Even more important, case-control studies indicate that increased levels of M1dG could be related to the development and progression of breast and lung tumours (60, 63). The relevance of the M1dG adduct as a possible biomarker of exposure to silica stems from its possible induction by ROS released by silica particles in the form of free radical (Si*) or through integration with oxygen in an aqueous environment. ROS can also be induced by cytokines and growth factors released by neutrophils and macrophages in the lung tissue following the inflammatory process caused by contact with silica particles. ROS are reactive molecules capable of interacting with DNA and lipids in the cell membrane, thus inducing oxidative damage and lipid peroxidation, resulting in the formation of malondialdehyde (MDA). MDA, in turn, is capable of interacting with DNA thus inducing exocyclic adducts, including M1dG. M1dG adduct can also be formed through ROS-induced propenals. Its carcinogenetic role might be linked to its ability to induce mutations.

Any increase in M1dG level in the nasal mucosa among silica-exposed workers, compared to an unexposed reference group, could represent a reliable indicator of lung cancer risk. Therefore, M1dG analysis has great potential to become a major tool for risk assessment and primary prevention (65).

Future NIS studies will apply a cross-sectional design to compare the M1dG adduct level in silica- exposed workers with an appropriate unexposed reference group. Following informed consent to participate in the study, nasal mucosa cells will be sampled by gentle brushing of the inferior turbinate of the nose with a cyto-brush (64) in

200 silica-exposed workers and 100 unexposed subjects. M1dG will be analysed on the DNA extracted from the nasal mucosa by ^{32}P-DNA-post-labelling. All participants will also complete a questionnaire gathering information on life style, residence and dietary habits. Dust samples will be collected by individual samplers with a specific selector (type CIP10). Silica levels will be measured by X-ray diffraction and scanning electronic microscopy.

The Network's experience with public occupational health and safety services

Several local initiatives resulted from the creation of an inter-regional coordinating technical committee of public OSH services within the NIS aiming to assess silica exposure and its related effects in the respective territories of each service. The initiatives were aimed at identifying exposed subjects and current exposure levels, as well as feasible standard preventive measures and adequate tools for enforcing application and efficacy of these preventive measures. A survey of silica-related health effects, such as pneumoconiosis and lung cancer, was also included in these initiatives. The following is a description of the experiences in Tuscany and Emilia Romagna and how they are integrated with the above mentioned research programmes.

The Tuscany experience

The activity of the Tuscany working group started with the identification of the workplaces where silica exposure occurs or might occur, with the aim of introducing measures to reduce exposure levels and of assessing possible silica-related adverse health effects. The industries involved in the project include sandstone quarries, stone cutting and finishing workshops, ceramics factories, special local tile manufacture ("*cotto dell'Impruneta*"), goldsmith workshops, sandblasting workshops, foundries, and the construction industry. In at least one structure for each type of trade inspections were carried out, respirable dust and the SiO_2 concentration were measured, and the application of the best available techniques verified, as indicated by NIS and/or the agreement European Network for Silica (NEPSI) established by the European Employee and Employer trade associations (http://www.nepsi.eu/media/2115/agreement%20-%20italian%20disclaimer. pdf). Inspections of the sandstone quarries also included geological details, including type of ore, its silica content and physical and chemical status, and the conditions of the working environment. Overall, 757 personal samples were collected in various workplaces from 2003 onwards. Samples were analyzed using X-ray diffractometry at the Laboratory of Public Health in Siena. Bulk dust samples were analyzed at the Department of Chemistry of the University of Florence in collaboration with the Tuscany Regional Agency for Environmental Protection (ARPAT). To test the relationship between silica surface and its chemical reactivity, bulk dust samples were analyzed at the Department of Chemistry of the Florence University, in collaboration with the Tuscany Agency for Environmental Protection (ARPAT), by electron microscopy, electron paramagnetic resonance (EPR) spectroscopy, aiming to identify surface contaminant ions and organic and inorganic radicals, and by x-ray absorption spectroscopy (XAS) aiming to define the chemical structure and morphology of the silica particle surface. The modifying effect of aging on particle surface changes and reactivity, including interaction with atmospheric agents, humidity, and chemicals, was also explored with the same spectroscopic techniques.

Out of a total of 757 measurements 350 (46.2%) were below the limit of quantification (LOQ) where the range of values is between 11 and 127 $\mu g/m^3$ depending on the method of measurement (7, 8, 74). This means that several measurements below the LOQ might have been greater than the limit value, and particularly the ACGIH TLV of 25 $\mu g/m^3$, which in turn implies that some selectors that were used do not meet the requirements to test current TLVs. Such findings are consistent with other reports in the literature (12). According to UNI EN 689/1997 criteria, which Italian Law (D.L. 81/08) takes as a reference, at expectedly low

airborne silica levels a good sampling and analyzing procedure should allow measuring a concentration of one tenth of the TLV. The only sampling device that meets such requirement for a 7-hour sampling period is the CIP10 sampler. Another source of significant sampling variation in silica content was associated with positioning two identical selectors on the left or right side of the same worker, which adds to the complexity of implementing an effective sampling procedure (75). The geometric mean of measurements above the LOQ (39.2 μg/m^3) was well above the TLV, as was the case for 283 out of the total 407 measurements above the LOQ (69.5%, corresponding to 37.4% of total measurements). Such instances appear to occur more frequently, ranging from 49.5 to 100%, in the ceramics industry, tunnelling, sandstone and "*pietra serena*" quarries, tobacco curing, and clay milling and moulding. It is worth noting that the inadequacy of some sampling devices might also have led to an underestimation of the percentage of samples above the TLV.

Using the EPR technique, changes in type and amount of silica radicals were observed following any mechanical or thermomechanical wet processing. ESE spectroscopy of the raw materials in ceramic tile manufacturing allowed distinguishing differences in the EPR spectrum related to changes in quartz particles induced by the work process from those induced by chemical interactions, for instance with aluminium, suggesting changes in silica bioreactivity capable of modifying its biological effects.

Differences in the chemical characteristics of iron binding silica particles, particularly in relation to Fe^{2+} and Fe^{3+} ions, were observed in bulk dust samples and by surface analysis with XAS techniques of model samples to assess the ability of iron to modulate ROS release and the resulting biological effects. Parallel high field EPR investigations showed that in the grinding process Fe^{3+} ions migrate from the inner quartz particle to the surface from where they are released as nano-sized oxides (18). The biological effects of such particulate are related to the duration of its suspension in the air of the environment, which is expected to be longer than that of the larger sized particles making up the respiratory fraction of free crystalline silica, which deposits faster. These results suggest that the catalytic activity of the various iron species depends on the processing of quartz particles, and that their bioavailability affects ROS formation.

The silica project of the Tuscany working group was completed with the implementation of several preventive measures, including introduction of modified ventilation devices, maintenance of the ventilation ducts and the water stream ducts carrying the suspended particles, and more frequent schedules of dust removal in the workplace. Overall, these measures contributed to a substantial reduction in the airborne dust concentration. However, particularly in dry process areas, levels continued to be higher than the ACGIH TLV, which required the use of expiratory valve-equipped personal respiratory protective equipment (PPE).

The Emilia Romagna experience

In the Emilia Romagna Region, based on 2008 INAIL data, about 31000 workers are estimated as being potentially exposed to silica. A trade-process/exposure matrix was created with the participation of the OSH services of six out of the 11 Emilia Romagna Health Units.

Overall, 243 measurements using 6,53 multi inlet sampler, for 6-8 hours sampling periods) were performed, 61 of which were below (10 μg) (1) the LOQ. Table 2 shows the mean airborne silica con-

Table 2 - Average silica exposure levels in Emilia Romagna, dusty trades in Italy

	Trades	No. samples	Aritmetic mean (Gds) (μg/m^3)
25-50 μg/m^3	Tile manufacture	64	49 (2.5)
	Foundries	32	44 (2.8)
	Stone crushing and milling plants	16	32 (4.4)
> 50 μg/m^3	Marble and granite works	6	186 (3.9)
	High speed railway tunnelling	24	90 (4.2)
	Construction	20	55 (4.2)

centration by type of industry, classified as below or above 50 μg/m^3. Preventive measures were set up based on the identified exposure levels classified into four categories of increasing level. A check list was also created to allow the employer to self-assess risk and the OSH services to plan inspection programmes. The survey is still in progress and aims at testing the adequacy of the preventive measures taken and at identifying instances of successful outcomes capable of providing highly efficient solutions that can be applied in other enterprises in the same trade and/or in other trades.

In 2000-2008, only twelve cases of pneumoconiosis were compensated by the regional INAIL office, two of which were confirmed with CT scan, and another 13 claims were rejected: this appears in contrast with the consistently reported measurable levels of silica exposure (1, 86, 88) in a substantial number of workers. A possible reason might be the difficulties in reading and classifying the radiographs. Therefore, following standard procedures (57), three B-Readers used the ILO criteria to examine technical features and classify the chest X-rays of 242 male workers exposed to silica in different areas (clay storage, milling, stamping presses) of five ceramics industries. The results of this survey (two new cases of silicosi ≥ILO 1/0 detected) suggested that a normal radiograph is not sufficient to detect the early stages of pneumoconiosis, where top quality techniques are required. A second issue is related to the loss of radiographs over time when stored improperly, which creates difficulties in following up the evolution of the radiological aspects at both individual and group level (http://www.ausl.re.it/Home/Custom.aspx?IDSottoCategoria=276). Such limits suggest a too much prudent attitude in inferring a low prevalence of silicosis, instead silicosis cases were about 8% among workers exposed more than 25 years, although previous exposures at higher levels might have most likely accounted for the observed cases (88). Concurrent exposure to smoking may act synergically with silica to cause lung damage, which further increases the need for a permanent prevention programme.

Conclusion

NIS initiatives to prevent the health effects related to occupational exposure to silica have set a model of efficient and advanced territorial OSH intervention, which creates the conditions to comply with the objectives of the global WHO programme to eradicate silica-related diseases also in Italy. A major obstacle is represented by the low compliance of small industries and workshops, which continue to represent a challenge for the public OSH services and the social partners to fulfil their responsibilities.

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