The "Carcinogens and Mutagens Directive" and the crystalline silica exposure at work place

Maurizio Coggiola*

* DSSPP, Dipartimento di Scienze della Sanità Pubblica e Pediatriche, Università degli Studi di Torino

The recent directive on the protection of workers from risks related to exposure to carcinogens and mutagens addresses the problem of exposure to crystalline silica.
In view of current scientific knowledge, the directive assigns the role of carcinogen to work processes that generate exposure to crystalline silica in the respirable fraction and not to silica as such. Therefore, this choice does not determine the obligation to classify and label as carcinogenic the products containing more than 0.1% of crystalline silica in the respirable fraction. Considering that the Scientific Committee of Occupational Level defines the silica substance for which a "practical" limit value can be identified, the directive has established an OEL of 0.1 mg / m^3. According to the directive, compliance with the limit value does not exempt the application of prevention measures provided for by the directive itself and by national regulations. However, in relation to the available literature data, it is considered possible to identify an action level lower than the OEL whose compliance guarantees a level of protection that does not make it necessary to activate some of the planned actions (replacement and processing in closed systems). At the current state of knowledge, an action level of 0.05 mg / m^3 could be indicated.
Keywords: *European Directive carcinogenics*

La "Direttiva sui cancerogeni e mutageni" e l'esposizione alla silice cristallina sul posto di lavoro. *La recente direttiva sulla protezione dei lavoratori dai rischi correlati all'esposizione ad agenti cancerogeni e mutageni affronta il problema dell'esposizione a silice cristallina.*
Alla luce delle attuali conoscenze scientifiche la direttiva attribuisce il ruolo di cancerogeno ai processi di lavoro che generano una esposizione a silice cristallina in frazione respirabile e non alla silice come tale. Tale scelta non determina pertanto l'obbligo di classificare ed etichettare come cancerogeni i prodotti contenenti più dello 0.1% di silice cristallina in frazione respirabile. In considerazione che lo Scientific Committee of Occupational Level definisce la silice sostanza per la quale è possibile identificare un valore limite "pratico" la direttiva ha stabilito un OEL pari a 0.1 mg/m^3. Secondo la direttiva il rispetto del valore limite non esime dall'applicazione degli interventi di prevenzione previsti dalla direttiva stessa e dalle norme nazionali. Tuttavia in relazione ai dati di letteratura disponibili si ritiene sia possibile identificare un livello di azione inferiore allo OEL il cui rispetto garantisca un livello di tutela tale da non rendere necessario attivare alcune delle azioni previste (sostituzione e lavorazioni in sistema chiuso). Allo stato delle conoscenze attuale potrebbe essere indicato un livello di azione pari a 0.05 mg/m^3.
Parole chiave: *direttiva europea cancerogeni.*

La "directive sur les agents cancérigènes et mutagènes" et l'exposition à la silice cristalline sur le lieu de travail. *La récente directive sur la protection des travailleurs des risques liés à l'exposition à des agents cancérigènes et mutagènes aborde le problème de l'exposition à la silice cristalline.*
Dans le contexte des connaissances scientifiques actuelles, la directive attribue le rôle de cancérigène aux processus de travail qui génèrent une exposition à la silice cristalline dans la fraction respirable et non à la silice en tant que telle. Par conséquece, ce choix ne détermine pas l'obligation de classer et d'étiqueter comme cancérogènes les produits contenant plus de 0,1% de silice cristalline dans la fraction respirable. Considérant que le comité scientifique de niveau professionnel Scientific Committee of Occupational Level définit la substance à base de silice pour laquelle une valeur limite "pratique" peut être identifiée, la directive a établi une VLEP de 0,1 mg / m^3. Selon la directive, le respect de la valeur limite ne dispense pas de

The directive (EU) 2017/2398 of the European Parliament and of the Council of 12 December 2017 amending Directive 2004/37/EC on the protection of workers from the risks related to exposure to carcinogens or mutagens at work introduces some important general criteria.

Particularly the Carcinogens and Mutagens Directive – CMD approach the problems of Occupational Exposure Level – OEL in case of carcinogens or mutagens agents' exposure.

In fact the CMD states "For *most carcinogens and mutagens, it is not scientifically possible to identify levels below which exposure would not lead to adverse effects. While setting the limit values at the workplace in relation to carcinogens and mutagens pursuant to this Directive does not completely eliminate risks to the health and safety of workers arising from exposure at work (residual risk), it nonetheless contributes to a significant reduction of risks arising from such exposure in the stepwise and goal-setting approach pursuant to Directive 2004/37/EC. For other carcinogens and mutagens, it is scientifically possible to identify levels below which exposure is not expected to lead to adverse effects".*

This statement is coherent with the recommendation proposed by Bolt *et al.* in 2008. In their paper the authors suggested the classification reported in figure 1

The classification provides for the identification of four categories of carcinogen agents: two groups (A and B) without OEL and two group (C and D) with OEL. In the category C the OEL is a practi-

l'application des mesures de prévention prévues par la directive elle-même et par les réglementations nationales. Cependant, en ce qui concerne les données disponibles de la littérature, il est possible d'identifier un niveau d'action inférieur à l'OEL dont la conformité garantit un niveau de protection qui ne nécessite pas d'activer certaines actions planifiées (remplacement et traitement en systèmes fermés). Dans l'état actuel des connaissances, un niveau d'action de 0,05 mg / m³ pourrait être indiqué.

***Mots clés**: directive européenne sur les agents cancérogènes*

cal threshold likely and in the category D is true/perfect threshold. Both are setting a health-based OEL.

In the group C are classified the agents with a weak genotoxicity and a secondary important mechanism. In the group D are classified the agents with a genotoxicity only on chromosome level or with an epigenetic action.

In the table 1 some example of carcinogens classification is reported.

Regarding the crystalline silica the CMD affirms " *There is sufficient evidence of the carcinogenicity of respirable crystalline silica dust. On the basis of available information, including scientific and technical data, a limit value for respirable crystalline silica dust should be established. Respirable crystalline silica dust generated by a work process is not subject to classification in accordance with Regulation (EC) No 1272/2008. It is therefore appropriate to include work involving exposure to respirable crystalline silica dust generated by a work process in Annex I to Directive 2004/37/EC and to establish a limit value for respirable crystalline silica dust ('respirable fraction') that should be subject to review, in particular in light of the number of workers exposed"*

The chose to introduce in the CMD the work process involving exposure to Respirable Crystalline Silica – RCS and not silica it self derives from the difficult to correctly understand the results of toxicological and epidemiological studies. In the toxicological studies the direct genotoxicity was observed in very few cases and the main mechanism observed seems to be the oxidative stress. The oxidative stress is related with the surface reactivity and the surface reactivity decreases proportionally at the time of the mechanical fracture.

The epidemiological studies did not show a risk excess of lung cancer in all conditions of exposure. When the risk excess was observed the exposure levels were very high, generally higher than the exposure levels able to causes the silicosis. The rule of silicosis is still uncertain (marker of high level of exposure or necessary condition to de-

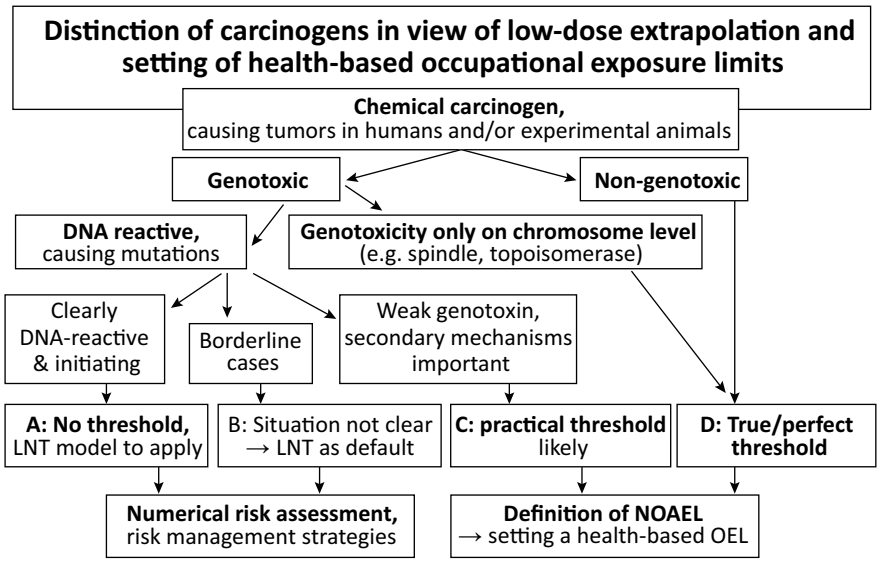

Fig. 1. Flow-chart to distinguisch between groups of carcinogens (S-D) for the purpose of risk assessment and standard serring (OELs). From Bolt *et al.*, 2008.
Diagramma di flusso per distinguere tra gruppi di agenti cancerogeni (S-D) ai fini della valutazione del rischio e degli standard (OEL). Da Bolt et al., *2008.*

Tab. I Results of SCOEL discussions on individual carcinogens (by 2007) and assignment to the groups of carcinogens based on mode of action, see SCOEL Summary Documents (SCOEL 1998. 2007). From Bolt *et al.* 2008.
Risultati delle discussioni SCOEL sui singoli agenti cancerogeni (entro il 2007) e assegnazione ai gruppi di agenti cancerogeni basati sul meccanismo di azione, cfr. Documenti riassuntivi SCOEL (SCOEL 1998. 2007). Da Bolt et al., *2008.*

A) Non-threshold genotoxic carcinogens: for risk lon-dose assessment the linear non-threshold ILNT) model appears appropriate:
1,3-butadiene (quantitative risk assessment performed), vinyl chloride (quantitative risk assessment performed), methylene dianiline (MI)A: 4.4'-diamono-diphenyl-methane). dimethyl sulphate

B) Genotoxic carcinogens, for which the existence of a threshold cannot be sufficiently supported at present. In these cases the LNT model may be used as a default assumption, based on the scientific uncertainty:
Acrylonitrile. benzene, naphthalene, wood dust, hexavalent chromium compounds (quantitative risk assessment performed)

C) *Genotoxic carcinogens for which a* practical *threshold is supported and for which a health-based OEL has been proposed:*
Formaldehyde, vinyl acetate, pyridine, silica, lead (provisional OEL proposed)

D) Non-genotoxic carcinogens and/or non-DNA-reactive carcinogens: for these compounds a true *("perfect") threshold is associated with a clearly founded NOAEL A health-based OEL has been proposed:*
Carbon tetrachloride, chloroform, nitrobenzene

velopment of the lung cancer). In the 2003 the Scientific Committee of Occupational Exposure Level affirmed "*The main effect in human of the inhalation of respirable silica dust is silicosis. There is sufficient information to conclude that the relative risk of lung cancer is increased in persons with silicosis (and apparently, not in employees without silicosis exposed to silica dust in quarries and in the ceramic industry). Therefore preventing the onset of silicosis will also reduce the cancer risk. Since a clear threshold for silicosis development cannot be identified, any reduction of exposure will reduce the risk of silicosis. (...) It arises that an OEL should lie below 0,05 mg/m*^{3}" (Scoel Sum Doc 94 final, June 2003).

Considering these data the CMD classified the work process and not the substance "silica". The work process causes an exposure to respirable silica with "freshly fracture" and the presence of "freshly fracture" increases the surface reactivity and the silica toxicity.

As reported in table 1 (Bolt *et al*. 2008) silica is considered a carcinogen with a "practical threshold likely" (category C). Consequently the CMD states "*It is therefore appropriate to include work involving exposure to respirable crystalline silica dust generated by a work process in Annex I to Directive 2004/37/EC and to establish a limit value for respirable crystalline silica dust ('respirable fraction') that should be subject to review, in particular in light of the number of workers exposed*."

In the Annex 1 the CMD reports for the crystalline silica an OEL of 0.1 mg/m^3. This value is a binding value. That means the member states could adopt an occupational exposure level equal or lower the OEL reported in the Annex 1.

The inclusion in the CMD the process involving exposure to Respirable Crystalline Silica – RCS– and no silica it self is not relevant for the classification and the labelling of the products containing RCS.

The FAQ prepared from EUROSIL for the associated companies states "*The directive is put forward only in the context of occupational workers' health protection legislation. In the EU the classification and labelling of products is ruled by other separate legislation (the CLP Regulation 1278/2008). There is no direct link between these two legislative frameworks. Directive 2017/2398 addresses respirable dust generated by work processes, not the substance itself. Crystalline silica placed on the market is subject to the classification obligation under Regulation (EC) 1272/2008, while crystalline silica dust generated by a work process is not placed on the market and therefore is not classified in accordance with that Regulation*".

Consequently the work process

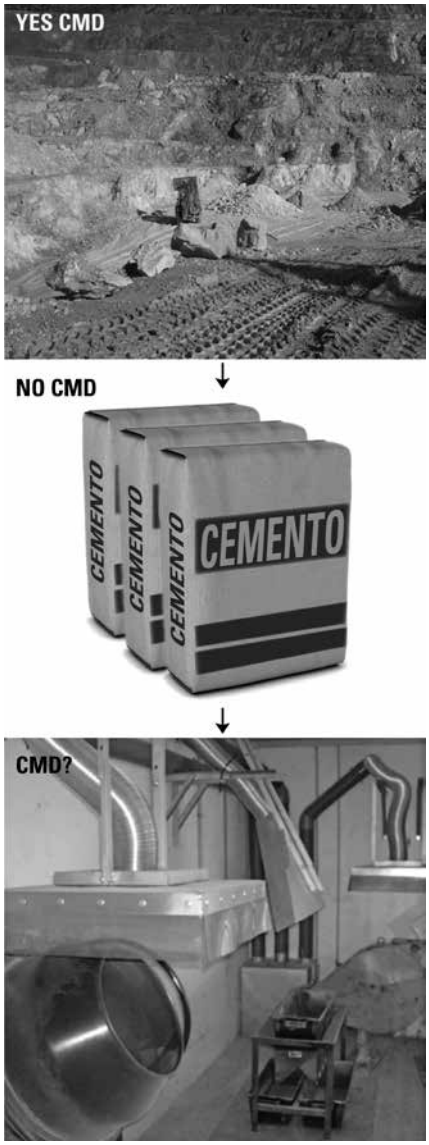

Fig. 2. The flow of the CMD application.
Il flusso di applicazione del CMD.

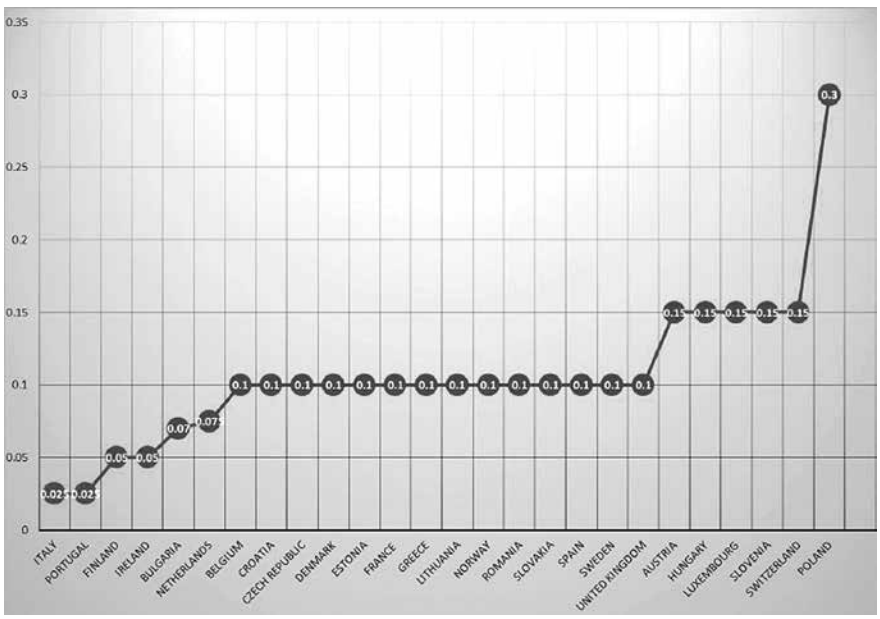

Fig. 3. Occupational Exposure Limits[15] in mg/m^3 8 hours TWA (time weighted average) – Respirable Crystalline Silica in EU-28[16], Norway and Switzerland.
Limiti di esposizione professionale[15] in mg/m^3 8 ore TWA (media ponderata nel tempo) per silice cristallina respirabile in EU-28, Norvegia e Svizzera.


IOM
WORKING FOR A HEALTHY FUTURE

IOM Research Project: P937/99
May 2011

Health, socio-economic and environmental aspects of possible amendments to the EU Directive on the protection of workers from the risks related to exposure to carcinogens and mutagens at work

Fig. 4. Document elaborated by IOM.
Documento elaborato da IOM.

and no the substance is considered carcinogen.

In the figure 2 the flow of the CMD application is reported: the work process extracting a mineral must be classified "carcinogen" in case of exposure to RCS, the distribution of the final product on the market is not covered from the CMD while the use of the product in a new work process could be fall under CMD in case of the presence RCS exposure.

Similarly to the work process extracting a mineral the drilling rock activity could fall under the scope of the CMD.

The CMD identified for RCS an occupational exposure level at 0.1 mg/m^3. The figure 3 reports the OEL adopted at today in the different European countries.

The chose of an OEL at 0.1 mg/m^3 derives from the document elaborated from the Institute of Occupational Medicine of Edinburgh (IOM) (Fig.4).

About the mean of the OEL in case of exposure the carcinogens the CMD states "*Occupational exposure limit values are part of risk management under Directive 2004/37/EC. Compliance with those limit values is without prejudice to other obligations on employers pursuant to that Directive, in particular the reduction of the use of carcinogens and mutagens at the workplace, the prevention or reduction of workers' exposure to carcinogens or mutagens and the measures which should be implemented to that effect. Those measures should include, in so far as is technically possible, the replacement of the carcinogen or mutagen by a substance, mixture or process which is not dangerous or is less dangerous to workers' health, the use of a closed system or other measures aiming to reduce the level of workers' exposure. In that context, it is essential to take the precautionary principle into account where there are uncertainties.*"

Therefore, in case of work involving exposure to respirable crystalline silica dust generated by a work process, the respect of the OEL is not sufficient to exclude to follow the approach reported in the CMD or in the national legislation.

Now the new challenge is to evaluated the possibility to identify an "action level" (AL) below 0.1 mg/m^3 able to prevent the risk of lung cancer. The respect of the AL (if it will be identifying it) could permit to avoid applying some actions required from the CMD directive (substitution and closed system).

At today the curve dose/response on RCS and lung cancer is not still well defined and universally accepted.

The pooled analysis published from Steenland in 2001 is generally used as reference to identify the relationship between the exposure level to RCS and risk excess for lung cancer. Using the data of Steenland Morfeld affirms (2011) the risk excess is related to the cumulative exposure higher than 6 mg/m^3/years. If we assume an occupational life of 40 years this value corresponds to an OEL higher than 0.15 mg/m^3. The Morfeld's evaluation is still under discussion but probably is the more realistic approach available at today. Therefore it is possible to propose a practical Action Level for RCS with a value of 0.05 mg/m^3.

In the figure 5 is reported a strategy model for the RCS risk assessment (NEPSI).

The respect of the OEL is mandatory. In case of RCS exposure lower than the action level (if adopted) some obligations reported in the CMD and national legislation could be no mandatory.

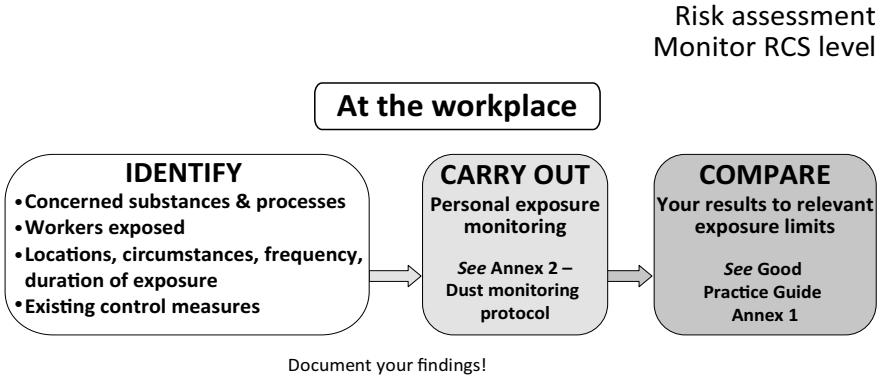

Fig. 5. The RCS Risk Assessment Monitor level proposed by NEPSI.
Il modello di valutazione e livello di monitoraggio della RCS proposto dal NEPSI

References

Agreement on Workers Health Protection through the Good Handling and Use of Crystalline Silica and Products containing it www.nepsi.eu

Bolt, H.M., Huici-Montagud A., 2008. *Strategy of the scientific committee on occupational exposure limits (SCOEL) in the derivation of occupational exposure limits for carcinogens and mutagens*. Arch Toxicol, 82: 61-64, DOI 10.1007/s00204-007-0260-z

Directive (EU) 2017/2398 of the European Parliament and of the Council of 12 December 2017 amending Directive 2004/37/EC on the protection of workers from the risks related to exposure to carcinogens or mutagens at work

Morfeld, P., *Respirable Crystalline Silica: Rationale For Classification According to the CLP* Regulation and within the Framework of the Globally Harmonised System (GHS) of Classification and Labelling of Chemicals*. www.crystallinesilica.eu

Steenland, K., Mannetje, A., Boffetta, P., Stayner, L., Attfield, M., Chen, J., Dosemeci, M., DeKlerkm N., Hnizdo, E., Koskela, R., Checkoway, H., International Agency for Research on Cancer, 2001. *Pooled exposure-response analyses and risk assessment for lung cancer in 10 cohorts of silica-exposed workers: an IARC multicentre study,* Cancer Causes Control, Nov., 12(9): 773-84.