COLL-CT-2003-500896

SILICERAM

- Studies aimed at assisting legislation and encouraging continual improvement strategies in the field of respirable crystalline silica -

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SILICERAM
Health and productivity

Project SILICERAM
Contract no COLL-CT-2003-500896

Studies aimed at assisting legislation and encouraging continual improvement strategies in the field of respirable crystalline silica

1. Project execution

Intrduction

Philippus Theophrastus Aureolus Bombastus Von Hohenheim (Paracelsus) lived in the fifteenth century and has variously been described as the father of toxicology. Amongst his many contributions to toxicology is one which has equal resonance today as it ever did during Paracelsus' life; that being,

"All things are poison and nothing is without poison, only the dose permits something to not be poisonous".

In other words, all substances have toxic potential but whereas some toxic substances have a beneficial effect in small doses, apparently benign substances can be lethal if consumed in vast quantities.

All this might sound like good common sense and lead us to a balanced and proportionate approach to regulation, but (and it is a big but) today we live in a society which harbours zero tolerance towards risk and which therefore continuously presses legislators and scientists to deliver a risk free environment; all of which is aided and abetted by a voracious tabloid press and the inevitability of endless debate on TV and radio by the usual "so called" experts.

If a risk free environment cannot be delivered any reassurance from politicians and scientists that the level of risk is miniscule will not be believed, let alone accepted by many. A good deal of this is born from the misguided notion that science can and should deliver definitive answers all the time, whereas invariably the process and techniques used in science often only deliver the next set of questions, but in seeking answers to such questions the body of knowledge builds and progress is made.

This process is invaluable in tackling occupational health and has been the driving force behind a major research project (SILICERAM) which has recently been completed. In a nut-shell the objective of the project was to pursue some of those unanswered questions which still plague our understanding surrounding the toxicology of respirable crystalline silica.

The whole debate relating to harmful effects of crystalline silica is very mature, in fact since the early 1900s occupational hygienists and physicians have known that prolonged and excessive exposure to respirable crystalline silica-containing dusts may cause silicosis, a particular form of pulmonary fibrosis leading to incapacity and premature death.

During the 1930s these principles were better understood and employers and regulators had started to introduce risk reduction measures. These included replacement where possible of fine crystalline silica as a process material, setting of occupational exposure limits, installing

dust extraction to reduce airborne concentrations and the introduction of efficient respiratory protective equipment.

Throughout the decades since, experience and technology advances have resulted in a degree of protection which has all but eliminated silicosis from the Industry. At the same time, stalking all this has been a range of questions, one of the most compelling of which is;

"*Are all the different forms of crystalline silica equally hazardous?"*

And in this regard conventional wisdom now inclines to the view that the answer to the question is a resounding "no". This being the case one could be forgiven for thinking that in the time honoured tradition of risk assessment then occupational exposure levels should be set at a level commensurate with risk and that therefore different forms of silica would attract different exposure levels, but they don't and the reason they don't is because to date scientists have been unable to really get to the bottom of the reasons why exposure to different silica dusts result in different health effects and whilst various theories exist none are sufficiently convincing in themselves to give the confidence to tackle variable toxicity in the regulation and standards setting arena.

Hovering around the debate are questions such as;

What happens to tissue cells in the lung when they are exposed to crystalline silica?

How much silica in the atmosphere actually ends up in the inner most recesses of the lung?

To what extent does the chemistry particle size and surface properties of different respirable crystalline silica affect their toxicity?

By definition, the answers to such questions will give us a better understanding of relative risk and therefore enable us to focus attention where it is needed most and not waste money and time in relatively risk free environments. It is to those issues that the Siliceram project turned its attention.

The project itself owes its existence to the European Commission without whose funding and support the project would never have got off the ground, but fundamental to the project has been the considerable effort and hard work of a range of stakeholders ranging from laboratories through to representatives from ceramic associations across the European Community.

The real meat of the project centred on the following actions:-

- The collection of dust samples taken from each of the principle ceramic sectors, i.e. brick manufacture, wall tiles, tableware and refractories and sanitary ware.

- The examination of these particles through x-ray to determine the extent to which their surface chemistry size and surface properties have a bearing on their toxicity.

- The conducting of laboratory (In-vitro) and animal (in-vivo) experiments to compare the effect of the various factory dust samples containing silica on tissue.

- The comparison of these results against control samples.

- The provision of measured data showing the Particle Size Distribution of quartz present in factory samples. This is important data since the likelihood of particles reaching the inner lung is size dependent.

The project involves a good deal more that this though. Inherent within the project are other priorities. These priorities are all about making sure that whatever lessons are learnt are put to maximum use in the interests of advancing the safety of all whose work involves exposure to respirable crystalline silica in the ceramic industry.

What this means in reality is;

1. Development of a first rate training resource to enhance the industries knowledge of the risks of exposure and the most effective means of controlling the risk.

2. Design of a comprehensive programme to share (disseminate) the findings with all interested parties, be they regulators, the scientific community, industry representatives and so.

Clearly in order to achieve such ambitious and challenging objectives the work has needed to be undertaken on a determined and systematic basis with all stakeholders being prepared to take responsibility and to this end the work has been split into a range of work packages (WPs); these are:

WP1. Determination of base line ‘’toxic’’ silica
WP2. Development of sampling apparatus
WP3. Collection and analysis of respirable crystalline silica samples.
WP4. The testing of RCS samples on animal tissue.
WP5. SME factory monitoring and training on abatement technologies
WP6. The sharing of the findings (dissemination)
WP7. Project management

What follows is a summary of the work of each work package, the lessons learnt at each stage and what implications the findings hold for the future of the industry across the European community in its continuous quest for improvement in the health of the industry’s employees.

WP1: Determination of base line “toxic” silica

As has already been stated one of the main purposes of the Siliceram Project was to conduct laboratory (in-vitro) and animal (in-vivo) experiments in order to compare the effect of various factory dust samples containing silica on cell tissue. In order for these experiments to yield any meaningful findings it was necessary to compare the findings relating to the factory dusts against various “controls”.

The purpose therefore of the work of WP 1 was to identify the most appropriate "controls". In undertaking this task WP1 set out to select (1) a highly toxic silica representing a "positive" control (2) a totally benign dust representing a negative control and finally (3) a contrived dust comprising various ingredients.

In addition the other principal objective was to select the most appropriate in-vitro tests for the project.

Results

1. DQ12 was selcted as the most appropriate positive control. DQ12 is pure quartz and is manufactured specifically for experimental purposes because it is highly toxic due to its constant biological activity which does not diminish overtime.

2. Fumed aluminium oxide was identified as the best negative control for all in-vitro assays. However for the in-vivo studies a modification of titanium dioxide ($Ti0_2$) was considered the most appropriate negative control because, like DQ12, $Ti0_2$ is the favoured negative control dust for in-vivo testing.

3. In addition to these lower and upper control materials a contrived sample was developed. Although the contrived sample does not actually exist in the work environment it did represent a useful control since it mimicked as far as is possible the kind of dusts one would expect to find in the workplace where typically any silica present is combined with a whole range of other dusts. The composition of the contrived sample was 30% quartz (DQ12), 20% feldspa and 50% china clay.

4. Several different in-vitro assays were selected each of which would inform the project of the differing effect each might have on cell tissue and their usefulness in differentiaiting between different dust samples, see Table 1.

Table 1: Final pattern of the assays used for *in vitro* screening

Assays used for *in vitro* screening of RCS-containing ceramic dusts
Comet-Assay - DNA damage test
Lactate dehydrogenase (LDH) – Enzyme liberation test
Prostaglandin E_2 (PGE_2) release – Prostaglandin liberation test
TNF-α mRNA expression by RT-PCR – cell inflamation test
MTT-Assay – cytotoxicity (cell killing) test

WP2: Development of high volume sampling apparatus, definition of sampling protocol

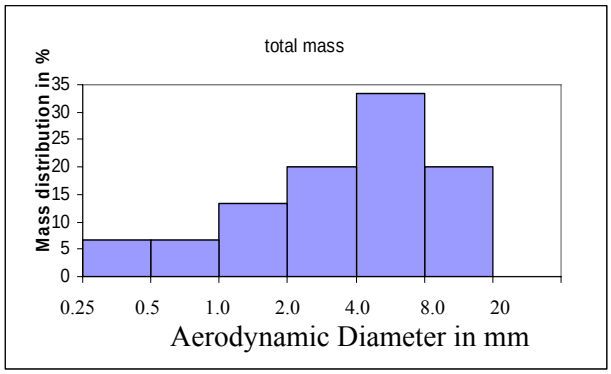
The main objectives of WP2 were:
- To design and manufacture a high-volume sampling apparatus.
- To optimise the current WRAS sampler.

Two High Volume Samplers (HVS) were designed on a cyclone based size-selective inlet with an aerodynamic diameter cut off of 4µm . The unique features of the high volume

samplers relates to the very low sensitivity of the cut off device to the flow rate with a relatively high sampling flow rate (~1,000 l/m) which had not been achieved before.

In addition three WRAS (Wide Range Aerosol Samplers) were delivered. The basic WRAS sampler developed earlier by Middlesex University had been modified to meet the requirements of the project. These modifications included the fitting of a new isokinetic inlet, the purpose of which was to reduce the loss of particles in the inlet.

The WRAS sampler was used on all SME factories for factory sampling and was vital for the collection of sufficient quantities of dust to allow the analysis of particle size distributuion (see graph below which shows how much of the total sample (%) was within a given size range)



Conclusions

The High Volume sampler has proved a very effective machine for collecting samples for toxicolgy testing. The WRAS has proved capable for collecting respirable fractions over a wide range of particle sizes.

WP3: Collection and surface analysis of RCS samples

The work of WP3 involved the collection of dust samples from each of the SMEs using the High Volume Sampler. Each RTD performer was responsible for testing on a selected factory from a different ceramic sector and samples were taken from a comination of the following process areas:

High Volume Sampler (HVS)

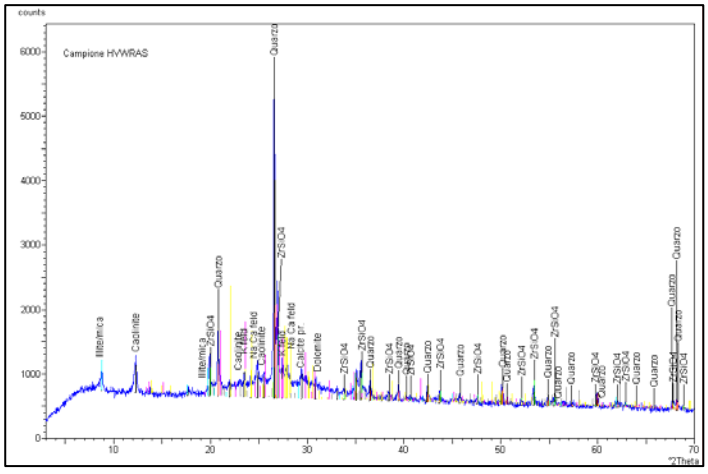
- Raw material processing
- Ceramic body mixing
- Forming/Making/Pressing
- Glazing/Cutting/Kiln Placing etc

The chosen areas were identified in order to ensure the collection of a sufficient quantity of dust. RTD performers carried out testing in the following ceramic sectors:

- Tableware (Granulate)
- Bricks
- Tiles
- Tableware (Slip Cast)
- Refractories

The collected samples were used for both surface analysis and toxicology studies. Surface analysis was carried out in each of the RTD performer's laboratories using X Ray Diffraction and Scanning Electron Microscopey/energy dispersive analysis SEM/EDA).

The respirable crystalline silica content (RCS) of the collected sample was determined by X Ray Diffraction (XRD)



XRD graph of a factory powder collected by HVS

The Quartz % of RCS for the five factory dusts are detailed in the table below.

	Brick	Tile	Tableware (Granulate)	Refractory	Tableware (Slip Cast)
RCS by XRD	7.8	8.1	5.8	3.7	3.1

The surface analysis was carried out by energy-dispersive X-ray microanalysis (EDA). 25 random samples were taken and the mean analysis determined.

An average of all the EDA results per sample was taken. The results can be found in the table below:

	Brick	Tile	Tableware (Granulate)	Refractory	Tableware (Slip Cast)
Al_2O_3	20.76	22.23	26.95	15.10	20.4
SiO_2	65.65	57.58	69.55	34.59	64.0

It was noticed that there was a big variation in both the SiO_2 and Al_2O_3 content of the samples, it was also noted that the RCS measured by XRD is considerably lower in all cases than the SiO_2 content measured in the dust samples by EDA.

The multiple-voltage scanning electron microscopy-energy dispersive X-ray spectroscopy allows us to undertake the following:

Scanning at 20 keV the X-rays excite to a few micrometer depth in mineral particles enabling us to indentify'bulk' silica particles whereas scanning at 8 keV the X-ray excitation depth drops to near 0.1 micrometer and so only identifies 'surface' composition. The brick, tile, refractory and tableware (granulate) samples were retested at both of these voltages, with the following results:

Sector	keV	Al_2O_3	SiO_2
Tile	20	22.2	57.6
	8	23.0	55.9
Tableware (Granulate)	20	1.7	98.0
	8	5.4	94.3
Refractory	20	21.3	51.8
	8	18.1	39.6
Brick	20	14.3	71.4
	8	16.4	72.0

The tile, refractory and tableware (granulate) samples performed in accordance with the hypothesis i.e. lower silica levels for the surface measurements, whereas the brick sample performed differently. The hypothesis put forward for this result is that the brick sample is a mixture of three clays hence no quartz is added as a separate entity unlike the tile, refractory and tableware (granulate) samples therefore scanning at different voltages will not differentiate between bulk and surface compositions.

WP4: In-vitro and in-vivo testing of RCS samples

Some exposures to crystalline silica have long been known to cause silicosis and other inflammatory diseases but attention to the pathogenic nature of silica was increased when the International Agency for Cancer Research (IARC) classified some occupational exposures to silica as being carcinogenic. The IARC stressed that not all exposures were active and that the toxicity of silica is very variable. In the same volume of the IARC monograph series coal dusts containing about 20% crystalline silica were not found to be active. Silica is used in many forms in the ceramic industry and there are many different exposures. This part of the Siliceram project sought to examine the biological activities of various dusts in several tests for toxicity primarily in cells in culture and secondly using a smaller range of dusts in whole animals.

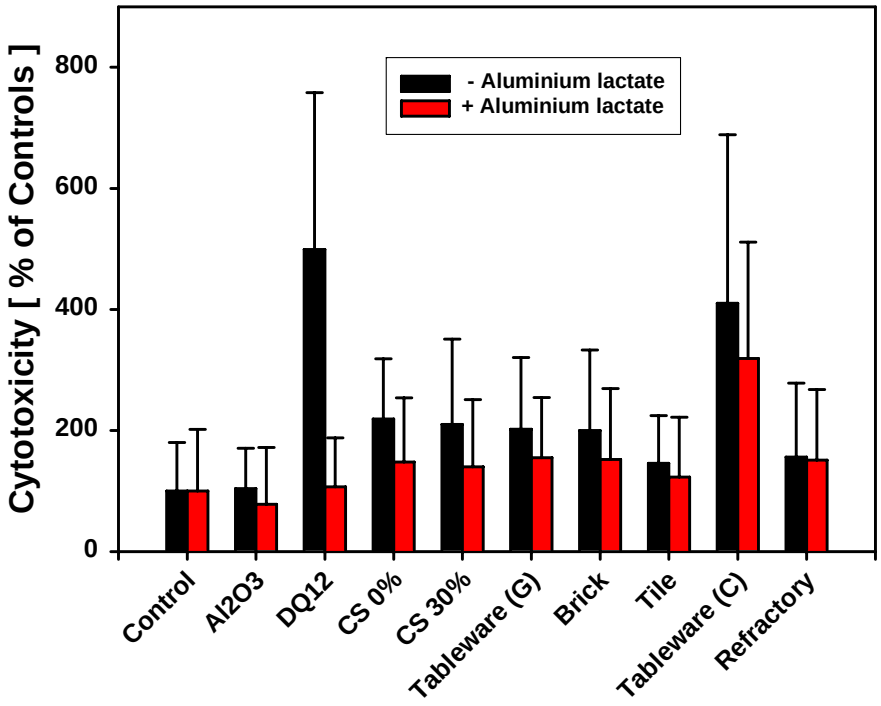
There is ample evidence, and a general agreement, that the first and, probably the key target for crystalline silica is the population of macrophages “patrolling” the non-ciliated alveolar regions of the lungs. The normal role of these cells is to engulf particles deposited in these regions and clear them mostly by being swept up the larger airways and then swallowed. Less important routes for clearance are through the lung lymphatic drainage or into the pleural spaces through pores on the surface of the lung. Crystalline silica is especially toxic to macrophages while having relatively less effect on other cell types. By poisoning the mechanism that should clear dusts and microbes, silica can itself accumulate in the lung, enhance the retention of other dusts and prevent some of the mechanisms which normally destroy invading micro organisms.

<u>The Siliceram project</u>
In this work a number of dusts were tested for their toxicity to primary macrophages or immortalised macrophage-like cells in 5 different assays at two centres. These tests can be regarded as forming a series capable of detecting different stages in a cascade of toxic events. The first effects are the production of a number of inflammatory mediators or cytokines this is perhaps a normal response of these cells to phagocytosis. In this project these effects are represented by the release of a prostaglandin (PGE2-Liberation) and the production of messenger RNA for TNF-α. When the cells are moderately damaged their energy metabolism is inhibited and this was monitored using the production of a formazan from a tetrazolium salt by metabolic reduction. In this work the MTT assay was used and the effects studied at two time points 2 and 24h. When the macrophages are severely damaged, or even burst, then components of the cytoplasm can be released and in this study this was monitored by the release of the enzyme lactic dehydrogenase (LDH). A further test, the comet assay, stands somewhat outside this cascade of events. This assay involved the exposure of the cells to dusts and then their concentration and re-suspension in an alkaline sol/gel followed by the separation of released DNA by electrophoresis. The DNA was then visualized by staining and imaging the released DNA “Comets”. Each comet originated from individual cells and crudely the more DNA damage then the bigger the stained area.

In this assay DNA damage can occur during the initial period of incubation of the cell/dust mixture. Alternatively when this mixture is concentrated into a pellet the cells are exposed to a much higher concentration of dust. Nuclei could be released and DNA damage occur in the cell dust concentrate. Finally damage could even occur once the DNA is released into the gel prior to and during electrophoresis. These problems would not be possible with the more usual soluble genotoxic agents as when the cells are sedimented the concentrations of toxin to which the cells are exposed reduces dramatically, with dusts it increases as both dust and cells are pelleted. These effects may have been responsible for the early finding that a sample of titanium dioxide, previously used as a negative control, was positive in this test. A sample of alumina was substituted as the negative control; however the titanium dioxide was the negative control in the animal test where the response was, as expected, minimal. However this test holds a great potential for identifying possible catalytic damage to DNA caused even by dusts previously thought to lack such activity.

There are several components in the dusts that could be toxic to cultured cells, which are very sensitive, and some that might even express effects in animals. These range from the lead compounds seen in the tile dusts to low toxicity materials affecting cells or animals due to the bolus added to tissue cultures or instilled into animal lungs. In order to detect specific effects due to silica we used a relatively novel approach comparing toxic activities in both the presence and absence of aluminium lactate. The concentration of this aluminum salt used was sufficient to inhibit silica toxicity but have relatively little effect on other toxicities. The use of this method was amply supported by the results with the control and “contrived” dusts. These were made from mixtures of kaolin and feldspar with added silica. At the outset the workplace dusts were thought likely to contain about 30% crystalline silica as this was the stated compositions of the materials being used at the sampling sites. The exception to this being in the brickworks studies where the raw materials relay on silica in the clay used and is not added as a separate material. . However when the crystalline silica content of the dust was measured all the samples contained only between 3 and 9%.

In the in vitro studies there are no effects, which can definitely be attributed to the silica in the dusts collected at ceramic works. Interestingly the 30% contrived sample, despite the silica content being much higher, often had similar or less silica activity than the workplace dusts. See figure below.



The samples were usually studied without sterilization; the microbial contamination the effect of heating the samples was investigated. There was a general reduction in activity on heat treatment. This is particularly interesting as it also happened with the standard silica (DQ12) this sample has little viable microbial contamination and it is not thought to be due to endotoxin that would be detected by the limulus amoebocyte lysate test. . Normal culture media only detect a minority of bacteria and many bacteria have never been cultured and the endotoxin detection systems are even more specific. So that not detecting contamination does not mean it is not present. It is primarily the supposed carcinogenic activity of this DQ12 sample of silica that is responsible for the IARC view that quartz is an animal carcinogen. It would be remarkable if the activities believed to be due to silica were instead due to some heat labile contaminant. A brief survey of the literature shows that some studies have used sterilized dusts and others non-heated samples relying on antibiotics in their culture media.

Animal studies (in-vivo)

Two samples of dust from the tableware industries were selected for study in animals, the two samples having displayed relatively different levels of overall toxicity in the in-vitro tests. Samples were instilled into the lungs of rats as suspensions. In these experiments the doses administered were matched for their silica content.

Again neither of the tableware dusts were very toxic but did produce statistically significant effects which did not progress with time, unlike those with the pure silica positive control. Again the activity of the silica in the contrived sample was significantly reduced. If the results using the various endpoints are ranked in this study, there was fairly good agreement. The tableware dusts being more active than the contrived samples and with the pure silica highest of all. However, the aluminium lactate method was not suitable for use in whole animals so that any effects seen could be due to silica or to other components of the dust.

In summary:-

For the cell studies *(in vitro)*:-

- The doses and/or the activities of the silica in workplace dusts were too low to reveal sufficient heterogeneity for any meaningful ranking of response.

- Inhibition of silica toxicity with aluminium lactate enables the quantification of silica toxicity in mixed dusts which also express other toxic effects. This is a method which should be used in a wider range of silica exposures where perhaps there is more risk of silicosis than the small risk in the ceramic industry.

In the animal studies *(in vivo)*:-

- All the dusts tested produced some, probably non-specific, inflammatory effects.

- The two tableware samples were much less active than the standard silica even though the doses of silica were similar.

- The effects produced did not become more severe with time progress unlike those due to the standard DQ12 silica. Perhaps the less active dusts could be cleared while DQ12 had damaged the macrophage clearance and remained in the lung causing further damage.

- There was considerable, but not complete, agreement between the activities of the dusts whatever the endpoint studied.

Relevant to both types of test:

- A contrived sample containing 30% of DQ12 crystalline silica in a mixture of kaolin and feldspar was less active than predicted by the content of silica; that is the mixture inactivated the toxicity of the silica contained. This low toxicity of silica mixed with the other ingredients of typical ceramic bodies is consistent with many previous observations. These include the fact that the clay mineral content of coal mine dusts is inversely related to the risk of silicosis and that the risk of silicosis in the ceramic industries is low and the dose response shallower than for many other silica exposures.

- Heating reduced the toxicity of both the workplace samples and the standard silica; a phenomenon that requires further study.

There are many other results that will be useful in planning further studies and all the results are reported fully in the body of this report. Further detailed statistical analysis will be undertaken before submitting these results for publication.

WP5: SME factory monitoring / Training on abatement technologies
The WP5 activities, were organised in three tasks as detailed below:

Task 5.1: SMEs factory exposure monitoring
The purpose of this work package was to collect dust samples from the various SMEs and in order to ensure a full range of results were collected dust samples were taken from all participating SMEs using both MDHS 14/3 method (or equivalent one) and the optimised WRAS sampler.

The factories monitored belonged to five different ceramic industry sectors: tiles, tableware, sanitaryware, refractory, bricks and roofing tiles. 255 personal sampling measurements (RCS) were carried out, together with 44 static sampling measurements (total/resp. dust) and 53 WRAS measurements.

The results were evaluated by process, i.e. raw materials, handling and preparation, "dry" shaping, "wet" shaping, glazing, firing, sorting-packaging-storage, maintenance. Regardless of the factory area sampled, plots of mg/m^3 airborne crystalline silica versus sample number show a characteristic plot (Figure 1).

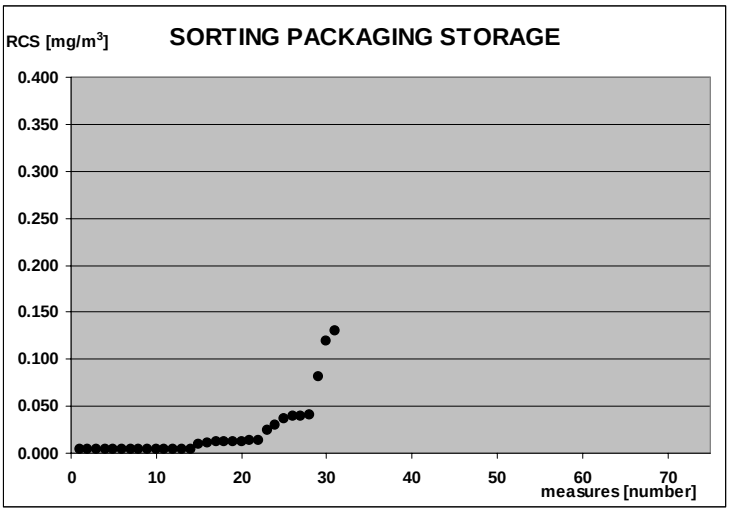


Figure 1: Results of samplings carried out in the same department of different factories

Most values are very low which indicates good control standards although these are only "one off" samples and the industry does monitor on a regular basis and only by doing this can a fuller picture emerge.

Ancon reviewed the factory sampling data and predicted the deposition of various samples in the respiratory tract with the folllowing conclusions:

Respiratory system provides the main pathway for airborne particulate matter to enter body compartments. Quantification and management of the health risks are important issues that the ceramic industry faces. From a dosimetric viewpoint, the size is crucial. For example, consider the distinction between inhaled aerosols with a median diameter of 0.3 μm versus one of 3 μm. Particle size affects the site and amount of particle deposition as well as subsequent clearance. The total deposition of 3 μm particles is 7 times greater than predicted for 0.3 μm particles, ICRP (1994). Moreover, the site of deposition in the lung is also affected

by particle size. Therefore, for the same mass of these aerosols in the air the mass of deposited particles into respiratory system is quite different.

Particles in the air are characterised by size distribution functions, for instance number particle size distributions, surface area size distributions and particle mass size distributions. Often size distributions are very complicated. There are observations of bi-modal and three-modal particle size distributions, e.g. Whitby (1978). Particle size distributions of airborne silica are influenced by the sources and sinks of aerosol particles at a factory, the history of the air mass as well as the meteorological and local conditions. Thus, distributions are different in different environment and subject to temporal and spatial variations.

Deposition of silica particles in the human respiratory system is a complex phenomenon that involves many physical and chemical processes including diffusion as well as interception and influenced by inertial properties of particles. All these processes depend upon the particle size. Exposure to the air containing particulate matter leads to deposition of airborne material in the lung.

The average deposition efficiency of respirable quartz particles is considerably lower than 100%; it ranges from 53% to 70% (based on sampling carried out during the project). Dose evaluation based upon the total MDHS 14/3 occupational hygiene samplers overestimates the health risk by factor of 1.4 to 2. Therefore it is logical to assume that to obtain correct health risk evaluation size-resolved sampling is required using modern fractionating technologies like the WRAS sampling technology used during this project.

Task 5.2: Training on abatement techniques

The factory sampling results were then discussed between each SME and the RTD on a country by country basis in order to ensure that all affected employees became better acquainted with the health effects related to processing of materials containing respirable crystalline silica. In addition it was also decided to prepare a comprehensive training course.

The course is intended to satisfy the needs of employees and organisations having different priorities. Whilst this material was being prepared, the European Social Partners Agreement on crystalline silica was signed. In the light of this it was decided that the Siliceram training course material should take into account, as much as possible, the contents of the “Good Practice Guide on Workers Health Protection through the Good Handling and Use of Crystalline Silica and Products Containing it”.

Task 5.3: SMEs factory monitoring retesting

Most companies, in which some measures exceeded the recommended values, planned to introduce some modifications in their processes (mainly abatement techniques), however many were not in a position to complete the introduction of these modifications during the project.

WP6: Dissemination activities, Exploitation

Dissemination

Several methods have and will be used to ensure an efficient and complete dissemination of the objectives and results of the SILICERAM project. The full results will be disseminated to a selection of target audiences, i.e. the Industry, legislators, the scientific community and other silica using industries.

Many methods have been used to exploit the largest range of dissemination tools, such as:

- Distribution of brochure outlining SILICERAM project / objectives
- Oral presentations and press releases
- Organization of local events/open workshops
- Conference communications, posters
- Scientific publications and revues
- Updates at RTDs technical meetings
- Newsletters, web sites

See list of dissemination items at the end of the report.

One of the most efficient tools is the SILICERAM Newsletter, written and distributed during the whole project's duration.

The Newsletters were formatted in A4 standard, and released in .pdf format to be distributed by electronic means: E-mailing, web sites. They were translated and distributed by IAG/RTD in each partner's language.

Many other dissemination vectors have been used to ensure the dissemination process:
The Technical Committees organized and managed by each RTDs with direct participation of the country SMES were used to perform dedicated presentations of SILICERAM updates at these sectorial assemblies. And these actions were performed at different level for SMEs, at the operational level (company personnel) and at the management level (company directors).

Concerning the web publications , the consortium choose to use the existing RTD, IAG web-sites, instead of a unique web-site dedicated to the project : this was to ensure a more powerful tool, which updating would be more efficient to disseminate the SILICERAM information releases.

Other vectors have been successfully used in the process of dissemination, mainly with the student courses performed by RTDs and the ceramic connected network events which the RTDs are involved.

After the project, a good deal of further dissemination has been planned which includes the presentation of papers at international conferences, the writing of an executive summary and a range of different articles in a variety of different journals to ensure maximum coverage. The consortium anticipates that this process will continue for some years.

Exploitation

Exploitation means taking the project outcomes and putting them to the maximum benefit of all stakeholders towards improvement in regulation and health in the workplace.

Knowledge arising from work carried out under the project is the joint property of the IAGs who have met on a number of occasions in order to agree their strategy on exploitation. This strategy is outlined below.

The Siliceram Project required the use of hardware equipment, some of which was developed specifically for the project.

The four pieces of hardware used during the Siliceram Project were;

a) Wide Ranging Aersol Sampler x 2
b) High Volume Sampler x 2

At the end of the Project the IAGs will retain ownership and will make the equipment freely available to all IAGs and SMEs provided that they undertake to service and re-calibrate the equipment.

The IAGs will also make the equipment freely available to any follow up Siliceram Project provided they are satisfied that the intentions are, in the opinion of the IAGs, consistent with the ongoing development of sound research and improvements in health and safety.

With regard to the ultimate results of the project the IAGS have clear priorities.

1 Improvements in health of employees in the Ceramics Industry. In terms of the knowledge gained from the project which relates to improvements in health and safety the IAGs agree to, independently, train SMEs in the appropriate findings.
2 Dependent upon the results the IAGs undertake to communicate with the regulatory authorities in member states and at Commission level with a view to improving the regulatory framework. In these endeavours ongoing collaborative effort is almost inevitable.

WP7: Management

The work package included the carrying out the technical, administrative, financial and strategic coordination of the project and the animation of the consortium:

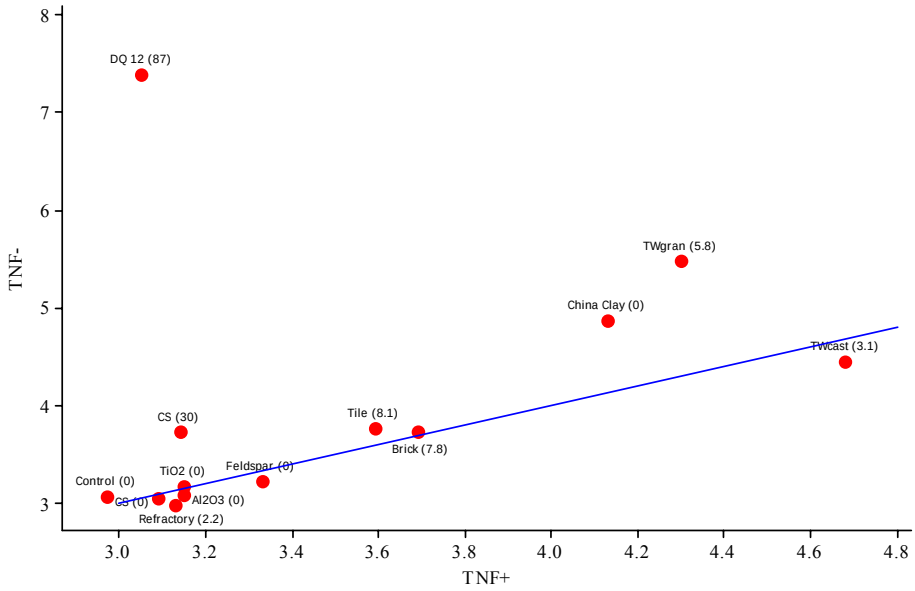
- Building up the SILICERAM communication platform "PRODIGE" with administrative, financial, technical, communication and archive sections,
- Producing and updating the Project Quality Assurance Plan detailing, for example, practices and advancements of the project
- Collection and submission of activity, management and financial reports on due dates,
- Organisation of the periodic project meetings,
- Creation of the project logo as well as a brochure for external diffusion,
- Management of contract and Consortium Agreement amendments, …

The completion of the management tasks in WP7 strongly depended on the efficiency and reactivity of the consortium and also a good communication between partners. A well-scheduled and quality methods according to standard and efficient procedures and followed by all partners, made easier the full accomplishment of these activities.

End results achieved and perspectives

It is considered by all the partners that the project has been succesful and has a number of positive conclusions.

- The project has identified potential and practical ways to render RCS safer. When silica is mixed with aluminium oxide i.e. clays. Some respirable silica particles in some mixed dusts are surface-occluded by adherent alumino-silicate surface coatings, while adherent, these coatings modify (diminish) the biological availability of the crystalline silica particle surface and so modify fibrogenic activity.
- We have shown that we can detect silica activity in mixed dusts and developed a useful battery of tests.
- We have shown that we can collect enough workplace dust to use in experiments.
- The *in-vivo* and *in-vitro* tests have provided reassurance that there is little serious silica-like activity in the factory dusts and that whatever toxicity exists occurs due to factors other than crystalline silica. It is therefore questionable whether targeting crystalline silica in itself actually addresses the issue to hand.
- The project has proved that it is possible to test for silicosis risk – using biological and crystallographic methods - needed in other industries using silica as a raw material e.g. the construction industry and quarrying industries.
- Of particular value was the findings of statistical analysis carried out by Middlesex University, an example of which is shown below. In this example the y-axis represents the original assay, the x-axis the aluminium lactate addition.



This method of showing the data provides an opportunity to see overall toxicity and implied toxicity from RCS for each sample tested. If the test without aluminium lactate and with aluminium lactate gives the same result, then the implied toxicity of RCS in the sample is zero. This theoretical relationship is indicated by the blue line on the figure which is a line of gradient one and intercept zero and has been labelled the "line of zero effect" from RCS.

Put simply, if RCS provided zero contribution to the overall toxicity of the sample then all points should lie on, or be very close to the blue line. Thus, any sample points lying above and to the left of the line exhibit toxicities which have contributions from RCS. The further the points lie from the line, the greater is the RCS-related toxicity in the sample.

All the analyses implied that there was very little RCS related toxicity for all the dust samples tested.

2. Dissemination and use

The below tables give some details on the already publishable results and non-confidential knowledge like publications available from the project. For any inquiries (like for publications), please contact:

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Ceram Research Limited (UK)

2.1. Main publishable results identified and their status

Result no	Description of knowledge
R1.1	**Determination of base line "toxic" silica** - Identification of crystalline silica that is considered "toxic". - Identification of a negative reference control - Definition of contrived RCS samples and individual ceramic body ingredients - Preparation of reference materials with a composition similar to RCS's in the ceramic industry/ characterisation of the reference materials and their ingredients - Optimisation of in-vitro assay conditions with the chosen reference materials
R2.1	**3 Optimised Wide Range Aerosol Sampler (WRAS) samplers and protocol**
R2.2	**2 High Volume (HV) samplers and protocol**
R3.1	**RCS samples from 5 ceramic sector** - Contrived quartz samples (protocol for making samples)
R3.2	**In-vitro and in-vivo testing of RCS samples** - Toxicology information for mixed dust samples - Toxic effects ranking induced by these samples - Identification of samples representative for a work process/factory - Trends and correlations (if existing) between surface chemistry (R3.2) - In-vivo analyses of inflammatory and genotoxic endpoints; comparison of effects to those of a mimicked 'RCS'
R4.1	**In-vitro and in-vivo testing of RCS samples** - Toxicology information for mixed dust samples - Toxic effects ranking induced by these samples - Identification of samples representative for a work process/factory - Trends and correlations (if existing) between surface chemistry (R3.2) - In-vivo analyses of inflammatory and genotoxic endpoints; comparison of effects to those of a mimicked 'RCS'
R5.1	**RCS sampling measurements and workers information on correct RCS handling procedures** - Results of the RCS sampling measurements carried out during factory monitoring - Better understanding of different risks, depending on production process/process step, worst process step - Evaluation, together with SMEs technicians, of new abatement apparatus or new procedure to reduce the dust level of the factory
R5.2	**Training workshops materials (copyright)** Educational material to be used in a short course of 5 one-day modules: 1. Dusts and sampling 2. Factory sampling

Result no	Description of knowledge
	3. Laboratory techniques 4. The ceramic process and production processes of ceramics 5. Abatement techniques

2.2. Main publications

Result no (if applicable)	Partner responsible /involved	Type of dissemination means	Relevant details: Title/Subject/Reference/Place	Actual/planned date or status
-	SFC/BCC	SILICERAM Newsletter	2 Newsletters released in English, German, French and Portuguese	December 2006 July 2007
-	ITC	Presentation of project, press release	Cerámica Información nº 316 marzo 2005	March 2005
-	CCB	Oral presentation of project, Conference	Il progetto SILICERAM: una ricerca collettiva nell'ambito del VI Programma Quadro, Ceramica e Ambiente, Bologna, Italy	15-17/6/2005
-	CERAM	Poster presentation of project, Conference	IX Conference & Exhibition of the European Ceramic Society (ECERS), Portorož, Slovenia, http://www.ecers2005portoroz.com/	19-23/6/2005
-	PROCEMA	Poster presentation of project, Conference	The 4th National Conference "New Research Trends in Materials Science" ARM - 4 2005, Constanta, Romania http://www.icpe-ca.ro/fp6/conferences/arm/index.htm	4-6/9/2005
R1.1	UHP	Poster presentation, Conference	"Evaluation of the cytotoxicity of silica samples using a co-culture of macrophages and transgenic fibroblasts", Congrès Annuel de la SFT 2005 "Allergies et Toxiques", Brest, France, http://www.sftox.com/	13-14/10/2005
-	ZIEGEL	Oral presentation of project, Press release	"Respirable crystalline silica – labelling in compliance with Germany's Equipment and Product Safety Act, Ziegelindustrie International (ZI) Vol3/2006	Nov. 2005, Feb. 2006
-	CERAM	General information about Siliceram topics	Input on R&D topics in fields of nano(eco)toxicology for preparation in FP7 to implement the action plan at: (http://www.cordis.lu/nanotechnology/actionplan.htm)	Submitted in Jan 2006
-	ITC	Presentation of project: newsletter	Cevisama Fair 2006, Valencia, Spain, http://cevisama.feriavalencia.com/	7-11/2/2006
-	ITC	Presentation of project: newsletter	Qualicer'06, Castellon, Spain, http://www.qualicer.org	12-15/2/2006

-	CERAM	General information about Siliceram topics	CERAMITEC 2006, Munich, Germany, www.ceramitec.de	16-19/5/2006
R1.1, R4.1	ITEM, CERAM, Toxservices	Poster/oral presentation, Conference	"The Comet Assay *in vitro* with Alveolar Macrophages: a Suitable Tool for Genotoxicity testing of Quartz-Containing Ceramic Dusts", INIS 10th InterNational Inhalation Symposium: Airborne particulate matter: Relevance of particle components and size for health effects and risk assessment, Hannover, Germany, http://www.inis-symposium.com/	31/5-3/6/2006
R2.1-2.2	CERAM, ANCON	Oral presentation of project, Conference, publication	"Sampling Techniques for Airborne Crystalline Silica"-J.7, 11th International Conferences on Modern Materials and Technologies (CIMTEC 2006), Acireale, Sicily, Italy, http://www.cimtec-congress.org/, publication in "Industrial Ceramics"	4-9/6/2006
-	APICER	Oral presentation and Press release	"Respirable Crystalline Silica", "Kéramica", nº279, 50-54.	July-August 2006
R1.1, R4.1	ITEM, CERAM, Toxservices	Poster/oral presentation, Conference, Publication	"The alkaline Comet Assay *in vitro* with primary rat alveolar macrophages: a suitable tool for genotoxicity testing of quartz-containing ceramic dusts", EUROTOX 2006/6 CTDC - 43rd Congress of The European Societies of Toxicology and 6th Congress of Toxicology in Developing Countries, Dubrovnik, Croatia, www.spektar-putovanja.hr/spektar/eurotox2006/ Toxicology letters 164 (2006), Suppl.1, pp.290	20-24/9/2006
R1.1	UHP, CERAM, Toxservices, ITEM	Poster presentation, Conference	"Cytotoxicity and TNFalfa expression evaluations for silica containing dusts", Congrès Annuel de la SFT 2006, Paris, France, http://www.sftox.com/	23-24/10/2006
-	ITC, ASCER, Hispalyt	Poster presentation: General information about Siliceram topics, Conference	« Initiatives for preventing exposure to respiraple crystalline silica in the ceramic industries », II Congreso Europeo de Seguridad y Salud en el Trabajo http://www.congresoseguridadysalud.com/	30/5-1/6/2007

-	ITC, ASCER, Hispalyt	Article	« La Problemática de la Exposición a Sílice Cristalina Respirable en las Industrias Cerámicas », Técnica Cerámica 354, 348-358 (2007)	2007
R1.1, R4.1	UHP, CERAM, ITEM	Poster presentation, Conference	"Internalization, cytotoxicity, apoptosis and TNF-a expression in rat alveolar macrophages exposed to silica containing dust", The 11th International Congress of Toxicology , Montréal, Canada, http://www.ict2007.org/)	15-19/72007
R3.2	ITC, CCB	Poster presentation	"XRD determination of respirable crystalline silica in environmental samples", QUALICER 2008 (Xth World Congress on ceramic tiles quality), Castellon, Spain, http://www.qualicer.org	10-13/2/2008
R1.1, R4.1	UHP, CERAM, Toxservices, ITEM	Publication	Internalization, cytotoxicity, apoptosis and tumor necrosis factor-□ expression in rat alveolar macrophages exposed to various dusts	End of 2007
R1.1, R4.1	UHP	PhD Thesis	Title to be determined	February 2008
R1.1, R4.1	UHP, CERAM, Toxservices, ITEM	Poster presentation, Conference	"Internalization, cytotoxicity, apoptosis and TNF-a expression in rat alveolar macrophages exposed to silica containing dust", 33ème Congrès Annuel de la SFT, Montpellier, France	25–26/10/2007
R1.1, R1.2, R4.1, R4.2	ITEM, Jackson, CERAM, TOXSERVICES	Poster/Oral presentation, Conference, Publication	In vivo study with quartz containing ceramic dust samples: Inflammatory effects of two factory samples in lungs after intratracheal instillation in a 28-day study with rats 47th Annual Meeting, Society of Toxicology, Seattle, Washington, USA, http://www.toxicology.org/ai/meet/conferences.asp Inhaled Particles X, Manchester, UK, http://www.hse.gov.uk/campaigns/conferences/ipx.htm	16-20/3/2008 23-25/9/2008
R1.1, R1.2, R4.1, R4.2	ITEM, CERAM, TOXSERVICES, UHP	Poster/Oral presentation, Conference, Publication	In vitro study with quartz containing ceramic dusts samples: Screening of the biological effects of five factory dusts using various cytotoxicity and genotoxicity assays Conferences idem above	Idem