

Safety In Mines Research Advisory Committee

Project Summary : SIM 030803 Phase 2

Project Title:	Validation of biomarkers for improved assessment of exposure and early effect from exposure to crystalline silica (1 volume, 45 pages)
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Report Date:	7 th March 2006	Related Projects:	Phases I and II of SIM 03-08-03 SIM
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Category:	Generic	Applied Research	Yes
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Summary

This is Phase II of a project to identify and operationalise biomarkers for silica dust exposure that can be used as very early (leading) indicators for silicosis in environmental surveillance. Phase I identified a short-list of 10 biomarkers worthy of further investigation from the published literature.

In this phase the aims were to identify which of the 10 biomarkers identified in Phase I showed raised or suppressed concentrations in the presence of silica dust exposure, irrespective of the presence of clinical silicosis, over and above any effects due to HIV infection smoking and age. In addition the study had the aim of developing the capacity to perform biomarker assays in South Africa.

The study involved the measurement of the 10 biomarker levels in four groups of volunteers who knew their HIV sero-status:

1. A group of 20 African male underground gold miners who were HIV sero-positive.
2. A group of 28 African male attendees at the HIV wellness clinic of the Johannesburg hospital who had never been exposed to occupational silica dust.
3. A group of 40 African male underground gold miners who were HIV sero-negative
4. A group of 32 African male blood donors who had never been exposed to silica dust

Groups 1 and 3 combined were also subdivided into those with and without silicosis.

Volunteers were asked about their age, work history, medication, and smoking history.

The following biomarkers were investigated: Chemiluminescence of isolated peripheral neutrophils exposed to silica, Red Cell Glutathione S Transferase (GST), Red Cell Glutathione (GSH), Red Cell

Derived Growth Factor (PDGF), Clara cell protein (16) (CC16) and Total Antioxidant Status as a trolox equivalent (TAS).

The results showed that there are three out of the 10 biomarkers that are significantly affected by exposure to silica dust, to an extent that would enable them to be used as biomarkers of silica dust exposure, independently of any effects due to HIV infection, ARV treatment, smoking, or age. Their levels were significantly suppressed, equally in those who were exposed and who did or did not have silicosis. These are GPX, n-8 isoprostane and CC16.

Analysis showed that if GPX is used as an indicator of silica dust exposure the area under the receiver operating characteristic curve (ROC curve) would be 0.89. The corresponding statistic for n-8 isoprostane was 0.73 and for CC16 it was 0.71.

It is recommended that Phase III of this project concentrates on these three biomarkers and addresses their operationalisation for field use. Phase IV should then study the biomarker levels prospectively alongside dust (dosimetry) and clinical (chest radiograph) measurements.