PROGRESS REPORT 6
Pooled Analysis of Three Case Control Studies

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Administration:
A face to face meeting with the Scientific Review Panel (SRP) took place in November. Their suggestions are being considered and acted upon as appropriate.
Every effort will be made to complete the project by the end of 2009. We will present a discussion of the exposure assessment rationalisation meeting at the "X2009" meeting in Boston in August and at the 2009 benzene symposium, in Munich in September 2009.
We have the following time lines with further details below:

Exposure Estimation	**Stage**
Job histories assembled, new sites characterised	Done
New refinery data identifed (%b in petrol)	Done
Review of previous work history/exposure assessment	Done
New job histories estimated where same as exisiting	Done
New exp assessment, novel job/site	Done
Certainty scores individual lines	Done
Certainty scores for whole work history	June
Peaks - absolute	Done
Comparison of WEs between studies	Done
Adjustment of study WE(s) where required	Done
Compare and re-adjust certainty scores as reqd	Done
Discussion with DV	June
Final adjusted WEs	June
Administration	
Final Approval to share from StatCan	Pending
Disease Classification	
Coded data from death cert/cancer registries assembled	Done
Underlying data from Cancer Registries	Done
Supplementary data from Hospitals where required	June
Scan last dx data for classification	June
Finalize dx assignment	July
Data Assembly	
Final list of variables to include	Done
Data cleaning/consistency checks	August
Data Analysis	September
Meeting @ Pitt	October

Report Writing December

Ethical reviews: Ethical approval is now available for AIP and IP for the study, including allowing sharing of data. The Canadian study is still not formally approved. It is now approved by the Statistics Canada policy committee and pathology reports from the provinces, as well as all data from the first update are also cleared to be shared. However, a few provinces still need to sign off on sharing cancer registry data. All appropriate forms have been sent to Statistics Canada who are liaising with the provinces, and the issue is in their hands. The data cannot be shared in a public forum until provincial approvals are obtained. We are hoping for these within a month.

Data handling:
AIP: Work histories have been checked and non-AIP company jobs have been removed, gaps in job histories have been checked.

IP: As part of the current contract it was agreed that documentation needed for construction of work histories should be extracted from microfilmed personnel records for the NHL and MM cases and their controls in addition to those of the leukaemia and other myelodysplasias. This work is almost complete. The construction of the work histories is, however, outside the current contract

IOL: EMBSI has processed the work histories.

All: A data set of all the original cases from each of the 3 studies has been sent to the University of Pittsburgh, in a unified form ready for analysis. A face to face meeting between the PIs and Gong Tang from University of Pittsburgh took place in New Jersey in February which was fruitful. Tang is now working through the preliminary data and setting up analysis programs so that when the final data are delivered, he will be in shape to analyze it. We have tentatively planned a further face to face meeting in mid October, although additional funds for travel for AIP and IP investigators may be necessary.

Exposure Assessment:
AIP: The agreed skin, peak and uncertainty scores were added for new and old cases. The external consultant has updated a spreadsheet listing the percentage of benzene in petrol and avgas by type and refinery by year. The % benzene in crude processed in Australia is being checked.

IP: The 2 week face to face meeting in November between Deborah Glass, Eileen Pearlman and Lesley Rushton in London completed the exposure assessment for the new cases and controls. In addition the new benzene peak definition was applied to the existing cases and controls.

IOL: Exposure assessment was completed for the new cases and controls. The agreed skin, peak and uncertainty scores were added for the new cases. The peak exposure metric was added for the old cases and controls.

The Retrospective Exposure Assessment Team (REAT) met face to face in New Jersey in February 2009 over a week. The meeting was very productive.
We agreed on the job groups and the definitions of who should be in each of the groups. We agreed on how the job groups should be amalgamated into categories for analyses. We agreed on the skin and peak scores to be associated with each job group.

We compared between studies, the means and range of the WEs grouped by job group and era. Some means were close but in other cases the process highlighted differences in exposure assessments. A number of changes were made to individual studies, to background and other BEs.
The uncertainty scores for each job line were compared by study and brought into line. A methodology for combining the job score into a career uncertainty score was discussed and is being developed.
The meeting was followed up with a teleconference at which the revisions were compared and agreed.
The exposure assessment rationalisation methods are being documented.

Case Diagnoses:
Pathology records are currently being requested for all new cases. The records of a sample of about 10 cases were examined in a web-based meeting in October to look at the data quality.

AIP: Some pathology records have been obtained from NSW, Queensland and SA. Pathology data is now available for 94 of 118 cases. We are still awaiting 5 requested pathology records from SA. We have completed ethics applications to receive data from the Death Registry in SA and Victoria but have not yet received the data. Victoria will not supply a copy of the death certificate but have agreed to send extracted data. Copies of the death certificates from the UK (1), WA (2), NSW (14) and Queensland (8), have been received. All available data has been scanned into a single pdf for each case.

IP: Some cases from the previous study have associated pathology records and all death certifcates are available. Death certificates have been collected for the new cases. A process is on-going to contact relevant hospitals to obtain pathology data for the new cases. Some information has been successfully obtained; for others it has been established that records have been destroyed; we are awaiting others or still pursuing hospital departments.

IOL: Statistics Canada are supplying the hospitals contacts for each case. They will also serve as a liaison with provincial authorities. Approximately 20 pathology reports have been obtained from Ontario, Saskatchewan, Manitoba, New Brunswick and Quebec. Records from BC, Alberta, and Nova Scotia have not been received. It is estimated that approximately one third of cases will have pathology reports. Death certificate literal information has also been obtained for all case deaths recorded in Statistics Canada records.

All: The search for pathology records has been in process for several months. We will continue to search for records until a firm date has been set for the disease classification and then set a cut off date.

Disease Classification Team
The team have completed a draft of how the data are to be classified but have not yet tested it. They have asked for a spreadsheet for each study listing fields in a consistent manner. The PI's have done this to a large degree. Scheduling for the team to get together to begin disease classification is in progress.
They have also prepared method to describe certainty of diagnosis.

Protocol:
The protocol is being expanded to clarify the exposure assessment methodology and the disease classification work as requested by the SRP. The revised protocol will circulated when complete.

Summary:

We anticipate to finish the project by December 2009. There are two issues that are causing concern:

1. Obtaining full permission from Statistics Canada to share the IOL data
2. The delay in starting the disease classification process

We are currently working to resolve these issues and do not expect them to prevent completion with the proposed timescales.