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Sent: Monday, August 22, 2005 3:36 PM (GMT)
To: benzconsort-tc@listserve.api.org
Cc: benzconsort-oc@listserve.api.org; benzconsort-cc@listserve.api.org
Subject: BHRC-TC... 3rd Mid-Year SHS Progress Report: Exposure Assessment
Attach: Fudan Progress Rpt 08 2005.pdf

BHRC Technical Committee (-TC)
With copy to Oversight, Technical Committees

Attached is a copy of the mid-year 2005 SHS Progress Report from Dr. Fu Hua (Fudan University). This is the final pending semi-annual report; those received from Drs. Irons (DP & ME Studies) and Wong (CC Study) were sent under separate cover last week.

Copies of all progress reports are also available on the SHS web site...

With best regards - Bruce.

PDF Attach.

SHS Semi-annual Report

July 14, 2005

By Fudan University School of Public Health

1. Summary

During the last 6 months, Questionnaire Takers interviewed 830 subjects for CC/DP Study, for an average of about 40 cases per week. The EA team visited 15 factories, gathered historical industry information and drafted a comprehensive benzene exposure historical summaries for shoe-making and textile printing industries; conducted site monitoring at 25 factories and collected 350 personal, area and bulk samples. Out of the total of 3775 Questionnaires collected so far, 3308 went through preliminary exposure assessment and the current “benzene exposed rate” remains around 7%. Due to the lack of availability and accessibility of complete historical IPHS information, Exposure assessment for the CC/DP study has shifted its focus from a case-to-case based study to sector analysis.

For the ME phase I study, medical records of 1600 cases were collected and entered into an Access database. Exposure Assessment, although slower than expected due to limited factory and information access, is progressing. So far, the EA team visited 11 factories for the ME Phase I, and additional 7 factories have exposure assessment site investigations pending.

No progress was made for ME phase II study because factory managers couldn't accept consent forms.

Issues, challenges and suggestions were summarized as follows:

- Evaluate second level questionnaires to make them more feasible and valuable
- Inadequate involvement of IPHS is still an obstacle against prompting the EA process. More efforts (resources) are needed from IPHS to speed up factory visit.
- Very limited access to IPHS database. Negotiation with CDC is necessary to get more data.
- Fudan investigators should be kept informed on the exposure assessment focus and strategy.
- More workers are needed for ME phase I study. But, it seems difficult to find information out of Shanghai.
- Factories couldn't accept ethical requirements of ME phase II study. A meeting is proposed to discuss factory enrollment in August. Senior occupational physicians and bioethical scientists should attend this meeting.

2. General Management

After dialog and interaction among the PIs of the study during the early part of the year, the Fudan EA team has worked on improving communications. Through weekly staff meetings and monthly reports to PIs, the Fudan team maintained communication with both the team members and the PIs overseas. These monthly reports not only captured progress made, but also communicated the technical questions raised by the EA team.

During this period, the team welcomed two new members who joined the team to fill in gaps left by a graduation and a pregnancy. With the project deadline approaches so far, we have not lost any team members. Keeping the team together in a cohesive and motivated unit is increasingly important as we get closer to the project completion.

The Fudan EA team also played a key role in interacting with IPHS. Fudan has initiated meetings with IPHS at least once a month to address issues related to data and factory access.

However, keeping EA team members of Fudan fully informed and transparent on a strategic basis of foreseeing EA approaches remains to be further prompted. In addition to the “personnel management”, more technical supports and team capacity building are preferably appreciated. Task should ideally assign through the group leader instead of delivering to individual team member directly.

3. Technical PROGRESS

3.1 CC and DP studies

3.1.1 Questionnaire administration

Up to June 25th, 2005, 3375 subjects have been interviewed; 1885 secondary questionnaires were applied. A total number of 850 subjects, including both case and controls, were interviewed in the last half year, and of these, 484 subjects had the secondary questionnaires applied.

Data collected from the Questionnaires was reviewed immediately after the collection and phone interviews were used as follow up to further clarify any questions that the QA coordinator may have. The first time pass rate is at around 89%.

3.1.2 Control selection

QA has worked closely with the hospital coordinators to ensure that control

selection adheres to the selection criteria, only 1.1% was found being selected from the same departments of the relevant hospitals; and 2 controls (0.4%) were repeatedly selected. All of these selected controls were excluded out; and the new controls were selected according to the selection criteria.

Control distribution: see the annexed table: distribution of inpatients in 68 hospitals (2002, Shanghai) vs. CC/DP controls.

3.1.3 Data entry and validation

In the last six months, data entry has kept with the pace of Questionnaires Administration, only one week lag behind the interview.. The data entry error rate remained at about 2%.

3.1.4 Exposure assessment

The EA team has taken on an active role to pursuing information related to the potential exposure scenarios. Main activities and accomplishment by the EA team include:

- Coded all cases and controls with industry coding developed during the third National Census Guideline.
- Completed preliminary assessments and make qualitative judgments of cases or controls that are exposed to benzene and other substances based on information on the Questionnaires.
- Gathered historical exposure data from IPHS or follow-up site investigations. During the last six months, the EA team visited 15 factories and collected personal, area and bulk samples.
- Completed summary reports and documented information collected for all cases and controls accumulated since last year.

Table 1 Current status of the case distribution in CC/DP Study.

Table 1 Summary of CC/DP exposure assessment (2003.5-2005.5)

Preliminary exposure assessment Completed to date	No. subjects that needs further follow-up by EAC	No. of subjects exposed to other substances	Interim benzene exposure rate (7%)	
			Benzene exposed	Benzene potentially exposed
3308	277	2631	112	121

During the last 6 months, 1228 subjects were assessed to clarify their potential exposures. 1130 of the 1228 subjects (92.02%) were identified as “non-exposed” or “exposed to other chemicals only except benzene”; 98

subjects (7.98%) were identified as “potentially benzene exposed” that were followed-up for further quantitative assessment. Of these, 52 subjects were accomplished for a qualitative EA; and 4 for the quantitative EA.

Although the estimated benzene exposure rate is at about 7%, the final assessment may be slightly lower. These “potentially benzene exposed” subjects are mainly from the following industries.

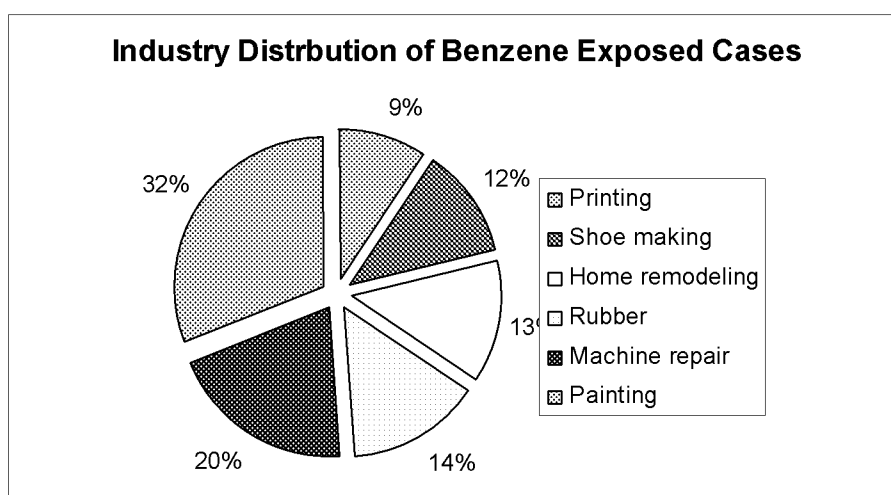


Figure 1. The distribution of Benzene exposed subjects by industry

During the last six months, the EA team has found that one-on-one matching of a subject’s working place based on IPHS database has proven to be far from fully effective. Only 3-5% factories of the subjects worked can be identified in the IPHS database, and the area samples taken often do not match the work area/task or time period the subject worked in that factory.

Therefore, the project is forced to further evaluate an alternative from the protocol for the retrospective Exposure Assessment strategy. A closer look at the IPHS database by industry, breaking down the database by the factors that contribute most to the exposure level – production scale and facility environment, time period, location and task could render some useful information, at least on the range of exposure level. Such information needs to be further verified through other information resources such as published literature, expert input and most important of all when possible, site investigations.

The access of the whole database has been withheld by IPHS and that has hindered the effort for sector analysis. Nevertheless, the Fudan EA team has been focusing on the following areas:

- Continued efforts to follow up on information regarding the exposure of each individual subjects
- Grouped all cases from the same industry together and analyze its commonalities and difference
- Sought information to better understand the industrial process and job/tasks that are related to benzene exposure and gather information that could contribute to the re-construction of historical exposure scenarios.
- Collected over 200 Chinese literature related to the benzene exposure
- Visit to factories and district IPHS, worked with people who directly conducted site monitoring, interviewed service personnel, and conducted current site exposure monitoring.

3.2 ME Study

3.2.1 ME phase I

3.2.1.1 Medical records collection

For 2221 cases, historical medical records from 25 factories were collected by the Yangpu Central Hospital. Historical IH background information and monitoring data were collected from three sources – factory records, IPHS database and/or occupational hospital records. As the critical regulatory requirements for record keeping did not effectively enforced until the passage of Occupational Disease Prevention and Control Act in 2001, often historical data were no longer available. Two factories with a total of 255 cases were disqualified due to inadequate supporting records.

3.2.1.2 Standardization and data entry

Before data entry, names of job titles of workers were standardized through factory managers, senior workers. Medical records from 15 of the 20 factories were double-entered per QA procedures, and validation is currently under way.

3.2.1.3 Exposure Assessment

Re-construction of historical exposure levels takes several steps and the only way to reconcile historical hematological data is through site investigations.

So far, 10 of the 18 factories were visited by the EA team, with a total of 250 exposure assessment samples taken at the sites.

Once the data are available, the EA team associates each of the worker's historical exposures to a job location/task through a coding system. So far, re-construction of historical exposure is completed for about 300 cases from 6

factories.

3.2.2 ME phase II

Although Fudan has been negotiating with factories, no worker has been successfully recruited for ME II study. A file has been submitted to Dr Irons to help him understand the critical problems of ME II study.

4. Issues, Challenges and suggestions

4.1 CC and DP studies

4.1.1 The second level questionnaires

FUSPH (Fudan School of Public Health) translated all the 63 types of occupations/jobs into Chinese. Although the second level questionnaires were used successfully in USA, the questionnaires often make both interviewer and interviewee confused and lost confidence in responding them. Very limited valuable information could be collected through 2nd questionnaire. Fewer questionnaires were used by EAC to support exposure assessment. Comments on 2nd questionnaires were collected from questionnaire administrators. The Fudan team would like to suggest that US experts evaluate current status of 2nd questionnaire usage and make them more feasible and more useful.

4.1.2 Inadequate involvement of IPHS

Inadequate involvement of IPHS is still an obstacle against prompting the EA process. It was agreed early this year that IPHS staff would participate weekly EAC meeting. However, IPHS participated in only 2 EAC meetings. Field visits to 17 factories were arranged in the first half of this year. The IPHS coordinator could spend only 1 day per week for CC/DP and ME studies. Recruitment of a full-time staff, which is ideally familiar with the role of IPHSs and the trendy changes of relevant industries, is needed, so that we can visit factory under a more responsive and effective way.

4.1.3 Access to IPHS database

Full access to the IPHS database is essential to the sector analysis approach. Currently, IPHS has refused to provide full access, citing complains from other study parties with which IPHS is collaborating. Actions to prompt IPHS re-engaging are under reviewed.

4.1.4 Technical supports to exposure assessment team

EAC was directed to focus on “sector analysis” and to estimate the exposure level in terms of ‘high’, ‘medium’ and ‘low’ according to the factory size in May. The questions are: 1) how to define factory size; and 2) the factory size doesn't

necessary proportionally relate to exposure level. However, no further clear and constructive guidelines have been provided by US experts, which need to be more transparent and technically supportive.

Further communication between US and Fudan investigators is needed. Fudan investigators should be kept informed about the adjustment of exposure assessment strategy. Fudan investigators understand that the EA is one of the most complicated issues for SHS, and it's difficult to answer all questions at the moment. However, we are hoping that all important decisions would be made based on scientific judgment and agreed with the PIs .

4.2 ME study

4.2.1 ME phase I study

After the qualification process, only a little more than half of the cases collected for ME Phase I study will be usable. Therefore, more factories need to be recruited. The Fudan Team and Dr. Ni both explored the possibility of reaching out to other sources for the information out-side Shanghai. However, historical records were not kept in these areas as complete and systematic as in Shanghai.

4.2.2 ME Phase II Study

Several candidate factories were approached but none of them could accept the ethical requirements and were willing to sign the consent form on behalf of workers. The ME II study would not be approachable unless the Ethical Committee would consider a different approach.

**Annexed table 1 : Disease distribution of inpatients in
68 hospitals (2002, Shanghai) vs. CC/DP controls (between Jan. to Jun.
2005)**

sort of disease	number of discharged patient	proportion(%)	Number of SHS controls	Proportion (%)
infectious disease and verminosis	12952	1.90	5	0.94
cancer	74460	10.92	82	15.36
incretinary disease,nutrition related	15859	2.33	31	5.81
disease, metabolic disease,immune disease				
blood and hematopoietic organ related disease	4448	0.65	0	0.00
mental disease	941	0.14	0	0.00
Neurologic system disease and sense organ related disease	27642	4.05	51	9.55
Cirulation system disease	100827	14.79	84	15.73
Respiratory system disease	93602	13.73	55	10.30
Digestive system disease	105418	15.46	76	14.23
Urinary system disease	40459	5.93	64	11.99
cyesis,delivery and complication of the puerperium	82255	12.06	5	0.94
dermal and hypodermis disease	4542	0.67	5	0.94
muscle and skeletal system disease, connective tissue disease	16156	2.37	54	10.11
inherent abnormality	4472	0.66	0	0.00
condition from perinatal period	3461	0.51	0	0.00
unknown of sign and symptom	6040	0.89	12	2.25
impairment and intoxication	54607	8.01	5	0.94
others	43742	6.41	5	0.94

total	681883	100.00	534	100
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