PROGRESS REPORT
June, 2004

I. ANALYSIS OF DISEASE PROGRESSION FOR APLASTIC ANEMIA, MYELODYSPLASTIC SYNDROME, ACUTE MYELOGENOUS LEUKEMIA AND BENZENE POISONING IN SHANGHAI, CHINA

II. MOLECULAR EPIDEMIOLOGY OF BENZENE-EXPOSED WORKERS IN SHANGHAI, CHINA

Richard D. Irons

A MULTICENTER INTERNATIONAL STUDY

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PROGRESS REPORT

JCML Clinical Activities

Overall Case Accrual

JCML began routine full service clinical operations in the middle of August 2003 with September 2003 being the first full month of operation. Prior to this JCML activity had been limited to a few cases in July. Currently, JCML laboratory diagnoses involves routine hematology, bone marrow aspirate analysis, bone marrow and lymph node histopathology, clinical chemistry-liver enzymes, serology, flow cytometric analysis of blood, bone marrow and lymph node preparations, cytogenetics, FISH and molecular genetics. The rate of patient referral has continued to escalate such that, as of June 30th, 2004, a total of 565 cases have been referred to JCML for diagnosis as part of the clinical operation. Based on the current laboratory caseload, JCML is expected to diagnose 650 new patients by September 1, 2004, which represents one year of full operation. This exceeds our original prediction of 500 cases per year by 30%. This escalation in case contact appears to be, in large part, due to our growing reputation as a service provider within the clinical community in Shanghai. There are several examples of JCML diagnoses having resulted in modified therapeutic treatment plans and favorable clinical responses. This has resulted in the increased integration of JCML in the diagnosis, management and follow-up of patients with lymphohematopoietic disease presenting at area hospitals. Further, the population of Shanghai is also increasing at a rate of over 1 million per year, according to official reports.

In addition, we have begun six month follow-up evaluations as called for in the DP protocol. This resulted in an additional 8 cases in the month of June, including BP, and the follow-up caseload is expected to increase with time. Even based on this modest sampling it appears that follow-up evaluations are going to yield valuable information on disease progression. Finally, in partnership with Professor Ni and the Shanghai Occupational Hospital, JCML has signed a contract with the city of Nanjing to provide laboratory diagnostic support and follow-up of benzene poisoning cases occurring in that city. This has resulted in an additional 7 hospital-based BP cases accrued to the DP study over the last 3 months for a total of 12 since we began laboratory operation. This number is expected to increase with time.

The turn-around time (TAT) for routine hematology continues to average less than 2 hours with a onetime excursion beyond 4 hours. Routine analyses of bone marrow aspirates average 2-7 days. For acute cases, preliminary aspirate analyses are available within 1-3 days. Flow cytometric analysis of bone marrow or lymph node preparations are normally completed within 1-2 days. The TAT for cytogenetics analyses averages 7-9 days with 70-80% being completed within 7 days. FISH analyses are 90% completed within less than 7 days. For acute cases, cytogenetics are completed within 5 days and FISH analyses within 2-3 days. This exceeds the American College of Medical Genetics (ACMG) TAT requirement of 21 days. The TAT for analysis of bone marrow core biopsy with hematoxylin and eosin (H&E) is now 1-2 days. The availability of histology for analysis of lymph node biopsies has historically been 7-10 days for immunohistochemistry for analysis of bone marrow or lymph node biopsies. However, we have

recently purchased additional processing equipment which will reduce the average TAT for H&E and immunochemistry to 1-2 days.

DNA and RNA are routinely isolated from samples received the same day, with all samples processed within 24 hours. Random RNA samples are subjected to electrophoresis, with visual confirmation of the 18S and 28S fractions demonstrating quality RNA. Additional quality control for DNA samples is provided by the amplification of the FLT-3 gene, performed on all samples from a given week on the first day of the following week. At present, routine molecular analyses performed in the laboratory include analysis of FLT-3 internal tandem duplication by PCR and FLT-3 amino acid substitution at D835 using RFLP, BCR/ABL confirmation by rtPCR, and TCR beta or gamma chain gene rearrangements by PCR and hetero/homoduplex analysis. Additional protocol-mandated molecular analyses (HHV8, NQ01) are not time sensitive and will be processed as time allows. The frequency of FLT-3 mutations in AML cases diagnosed at JCML varies significantly from the published Western literature and is likely to be of prognostic significance. Therefore, in order to support publication of these results we are sequencing FLT-3 alleles of interest in all AML cases diagnosed at JCML.

JCML is a designated tissue bank according to international standards and in accordance with its US and Chinese human use approvals. Mononuclear cells (MNC) from all blood samples coming into JCML are cryopreserved along with tumor RNA, DNA and serum aliquots. Randomly selected samples demonstrate greater than 99.4% viability upon thawing. However, immortalization of patient cells continues to present a challenge. EBV viral lots obtained in China have failed to transform both patient samples and test samples. Therefore, EBV supernatant was prepared in Colorado and shipped to Shanghai, and this material has been used to successfully immortalize test cultures. However, the volume of starting material (blood) originally obtained for this purpose has proved to be suboptimal in many cases. Efforts are underway to increase the transformation efficiency of the culturing process, and a protocol amendment was approved to increase the starting blood sample volume. Patient cultures are now in the process of being immortalized using cryopreserved MNC as well as peripheral blood MNC obtained from fresh blood.

Routine screening of patients for HIV and HCV continues. In addition, HIV screening has been extended to controls. During the last 6 months HIV screening also has been instituted at area hospitals, posing a problem in the recruitment of some controls for NHL. Therefore, JCML has agreed to share HIV results with participating hospitals in accordance with established clinical guidelines and consistent with informed consent procedures. This notwithstanding, our results over the first 10 months of operation suggest that, at least for the present, HIV will not pose a problem in the interpretation of study results.

Site visits and hematopathology reviews of JCML diagnoses were conducted in October 2003, and April 2004, by Dr. John Ryder, a board-certified hematopathologist. These visits involved independent histopathologic review of previously established JCML diagnoses. In October, there was approximately a 95% overall concordance between the previously recorded JCML diagnosis and secondary pathology review. Greater detail was provided for the April visit in which secondary review agreed with the previously established JCML diagnosis in 150 out of 161 cases. This represents a concordance rate of 93%. For 10 of the 11 disagreements, minor

issues were raised involving subtleties related to classification which were judged by Dr. Ryder to be of no clinical or therapeutic significance. Excluding these cases where there were minor differences, the concordance rate is greater than 99%. In general, a 90% interlaboratory concordance rate is considered acceptable.

Inter-laboratory validation of peripheral hematology parameters is now conducted monthly in cooperation with two other clinical laboratories in Shanghai. In the most recent split sample analysis a total of 7 JCML CBC samples were chosen at random and 8 parameters compared. JCML results were within 1 S.D. of the mean for 52 of 56 measurements and within 2 S.D. for all measurements.

Cytogenetic analyses have also been subject to statistical review, according to guidelines established by the ACMG that require that reference laboratories maintain at least a 50% rate of detection of abnormalities for acute myelogenous leukemia (not including MDS). The results place JCML in the top echelon of US cytogenetic reference laboratories. The cumulative rate of detection of clonal abnormalities at JCML is as follows:

AML:	60%
MDS:	28.33%
NHL:	80%
ALL :	51.85%

A long-standing objective of JCML has been to obtain CAP certification before completion of the project. To this end, we have met performance standards in all areas of clinical laboratory operations and are continually striving to improve process documentation. Other remaining requirements include among other things: documentation of parent institutional fiscal support, institutional documentation of a suitable health and safety program, chemical and radioactive waste disposal and personnel training. In addition, all sister laboratories must meet the same standards and undergo physical inspection. We have determined that successful performance on the latter is a virtual impossibility. Accordingly, we have embarked on a strategy to bring all hematology specimen staining and slide production out of Huashan Hospital and exclusively into JCML. Resolution of the same issue with respect to immunohistochemistry performed at the Tumor Hospital remains an outstanding challenge.

Case Control (CC) /Disease Progression (DP) Case Accrual

Based on JCML diagnoses made through June 2004, representing 10 months of full operation, we have projected the following hospital-based case accrual for diseases qualifying for inclusion in the CC and DP studies for the first year ending September 1, 2004:

AML:	>150(120)
MDS:	97(60)
AA:	58(50)
BP:	12(10)
$NHL_{WHO:}$	139(200)
$NHL_{ICD-9:}$	108

When interpreting these numbers there are several issues that should be kept in mind. First, while most of these numbers exceed initial study projections, we are in year 3 of the project and only year 1 of case accrual so we are not exceeding the original goals of the study. Second, all projections of case accrual rate have always been based on WHO diagnostic criteria, which are the current international clinical standard and the criteria to be used for JCML study diagnosis as defined by study protocol. All case accrual numbers appearing in JCML reports reflect WHO diagnoses unless specifically stated otherwise. While WHO incidence data is emerging in the international literature, there remain no established benchmarks for predicting the prevalence of many of the disease subtypes embraced within the WHO guidelines, and the incidence and prevalence of some of these diseases varies from region to region. Moreover, the WHO classification is dynamic, and it is anticipated that it will be modified at least once again before the conclusion of this study. The disparity between NHL_{WHO} and NHL_{ICD-9} classifications is borne in large part by the inclusion of ALL in the former but not the latter, although there is no simple algorithm that enables translation between the two classifications. Finally, the initial projections for case accrual in this project were primarily based on local anecdotal information and not on quantitative epidemiology.

These issues notwithstanding, we believe that some cases of NHL presenting at participating Shanghai hospitals over the last 10 months were not accrued to the study because of logistical problems in the recruitment process. It is impossible to accurately determine what this number might have been. In order to minimize the number of case contacts presenting with non-neoplastic lymphoid diseases (traditionally thought to be on the order of 50%) and thus control costs, it was decided to screen initial biopsy material for suitability prior to recruiting subjects to the study and to subsequently recruit subjects and obtain additional sampling. Because approximately 50% of NHL cases initially present as outpatients and tracking outpatients in China is problematic, this resulted in an undisclosed number of cases being lost to follow-up. Based on actual experience, we now believe that non-neoplastic conditions represent only about 11% and Hodgkin lymphoma 13% of the total subject population presenting with solid tissue lymphoid disease, resulting in a 23% exclusion rate. Therefore, we have decided to recruit these subjects at the time of initial presentation and forego any initial screening. The impact this change will have on NHL study accrual is presently unknown but it is expected to result in an increased study accrual rate.

Assuming our *present** rate of case contact, we project the following numbers to be accrued to CC and DP studies by the end of 2006:

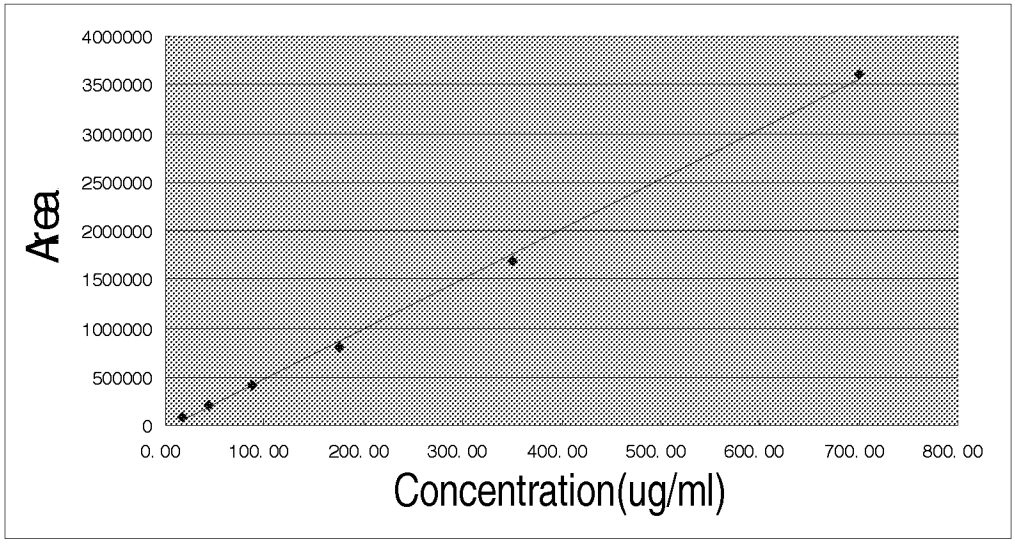
AML:	500 - 600
MDS:	250 - 350
AA:	200 - 250
BP:	30 - 50
$NHL_{ICD-9:}$	300 - 350*

Benzene and Metabolite Analyses

Benzene

During the last 6 months we have been developing in-house analytical capability in support of IH and metabolism activities. Protocols for the measurement of benzene, cyclohexane, toluene and xylenes have been developed and validated for area monitoring, personal sample analysis, exhaled breath measurements and analysis of benzene in solvents and glue components. The instrumental MDL for benzene is 0.12 ug/ml which corresponds to an MDL in air of 0.12 mg/m^3 or 0.038 ppm. Linearity for these analytes is maintained over a wide range of concentrations: (Benzene: 17.5~701.2ug/ml (R=0.9998); Cyclohexane:15.6~622.8ug/ml(R=0.9999); Toluene:17.3~693.5ug/ml (R= 0.9999); Xylene: 17.2~688.9ug/ml(R=0.9999)). Figure 2 illustrates this standard curve for benzene:

Figure 2: Standard Curve for Benzene



In June, three sets of 3M-3500 badges were sent from EMBSI to JCML as quality assurance check samples for split sample analysis. These were prepared by spiking 3M-3500 badges with known amounts of mixtures containing four of the five following components: n-hexane, benzene, cyclohexane, toluene and p-xylene. The results for each analyte were within acceptable performance limits for all three sets (See Appendix B).

Benzene Metabolites

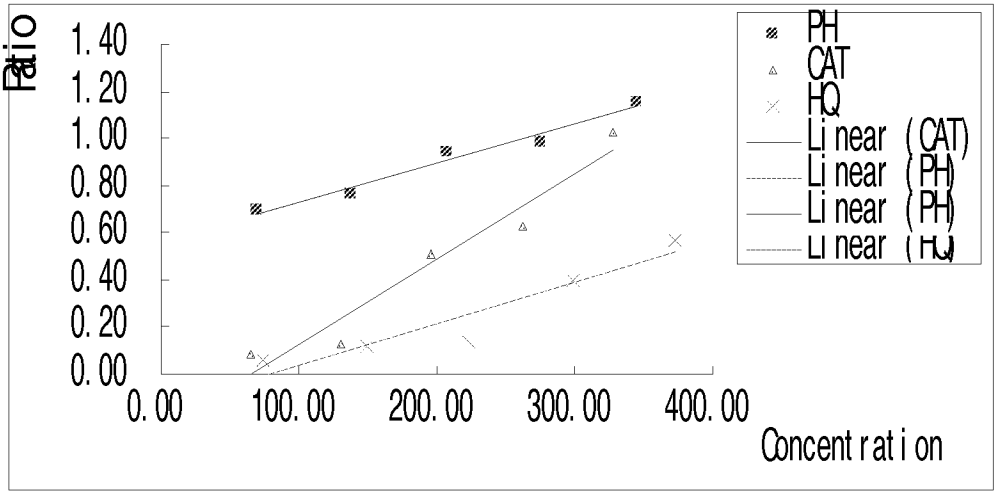
We have succeeded in developing and implementing in the field a method for the extraction, derivation and analysis of phenol, catechol, hydroquinone and trans-,trans- muconic acid in human blood and bone marrow. The method employs deuterated internal standards and a two-step acetonitrile-dichloromethane, Na_2SO_4-toluene extraction procedure, followed by derivation with pentaflurobenzyl bromide and analysis by GCMS. A graph of recovery versus concentration for phenol, catechol and hydroquinone is presented in Figure 3. Linearity for these

three metabolites is: PH: r = 0.9840 (68.94 ~ 344.68pmol/ml), CAT: r = 0.9719 (64.45 ~ 327.27pmol/ml) and HQ: r = 0.9423 (74.62 ~ 373.09pmol/ml), with limits of detection of 68.9 nM, 64.45 nM and 149 nM, respectively. The limit of detection for trans-, trans- muconic acid is 25ng/ml over a linear range of 10 ~ 100 ng/ml.

We are presently working to improve the recovery rate, lower the limits of detection and establish background concentrations of these metabolites in human subjects. However, studies conducted in my laboratory and others over the years have established that the most toxic metabolite, HQ, produces effects in human bone marrow cells over a concentration range of 1 ~ 10 uM. Therefore, we believe that our method is currently sufficiently sensitive to monitor effective target organ concentrations in human subjects.

Figure 3: Recovery vs. Concentration for Phenol, Catechol and Hydroquinone

(Y: Area ratio of X/X-d6, X: the concentration of benzene metabolites- pmoles/ml)



Exposure Assessment

Questionnaire administration

Case and control recruitment for CC/DP studies is progressing smoothly with notable gains in efficiency over the last 12 months. The questionnaire administration and data entry teams have kept pace with the caseload that has doubled over the last several months. Following identification of validity and quality control issues concerning control selection at certain hospitals, the questionnaire administration team has successfully implemented and verified an improved control selection process. However, certain items require continued improvement. An unacceptably high fraction of questionnaires are missing essential information in key fields necessary for exposure assessment, and the dual entry and error checking routine for questionnaire validation is slow. We are upgrading the quality assurance process by reassigning personnel, authorities and duties to specifically address these issues. The focus will be on reducing the error/omission rate and to improve database response time.

Exposure Assessment

The US based investigators have spent significant time establishing procedures, working through examples, and repeatedly reviewing and monitoring progress of the Exposure Assessment Committee (EAC). As a result, the EAC has improved the organization and implemented processes for qualitative and quantitative exposure assessment. Even with the high caseload, the EAC has been able to maintain a completion rate of about 90% for all data that has been validated for qualitative assessment on benzene and other substances.

At the present time, 1098 primary questionnaires have been validated and are in the Exposure Assessment Database. Initial exposure assessments indicated 687 with no exposure, zero benzene only exposures, 48 with benzene and other exposures, 360 exposures to other agents not including benzene and 3 pending. A total of 124 requests to the IPHS database and 8 site inspections were made. Final assessments completed by the EAC included 688 with no exposure, 2 exposed to benzene only, 28 exposed to benzene and other compounds, 359 exposed to other agents and 23 pending. These were reviewed in July by Tom Armstrong and Yemei Zhou and 15 referred for further clarification. Since January, 5 factories representing spray-painting, chemical, color printing, stationery and rubber industries have been visited and exposures characterized. Issues and concerns previously identified over hospital based selection of control cases have been addressed with clinical coordinators and measures put in place to track performance. We will continue to closely track performance in this area.

Several areas of concern leave additional room for improvement. The EAC currently relies on the IPHS database to provide historical data and background information on factories or their surrogates. However, IPHS cooperation has been less than anticipated, and responses to database requests have been sporadic and slow. At present, our access to the IPHS benzene database is only piecemeal through them, resulting in a slow response time. This has hindered progress in exposure assessment. Independently, IPHS has failed to provide the level of access for CC/DP investigators to factories as originally negotiated. According to the negotiated work plans, Fudan University and the EAC rely on the municipal IPHS to contact district IPHS, who in turn contacts the factory to arrange access to the factory. This has been inefficient and cumbersome. These issues were raised in June with the IPHS director who has made specific promises to allocate more structured time and organizational priority to streamline our access to their database. Factory access issues appear to involve a number of issues internal to IPHS, most related to the complexity of that organization and difficulties in communication between the central municipal IPHS and local IPHS offices. Therefore, we are making our own initiatives to improve networking with local IPHS offices through direct face-to-face contact, independent of the Municipal Office. At present it is impossible to gauge how successful this strategy will be.

Molecular Epidemiology (ME) Study

Phase 2a and 2b activities

To date, a total of 114 workers have been recruited to the 2a study from three factories, including a shoe factory and two rubber factories. The exposure assessment team has completed in-depth exposure surveys during site exposure assessments and can now independently complete these assignments. Summary data from the last Rubber Products Factory Survey is provided in Appendix A (figures 1, 2 & 3). Phase 2a clinical laboratory screening and physical examinations from 28 workers identified 8 individuals with abnormal hematology values, and 3 of these individuals were recruited to Phase 2b studies which were conducted in July. These results confirm that high occupational exposure to benzene still exists in Shanghai and the surrounding provinces, although we believe that IPHS efforts to reduce benzene exposure are resulting in fewer factories with existing high exposure concentrations.

Despite some limited success, factory participation in the ME study has proven to be uneven and inconsistent. Similarly, the response of both factory management and workers to Phase 2b recruitment efforts have been markedly different from one facility to another, ranging from a high degree of enthusiasm on the part of workers but heavy resistance from management to a general reluctance on the part of workers and mediocre support of management. Although cultural biases against blood and bone marrow sampling exist, employee-management relations appear to play an equal or greater role in the recruitment process. Study subject compensation has variously been reported to be either too high or two low as an explanation for conflicting responses at different factories. Throughout this process we have experienced significant push back from the municipal IPHS to recruit factories with high benzene exposures to the Phase 2b study. We believe that, as the result of a national mandated reform to reduce benzene exposures that began two years ago, some representatives of the municipal IPHS may view the potential publication of existing high exposure levels in some factories as a tacit admission of their failure to meet national goals. Moreover, failure of the municipal IPHS to communicate with and provide study support to local IPHS and factory management has resulted in a lack of incentive on the part of these groups to cooperate effectively in meeting study goals. At this point in time we believe that the only effective solution to this problem is for IPHS senior management to provide effective leadership and personally present study objectives to prospective factory management.

These issues have caused us to modify our existing strategy for factory recruitment. Although, we are continuing to mount pressure on top level IPHS management to fulfill their contractual obligations to the project, we no longer are relying on IPHS staff to identify candidate factories or to introduce the project to factory management. It appears that a major requirement for successful interaction with factory management is routine high-level participation by senior Chinese faculty and physicians in the initial recruitment process. Independently, we have accelerated our initial plans to recruit factories and subjects from adjacent or even distant provinces. We are directly undertaking the identification of candidate facilities at several sites outside of Shanghai, and, as part of our ongoing collaboration with Professor Ni, President of the Chinese Academy of Occupational Medicine, we are pursuing recruitment of factories in Nanjing that have referred BP cases to JCML. Specifically, we have identified a single factory in Nanjing which is the source for 7 cases of putative benzene poisoning that we have evaluated in 2003-2004 as part of the BP study. This facility will be visited during August 2004. We are also exploring some procedural changes in order to streamline the factory survey and recruitment process. These include reducing the period necessary for exposure assessment, minimizing contact between the exposure assessment team and factory workers, and moving the physical examination and review process to a hospital setting where appropriate.

CONCLUSIONS

Since the last reporting period we have solved many of the problems confronting us, and we are now focused on meeting new and continuing challenges. During the last 6 months we have undergone a transition from inauguration of study activities to routine clinical and research activities. Our clinical operations have experienced a marked increase in case contact, and JCML has emerged as the major service provider for diagnosis of blood and lymphoid diseases for the 23 participating hospitals in Shanghai. We currently meet or exceed statistical measures

used to gauge clinical laboratory performance in the US. The increased rate of patient contact and subject accrual now presents us with a number of challenges, namely to continue to meet performance standards and remain on budget. In the research arena, all procedures are up to speed except immortalization of cell lines. Analytical capabilities have been developed at JCML in support of IH and metabolism requirements. We are accruing a greater than predicted number of study cases based on our initial projections, and the rate continues to grow. This increase in the rate of case accrual must be gauged against the fact that we are in year 1 of accrual but year 3 of the project.

Over the past 6 months we have confirmed that exposure to high concentrations of benzene is still ongoing in the workplace in certain facets of Chinese industry despite central government initiatives to reduce its use. However, we face some remaining hurdles that will be the focus of continued attention over the next year. These include: improving leadership continuity for EAC, QA/QC and ME projects, and developing a different strategy and logistical approach to identifying factories and encouraging the participation of factory management in the ME study.

Appendix A

Benzene Exposure Data for Rubber Products Factory

Figures 1 and 2 are histograms that present the number of samples within the concentration ranges given on the X axes. These data cover several work areas of the factory over the two-week assessment period. Approximately 47% of the full shift personnel samples were at or above 20 ppm. For the 20-minute area samples, 54% were at or above 20 ppm.

Figure 3 summarizes the area samples (average, minimum and maximum in mg/m^3) on an illustration of the factory floor layout. Note that the charcoal tube samples followed the IPHS standard 20-minute collection time. The UltraRAE samples (a benzene selective detector) represent a 1-minute averaging time. These samples give an idea of the short-term concentrations of benzene encountered in this factory. The upper end for the charcoal tube (20 minutes) samples was 640 mg/m^3 and the highest reading on the UltraRAE (1 minute sample) was 1440 mg/m^3. These were worker breathing zone samples.

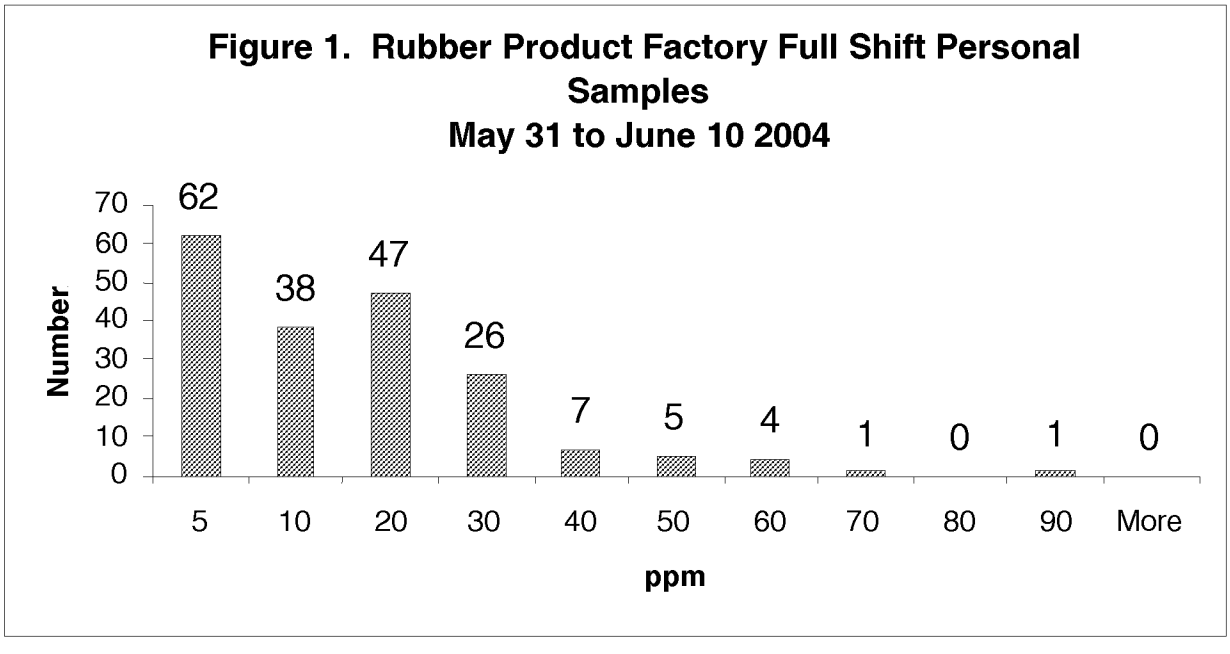
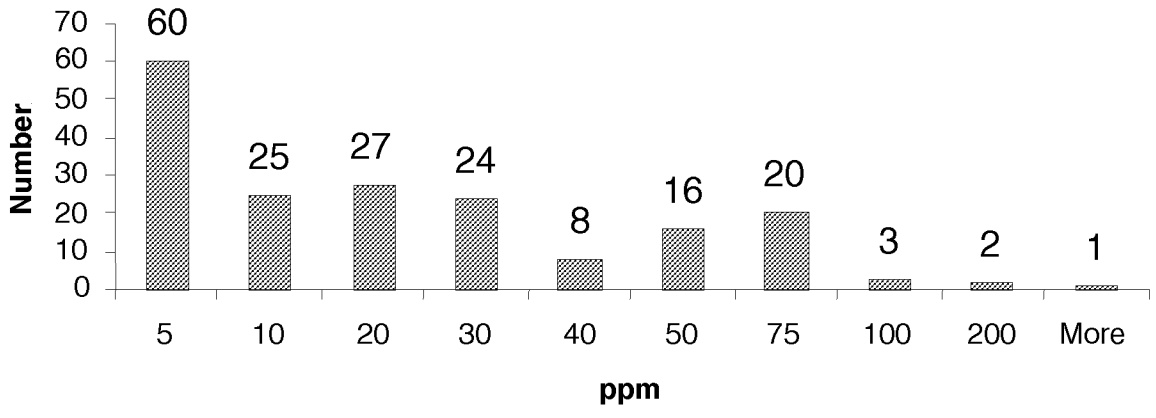


Figure 2. Rubber Products Factory Area Samples
31 May to 10 June 2004



Appendix B

July 6, 2004

QA Results for Fudan University Lab

04EMBSI 348

Thomas W. Armstrong
ExxonMobil Biomedical Sciences, Inc.
1545 Route 22 East, P.O. Box 971
Annandale, New Jersey 08801-0971

Dear Tom;

Attached are summary tables and plots of the data for three sets of 3M-3500 badges that were sent to Fudan University as quality assurance check samples. The following table contains the overall performance summary indicating the number of outliers that were obtained by each set. Each set consisted of three spiked badges at two concentration levels (a duplicate sample at one of the concentration levels) and a blank

Laboratory: Fudan University			
	3M-3500 OVM		
Overall Lab Performance:	Set #3	Set #8	Set #13
Acceptable (≤ 10% Outliers) Unacceptable (>10% but ≤25% Outliers) Unacceptable (>25% Outliers)	_X_ ___ ___	_X _ ___ ___	_X_ ___ ___
% Data Points Acceptable:	100%	100%	100%
# Results Received:	12	12	12
# Outliers (> ± 20% Reference Value)	0	0	0

Reference samples were prepared by spiking 3M-3500 badges with known amounts of mixtures containing four of the five following components: n-hexane, benzene, cyclohexane, toluene and p-xylene. The laboratory was requested to determine the mass of the components of interest using their normal analytical procedure for a complex mixture.

An acceptable performance limit was established for each analyte at each spike level. The limits were established at ± 20 % of the reference value based on the Quality Control Guidelines for Industrial Hygiene Analytical Services (MR.15DQ.88). The 20% criteria was established to

reflect the accuracy requirements of a Class A sampling method as established by the ExxonMobil Industrial Hygiene Monitoring Committee. Class A methods are established for compounds with high levels of concern (such as benzene, toluene and xylene).

A Class A method requires that an industrial hygiene monitoring method is able to determine the actual analyte concentration within ±25%. This 25% includes sampling pump error and maximum analytical error (MAE). The generation of reference samples also has a degree of uncertainty (approximately 5%). Combination of the appropriate errors results in our selection of the ±20% criteria. Any analyte result that exceeded the ±20% criteria was identified as an outlier. Each sample set had a maximum of 12 results. In establishing overall performance criteria, 1 outlier (8.33%) was allowed to achieve an acceptable score.

The intermediate performance category (>10% but < or = 25% outliners) is indicated on the lab performance summary. Although these labs do not meet the criteria of acceptability, they are the most likely candidates to be able to improve with a minimum of effort. The current American Industrial Hygiene Association (AIHA) criteria of acceptability allows participating laboratories to have 25% outliers and still be classified as proficient. Laboratories that have greater than 25% outliers are considered to have unacceptable performance.

The recommendation is to inform the management of unacceptable performance and to allow them to determine the causes of the errors. The lab should be allowed to make the appropriate changes and to correct the deficiencies noted. Submission of spiked samples on a regular basis is a good practice. It is especially warranted with poor performing laboratories to assure that deficiencies have been corrected and that data is of acceptable quality.

If any additional information or assistance is required, please do not hesitate to contact me (x1058).

Sincerely,

Mary O'Donnell

cc:

D.Y. Chang
J.J. Freeman
J.L. Martin Jr.
A.R. Schnatter

Fudan University QA Lab Results

Contact :Professor Zheng
Date Results Received by EMBSI:6/30/04
QA Set # 3
3M 3500 Data

Compound	A173 Lab Results ug	A183 Lab Results ug	Ref. Value Ug	% Bias	% Bias	CV%	A193 Lab Results ug	Ref. Value ug	% Bias
n-Hexane	113	113	131	-13.7	-13.7	0.00	308	328	-6.03
Benzene	35	36	43.7	-19.9	-17.6	1.99	101	109	-7.55
Cyclohexane	116	117	119	-2.27	-1.43	0.61	302	297	1.77
Toluene	126	127	130	-3.00	-2.23	0.56	326	325	0.38
p-Xylene	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

Coefficient of Variation % (CV%) = Standard Deviation/Mean x 100 Avg. CV%: 0.79
% Bias = (Lab Result - Ref. Value) / Ref. Value x 100 Avg. % Bias: 7.46

Fudan University QA Lab Results

Contact : Professor Zheng
Date Results Received by EMBSI: 6/30/04
QA Set # 8
3M 3500 Data

Compound	B273 Lab Results ug	B283 Lab Results ug	Ref. Value Ug	% Bias	% Bias	CV %	B293 Lab Results ug	Ref. Value ug	% Bias
n-Hexane	142	132	133	6.77	-0.75	5.16	324	333	-2.70
Benzene	41	41	44.2	-7.24	-7.24	0.00	103	111	-6.79
Cyclohexane	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Toluene	140	141	130	7.44	8.21	0.50	334	326	2.53
p-Xylene	137	138	129	6.04	6.81	0.51	333	323	3.10

Coefficient of Variation % (CV%) = Standard Deviation/Mean x 100 Avg. CV%: 1.54
% Bias = (Lab Result - Ref. Value) / Ref. Value x 100 Avg. % Bias: 5.47

Fudan University QA Lab Results

Contact : Professor Zheng

Date Results Received by EMBSI: 6/30/04

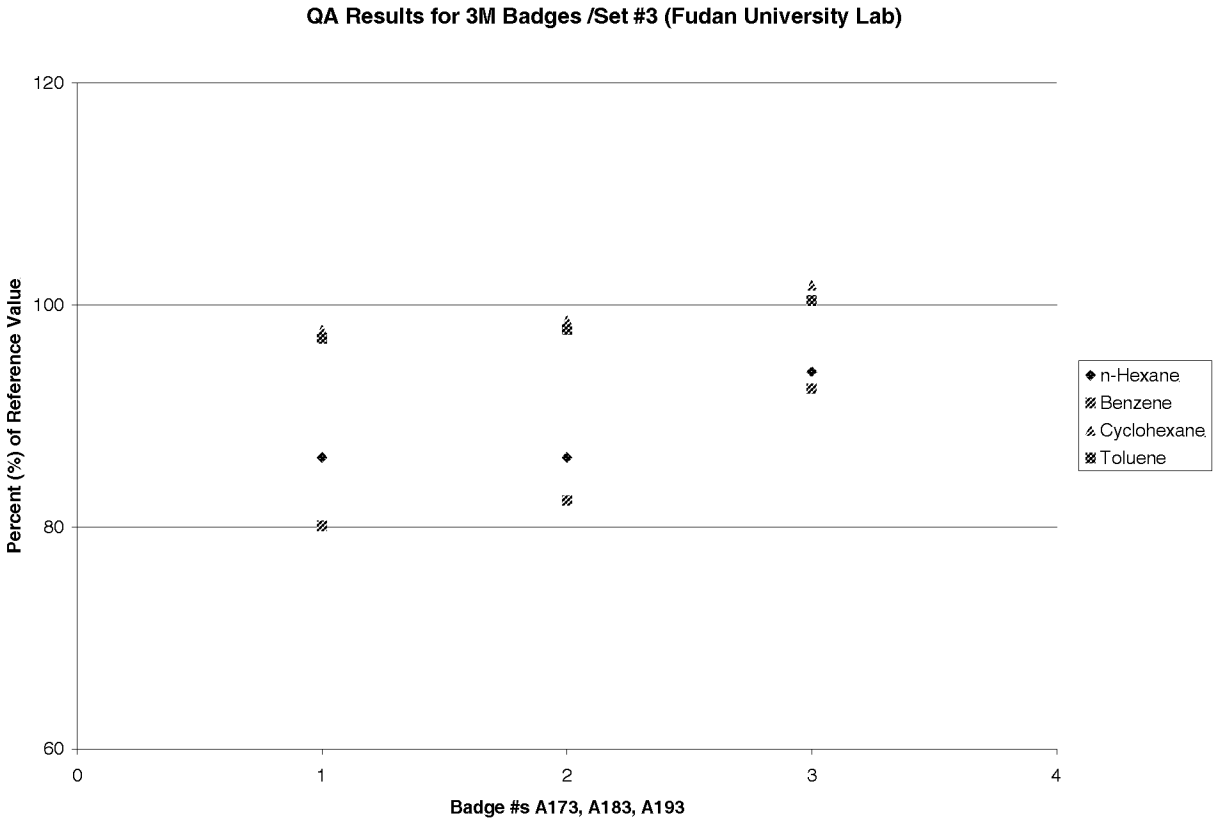
QA Set # 13

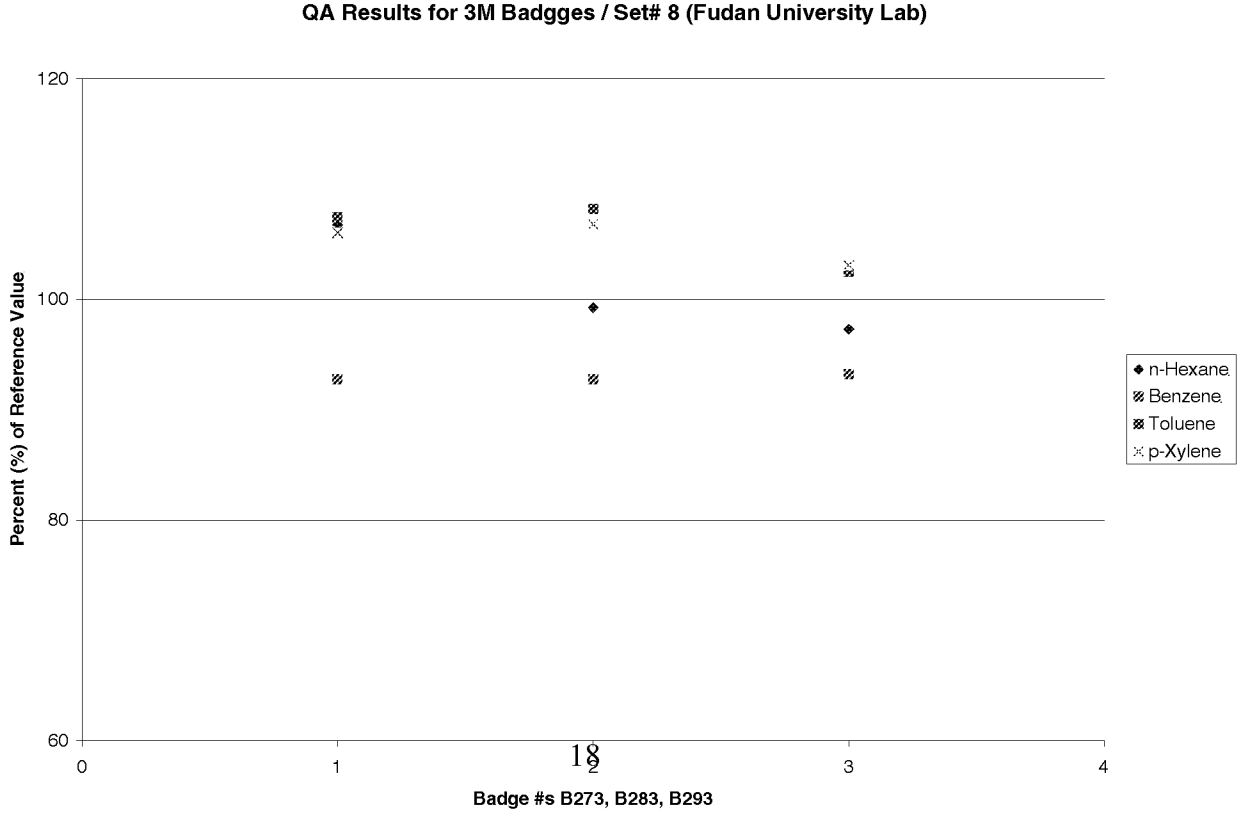
3M 3500 Data

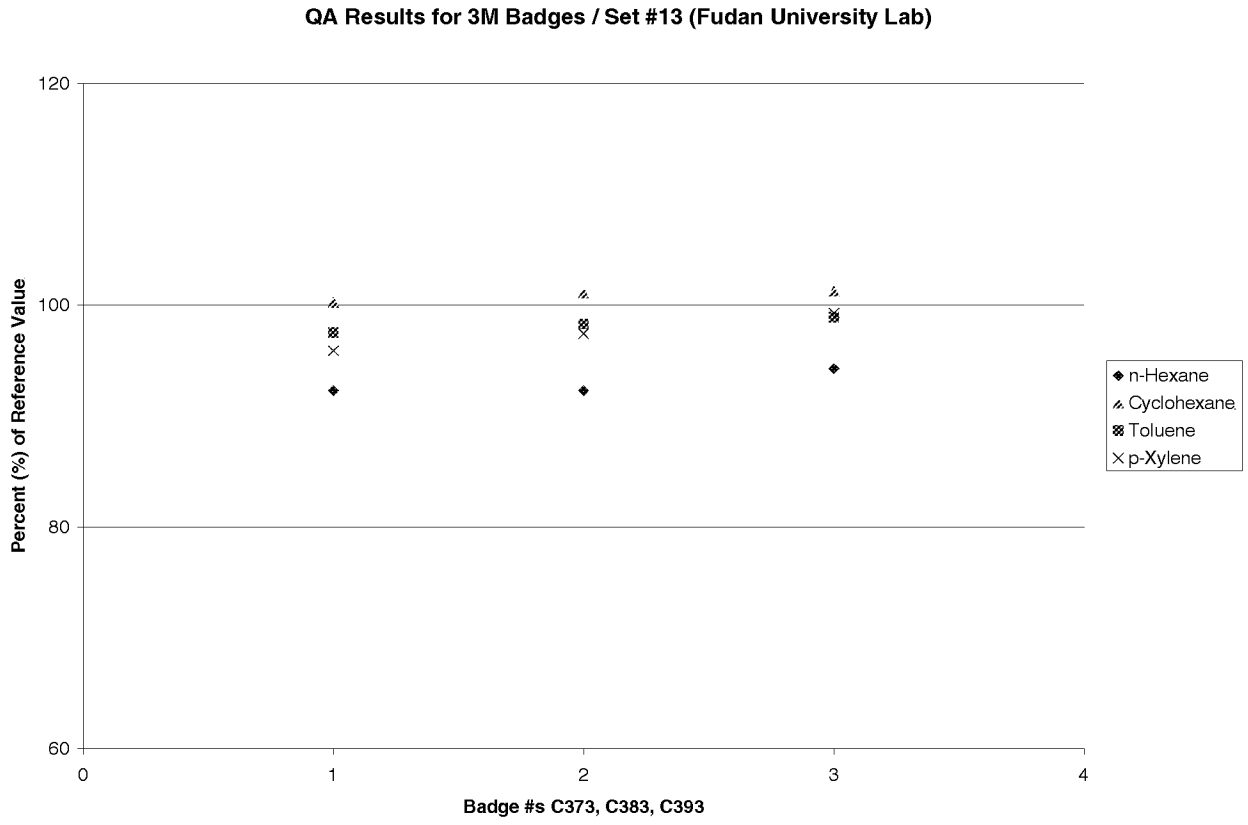
Compound	C373 C383						C393		
	Lab Results ug	Lab Results ug	Ref. Value Ug	% Bias	% Bias	CV%	Lab Results ug	Ref. Value ug	% Bias
n-Hexane	121	121	131	-7.70	-7.70	0.00	309	328	-5.72
Benzene	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Cyclohexane	118	119	118	0.25	1.10	0.60	298	294	1.27
Toluene	127	128	130	-2.46	-1.69	0.55	322	326	-1.08
p-Xylene	124	126	129	-4.10	-2.55	1.13	321	323	-0.70

Coefficient of Variation % (CV%) = Standard Deviation/Mean x 100 Avg. CV%: 0.57

% Bias = (Lab Result - Ref. Value) / Ref. Value x 100 Avg. % Bias: 3.03







To:	benzconsort-tc@listserve.api.org <benzconsort-tc@listserve.api.org>
From:	Bruce Jarnot <jarnotb@api.org>
Cc:	
Bcc:	
Received Date:	2004-08-05 20:00:15 GMT
Subject:	BHRC-TC... draft 2Q04 Financial Report (for Friday 8/13 conf call)

BHRC Technical Committee (TC) -

Attached is the draft 2Q04 Financial Report for the Shanghai Health Study, which includes UCHSC financial data from Richard's mid-year progress report.

And please check your calendar: a Financial Subcommittee / Technical Committee conference call is scheduled next Friday, August 13th to review and approve this report prior to formal distribution to the Oversight Committee:

Schedule & Dial-In Information
-- Friday August 13th
-- 7am MDT (6am California, 8am Houston, 9am DC)
-- Phone: 763/315-6900 (toll-free 866/448-6756)
-- PIN: 6828319#

Best Regards - Bruce.

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Attachments:

BHRC Program Expenses 2Q04 rpt.xls

Benzene Health Research Consortium
2Q04 Financial Report Overview

RESEARCH PROGRESS:

Case Diagnosis: JCML clinical lab operating at 100% capacity, processing 30% more cases than anticipated with 99+% concordance between primary diagnosis & secondary pathology review. CDC

Case Accrual: Logistical issues affecting NHL accrual rate have been successfully resolved. All

Exposure Assessment: Exposure Assessment fully operational, and Exposure Re-creation Committee reorganized apart from IPHS. Exposure activities will be highlighted at annual meeting.

External Review Panels: ERP Chair will be chosen at Asilomar, and Ethics panel will resume

EXPENSE DISCUSSION:

Fund Balance at API 1Q04 = $5,193,061

General: 2Q04 report generation went like clockwork, with mininal API time required to general report

Irons Field Expenses: Total T&E expenses are currently 1% ($15K) over budget and need to be

UCHSC: $874,031 was disbursed in 2Q04. First-half 2004 total expenses were 100^{+}% (~$1MM) above

Subcontracts: Total UCHSC Subcontractor expenses were ~$800K above projected budget, attibuted

AHS: 2Q04 expenses include both 1Q & 2Q due to timing of new AHS contract. Labor costs high due length of time in Shanghai, but travel savings have kept total expenses 1% ($28K) under budget.

Fudan University: 30% additional case load, and transfer of CDC & IPHS activities has increased

SRP/ERP: Total expenses 2% ($9K) over budget following 1Q04 budget adjustment and unanticipated

Communications (APCO): No 2Q04 communication expenses.