

Shanghai Health Study
Proposal for Bringing Study to Successful Closure

Draft: August 16, 2006

Background:

July 31-Aug 2 2006, the investigators, Scientific Review Panel, and Ethics Review Panel met to evaluate progress towards meeting the study aims of the Shanghai Health Study. Members of the sponsoring companies attended as observers. Sponsors did not participate in the technical session.

At about the same time, the sponsors received Dr. Irons and Dr. Wong's mid-year reports. Dr. Irons submitted a technical study update to the SRP and ERP. The sponsors received a financial report from Dr. Irons. While good progress is being made, there have been some challenges, which could cause the study to run longer than previously predicted. Loss of lab and exposure personnel is the most significant issue.

Options:

Irons Budget	18.3MM	18.8MM	19.3MM	22.3MM
Additional \$	0	+ 0.5MM	+ ~ 1.0MM	+ ~ 4.0MM
Shell Share	0	0 (take from contingency \$)	+ ~ 100K	+ ~ 600-700K

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Options:

	Option 1	Option 2	Option 3	Option 4
Irons Budget	18.3MM	18.8MM	19.3MM	22.3MM
Additional \$	0	+ 0.5MM	+ ~ 1.0MM	+ ~ 4.0MM
Shell Share	0	0 (take from contingency \$)	+ ~ 100K	+ ~ 600-700K
Impact on Time Line	Stop case accrual YE06	- Stop case accrual YE06 - Exposure assessment not as robust	- Stop case accrual May 07 - Exposure assessment completed	- Stop case accrual May 07 - Exposure assessment completed - Full data analysis
Impact on Case Accrual	NHL = 336	NHL = 433	NHL = 500	NHL = 500
Achievements	- Built and gifted to Fudan University state of art diagnostic lab - Provided free diagnostics to 1000s of Shanghai residents - First study to use WHO tumor classifications - Demonstrated commitment to learning about benzene - Publications			
Positives	Case Control paper	Honor time line		
		>400 AML/NHL cases for Case Control Study	500 AML/NHL cases	
Negatives	<400 AML/NHL cases			
	Do not achieve	Do not achieve		

	protocols	protocols		
	Did not achieve study goals	Did not achieve study goals		

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Recommendation to API Executive Committee

April 3, 2007

- Shell supports request for additional funding up to \$9.1M
 - Shell share is 1.6M
- API Exec Comm approved funding in Dec
- Sponsors recommending:
 - Advance of up to \$2M to support lab while new contracts are being executed
 - CinPathogen - Fudan University contract executed
 - CinPathogen – University of Colorado letter of understanding received
 - API – Sponsor contract amendments ready for signatures
 - CinPathogen as new entity for funding
 - Delaware Certificate of Incorporation in hand
 - State of Colorado Certificate of Good Standing in hand

DRAFT

Shanghai Health Study – December 15, 2006

Study Status	<u>Current</u>	<u>Desired</u>
 Case Control	425 AML/ 240 NHL cases	500 each
 Molecular Epi	Factory worker evaluations	Biomarkers
 Disease Progression	40% AMLs/NHLs followed	Knowledge in Benzene Poisoning and MDS progressing to AML

Funding Request	- Up to 10.4MM – Shell's share about \$2MM
Funding Level recommended by sponsors' oversight committee	- Up to 9.1MM – Shell's share about \$1.7MM

- Options considered by Sponsors

No additional \$	Fully Fund	Manage Risk Recommended Option
Cost limited to current - 5MM (Shell share)	Shell share increased to \$2MM	Support additional funding if conditions met
Contractual exposure	Future \$ increases unknown	Shell Share increased by \$1.7MM
Reputation		

Shanghai Health Study – December 15, 2006

- Conditions to support additional funding agreed by consortium
 - Robust QA/QC process to be implemented; led by Dr Rice, Scientific Review Panel chair, with Dr. Wong, Case Control Study principal investigator and Judy Baldwin, professional QA/QC expert. QA/QC Team has full access to study database.
 - Case Control study accruals to achieve 500 AMLs and 500 NHLs or end by YE07 – whichever comes first
 - Progress on Disease Progression and Molecular Epi studies based on funding
 - Grant payments to University of Colorado tied to study progress
 - University of Colorado funding capped
 - Benzene Health Research Consortium (BHRC) to terminate YE08
 - Monthly metrics on case accruals reported to Scientific Review Panel and BHRC Oversight Committee

Shanghai Health Study – December 15, 2006

- Study Time Line

- 07: Complete data collection
- 08: Data analysis
Closing Ceremony in Shanghai (cultural and ethics expectation)
Sponsors consortium terminates
- 08-09: Publications