To: OttoWong@aol.com <OttoWong@aol.com>; Cagen, Stuart Z SHLOIL-SHOIL-SHS <stuart.cagen@shell.com>
From: Russell White <whiter@api.org>
Cc: Bruce Jarnot <jarnotb@api.org>
Bcc:
Received Date: 2006-12-08 18:03:25 GMT
Subject: RE: SHS. please revise / resubmit the newest AHS budget

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Otto,

Are these subtypes from WHO or the ICD-9 classification?

From: OttoWong@aol.com [mailto:OttoWong@aol.com]
Sent: Friday, December 08, 2006 12:55 PM
To: stuart.cagen@shell.com
Cc: Bruce Jarnot; Russell White
Subject: Re: SHS. please revise / resubmit the newest AHS budget

Dear Stuart:

By "diagnostic subtypes," I mean different subgroups of AML or NHL. Here are some examples. According to the test datasets that we received from Gail Jorgensen in July, the largest subgroups of AML and NHL are as follows. (These are preliminary numbers, please do not quote them.)

AML (15 subtypes)

"AML MD" = 28%
"APL with t(15;17)" = 19%
"AMML" = 11%
"AML with t(8;21)" = 11%

NHL (20+ subgroups)

"Diffuse large B-cell lymphoma" = 42%
"Follicular lymphoma" = 12%
"Peripheral T-cell lymphoma" = 9%

Subtype analysis is one of the objectives stated in our original protocol. Analysis by subtype is important, because epidemiologic studies have demonstrated that certain subtypes of AML are related to smoking and certain subtypes of NHL with pesticide exposures. As we get closer to the end of case accrual, I need to work with Dr. Irons to combine some of the subgroups that will provide us with higher statistical power and at the same time that will make biological sense. At this point, I do not know exactly how large these subgroups will be. If I have to make an educated guess, the largest subgroups may be 30% to 50% of the total sample. This underscores the importance of having an adequate overall study size.

At this time, one can question how much additional gain we would have if we have a sample size of 400 instead of 500. To answer this question, we need to know the exposure prevalence of the cases and controls, the distribution by exposure level, the distribution by occupation/industry, the magnitude of risk, and the distribution by diagnostic subtype. We don't have all the information yet. All I can say at this point is that 500 is better than 400. In fact, 600 would be even better, but I am not proposing that. The original target of 500 was based on a consideration of statistical power and was accepted by the SRP. I strongly recommend keeping our original aim of 500.

If I can answer additional questions, please let me know.

Regards,

Otto

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--- Original message ---

Subj: RE: SHS. please revise / resubmit the newest AHS budget
Date: 12/8/2006 7:41:55 AM Pacific Standard Time
From: stuart.cagen@shell.com
To: OttoWong@aol.com
Sent from the Internet (Details)

Otto:

Thanks for the clarity on your situation and its uncertainties.

I am not sure what you mean about diagnostic subtypes. Does this imply something new regarding required sample sizes ? Also, is there something special about 500 cases; what about 400 with an earlier end to accruing cases.

Stuart Cagen, Ph.D.

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-----Original Message-----
From: OttoWong@aol.com [mailto:OttoWong@aol.com]
Sent: Friday, December 08, 2006 2:07 AM

To: jarnotb@api.org
Cc: whiter@api.org; Cagen, Stuart Z SHLOIL-SHOIL-SHS
Subject: Re: SHS. please revise / resubmit the newest AHS budget

Dear Bruce:

After talking to you about the increased airfares to Shanghai, I looked up the airfares on United Airline's website again. On the average, I underestimated my estimate for airfares in my previous budget proposal by about $1,500 per trip. I have revised my budget proposal accordingly (attached, dated 2006-12-8). Although the total increase ($11,418) over the previously estimated budget is relatively minor, I agree with your advice that it is far better to request an adequate budget upfront than to ask for supplemental funds later.

In my revised cover letter (attached, dated 2006-12-8), I have added a couple of sentences (in the second paragraph) emphasizing the importance of an adequate study sample size. Specifically, I added the following sentences. "An adequate sample size of both AML and NHL cases is important for analyses stratified by exposure level, occupation/industry, diagnostic subtype, etc. Recent studies suggest that different subtypes of AML and NHL are associated with different risk factors." Please make sure that the sponsors understand this point.

If you have any questions or need additional information, please let me know.

Regards,

Otto

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--- Original message ---

Subj: Shanghai Health Study... please revise / resubmit the newest AHS budget
Date: 12/4/2006 9:27:11 AM Pacific Standard Time
From: jarnotb@api.org
To: OttoWong@aol.com
CC: whiter@api.org
Sent from the Internet (Details)

Dear Otto –

Repeating my rambling voicemail message…

1) At your earliest convenience, please revise and resubmit the most recent AHS budget, which you developed in response to the revised NHL case collection timeline;

2) Also, I would like to pick your brain for potential metrics of study progress that can be easily checked on a regular (monthly?) basis, and that will – in total – provide reasonable assurance that "all systems are go"

Best Regards – Bruce (202/682-8473)
