From: Schmitt, Michael
To: Martha Carraway
Cc: Ghio, Andrew; ~~Diaz-Sanchez, David~~; ~~CN=Heidi Hiers/OU=RTP/O=USEPA/C=US@EPA~~; ~~CN=Kelly Duncan/OU=RTP/O=USEPA/C=US@EPA~~; ~~Dailey, Lisa~~; ~~Martha Carraway~~; ~~Maryann Bassett~~; ~~CN=Melanie Jardim/OU=RTP/O=USEPA/C=US@EPA~~; ~~Devlin, Robert~~; ~~Montilla, Tracey~~; ~~Schmitt, Michael~~
Subject: Re: Fw: Bronchoscopy for Lamarck
Date: Wednesday, July 14, 2010 9:15:26 AM
Attachments: lamarck IRB 06032010_clean.doc
Lamarck_Study Consent_IRBstamped_6-3-10.pdf

Hey MSC,

Melanie just informed me that we never made an atropine change in this protocol. Please advise with correct wording.

All,

Since this also came out as another oversight, I am attaching the most current copy of the protocol and consent. Please look over these and make us aware of any other oversights that may be associated with the bronchoscopy. We would appreciate any input to ensure that we have the correct language in the protocol and consent concerning the bronchoscopy, bronch risks, and any other section/wording that is associated with this process.

Thank you for the valuable input and I look forward to getting in place an agreed upon Lamarck protocol.

mike

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From:

Mike Schmitt/RTP/USEPA/US

To:

Martha Carraway/RTP/USEPA/US@EPA
Cc:

Andy Ghio/RTP/USEPA/US@EPA, David Diaz-Sanchez/RTP/USEPA/US@EPA, Heidi Hiers/RTP/USEPA/US@EPA, Kelly Duncan/RTP/USEPA/US@EPA, Lisa Dailey/RTP/USEPA/US@EPA, Maryann Bassett/RTP/USEPA/US@EPA, Melanie Jardim/RTP/USEPA/US@EPA, Robert Devlin/RTP/USEPA/US@EPA, Tracey Montilla/RTP/USEPA/US@EPA
Date: 07/14/2010 08:36 AM

Subject: Re: Fw: Bronchoscopy for Lamarck

Thanks MSC!

In the original protocol we have language saying we will premedicate with atropine. I was not aware that this needed to be amended not can I find where it was changed. I may be over looking something. Melanie can you confirm this?

thanks,

mike

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From: Martha Carraway/RTP/USEPA/US
To: Mike Schmitt/RTP/USEPA/US@EPA
Cc: Andy Ghio/RTP/USEPA/US@EPA, David Diaz-Sanchez/RTP/USEPA/US@EPA, Heidi Hiers/RTP/USEPA/US@EPA, Kelly Duncan/RTP/USEPA/US@EPA, Lisa Dailey/RTP/USEPA/US@EPA, Maryann Bassett/RTP/USEPA/US@EPA, Melanie Jardim/RTP/USEPA/US@EPA, Mike Schmitt/RTP/USEPA/US@EPA, Robert Devlin/RTP/USEPA/US@EPA, Tracey Montilla/RTP/USEPA/US@EPA
Date: 07/13/2010 05:27 PM
Subject: Re: Fw: Bronchoscopy for Lamarck

Mike,

I don't think this is the most updated version of the bronchoscopy protocol. An amendment should have been done to make administration of atropine optional, and the protocol and consent form modified to reflect the amendment. Can you check to make sure that was done.

For the first two highlighted sentences, change to:

Bronchoalveolar lavage will be performed using a total volume of up to 250 cc of sterile 0.9% saline; up to 5 aliquots of 50 cc each will be injected and immediately aspirated through the channel in the bronchoscope using a syringe.

Keep the second sentences as they are.

Thank you!

Martha Sue

From: Mike Schmitt/RTP/USEPA/US
To: Martha Carraway/RTP/USEPA/US@EPA
Cc: Robert Devlin/RTP/USEPA/US@EPA, David Diaz-Sanchez/RTP/USEPA/US@EPA, Maryann Bassett/RTP/USEPA/US@EPA, Tracey Montilla/RTP/USEPA/US@EPA, Heidi Hiers/RTP/USEPA/US@EPA, Kelly Duncan/RTP/USEPA/US@EPA, Melanie Jardim/RTP/USEPA/US@EPA, Andy Ghio/RTP/USEPA/US@EPA, Lisa Dailey/RTP/USEPA/US@EPA, Mike Schmitt/RTP/USEPA/US@EPA
Date: 07/13/2010 03:09 PM
Subject: Fw: Bronchoscopy for Lamarck

MSC,

Here is the current language in Lamarck protocol for the bronchoscopy. If you would, please look over this and give me feed back on what might be appropriate language to

suit all parties involved.

We may/need to change more than just the highlight portion depending on what comments/suggestions everyone has on this subject (keeping in mind that some of this

language is very specific)

A total volume of up to 250 cc of sterile saline, (5 aliquots of 50 cc each), will be injected and immediately aspirated through the channel in the bronchoscope using a syringe.

thanks and I look forward to your input,

mike

6. **Bronchoscopy.** Subjects will have undergone a physical examination including assessment for suitability for transnasal fiberoptic bronchoscopy at the Human Studies Facility by a board certified or board eligible pulmonologist.

Prior to the procedure, subjects will perform spirometry (as above); bronchoscopy will not be performed if lung function does not meet the recommended performance level (NIH guidelines; FEV1≥ 60 % predicted). Prior to bronchoscopy, a small tube (IV) will be placed in a vein for potential use in administering fluids. Subjects will receive inhaled albuterol prior to the bronchoscopy at the discretion of the pulmonary physician performing the procedure. Bronchoscopy with bronchoalveolar lavage and brush biopsy will be performed by a licensed physician who is Board certified or board eligible in pulmonary medicine and is experienced in fiberoptic bronchoscopy. The physician will be assisted by at least one R.N experienced in bronchoscopy. The subjects will be monitored closely throughout the procedure in the following manner: 1) Chest electrodes for continuous electrocardiogram, 2) Pulse oximetry of arterial blood, and 3) blood pressure monitoring using an electronic sphygmomanometer. Subjects will be premedicated with IV atropine (0.6 mg) to prevent bradycardia and hypotension that could result from vagal stimulation provoked by passing the bronchoscope through the subject's larynx and to minimize the amount of airways secretions. Nasal oxygen will be administered during the procedure. No sedatives and/or narcotics are administered at any time during bronchoscopy. We have found that premedication with sedatives (midazolam) or with opiates (demerol) is not required for research bronchoscopy subjects. Avoidance of these drugs reduces procedure risk and markedly shortens post-procedure recovery time. Topical lidocaine anesthesia will be used for subject comfort and to prevent cough, with a maximum dose of 15 ml of 2% lidocaine solution (360 mg lidocaine). Electrocardiographic and pulse oximeter will be monitored throughout the procedure. After the airways are visualized, the bronchoscope tip is wedged in a 4th-6th order bronchus (right middle lobe) for bronchial lavage. A volume of 20 cc of

sterile saline will be injected and immediately aspirated through the channel in the bronchoscope using a syringe. An additional 30 mls of saline will be injected and aspirated into the same lobe. The lavage fluid aliquots will be put in polypropylene tubes and kept on ice until processed. Up to 8 brush biopsies will then be obtained from the lower trachea, main, and lobar bronchi after topical application of 1% lidocaine. A cytology brush (Bronchoscope Cytology Brush; Bard, Tewksbury, MA) is applied to the region under direct visualization. For a single brushing, six passes, each with a linear excursion of 2-5 cm, are made with the brush along the endobronchial surface.

Subjects are observed and monitored for a minimum of 1 to hours after the procedure in the on-site medical station by a registered nurse with physician supervision. At discharge subjects will be symptom-free. At least 2 physicians, including the responsible bronchoscopist, will be available (24 hours daily) to subjects who develop any symptoms after discharge. The subject is discharged by a physician and is provided with the names and telephone numbers of the bronchoscopist and one other physician. The subject is contacted 24 hours post-bronchoscopy to ask about any untoward effects.

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----- Forwarded by Mike Schmitt/RTP/USEPA/US on 07/13/2010 02:54 PM -----

From: Robert Devlin/RTP/USEPA/US
To: Maryann Bassett/RTP/USEPA/US@EPA
Cc: Mike Schmitt/RTP/USEPA/US@EPA
Date: 07/13/2010 02:13 PM
Subject: Re: Bronchoscopy for Lamarck

No, I usually like to keep Mike in the dark as much as possible, but since he's the one writing the amendment, I guess I'll have to bring him into the loop this one time.

From: Maryann Bassett/RTP/USEPA/US
To: Robert Devlin/RTP/USEPA/US@EPA
Date: 07/13/2010 02:01 PM
Subject: Re: Bronchoscopy for Lamarck

Bob,

Thanks for the information. I noticed that Mike Schmitt wasn't on the e-mail. Do you want me to forward on to him?

Maryann

Maryann Bassett R.N.

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Chapel Hill, NC 27514

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From: Robert Devlin/RTP/USEPA/US
To: Maryann Bassett/RTP/USEPA/US@EPA, Tracey Montilla/RTP/USEPA/US@EPA, Heidi Hiers/RTP/USEPA/US@EPA, Martha Carraway/RTP/USEPA/US@EPA, Andy Ghio/RTP/USEPA/US@EPA, David Diaz-Sanchez/RTP/USEPA/US@EPA, Kelly Duncan/RTP/USEPA/US@EPA, Melanie Jardim/RTP/USEPA/US@EPA, Lisa Dailey/RTP/USEPA/US@EPA
Date: 07/13/2010 11:21 AM
Subject: Bronchoscopy for Lamarck

This morning the first bronchoscopy was performed for Lamarck. I would make the following recommendation for future Lamarck bronchs.

The protocol currently specifies that we will do a single 20 ml wash, followed by a single 30 ml wash. While this provides adequate fluid for our needs, it precludes the possibility of obtaining macrophages for in vitro work. It would be better if we had a more generic sentence in the protocol that indicated up to 4 (or 5?) washes may be performed. We do not need to specify the volume (or even location?) of the washes.

Although the protocol does not need to specify the order of brushes vs washes, I would recommend that the brushes go first. Otherwise we run the risk that we might have to stop the procedure before obtaining the required brushes and brushes are the #1 priority of this study.

If the brushes go first, then washes can be done (up to 4 or 5) until medical personnel or subject comfort dictates stopping. This will maximize the number of macrophages that can be obtained.

There is the likelihood that doing brushes first may contaminate the lavage fluid with plasma and/or epithelial cells, but I think this can be minimized by doing the brushes on one side and the lavage on the other.

Something else that doesn't need to be in the protocol but which is worth discussing is the volume of the first wash. When we and others started doing lavages for research purposes, the "standard" procedure was to do 6 50 ml washes. But about 1990 some papers from Rennard et al. showed that if only 20 mls was used for the first wash, it preferentially sampled the large airways. So we and others incorporated this modification into our standard procedure and analyzed the first wash separately from the others.

However, for this study, we don't care all that much about sampling the large airways. The primary purpose for obtaining BAL fluid is for proteomics analysis of that fluid. We don't recover enough fluid from a 20 ml first wash for proteomics so it makes more sense to me to just do 50 ml washes. Otherwise we will likely end up just throwing away that first aliquot anyway and 4-5 50 ml washes will provide a higher macrophage yield.

So... unless someone objects, I suggest that Mike talk with Martha Sue about appropriate language to put into an amendment.