NIH ARDS NETWORK

PROSPECTIVE, RANDOMIZED, MULTI-CENTER TRIAL OF HIGHER END-EXPIRATORY LUNG VOLUME/LOWER FiO_2 VERSUS LOWER END-EXPIRATORY LUNG VOLUME/HIGHER FiO_2 VENTILATION IN ALI/ARDS

(ALVEOLI)

CASE REPORT FORM INSTRUCTIONS
Version 1

October 27, 1999

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This manual contains instructions for completing the case report forms on patients enrolled in the ARDS Network study entitled "Prospective, randomized, multi-center trial of higher end-expiratory lung volume/lower FiO2 vs. lower end-expiratory lung volume/higher FiO2 ventilation in ALI/ARDS" (ALVEOLI).

- The format of the instructions is similar to the format of the case report form. Each section of the instructions has a title at the top of the first page similar to the title of the corresponding case report form pages. Within each section, the sequence of instructions is identical to the sequence of the questions on the case report form pages.
- A 💻 symbol indicates instructions specific to using a form in the MetaTrial system.

- In the MetaTrial CRFs: for questions with radio buttons, the option "No Answer" indicates that there has been no data entered, i.e., the question is blank.

- ADDITIONAL COMMENTS: Single or multiple comments can be entered on any field in the CRFs in the MetaTrial system. Use this option in place of the previous "additional comment" form to document any additional information regarding a data point. Comments can be entered or viewed by clicking on the "Show Info" button in the Form Toolbar and selecting "Comments" from the pull-down menu.

- Some of the case report form pages must be completed only once on each patient (e.g., "INCLUSION CRITERIA" and "BASELINE VENTILATOR PARAMETERS"). For these pages, the corresponding instruction manual pages will be required only once. Other case report form pages must be completed on several dates after enrollment (e.g., "ON STUDY VITAL SIGNS" AND "WEANING FORM"). For these pages, the corresponding instruction manual pages should be used each time the case report form page is completed.

- Most of the questions on the case report form screens are self-explanatory, and the corresponding instructions are brief. For other questions, additional information is provided in the instructions or a reference to a specific protocol section or operating procedure is given.

- For some of the questions, a value will not be available when the case report forms are being completed. This may occur because a value is pending or the chart was unavailable. In these instances, the coordinator should leave the field blank until the data can be obtained.

ALI SCREENING FORM

This form should be completed on all patients meeting the study inclusion criteria in regularly screened ICUs. It should also be completed for patients meeting the inclusion criteria identified in other ICUs.

Inclusion Criteria

Acute onset of:

1. **$PaO_2/FiO_2 \leq 300$. If altitude > 1000m, use $(PaO_2/FiO_2) \leq (300) * (B.P./760)$**
2. **Bilateral infiltrates consistent with pulmonary edema on frontal chest radiograph. The infiltrates may be patchy, diffuse, homogenous, or asymmetric.**
3. **Requirement for positive pressure ventilation via endotracheal tube.**
4. **No evidence of left atrial hypertension (if measured, pulmonary arterial wedge pressure < 18 mmHg x 12 hours).**

ITEM	DEFINITION	DATA RULES
	If a patient meets all inclusion criteria and no exclusion criteria AND it has been < 36 hours since all inclusion criteria were first met, she/he is eligible for study enrollment.	
1. Acute Onset	Select (Yes) or (No). Acute onset is defined as follows: PaO_2/FiO_2 ratio $\leq$ 300 (corrected for altitude) and bilateral infiltrates must be present for $\leq$ 28 days. If either is present continuously for > 28 days, the condition is not considered "acute", and the patient is not eligible for enrollment.	Required field.
	THE FOLLOWING INCLUSION CRITERIA (2a-c,3) MUST OCCUR WITHIN A SINGLE 24 HOUR INTERVAL (PROTOCOL SEC. 3.2).	
2a. $PaO_2/FiO_2 \leq 300$ (corrected for altitude)	Example PaO_2/FiO_2 calculation: If PaO_2=89 and FiO_2=.50, then PaO_2/FiO_2=89/.50 = 178.	Required field.
2b. Bilateral infiltrates consistent with pulmonary edema?	The infiltrates may be patchy, diffuse, homogeneous, or asymmetric. Infiltrates must not be caused solely by atelectasis, effusions, mass, plump or indistinct vessels, or shadows known to be chronic.	Required field.
2bb. Date/Time of CXR used to answer question 2b.	Select the date (click on the *date* button to activate the pop-up calendar) and time (military) of the QUALIFYING chest radiograph. Source documentation of qualifying chest film (date and signature of reader) is required.	Required field.
2c. Receiving positive pressure ventilation via endotracheal tube?	"Positive pressure ventilation" is defined as ventilation assistance wherein airway pressure is raised during inspiration and lowered during expiration. This excludes CPAP but includes Pressure Support, Pressure Control, and Assist/Control modes. "Endotracheal tube" may be an orotracheal, nasotracheal, or tracheostomy tube.	Required field.
3. No clinical evidence of left atrial hypertension. If measured, pulmonary arterial wedge pressure $\leq$ 18 mmHg.	Select the option that best applies. **Yes =NO evidence of left atrial hypertension; NO = evidence of left atrial hypertension is PRESENT.**	Required field.
4. PaO_2	Enter the PaO_2 used to calculate the P/F ratio in 2a above	Required field.
5. FiO_2	Enter the FiO_2 used to calculate the P/F ratio in 2a above. Enter as a decimal (e.g., 50% should be entered as .50).	Required field.

ALI SCREENING FORM

(Continuation)

6. Enter the first date that all these criteria exist simultaneously	Select the first calendar date from the pop-up calendar when ALL inclusion criteria (2a-c, 3) first occur together. Example: If the P/F criterion was first met on 1/30/96 but the chest x-ray did not show bilateral infiltrates until 2/1/96 and the patient STILL met the P/F criterion on 2/1/96, then the first date both were met would be 2/1/96	Required field.
7. Gender	Select the appropriate option.	Required field.
8. Ethnicity	Select the option that best applies: 1=White, not of Hispanic Origin, 2=Black, not of Hispanic Origin, 3=Hispanic, 4=Asian/Pacific Islander, 5=American Indian/Alaskan Native, 6=Other.	Required field.
9. Age	Enter patient's age in years at last birthday.	Required field.
10. Location	Select the option that indicates patient's current location: MICU, SICU, Cardiac SICU, CCU, Neuro ICU, Burn, Trauma, Cancer Unit, MICU/SICU, Other.	Required field.
11. Regularly Screened ICU	Enter (Yes) if this ICU is screened at least 5 days each week for ARDSNet studies.	Required field.
12a. Primary Reason for Exclusion	Select the option from the list that indicates the most important condition that led to exclusion (if any). Refer to protocol section 3.3 (pg 16) and Appendix A for definitions of specified exclusion criteria such as chronic lung disease, terminal illness, chronic liver disease, acute liver disease, morbid obesity.	Required field.
12 b. If not excluded but not enrolled, explain.	Occasionally patients meet all inclusion criteria and no exclusion criteria but are not enrolled because they improve quickly or die quickly within the 36 hour enrollment window. For these patients, complete this item.	Required field if 13a = not excluded.
13. If chronic liver disease, enter Child-Pugh	If the patient has chronic liver disease, compute Child-Pugh. The patient is excluded if the score is $\geq$ 10. See Appendix A of the protocol for Child-Pugh formula.	
14. Lung Injury Category	Enter one primary and 0-4 secondary causes of lung injury: Trauma, Aspiration, Sepsis, Multiple Transfusions, Other. The "primary" category should be the most immediate cause. E.g., a patient with multiple trauma who develops sepsis and then ALI: primary category = sepsis; secondary category = trauma.	Required field.
COMPLETE THE FOLLOWING QUESTIONS FOR SCREENED PATIENTS ONLY – NOT FOR PATIENTS ENROLLED IN ARDSNET 04		
15. Patient able to sustain a period of unassisted breathing for 48 hours during the first 60 days?	Select (Yes) or (No) to indicate if patient achieved 48 hours of unassisted breathing anytime during the first 60 days after the date of screening.	If available.
15a. If yes, enter the START date that the first period of unassisted breathing was achieved that lasted for 48 hours or more.	Select the date from the pop-up calendar that unassisted breathing began.	Required field for all patients who are screened but not enrolled in the study
16. Was patient discharged from study hospital during the first 60 days?	Enter (Yes) or (No) to indicate if patient was discharged (alive or dead) from the study hospital during the first 60 days following the date of screening.	Required field for all patients who are screened but not enrolled in the study
16a. If yes, give discharge date:	Select the date from the pop-up calendar that the patient was discharged.	Required field if 16 =Yes.
17. Status at discharge:	Select (Alive) or (Dead) to indicate the patient's status at time of discharge.	Required field if 16 =Yes.

ENROLLMENT FORM

Complete this form on all patients who are being enrolled in the study.

ITEM	DEFINITIONS	DATA RULES
1. Has informed consent been obtained?	For questions a, b, & c indicate if patient/family consent has been obtained for *each* of the 3 layers of consent:.	
1a. For participation in ALVEOLI?	Informed consent **must** be obtained before any study procedures are initiated. Select "Yes" (1) if informed consent has been obtained. Select "No" (2) if informed consent has not been obtained.	Required field.
GENETIC TESTING	**PATIENT OR SURROGATE CAN REFUSE THEIR CONSENT FOR GENETIC TESTING AND PARTICIPATE IN THE STUDY**	
1b. For genetic testing related to ALVEOLI?	If the patient or surrogate has given consent for genetic testing only for this study, Select “Yes” (1), otherwise, select “No” (2).	Required field.
1c. For genetic testing related to future studies?	If the patient or surrogate has given consent for genetic testing not limited to this study, select “Yes”, otherwise, enter “No”.	Required field.
2. Enter randomization number	Enter the nine-digit study number assigned by the coordinating center voice randomization system (IVRS).	Required field.
3. Patient randomized to:	Select the treatment assignment given by the CCC IVRS: either (1) lower PEEP/high FiO2; (2) higher PEEP/low FiO2 with Recruitment maneuvers on Days 1& 3; or (3) higher PEEP/low Fi02 with Recruitment maneuvers on Days 2 & 4.	Required field.
4. Date/Time (military) of initial ventilator change.	Select the date from the pop-up calendar and time (24-hour clock) of initial study ventilator changes, if any. If no ventilator changes were necessary to initiate study, enter time that ventilator changes would have been made if they were necessary.	Required field.

APACHE III - DEMOGRAPHICS
Enrollment

Complete this form on all patients enrolled into the study.

ITEM	DEFINITION	DATA RULES
1. Hospital Admission Date	Select the date from the pop-up calendar the patient was admitted to the study hospital.	Required field.
2. ICU Admission Date	Select the date from the pop-up calendar of the current ICU admission.	Required field.
3. Time of ICU Admission	Enter the time the patient was admitted to the current ICU.	Required field.
4. Patient Admitted Directly From:	Select the location where the patient was **immediately prior** to this ICU admission (OR, Recovery Room, ER, Floor, Another Special Care Unit, Another Hospital, Direct Admit, Step-down Unit).	Required field.
5. Is the patient immediately post-operative from elective surgery?	Select the option that best applies.	Required field.
6. ICU Readmit?	During this hospitalization, was the patient in an ICU prior to this current ICU admission? (Yes/No)	Required field.
7. ICU Readmit within 24 hours?	If item 6 is answered "yes", was the readmission to the ICU within 24 hours of a previous ICU discharge?	Required field.
8a. Chronic Health Information Available?	Select (Yes) or (No). Chronic health information may be updated at any time during the admission. If any of the following chronic health items (items 8b-9h) are diagnosed during the hospital admission AND **PRIOR** to study entry, record the item as present on study entry.	Required field. If item 8a = (No), then skip to question 10.
8b. Is the patient on chronic dialysis or peritoneal dialysis?	Select (Yes) or (No) to indicate if the patient required dialysis prior to hospitalization.	Required field only if 8a = (Yes).
9a. AIDS?	Select (Yes) or (No). Enter (No) if HIV positive but without other AIDS criteria.	Required field only if 8a =(Yes).
9b. Leukemia (AML, CML, all lymphocytic leuk., multiple myeloma)	Select (Yes) or (No).	Required field only if 8a =(Yes).
9c. Non-Hodgkins Lymphoma	Select (Yes) or (No).	Required field only if 8a =(Yes).
9d. Solid Tumor with metastasis	Select (Yes) or (No).	Required field only if 8a =(Yes).
9e. Immune Suppression	Select (Yes) or (No) to indicate if the patient is immunocompromised secondary to chemotherapy, radiation therapy, use of anti-rejection drugs taken after organ transplant, or the daily use of high doses of steroids (0.3 mg Prednisone kg/day or equivalent therapy) within part of or the entire previous six months.	Required field only if 8a = (Yes).

9f. Hepatic Failure	Select (Yes) or (No) to indicate if the patient has decompensated cirrhosis (Hepatic Failure) as evidenced by one or more episodes of jaundice and ascites, upper gastrointestinal bleeding or hepatic encephalopathy or comas.	Required field only if 8a =(Yes).

APACHE III - DEMOGRAPHICS
Enrollment (Continuation)

9g. Compensated cirrhosis.	Select "1" (Yes) or "2" (No) to indicate if the patient has cirrhosis without the stigmata indicated above in 9f. If the patient has a functioning liver transplant, this chronic health item would not apply.	Required field only if 8a = (Yes).
9h. Diabetes Mellitus	Select (Yes) or (No).	Required field only if 8a = (Yes).
10. Vasopressors last 24 hours?	Select (Yes) or (No) to indicate if the pt has received any vasopressors within the last 24 hours prior to initial vent changes.	Required field.
11. Protocol defined ethanol use?	Select (Yes) or (No) to indicate if patient consumes alcohol.	Required field.

APACHE III PHYSIOLOGY
Enrollment

COMPLETE ON DAY 0. ALL DATA SHOULD BE TAKEN FROM THE 24 HOURS PRECEDING INITIAL VENTILATOR CHANGES (IF ANY). DO NOT INCLUDE INTRAOPERATIVE VALUES OR VALUES RELATED TO DEATH OR CARDIO/RESPIRATORY ARREST SITUATIONS.

For items on this table indicated with "*" (items 8-18), if no values were obtained for clinical purposes during the 24 hours preceding initial study procedures, the lab tests must be obtained before initiating study procedures.

ITEM	DEFINITION	DATA RULES
1. Temperature	Enter the highest and lowest temperatures in Centigrade or Fahrenheit. Add 1 degree Centigrade or 2 degrees Fahrenheit if axillary temperatures.	Required field.
2. Systolic BP	Enter the highest and lowest.	Required field.
3. Mean Arterial Pressure	Enter the highest and lowest.	Required field.
4. Heart Rate	Enter the highest and the lowest.	Required field.
5. Respiratory Rate	Enter the highest and the lowest.	Required field.
6a. Was patient ventilated when the lowest respiratory rate occurred?	Select (Yes) or (No).	Required field.
6b. Was patient ventilated when the highest respiratory rate occurred?	Select (Yes) or (No).	Required field.
7. Urine Output 24 hr	Enter the amount of urine output (ml) in the 24 hrs prior to initial ventilator changes (if any). E.g., if initial ventilator changes occur on 2/1/96 at 1400, then the urinary output listed should be from 1/31/96 at 1400 to 2/1/96 at 1400). If a large volume of urine was inadvertently spilled or the urine was not measured, leave the field blank. A urine output value of zero indicates that the patient produced no urine.	Required field.
8 Hematocrit*	Enter highest and lowest values as "00.0" (e.g., "35.2", not " .352"). If only one value is present for 24 hour period, enter this value as both the highest and lowest.	Required field.
9. WBC* (White Blood Cell count).	Enter highest and lowest as "00000" (e.g., a WBC of 14,200 should be entered as "14200" Do not add comma.). If only one value present for 24 hour period, enter it as both the highest and lowest.	Required field.
10. Platelets*	Enter only the lowest value during the 24 hours. Enter as "000" (e.g., a platelet count of 258,000 should be entered as "258".	Required field.
11. Serum Sodium*	Enter highest and lowest. If only one value present for 24 hour period, it should be entered as both the highest and lowest.	Required field.

APACHE III – PHYSIOLOGY
Enrollment (Continuation)

12. Serum Potassium*	Enter highest and lowest. If only one value present for 24 hour period, it should be entered as both the highest and lowest.	Required field.
13. Serum BUN*	Enter only highest value.	Required field.
14. Serum Creatinine*	Enter highest and lowest. If only one value present for 24 hour period, it should be entered as both the highest and lowest.	Required field.
15. Serum Glucose*	Enter highest and lowest. If only one value present for 24 hour period, it should be entered as both the highest and lowest.	Required field.
16. Serum Albumin*	Enter highest and lowest. If only one value present for 24 hour period, it should be entered as both the highest and lowest.	Required field.
17. Serum Bilirubin*	Enter only highest value.	Required field.
18. Serum Bicarbonate*	Enter only lowest value.	Required field.

APACHE ARTERIAL BLOOD GASES
Enrollment

Record ALL ABG's in the 24 hours preceding initial study ventilator changes, if any. One set of ABG values is required for the study. Record "Yes" or "No" if the patient was intubated (with or without positive pressure ventilation) when each ABG was obtained.

Select "New Copy" from the menu to the left of the form to create another copy of the row if there is more than one set of ABG values to enter. Repeat this process to record all available ABG values. Use the "Next Copy" and "Previous Copy" buttons to navigate between individual entries. Scroll through the lower section at the bottom of the form to view all entries at once.

	FiO_2	PaO_2	$PaCO_2$	pH	Intubated?	DATA RULES
NEW COPY						Required field.
						Record values, if available.
SAVE						Record values, if available.
						Record values, if available.
EDIT						Record values, if available.
						Record values, if available.
NEXT COPY						Record values, if available.
						Record values, if available.
PREVIOUS COPY						Record values, if available.
						Record values, if available.
						Record values, if available.
NAVIGATE						Record values, if available.

VITAL SIGNS DAY-0

VALUES FOR ITEMS 2-5 SHOULD BE OBTAINED IN THE 4 HOUR INTERVAL THAT PRECEDES INITIAL STUDY VENTILATOR CHANGES, IF ANY. IF MORE THAN ONE VALUE IS AVAILABLE DURING THIS INTERVAL, RECORD THE VALUE CLOSEST TO THE TIME THAT STUDY PROCEDURES WERE INITIATED.

Values for items 6-21 may be obtained during the 24 hour interval preceding initial study ventilator changes, if any. If no values were obtained for clinical purposes during this interval, a blood specimen or measurement should be drawn and sent prior to study initiation. If more than one value is available, use the most recent value before study initiation.

ITEM	DEFINITION	DATA RULES
1. Date and Time of current intubation	Select the date from the pop-up calendar and time (24 hour clock) that indicates when positive pressure ventilation was initiated via endotracheal tube.	Required field.
	ITEMS 2-5 ARE MOST RECENT IN THE 4 HOURS PRECEDING INITIAL VENT CHANGE	
2. Heart Rate	Use last value prior to study initiation.	Required field.
3. Systolic BP	Use last value prior to study initiation.	Required field.
4. Diastolic BP	Use last value prior to study initiation.	Required field.
5. Temperature	Use last value prior to study initiation. Prefer rectal, tympanic, or core temperature. If axillary used, add 1 degree Centigrade or 2 degrees Fahrenheit.	Required field.
6. Height	Record patient's height from heel to crown. Patient should be supine with legs straight (no flexion or extension of hips and knees, if possible), during measurement. This value should be documented in the source documents (ie, pt chart or study file).	Required field.
7. PBW (Predicted Body Weight)	Enter Predicted Body Weight in kilograms. This value should be documented in the source documents (ie, pt chart or study file). Utilize the formula below to calculate PBW: Males: IBW = 50 + 2.3(inches – 60) Female: IBW = 45.5 + 2.3(inches – 60)	Required field.
8. Measured Weight	Enter most recent measured body weight. If weight not available during preceding 24 hours, enter most recent weight. Note technique for weighing patient (bed-scale, lift, etc.) on medical record.	Collect data, when available.
9. Pulmonary Artery Catheter?	Select (Yes) or (No) if patient has a PA catheter at time of enrollment. If (No) skip to item 10.	Required field.
a. PA systolic	Enter value in mm Hg.	Required field, if 9 is (Yes).
b. PA diastolic	Enter value in mm Hg.	Required field, if 9 is (Yes).
c. PA mean	Enter value in mm Hg.	Required field, if 9 is (Yes).
d. PAOP (Pulmonary Artery Occlusion Pressure or *wedge pressure*)	Enter value in mm Hg.	Required field, if 9 is (Yes).

VITAL SIGNS DAY 0
(continued)

e. CVP (Central Venous Pressure)	Enter value in mm Hg.	Required field, if 9 is (Yes).
f. Cardiac index	Enter the cardiac output, indexed to the pt's BSA, in L/min/m^2	Required field, if 9 is (Yes).
10. Hct	Enter value as "00.0" (e.g., 39.3).	Required field
11. WBC	Enter value as "00000" (e.g., if WBC = 14,200, enter "14200". Do not use comma.	Required field.
12. Platelets	Enter as "000" (e.g., a platelet count of 258,000 should be entered as "258".	Required field.
13. Albumin	Enter value as g/dL.	Required field.
14. Sodium	Enter value as mEq/L	Required field.
15. Potassium	Enter value as mEq/L	Required field.
16. Glucose	Enter value as mg/dL	Required field.
17. Creatinine	Enter value as mg/dL	Required field.
18. BUN	Enter value as mg/dL	Required field.
19. HCO3	Enter value as mEq/L	Required field.
20. HCG (pregnancy test)	Select (Positive) or (Negative). All females of childbearing potential should be tested prior to initiation of study procedures. Use (N/A) for instances where this test would not apply, i.e., male patients or females with hysterectomy. 💻 Document N/A selections due to hysterectomy in a comment to the field.	Required field.

Collect blood for cytokines prior to initial vent change.	Collect plasma for blood cytokines as follows: 1. Draw blood from patient via arterial line, venous line, or by venipuncture. Use at least an 18 gauge needle for venipuncture and when instilling blood into the purple top vacutainer to prevent hemolysis of the specimen. Hemolyzed samples should be redrawn if possible. 2. Gently invert the vacutainer 2-3 times to mix. 3. Place on ice if unable to centrifuge immediately. 4. Centrifuge for 10 minutes at approximately 1500-3000 rpm (standard table-top centrifuge may be used). 5. Withdraw plasma (do not remove buffy coat) using a pipette or syringe and fill purple top micro tubes (1 ML OF PLASMA IN EACH OF 12 TUBES) with plasma. 6. Attach appropriate bar-coded label, which contains an ID number and contents of tube. 7. Place on ice until able to freeze at -70° C (ASAP). 8. Comment on any deviation from protocol, such as late sampling or hemolyzed samples.	

BASELINE VENTILATOR PARAMETERS
Enrollment

The following information should be taken from the four-hour interval that immediately precedes initial study ventilator changes, if any. If more than one value is available during this four-hour interval, enter the last value prior to initial study ventilator changes. Enter date and time of initial ventilator changes in the indicated field.

ITEM	DEFINITION	DATA RULES
1. Ventilator manufacturer and model	Select the type of ventilator that the patient is on: Puritan 7200, Servo 9000, Servo 300, Hamilton Veolar/Amadeus, Bird 8400, Bear 1000, other ventilator, or Draeger.	Required field.
2. Ventilator mode	Indicate what mode of ventilation the pt is receiving. Select all that apply: (SIMV, Pressure Support, Assist/Control, Pressure Control, PCIRV, Other.	Required field.
3. Calculated delivered tidal volume	Enter the corrected inspired tidal volume: inspired tidal volume (ml) set on the ventilator minus any additional tidal volume added to correct for has compression and ventilator tube expansion (this should = the tidal volume called for by the protocol; this will not = the volume set on the ventilator unless the ventilator makes automatic adjustments for gas compression/tube expansion). Puritan-Bennett 7200's and some other ventilators make this correction automatically (for these vents the value set on the vent = the calculated delivered tidal volume).	Required field for SIMV and A/C modes.
4. Pressure Control Level	Enter the pressure control level (cm H_2O) on the ventilator if the patient is on Pressure Control Ventilation or PCIRV.	Required field for PC and PCIVR modes.
5. Pressure Support	Enter the level of Pressure Support (in cmH_2O) if the patient is receiving pressure support ventilation either in the Pressure Support or SIMV with Pressure Support mode. The Pressure Support level indicates the increment in airway pressure during inspiration above its level during expiration. For example, if PEEP = 5 and inspired airway pressure = 20, then enter Pressure Support = 15.	Required field for PS and SIMV +PS modes.
6. Set Rate	Enter the rate set on the ventilator if the patient is on the SIMV, SIMV with Pressure Support, Assist/Control, or Pressure Control mode. (This is the minimum rate set on the ventilator, not the patient rate).	Required field.
7. Total Respiratory Rate	Enter the total respiratory rate, which may exceed the Set Rate above if the patient is making additional inspiratory efforts.	Required field.
8. Total Minute Ventilation (V_E)	Enter the total minute ventilation in liters per minute. This value is available from a digital report on the ventilator.	Required field.
9. PEEP	Enter the PEEP applied on the ventilator in cmH_2O. This is the external or applied PEEP, not the total PEEP, auto-PEEP, or intrinsic PEEP.	Required field.

(Continuation)

10. Plateau Pressure (Pplat)	Enter the value for plateau pressure measurement in cm H20. The plateau pressure measurement should be made with a 0.5 second inspiratory pause.	Required field for SIMV and A/C modes.
11. Peak Inspiratory Pressure	Enter the peak inspiratory airway pressure (cmH_2O). This should be obtained while the patient is relaxed, not coughing or moving in bed.	Required field for SIMV and A/C modes.
12. I:E Ratio	Enter the ratio of the duration of inspiration to expiration. Monitor the I:E ratio for at least one minute and enter a representative value.	Required field.
13. Mean Airway Pressure	Enter the mean airway pressure (cmH_2O). This should be obtained while the patient is relaxed, not coughing or moving in bed.	Required field.
14. FiO_2	Enter the fraction of inspired oxygen as decimal (e.g., ".50", not 50%)	Required field.
15,16,17: PaO_2, $PaCO_2$, and Arterial pH	Enter results of the last arterial blood gas prior to initial study ventilator changes.	Required field.
18. SpO_2	Enter pulse oximetry value prior to study ventilator changes. Observe the oximeter values for at least one minute and enter a representative value.	Required field.
INITIAL RECRUITMENT MANEUVER MEASUREMENTS	OBTAIN ITEMS 19-21 BELOW AFTER INITIAL VENT CHANGES (IF ANY) HAVE BEEN INITIATED. VALUES SHOULD BE OBTAINED ON A TIDAL VOLUME OF 6-8 ML/KG PBW BUT BEFORE OTHER PROTOCOL DIRECTED CHANGES	
19. Calculated delivered tidal volume	Enter the corrected inspired tidal volume: inspired tidal volume (ml) set on the ventilator minus any additional tidal volume added to correct for has compression and ventilator tube expansion (this should = the tidal volume called for by the protocol; this will not = the volume set on the ventilator unless the ventilator makes automatic adjustments for gas compression/tube expansion). Puritan-Bennett 7200's and some other ventilators make this correction automatically (for these vents the value set on the vent = the calculated delivered tidal volume).	Required field.
20. Pplat	Enter the value for plateau pressure measurement in cm H20.	Required field.
21. PEEP	Enter the PEEP applied on the ventilator in cmH_2O. This is the external or applied PEEP, not the total PEEP, auto-PEEP, or intrinsic PEEP.	Required field.

CHEST X-RAY/BAROTRAUMA
Enrollment

Use the most recent chest radiograph *prior to initial ventilator changes*. This film may not necessarily be the "qualifying" x-ray that was used to determine ARDS onset. This film is used to assess the patient's baseline for barotrauma for comparison to on-study films. On-study barotrauma occurrence will be captured on the new *Barotrauma Form*.

ITEM	DEFINITION	DATA RULES
1. Number of quadrants with infiltrates.	Enter a number from 0 through 4 that indicates the number of quadrants with pulmonary infiltrate. Shadows interpreted as infiltrates may not be caused by effusions, atelectasis, masses, indistinct or plump blood vessels, or shadows known to be chronic.	Required field.
2. Barotrauma: Pneumothoraces	Select the appropriate item to indicate if there is a pneumothorax on the right side (1), on the left side (2), on both sides, bilateral (3), or none (4).	Required field.
Subcutaneous emphysema	Select (Yes) or (No) to indicate presence of subcutaneous emphysema apparent on the chest x-ray or by physical exam that is attributed to barotrauma.	Required field.
Pneumomediastinum	Select (Yes) or (No) to indicate if the chest x-ray shows air in the mediastinum attributed to barotrauma.	Required field.
Pneumatoceles > 2 cm diameter	Select the appropriate item to indicate if there are one or more pneumatoceles > 2 cm minimum diameter (a bubble or hole in the parenchyma that is not attributed to a chronic bleb or bullous lesion), on the right side (1), the left side (2), on both sides, bilateral (3), or on neither side (4).	Required field.
3. Chest Tube	Select the appropriate item to indicate if there are one or more chest tubes on the right side (1), on the left side (2), on both sides (3), or on neither side (4).	Required field.

MEDICATION REPORT
Enrollment

Complete this form using information pertaining to the 24 hour interval that precedes initial study ventilator changes.

ITEM	DEFINITION	DATA RULES
1 Neuromuscular blocking agents.	Select (Yes) or (No) to indicate if patient has received pancuronium, vecuronium, atracurium, succinylcholine, or other medication for neuromuscular blockade within 24 hours prior to study initiation.	Required field.
2. Vasopressors	Select (Yes) or (No) to indicate if vasopressors are in use at the time of initial vent change.	Required field.
a. Dopamine $\geq$ 6 mcg/kg/min b. Norepinephrine c. Neo-Synephrine d. Epinephrine	If 2 =yes, enter the infusion rate for all that apply at the time of initial vent change. "Vasopressor" is defined as: I. Dopamine $\geq$ 6 mcg/kg/min; dopamine at a rate < 6 is not considered a vasopressor. II. II. Norepinephrine, Neo-Synephrine, or epinephrine (in mcg/min). Dobutamine is not considered a vasopressor.	Do NOT use a "0" to indicate a pressor that the pt is not receiving, leave the field blank.
Sedatives/analgesics	Enter the IV infusion (hourly rate) at the time of initial vent change (left column fields) **AND** the total amount of boluses given in the one hour period PRIOR TO initial vent change (right column fields).	
5-14. Diazepam (Valium), Other benzo, Propofol, Morphine, Demerol (Meperidine), Other narcotic, Haldol (Haloperidol), Droperidol, Other drug:	I. Enter the infusion rate in mg/hr for all that apply. II. Enter the TOTAL amount of boluses in mg received in the 1 hour period prior to initial vent changes. III. For "other" items enter the name of the drug in the corresponding field.	Do NOT use a "0" to indicate a drug that the pt is not receiving, leave the field blank.
(#9.) Fentanyl:	Enter as above in mcg/hr and mcg respectively.	

GLASGOW COMA SCORE
Day 0

Complete this form on Day 0 Only. Use the worst values for the date.

ITEM	DEFINITION	DATA RULES
Glasgow Coma Score (GCS)	Use the options listed on the CRF to calculate the worst GCS for this calendar date. All three components should originate from the same time point.	Required field.
1. Pt on sedative or neuromuscular blocker?	Select (Yes) or (No).	Required field.
1. Eye Opening Score	Select the option that indicates the best response. If patient's eyes are swollen shut, estimate best response.	Required field.
2. Motor Response Score	Select the option that indicates the best response.	Required field.
3. Verbal Response Score	Select the option that indicates the best response. If patient was intubated on this date select from the “on vent” pick-list and use clinical judgment to estimate best response. If unsure, enter "3".	Required field.
4. GCS (total)	Computer calculated total Glasgow Coma Score.	Calculated value.

ON STUDY VITAL SIGNS
Dates after Date of Enrollment: 1, 2, 3, 4, 7, 14, 21, and 28

Complete this form on the dates following the date of enrollment shown above if the patient is alive and receiving mechanical ventilation or is attempting a 48 hour period of unassisted breathing. Discontinue completing this form after the patient has achieved 48 hours of unassisted breathing.

PARAMETERS INDICATED WITH "*" MUST BE MEASURED DURING THE REFERENCE PERIOD 0600-1000 ON THE CALENDAR DATE. IF MORE THAN ONE VALUE IS AVAILABLE FROM 0600-1000, RECORD THE VALUE CLOSEST TO 0800.

FOR PARAMETERS NOT INDICATED WITH "*", USE VALUES CLOSEST TO 0800, IF AVAILABLE. IF VALUES ARE NOT AVAILABLE FROM 0600-1000, USE VALUES CLOSEST TO 0600-1000 ON THIS CALENDAR DATE.

ITEM	DEFINITION	DATA RULES
1. Heart Rate*	Enter value recorded between 0600-1000. If more that one, enter the value closest to 0800.	Required field.
2. Systolic BP*	Enter value recorded between 0600-1000. If more that one, enter the value closest to 0800.	Required field.
3. Diastolic BP*	Enter value recorded between 0600-1000. If more that one, enter the value closest to 0800.	Required field.
4. Temperature*	Rectal, tympanic, or core temperature preferred. If axillary temperature used, add 1^{o} C or 2^{o} F.	Required field.
5. Weight	Enter actual body weight measured on this date, if available.	Required field.
6. Fluid Intake	Record total fluid intake (parenteral and enteral) during 24 hours preceding the reference interval 0600-1000.	Required field.
7. Urine Output	Record total urine output during 24 hours preceding the reference interval 0600-1000.	Required field.
8. Hematocrit	Record Hematocrit if measured on this calendar date. Enter as "00.0".	Required field.
9. WBC	Record white blood cell count if measured on this calendar date. Record as "00000" (e.g., if WBC = 14,300, enter as "14300". Do not use a comma.	Required field.

ON STUDY VITAL SIGNS
(Continuation)

Collect blood for cytokines on Days 1, 3, 7.	Collect plasma for blood cytokines **only on on-study Days 1, 3, and 7**: 1. Draw blood from patient via arterial line, venous line, or by venipuncture. Use at least an 18 gauge needle for venipuncture and when instilling blood into two 10 mL purple-top vacutainers to prevent hemolysis of the specimen. Hemolyzed samples should be redrawn if possible. 2. Gently invert the vacutainer 2-3 times to mix. 3. Place on ice if unable to centrifuge immediately. 4. Centrifuge for 10 minutes at approximately 1500-3000 rpm (standard table-top centrifuge may be used). 5. Withdraw plasma (do not remove buffy coat) using a pipette or syringe and fill purple top micro tubes (1 ML OF PLASMA IN EACH OF 12 TUBES) with plasma. 6. Attach appropriate bar-coded label, which contains an ID number and contents of tube. 7. Place on ice until able to freeze at -70^{o} C (ASAP). 8. Comment on any deviation from protocol, such as late sampling or hemolyzed samples.	Required field.

ON STUDY VENTILATOR PARAMETERS
Dates after Date of Enrollment: 1, 2, 3, 4, 7, 14, 21, and 28

Complete this form on the dates after the date of enrollment shown above if the patient is alive and receiving mechanical ventilation or is attempting a 48 hour period of unassisted breathing. Record data from the Reference Interval from 0600-1000. When more than one value is available during this interval, record the value closest to 0800. ***Discontinue this form after the patient has achieved 48 hours of unassisted breathing.***

ITEM	DEFINITION	DATA RULES
1. Calculated delivered tidal volume	Enter the corrected inspired tidal volume: inspired tidal volume (ml) set on the ventilator minus any additional tidal volume added to correct for has compression and ventilator tube expansion (this should = the tidal volume called for by the protocol; this will not = the volume set on the ventilator unless the ventilator makes automatic adjustments for gas compression/tube expansion). Puritan-Bennett 7200's and some other ventilators make this correction automatically (for these vents the value set on the vent = the calculated delivered tidal volume).	Required field.
2. Pressure Support	Enter the level of Pressure Support (in cmH_2O) if the patient is receiving pressure support ventilation either in the Pressure Support or SIMV with Pressure Support mode. The Pressure Support level indicates the increment in airway pressure during inspiration above its level during expiration. For example, if PEEP = 5 and inspired airway pressure = 20, then enter Pressure Support = 15.	
3. Set Rate	Enter the rate set on the ventilator if the patient is on the SIMV, SIMV with Pressure Support, Assist/Control, or Pressure Control mode. (This is the minimum rate set on the ventilator, not the patient rate).	Required field.
4. Total Respiratory Rate	Enter the total respiratory rate, which may exceed the Set Rate above if the patient is making additional inspiratory efforts.	Required field.
5. Total Minute Ventilation	Enter the total minute ventilation in liters per minute. This value is available from a digital report on the ventilator.	Required field.
6. PEEP	Enter the PEEP applied on the ventilator in cmH_2O. This is the external or applied PEEP, not the total PEEP, auto-PEEP, or intrinsic PEEP.	Required field.
7. Plateau Pressure	The plateau pressure measurement should be made with a 0.5 second inspiratory pause.	Required field.
8. Peak Inspiratory Pressure	Enter the peak inspiratory airway pressure (cmH_2O). This should be obtained while the patient is relaxed, not coughing or moving in bed.	Required field.

(continued)

9. I:E Ratio	Enter the "True I:E" if patient is on a ventilator that displays actual I:E ratios with each breath (Puritan Bennett ventilators do this). Enter the "set I:E" if the patient is on a ventilator that does not display actual I:E ratios (Siemens 900 ventilators do not). (On ventilators that do not display actual I:E ratios, the therapist selects a % Inspiratory Time to achieve a Set I:E ratio, assuming the Total Respiratory Rate = Set Rate. If the % Inspiratory Time = 33%, then the Set I:E ratio = 1:2. If % Inspiratory Time = 25%, then the Set I:E ratio = 1:3. If the % Inspiratory Time = 50%, the Set I:E ratio = 1:1	Required field.
10. Mean Airway Pressure	Enter the mean airway pressure (cmH_2O). This should be obtained while the patient is relaxed, not coughing or moving in bed.	Required field.
11. FiO_2	Enter the fraction of inspired oxygen as decimal (e.g., ".50", not 50%)	Required item.
12, 13, 14. PaO_2, $PaCO_2$, and Arterial pH	Enter results of arterial blood gas analysis. If no ABG obtained during 0600-1000, record value closest in time to this interval on this calendar date.	Required item.
15: SpO_2:	Enter pulse oximetry value. Observe the oximeter values for at least one minute and enter a representative value.	Required item.

ON STUDY RECRUITMENT MANEUVER

Complete this form on Days 1-4 for ALL patients, Hi PEEP *AND* Lo PEEP:

1) **Patients will be randomized to RMs on either EVEN days (study days 2 & 4) or ODD days (study days 1 & 3). RMs should be performed closest to 8 AM in the reference period. Data collection on days when a RM is not performed is also required and should start at 8 AM (as "Time Zero") in the reference period.**
2) **For Lo PEEP pts: answer questions 1-12, 23, and 24 for ALL pts. Use "Time Zero" in place of the recruitment maneuver.**
3) **For source documentation, record data on the "ALVEOLI RM Log" (provided in the SOP section of the study binder) and retain in pt chart or study file.**

ITEM	DEFINITION	DATA RULES
1a. Was RM performed?	Select (Yes), (No), or Not Required (for non-RM days or Lower PEEP pts) if a RM was performed on this date.	Required item.
1b. If no state why.	State why the RM was not performed.	Required item if 1a= (No).
2. Time RM started or Time Zero (non-RM days or Lo PEEP pts)	Enter the time that RM was initiated or Time Zero for non-RM days and Lo PEEP pts.	Required item.
3. RM pressure	Enter the pressure used in cm H20 (for Hi PEEP pts).	Required item if 1a =(Yes).
4. RM duration	Enter the total time of RM in seconds.	Required item if 1a= (Yes).
PRE-RECRUITMENT	FOR ITEMS 5-10 ENTER BASELINE VALUES IMMEDIATELY PRECEDING THE TIME IN ITEM 2	COLLECT ON ALL PTS (Hi PEEP AND Lo PEEP)
5. Pre-RM SpO2:	Enter the pulse oxymetry value immediately prior to the RM time (or Time Zero) entered in item 2.	Required item.
6. Pre-RM FiO2:	Enter the Fi02 that the pt was receiving when the Sp02 was recorded in item 5 above.	Required item.
7. Pre-RM PEEP:	Enter the amount of PEEP pt was receiving immediately prior to the RM time (or Time Zero) entered in item 2.	Required item.
8. Pre-RM Plateau pressure:	Enter the plateau pressure measured immediately prior to the RM time (or Time Zero) entered in item 2.	Required item
9. Pre-RM Calculated VT:	Enter the calculated tidal volume that the pt was receiving (in mL) immediately prior to the RM time (or Time Zero) entered in item 2	Required item.
10. Pre-RM SBP:	Enter the blood pressure (S/D) recorded immediately prior to the RM time (or Time Zero) entered in item 2.	Required items.
11. Pre-RM DBP:		
12. Pre-RM HR:	Enter the heart rate recorded immediately prior to the RM time (or Time Zero) in item 2.	Required item.
DURING RECRUITMENT	FOR ITEMS 13-18 ENTER VALUES FROM THE 10 MINUTE INTERVAL BEGINNING AT TIME IN ITEM 2	COLLECT ON Hi PEEP PATIENTS ONLY
13. Lowest SpO2:	Enter the lowest SpO2 that occurred in the 10-minute period from the time in item 2.	Required item.
14. Highest SpO2:	Enter the highest SpO2 that occurred in the 10-minute period from the time in item 2.	Required item.

RECRUITMENT MANEUVER (RM)
(Continued)

15. Lowest SBP: 16: Lowest DBP:	Enter the lowest blood pressure (S/D) recorded in the 10-minute period from the time in item 2.	Required item
17. Lowest HR	Enter the lowest heart rate that occurred in the 10-minute period from the time in item 2.	Required item
18. Highest HR	Enter the highest heart rate that occurred in the 10-minute period from the time in item 3.	Required item
POST RECRUITMENT	**ENTER VALUES AT THE SPECIFIED TIMES UP TO 8 HOURS FROM THE TIME ENTERED IN ITEM 2 (EITHER RM OR TIME ZERO).**	**Hi PEEP PTS: ALL Lo PEEP PTS: ITEMS 23 AND 24 ONLY**
19. 10 minutes post RM:	Enter SpO2, FiO2, and PEEP values at 10 minutes post RM time or Time Zero (item 2 above).	Required item
20. 30 minutes post RM:	Enter Sp02, Fi02, and PEEP values at 30 minutes post RM time or Time Zero.	Required item
21. *60 minutes post RM:	Enter Sp02, Fi02, PEEP, **Pplat**, and **VT** values at 60 minutes post RM time or Time Zero.	Required item
22. 2 hours post RM:	Enter only Sp02, Fi02, and PEEP values at 2 hours post RM time or Time Zero.	Required item
23. *4 hours post RM:	Enter Sp02, Fi02, PEEP**, Pplat, and VT** values at 4 hours post RM time or Time Zero.	Required item
24. *8 hours post RM:	Enter Sp02, Fi02, PEEP, **Pplat, and VT** values at 8 hours post RM time or Time Zero.	Required item
25. Number of RMs performed?	Enter the total number of RMs that were performed on this calendar date (do not exceed 4 RMs in a 24 hour period).	
**********	**IF AN ADVERSE EVENT OCCURRED DURING OR AFTER RM OR TIME ZERO COMPLETE AN AE REPORT**	**********

ON-STUDY BAROTRAUMA

Complete this form for each new occurrence of barotrauma during Days 1-28 if the patient is alive and receiving mechanical ventilation or is attempting a 48 hour period of unassisted breathing. Use this form only once per day (if indicated) and discontinue after the patient has achieved 48 hours of unassisted breathing**. For source documentation of data record data on the "ALVEOLI Barotrauma Assessment Log" and retain in study file**.

ITEM	DEFINITION	DATA RULES
1. Barotrauma: Pneumothoraces ~	Enter (1) "right side", (2) "left side", (3) "bilateral", or (4) "none" to indicate location or absence of a pneumothorax.	Required field.
Subcutaneous emphysema ~	Indicate with "1" (Yes) or "2" (No) if there is subcutaneous emphysema apparent on the chest x-ray or by physical exam that is attributed to barotrauma.	Required field.
Pneumomediastinum ~	Indicate with "1" (Yes) or "2" (No) if the chest x-ray shows air in the mediastinum attributed to barotrauma.	Required field.
Pneumatoceles >2 cm diameter~	Indicate if there are one or more pneumatoceles > 2 cm minimum diameter (a bubble or hole in the parenchyma that is not attributed to a chronic bleb or bullous lesion), on the right side (1), the left side (2), on both sides, bilateral (3), or on neither side (4).	Required field.
2. Chest Tube:	Indicate if there are one or more chest tubes on the right side (1), on the left side (2), on both sides (3), or on neither side (4).	Required field.
3. Is chest tube to treat pneumothorax?	If a chest tube is present, select (Yes) or (No) to indicate if it was placed to treat a pneumothorax.	Required field if item 2= (1),(2), or (3).

MEDICATION REPORT
STUDY DAYS 1-28

Complete this form on study days 1-5, 7, 14, 21, and 28 if the patient is alive and receiving mechanical ventilation or is attempting a 48 hour period of unassisted breathing. Discontinue this form after patient has completed 48 hours of unassisted breathing.

ITEM	DEFINITION	DATA RULES
1 Neuromuscular blocking agents.	Select Yes (1) or No (2) to indicate if patient has received pancuronium, vecuronium, atracurium, succinylcholine, or other medication for neuromuscular blockade on this calendar date (midnight to midnight).	Required field.
2. Methylprednisolone > 12 mg/day, If yes, check one:	Select Yes (1) or No (2) to indicate if patient has received steroids on this calendar date. If yes, select the one that applies: a. Daily dose 13 – 60 mg b. 61 – 200 mg c. > 200 mg	Required field.
3. Experimental therapies?	Select Yes (1) or No (2) to indicate if patient has received any experimental therapies listed below on this calendar date (midnight to midnight).	Required field.
Nitric Oxide, Surfactant, Liquid Ventilation, ECMO, IVOX, High Frequency Ventilation or Oscillation, Prone Positioning, Inhaled PGI or PGE, Intravenous PGI or PGE.	If 4 = "Yes" select all that apply for this calendar date.	Required if #3 = Yes.
4. New episode of barotrauma?	Select Yes (1) or No (2) to indicate if a NEW incidence of barotrauma has occurred on this calendar date. If yes complete a barotrauma form.	Re
**********	USE THE COMPUTER GENERATED **RANDOM MEDICATION CHECK TIME** TO ANSWER QUESTIONS 5-17	*
5. Vasopressors	Select Yes (1) or No (2) to indicate if the patient has received any vasopressors at the time of random med check.	Re
a. Dopamine ≥ 6 mcg/kg/min b. Norepinephrine c. Neo-Synephrine d. Epinephrine	If 5=yes, enter the infusion rate for all that apply. "Vasopressor" is defined as: I. Dopamine ≥ 6 mcg/kg/min; II. Norepinephrine, Neo-Synephrine, or epinephrine (in mcg/min). Dobutamine is not considered a vasopressor.	Do NOT use a "0" to indicate a pressor that the pt is not receiving, leave the field blank.
Sedatives/analgesics	**A)** Enter the IV infusion (hourly rate) at the time of the random medication check (computer generated). **AND** **B)** Enter the total amount of BOLUSES given in the one hour period PRIOR TO the random medication check time.	

ON-STUDY MEDICATIONS
(Continued)

6-17. Diazepam (Valium), Other benzo, Propofol, Morphine, Demerol (Meperidine), Other narcotic, Haldol (Haloperidol), Droperidol, Other drug:	I. Enter the infusion rate in mg/hr for all that apply. II. Enter the TOTAL amount of boluses in mg received in the 1 hour period *prior to* random med check. III. For "other" items enter the name of the drug in the corresponding field.	Do NOT use a "0" to indicate a drug that the pt is not receiving, leave the field blank.
(#12.) Fentanyl:	Enter as above in mcg/hr and mcg respectively.	

WEANING/VENTILATOR MONITORING
Dates after Date of Enrollment: 1-28

Complete this form on all patients on Days 1-28 if the patient is alive and receiving mechanical ventilation or is attempting a 48 hour period of unassisted breathing. Use information from the calendar date (midnight-midnight) shown on the computer screen.

ITEM	DEFINITION	DATA RULES
1. At 0600 the patient was on:	Indicate the appropriate ventilator mode. Select the mode that the patient was on at 06:00: Volume Assist/Control (1), Pressure Support (2), or Unassisted Breathing (3).	Required field. If answer = (PS), go to Weaning History, #4 a-h. If UAB go to #5.
2. Did patient meet weaning evaluation criteria?	Select Yes (1), No (2), or Not tried/Evaluated (3) to indicate if the patient met the following criteria for weaning: (a) $\geq$ 12 hours since initial protocol ventilator changes, if any. (b) $FiO_2 \leq .40$. (c) Values of both PEEP and $FiO_2 \leq$ values from the previous day (comparing reference measurement values). (d) Not receiving neuromuscular blocking agents, and without neuromuscular blockade. (e) Patient exhibiting inspiratory efforts (ventilator rate should be decreased to 50% of baseline level for up to 5 minutes to detect inspiratory efforts if no efforts are evident at baseline ventilator rate.	Required field. If answer = (No) or (Not tried/Evaluated) go to #5, "did patient tolerate trial...."
3. If 2 is Yes, did the patient pass the 5 min. CPAP trial?	Select Yes (1) if a 5-minute CPAP trial was conducted and the patient's respiratory rate remained $\leq$ 35 breaths/min. Select No (2) if RR > 35 during the CPAP trial. Select Not tried/Evaluated (3) if the CPAP trial was not conducted.	Required field if #2= (Yes). If answer = (No), go to #7, on A/C continuously…?
4. Did patient go to pressure support?	Select Yes (1), No (2), or Not tried/Evaluated (3) to indicate if the patient tolerated reductions in Pressure Support to 5 cmH_2O. The criteria for tolerance are in Section 4.1.2.3 of the protocol. If no attempts were made to wean PS, enter the reason in the text field. A Yes answer will enable access to the weaning history section, 4a-h.	This question is always available. Use "No answer" if not applicable. Go directly to the field and click on it to access.
4a-h. Weaning History	Record **initial** and subsequent pressure support levels along with their corresponding starting times (military) each time the Pressure Support Level is changed.	Required field if #4 = (Yes).
5. Did patient tolerate a trial of spontaneous breathing > 2 hours?	Select Yes (1), No (2), or Not tried/Evaluated (3) to indicate if the patient tolerated a trial of spontaneous breathing > 2 hrs. Spontaneous breathing trial = CPAP 5, T-piece, or trach mask with FiO2 $\leq$ .50. The pt must meet all criteria specified in protocol section 4.1.2.5	Required field.
6. Did patient complete 48 hours of unassisted breathing?	Select Yes (1) or No (2) to indicate if patient **COMPLETED** 48 hours of "Unassisted Breathing" on this calendar date (the **START** date is captured on the Study Termination form). See section 4.1.2.6 of the protocol for definition of "Unassisted Breathing".	Required field.

WEANING/VENTILATOR MONITORING
(Continuation)

7. Was patient on A/C continuously during 4 hours preceding and 4 hours following selected time of ventilator check?	Select Yes (1) or No (2) to indicate if the pt was on A/C continuously for 4 hours before and after random vent check time. If a CPAP trial has been conducted, A/C is **not** considered "continuous". Tracheal suctioning during this period still qualifies as "continuous".	Required field.
RANDOM VENTILATOR CHECK	FOR ITEMS 8-12 ENTER FIRST VALUE IN FOUR HOUR INTERVAL **ON OR AFTER** THE TIME INDICATED ON THE SCREEN FOR THE RANDOM VENTILATOR CHECK	
8. FiO_2	Enter the FiO_2 as a decimal (e.g. .50).	Required field if #7=Yes.
9a. Calculated delivered tidal volume (if on A/C)	Enter the inspired tidal volume (ml) set on the ventilator minus any additional tidal volume added to correct for gas compression and ventilator tube expansion (this should = the tidal volume called for by the protocol; this will not = the volume set on the ventilator unless the ventilator makes automatic adjustments for gas compression/tube expansion). Puritan-Bennett 7200's and some other ventilators make this correction automatically, in which case the tidal volume set on the ventilator should = the tidal volume called for in the protocol. For patients on these ventilators, enter the tidal volume set on the ventilator.	Required field if #7 =Yes.
9b. V_T increased due to severe dyspnea?	Select Yes (1) or No (2) to indicate if the tidal volume was increased because of the conditions described in protocol section 4.1.1.2b(ii).	Required field if #7 =Yes.
10. PEEP	Enter the level of PEEP in cmH_2O.	Required field if #7 =Yes.
11. Set Rate	Enter the minimum respiratory rate set on the ventilator (not the actual rate, which may exceed the set rate).	Required field if #7 =Yes.
12. Pplat (plateau pressure)	Enter the plateau pressure measured. *The Pplat measurement should be source documented in the pt study file or the pt chart.*	Required field if #7 =Yes.
RANDOM VENTILATOR CHECK	FOR ITEMS 13-16 ENTER THE LAST VALUE IN THE FOUR HOUR INTERVAL **IMMEDEATELY PRIOR TO (BUT NOT ON)** THE TIME OF THE RANDOM VENTILATOR CHECK.	
13a. pH	Enter the most recent value during the four hour interval **PRIOR TO** the random ventilator check, if available.	
13b. If pH available, was set rate changed in the 4 hr interval between measurement and time set rate recorded?	Select Yes (1) or No (2).	Required field if 13a is available.
SpO2 vs. PaO2	IF BOTH SpO2 AND PaO2 WERE AVAILABLE DURING THE 4 HOUR INTERVAL, ENTER **ONLY** ONE (EITHER SpO2 **OR** PaO2) USED TO SET OR ASSESS THE VALUES OF FiO2 OR PEEP IN ITEMS 8 AND 10	
14a. SpO_2	If SpO2 was used to set or assess PEEP and FiO2 enter the most recent pulse oximetry value **PRIOR** to the time of the random ventilator check.	
14b. If SpO2 available was FiO2 or PEEP changed...?	Select Yes (1) or No (2)	Required field if Sp02 available.

WEANING/VENTILATOR MONITORING
(Continuation)

15a. PaO2	If PaO2 was used to set or assess PEEP and FiO2 enter the most recent pulse oximetry value **PRIOR** to the time of the random ventilator check.	
15b. If PaO2 available was FiO2 or PEEP changed..?	Select Yes (1) or No (2).	Required field if Pa02 available.
16. If no pH available for #13a. then enter most recent.	In no pH available in the 4 hour interval prior to random vent check but WAS available on this calendar date enter the most recent value.	

BRUSSELS TABLE
Study Days: 1-28

Complete this form using *clinically available* data on each date after the date of enrollment through Day 28 until death or study hospital discharge, whichever comes first.

Use t**he pop-up table on the Brussels form to enter data. Click on the *DATA ENTRY GRID* button to access the table. Data can be entered either across or down in the table.**

In the row labeled "Day 0.5", enter data pertaining to the date of enrollment from the time immediately following initial study procedures until 2359.59 (11:59.59 pm). If no values are available during this interval, enter most recent values from before this interval.

In the rows for Days 1-28, enter data from the first through the 28th calendar date after the date of enrollment. Each of these calendar dates includes the interval from 0000 (Midnight) until 23:59.59.

Record the worst values for each of the five variables shown at the headings of the columns.

Worst values are defined below:

Systolic	**Lowest** value for the date.
P/F Ratio	**Lowest** value for the date.
Platelets	**Lowest** value for the date.
Creatinine	**Highest** value for the date.
Total Bilirubin	**Highest** value for the date.

Vasopressors yes/no: Enter "1" (Yes) to indicate that one or more vasopressors were used on the calendar date. Enter "2" (No) if no vasopressors were used on the calendar date. "Vasopressor" is defined as: Dopamine ≥ 6 mcg/kg/min and Neo-Synephrine, epinephrine, or Levophed at any rate. Dobutamine is NOT considered a vasopressor.

ADVERSE EVENT REPORTING FORM

I. AE REPORTING:

This form should be used to capture All CLINICALLY IMPORTANT **and** UNEXPECTED adverse events that occur from time of initial ventilator changes through completion of 48 hours of unassisted breathing, **OR** day 60 whichever comes first.

Deaths will be captured on the study termination form and will NOT require a "death report form". Deaths resulting from an adverse event will fall under the reporting requirements of an IMMEDIATELY REPORTABLE AE outlined below.

The Adverse Event Form should not be used to report organ failures related to ARDS as these are systematically captured by the protocol.

II. IMMEDIATELY REPORTABLE AE: SERIOUS + UNEXPECTED + STUDY RELATED AE REPORTING:

All SERIOUS **AND** UNEXPECTED **AND** STUDY-RELATED adverse events should be reported to the Clinical Coordinating Center *within 24 hours by phone*. The investigator must submit a detailed, written report to the Clinical Coordinating Center within **5 working days**. The Institutional Review Board should be notified based on institutional policy, but no later than 5 working days after the event is discovered.

To report multiple events on the same patient, click on "New Copy" in the menu to the left of the form to create another copy of the AE form. Use *NEXT COPY* and *PREVIOUS COPY* from the menu to move between copies. When there are 2 or more copies a summary view is present at the bottom of the screen: Use the scroll bar on the right to see all copies. You can go directly to each form by clicking on the field *LOAD* next to each record in the summary view.

ITEM	DEFINITION	DATA RULES
1. Date of event	Select the date from the pop-up calendar that the event first occurred.	Required field.
2. Time of event	Enter the time (military) the event began.	Required field.
3. Name of event	Select the term from the COSTART pick-list that best categorizes the event.	Required field.
4. Describe event or problem	Give a brief narrative description of problem. If death, give cause.	Required field.
5. Severity of event	Select one: **MILD-**Any event that is usually transient requires no special treatment and does not interfere with the patient's daily activities. **MODERATE**- Any event that introduces a low level of inconvenience or concern to the patient and may interfere with daily activities. Usually ameliorated by simple measures. **SERIOUS**-Any event that if fatal or immediately life threatening, is permanently disabling, or severely incapacitating, or requires or prolongs inpatient hospitalization. SEE APENDIX B IN THE PROTOCOL FOR DEFINITION OF SERIOUS AE.	Required field. **CCC MUST BE NOTIFIED WITHIN 24 HOURS FOR SERIOUS, UNEXPECTED AND STUDY RELATED EVENTS!!!!!**
6. Therapeutic intervention?	Select Yes (1) or No (2) to indicate if therapeutic intervention was required to prevent permanent impairment or damage.	Required field.
7. Immediate risk of death?	Select Yes (1) or No (2)	Required field.
8. Unexpected or more severe than expected in ARDS or ALI?	Select Yes (1), No (2), or Unknown (3) to indicate if the event is unexpected in ARDS/ALI or more severe or frequent than expected in ARDS/ALI.	Required field.

AE Reporting
(continued)

9. Causal relationship to study procedures?	Select the answer, which best describes the event's relationship to the study drug. **1= Definitely Associated- The event follows** 1) A reasonable, temporal sequence from administration of study procedures. 2) Cannot be explained by the known characteristics of the patient's clinical state or other therapies. 3) Evaluation of the patient's clinical state indicates to the investigator that the experience is definitely related to study procedures. **2=Probably or 3=Possibly Associated:** The event should be assessed following the same criteria for "Definitely Associated". If in the investigator's opinion at least one or more of the criteria are not present, then "probably" or "possibly" associated should be selected. **4=Probably Not Associated:** The event occurred while the patient was on the study but can reasonably be explained by the known characteristics of the patient's clinical state or other therapies. **5=Definitely Not Associated:** The event is definitely produced by the patient's clinical state or by other modes of therapy administered to the patient. **6=Uncertain Association:** The event does not meet any of the criteria previously outlined.	Required field.
10. Withdrawn from study?	Select Yes (1) or No (2) to indicate if the patient was withdrawn from the **protocol** as a result of this event.	Required field.
11. Status of the EVENT at time of initial AE report.	Select Recovered, date (1), AE present, no tx (2), AE present, being treated (3), Residual effect/no tx (4), Residual effect/being treated (5), Deceased (6) as a result of this event. *Select deceased ONLY if the patient died as a result of the event.*	Required field.
If recovered, date	If the answer selected is Recovered (1) select the date from the pop-up calendar of recovery from the event.	Required field if "recovered" selected.
12. FINAL outcome of AE (at resolution or 48h unassisted breathing).	The final outcome should be reflective of the status of the event at resolution of the event OR patient achieving 48 hours of unassisted breathing, whichever comes first.	Required field if #12 = 2,3,4, or 5.
If recovered, date:	If the answer selected is Recovered (1) select the date from the pop-up calendar of recovery from the event.	Required field if "recovered" selected.

SPECIMEN COLLECTION
Study Days 0,1, 3, and 7

Collect blood samples for cytokines on Study Days: 0,1, 3, and 7. Collect buccal smears for genetic testing ONE time only on Day 0. Document in the comment field any missed specimens and the reason why.

****************************FAX SPECIMEN COLLECTION LOGS TO THE CCC***************************

ITEM	DEFINITION	DATA RULES
Day 0 blood for cytokines	Select (Yes) or (No) to indicate if blood was drawn this calendar day for cytokines. For "No" answers document in the comment field why the specimen was not drawn.	Required field.
Day 0 date	If above = Yes enter the date that the sample was obtained.	Required field if above = (Yes).
Day 1 blood for cytokines	Select (Yes) or (No) to indicate if blood was drawn this calendar day for cytokines. For "No" answers document in the comment field why the specimen was not drawn.	Required field.
Day 1 date	If above = Yes enter the date that the sample was obtained.	Required field if above = (Yes).
Day 3 blood for cytokines	Enter (Yes) or (No) to indicate if blood was drawn this calendar day for cytokines. For "No" answers document in the comment field why the specimen was not drawn.	Required field.
Day 3 date	If above = Yes enter the date that the sample was obtained.	Required field if above = (Yes).
Day 7 blood for cytokines	Enter (Yes) or (No) to indicate if blood was drawn this calendar day for cytokines. For "No" answers document in the comment field why the specimen was not drawn.	Required field.
Day 7 date	If above = Yes enter the date that the sample was obtained.	Required field if above = "1" (Yes).
GENETIC TESTING	DO NOT OBTAIN UNLESS PATIENT/SURROGATE HAS CONSENTED TO GENETIC TESTING	
Buccal smear	Collect only for pts (who have consented to genetic testing) who have been transfused within 5 days of the (genetic) blood specimen collection date. Enter (Yes) or (No) to indicate if a buccal smear was collected on this calendar date.	Required field if consent obtained for genetic testing.
Buccal specimen collection date:	If above = Yes enter the date that the sample was obtained.	Required field if above = (Yes).

STUDY TERMINATION

I. Begin completion of this form by Day 28. For patients who are not home with UAB before Day 28, follow at weekly intervals until the patient is home with UAB, expires, or until Day 90, whichever occurs first. Enter data in question 1 by Day 28. If status at Day 28 is "other" and changes prior to Day 90, update this field to reflect the change.

II. Up to Day 90 Capture: 1) ICU discharge date (and ALL ICU re-admissions in study hospital if applicable); 2) Study hospital discharge date; and 3) On/Off assisted breathing dates.

III. Use the "ALVEOLI Patient Outcome Follow-up Log" (located in SOP section of study binder) to document patient tracking.

ITEM	DEFINITION	DATA RULES
1. Patient Status (through Day 90):	Select "home with UAB" if the patient is home with unassisted breathing. "Home" is defined as the place the patient lived prior to study hospital admission (i.e., pt living in a nursing home→admitted to study hospital and enrolled into ALVEOLI→dc'd back to nursing home on UAB. The nursing home would qualify as "home on UAB". Pts previously living at home who are discharged to a rehab facility on UAB from study hospital would NOT qualify as being "home on UAB".) See section 4.1.2.6 of the ALVEOLI protocol for definition of UAB. Select "Dead…" if the patient died prior to discharge home with unassisted breathing or died prior to achieving unassisted breathing at home for 48 hours. Select "Other" if neither condition above applies. E.g., if the patient went home on assisted breathing and has not achieved unassisted breathing for 48 hours, continues on assisted breathing, or has been transferred to another facility, other than home, on unassisted breathing.	Required field.
1a,b,c. Dates	💻 Select the appropriate date (from the pop-up calendar) of discharge home with unassisted breathing (if condition 1 above), date of death prior to discharge home with unassisted breathing (if condition 2, above), or date of last KNOWN patient status, i.e., date that the patient was last know to be alive and does not meet the other 2 criteria (if condition 3 above).	Required field. There should be only ONE date entered to correspond with the selected status option.
2. Was pt permanently withdrawn from the ALVEOLI study?	Select the option (yes/no) that applies. Pts who are off vent secondary to achieving 48 hours of unassisted breathing are considered to have COMPLETED the study and do not qualify as "withdrawn". Patients who are off protocol temporarily (i.e., a few days) then resume study procedures can be counted as a "No".	Required field.
3. Patient discharged from study hospital?	Select the option (yes/no) that applies to indicate if the patient was discharged (alive or dead) from the study hospital up through Day 90.	Required field.
3a. Date	If 3= Yes, give the date of discharge.	Required field if 3= Yes.
3b. Status at discharge:	Select the option (alive/dead) that describes the patient's vital status at hospital discharge.	Required field.
4. Patient discharged to home? If yes give date.	Select the option (yes/no) that applies to indicate if the pt was discharged to home, *ON OR OFF UAB*. If discharged home with assisted breathing, continue to follow until the pt achieves UAB at home and complete question 6.	Required field.

	FOR QUESTION 5a-e DOCUMENT ALL INCIDENCES OF ICU ADMISSIONS AND DISCHARGES *DURING THE STUDY HOSPITALIZATION* UP THROUGH DAY 90	Questions are required until a "No" or "Unknown" response is selected, then skip to 6a.
5a. Was the patient discharged from an ICU? If yes, enter date.	Select the option that best applies. 💻 Select the date of discharge from the pop-up calendar by clicking on the "date" button.	Required field. Date required if "Yes" selected.
5b. Pt readmitted to an ICU? If yes, enter date.	Was the pt readmitted to an ICU during study hospitalization? This includes any ICU within the study hospital. Select the option that best applies. 💻 Select the date of readmission from the pop-up calendar.	Required field. Date required if "Yes " selected.
Discharged after ICU readmission? If yes, enter date.	Was the pt discharged (alive or dead) after readmission to the ICU? Select the option that best applies. 💻 Select the date of discharge from the pop-up calendar. If pt died while in an ICU, the date in this field should be the same as in 3b.	Required field if #5b =Yes. Date required if "Yes" selected.
5c. If 5b= Yes, was pt readmitted a 2nd time? If yes, enter date.	Was the pt readmitted to an ICU at any time after the DC date entered in 5b? If yes, enter the date of the 2nd readmission.	Required field if a DC date is present in 5b.
5d-e.	Use these questions to capture all other ICU readmissions and discharges, occurring in study hospital, up through Day 90 when applicable.	
	FOR QUESTIONS 6a-g CAPTURE ALL INCIDENCES OF UNASSISTED BREATHING UNTIL DC HOME, DEATH, OR UNTIL PT HAS BEEN FOLLOWED TO DAY 90	Questions are required until a "No" or "Unknown" response is selected, then skip to 7.
6a. Did pt achieve unassisted breathing?	Select the option that applies. **See section 4.1.2.6 of version I of the ALVEOLI protocol for definition of unassisted breathing.**	Required field.
Date of the FIRST episode of UAB:	Select the first date that the pt was on UAB from midnight to midnight (i.e., If the pt was extubated on Day 2 and remained off the vent through Day 3, Day 3 would be the date of first **UAB**).	Required field if UAB =Yes.
6b. Did pt return to assisted breathing? If yes, enter date.	Select the option that best applies. If Yes, enter the date that the pt returned to assisted breathing.	Required field if 6a =Yes.
6c. If pt returned to assisted breathing, was a 2nd episode of UAB achieved?	Select the option that best applies. If yes, enter the SECOND date that the pt was on UAB (from midnight to midnight).	Required field if 6b =Yes.
6d. Pt returned to assisted breathing after 2nd episode of UAB?	Select the option that best applies. If yes, enter the date that the pt returned to assisted breathing after the 2nd period of UAB.	Required field if 6c = Yes.

6e-g.	Use these questions to capture ALL other incidences of UAB occurring at any location until dc home, death, or pt is followed to Day 90.	

STUDY TERMINATION
(continued)

7. End of Life Decision Making:	This field is intended to capture information on end of life decision making for all pts that died. "Life Support" includes (but is not limited to): mechanical ventilation, vasopressors, IV fluids, antibiotics, dialysis, and blood products. *Select the option that best applies: 1) No DNR decision made (includes pts receiving aggressive management, including failed CPR) 2) DNR Decision made: withhold only CPR (includes pts receiving aggressive management up to but not including CPR) 3) DNR Decision made: withhold life support in addition to CPR (includes pts with an identified antemortem decision to withhold some form of life support, i.e., in the event of renal failure will not dialyze or if respiratory failure occurs will not intubate) 4) DNR Decision made: withdraw life support (includes **removal** of mechanical ventilation, dialysis, or discontinuation of vasopressors) 5) Diagnosis of Brain Death (per study site institutional standards for brain death criteria) 6) Unknown/can't tell	Required field if item 1="Dead…".

***** Criteria for DNR grading adapted from: Prendergast T, Claessens M, and Luce J. *A National Survey of End-of-life Care for Critically Ill Patients*. Am. J. Respir. Crit. Care Med., Volume 158, Number 4, October 1998, 1163-1167