GW IRB Application (Version 1.2)

1.0 General Information

***Please enter the full title of your study:**

What is the ideal dose of whole blood in massively bleeding trauma patients?

***Study Short Title:**

Whole blood dosing
* This field allows you to enter an abbreviated version of the Study Title to quickly identify this study.

Is this a multi-site study in which GW will be the lead site and will enter into a reliance agreement (IAA) with other collaborating institutions who will rely on our review?

No

2.0 Add Department(s)

2.1 List departments associated with this study:

Primary Dept?	Department Name
◉	**GW** - SURGERY-SCHOOL-INSTRUCTION

3.0 Assign key study personnel (KSP) access to the study

3.1 *Please add a Principal Investigator for the study (Students are not eligible to be Principal Investigators)

Sarani, Babak, MD

3.2 If applicable, please select the Research Staff personnel:

A) Additional Investigators

Estroff, Jordan, MD
Co-Investigator
Kartiko, Susan, MD, PhD
Co-Investigator
Quintana, Megan, MD
Co-Investigator
Wanersdorfer, Karen, DO
Co-Investigator

B) Research Support Staff

Brock, Tremaine

Research Staff

3.3 *Please add a Study Contact:

Brock, Tremaine
Sarani, Babak, MD

The Study Contact(s) will receive all important system notifications along with the Principal Investigator. (e.g. The study contact(s) are typically either the Study Coordinator or the Principal Investigator themselves). Anyone **not** added here will NOT receive email or correspondence from the system for this study

3.4 Please select the Designated Department Approval(s):

Aly, Radwa
Scientific Reviewer
Gomberg-Maitland, Mardi, MD
Research Integrity Officer
Sidawy, Anton, MD
Department Chair

Add the name of the individual authorized to approve and sign off on this protocol from your Department (e.g. the Department Chair or Dean). **All new submissions MUST be signed off by a Department Chair before the IRB will review a submission.**
For ALL MFA Studies: In addition to having your Department Chair sign off (for Dept of Medicine, please add Dr. William Borden as Department Chair), all studies need to be signed off by **Radwa Aly and Mardi Gomberg-Maitland**. Please add them **here** or during final routing of signatures after your application has been completed.

4.0 Study Personnel Information

4.1 Do you or any research team personnel have any outside interests related to this research (ex: personal stock in the company sponsoring the research, receipt of income, including royalties and entitlement to royalties, from the sponsor of this research for purposes other than this research, etc.) that could possibly be perceived as introducing bias into the research or as a conflict of interest?

○ Yes ◉ No

4.2 Is the PI a regular service faculty member?

◉ Yes ○ No

5.0 Review Determination

5.1 Are you applying for an Exempt study?

○ Yes ◉ No

5.2 Please indicate which of the categories below describe this study:

◉ Minimal Risk
○ Greater than Minimal Risk

6.0 GW's Role

6.1 Select GW's Role in the Project:

- ○ Sole Site (GW is the only IRB involved in this study)
- ○ GW is the Lead Site (and the other site(s) will be relying on GW)
- ◉ GW is the Lead Site (and each site is doing their own review)
- ○ GW is a Participating Site (and will rely on another IRB for review)
- ○ GW is a Participating site (and each site is doing their own review)

The 2018 Common Rule requires use of a Single IRB (sIRB) for all cooperative research that is subject to the Common Rule. These requirements apply to any studies approved by the IRB on or after January 20, 2020 and so it is possible that your study may require the use of a Single IRB unless:

i. The study is NOT federally funded
ii. The study is federally funded AND solely involves international sites besides GW
iii. The collaborating site is the VA, or another national IRB required by law (such as a tribal IRB)

6.2 Is GW acting only as a data coordinating site for this study, where the sole role of GW personnel is to receive data or otherwise coordinate data, and will not be involved in active data collection?

○ Yes ◉ No

7.0 Funding

7.1 Is this study externally funded?

○ Yes ◉ No

8.0 Objectives and Justifications

8.1 Summary of the study using lay language (200 words or less):

Use of stored, cold whole blood is becoming increasingly common in the civilian trauma setting and is now routinely used at GW Hospital in severely bleeding trauma patients. Use of this product as an adjunct to standard component therapy is predicated on the premise that whole blood has better hemostatic efficacy than component transfusion. However, there are no studies evaluating how many units of whole blood should be transfused during a massive hemorrhage episode. As such, trauma centers vary the amount of whole blood given to each patient based on their supply, locally written protocol, and/or physician judgement. The purpose of this study is to determine if there is an optimal ratio of whole blood to either packed red blood cell or plasma transfusion in massively bleeding trauma patients. We seek to determine what ratio mitigates ongoing blood loss and thus transfusion need. Because the need for whole blood transfusion is not common across most trauma centers, we seek to perform a multicenter, prospective, observational study in order to enroll a sufficient number of patients to answer this question in a reasonably timely fashion.
This study will enroll actively bleeding, unstable patients who will not be able to render informed consent on arrival. We will obtain informed consent from patients if their condition stabilizes to the point where this is possible. If the patients are left with injury which precludes them from being able to render informed consent (for example, persistent coma or severe brain injury), we will obtain informed consent from a LAR. A member of the reserach team will approach the patient or the LAR and explain the study. This will occur in a private setting in GWUH. Consent can be obtained at any point during the hospital stay. A copy of the signed informed consent document will be given to the patient or to the LAR. In instances where a LAR signs the consent form and the patient subsequently is able to consent him/herself, he/she will be told about the study and allowed to withdraw as needed. However, any information already entered into the database will be kept.

8.2 Objective(s) and justification of the study including the purpose, research question(s), hypothesis and relevant background information:

We hypothesize that there is a dose-response relationship between whole blood transfusion and hemostasis. The specific aims of this study are:
Primary Aim: To determine if there is a dose-response relationship between number of units of whole blood given and total transfusion need within the first 2, 4, 6, 12 and 24 hours following onset of hemorrhage.

Secondary Aim: To determine if there is a relationship between number of units of whole blood given and need for mechanical ventilation, ICU/hospital length of stay, resolution of acidosis, normalization of vesicoelastography and conventional coagulation indices, morbidity (as defined below) and death.

Primary Outcome: Total number of blood components transfused at hours 2, 4, 6, 12,and 24 hours following arrival to the trauma center
Secondary Outcome(s): Hospital and ICU length of stay, duration of mechanical ventilation, vesicoelastrophy and conventional coagulation results (when available) before/after the massive transfusion even, incidence of ARDS, ventilator associated pneumonia, acute kidney injury, and pulmonary embolism, mortality

8.3 Describe how the research results will be used and will contribute to generalizable knowledge:

The results of this study will be presented at peer society meetings and published in a peer reviewed journal. By better elucidating how whole blood should be transfused, this study will contribute to the evolving medical literature on this topic.

8.4 How will the data be analyzed to answer the research question? Briefly describe the data analysis procedures (e.g., statistical tests, thematic analysis, factors to be compared):

Briefly describe statistical tests, thematic analysis, and the factors to be compared.

Data will be analyzed using parametric and/or non-parametric tests as appropriate. Multivariable analysis will be done to control for known confounders and also to control for univariate factors found to be significant at the p=0.2 threshold. We aim for determine if there is a ratio of whole blood infused as a part of the total amount of blood products given within specific time intervals with the prmiary outcome being cessation of hemorrhage, which is defined as a decreased need for ongoing transfusion. Data will be analyzed and reported in aggregate using de-identified information.

8.5 Please choose "Yes" for at least one of the following questions. Your study is Social and Behavioral in nature and/or it is Biomedical. In some cases it may be both, but it is never neither.

Are you performing a social or behavioral study?

○ Yes ◉ No

Are you performing a biomedical study?

◉ Yes ○ No

8.6 Are you performing a clinical trial?

○ Yes ◉ No

8.8 Are you only conducting a chart review or does the research consist only of secondary analysis of an already existing dataset?

◉ Yes ○ No

9.0 Study Details - Chart Review

9.1 Please list the variables accessed for data analysis:

Variables
See attached data collection tool

9.2 Indicate where, how and from whom existing data will be accessed, obtained or otherwise determined:

Members of the American Association for the Surgery of Trauma (AAST), a peer trauma society, will be invited to participate in this study. Sites that agree to participate will then designate a site-PI. All information will be collected from the patient's medical record by each site-PI. The data will be entered into REDCap by each site. Each site will only have access to their own data in REDCap. Only Dr. Sarani, as the overall study PI, will be able to access all information that is entered into REDCap by any site.
A modification request will be submitted to GW IRB listing out each of the confirmed sites that are engaged in this research

9.3 If the study involves retrospective analysis, please state the exact date range from which data will be accessed:

- Please note that all data accessed for this research must be in existence at the time of the initial IRB application in order to meet the definition of "retrospective."

From:

To:

9.4 If study involves retrospective AND prospective analysis, detail how consent for the prospective component will be obtained:

This is purely a prospective, observational study. There is no retrospective component

9.5 Which personal or demographic data will be collected?

- [ ] Name
- [ ] SSN
- [x] Medical Record # (MRN)
- [ ] DOB or
- [x] Age
- [ ] Phone #
- [ ] Home Address
- [ ] Email
- [x] Date of medical procedures
- [x] Race / Ethnicity
- [x] Gender
- [ ] Employer / School Name
- [ ] Department / Division
- [x] Disease Status
- [ ] City
- [ ] State/other
- [ ] Zip Code

10.0 Subject Population

10.1 General description of the study population:

The study population will consist of all injured patients, age 18-80 years old, who require whole blood transfusion during their initial resuscitation

10.2 Locations where subjects will participate in GW IRB supervised research activities, and/or from which data are retrieved:

Organization / Facility/ Location	Research Activities Performed (recruitment, consenting subject/researcher interaction or data retrieval):
GWUH	subject enrollment, data collection

Does the study involve Medical Faculty Associates (MFA) patients or George Washington University Hospital (GWUH) patients?

(•) Yes ( ) No

Does the study involve MFA data or records, or GWUH data or records?

(•) Yes ( ) No

Is either the MFA or GWUH being used as a study site?

(•) Yes ( ) No

Is the PI employed by the MFA?

(•) Yes ( ) No

Your study application will need to be signed off by both **Dr. Mardi Gomberg-Maitland** and **Radwa Aly.** Please add them to section 3.4 as departmental reviewers and include them in the signature routing when submitting your Initial Review Submission Packet.

10.3 If your study involves research activities at external (non-GW) sites, do you need permission to perform the activities at those sites? (NOTE: this is NOT informed consent from participants, but is gaining administrative permission for involvement of the site)

(•) Yes
( ) No
( ) N/A (Does not involve non-GW Sites)

Do you have permission from the site?

( ) Yes (•) No

What is your plan for obtaining permission from the site?

We will obtain a data use agreement from each participating site before allowing them to participate in this study

10.4 Maximum number of subjects:

- For a multi-center study, both local and total accrual numbers must be provided if GW is acting as the IRB of Record.
- If this study does not involve multiple sites or the number of subjects at other sites is unknown, complete only the "Locally" row.
- Subjects are considered to be enrolled and count towards your total number of subjects once they begin study procedures, which excludes screening procedures. A list of subjects who sign the informed consent document but did not meet inclusion criteria should be kept for your files.

Maximum Number of Subjects to be Enrolled

	Annually	Entire Study
Locally (by GW researchers)	15	30
Study-wide (Multi-center)	100	200

10.5 If existing data or records will be accessed, maximum number of records:

Maximum Number of Charts to be Reviewed:

	Annually	Entire Study
Locally (by GW researchers)	15	30

10.6 Age range of subjects:

18-80 years old

10.7 Inclusion Criteria:

Order Number	Criteria
1	Age 18-80 years old
1	Acute injury (any mechanism)
1	Received blood transfusion via a dedicated massive transfusion protocol on arrival to the hospital
1	Received both whole blood and component therapy during their initial resuscitation

10.8 Exclusion Criteria*:

These are the characteristics that a participant must NOT have in order to be eligible to participate in the study.

Order Number	Criteria
1	Age less than 18 or greater than 80 years old
1	Pregnant
1	Prisoner
1	Moribund/expected to die
1	Dead on arrival
1	Died in the trauma bay
1	Transfer from an outside hospital/facility
1	Known use of anticoagulant within 48 hours of injury
1	Head abbreviated injury score 3 or higher

***If excluding a population or group that may benefit from the research, please provide justification:**

There is no direct benefit to any of the above noted groups because this is an observational study and does not direct the care actually provided or received

10.9 Special populations to be involved in the research:

- ☐ Research conducted internationally
- ☐ Non-English speaking
- ☐ Educationally Disadvantaged
- ☐ Economically Disadvantaged
- ☐ Mentally Ill
- ☐ Decisionally-Impaired
- ☐ Illiterate
- ☐ Students
- ☐ Employees
- ☐ Other

For any population listed above, please explain why the population is necessary and explain additional steps that will be taken to protect the subjects:

10.10 Does the research involve prisoners?

- ☐ Prisoners

10.11 Does the research involve children?

- ☐ Children

10.12 Does the research target pregnant women, fetuses or Neonates?

- ☐ Pregnant women, fetuses or neonates

10.13 Does the study involve wards of the state or any other agency, institution, or entity?

- ○ Yes ◉ No

11.0 Subject Recruitment

11.1 Does any member of the research team have an existing relationship with any potential subjects (such as a medical care provider, professional colleague, or instructor)?

- ◉ Yes ○ No

Please explain the relationship and describe steps that will be taken to minimize risks to subjects and reduce potential for bias. Address any conflict of role that this relationship poses:

Members of the GW Trauma Team are all co-investigators on this study and will direct the decision to transfuse and how to transfuse the patients. However, this study is observational in nature and will have no bearing on this decision making. Use of whole blood at GW Hospital is already established, common practice. Therefore the risk of bias is minimal.
It is possible that a patient will be cared for by a member of the research team, but this will not impact care rendered because the study does not govern or direct care to be given. This is an observational study evaluating care that was rendered.

11.4 Retrospective data analysis only: Provide the exact date range (MM/DD/YYYY- MM/DD/YYYY) from which data will be accessed. All data accessed for this research must be in existence at the time of the initial IRB submission in order to meet the definition of "retrospective.":

12.0 Informed Consent Process

12.1 Consent method being requested for the study:

- [x] Written Consent Document with Signature (obtaining subject or Legally Authorized Representative signature).
- [ ] Waiver of Documentation of Consent (electronic or verbal consent)
- [ ] Waiver of Consent process
- [ ] Waiver or Alteration of Some of the Required Elements of Consent

Study Population:

All injured patients age 18-80 years old who receive whole blood during their initiation resuscitation

12.2 Describe the informed consent process, assent process, and parental permission process:

- Who is obtaining the consent/assent/parental or guardian permission (e.g, research team, etc.)?
- Where is the consenting/assenting/parental or guardian permission occurring?
- At what point will consent/assent/parental or guardian permission be obtained?
- How will participants receive the consent/assent/parental or guardian permission document(s) (e. g., email, in-person, etc.)?
- At what point will participants receive the consent/assent/parental or guardian permission document(s)?
- Will participants receive a copy of the consent/assent/parental or guardian permission documents (s)?
- Describe if participants will have ample time to review the consent/assent/parental or guardian permission form(s) and ask questions to the research team before providing consent/assent /parental or guardian permission.

For efficiency of review, if a research study involves multiple research methods (e.g., survey, interview, focus group, etc.) and multiple study populations, please explain each consent/assent/parental or guardian permission process by research method or study population separately. For example: The research team is obtaining verbal consent and requesting a waiver of documentation of consent for A and B procedures with X study population. Also, the research team is obtaining signed consent forms from Y study population for C and D procedures.

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This study will enroll actively bleeding, unstable patients who will not be able to render informed consent on arrival. We will obtain informed consent from patients if their condition stabilizes to the point where this is possible. If the patients are left with injury which precludes them from being able to render informed consent (for example, persistent coma or severe brain injury), we will obtain informed consent from a LAR. A member of the reserach team will approach the patient or the LAR and explain the study. This will occur in a private setting in GWUH. Consent can be obtained at any point during the hospital stay. A copy of the signed informed consent document will be given to the patient or to the LAR. In instances where a LAR signs the consent form and the patient subsequently is able to consent him/herself, he/she will be told about the study and allowed to withdraw as needed. However, any information already entered into the database will be kept.

12.3 Where and how long signed consent documents will be securely maintained:

Studies under HIPAA: Consents and research records must be maintained a minimum of 6 years following study closure.
Studies under HHS: Consents and research records must be maintained a minimum of 3 years following study closure.
Studies involving children: Please look into storage requirements for studies that involve minors /children

All consent documents will be kept in Dr. Sarani's office for 6 years

13.0 Risks and Benefits

13.1 Risks to subjects:

Note: All research studies have some risk, such as possible loss of confidentiality. You may not answer this question "N/A" or "no risk". All must be included.

The only risk to subjects is release of information (loss of confidentiality) gathered for this study.

13.2 Steps taken to minimize risks and to protect subjects' welfare:

All information will be entered into REDCap by a member of the research team. There will be no paper records kept. We will create a separate excel spreadsheet that cross references the MRN to the unique REDCap patient identifier, which is created automatically by REDCap each time a new entry is created. The excel spreadsheet will be kept on Dr. Sarani's password protected computer in his locked office in the basement of GWUH. The excel spreasheet will be permanently deleted by Dr. Sarani upon acceptance of the mansucript from this study for publication in a peer reviewed journal. Data will be analyzed and reported in aggregate using de-identified information.

13.4 Benefits of this research for society:

This study may help eluidate optimal transfusion ratio for whole blood. This will impact how this novel therapy will be used in trauma centers.

14.0 Use of Protected Health Information (PHI): HIPAA Requirements

14.1 If obtaining, viewing, or collecting records or data from medical or clinical settings to support subject selection, will any potential subjects currently be under treatment by a member of the research study team?

(•) Yes ( ) No

14.2 Will this study involve access to, or use of, any subjects' 18 identifiable pieces of protected health information (PHI) defined under HIPAA (45 CFR 164.514(A)(2)) from a covered entity?

- Visit **https://www.hhs.gov/hipaa/** for more information about the Health Insurance Portability and Accountability Act (HIPAA).
- Please note, exact age if over 89 would be considered identifiable

(•) Yes
( ) No

Select one or more options that apply:

[x] I will create a HIPAA Authorization to be included in the consent document.
[ ] I am requesting a HIPAA Partial Waiver (for recruitment purposes only)
[ ] I am requesting a HIPAA Full Waiver (to be used when viewing PHI or collecting PHI without consent)

15.0 Application Questions Complete

15.1 Please click Save & Continue to proceed to the Initial Review Submission Packet.

The Initial Review Submission Packet is a short form filled out after the protocol application has been completed. This is an area to attach protocol-related documents, consent forms, and review the application.