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Award Number: W81XWH-12-1-0530

TITLE: Fluid Lavage of Open Wounds (FLOW): A Multicenter, Blinded, Factorial Trial Comparing Alternative Irrigating Solutions and Pressures in Patients with Open Fractures

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CONTRACTING ORGANIZATION: Greenville Hospital System, Greenville, SC 29605

REPORT DATE: October 2013

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
October-2013	Annual	30 September 2012-29 September 2013

4. TITLE AND SUBTITLE
Fluid Lavage of Open Wounds (FLOW): A Multicenter, Blinded, Factorial Trial Comparing Alternative Irrigating Solutions and Pressures in Patients with Open Fractures

5a. CONTRACT NUMBER

5b. GRANT NUMBER
W81XWH-12-1-0530

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
Kyle J. Jeray, MD; Stephanie L. Tanner, MS

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) A ND ADDRESS(ES) AND ADDRESS(ES)
Greenville Hospital System
701 Grove Road
Greenville, SC 29605

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTE

14. ABSTRACT

Thorough irrigation and debridement is the most important initial step in preventing infection in open fractures. However, there is little clinical evidence as to the best irrigation methods and additives. This is a blinded (patients and outcome assessors), 2x3 factorial design randomized trial to investigate whether irrigation solution (soap vs. saline solution), or irrigation pressure (high vs. low vs. gravity flow) will decrease the reoperation rate among patients with open fractures. The hypotheses are that a soap solution will result in fewer reoperations in patients with open fractures compared to saline solution, and that low-pressure irrigation and gravity flow will result in fewer reoperations than high-pressure irrigation. Study follow-up will be for one year post-injury. The primary outcome is reoperation for infection, wound healing or fracture healing problem. Secondary outcomes include health related quality of life. Enrollment was completed on September 30, 2013, with 2545 patients enrolled internationally, and 149 covered under this grant.

15. SUBJECT TERMS
Open fracture; irrigation; infection

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRMC
U	U	U	UU	206	19b. TELEPHONE NUMBER *(include area code)*

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INTRODUCTION:

Thorough irrigation and debridement is the most important initial step in preventing infection in open fractures. However, there is little clinical evidence as to the best irrigation methods and additives. This is a blinded (patients and outcome assessors), 2x3 factorial design randomized trial to investigate whether irrigation solution (soap vs. saline solution), or irrigation pressure (high vs. low vs. gravity flow) will decrease the infection rate among patients with open fractures. The hypotheses are that a soap solution will result in fewer reoperations in patients with open fractures compared to saline solution, and that low-pressure irrigation and gravity flow will result in fewer reoperations than high-pressure irrigation.

BODY:

Study Objectives

The primary objective of this trial is to assess the impact of the following on re-operations at one year in patients operatively treated for open fractures of the extremity:

1. Irrigation solutions (soap vs. normal saline).
2. Irrigation pressures (high pressure vs. low pressure vs. gravity flow).

The secondary objective is to assess the impact of the following on patient function and quality of life at one year in patients operatively treated for open fractures of the extremity:

1. Irrigation solutions (soap vs. normal saline).
2. Irrigation pressures (high pressure vs. low pressure vs. gravity flow).
3. Patient beliefs on function and quality of life at one year.

Inclusion Criteria

1) Men or women who are 18 years of age or older.
2) Fracture of any extremity with complete radiographs.
3) Open fractures (Gustilo-Anderson Types I-IIIB)
4) Fracture requiring operative fixation.
5) Provision of informed consent.

* For patients with multiple open fractures, the fracture with the greatest Gustilo-Anderson Type, that does not meet exclusion criteria, will be the included fracture.

Exclusion Criteria

1) Open fractures with an associated vascular deficit (Gustilo-Anderson Type IIIC).
2) Known allergy to detergents or castile soap ingredients.
3) Previous wound infection or history of osteomyelitis in the injured extremity.
4) Previous fracture with retained hardware in injured extremity that will interfere with new implant fixation.
5) Surgical delay to operative wound management greater than 24 hours from hospital admission.
6) Use of immunosuppressive medication within 6 months.
7) Immunological deficient disease conditions (e.g. HIV).
8) Fracture of the hand (metacarpals and phalanges).
9) Fracture of the toes (phalanges).
10) Likely problems, in the judgment of the investigators, with maintaining follow-up. We will, for example, exclude patients with no fixed address, those who report a plan to move out of town in the next year, or intellectually challenged patients without adequate family support.
11) Previous randomization in this study or a competing study.
12) Patient is a prisoner or is at high risk of incarceration during the follow-up period.

Task 1. Begin enrollment of the 150 patients funded by this grant. (0-6 months)

1 a. Obtain regulatory approval to begin enrollment (0-6 months)

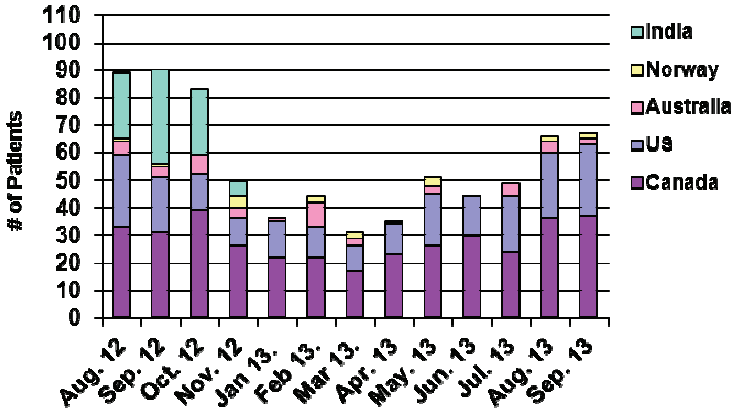
Accomplishments: As the study was ongoing with previous funding by the Department of Defense through the Orthopaedic Trauma Research Program, all participating US sites had local IRB and HRPO approval. Enrollment on this grant began on December 15, 2012 following regulatory approval from HRPO under a new HRPO log number (A. 17451) to correspond with this grant..

1b. Enrollment of at least 150 patients (0-12 months)

Accomplishments: Enrollment was stopped on September 30, 2013. Final international enrollment was 2545, with 149 of those funded by this grant.

The Statement of Work was revised in February 2013 to increase the overall study enrollment size. It was noticed that the sample size calculation of 2280 did not include appropriate calculations for loss to follow-up. Therefore, the sample size was increased to 2520. The increase in sample size did not require any changes to the US enrollment goals under this grant. The additional needed participants were enrolled at international sites. The final enrollment did exceed the sample size by 25 participants. As the enrollment approached the expected enrollment numbers, we were re-evaluating all times that that randomization system was access to ensure the correct enrollment numbers. (There were times in which the randomization system had been accessed multiple times for an individual patient, or accessed prior to consent, therefore those “randomizations” were removed from the total number.) Once it was validated that we had reached the expected enrollment, emails were sent to all centers that the randomization system would be shut down and that enrollment was complete. Appendix A shows the final enrollment for each site on this grant. Table 1 shows the enrollment per country, per month from August 2012- September 2013.

Table 1. Enrollment per country per month from August 2012- September 2013.



Task 2. Conduct Yearly Investigator Meetings (0-48 months)

2a. Conduct yearly Investigator Meeting with study investigators and coordinators, to be held during Orthopaedic Trauma Association Annual Meeting in October of each year. Additional Investigators Meetings may be held during the American Academy of Orthopaedic Surgeons meeting each spring.

Accomplishments: The yearly Investigator Meeting with study investigators and coordinators was held during Orthopaedic Trauma Association Annual Meeting in October 2012 in Minneapolis, MN.

Task 3. Maintain current IRB, HRPO and other regulatory files for all DoD funded participating centers. Regulatory files will be kept current throughout the grant cycle (0-48 months)

Accomplishments: All sites have HRPO approval.

Task 4. Continuation of data validation and quality control (0-36 months)

4a. It is estimated that all data will be collected and validated with all quality controls completed within 36 months. Quality control is ongoing and will continue until all queries have been resolved and all outcomes have been adjudicated.

Accomplishments: Quality control is ongoing and will continue until all queries have been resolved and all outcomes have been adjudicated. A sample of a Quality Control Report is attached as Appendix B.

Task 5. Conduct site monitoring and close-out visits as necessary (0-48 months)

Accomplishments: Site monitoring visits have occurred for University of Alabama-Birmingham, University of Missouri, and the University of Pittsburgh. A monitoring visit has been scheduled for Scottsdale Health. Other monitoring visits are currently being scheduled.

Task 6. Data Monitoring Committee meetings

6a. DMC meetings are to be held at least twice per calendar year (0-48 months)

Accomplishments: The Data Monitoring Committee met in January 2013 to review the interim analysis. Since the purpose of this meeting to review the interim analysis, a standard DMC meeting was not held. Due to the confidentiality of the data discussed at this meeting, formal meeting minutes were not distributed. However, the following action items were released from the meeting:

1. The statistician will update the power analysis table to include lower control event rates and calculate a sample size increase required to achieve 80% power or higher.
2. The study team will discuss the feasibility of increasing the sample size, and the magnitude of the sample size increase, if applicable.

The email response from the Steering committee regarding these action items is included in Appendix C. These actions were completed with the Amendment to Version 6 of the protocol, and updating the Statement of Work (February 2013).

The next DMC meeting is scheduled for December 9, 2013.

Task 7. Project coordinators will have at least one in person Study update meeting per year. (0-48 months)

Accomplishments: The Project coordinators held a Study update meeting during in Minneapolis, MN in October 2012 in conjunction with the Orthopaedic Trauma Association Annual meeting.

Task 8. Final one year follow-up for patients (12-42 months)

8a. Data cleaning of all patients with 1 year follow-up complete

Accomplishments: Data cleaning is ongoing.

Task 9. Adjudication of clinical outcomes (0-48 months)

A blinded Central Adjudication Committee will judge whether our primary endpoint (re-operation for infection, wound healing problem or fracture healing problem) has occurred. Adjudication of outcomes is completed in small batches (<20 patients at a time). Adjudication will be completed for all situations where eligibility is in doubt, all re-operations to treat infection, wound healing problems, or fracture healing problems (delayed unions and nonunions), all soft tissue procedures without infection or wound healing problems in patients who have undergone more than 3 re-operations, and all non-operatively managed infections, wound healing problems and fracture healing problems. Soft tissue procedures without infection will also be adjudicated by this committee, but only for patients who have undergone more than 3 re-operations.

9a. Adjudication of all primary outcomes (reoperation) The primary study endpoint is re-operation within 12 months post initial surgery to treat an infection, manage a wound healing problem, or promote fracture healing. Re-operation is defined as a surgery that occurs subsequent to the initial procedure. This composite endpoint of re-operation will include a narrow spectrum of patient-important procedures:

- irrigation and debridement for infection wound,
- revision and closure for wound dehiscence,
- wound coverage procedures for infected or necrotic wound,
- drainage of a hematoma,
- re-operation for hardware failure that is likely related to an infection, wound healing problem, or bone healing problem (delayed union or non-union),
- bone grafts or implant exchange procedures for established nonunion in patients with postoperative fracture gaps less than 1cm,
- intramedullary nail dynamizations in the operating room, and
- fasciotomies for compartment syndrome.

We will assess whether a patient has had a re-operation at 1 week, 2 weeks, 6 weeks, 3 months, 6 months, 9 months, and 1 year follow up visits.

9b. Adjudication of Infections

Infections will be classified according to a modification of the Center for Disease Control Criteria (CDC). We will define infection in patients as a constellation of clinical symptoms and laboratory examinations. These will include (but are not limited to) fever, erythema/cellulites, positive tissue cultures, and frank purulent drainage. When interpreting the criteria, any infections that are superficial to the fascia will be considered "Superficial Incisional SSI" and any infections that are deep to the fascia will be considered "Deep Incisional SSI" (including infections of the bone (osteomyelitis)). Organ/Space SSI will refer to any infections that affect an organ, other than bone.

9c. Adjudication of Wound Healing Problems

Our definition for wound healing problems will follow previously published criteria (Anglen, 2005). Any re-operations related to problems with primary wound healing will be documented. These include: 1) a dehiscence of a suture line, death of a flap or graft, or failure to heal which is not due to underlying deep infection (drainage of purulent fluid and positive cultures) or 2) problems with secondary healing that include failure of the wound to progress to satisfactory closure (wound becomes larger over time, failed granulation, or development of necrosis all requiring further intervention).

9d. Adjudication of Bone Healing Problems

Diagnosis of nonunion will include a failure of the fracture to progress towards healing as observed by the treating surgeon and that requires further intervention to promote healing either surgical (i.e. bone graft) or non-surgical (i.e. bone stimulator). Final consensus on nonunion will be determined by the Central Adjudication Committee (CAC).

9d. Adjudication of Non-Events

The following conditions are not considered outcome events:

1) planned secondary interventions from initial surgical procedures

2) any re-operations to promote fracture healing in patients with post-operative fracture gaps greater than 1 cm.

Accomplishments: Task 9a-d.

The blinded Central Adjudication Committee has met regularly via teleconference to evaluate the above events. To date, of the 2545 enrolled patients, 1559 have reached one year of follow-up. Adjudication of events has been completed for 494 patients, and is pending for 198. Adjudication was not required for 867 patients. The current Adjudication Charter is attached as Appendix D.

Task 10. Assessment of Secondary Study Outcomes (0-48 months)

The secondary study outcomes include:

- patient function and quality of life measured by the Short Form-12 (SF-12) and the EuroQol-5D (EQ-5D) at 1 week, 2 weeks, 6 weeks, 3 months, 6 months, 9 months, and 12 months,
- non-operatively managed infections, wound healing problems and fracture healing problems within 12 months, and

- patient's illness beliefs with the Somatic Pre-Occupation and Coping (SPOC) questionnaire at 1 week and 6 weeks.

10a. SF-12

The SF-12 questionnaire is a self-administered, 12-item questionnaire that measures health-related quality of life in eight domains that can be aggregated into a physical and mental summary scores. Each domain is scored separately from 0 (lowest level) to 100 (highest level).

10b. EQ-5D

The EQ-5D is a standardized instrument for use as a measure of health outcome (Brooks et al, 2003). The EQ-5D will be administered at North American sites only. We will conduct economic analysis in the context of North American setting, when additional funding is obtained. We will thus collect quality of life data measured by EQ-5D which is appropriate for economic analysis, in North American sites only. Patients who are completing the self-administered version of the EQ-5D will also be asked to complete a test version of the EQ-5D questions that uses 5-level response options. This data will be used in a sub-study comparing the test version to the validated version, which uses 3-level response options.

10c. SPOC

The SPOC questionnaire is a validated self-administered, 27-item questionnaire that measures illness beliefs.

10d. Non-operatively managed infections, wound healing problems and fracture healing problems.

The blinded CAC will adjudicate all reported events including non-operatively managed infections, wound healing problems and fracture healing problems following the definitions listed above (Task 9).

Task 10a-10d.

Accomplishments: Secondary outcomes are currently being collected and will be analyzed once study data collection is complete. Non-operatively managed infections, wound healing problems and fracture healing problems are being adjudicated with other outcomes. Please see Task 9.

Task 11. Data Analysis and manuscript preparation (32 – 48 months)

11a. Following data cleaning and adjudication of all patients, data analysis will be Conducted and primary manuscript preparation will begin.

11b. The final manuscript should be submitted for publication with 36-48 months of funding.

KEY RESEARCH ACCOMPLISHMENTS:

- The Study Protocol, Randomization System and regulatory documents were updated to increase the overall study enrollment to 2520. (The latest version of the study protocol and current CRFs are included as Appendix E and F).
- Study-wide enrollment was completed on September 30, 2013 with2545 patients enrolled internationally,149 on this grant at US sites.
- An investigator meeting was held in October 2012.
- The Central Adjudication Committee continues to adjudicate outcomes.

REPORTABLE OUTCOMES:

During the first year of funding, there were no publications or presentations based off of this work.

However, Dr. Jeray has been invited to give an presentation at the 2013 Orthopaedic Trauma Association Annual Meeting, Basic Science Research Forum regarding this study. The session was on International Research Studies. Below is the citation for his presentation:

Jeray, KJ. “International Randomized Control Trial: FLOW”, Basic Science Research Forum, Orthopaedic Trauma Association Annual Meeting, Phoenix, AZ. October 9, 2013.

CONCLUSION:

The removal of foreign material from open fractures wounds by adequate irrigation should reduce the risks of infection. However, there is a lack of clinical evidence as to the most effective methods of wound irrigation. A clinical trial comparing the effect of soap solution vs. saline, and high- vs. low-pressure lavage vs. gravity flow irrigation on reoperation rates following open wounds is warranted and is a question of importance in the field of orthopaedic trauma, both in civilian and combat situations.

As a result of the support from the CDMRP-PRORP Award, we have been successful in completing the large international randomized control trial. As we are in the final data collection phase, we are unable to make any clinical conclusions. However, all of our first year goals have been met and/or exceeded.

We believe that this study has the potential to resolve the current controversy on irrigation solutions and pressures for care of open fracture wounds. By answering these questions, we should be able to improve the current practices across both civilian and military medicine, to improve patient outcomes, and to potentially reduce health care costs. Additionally, upon completion this study has the potential to be the largest randomized controlled trial in the field of orthopaedic trauma.

REFERENCES

Flow Investigators. Fluid lavage of open wounds (FLOW): design and rationale for a large, multicenter collaborative 2 x 3 factorial trial of irrigating pressures and solutions in patients with open fractures. BMC Musculoskelet Disord. 2010 May 6;11:85.

Additional references supporting the study are included in the study protocol (Appendix E).

APPENDICES

Appendix A: Final Enrollment Numbers (Sites funded by this award)

FLOW Final Enrollment Numbers

Site Name	Site PI	Total Enrolled	Total Enrolled under W81XWH-12-1-0530
Greenville Hospital System	Kyle J. Jeray	179	29
Duke University	Robert Zura	50	2
Orthopaedic Associates of Michigan	Clifford Jones	138	46
University of Missouri	Gregory Della Rocca	58	15
Indiana University	Jan Ertl	86	13
Wright State University	Michael Prayson	21	2
Lahey Clinic	Andrew Marcantonio	30	6
University of Pittsburgh	Ivan Tarkin	15	9
University of Alabama – Birmingham	William Min	100	15
University of California-Irvine	David Zamorano	22	7
Scottsdale Healthcare	Anthony Rhorer	16	4

Appendix B: Sample Quality Control Report

Quality Control Report

015-090827

Study Coordinator Sign and Date _____

QUALITY CONTROL REPORT # 015-090827-01 (Stephanie L. Tanner, Greenville Hospital System)

PATIENT STATUS SUMMARY (* identifies patients with data queries in this report)

PATIENT	ENTRY VISIT	LAST FOLLOW-UP	NEXT FOLLOW-UP
151001*	Scrn: 28/07/2009	2W F/U: 18/08/2009	6W F/U: 08/09/2009
151002*	Scrn: 01/08/2009	2W F/U: 14/08/2009	6W F/U: 12/09/2009
151003*	Scrn: 01/08/2009	6W F/U: unknown	3M F/U: 02/11/2009
151004*	Scrn: 13/08/2009	1W F/U: 17/08/2009	2W F/U: 28/08/2009
151005	Scrn: 22/08/2009	1W F/U: 24/08/2009	2W F/U: 05/09/2009
151006*	Scrn: 22/08/2009	RBlSrg: 22/08/2009	1W F/U: 29/08/2009
153001	Scrn: 09/07/2009	Scrn: 09/07/2009	: done
153002	Scrn: 14/07/2009	Scrn: 14/07/2009	: done
153003	Scrn: 17/07/2009	Scrn: 17/07/2009	: done
153004	Scrn: 19/07/2009	Scrn: 19/07/2009	: done
153005	Scrn: 23/07/2009	Scrn: 23/07/2009	: done
153006	Scrn: 30/07/2009	Scrn: 30/07/2009	: done
153007	Scrn: 03/08/2009	Scrn: 03/08/2009	: done
153008	Scrn: 03/08/2009	Scrn: 03/08/2009	: done
153009	Scrn: 05/08/2009	Scrn: 05/08/2009	: done
153010	Scrn: 15/08/2009	Scrn: 15/08/2009	: done
153011	Scrn: 16/08/2009	Scrn: 16/08/2009	: done
153012	Scrn: 16/08/2009	Scrn: 16/08/2009	: done
153013	Scrn: 23/08/2009	Scrn: 23/08/2009	: done

TOTAL CASES = 19

FAX/REFAX LIST (Please locate/correct and then fax the following pages of the CRF)
BE SURE TO INITIAL AND DATE ALL CHANGES.

PATIENT	Forms & Visits	PROBLEM
151001	Peri Op 7.1	1. Date of discharge = (Inconsistent) REMINDER: Please re-fax form when discharge date is available.
151001	Peri Op 7.1	2. Where discharged to? = None chosen (Inconsistent) REMINDER: Please re-fax form when discharge location is available.
151002	Baseline 3.3	11. Use tobacco products = Yes (Missing Value) Please complete all items in question 11 if the patient's answer is "yes". Thank you.
151002	Peri Op 7.1	1. Wound vac = Yes (Inconsistent) For question "1. Wound vac": All of the next 2 fields are required, but some of them are not completed. Either change the response for this question, or fill in the next 2 fields.

015-090827

Study Coordinator Sign and Date _____

QUALITY CONTROL REPORT # 015-090827-02 (Stephanie L. Tanner, Greenville Hospital System)

FAX/REFAX LIST (Please locate/correct and then fax the following pages of the CRF)
BE SURE TO INITIAL AND DATE ALL CHANGES.

PATIENT	Forms & Visits	PROBLEM
151002	Peri Op 7.1	1. Date of removal = (Missing Value) When it is available, please specify the date of removal of the wound vac.
151002	F/U Rpt 8.4 1W	18. Wound vac = Yes (Inconsistent) For question "18. Wound vac": All of the next 2 fields are required, but some of them are not completed. Either change the response for this question, or fill in the next 2 fields.
151002	F/U Rpt 8.4 1W	18. Date of removal = (Missing Value) Please record the date of wound vac removal. Thank you.
151002	F/U Rpt 8.4 2W	18. Wound vac = Yes (Inconsistent) For question "18. Wound vac": All of the next 2 fields are required, but some of them are not completed. Either change the response for this question, or fill in the next 2 fields.
151003	F/U Rpt 8.1 6W	(Missing Page)
151003	F/U Rpt 8.3 6W	(Missing Page)
151003	F/U Rpt 8.4 6W	(Missing Page)
151004	Baseline 3.3	11. Use tobacco products = Yes (Inconsistent) Iconsistency in responses to question" 11. Use tobacco products".
151004	Baseline 3.3	11. How long (yrs) = (Inconsistent) This field is required; please supply a value or enter a missing code.
151004	Baseline 3.3	11. Yes, cigars/week = (Inconsistent) This field is required; please supply a value or enter a missing code.
151004	Baseline 3.3	11. Yes, chewing/week = (Inconsistent) This field is required; please supply a value or enter a missing code.
151004	Baseline 3.3	12. Drinks per week = 01.0 (Other Problem) Should this be 7 drinks per week?
151004	Meds Log 4.1	(Missing Page)

Quality Control Report

015-090827

Study Coordinator Sign and Date _____

QUALITY CONTROL REPORT # 015-090827-03 (Stephanie L. Tanner, Greenville Hospital System)

FAX/REFAX LIST (Please locate/correct and then fax the following pages of the CRF)
BE SURE TO INITIAL AND DATE ALL CHANGES.

PATIENT	Forms & Visits	PROBLEM
151006	Baseline 3.3	16. No (not any of class) = Not checked (Inconsistent) For question 16: At least one of the next 6 fields are required, but none of them are completed. Either change the response for this question, or fill in one of the next 6 fields.
151006	Peri Op 7.1	1. Date of discharge = (Inconsistent) REMINDER: Please re-fax form when discharge date is available.
151006	Peri Op 7.1	2. Where discharged to? = None chosen (Inconsistent) REMINDER: Please re-fax form when discharge location is available.
151006	Peri Op 7.1	1. Wound vac = None chosen (Missing Value) Please remember to indicate whether a wound vac was used. Thank you.

Appendix C:Email Chain Regarding Action Items from the Interim Analysis

From: Doug Altman [mailto:doug.altman@csm.ox.ac.uk]
Sent: Wednesday, February 13, 2013 10:10 AM
To: Gandhi, Dr. Rajiv; Bhandari, Mohit; McKay, Paula; Markus Bischoff
Cc: Heels-Ansdell, Diane (ansdell); Madden, Kim
Subject: RE: Response to DMC -FLOW Study

Yes I agree. It's a very pragmatic way to proceed.
Best wishes
Doug

From: Gandhi, Dr. Rajiv [mailto:Rajiv.Gandhi@uhn.ca]
Sent: 13 February 2013 13:25
To: 'Bhandari, Mohit'; McKay, Paula; Doug Altman; Markus Bischoff
Cc: Heels-Ansdell, Diane (ansdell); Madden, Kim
Subject: RE: Response to DMC -FLOW Study

Dear Mo

I have no concerns – congratulations on finding some greater efficiencies to enrol more patients

Best of luck
Rajiv

From: Bhandari, Mohit [mailto:bhandam@mcmaster.ca]
Sent: Tuesday, February 12, 2013 3:27 PM
To: McKay, Paula; Doug Altman; Gandhi, Dr. Rajiv; Markus Bischoff
Cc: Heels-Ansdell, Diane (ansdell); Madden, Kim
Subject: Response to DMC -FLOW Study

Dear FLOW DMC members,

Thanks again for participating in our recent call to review the interim analysis data for FLOW. We have investigated the possibility of obtaining additional funding and it seems highly unlikely we can raise another several hundred thousand dollars to increase our sample size by about 1000 patients, as per Diane's revised power analyses. However, we have identified some efficiencies in our current budget that would allow us to increase the sample size to 2520 patients recruited (which is another 240 patients enrolled). While less than ideal, this provides for a modest increase in sample size without the need to have the sites stop enrollment while we approach the CHIR or other agencies for additional funds without any assurance that additional funds are forthcoming.

Based on the aggregate data on overall event rate, we have no idea what the treatment effect is, and we could still be powered if low pressure performs better than 30% reduction in risk. We are not as concerned about the soap comparison as this is likely a powered analysis.

We look forward to your comments on this plan, which we feel is the best way forward given our current circumstances.

Sincerely,
Mo

Mohit Bhandari

Appendix D: Updated Adjudication Charter

ADJUDICATION CHARTER

Fluid Lavage of Open Wounds (FLOW): A Multi-center, Blinded, Factorial Trial Comparing Alternative Irrigating Solutions and Pressures in Patients with Open Fractures

Version: 3.0

Date: June 1, 2011

SIGNATURE PAGE

Reviewed and Approved by:		
(Adjudication Committee Chair) ***Emil Schemitsch***	***Signature:***	***Date:***
(Adjudication Committee Chair Alternate) ***Mohit Bhandari***	***Signature:***	***Date:***
(Adjudication Committee Member) ***Kyle Jeray***	***Signature:***	***Date:***
(Adjudication Committee Member) ***Brad Petrisor***	***Signature:***	***Date:***
(Adjudication Committee Member) ***Gregory Della Rocca***	***Signature:***	***Date:***

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LIST OF ABBREVIATIONS

Abbreviation	Definition
AP	Anterior Posterior
CAC	Central Adjudication Committee
CV	Curriculum Vitae
EDC	Electronic Data Capture
SOPs	Standard Operating Procedures
SSI	Surgical Site Infection

DOCUMENT REVISION HISTORY

Date	Version Number	Section(s) affected	Summary of Changes(s)	Author(s)
August 13, 2010	1.0	Entire Document	Initial Version	S. Sprague C. Vannabouathong
January 20, 2010	2.0	Signature Page Section 3 Section 4 Section 5 Section 6 Section 9 Section 10 Appendix I Appendix II	• Gregory Della Rocca added to the Adjudication Committee • Emil Schemitsch to replace Mohit Bhandari as the Adjudication Committee chair • Mohit Bhandari's role as Adjudication Committee Chair revised • Added "drainage of a hematoma" as a study event. • Added "re-operation for hardware failure that is likely related to an infection, wound healing problem, or bone healing problem" as a study event • Added information regarding adjudication of early re-operations. • Revised information regarding adjudication of "planned" re-operations.	P. Mckay S. Sprague S. Resendes
June 1, 2011	3.0	Section 9 Section 10 Appendix I	• Modified the CDC infection criteria to exclude the timeline restrictions pertaining to superficial, deep and organ space surgical site infections.	S. Resendes P. McKay

1.0 INTRODUCTION

The purpose of the Adjudication Charter is to describe the responsibilities and processes for the Adjudication Committee for the FLOW study. The primary responsibility of the Adjudication Committee is to confirm fracture eligibility and adjudicate secondary procedures and non-operatively treated fracture related adverse events. This document details the procedures for the Adjudication Committee to confirm subject eligibility and adjudicate the study endpoints. For details on the collection of adjudication materials, preparation of the adjudication materials, and quality control with the clinical sites, please refer to the Standard Operating Procedures (SOPs), FLOW Adjudication Operations Manual, and the FLOW Adjudication Communication and Escalation Plan.

Adjudication Charter Sign-Off

The Adjudication Committee members will review and approve the processes outlined in the Adjudication Charter prior to beginning the adjudication for FLOW. This sign-off will confirm that Adjudication Committee approves the processes and the decision rules. The Adjudication Committee members will also review and sign-off on any charter amendments.

2.0 PROTOCOL SUMMARY

Methodology	Multi-center, Blinded, Factorial Randomized Trial
Study Duration	June 2009 to December 2012
Study Center(s)	Multi-Center
Primary Study Questions	1) In patients operatively treated for open fractures of the extremity, is there any difference in effects of solutions (soap vs. normal saline) on re-operations at one year? 2) In patients operatively treated for open fractures of the extremity, is there any difference in effects of the pairs of irrigation pressures (high vs. low; high vs. gravity flow; low vs. gravity flow) on re-operations at one year?
Number of Subjects	2,280
Diagnosis and Main Inclusion Criteria	Acute open fractures (Gustilo-Anderson Types I-IIIB) of the extremities requiring operative treatment
Study Product, Dose, Route, Regimen	Irrigation solutions: normal saline, and soap solution Irrigation pressures: high pressure (>20 psi), low pressure (5-10 psi), and low gravity flow (1-2 psi)

3.0 ADJUDICATION COMMITTEE MEMBERSHIP

3.1 Chair of the Adjudication Committee

The Adjudication Committee is chaired by Dr. Emil Schemitsch (**Figure 1**). Dr. Schemitsch is an orthopaedic surgeon who specializes in orthopaedic trauma with expertise in research methodology and prior experience with clinical trials and adjudication. His curriculum vitae (CV) is on file at the FLOW Methods Centre**.**

Figure 1: Dr. Emil Schemitsch

3.2 Adjudication Committee Chair Alternate

The Trial Principal Investigator, Dr. Mohit Bhandari (**Figure 2**), will serve as the Adjudication Committee Chair Alternate. Dr. Bhandari will not routinely adjudicate study outcomes for each patient, but may propose consensus decisions and/or chair the consensus meeting should the chair, Dr. Emil Schemitsch, be unavailable. Dr. Bhandari's CV is on file at the FLOW Methods Centre.

Figure 2: Dr. Mohit Bhandari

3.3 Members of the Adjudication Committee

The Adjudication Committee is composed of three members (**Figure 3**), in addition to the Chair. The members are Dr. Kyle Jeray, Dr. Brad Petrisor, and Dr. Gregory Della Rocca. All members are orthopaedic surgeons who specialize in orthopaedic trauma with expertise in research

methodology and prior experience with clinical trials and adjudication. The Adjudication Committee members' CVs are on file at the FLOW Methods Centre.


Dr. Kyle Jeray


Dr. Brad Petrisor

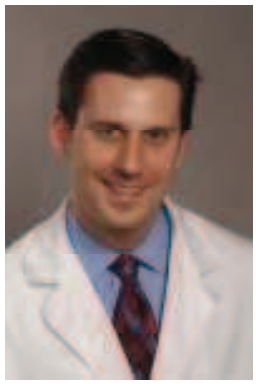
Dr. Gregory Della Rocca

Figure 3: Adjudication Committee Members

3.4 Contact Information for Adjudication Committee Members

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Adjudication Committee Member
Co-director, orthopaedic trauma service
Associate program director
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Columbia, Missouri 65212
Office phone 573-884-6633
Office fax 573-884-0438
Email: dellaroccag@health.missouri.edu

4.0 ROLE OF THE ADJUDICATION COMMITTEE CHAIR

The Chair of the Adjudication Committee, Dr. Emil Schemitsch, is responsible for ensuring that the procedures described in the Adjudication Charter are followed and that all adjudication is completed on time. He is also responsible for addressing any problems or delays that occur. In addition, the Chair of the Adjudication Committee will chair each Adjudication Consensus meeting and ensure that a decision is reached on each disagreement.

The Chair of the Adjudication Committee will select the Adjudication Committee members. The Chair of the Adjudication Committee is also responsible for writing and updating the Adjudication Charter and developing the adjudication decision rules **(Appendix I)** within the Adjudication Charter. The Chair of the Adjudication Committee will ensure that all adjudication is completed on time and that the decision rules are applied to each question that is being adjudicated. The Global Adjudicator™ (Section 7.0), an internal system to facilitate the adjudication process, will help to ensure that the decision rules are followed through programmed logic checks. In addition, the minutes from each consensus call will document the decisions made at the consensus meetings.

The Chair of the Adjudication Committee is responsible for communicating as necessary with Adjudication Committee members and addressing any queries and concerns that arise from the Adjudication Committee members. The Chair of the Adjudication Committee is responsible for communicating with the Steering Committee, as appropriate, should any problems or issues arise with adjudication. The Chair may also communicate with the investigative site as necessary.

The Chair of the Adjudication Committee will lead each of the consensus meetings, which includes reviewing and presenting minutes of the last consensus meetings, presenting outstanding issues from previous meetings, providing a summary of key decisions from previous meetings, arbitrating discussions on disagreements, and ensuring a decision is reached on all disagreements. Should the Chair not be available, Dr. Mohit Bhandari or another member of the Adjudication Committee may Chair the consensus meeting.

5.0 ROLE OF THE ADJUDICATION COMMITTEE MEMBERS

5.1 Completion of Adjudication

The Adjudication Committee members are responsible for assessing and adjudicating the following:

- Patients whose eligibility is in doubt (Section 8.0)
- Re-operations to treat infection, wound healing problems, hematomas, or fracture healing problems (delayed unions, nonunions and hardware failures) and soft tissue procedures without infection in patients who have undergone more than 3 re-operations
- Non-operatively managed infections, wound healing problems, and fracture healing problems (Section 9.0)

The adjudication material, including X-rays, clinical notes, and/or case report forms will be posted on the Global Adjudicator™ website (Section 7.0). Each Adjudication Committee member is responsible for the careful review of the adjudication material and answering the appropriate adjudication questions **(Appendix II)** on the Global Adjudicator™. They are also responsible for applying the adjudication decision rules **(Appendix I)** to all adjudication questions.

The Adjudication Committee members are responsible for communicating any technical issues, problems with the Global Adjudicator™ website, or errors or inconsistencies in the posted adjudication material to the Research Associate. They are also responsible for maintaining data quality.

5.2 Adjudication Committee Training

Prior to beginning adjudication the Adjudication Committee members will review the Adjudication Charter and the Global Adjudicator User's Guide for Adjudication and may contact the Chair with any questions or concerns.

5.3 Participation in Consensus Meetings

The members of the Adjudication Committee will be required to participate in regularly scheduled consensus calls. At least three of the four members of the Adjudication Committee members should participate in the consensus calls where disagreements are discussed, as disagreements will be resolved by consensus. The Chair of the Committee (or designee) may follow-up with any members who are unable to participate in the consensus meeting. If after extensive deliberation a consensus is not acquired, a vote will be permitted at the discretion of the Chair and recorded in the minutes of the call. Once consensus has been reached by the Adjudication Committee members, either by consensus or vote, the consensus data will be entered into the consensus section of the Global Adjudicator™ system.

5.4 Replacement of an Adjudication Committee Member

In the event that it is necessary to replace a member of the Adjudication Committee, it is the responsibility of the Chair of the Adjudication Committee to select a new member. Potential reasons for replacing an Adjudication Committee member include:

- Resignation of an Adjudication Committee member. Adjudication Committee members must provide at least 30 days notice prior to resignation.
- Inadequate performance in the opinion of the Chair of the Adjudication Committee, including failure to meet adjudication deadlines, lack of participation in consensus meetings, or inability to meet any of the responsibilities of an Adjudication Committee member as detailed in the Adjudication Charter

The decision to replace an Adjudication Committee member will be made by the Chair of the Adjudication Committee. The Chair of the Adjudication Committee will be responsible for recommending a replacement Adjudication Committee member. The new Adjudication Committee member must be a trauma-fellowship trained orthopaedic surgeon with previous experience with clinical research. The Adjudication Charter will be updated to reflect the change in Committee membership.

6.0 ADJUDICATION PROCESS

6.1 Administration

The primary objective of this trial is to assess re-operation rates within 12 months after initial surgery across soap vs. saline, and low vs. high, gravity flow vs. high, and low vs. gravity flow pressure irrigation. The primary study endpoint is re-operation within 12 months post initial surgery to treat an infection, manage a wound healing problem, drain a hematoma, or promote fracture healing. Re-operation is defined as a surgery that occurs subsequent to the initial procedure. This composite endpoint of re-operation will include a narrow spectrum of patient-important procedures:

- irrigation and debridement for infected wound,
- revision and closure for wound dehiscence,
- wound coverage procedures for infected or necrotic wound,
- drainage of a hematoma,
- re-operation for hardware failure that is likely related to an infection, wound healing problem, or bone healing problem (delayed union or nonunion)
- bone grafts or implant exchange procedures for established nonunion in patients with postoperative fracture gaps less than 1cm,
- intramedullary nail dynamizations in the operating room, and
- fasciotomies for compartment syndrome.

The secondary study endpoints include non-operatively managed infections, wound healing problems, and fracture healing problems within 12 months.

Patient fracture eligibility, re-operations, and non-operatively managed infections, wound healing problems, and fracture healing problems will be adjudicated for patients following their

12 month visit. Patient fracture eligibility will only be adjudicated in situations where patient eligibility is in doubt.

Completed cases will be posted on the Global Adjudicator™ website by the Research Associate in batches. The information for adjudication will remain on the website for the duration of the trial so that Adjudication Committee members may view cases previously adjudicated. This includes both the consensus answers as well as their individual answers. They will not be able to change previously adjudicated answers, unless the Adjudication Committee agrees that an error has been made or unless additional data becomes available. The FLOW Adjudication Operations Manual describes the process for making changes to adjudication data. The Global Adjudicator™ website will prompt the adjudicators on which items require adjudication and the questions that need to be addressed for each item. The adjudicators will review the appropriate X-rays, clinical notes, and/or case report forms to answer each question.

Each adjudicator will be notified by email when cases are available for adjudication. The Research Associate will send reminders to the Adjudication Committee members to help ensure the adjudication is completed on time. The reminders will be sent by email, with follow-up telephone calls as necessary. The details are outlined in the FLOW Adjudication Communication and Escalation Plan.

The Adjudication Committee members will complete the adjudication using the information that is available. The Research Associates will work with the clinical sites to ensure that the required adjudication materials, including the radiographs, clinical notes, and/or case report forms are available. If insufficient information is posted, the Adjudication Committee members may request additional information from the clinical sites. The Research Associate will facilitate the requests for additional information from the clinical sites. In circumstances where some materials are not available, the Adjudication Committee members will answer the questions to the best of their ability using the information available.

The Adjudication Committee members will participate in conference calls to reach consensus on any disagreements. If the Adjudication Committee members disagree on any of the adjudication questions, they will resolve these disagreements during the consensus conference calls. The Research Associate will schedule the teleconferences in advance and will ensure that the Adjudication Committee members are available for participation. The successful completion of the trial is dependent upon the adjudication being completed in a timely manner.

The Adjudication Committee members will complete the adjudication questions using the Global Adjudicator™'s electronic data capture system (EDC) with built-in logic checks. After answering the adjudication questions, the Adjudication Committee members will electronically sign-off on their answers. Should the Global Adjudicator™ system not be available, paper case report forms will be used.

The Adjudication Charter and the Decision Rules **(Appendix I)** will be posted on the Global Adjudicator™ in read-only format. If the Adjudication Committee members have questions regarding a decision rule, they should immediately contact the Program Manager or Research Associate, who may defer the question to the Adjudication Committee Chair as appropriate.

The Adjudication Committee members will view the X-rays in read-only format and they are not permitted to edit the X-rays in any form. They can scroll through and pan the X-rays, as well as zoom in and out on the X-rays.

6.2 De-identifying of Adjudication Material

All Adjudication Committee members will be blinded to subject's treatment allocation and blinded to the name of the clinical site. The clinical sites will ensure that subject's personal identifiers are removed from the X-ray image prior to sending them to the FLOW Methods Centre. Information such as the clinical site identification number and clinical site name and location will be removed prior to posting the material on the Global Adjudicator™. To identify the clinical site, a letter code will be used instead of the site identification number. The Research Associate will be responsible for assigning the letter coding to each participating clinical site in the Global Adjudicator™ system. A list will be kept on file at the FLOW Methods Centre that identifies the letter code assigned to each clinical site. The procedures to ensure quality control are outlined in the FLOW Adjudication Operations Manual.

If an Adjudication Committee member identifies adjudication materials that have not had the clinical site and subject identifiers removed, they must notify the Research Associate. The Research Associate will ensure that the item is withdrawn from the Global Adjudicator™ immediately. The Research Associate will notify the clinical site if the problem is with an X-ray or clinical note. The details are outlined in the FLOW Adjudication Communication and Escalation Plan and in FLOW Adjudication Operations Manual.

6.3 Communications

Details of the communications are summarized in the FLOW Adjudication Communication and Escalation Plan and in the FLOW Adjudication Operations Manual.

Briefly, Chair of the Adjudication Committee, the Program Manager, and/or the Research Associates may provide feedback to the clinical sites on the following parameters:

- Issues with X-ray quality
- Issues with clinical notes
- Inconsistencies identified within the adjudication materials (i.e. discrepancies between X-ray dates or information from the clinical notes)
- Issues with data quality

6.4 X-ray Quality

Every effort will be made to ensure that high quality X-rays are taken and available for adjudication (**Figure 4**). If an Adjudication Committee member finds the quality of an X-ray to be unacceptable (**Figure 5**), they will inform the Research Associate as necessary.

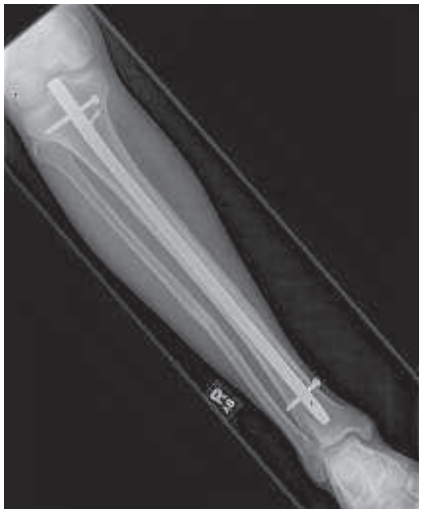
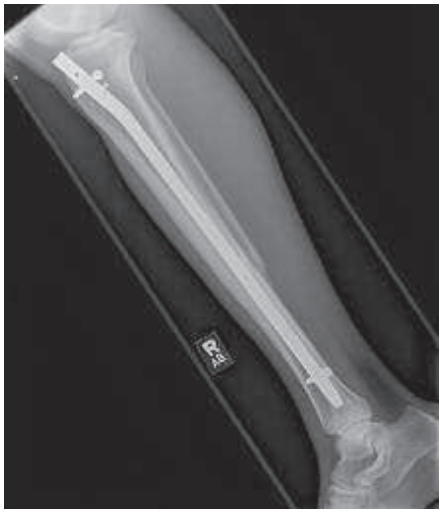
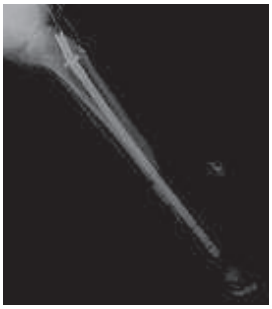
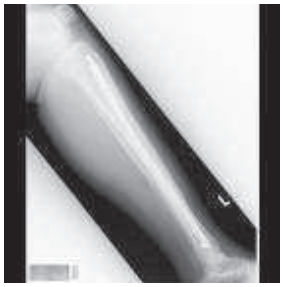
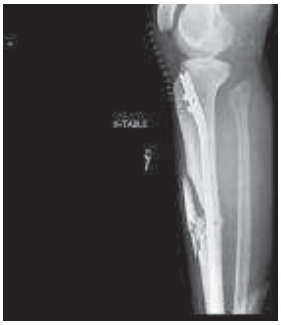



Figure 4: Example of Acceptable X-rays

Underexposed **Overexposed** **Full tibia not shown**

Figure 5: Examples of Unacceptable X-rays

6.5 Clinical Notes

The Adjudication Committee may require clinical notes to adjudicate fracture eligibility, re-operations and non-operatively managed infections, wound healing problems, and fracture healing problems. Clinical notes include the subject's in-hospital notes (initial consultation note, surgical note, and discharge note) and follow-up notes (clinic notes and surgical notes).

Should the Adjudication Committee members find that there is insufficient information available, they will notify the Research Associate as necessary. Every attempt will be made to obtain the required information from the clinical site. Once the missing information has been obtained, it will be posted on the Global Adjudicator™ website. The Adjudication Committee members will be notified that additional information is posted via email.

6.6 Data from the Case Report Forms

The Adjudication Committee may require completed case report forms to adjudicate fracture eligibility, re-operations and non-operatively managed infections, wound healing problems, and

fracture healing problems. Should the Adjudication Committee members find that there is insufficient information available, they will notify the Research Associate as necessary. Every attempt will be made to obtain the required information from the clinical site. Once the missing information has been obtained, it will be posted on the Global Adjudicator™ website. The Adjudication Committee members will be notified that additional information is posted via email.

6.7 Quality Control

The Adjudication Committee members should look for inconsistencies in X-rays and clinical notes due to clinical site errors. If an Adjudication Committee member notices an inconsistency, they are to notify the Research Associate immediately. Any inconsistencies within X-rays and clinical notes, between two different sets of clinical notes, or between two X-rays will be brought to the attention of the clinical site. The clinical site must resolve the inconsistency promptly. The details are outlined in the FLOW Adjudication Communication and Escalation Plan.

7.0 GLOBAL ADJUDICATOR™

The Global Adjudicator™ (**Figure 6**) has been specifically designed to facilitate the adjudication of orthopaedic clinical trials. The Global Adjudicator™ will be used as an internal system to facilitate the adjudication process for FLOW. Administrative access to the Global Adjudicator™ system is limited to study personnel. The Adjudication Committee members will have access to review the adjudication materials and to answer their adjudication questions in the Global Adjudicator™'s electronic data capture system. Logic checks have been built into the system to help ensure that the decision rules are followed.

The adjudication material will be posted on the Global Adjudicator™ website at www.globaladjudicator.ca. The Adjudication Committee members will review the Global Adjudicator™ Users Guide for instructions on how to use the Global Adjudicator™ system. The Adjudication Committee members will review the appropriate adjudication materials and then independently record their answers to the adjudication questions in the Global Adjudicator™ system. The system will export their answers into consensus tables, which will be reviewed and discussed at each consensus call. The final consensus answers will also be recorded in the Global Adjudicator™ system. The consensus procedures are documented in the FLOW Adjudication Operations Manual.

Figure 6: Global Adjudicator™ Home Page

8.0 ADJUDICATION OF FRACTURE ELIGIBILITY

8.1 Fracture Eligibility Adjudication Process

All members of the Adjudication Committee will adjudicate fracture eligibility in cases where eligibility is in doubt. The adjudication will be completed when the patient has completed their one-year follow-up. They will review the patient's radiographs, clinical notes, and completed case report forms. The Global Adjudicator™ website will have the subject's pre-surgery X-rays, post-surgery X-rays, and the subject's in-hospital clinical notes for review. If the immediate post-surgery X-rays are not available, the Adjudication Committee members will review the next available X-rays.

8.2 Fracture Eligibility Adjudication Questions

Each Adjudication Committee member will review the available information for patients whose eligibility is in doubt and answer the questions below:

1. Does this fracture meet the eligibility criteria?
   Yes
   No
   Unable to assess

2. Why is this ineligible? Please indicate which exclusion criteria the fracture met that made it ineligible for the trial. Please check all that apply.

a) Open fractures with an associated with a vascular deficit (Gustillo-Anderson Type IIIC)?
Yes (Fracture is ineligible)
No

b) Previous wound infection or history of osteomyelitis in the injured extremity?
Yes (Fracture is ineligible)
No

c) Previous fracture with retained hardware in the injured extremity that will interfere with the new implant fixation?
Yes (Fracture is ineligible)
No

d) Fracture of the hand (metacarpals and phalanges)?
Yes (Fracture is ineligible)
No

e) Fracture of the toes (phalanges)?
Yes (Fracture is ineligible)
No

f) Other reason for exclusion?
Yes (Fracture is ineligible): Specify:_____
No

3. Comments:_____

Each adjudicator will record his responses to the above questions on the Global Adjudicator™. If the patient meets one of the exclusion criteria, the patient will be deemed ineligible. Any disagreements will be resolved during the next consensus meeting.

8.3 Decision Rules for Fracture Eligibility

The following decision rules will be applied to the confirmation of fracture eligibility:

1. The Adjudication Committee will determine if the fracture meets the eligibility criteria based upon review of the available X-rays, clinical notes and case report forms.

2. The fracture will be eligible if it meets the eligibility criteria.

3. A subject will be deemed ineligible if they meet at least one of the exclusion criteria.

4. The Adjudication Committee will document all reasons for ineligibility.

5. If a fracture is deemed ineligible, the Adjudication Committee will continue to adjudicate re-operations and non-operatively treated infections, wound healing problems, and fracture healing problems as per the study protocol and the Adjudication Charter.

9.0 RE-OPERATIONS

9.1 Secondary Procedures Adjudication Process

All members of the Adjudication Committee will adjudicate re-operations after each patient has completed their 12 month follow-up. Specifically the Adjudication Committee will adjudicate all re-operations to treat infection, wound healing problems, drainage of hematomas, or fracture healing problems (delayed unions and nonunions), and soft tissue procedures without infection in patients who have undergone more than 3 re-operations. The Adjudication Committee will also adjudicate any re-operations for hardware failure that are likely related to an infection, wound healing problem, or bone healing problem (delayed unions and nonunions).

The Research Associates will post the clinical notes and operative reports for any secondary procedures, along with the patient's completed case report forms and any additional X-rays, on the Global Adjudicator™ website for the adjudicators to review. Secondary procedures may fall between the scheduled visits or it may occur within a scheduled visit.

The primary study endpoint is re-operation within 12 months post initial surgery to treat an infection, manage a wound healing problem, drain a hematoma, or promote fracture healing. Re-operation is defined as a surgery that occurs subsequent to the initial procedure. This composite endpoint of re-operation will include a narrow spectrum of patient-important procedures:

- irrigation and debridement for infected wound,
- revision and closure for wound dehiscence,
- wound coverage procedures for infected or necrotic wound,
- drainage of a hematoma,
- re-operation for hardware failure that is likely related to an infection, wound healing problem, or bone healing problem (delayed union or nonunion)
- bone grafts or implant exchange procedures for established nonunion in patients with postoperative fracture gaps less than 1cm,
- intramedullary nail dynamizations in the operating room, and
- fasciotomies for compartment syndrome.

When making judgements on early re-operations, the Adjudication Committee will take into consideration the clinical information from subsequent visits. If the patient later developed an infection, wound healing problem, etc., this would be indicative that the re-operation may be related to this complication, and should be considered a study event. If the patient does not develop any future complications, the re-operation is likely due to a technical issue and should not be considered a study event.

Any planned re-operations that result in the discovery of an unknown underlying problem will be considered a study event (e.g. planned second look irrigation and debridement that results in the discovery of an infection).

The Adjudication Committee will independently review the available adjudication materials and determine if the re-operation meets the criteria for being a study event. Any disagreements will be resolved during the next consensus meeting. The consensus decisions will be recorded into the Global Adjudicator™ system following the consensus meeting.

If the Adjudication Committee is unsure if the re-operation meets the criteria for being a study event, they may request additional information from the clinical site. The Research Associate will facilitate the collection of this additional information. The details are outlined in the FLOW Adjudication Communication and Escalation Plan.

9.2 Re-Operation Adjudication Questions

Each Adjudication Committee member will independently answer the following questions for secondary procedures on the Global Adjudicator™.

1. Does this re-operation meet the criteria for being a study event?
   - o Yes (Complete question 2)
   - o No (Complete question 4)
   - o Unable to assess

2. If the re-operation is a study event, specify the type of study event:
   - o Irrigation and debridement for infected wound (Complete question 3)
   - o Revision and closure for wound dehiscence
   - o Wound coverage procedures for infected (Complete question 3) or necrotic wound
   - o Drainage of a hematoma
   - o Re-operation for hardware failure that is likely related to an infection, wound healing problem, or bone healing problem (delayed union or nonunion)
   - o Bone grafts for established nonunion in patients with postoperative fracture gaps less than 1cm
   - o Implant exchange procedures for established nonunion in patients with postoperative fracture gaps less than 1cm
   - o Intramedullary nail dynamizations in the operating room
   - o Fasciotomies for compartment syndrome
   - o Other, please specify: _____
   - o Unable to assess

3. If this patient had a re-operation to treat infection, please classify the infection according to the modified CDC criteria:
   - o Superficial SSI
   - o Deep SSI
   - o Organ/space SSI

- Unable to assess

4. If the surgery is not a study event, please indicate why:
   - Secondary procedure planned at the time of initial surgery
   - Removal of locking screws that do not dynamize the fracture
   - Soft tissue coverage in the absence of infection
   - Irrigation and debridement in the absence of infection
   - Re-operation for hardware failure that is not likely related to an infection, wound healing problem, or bone healing problem (delayed union or nonunion)
   - Secondary procedure to correct an unacceptable degree of malalignment following the initial surgery
   - Bone grafts for established nonunion in patients with postoperative fracture gaps greater or equal to 1cm
   - Implant exchange procedures for established nonunion in patients with postoperative fracture gaps greater to or equal to 1cm
   - Other, please specify: _____
   - Unable to assess

5. Comments:_____

9.3 Decision Rules for the Adjudication of Secondary Procedures

The following decision rules are to be applied to the adjudication of secondary procedures:

1. The following secondary procedures performed within 12 months of the patient's initial surgery will be adjudicated:
   - All re-operations to treat infection, wound healing problems, hematomas, or fracture healing problems (delayed unions, nonunions, and hardware failures)
   - Soft tissue procedures without infection in patients who have undergone more than 3 re-operations.

2. The Adjudication Committee will determine if a secondary procedure is a study event according to the definitions outlined in the study protocol and adjudication charter.

3. Secondary procedures that will be classified as events include:
   - Irrigation and debridement for infected wound
   - Revision and closure for wound dehiscence
   - Wound coverage procedures for infected or necrotic wound
   - Drainage of a hematoma
   - Re-operation for hardware failure that is likely related to an infection, wound healing problem, or bone healing problem (delayed union or nonunion)
   - Bone grafts for established nonunion in patients with postoperative fracture gaps less than 1cm
   - Implant exchange procedures for established nonunion in patients with postoperative fracture gaps less than 1cm

- Intramedullary nail dynamizations in the operating room
- Fasciotomies for compartment syndrome

Secondary procedures that will not be classified as events include:
- Secondary procedure planned at the time of initial surgery
- Removal of locking screws that do not dynamize the fracture
- Soft tissue coverage in the absence of infection
- Irrigation and debridement in the absence of infection
- Re-operation for hardware failure that is not likely related to an infection, wound healing problem, or bone healing problem (delayed union or nonunion)
- Secondary procedure to correct an unacceptable degree of malalignment following the initial surgery
- Bone grafts for established nonunion in patients with postoperative fracture gaps greater than or equal to 1cm
- Implant exchange procedures for established nonunion in patients with postoperative fracture gaps greater than or equal to 1cm

4. Diagnosis of nonunion will include a failure of the fracture to progress towards healing as observed by the treating surgeon and that requires further intervention to promote healing either surgical (i.e. bone graft) or non-surgical (i.e. bone stimulator).

5. The fracture gap is defined by the widest separation on the available post-definitive fixation X-rays. If there is some bone present in the fracture gap, this area does not count as part of the gap. If the percentage of cortical continuity is 50% or greater, the fracture gap will be zero by definition. If the percentage of cortical continuity is 0 or 25%, there is by definition a fracture gap. If there is a gap (defined as 0 or 25% cortical continuity), the Adjudication Committee will determine if the fracture gap is less than 1 cm. The Adjudication Committee members will estimate the size of gap in mm at its largest point on the Global Adjudicator™ viewer.

6. Infections will be classified according to a modification of the CDC criteria.

Superficial incisional surgical site infection (SSI) is defined as an infection that involves only the skin or subcutaneous tissue and at least one of the following:
- Purulent drainage, with or without laboratory confirmation, from the superficial incision.
- Organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision.
- At least one of the following signs or symptoms of infection: pain or tenderness, localized swelling, redness, or heat and superficial incision is deliberately opened by the surgeon, unless incision is culture-negative.

Deep incisional SSI is an infection that involves deep soft tissues (e.g., fascial and muscle layers) and at least one of the following:
- Purulent drainage from the deep incision but not from the organ/space component of the surgical site.

- A deep incision spontaneously dehisces or is deliberately opened by the surgeon when the patient has at least one of the following signs or symptoms: fever (>38ºC), localized pain, or tenderness, unless the site culture is negative.
- An abscess or other evidence of infection involving the deep incision found on direct examination, during re-operation, or by histopathologic or radiologic examination.

Organ/space SSI is an infection that involves any part of the anatomy (e.g., organs or spaces), other than the incision, which was opened or manipulated during an operation and at least one of the following:

- Purulent drainage from a drain that is placed through a stab wound into the organ/space.
- Organisms isolated from an aseptically obtained culture of fluid or tissue in the organ/space.
- An abscess or other evidence of infection involving the organ/space that is found on direct examination, during reoperation, or by histopathologic or radiologic examination.

When interpreting these criteria, any infections that are superficial to the fascia will be considered "Superficial Incisional SSI" and any infections that are deep to the fascia will be considered "Deep Incisional SSI" (including infections of bone (osteomyelitis)). Organ/Space SSI will refer to any infections that affect an organ, other than bone.

7. A secondary procedure to correct 0 percent cortical continuity is not to be regarded as a study event. Once a procedure has been performed and cortical continuity achieved, however, subsequent procedures may be identified as study events.

8. The Adjudication Committee will review the information from the operative reports, surgical consultation notes and case report forms to verify whether the secondary procedure was planned at the time of the initial procedure. The secondary procedure will not be considered planned unless it is clearly stated in the information that it was planned at the time of the initial procedure. The secondary procedure will be considered planned only if ALL parts of the procedure were planned. The following exceptions to this rule apply: 1) If the secondary procedure was planned but results in the discovery of an underlying problem, it will be considered a study event (e.g. planned second look irrigation and debridement that results in the discovery of an infection); 2) When antibiotic beads have been used (in which case the secondary procedure only to remove the beads, will be considered planned even if it is not explicitly stated).

9. For subjects who have had a second re-operation following an implant exchange, the second re-operation may be classified as a secondary procedure if the fracture was not healed.

10. If a subject required multiple re-operations for one indication, each re-operation will be considered a study event.

10.0 NON-OPERATIVELY MANAGED INFECTIONS, WOUND HEALING PROBLEMS AND FRACTURE HEALING PROBLEMS

10.1 Non-Operatively Managed Infections, Wound Healing Problems and Fracture Healing Problems Adjudication Process

All members of the Adjudication Committee will adjudicate all reported non-operatively managed infections, wound healing problems, and fracture healing problems after each patient has completed their 12 month follow-up.

The Research Associate will post clinical notes and the patient's completed case report forms for the adjudication of non-operatively managed infections, wound healing problems and fracture healing problems, along with any additional X-rays (as appropriate), on the Global Adjudicator™ web site for the Adjudication Committee to review. Any disagreements will be resolved during the next consensus meeting. The consensus decisions will be recorded into the Global Adjudicator™ system following the consensus meeting. Non-operatively managed infections, wound healing problems, and fracture healing problems may fall between the scheduled visits or it may occur within a scheduled visit.

If the Adjudication Committee is unsure if the non-operatively managed infection, wound healing problem, or fracture healing problem meets the criteria for being a study event, they may request additional information from the clinical site. The Research Associate will facilitate the collection of this additional information. The details are outlined in the FLOW Adjudication Communication and Escalation Plan.

10.2 Non-Operatively Managed Infections, Wound Healing Problems, and Fracture Healing Problems Adjudication Questions

Each Adjudication Committee member will independently answer the following questions for non-operatively managed infections, wound healing problems or fracture healing problems on the Global Adjudicator™.

1. Does this non-operatively managed infection, wound healing problem, or fracture healing problem meet the criteria for being a study event?
   - o Yes (Complete question 2)
   - o No
   - o Unable to assess

2. If the non-operatively managed infection, wound healing problems, and fracture healing problems event meet the criteria for being a study event, specify the type of event (please select one):
   - o Infection → Please classify according to the modified CDC criteria:
     - o Superficial incisional SSI
     - o Deep incisional SSI
     - o Organ/space SSI
   - o Wound Healing Problem (Specify)
     - o Wound dehiscence

- Wound necrosis
- Death of a flap
- Death of a graft
- Failure of closure to heal
- Wound grew larger over time
- Failed granulation
- Other (Specify):_____

o Nonunion
o Delayed Union
o Other (Specify):_____
o Unable to assess

3. Comments:_____

10.3 Decision Rules for the Adjudication of Non-Operatively Managed Infections, Wound Healing Problems, and Fracture Healing Problems

The following decision rule is to be applied to the adjudication of non-operatively managed infections, wound healing problems, and fracture healing problems:

1. Non-operatively managed infections, wound healing problems, and fracture healing problems occurring during the first 12 months will be considered study events.

2. Infections will be classified according to the modified CDC criteria.

Superficial incisional surgical site infection (SSI) is defined as an infection involves only the skin or subcutaneous tissue and at least one of the following:

- Purulent drainage, with or without laboratory confirmation, from the superficial incision.
- Organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision.
- At least one of the following signs or symptoms of infection: pain or tenderness, localized swelling, redness, or heat and superficial incision is deliberately opened by the surgeon, unless incision is culture-negative.

Deep incisional SSI is an infection that involves deep soft tissues (e.g., fascial and muscle layers) and at least one of the following:

- Purulent drainage from the deep incision but not from the organ/space component of the surgical site.
- A deep incision spontaneously dehisces or is deliberately opened by the surgeon when the patient has at least one of the following signs or symptoms: fever (>38ºC), localized pain, or tenderness, unless the site culture is negative.
- An abscess or other evidence of infection involving the deep incision found on direct examination, during re-operation, or by histopathologic or radiologic examination.

Organ/space SSI is an infection that involves any part of the anatomy (e.g., organs or spaces), other than the incision, which was opened or manipulated during an operation and at least one of the following:

- Purulent drainage from a drain that is placed through a stab wound into the organ/space.
- Organisms isolated from an aseptically obtained culture of fluid or tissue in the organ/space.
- An abscess or other evidence of infection involving the organ/space that is found on direct examination, during reoperation, or by histopathologic or radiologic examination.

When interpreting these criteria, any infections that are superficial to the fascia will be considered "Superficial Incisional SSI" and any infections that are deep to the fascia will be considered "Deep Incisional SSI" (including infections of bone (osteomyelitis)). Organ/Space SSI will refer to any infections that affect an organ, other than bone.

3. The adjudicators will classify the type of wound healing problem.

4. Diagnosis of nonunion will include a failure of the fracture to progress towards healing as observed by the treating surgeon and that requires further intervention to promote healing either surgical (i.e. bone graft) or non-surgical (i.e. bone stimulator).

5. Delayed unions are defined as failure of progression of fracture healing for at least 2 or 3 successive months with pain at the fracture site.

11.0 CONSENSUS PROCESS

Posting of adjudication materials for review and Adjudication Committee consensus conference calls will commence after the first few batches of patients has completed their 12 month follow-up and will continue at regular intervals until the last patient has completed their 12 month follow-up. After all Adjudication Committee members have completed adjudication for each batch, the Research Associate will download the consensus tables from the Global Adjudicator™ website. The Chair of the Adjudication Committee or designee may then review the tabulated results and propose consensus decisions based on the individual responses of the Adjudication Committee members.

Prior to each Adjudication Committee conference call, each Adjudication Committee member will receive via email an agenda, a table summarizing the disagreements to be discussed during the conference call, and any proposed consensus decisions recommended by the Chair. For each proposed consensus decision, if all members of the Adjudication Committee are in full agreement, it will be recorded by the Research Associate as a final consensus decision. If all members of the Adjudication Committee are not in full agreement, the item will be discussed during the conference call. The Chair of the Adjudication Committee will arbitrate the discussion and ensure that each Adjudication Committee member has the opportunity to

participate in the discussions. The Chair of the Adjudication Committee will also ensure that all of the decision rules are appropriately followed. The Adjudication Committee members will attempt to reach consensus on all counts. If after extensive deliberation a consensus is not reached, a vote will be permitted at the discretion of the Chair. In this case, the Adjudication Committee members will proceed with voting and the final decision will be based on the majority vote. The Chair of the Adjudication Committee will not override any votes. The Research Associate will record all of the final consensus decisions made by the Adjudication Committee. The final decisions will be entered in the Global Adjudicator™ system. The Chair of the Adjudication Committee will electronically sign-off on the consensus answers.

The Research Associate is responsible for preparing the minutes from each Adjudication Committee consensus teleconference. The Chair of the Adjudication Committee will review and approve the minutes. The Research Associate will send a copy of the final minutes to the Adjudication Committee members.

APPENDIX I: Decision Rules

Fracture Eligibility

The following decision rules will be applied to the confirmation of fracture eligibility:

1. The Adjudication Committee will determine if the fracture meets the eligibility criteria based upon review of the available X-rays, clinical notes and case report forms.

2. The fracture will be eligible if it meets the eligibility criteria.

3. A subject will be deemed ineligible if they meet at least one of the exclusion criteria.

4. The Adjudication Committee will document all reasons for ineligibility.

5. If a fracture is deemed ineligible, the Adjudication Committee will continue to adjudicate re-operations and non-operatively treated infections, wound healing problems, and fracture healing problems as per the study protocol and the adjudication charter.

Secondary Procedures

The following decision rules are to be applied to the adjudication of secondary procedures:

1. The following secondary procedures performed within 12 months of the patient's initial surgery will be adjudicated:
   - All re-operations to treat infection, wound healing problems, hematomas, or fracture healing problems (delayed unions, nonunions, and hardware failures)
   - Soft tissue procedures without infection in patients who have undergone more than 3 re-operations.

2. The Adjudication Committee will determine if a secondary procedure is a study event according to the definitions outlined in the study protocol and adjudication charter.

3. Secondary procedures that will be classified as events include:
   - irrigation and debridement for infected wound,
   - revision and closure for wound dehiscence,
   - wound coverage procedures for infected or necrotic wound,
   - drainage of a hematoma,
   - re-operation for hardware failure that is likely related to an infection, wound healing problem, or bone healing problem (delayed union or nonunion)
   - bone grafts or implant exchange procedures for established nonunion in patients with postoperative fracture gaps less than 1cm,
   - intramedullary nail dynamizations in the operating room, and
   - fasciotomies for compartment syndrome.

Secondary procedures that will not be classified as events include:

- Secondary procedure planned at the time of initial surgery
- Removal of locking screws that do not dynamize the fracture
- Soft tissue coverage in the absence of infection
- Irrigation and debridement in the absence of infection
- Re-operation for hardware failure that is not likely related to an infection, wound healing problem, or bone healing problem (delayed unions and nonunions).
- Secondary procedure to correct an unacceptable degree of malalignment following the initial surgery
- Bone grafts for established nonunion in patients with postoperative fracture gaps greater than or equal to 1cm
- Implant exchange procedures for established nonunion in patients with postoperative fracture gaps greater than or equal to 1cm

4. Diagnosis of nonunion will include a failure of the fracture to progress towards healing as observed by the treating surgeon and that requires further intervention to promote healing either surgical (i.e. bone graft) or non-surgical (i.e. bone stimulator).

5. The fracture gap is defined by the widest separation on the available post-definitive fixation X-rays. If there is some bone present in the fracture gap, this area does not count as part of the gap. If the percentage of cortical continuity is 50% or greater, the fracture gap will be zero by definition. If the percentage of cortical continuity is 0 or 25%, there is by definition a fracture gap. If there is a gap (defined as 0 or 25% cortical continuity), the Adjudication Committee will determine if the fracture gap is less than 1 cm. The Adjudication Committee members will estimate the size of gap in mm at its largest point on the Global Adjudicator™ viewer.

6. Infections will be classified according to the modified CDC criteria.

Superficial incisional surgical site infection (SSI) is defined as an infection that involves only the skin or subcutaneous tissue and at least one of the following:

- Purulent drainage, with or without laboratory confirmation, from the superficial incision.
- Organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision.
- At least one of the following signs or symptoms of infection: pain or tenderness, localized swelling, redness, or heat and superficial incision is deliberately opened by the surgeon, unless incision is culture-negative.

Deep incisional SSI is an infection that involves deep soft tissues (e.g., fascial and muscle layers) and at least one of the following:

- Purulent drainage from the deep incision but not from the organ/space component of the surgical site.
- A deep incision spontaneously dehisces or is deliberately opened by the surgeon when the patient has at least one of the following signs or symptoms: fever (>38ºC), localized pain, or tenderness, unless the site culture is negative.

- An abscess or other evidence of infection involving the deep incision found on direct examination, during re-operation, or by histopathologic or radiologic examination.

Organ/space SSI is an infection that involves any part of the anatomy (e.g., organs or spaces), other than the incision, which was opened or manipulated during an operation and at least one of the following:

- Purulent drainage from a drain that is placed through a stab wound into the organ/space.
- Organisms isolated from an aseptically obtained culture of fluid or tissue in the organ/space.
- An abscess or other evidence of infection involving the organ/space that is found on direct examination, during reoperation, or by histopathologic or radiologic examination.

When interpreting these criteria, any infections that are superficial to the fascia will be considered "Superficial Incisional SSI" and any infections that are deep to the fascia will be considered "Deep Incisional SSI" (including infections of bone (osteomyelitis)). Organ/Space SSI will refer to any infections that affect an organ, other than bone.

7. A secondary procedure to correct 0 percent cortical continuity is not to be regarded as a study event. Once a procedure has been performed and cortical continuity achieved, however, subsequent procedures may be identified as study events.

8. The Adjudication Committee will review the information from the operative reports, surgical consultation notes and case report forms to verify whether the secondary procedure was planned at the time of the initial procedure. The secondary procedure will not be considered planned unless it is clearly stated in the information that it was planned at the time of the initial procedure. The secondary procedure will be considered planned only if ALL parts of the procedure were planned. The following exceptions to this rule apply: 1) If the secondary procedure was planned but results in the discovery of an underlying problem, it will be considered a study event (e.g. planned second look irrigation and debridement that results in the discovery of an infection); 2) When antibiotic beads have been used (in which case the secondary procedure only to remove the beads, will be considered planned even if it is not explicitly stated).

9. For subjects who have had a second re-operation following an implant exchange, the second re-operation may be classified as a secondary procedure if the fracture was not healed.

10. If a subject has two unplanned re-operations for one indication, the second re-operation will be considered a study event in addition to the first re-operation.

Non-Operatively Managed Infections, Wound Healing Problems, and Fracture Healing Problems

The following decision rule is to be applied to the adjudication of non-operatively managed infections, wound healing problems and fracture healing problems:

1. Non-operatively managed infections, wound healing problems, and fracture healing problems occurring during the first 12 months will be considered study events.

2. Infections will be classified according to the modified CDC criteria.

Superficial incisional surgical site infection (SSI) is defined as an infection that involves only the skin or subcutaneous tissue and at least one of the following:

- Purulent drainage, with or without laboratory confirmation, from the superficial incision.
- Organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision.
- At least one of the following signs or symptoms of infection: pain or tenderness, localized swelling, redness, or heat and superficial incision is deliberately opened by the surgeon, unless incision is culture-negative.

Deep incisional SSI is an infection that involves deep soft tissues (e.g., fascial and muscle layers) and at least one of the following:

- Purulent drainage from the deep incision but not from the organ/space component of the surgical site.
- A deep incision spontaneously dehisces or is deliberately opened by the surgeon when the patient has at least one of the following signs or symptoms: fever (>38ºC), localized pain, or tenderness, unless the site culture is negative.
- An abscess or other evidence of infection involving the deep incision found on direct examination, during re-operation, or by histopathologic or radiologic examination.

Organ/space SSI is an infection that involves any part of the anatomy (e.g., organs or spaces), other than the incision, which was opened or manipulated during an operation and at least one of the following:

- Purulent drainage from a drain that is placed through a stab wound into the organ/space.
- Organisms isolated from an aseptically obtained culture of fluid or tissue in the organ/space.
- An abscess or other evidence of infection involving the organ/space that is found on direct examination, during reoperation, or by histopathologic or radiologic examination.

When interpreting these criteria, any infections that are superficial to the fascia will be considered “Superficial Incisional SSI” and any infections that are deep to the fascia will be considered “Deep Incisional SSI” (including infections of bone (osteomyelitis)). Organ/Space SSI will refer to any infections that affect an organ, other than bone.

3. The adjudicators will classify the type of wound healing problem.

4. Diagnosis of nonunion will include a failure of the fracture to progress towards healing as observed by the treating surgeon and that requires further intervention to promote healing either surgical (i.e. bone graft) or non-surgical (i.e. bone stimulator).

5. Delayed unions are defined as failure of progression of fracture healing for at least 2 or 3 successive months with pain at the fracture site.

APPENDIX II: Adjudication Questions

Fracture Eligibility

Each Adjudication Committee member will review the available information for patients whose eligibility is in doubt and answer the questions below:

1. Does this fracture meet the eligibility criteria?
   Yes
   No
   Unable to assess

2. Why is this ineligible? Please indicate which exclusion criteria the fracture met that made it ineligible for the trial. Please check all that apply.

   a) Open fractures with an associated with a vascular deficit (Gustillo-Anderson Type IIIC)?
   Yes (Fracture is ineligible)
   No

   b) Previous wound infection or history of osteomyelitis in the injured extremity?
   Yes (Fracture is ineligible)
   No

   c) Previous fracture with retained hardware in the injured extremity that will interfere with the new implant fixation?
   Yes (Fracture is ineligible)
   No

   d) Fracture of the hand (metacarpals and phalanges)?
   Yes (Fracture is ineligible)
   No

   e) Fracture of the toes (phalanges)?
   Yes (Fracture is ineligible)
   No

   f) Other reason for exclusion?
   Yes (Fracture is ineligible): Specify:_____
   No

3. Comments:_____

Secondary Procedures

Each Adjudication Committee member will independently answer the following questions for secondary procedures on the Global Adjudicator™.

1. Does this re-operation meet the criteria for being a study event?
   - o Yes (Complete question 2)
   - o No (Complete question 4)
   - o Unable to assess

2. If the re-operation is a study event, specify the type of study event:
   - o Irrigation and debridement for infected wound (Complete question 3)
   - o Revision and closure for wound dehiscence
   - o Wound coverage procedures for infected (Complete question 3) or necrotic wound
   - o Drainage of a hematoma
   - o Re-operation for hardware failure that is likely related to an infection, wound healing problem, or bone healing problem (delayed union or nonunion)
   - o Bone grafts for established nonunion in patients with postoperative fracture gaps less than 1cm
   - o Implant exchange procedures for established nonunion in patients with postoperative fracture gaps less than 1cm
   - o Intramedullary nail dynamizations in the operating room
   - o Fasciotomies for compartment syndrome
   - o Other, please specify: _____
   - o Unable to assess

3. If this patient had a re-operation to treat infection, please classify the infection according to the modified CDC criteria:
   - o Superficial SSI
   - o Deep SSI
   - o Organ/space SSI
   - o Unable to assess

4. If the surgery is not a study event, please indicate why:
   - o Secondary procedure planned at the time of initial surgery
   - o Removal of locking screws that do not dynamize the fracture
   - o Soft tissue coverage in the absence of infection
   - o Irrigation and debridement in the absence of infection
   - o Re-operation for hardware failure that is not likely related to an infection, wound healing problem, or bone healing problem(delayed union or nonunion)
   - o Secondary procedure to correct an unacceptable degree of malalignment following the initial surgery
   - o Bone grafts for established nonunion in patients with postoperative fracture gaps greater or equal to 1cm
   - o Implant exchange procedures for established nonunion in patients with postoperative fracture gaps greater to or equal to 1cm

- o Other, please specify: _____
- o Unable to assess

5. Comments:_____

Non-Operatively Managed Infections, Wound Healing Problems, and Fracture Healing Problems

Each Adjudication Committee member will independently answer the following questions for non-operatively managed infections, wound healing problems, or fracture healing problems on the Global Adjudicator™.

1. Does this non-operatively managed infection, wound healing problem, or fracture healing problem meet the criteria for being a study event?

- o Yes (Complete question 2)
- o No
- o Unable to assess

2. If the non-operatively managed infection, wound healing problems, and fracture healing problems event meet the criteria for being a study event, specify the type of event (please select one):

- o Infection → Please classify according to the modified CDC criteria:
  - o Superficial incisional SSI
  - o Deep incisional SSI
  - o Organ/space SSI
- o Wound Healing Problem (Specify)
  - o Wound dehiscence
  - o Wound necrosis
  - o Death of a flap
  - o Death of a graft
  - o Failure of closure to heal
  - o Wound grew larger over time
  - o Failed granulation
  - o Other (Specify):_____
- o Nonunion
- o Delayed Union
- o Other (Specify):_____
- o Unable to assess

3. Comments:_____

Appendix E: Protocol Version 6

Fluid Lavage of Open Wounds (FLOW): A Multi-Center, Blinded, Factorial Trial Comparing Alternative Irrigating Solutions and Pressures in Patients with Open Fractures

Methods Center:

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United States Army Institute of Surgical Research, Orthopaedic Trauma Research Program (OTRP)

Congressionally Directed Medical Research Program, Peer Reviewed Orthopaedic Research Program

Association Internationale pour l'Ostéosynthèse Dynamique (AIOD)

Canadian Institutes of Health Research (CIHR)

Date: February 19, 2013
Version: 6.0

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List of Abbreviations

Abbreviations are listed in alphabetic order:

AE: adverse event
AIOD : Association Internationale pour l'Ostéosynthèse Dynamique
CAC: Central Outcomes Adjudication Committee
CDC: Center for Disease and Control
CRF: case report form
DMC: Data Monitoring Committee
EQ-5D or EuroQol-5D: European quality-of-life five-domain questionnaire
FDA: Food and Drug Administration
FLOW: Fluid Lavage of Open Wounds
GCP: Good Clinical Practice
HIPAA: Health Insurance Portability and Accountability Act
HRPO: Human Research Protection Office
HUI: Health Utilities Index
IRB: Institutional Review Board
LAR: legally authorized representative
MCS: mental component summary
ORP: Office of Research Protections
OTRP: United States Army Institute of Surgical Research, Orthopaedic Trauma Research Program
USARMMC: US Army Medical Research Materiel Command
PCS: physical component summary
PHI: protected health information
psi: pound per square inch
RCT: randomized controlled trial
REB: Research Ethics Board
SAE: serious adverse event
SF-12: Short Form-12 questionnaire
SPRINT: Study to Prospectively evaluate Reamed Intramedually Nails in Patients with Tibial fractures
SPOC: Somatic pre-occupation and coping questionnaire
SSI: Surgical Site Infection

Study Summary

Title	Fluid Lavage of Open Wounds (FLOW): A Multi-center, Blinded, Factorial Trial Comparing Alternative Irrigating Solutions and Pressures in Patients with Open Fractures
Short Title	FLOW
Methodology	Multi-center, Blinded, Factorial Randomized Trial
Study Duration	January 2009 to December 2014
Study Center(s)	Multi-Center
Primary Study Questions	1) In patients operatively treated for open fractures of the extremity, is there any difference in effects of solutions (soap vs. normal saline) on re-operations at one year? 2) In patients operatively treated for open fractures of the extremity, is there any difference in effects of the pairs of irrigation pressures (high vs. low; high vs. gravity flow; low vs. gravity flow) on re-operations at one year?
Number of Subjects	2520
Diagnosis and Main Inclusion Criteria	Acute open fractures (Gustilo-Anderson Types I-IIIB) of the extremities requiring operative treatment
Study Product, Dose, Route, Regimen	Irrigation solutions: normal saline, and soap solution Irrigation pressures: high pressure (>20 psi), low pressure (5-10 psi), and low gravity flow (1-2 psi)

1 Introduction

This document is a protocol for a human research study. This is a multi-center, blinded, randomized controlled trial, using a 2×3 factorial design, to investigate whether irrigation solution (soap vs. normal saline) or irrigation pressure (gravity flow vs. high; low vs. high; low vs. gravity flow) will decrease re-operations among patients with open fracture wounds. The rationale for the study is fuelled by: 1) mounting experimental evidence supporting the use of a novel irrigating solution and a specific irrigating pressure, 2) clinical uncertainty in the orthopaedic community, 3) lack of randomized controlled trial (RCT) evidence, 4) extensive investigator support for the proposed trials, and 5) a feasible and efficient study design.

1.1 Background

Orthopaedic injuries represent 67% of injury admissions to Canadian hospitals (CIHI, 2003). Fractures and dislocations of the upper and lower limbs represent 16% and 38% of all injury admissions, respectively, a total of nearly 86,000 injury admissions due to fractures (CIHI, 2003). It is estimated that by 2020, disability from traffic accidents (the major cause of fractures) will rank in the top 3 of all causes of disability (Dormans, 2001).

Orthopaedic injuries are even more prominent internationally. Accelerated urbanization and industrialization in India and China, which represent 40% of the world's population, have resulted in an alarming increase in traumatic injuries. A vehicular accident is reported every three minutes and a death every ten minutes on Indian roads. For every death, 3 patients survive and live with disability (Joshipura, 1996).

Open fractures (broken bones that break through the skin) account for an estimated 250,000 fractures in North America annually (Anglen, 2001). These open fractures are often complicated by infections, wound healing problems and failure of fracture healing—many of which necessitate a re-operation. Open fractures are designated as surgical emergencies and require urgent treatment.

Infections can occur in up to 50% of open fractures that are severe or become grossly contaminated due to the mechanism of their injury (Bhandari et al, 2001; Tsukayama & Schmidt, 2001). Infection can lead to both wound and fracture healing delays (Harley et al, 2002). The additional treatment required to treat infections, as well as wound and bone healing complications, leads to a significant increase in health care cost, and greater impact on the patients' quality of life.

Current management of grossly contaminated fractures include the careful handling of the damaged soft tissues and the stabilization of the bone (Chapman 1991, Russell 1992, Gustilo 1990). The single most important step in the initial management of open fractures is a thorough irrigation and debridement (Gustilo 1990, Anglen et al, 1996; Anglen, 2001). Removal of all contaminated tissue and foreign matter is necessary to prevent infection, support wound healing, and promote fracture healing. Surgeons accomplish debridement with careful removal of all visible debris and necrotic tissue along with copious irrigation of the wound. However, there is currently no consensus regarding the optimal approach to irrigating the wounds during the initial operative procedure. Multiple options exist for irrigation solutions and the delivery of fluids.

1.2 Preclinical Data

1.2.1 Experimental Studies Evaluating the Effect of High and Low Pressure Wound Irrigation

Advocates of high-pressure irrigation believe that higher pressures optimally remove all particulate matter and contamination (Bhaskar et al 1971; Brown et al 1978; Dirschl et al, 1998, Gross et al, 1971; Caprise et al, 2002; Lee et al, 2002, Granick et al, 2007). However, low-pressure advocates believe that low-pressure irrigation may damage bone to a lesser extent than high-pressure irrigation thus preserving

bone architecture (Dirschl et al 1998; Bhandari et al, 1998; Bhandari et al, 1999 Bhandari et al, 2000; Adili et al 2002; Hassinger et al, 2005, Draeger et al 2006).

We have conducted a series of laboratory investigations using in-vitro models of a contaminated tibial shaft fracture, rat models of fracture healing, and cell culture models of bone nodule formation. Our experimental data suggests high pressure lavage may be more effective than low pressure lavage for removing debris and bacteria from contaminated open wounds after a 3 hour delay (Bhandari et al, 1999; Bhandari et al, 2000; Bhandari et al, 2001). However, the efficacy in removing debris and bacteria comes at the expense of damage to the bone tissue (Bhandari et al, 1998; Bhandari et al, 1999), bacterial propagation into the intramedullary canal of the fractured bones (Bhandari et al, 1998), and promotion of stem cell differentiation away from bone forming cells (osteoblasts) toward the adipocyte cell types (Bhandari & Schemitsch, 2002). These cellular level effects also translate into a significant reduction in ***in-vivo*** fracture strength. Mechanical testing of 36 rat fractured femora after 3 weeks of healing revealed a 37% lower peak bending force and stiffness in animals treated with high pressure irrigation compared to the low pressure groups ($p<0.05$) (Adili et al, 2002).

While findings are not always consistent (Caprise et al, 2002; Lee et al, 2002), the weight of experimental evidence suggests a trade off between greater efficacy in removing particulate matter and bacteria with high pressure irrigation with the disadvantage being the potential for bone damage, driving particulate matter deeper into bone and tissues and delaying bone healing. The lack of compelling clinical evidence strongly supports a randomized trial of varying irrigating pressures in patients with open fractures.

1.2.2 Experimental Studies Evaluating the Effect of Various Irrigating Solutions

The type of irrigating solution and its effect on the efficacy of wound debridement remains controversial. Although experimental studies have evaluated several irrigation additives including antiseptics, antibiotics, and surfactants (soap), few have revealed promise beyond the current common standard solution--normal saline.

Experiments suggest antiseptics are toxic to the host cells (Kaysinger et al, 1995; Moussa et al, 1996; Gainor BJ et al, 1997; Tarbox et al, 1998; Conroy et al, 1999; Anglen, 2001). Although some investigators have promoted irrigation with antibiotic solutions (such as bacitracin), concerns about allergic reactions (Sprung et al 1990), increased cost (Anglen 2005), promotion of antibiotic resistance, and unproven efficacy have limited widespread use (Anglen 1994). In an in-vitro study evaluating multiple irrigating solutions, exposure of mouse calvarial cells to 10% ethanol, 10% povidone-iodine, 10% antimicrobial wash, or 4% chlorhexidine gluconate resulted in cell-density decreases of 70%, 63%, 70%, and 69% respectively (Bhandari et al, 2001). Normal saline solution or soap solutions were the only solutions that did not significantly decrease the cell numbers when compared with controls. The antimicrobial wash further led to a significant decline in in-vitro bone formation (bone nodule formed in-vitro) compared to saline solution (Bhandari et al, 2001).

The mechanism of action of soap, a detergent, is well known. When grease or oil (non-polar hydrocarbons) is mixed with a soap-water solution, the soap molecules work as a bridge between polar water molecules and non-polar oil molecules. Since soap molecules have both properties of non-polar and polar molecules, the soap can act as an emulsifier. An emulsifier is capable of dispersing one liquid into another immiscible liquid. This means that while oil (which attracts dirt) does not naturally mix with water, soap can suspend oil/dirt in such a way that it can be removed. The soap will form micelles and trap the oil/dirt within the micelle. Since the micelle is soluble in water, it can easily be washed away.

We, along with other investigators, have shown in laboratory and animal models that soap solution is more effective in removing bacteria and particular matter from wounds and bone than normal saline (Burd et al, 1999; Gainor et al 1997; Anglen et al, 1996; Bhandari et al, 2001; Anglen et al, 2003), without toxic effects to soft tissues and bone (Bhandari et al, 2001). We have further shown a possible synergy between soap and low pressure irrigation (Bhandari et al, 2001). The addition of a soap solution under low pressure pulsatile irrigation removed the greatest number of bacteria from the contaminated tibia when compared to either the soap alone, or low pressure irrigation alone ($p<0.01$) (Bhandari et al, 2001).

The potential efficacy of soap solution in removing particulate matter, oil and bacteria from contaminated open wounds requires confirmation in a definitive trial. At pennies per application, soap offers a low cost, globally applicable, simple intervention that may reduce infections, as well as wound and bone healing complications following open fractures.

1.3 Clinical Data

1.3.1 Inconclusive Clinical Evidence

Soap solution has been evaluated by a single surgeon in a randomized trial of 400 patients with 458 open fractures (Anglen, 2005). At a mean 1.3 year follow up, soap solution (80mL per 3L Normal Saline Bag) demonstrated a trend towards a decreased risk of infection compared to an antibiotic solution (100,000U of bacitracin per 3L Normal Saline) (13% vs. 18%, relative risk 0.74, 95% confidence interval 0.45-1.26, p=0.2). The study reported a significant reduction in wound healing complications with soap compared to antibiotic (4%, 8/199 vs. 9.5%, 19/199; p=0.03). While this study provides some support for the efficacy of soap solution, its findings are limited by relatively small sample size, lack of generalizability to other centers or countries, unconvincingly concealed randomization, and unblinded non-independent adjudication of primary outcome.

A recent RCT of 21 patients with traumatic open wounds (Granick et al, 2007) compared two alternative high pressure irrigating devices, one delivering 40 p.s.i. and the other delivering above 5,000 p.s.i. pressure to the wound. The investigators reported a similar efficacy in both high pressure devices. This study provides limited data suggesting that irrigation pressures of 40 p.s.i. or greater provide similar efficacy to higher pressures; the relative effect of lower pressure irrigation (less than 40 p.s.i.) remains unaddressed.

1.3.2 Multinational Survey: Uncertainty and Support for a Large Trial

We have conducted two surveys (Bhandari et al, 2002; Petrisor et al, 2008) to explore surgeons' views regarding wound irrigation. Of 577 orthopaedic surgeons managing open tibial fractures who responded to our first survey, 39% preferred high and 45% low-pressure irrigation in their treatment of open wounds (Bhandari et al, 2002).

We mailed our second survey to members of the Canadian Orthopaedic Association and delivered it to attendees of an international fracture course (AO, Davos, Switzerland) (Petrisor et al, 2008). Of the 1,764 surgeons who received the questionnaire, 984 (55.8%) responded. In the management of open wounds, 676 (70.5%), favoured normal saline alone. Only 12 surgeons (1.3%) routinely used a soap solution. Although the majority of surgeons, 695 (71%), preferred what they called "low pressure" when delivering the irrigating solution to the wound, there was considerable variation in what pressures that constituted high versus low pressure lavage. Based upon the definitions provided, the majority (63.7%) were actually delivering what would constitute "high" irrigating pressures to the wound. In summary, current practice reflects the use of normal saline and higher irrigating pressures (Petrisor et al, 2008).

Of the respondents, 803 (84.8%) supported a clinical trial evaluating outcomes following the use of different irrigating solutions and 730 (77.6%) supported a trial of irrigating pressures. Most surgeons [889 (94.2%)] reported they would change their practice if a large RCT showed a clear benefit of an irrigating solution**.** The majority of surgeons [765 (80.6%)] believed that a particular irrigating solution would need to reduce the risk of infection compared to a standard by at least 25% to change practice. As a final confirmation of support, 612 surgeons reported they would participate in a randomized trial to resolve the controversy (Petrisor et al, 2008)**.**

1.3.3 Pilot Randomized Trial

We have successfully completed a pilot RCT using a factorial design to assess the feasibility of the proposed definitive FLOW trial **(Table 1)**. One hundred and eleven patients with open extremity fractures were randomized in permuted blocks using a customized web-based/telephone randomization system, to

receive either soap or saline solution and either low or high pressure irrigation. Patients, outcome assessors and data analysts were blinded to treatment allocation. The primary outcomes of the pilot study were the rates of infection on open fracture wounds and the rates of wound healing, delayed/non-union, adverse events, and functional outcomes. Our pilot study demonstrates: 1) our ability to recruit patients for the definitive trial; 2) investigator's compliance with key aspects of the protocol; (3) maintenance of data quality; 4) maintenance of high follow up rates; 5) our ability to organize trial procedures (randomization, data management) in a multinational trial; and 6) provocative results that emphasize the potentially enormous impact of our study. We have also used the pilot to develop and revise case report forms, the Manual of Operations for Investigational Sites, and posters for the pivotal FLOW trial.

1.4 Risk/Benefits

Open fractures have inherent associated complications which include infection, delayed union, non-union, wound healing problems, scarring, pain, loss of motion, damage to neurovascular structures and reoperations to treat wound or fracture problems possibly including amputation. However, risks of the study include potentially more infections or reoperations in the less efficacious pressure or solution group. Additional risks of this study include the potential allergic reaction to the soap.

All subjects are expected to benefit from this study. Possible benefits may include a significant decrease in infection, a significant improvement in wound healing and fracture healing. The subjects will all receive treatment for their open fracture wounds in a manner in which is considered acceptable and within the current standards of care. In addition, the subjects may benefit from the additional surveillance provided through this study which is above standard of care.

2 Study Objectives

The objectives of this study are to determine the effects of irrigation solutions (soap vs. normal saline) and irrigation pressures (gravity flow vs. high; low vs. high; gravity flow vs. low) on open fractures of extremities. These objectives will be carried out by answering the following questions:

2.1 Primary Questions

1. In patients operatively treated for open fractures of the extremity, is there any difference in effects of solutions (soap vs. normal saline) on re-operations within one year after initial surgery?
2. In patients operatively treated for open fractures of the extremity, are there any differences in effects of the pairs of irrigation pressures (high vs. low; high vs. gravity flow; low vs. gravity flow) on re-operations within one year after initial surgery?

2.2 Secondary Questions

In patients operatively treated for open fractures of the extremity, what is the impact of either irrigation solutions (soap vs. normal saline) or pressures (high vs. low; high vs. gravity flow; low vs. gravity flow) or illness beliefs on patient function and quality of life at one year?

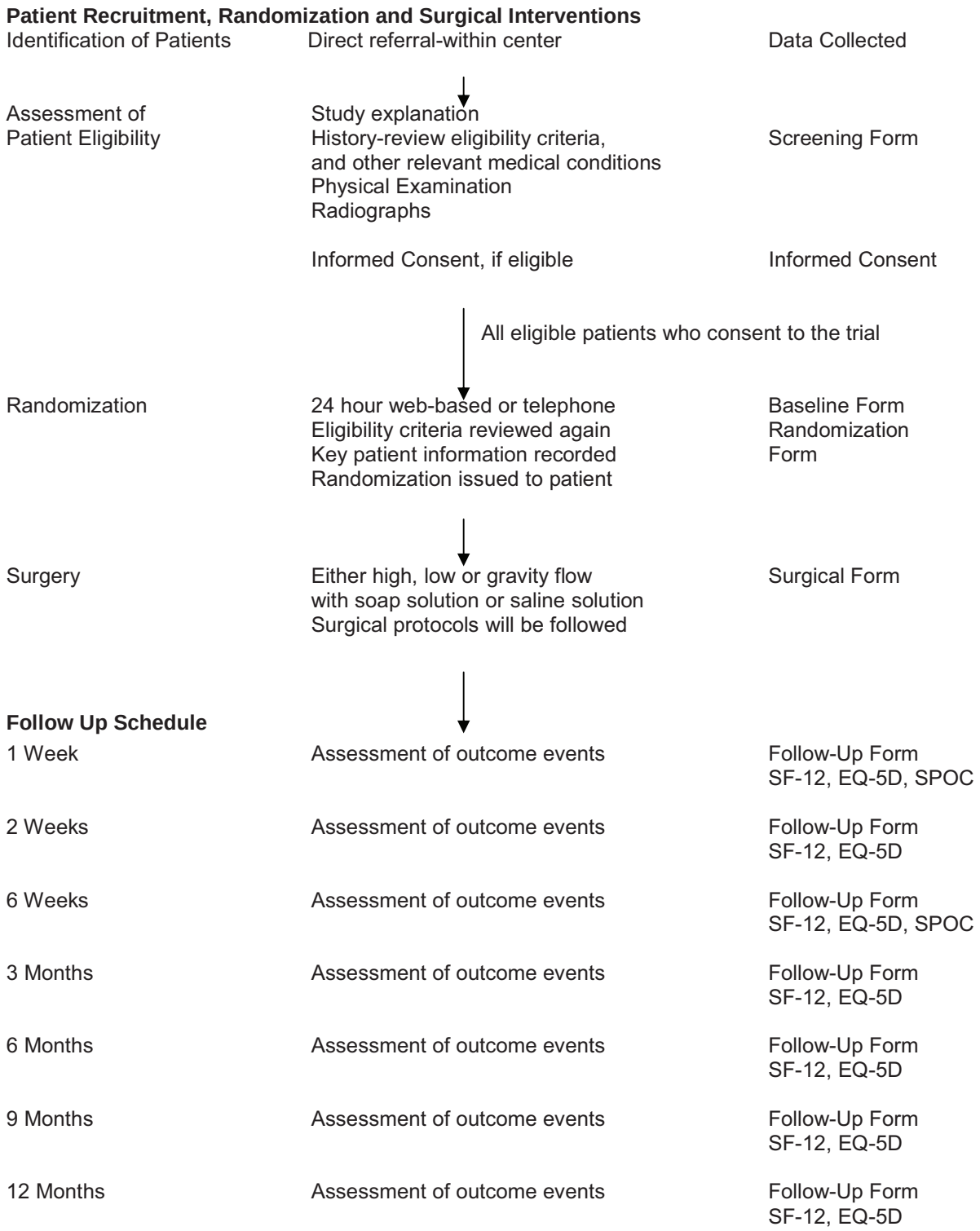
3 Study Design

This study is a multi-center, blinded, randomized controlled trial, using a 2×3 factorial design, to primarily investigate whether irrigation solution (soap vs. normal saline) or irrigation pressure (gravity flow vs. high; low vs. high; low vs. gravity flow) will decrease re-operations among patients with open fracture wounds. Patients are randomized, by using a central computer system that allows random variable block sizes, to one of 6 treatment arms (soap + gravity flow pressure; soap + low pressure; soap + high pressure; saline + gravity flow pressure; saline + low pressure; saline + high pressure) (**Table 1**). The randomization is stratified by center and the type of Gustilo-Anderson open fracture (Type I + Type II versus Type III) (Tsukayama & Schmidt, 2001). The period of patient enrolment is approximately 2 years and the enrolled patients will be followed for 1 year after surgery. We will assess re-operation rates within 12 months after initial surgery across soap vs. saline, and low vs. high, gravity flow vs. high, and low vs. gravity flow pressure irrigation. Patients, outcome adjudicators and data analysts will be blinded. We will measure function and quality of life at 1 week, 2 weeks, 6 weeks, 3 months, 6 months, 9 months, and 12 months. The schematic procedures are shown in **Figure 1**.

Table 1: 2x3 Factorial Design with a Total of 2520 Patients and 420 Patients per Cell

	Gravity Flow Pressure	Low Pressure	High Pressure	Total
Soap solution	420	420	420	1260
Saline	420	420	420	1260
Total	840	840	840	2520

Figure 1. Trial Conduct Procedure



* ***Follow Up Form includes antibiotic use, AEs, SAEs, infections, reoperations, protocol deviations or wound healing problems, and appropriate forms***.

3.1 Rationale for 2X3 Factorial Design

To optimize the efficiency and reduce overall trial cost, we propose to compare two different interventions with their respective controls (Pocock, 1984; McAlister et al, 2003; Montgomery et al, 2003). We will be able to efficiently and simultaneously investigate two interventions (irrigating pressure and irrigating solution) by including all participants in both analyses. The gravity flow irrigation arm is an addition since the pilot study. Feedback from surgeons, our survey results and United States Department of Defense-OETRP grants review committee argue for including a very low pressure group (gravity flow irrigation).

3.2 Primary Study Endpoints

The primary study endpoint is re-operation within 12 months post initial surgery to treat an infection, manage a wound healing problem, or promote fracture healing. Re-operation is defined as a surgery that occurs subsequent to the initial procedure. This composite endpoint of re-operation will include a narrow spectrum of patient-important procedures:

- irrigation and debridement for infection wound,
- revision and closure for wound dehiscence,
- wound coverage procedures for infected or necrotic wound,
- Drainage of a hematoma,
- Re-operation for hardware failure that is likely related to an infection, wound healing problem, or bone healing problem (delayed union or non-union),
- bone grafts or implant exchange procedures for established nonunion in patients with postoperative fracture gaps less than 1cm,
- intramedullary nail dynamizations in the operating room, and
- fasciotomies for compartment syndrome.

We will assess whether a patient has had a re-operation at 1 week, 2 weeks, 6 weeks, 3 months, 6 months, 9 months, and 1 year follow up visits.

Infections will be classified according to a modification of the Center for Disease Control Criteria (CDC). We will define infection in patients as a constellation of clinical symptoms and laboratory examinations. These will include (but are not limited to) fever, erythema/cellulites, positive tissue cultures, and frank purulent drainage. When interpreting the criteria, any infections that are superficial to the fascia will be considered “Superficial Incisional SSI” and any infections that are deep to the fascia will be considered “Deep Incisional SSI” (including infections of the bone (osteomyelitis)). Organ/Space SSI will refer to any infections that affect an organ, other than bone.

Our definition for wound healing problems will follow previously published criteria (Anglen, 2005). Any re-operations related to problems with primary wound healing will be documented. These include: 1) a dehiscence of a suture line, death of a flap or graft, or failure to heal which is not due to underlying deep infection (drainage of purulent fluid and positive cultures) or 2) problems with secondary healing that include failure of the wound to progress to satisfactory closure (wound becomes larger over time, failed granulation, or development of necrosis all requiring further intervention).

Diagnosis of nonunion will include a failure of the fracture to progress towards healing as observed by the treating surgeon and that requires further intervention to promote healing either surgical (i.e. bone graft) or non-surgical (i.e. bone stimulator). Final consensus on nonunion will be determined by the Central Adjudication Committee (CAC).

The following conditions are not considered outcome events: 1) planned secondary interventions from initial surgical procedures and 2) any re-operations to promote fracture healing in patients with post-operative fracture gaps greater than 1 cm.

A blinded CAC will judge whether our primary endpoint (re-operation for infection, wound healing problem or fracture healing problem) has occurred. Soft tissue procedures without infection will also be adjudicated by this committee, but ONLY for patients who have undergone more than 3 re-operations.

3.3 Secondary Study Endpoints

The secondary study endpoints include:

- patient function and quality of life measured by the Short Form-12 (SF-12) and the EuroQol-5D (EQ-5D) at 1 week, 2 weeks, 6 weeks, 3 months, 6 months, 9 months, and 12 months,
- non-operatively managed infections, wound healing problems and fracture healing problems within 12 months, and
- patient's illness beliefs with the Somatic Pre-Occupation and Coping (SPOC) questionnaire at 1 week and 6 weeks.

The SF-12 questionnaire is a self-administered, 12-item questionnaire that measures health-related quality of life in eight domains that can be aggregated into a physical and mental summary scores. Each domain is scored separately from 0 (lowest level) to 100 (highest level). The EQ-5D is a standardized instrument for use as a measure of health outcome (Brooks et al, 2003). The EQ-5D will be administered at North American sites only. We will conduct economic analysis in the context of North American setting, when additional funding is obtained. We will thus collect quality of life data measured by EQ-5D which is appropriate for economic analysis, in North American sites only. Patients who are completing the self-administered version of the EQ-5D will also be asked to complete a test version of the EQ-5D questions that uses 5-level response options. This data will be used in a sub-study comparing the test version to the validated version, which uses 3-level response options. The SPOC questionnaire is a validated self-administered, 27-item questionnaire that measures illness beliefs.

The blinded CAC will adjudicate all reported events including non-operatively managed infections, wound healing problems and fracture healing problems.

4 Subject Selection and Withdrawal

Patients who meet the eligibility criteria outlined below are to be included in the FLOW study. Only one fracture is to be included. For patients with multiple eligible open fractures, the eligible fracture with the most severe open injury that meets the below criteria is to be included.

4.1 Inclusion Criteria

1) Men or women who are 18 years of age or older.
2) Fracture of any extremity with complete radiographs.
3) Open fractures (Gustilo-Anderson Types I-IIIB) (**Table 2**)*.
4) Fracture requiring operative fixation.
5) Provision of informed consent.

* For patients with multiple open fractures, the fracture with the greatest Gustilo-Anderson Type, that does not meet exclusion criteria, will be the included fracture.

Table 2. Gustilo-Anderson Classification of Open Fractures (Gustilo et al, 1990)

Open fracture type	Characteristics
Type I	Clean wound smaller than 1 cm in diameter, simple fracture pattern, no skin crushing.
Type II	A laceration larger than 1 cm but without significant soft tissue crushing, including no flaps, degloving, or contusion. Fracture pattern may be more complex.
Type III	An open segmental fracture or a single fracture with extensive soft tissue injury. Also included are injuries older than 8 hours. Type III injuries are subdivided into three types.
Type IIIA	Adequate soft tissue coverage of the fracture despite high energy trauma or extensive laceration or skin flaps.
Type IIIB	Inadequate soft tissue coverage with periosteal stripping. Soft tissue reconstruction is usually necessary.

Type IIIC	Any open fracture that is associated with an arterial injury that requires repair.

4.2 Exclusion Criteria

1) Open fractures with an associated vascular deficit (Gustilo-Anderson Type IIIC).
2) Known allergy to detergents or castile soap ingredients.
3) Previous wound infection or history of osteomyelitis in the injured extremity.
4) Previous fracture with retained hardware in injured extremity that will interfere with new implant fixation.
5) Surgical delay to operative wound management greater than 24 hours from hospital admission.
6) Use of immunosuppressive medication within 6 months.
7) Immunological deficient disease conditions (e.g. HIV).
8) Fracture of the hand (metacarpals and phalanges).
9) Fracture of the toes (phalanges).
10) Likely problems, in the judgment of the investigators, with maintaining follow-up. We will, for example, exclude patients with no fixed address, those who report a plan to move out of town in the next year, or intellectually challenged patients without adequate family support.
11) Previous randomization in this study or a competing study.
12) Patient is a prisoner or is at high risk of incarceration during the follow-up period.*

* Clinical sites located outside of the United States may enroll prisoners or those at high risk of incarceration with the approval of their local IRB/REB.

4.3 Subject Recruitment and Screening

Participating centers will identify patients with open fractures through direct emergency department referral. The surgeon, designated fellow or resident conducts a history and physical examination and completes a Screening Form. If a patient meets the eligibility criteria for the study, an Investigator and/or designated study staff (as permitted by local regulations) then obtains informed consent. **Figure 1** outlines this process.

Informed consent will be obtained from each subject prior to enrolment in this study. If a patient is deemed unable to consent due to being temporarily incapacitated (i.e. due to trauma, pharmacological or other influence) informed consent may be obtained from the subjects legally authorized representative (LAR). The LAR will be determined based on site specific local regulations and policies. When the subject is deemed no longer incapacitated, the subject will be approached regarding the study and informed consent will be obtained from the patient for ongoing participation in the study. If the patient refuses continued participation, the patient will be withdrawn from the study.

We will register all patients who meet the inclusion criteria and document reasons for failure to randomize. We will document all patients screened for eligibility and record patients as: 1) eligible and included, 2) eligible and missed, and 3) excluded. Our CAC will adjudicate all situations where eligibility is in doubt. The CAC will also adjudicate the Gustilo-Anderson wound classification for all randomized patients.

4.4 Early Withdrawal of Subjects

4.4.1 When and How to Withdraw Subjects

We will only withdraw patients for the following scenarios:

- if patients withdraw consent for participation or
- if patients are deemed loss to follow-up after all exhaustive measures have been taken to locate the patient.

We will document the reasons for patient withdrawal from the trial.

We will not withdraw patients if the study protocol was not adhered (e.g., wrong irrigation solution and/or pressure used, occurrence of protocol deviations, missed follow-up visits, etc.).

4.4.2 Data Collection and Follow-up for Withdrawn Subjects

To maximize the integrity of the data, all possible attempts should be made to collect as much data as possible and to reduce loss to follow-up (Section 6.12). If a patient wishes to withdraw their consent from the study, the following strategies should be used to reduce the demands of the study and help to retain the subject:

- ask the patient if you can still collect clinical data from their medical and hospital charts; and
- ask the patient if you may contact them by telephone to ask about the primary and secondary outcomes.

Patients should not be deemed lost to follow-up until the 12 month visit is due and all attempts to contact the patient have been exhausted.

5 Study Interventions

5.1 Randomization Methods

We will randomize patients using random variable block sizes to avoid substantial imbalance in the number of patients assigned to each group. An automated internet-based randomization system based at the CLARITY Methods Center (available 24 hours/day), which we have used successfully for other multicenter trials, will ensure concealed randomization of eligible consenting patients. To ensure a prognostic balance between key factors, we will stratify patients by center and the type of Gustilo-Anderson open fracture (Types I and Type II versus Type III).

Once informed consent has been obtained from patient or proxy and the operating or attending surgeon has evaluated the open fracture wound, the investigator or designated study team member will contact the automated randomization system at the Methods Center to randomize the patient. Patients will be randomized to one of 6 treatment groups:

1) Castile soap solution & low pressure,
2) Castile soap solution & high pressure,
3) Castile soap solution & gravity flow pressure,
4) Saline solution & low pressure,
5) Saline solution & high pressure, and
6) Saline solution & gravity flow pressure.

The randomization system can be accessed by internet (please see details in the Manual of Operation for the Study Sites).

The Patient Study ID Number found at the top left of every data collection form is a six-digit number made up of two parts. The first two digits designate the patient's center and the last four digits designate the patient's sequential number within the center. Included patient study numbers are assigned by the computerized randomization system. Included patient numbers start at 1001, increment sequentially and can go as high as 1999 within any one center. For example, the first included patient from center 1 would have a Patient Study ID Number of 01 1001 and the 15th included patient at center 1 would have a Patient Study ID Number of 01 1015.

5.2 Irrigation Procedures

5.2.1 Irrigating Solutions

Patients will be randomized to have their open fracture wounds irrigated either with soap (experimental group) or normal saline (control group). In the operating room, surgeons will use sterile technique to inject 80mL of the clear liquid soap (Castile Soap, 16-21% concentration as supplied by the Methods Center) with a sterile syringe into a 3L bag of normal saline. Our choice of castile soap and dosing is based upon

a large body of experimental evidence, a recent clinical trial that used this formulation without adverse effects (Anglen, 2005), and our pilot study that confirmed its safety.

Patients randomized to the normal saline group (control) will receive sterile normal saline provided in 3L bags.

We will standardize the minimum amount of soap or saline solution based upon the severity of open fracture wound according to the Gustilo-Anderson Classification (Type I – 3 Litres, Types II and III - 6 Litres). We based these volumes on our international survey data (Petrisor et al, 2008) to reflect current standards and management protocols.

5.2.2 Irrigating Pressures

Patients will also be randomized to have the solutions delivered to the open fracture wounds by gravity flow (1-2 p.s.i.), low-pressure irrigation (5-10 p.s.i.), or high-pressure irrigation (>20 p.s.i.) (control group) with a battery operated irrigator [Stryker Surgilav or Zimmer Pulsavac Plus].

Gravity flow irrigation will be standardized across participating centers as 3L bags of normal saline (alone or with soap solution) suspended 6-8 feet above floor level (2-5 feet above the table) using an I.V. pole. Irrigation tubing (measuring 1/4 – 3/8 inch inner diameter) will be connected to the 3L bag and secured with a stopcock (or compressive device) until ready for use. At the time of irrigation, the stopcock (or compression device) will be released and gravity flow irrigation of the open wound will occur. A large basin collecting the runoff will be suctioned by standard intraoperative suction tubing. No pressure will be applied to the bag of solution.

To ensure standard low and high pressure delivery, we will standardize the irrigator to one of two devices [Stryker Surgilav or Zimmer Pulsavac Plus] to all participating sites. One of the irrigator manufacturers [Stryker] has agreed to provide Surgilav irrigators for the trial for sites in India and China.

Stryker Surgilav: For low pressure delivery, the high flow trauma tip will be used at the low pressure setting which delivers a pressure of 6 p.s.i. For the high pressure delivery, the multi-orifice tip will be used at the high setting which delivers a pressure of 30 p.s.i.

Zimmer Pulsavac Plus: For low pressure delivery, the shower tip will be used at the low pressure setting which delivers a pressure of 5.8 p.s.i. For the high pressure delivery the shower tip will be used at the high pressure setting which delivers a pressure of 23 p.s.i.

The irrigator tip will be held perpendicular to and 5cm above the wound.

5.3 Standardization of Procedures and Peri-Operative Care

We will standardize key aspects of peri-operative care and technical aspects of the initial irrigation and debridement procedure, as follows:

5.3.1 Antibiotics

Pre-operative I.V. antibiotics must be administered commencing on diagnosis. Postoperative, I.V. antibiotics must be administered for at least 24 hours post-surgery. Specific antibiotics will be used at the discretion of the attending surgeon. The recommended guidelines will include: Cephalosporin (Ancef) I.V. for Grade I-II injuries, Cephalosporin (Ancef) I.V. and Aminoglycoside (Gentamycin) I.V. for Grade III injuries, and Cephalosporin (Ancef) I.V., Aminoglycoside (Gentamycin I.V) and penicillin for gross contaminated injuries. For large open wounds (Types III), temporary local antibiotic administration will be permitted (bead pouch) until definitive wound closure. All antibiotics that are prescribed for the randomized fracture are to be recorded on the case report forms (CRFs).

5.3.2 Wound Management

Prior to randomization, we will record whether the attending surgeon plans to use antibiotic beads or antibiotic osteobiologics and if the attending surgeon plans to use negative pressure wound therapy (wound vacs) to treat the patient's randomized open fracture wound. The FLOW randomization system will capture this information prior to the treatment allocation being provided. Since the attending surgeons will not be blinded to the treatment allocation and bias may be introduced, we strongly encourage surgeons to use antibiotic beads or antibiotic osteobiologics, and negative pressure wound therapy (wound vacs) only if they indicated this prior to randomization. We will record the actual use of antibiotic beads or antibiotic osteobiologics and negative pressure wound therapy (wound vacs) on the case report forms and we will document any discrepancies.

Intra-operatively, surgeons will prepare and drape the injured extremity using sterile technique. Iodine-based or chlorhexidine-based initial wound scrubs will be allowed for extremity preparation. Surgeons will initially remove all gross debris, contaminants, and dead tissue (muscle, fat, fascia, skin, or bone). Adequacy of the debridement will be judged by colour, consistency, contractility, and bleeding of the muscle as well as complete eradication of contaminated and necrotic tissue including nonarticular devitalized bone. Surgeons will irrigate the open wound as prescribed by the randomization procedure and minimum volume standards of 3L for Gustilo-Anderson Type I and 6L for Gustilo-Anderson Type II and III. Delayed wound closure, split thickness skin grafting, or muscle flaps should occur by 7-14 days following the initial surgery when possible. Surgeons will repeat the irrigation and debridement procedure until the open wound is clean and soft tissues viable. **Patients will receive the same irrigating pressure and solution to which they were initially randomized for all subsequent irrigations and debridements.**

5.3.3 Fracture Stabilization

Fracture stabilization will be at the surgeon's discretion. Surgeons should stabilize the fractures using current best practices. These include the following guidelines based upon the best available evidence: 1) definitive fixation should be in place by 14 days from the initial operative wound irrigation and debridement as soft tissue allows, 2) temporizing fracture stabilization (external fixation) for grossly contaminated (Type II or Type III) wounds if used should be spanning external fixation outside the zone of the injury, 3) definitive fixation for shaft fractures of the lower extremity will include statically locked intramedullary nails (unless very proximal or very distal) (Bhandari et al, 2000), and 4) upper extremity fractures should be treated when possible with plates and screws (Bhandari et al, 2006). Due to the varying nature of these traumatic fractures, each fracture should be stabilized as the treating surgeon sees fit. To ensure both feasibility and generalizability, we will not standardize the implants.

5.4 Blinding

Patients, outcome adjudicators, and data analysts will be blinded to the study treatment. The operating room team (including the surgeon and study coordinator) cannot be blinded since the equipment they use for the irrigation pressures and the solutions are visually distinguishable.

6 Study Procedures

Completed forms recording patient status should be sent to the DataFax promptly (1-888-713-0434 [Canada and USA only], or 1-905-527-9637, via email, or via Electronic Data Capture), once each of the defined follow up visits are completed. Completed forms for patient screening, randomization, and surgical interventions should be as soon as they are completed. It is anticipated that completed forms will be sent in no more than seven days. See **Figure 1** for Study Follow-up Timeline.

6.1 Patient Screening and Consent

Research Coordinators and/or Investigators (or their designees) (as permitted by local regulations) should screen all emergency admissions on a daily basis. The Screening Form should be completed, and patient consent should be obtained using local IRB/REB approved Informed Consent Form to participate the trial.

6.2 Randomization

Patients should be randomized after the patient eligibility is established and the patient consent is obtained. Randomization Form and Baseline Characteristics Form should be completed.

6.3 Surgical Interventions

The surgical management of the open fracture wounds should occur within 24 hours after admission to the clinical site. The open fracture wounds should be irrigated following the treatment group that they are randomized. Fracture Characteristics Form, Surgical Report Form, Peri-operative Form, and Antibiotics Log should be completed. Only antibiotics that are prescribed for the randomized fracture are to be recorded on the Antibiotics Log. Patients should be assessed for any adverse events and protocol deviations.

6.4 1 Week Follow-up

The 1 week follow-up visit should occur between 24 hours and 1 week post surgery in person either at the hospital (if prior to discharge) or at the first clinic visit. The Follow-up Form should be completed. The SF-12 and EQ-5D (which is only administered at North American Sites), should be completed based on the patient's function **prior** to injury, and patients should also complete the SPOC. Patients should be assessed for any AEs, SAEs, infections, reoperations, protocol deviations, wound healing problems, and antibiotic use related to the fracture and the appropriate forms completed as necessary. A Missed Follow up Form should be completed if the patient misses the follow up visit. An Early Withdrawal Form should only be completed if the patient withdraws their consent.

* ***We will conduct economic analysis in the context of North American setting, when additional funding is obtained. We will thus collect quality of life data measured by EQ-5D which is appropriate for economic analysis, in North American sites only.***

6.5 2 Week Follow-up

The 2 week follow-up visit should occur in person either at the hospital (if prior to discharge) or at a clinic visit. The Follow-up Form should be completed. Additionally, SF-12, and EQ-5D (which is only used in North American Sites) should be completed. Patients should be assessed for any AEs, SAEs, infections, reoperations, protocol deviations, wound healing problems, and antibiotic use related to the fracture and the appropriate forms completed as necessary. A Missed Follow up Form should be completed if the patient misses the follow up visit. An Early Withdrawal Form should only be completed if the patient withdraws their consent.

6.6 6 Week Follow-up

The 6 week follow-up visit should occur in person either at the hospital (if prior to discharge) or at a clinic visit. The Follow-up Form should be completed. Additionally, SF-12, EQ-5D (which is only used in North American Sites), and SPOC should be completed. Patients should be assessed for any AEs, SAEs, infections, reoperations, protocol deviations, wound healing problems, and antibiotic use related to the fracture and the appropriate forms completed as necessary. A Missed Follow up Form should be completed if the patient misses the follow up visit. An Early Withdrawal Form should only be completed if the patient withdraws their consent.

6.7 3 Month Follow-up

The 3 month follow-up visit should occur in person either at the hospital (if patient is hospitalized) or at a clinic visit. The Follow-up Form should be completed. Additionally, SF-12, and EQ-5D (which is only used in North American Sites) should be completed. Patients should be assessed for any AEs, SAEs, infections, reoperations, protocol deviations, wound healing problems, and antibiotic use related to the fracture and the appropriate forms completed as necessary. A Missed Follow up Form should be completed if the patient misses the follow up visit. An Early Withdrawal Form should only be completed if the patient withdraws their consent.

6.8 6 Month Follow-up

The 6 month follow-up visit should occur in person either at the Hospital (if patient is hospitalized) or at a clinic visit. The Follow-up Form should be completed. Additionally, SF-12, and EQ-5D (which is only used in North American Sites) should be completed. Patients should be assessed for any AEs, SAEs, infections, reoperations, protocol deviations, wound healing problems, and antibiotic use related to the fracture and the appropriate forms completed as necessary. A Missed Follow up Form should be completed if the patient misses the follow up visit. An Early Withdrawal Form should only be completed if the patient withdraws their consent.

6.9 9 Month Follow-up

The 9 month follow-up visit should occur in person either at the hospital (if patient is hospitalized) or at a clinic visit. The Follow-up Form should be completed. Additionally, SF-12, and EQ-5D (which is only used in North American Sites) should be completed. Patients should be assessed for any AEs, SAEs, infections, reoperations, protocol deviations, wound healing problems, and antibiotic use related to the fracture and the appropriate forms completed as necessary. A Missed Follow up Form should be completed if the patient misses the follow up visit. An Early Withdrawal Form should only be completed if the patient withdraws their consent.

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6.10 12 Month Follow-up

The 12 month follow-up visit should occur in person either at the hospital (if patient is hospitalized) or at a clinic visit. The Follow-up Form should be completed. Additionally, SF-12, and EQ-5D (which is only used in North American Sites) should be completed. Patients should be assessed for any AEs, SAEs, infections, reoperations, protocol deviations, wound healing problems, antibiotic use related to the fracture, and planned re-operations and the appropriate forms completed as necessary. A Missed Follow up Form should be completed if the patient misses the follow up visit. An Early Withdrawal Form should be completed if the patient withdraws their consent or if the patient is deemed lost to follow-up and all methods to contact the patient have been exhausted.

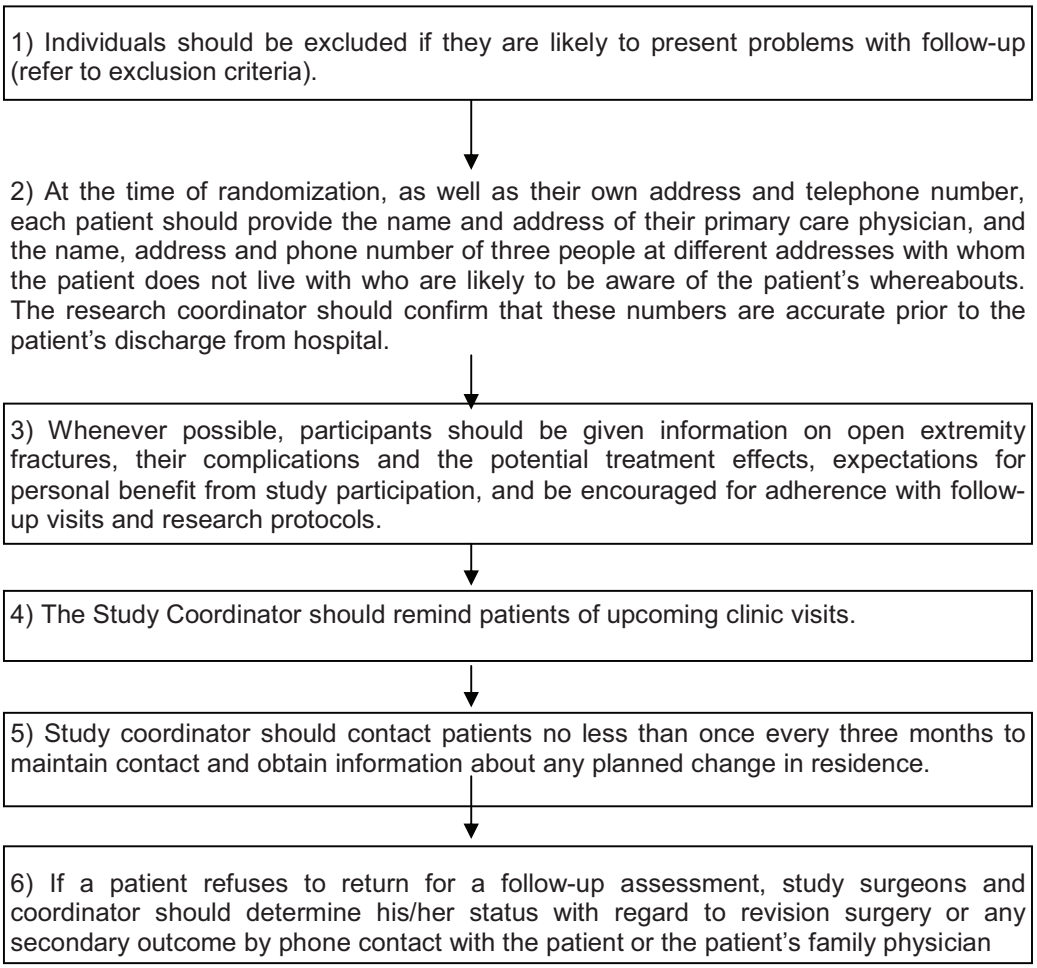
6.11 Telephone Follow up

If a patient is unable to or unwilling to return for follow-up in the confines of the allowable ranges of times for each follow-up period, then as much information as possible may be collected by telephone for the specified follow-up period.

6.12 Maximization of Follow up

It is extremely important to maintain patients follow up in the trial to ensure the completeness and integrity of the data. We will implement several procedures to limit loss of follow up, as described below **(Figure 2).**

Figure 2: Strategies to Limit Loss to Follow-Up



6.13 Minimization of Crossovers of Surgical Interventions

We require the patients to receive the surgical management to which they are randomized for the initial irrigation and debridement and for all subsequent irrigation and debridements. To prevent any patients from receiving the wrong solution or pressure, the following measures should be applied whenever possible:

- ensure FLOW posters with clear preparation guides are readily posted in all emergency operating rooms,
- ensure soap bottles are placed in all orthopaedic operating rooms in clearly marked boxes with instructions, and
- ensure that surgeons completing the subsequent irrigation and debridements are aware of the patient's treatment allocation.

If possible, the study coordinator of the individual clinical site should be present in any subsequent irrigation and debridements to further ensure that patients receive the treatment to which they were randomized.

Patients that do not receive the irrigation solution/pressure that they were randomized to will be followed as per the study protocol and they will be analyzed in the study in the group that they were randomized to following the intention to treat principle.

6.14 Adjudication Requirements

The CAC will adjudicate the following:

- all situations where eligibility is in doubt,
- re-operations to treat infection, wound healing problems, or fracture healing problems (delayed unions and nonunions),
- soft tissue procedures without infection in patients who have undergone more than 3 re-operations, and
- non-operatively managed infections, wound healing problems and fracture healing problems.

For the CAC to adjudicate situations when eligibility is in doubt, they will require:

- all initial hospital notes including the emergency room consultation note, the surgical consultation note, the operative report(s), in hospital progress reports, and the hospital discharge summary,
- pre-operative x-rays, and
- post-operative x-rays.

The CAC will require the following items to adjudicate re-operations to treat infection and wound healing problems:

- all initial hospital notes including the emergency room consultation note, the surgical consultation note, the operative report(s), in hospital progress reports, and the hospital discharge summary,
- all clinic notes,
- operative report(s),
- pre-operative x-rays,
- post-operative x-rays, and
- x-rays taken when the infection or wound healing problem was diagnosed.

To adjudicate re-operations to treat fracture healing problems (delayed unions and nonunions) the CAC will require:

- all initial hospital notes including the emergency room consultation note, the surgical consultation note, the operative report(s), in hospital progress reports, and the hospital discharge summary,
- all clinic notes,
- all operative reports,
- pre-operative x-rays,
- post-operative x-rays, and
- x-rays from the follow-up visits showing the fracture healing problem and its progression.

For the adjudication of non-operatively managed infections and wound healing problems, the CAC will require:

- all initial hospital notes including the emergency room consultation note, the surgical consultation note, the operative report(s), in hospital progress reports, and the hospital discharge summary,
- all clinic notes,
- pre-operative x-rays, and
- post-operative x-rays.

To adjudicate non-operatively treated fracture healing problems (delayed unions and nonunions) the CAC will require:

- all initial hospital notes including the emergency room consultation note, the surgical consultation note, the operative report(s), in hospital progress reports, and the hospital discharge summary,
- all clinic notes,
- pre-operative x-rays,
- post-operative x-rays, and

- x-rays from the follow-up visits showing the fracture healing problem and its progression.

The CAC will only require adjudication materials related to the randomized fracture. Upon request, the adjudication materials are to be forwarded to the Methods Center in a timely manner for preparation for adjudication.

7 Statistical Plan

7.1 Sample Size Determination

Our sample size is chosen to identify if there is any difference in effects of pairwise comparisons of the three irrigation pressure groups (high vs. low; high vs. gravity flow; low vs. gravity flow) on re-operations at 12 months (**Table 1**). This sample size will also allow us to establish if there is a difference between soap and saline (see below). For the comparisons of the three different pressures, we have chosen a two-sided alpha level of 0.05. Given that this applies to three pairwise comparisons, our alpha level for each individual comparison will be, according to Tukey's method, 0.0188 (Kleinbaum et al, 1997).

Our best estimate of the control group re-operation rate is 30%. In a previous randomized trial that involved lower limb open fractures (Anglen, 2005), the overall rate of re-operations due to infection, wound healing complications and delayed fracture healing was 46%. In the SPRINT trial, the reoperation rate in 400 patients with open tibial fractures was 27% (95%CI: 22.4-31.0). A 25% relative risk reduction associated with one or both of the lower pressures is plausible based on the pilot data. Furthermore, based upon our survey (Petrisor et al, 2008), 80% of surgeons will consider a 25% relative difference between treatments important enough to change practice.

We believe, given our experiences in the pilot study and centers that have committed to participate in the FLOW definitive study, that we will be able to recruit a total sample size of 2520, 840 per pressure group at the margin of table for a 2X3 factorial design (i.e. 420 per cell, **Table 2**). Based on our previous experiences, we estimate that approximately 10% of enrolled patients will be withdrawn due to withdrawal of consent or loss to follow-up prior to reaching the primary endpoint. Allowing for this rate of early withdrawal, our selected sample size will result in approximately 380 patients per cell with complete follow-up for our final analysis. **Table 3** shows our study power for the three pairwise comparisons of alternative pressures given our target sample size with complete follow-up (380 per cell) and given varying control event rates and relative risk reductions. Power is over 80% for relative risk reductions over 28% for control event rate as low as 25%. Power is over 80% for relative risk reduction as low as 24% if our control event rate is as high as 30%.

We have the same best estimate of control group re-operation rate for the saline solution (i.e. 30%), based on two randomized trials (Anglen 2005, SPRINT Investigators 2008). Given that our pilot data suggested a 37.5% relative risk reduction with soap versus saline, a relative risk reduction of 25% is plausible. For the saline versus soap comparison, we will have larger number of patients (i.e. 1,140) per group and a higher threshold p-value (0.05 vs. 0.018). Therefore, for any given baseline risk and relative risk reduction our power will be greater for the saline-soap comparison than for the pressure comparisons.

Table 3. The Power of Our Study to Detect the Relative Risk Reduction for Pairwise Comparison of Three Pressure Groups Given Varying Control Event Rate

		Relative risk reduction				
		20%	24%	28%	32%	35%
Control event rate	25%	0.49	0.68	**0.84**	**0.93**	**0.97**
	27%	0.54	0.73	**0.87**	**0.95**	**0.98**
	30%	0.61	**0.80**	**0.92**	**0.98**	**0.99**
	33%	0.68	**0.85**	**0.95**	**0.99**	**1.00**
	35%	0.72	**0.89**	**0.99**	**1.00**	**1.00**

* Note: We use a two-sided alpha level of 0.0188 for each pairwise comparison of three pressure groups, and the sample size per group at the margin is 760 (380 per cell).

For our secondary outcomes, we consider an important difference in SF-12 to correspond to a moderate effect as reported by Cohen (1992) as well as a minimally important difference in the SF-12 as reported by Ware (Ware, 1996). In both cases, the value is ½ the standard deviation, equivalent to 5 point difference in score. Specifying an alpha level=0.01, a beta=0.20 (study power=0.80), we require a sample of at least 405 patients (135 per pressure group at the margin of the table) to ensure detection of a ½ standard deviation improvement.

The EQ-5D correlates well with the Health Utilities Index (HUI) and both have been reported to provide similar estimates of utility (Bosch et al, 2000). Drummond et al (2001) report that 0.03- 0.04 incremental changes in HUI represent a patient-important difference. For adequate study power, we will need at least 329 patients per group at the margin of the table (alpha level=0.01, a beta=0.20, difference=0.04, σ =0.15). Thus, in all circumstances, our desired sample size of 2520 patients (840 per group at the margin of the table) will be sufficient to detect the minimally important differences in our secondary measures of outcome.

7.2 Statistical Methods

7.2.1 Primary Analysis

All analyses will include all patients in the groups to which they were randomized. The data analyst and investigators, while conducting the analyses, will be blind to which group represents high, low and gravity flow pressure and which represents soap and saline. We will use log-rank test and Kaplan-Meier survival curve to compare the main effects of irrigating solution (soap vs. saline) and irrigation pressure (high vs. low, high vs. gravity flow, low vs. gravity flow) at the margins of the 2X3 factorial design on time to the first re-operation after the initial surgery. We will use a two-sided alpha level of 0.05 for the comparison of irrigation solution and a two-sided alpha level of 0.0188 for pairwise comparison of irrigation solution. We will use Cox model to generate hazard ratio and its associated 95% confidence intervals for each comparison. The analyses will be stratified by center and the type of Gustilo-Anderson open fracture (Types I and II versus Type III).

Adjusted analyses, employing Cox regression, will examine and control for the influence of patient and surgical factors that might be associated with the risk of re-operation, including age, degree of soft tissue injury, upper or lower extremity injury, amount of fracture gap, type of internal fixation, and severity of fracture combination.

7.2.2 Secondary Analyses

We will also examine the interaction of soap with pressure by including the main effects and their interaction terms in the Cox regression with the outcome variable as re-operation. This secondary analysis will be underpowered and only large effects will be detectable.

In addition to re-operation, we will also compare the effects of irrigation solution (soap vs. saline) and pressure (low vs. high; gravity flow vs. high; gravity flow vs. low) on the component outcomes, including non-operatively treated fracture healing complications, wound healing problems, infection (deep and

superficial), using log-rank test and Kaplan-Meier survival curve. Adjusted analyses, using Cox model, will be used to examine and control for the influence of patients and surgical factors.

We will employ the generalized linear model for repeated-measure analysis of variance to look at time, treatment, and the interaction between the two to compare the change in functional status and quality of life for all comparison groups. We will construct multi-variable regression models to explore the association between SPOC scores and functional outcome at 1-year, as measured by short form-12 (SF-12) physical component summary (PCS) and mental component summary (MCS) scores. We will also examine if SPOC scores at 1 week and 6 weeks are similarly predictive.

7.2.3 Subgroup Analyses

We plan to conduct two subgroup analyses, both with strong biological rationale and possible interaction effects. The first will compare hazard ratios of re-operation based upon the degree of soft tissue injury (Gustilo-Anderson Type I/II open fractures vs. Gustilo-Anderson Type IIIA/B open fractures). The second will compare hazard ratios of re-operation between fractures of the upper and lower extremity. We will test if the treatment effects differ with fracture types and extremities by putting their main effect and interaction terms in the Cox regression. For the comparison of pressure, we anticipate that the low/gravity flow will be more effective in the Type IIIA-B open fracture than in the Type I/II open fracture, and be more effective in the upper extremity than the lower extremity. For the comparison of solution, we anticipate that soap will do better in the Type IIIA-B open fracture than in the Type I/II open fracture, and better in the upper extremity than the lower one.

7.2.4 Interim Analysis

We will conduct an interim analysis to monitor the treatment benefits. Interim analysis will be performed when two-thirds of the entire patient follow-up is completed (i.e. 1520 person-years). At this point, 91.7% (1886) patients have been recruited into the trial.

We will maintain the overall specified type I error rate of 0.05. For the interim analysis, we choose the 2-sided significance levels at 0.001. This significance level is a conservative one, making it unlikely the DMC will recommend stopping the trial early in the absence of a large and robust effect.

The data analyst will present the results of analysis, including confidence intervals, to an independent DMC. No one other than committee members will be aware of the data on which the committee makes its decision, and no one involved in the study will be aware of the content of their deliberations.

8 Safety and Adverse Events

8.1 Definitions

Adverse Event (AE)
An ***adverse event*** (AE) is any symptom, sign, illness or experience that develops or worsens in severity during the course of the study

Serious Adverse Event
Adverse events are classified as serious or non-serious. A ***serious adverse event*** is any AE that is:

- fatal,
- life-threatening,
- requires or prolongs hospital stay,
- results in persistent or significant disability or incapacity,
- a congenital anomaly or birth defect, or
- an important medical event.

Unanticipated Problems Resulting in Risk to Subjects or Others
Any incident, experience, or outcome that meets ~~all~~ of the following criteria:

- unexpected in nature, severity, or frequency (i.e. not described in study-related documents such as the IRB-approved protocol or consent form, the investigators brochure, etc),
- related or possibly related to participation in the research (i.e. possibly related means there is a reasonable possibility that the incident experience, or outcome may have been caused by the procedures involved in the research),
- suggests that the research places subjects or others at greater risk of harm (including physical, psychological, economic, or social harm).

Unanticipated problems resulting in risk to volunteers or others encompass more than what one usually thinks of as adverse events. "Problems involving risk" may not necessarily result in harm. For example, misplacing a volunteer's study records containing identifiable private information introduces the risk of breach of confidentiality. Confidentiality may or may not be breached, but either way this would be a reportable event. Risks to others must also be reported. For example, an unexpected outburst during questionnaire administration by a volunteer that puts study staff at risk would be a reportable event.

8.2 Reporting of Serious Adverse Events and Unanticipated Problems Resulting in Risk to Subjects or Others

All serious adverse events and unanticipated problems resulting in risk to subjects or others are to be reported to the Methods Center immediately.

8.2.1 Reporting and Responsibilities/Roles of the PI and Medical Monitor

The protocol will be conducted in accordance with the protocol submitted to and approved by the United States Army Medical Research and Materiel Command, Office of Research Protections, Human Research Protection Office (USAMRMC ORP HRPO) and will not be initiated until written notification of approval of the research project is issued by the USAMRMC ORP HRPO.

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Please Note: The USAMRMC ORP HRPO conducts site visits as part of its responsibility for compliance oversight. Accurate and complete study records must be maintained and made available to representatives of the USAMRMC as a part of their responsibility to protect human subjects in research. Research records must be stored in a confidential manner so as to protect the confidentiality of subject information.

Any changes of the IRB used to review and approve the research will be promptly reported to the USAMRMC ORP HRPO.

All unanticipated problems involving risk to subjects or others must be promptly reported by telephone (301-619-2165), by email (HRPO@amedd.army.mil), or by facsimile (301-619-7803) to the HRPO. A complete written report will follow the initial notification. In addition to the methods above, the complete report can be sent to the U.S. Army Medical Research and Materiel Command, ATTN: MCMR-RP, 504 Scott Street, Fort Detrick, Maryland 21702-5012.

Substantive modifications to the research protocol and any modifications that could potentially increase risk to subjects must be submitted to the HRPO for approval prior to implementation. The USAMRMC ORP HRPO defines a substantive modification as a change in Principal Investigator, change or addition of an institution, elimination or alteration of the consent process, change to the study population that has regulatory implications (e.g. adding children, adding active duty population, etc), significant change in study design (i.e. would prompt additional scientific review) or a change that could potentially increase risks to subjects.

A copy of the continuing review approval notification by the IRB of Record and a copy of the continuing review report approved by the IRB must be submitted to the HRPO as soon as possible after receipt. Please note that the HRPO also conducts random audits at the time of continuing review. Additional information and documentation may be requested at that time.

The final study report, including any acknowledgement documentation and supporting documents, must be submitted to the HRPO when available.

Suspensions, clinical holds (voluntary or involuntary), or terminations of this research by the Institutional Review Board (IRB), the institution, the Sponsor, or regulatory agencies will be promptly reported to the USAMRMC ORP HRPO.

The knowledge of any pending compliance inspection/visit by the FDA, DHHS Office of Human Research Protections (OHRP), or other government agency concerning this research, the issuance of Inspection Reports, FDA Form 483, warning letters or actions taken by any regulatory agencies including legal or medical actions and any instances of serious or continuing noncompliance with the regulations or requirements, must be promptly reported to the HRPO.

The medical monitor will review all unanticipated problems involving risk to subjects or others associated with the protocol and provide an unbiased written report of the event. At a minimum, the medical monitor must comment on the outcomes of the problem and comment on the relationship to participation in the study. The medical monitor must also indicate whether he/she concurs with the details of the report provided by the principal investigator. Reports for events determined by either the investigator or medical monitor to be possibly or definitely related to participation must be promptly forwarded to the USAMRMC ORP HRPO.

8.2.2 Investigator Reporting: Notifying the Methods Center

Any SAEs must be reported to the Methods Center by completing the SAE Form and submitting it to DataFax. The investigator will keep a copy of this SAE form on file at the study site. The SAE form should include of a written narrative and any other information that will assist the understanding of the event. Significant new information on ongoing serious adverse events should be provided promptly to the Methods Center by updating the SAE form.

Unanticipated problems resulting in risk to subjects or others are to be reported to the Methods Center by either fax or email.

8.2.3 Site Investigator – IRB/REB Reporting

Investigators are responsible for reporting AEs, SAEs, and unanticipated problems resulting in risk to subjects or others to their local IRB/REB. Investigators are responsible for complying with their local IRB's/REB's reporting requirements. Copies of each report and documentation of IRB/REB notification and receipt will be kept in the investigator's study file.

8.2.4 Methods Center Reporting: Notifying Participating Investigators

It is the responsibility of the Methods Center to notify all participating investigators, in a written safety report, of any adverse event associated with the use of the irrigation solutions and pressures that is both serious and unexpected.

8.3 Medical Monitoring

It is the responsibility of the Principal Investigator to oversee the safety of the study at his/her site. This safety monitoring will include careful assessment and appropriate reporting of adverse events as noted above, as well as the construction and implementation of a site data and safety-monitoring plan. Medical monitoring will include a regular assessment of the number and type of serious adverse events.

The CRFs and informed consent form will be reviewed primarily by study coordinators. If necessary, the medical monitor may be asked to further review the records. Data collectors and site investigators will be advised of the inappropriate documentation and further training may be conducted to ensure the compliance of records documentation. Statistical monitoring will also be used to check fraudulent data (Buyse et al 1999). Statistical monitoring will be conducted to detect strange patterns in the data including, but not limited to, outliers, inliers, overdispersion, underdispersion and correlations or lack thereof. A protocol will be prepared for review of case report forms and informed consent, and for conducting statistical monitoring.

8.3.1 Data Monitoring Committee

Our DMC will be comprised of 3 members: Doug Altman (Chair, Biostatistician, Oxford, UK), Rajiv Gandhi (Orthopaedic Surgeon, Toronto, Ontario, Canada) and Marcus Bischoff (Clinical Expert and Trialist, Milton, Canada). .They remain completely independent of the study investigators and have never received any honoraria from, or held stock in any of the manufacturers whose products are used in this trial. The terms of reference and functions are derived from the principles established by the Data and Safety Monitoring Boards: Lessons, Ethics, Statistics (DAMOCLES) Study Group charter.

9 Data Handling and Record Keeping

9.1 Confidentiality

Information about study subjects will be kept confidential and managed according to the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA). Those regulations require a signed subject authorization informing the subject of the following:

- what protected health information (PHI) will be collected from subjects in this study,
- who will have access to that information and why,
- who will use or disclose that information, and
- the rights of a research subject to revoke their authorization for use of their PHI.

In the event that a subject revokes authorization to collect or use PHI, the investigator, by regulation, retains the ability to use all information collected prior to the revocation of subject authorization. For subjects that have revoked authorization to collect or use PHI, attempts should be made to obtain permission to collect at least vital status (i.e. that the subject is alive) at the end of their scheduled study period.

9.2 Case Report Forms

The CRFs are the primary data collection instrument for the study. All data requested on the CRF must be recorded. All missing data must be explained. If a space on the CRF is left blank because the procedure was not done or the question was not asked, write “N/D”. If the item is not applicable to the individual case, write “N/A”. All entries should be printed legibly in black ink. If any entry error has been made, to correct such an error, draw a single straight line through the incorrect entry and enter the correct data above it. All such changes must be initialed and dated. DO NOT ERASE OR WHITE OUT ERRORS. For clarification of illegible or uncertain entries, print the clarification above, below, or to the side of the item, then initial and date it.

10 Ethical Considerations

This study is to be conducted according to US and international standards of Good Clinical Practice (FDA Title 21 part 312 and International Conference on Harmonization guidelines), applicable government regulations and Institutional research policies and procedures.

This protocol and any amendments will be submitted to a properly constituted independent REB or IRB, in agreement with local legal prescriptions, for formal approval of the study conduct. The decision of the REB /IRB concerning the conduct of the study will be made in writing to the investigator and a copy of this decision will be provided to the Methods Center before commencement of this study.

All subjects for this study will be provided a consent form describing this study and providing sufficient information for subjects to make an informed decision about their participation in this study. The consent form will be submitted with the protocol for review and approval by the REB /IRB for the study. The formal consent of a subject, using the REB /IRB-approved consent form, must be obtained before that subject undergoes any study procedure. The consent form must be signed by the subject or legally authorized representative, and the investigator-designated research professional obtaining the consent.

11 Study Finances

11.1 Funding Sources

This study is financed through grants from the AIOD, Canadian Institutes of Health Research and United States Department of Defense-Orthopaedic Extremity Trauma Research Program.

11.2 Subject Stipends or Payments

There is no payment to subjects for participation in this study.

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Appendix F: Case Report Forms

PLEASE DO NOT FAX THIS TO THE METHODS CENTRE

Centre # | Patient # | Patient Initials F L

PATIENT CONTACT FORM (1 of 2) - FORM L-1

In order to facilitate follow-up, it is important to collect contact information for you AND 3 alternate contacts that could assist us should you move during the course of the study. This information will not be given to anyone outside of the study.

Patient Contact Information

Patient: (please print) Last Name _____ First Names _____

Apt. No. _____ Street _____ Postal/Zip Code _____

Town/City _____ Province/State (if applicable) _____ Country _____

Home Phone # _____ Work Phone # _____

What is the best time to reach you? 24h clock HH MM : Day(s)? _____

E-mail: _____

Family Physician Contact - Clinic Address

Physician: (please print) Last Name _____ First Names _____

Apt. No. _____ Street _____ Postal/Zip Code _____

Town/City _____ Province/State(if applicable) _____ Country _____

Phone # _____ E-mail: _____

Trauma/Orthopaedic Surgeon Contact - Clinic Address

Surgeon: (please print) Last Name _____ First Names _____

Apt. No. _____ Street _____ Postal/Zip Code _____

Town/City _____ Province/State(if applicable) _____ Country _____

Phone # _____ E-mail: _____

PLEASE DO NOT FAX THIS TO THE METHODS CENTRE

Centre # | Patient # | Patient Initials F L

PATIENT CONTACT FORM (2 of 2) - FORM L-2

Alternate Contact Information

Contact #1: (please print)

Last Name _____ First Names _____

Apt. No. _____ Street _____ Postal/Zip Code _____

Town/City _____ Province/State(if applicable) _____ Country _____

Home Phone # _____ Work Phone # _____

E-mail: _____ Relationship to Patient: _____

Contact #2: (please print)

Last Name _____ First Names _____

Apt. No. _____ Street _____ Postal/Zip Code _____

Town/City _____ Province/State(if applicable) _____ Country _____

Home Phone # _____ Work Phone # _____

E-mail: _____ Relationship to Patient: _____

Contact #3: (please print)

Last Name _____ First Names _____

Apt. No. _____ Street _____ Postal/Zip Code _____

Town/City _____ Province/State(if applicable) _____ Country _____

Home Phone # _____ Work Phone # _____

E-mail: _____ Relationship to patient: _____

Instructions for Completing DataFax Case Report Forms (CRFs)

What is DataFax?

DataFax is a direct fax to computer data management system for collecting study Case Report Forms (CRFs). It includes Intelligent Character Recognition (ICR) and an automated Quality Control (QC) report system.

Why are we using DataFax for this study?

- To increase the speed and efficiency of data collection from participating clinical sites.
- To improve data quality through continuous monitoring and Quality Control (QC) reports.

Completing CRFs:

- Please print legibly using black ink.
- Record Patient ID on all forms.
- Record patient initials in the following format: first (F) / last (L).
- All text and explanatory comments should be brief and within the space provided.
- Answer every question explicitly, do not use ditto marks.
- Only enter data in the fields provided.
- If the answer is zero, do not leave the field blank, write "0".
- If a procedure was not done or a question was not asked, write "N/D".
- If the item is not applicable in the individual case, write "N/A".
- Mark choice and check fields with a ✓ or an ✗ inside the appropriate box.
- To maximize ICR accuracy, please print all numbers **inside** the boxes as shown here, trying not to touch the sides.

Dates:

0	1	2	3	4	5	6	7	8	9

- All dates are in the dd/mm/yyyy format. Enter the appropriate two digit number for months and days (e.g., use 01 for January, use 01 for the first of the month).

Example:

Day	Month	Year	
2 2	0 5	2 0 0 0	May 22, 2000

Correction of errors:

If an error occurs, please correct it in the following way:

Do not use "White-Out" or correction fluid.

1. Cross out the error with a single straight line.
2. Write the correct value above, below or to the side.
3. Initial and date the correction.
4. Ensure all corrections are completely clear.

Example:

Duration of treatment

~~0 2 4~~

(hours)

048 initial/date

Faxing:

- Before faxing, check CRFs for accuracy, completeness and legibility.
- Fax CRFs as soon as possible after patient assessment to the methods centre at **1-888-713-0434** for North America only and for local and overseas **1-905-527-9637**.
- Faxes should be sent in **standard mode** (fine mode works but costs more and is unnecessary).
- Be careful not to overload your fax machines paper tray or memory limitations.
- After transmitting the CRFs check that all pages of the fax were transmitted successfully.
- Scanned CRFs (saved in PDF format) can be sent to the Methods Centre via email at trauma4@mcmaster.ca.

What are Quality Control (QC) reports?

At regular intervals, you will receive QC reports by fax or email identifying items on the CRFs which are incomplete, unclear, illegible or discrepant. **Respond by making corrections to the original CRF and promptly refaxing the corrected page(s)**. Remember to initial and date all changes.

Instructions for Completing DataFax Case Report Forms (CRFs) (continued)

Patient numbering:

The Patient Study ID Number found at the top left of every data collection form is a six digit number made up of two parts. The first two digits designate the patient's centre and the last four digits designate the patient's sequential number within the centre.

Included Patients:

- Included patient study ID numbers are assigned by the computerized randomization system.
- Included patient numbers start at 1001, increment sequentially, and can go as high as 1999 within any one centre.

Example: The first included patient at centre 1 would be: **Patient Study ID Number** 0 1 (Centre #) 1 0 0 1 (Patient #)

The 15th included patient at centre 1 would be: **Patient Study ID Number** 0 1 (Centre #) 1 0 1 5 (Patient #)

Missed Patients:

- Missed patient study ID numbers are assigned by the individual site coordinators.
- Missed patient numbers start at 2001, increment sequentially, and can go as high as 2999 within any one centre.

Example: The first missed patient at centre 1 would be: **Patient Study ID Number** 0 1 (Centre #) 2 0 0 1 (Patient #)

The 15th missed patient at centre 1 would be: **Patient Study ID Number** 0 1 (Centre #) 2 0 1 5 (Patient #)

Excluded Patients:

- Excluded patient study ID numbers are assigned by the individual site coordinators.
- Excluded patient numbers start at 3001, increment sequentially, and can go as high as necessary.

Example: The first excluded patient at centre 1 would be: **Patient Study ID Number** 0 1 (Centre #) 3 0 0 1 (Patient #)

The 15th excluded patient at centre 1 would be: **Patient Study ID Number** 0 1 (Centre #) 3 0 1 5 (Patient #)

FLOW #103 **Plate #001** **Visit #000**

Patient Study ID Number [ ][ ] [ ][ ][ ][ ] **Patient Initials** [ ][ ]

Centre # **Patient #** **F L**

Date [ ][ ] [ ][ ] [2][0][ ][ ]

DD **MM** **YYYY**

SCREENING FORM (1 of 1) - FORM 1.1

Please complete this form for all patients with an open fracture wound.

For included patients you must answer yes to questions 1-5:	**Yes**	**No**
1. Male or female who is 18 years of age or older?	☐	☐
2. Fracture of any extremity with complete radiographs?	☐	☐
3. Open fractures (Gustilo-Anderson Types I, II, IIIA, or IIIB)?	☐	☐
4. Fracture requiring operative fixation?	☐	☐
5. Provision of informed consent?	☐	☐

If you answered no to any of items 1-5, the patient should be excluded.

For included fractures you must answer no to questions 6-17:	**Yes**	**No**	**N/A* (Non-US Sites Only)**
6. Open fractures with an associated vascular deficit (Gustilo-Anderson Type IIIC)?	☐	☐	
7. Known allergy to detergent or castile soap ingredients?	☐	☐	
8. Previous wound infection or history of osteomyelitis in the injured extremity?	☐	☐	
9. Previous fracture with retained hardware in the injured extremity that will interfere with new implant fixation?	☐	☐	
10. Surgical delay to operative wound management greater than 24 hours from hospital admission?	☐	☐	
11. Likely problems, in the judgment of the investigators, with maintaining follow-up?	☐	☐	
12. Previous randomization in this study or a competing study?	☐	☐	
13. Use of immunosuppressive medication within the last 6 months?	☐	☐	
14. Immunological deficient disease conditions (e.g.HIV)?	☐	☐	
15. Fracture of the hand (metacarpals and phalanges)?	☐	☐	
16. Fracture of the foot (phalanges)?	☐	☐	
17. Patient is a prisoner or is at high risk of incarceration during the follow-up period?	☐	☐	☐*
18. Other reason: _____	☐	☐	

If you answered yes to any of items 6-18 the patient should be excluded.

PATIENT STATUS - See previous page for coding Patient ID #

19. Please indicate the patient's status.

- ☐ INCLUDED (proceed to the **Randomization Form 2.1**)
- ☐ EXCLUDED
- ☐ MISSED (eligible, but was not randomized due to error)

***For use by Non-US sites with Ethics Committee approval to enroll prisoners only**

FLOW #103 **Plate #002** **Visit #001**

Patient Study ID Number ☐☐ (Centre #) ☐☐☐☐ (Patient #) **Patient Initials** ☐☐ (F L)

RANDOMIZATION FORM (1 of 1) - FORM 2.1

Please complete the following questions for all included patients prior to randomization. You will need to have this information available when you randomize the patient.

1. Patient date of birth: Day ☐☐ Month ☐☐ Year ☐☐☐☐

2. Does the patient have previous wound or bone infections or retained hardware in the same extremity?

☐ Yes → **Patient should be excluded**

☐ No

3. Type of fracture: ****<u>Only one fracture</u> is to be included in FLOW. For patients with multiple open fractures, please randomize the eligible fracture with the <u>most severe</u> open injury.**

*** For Use With Randomization System:**

*Stratum 1: ☐ Type I ☐ Type II

*Stratum 2: ☐ Type IIIA ☐ Type IIIB

Please randomize the patient using the Internet randomization system at http://clarityrand.mcmaster.ca/FLOW

4. Does the attending surgeon plan to use antibiotic beads or antibiotic osteobiologics in this patient's randomized open fracture? ☐ Yes ☐ No

5. Does the attending surgeon plan to use negative pressure wound therapy (wound vac) to treat this patient's randomized open fracture? ☐ Yes ☐ No

6. Date of randomization: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

7. Patient randomized to:

☐ Group 1: castile soap solution, low pressure

☐ Group 2: castile soap solution, high pressure

☐ Group 3: castile soap solution, gravity flow pressure

☐ Group 4: normal saline, low pressure

☐ Group 5: normal saline, high pressure

☐ Group 6: normal saline, gravity flow pressure

8. Initials of person who randomized patient: ☐☐ (F L)

Stryker Surgilav Pressure Settings:

1. For **high pressure** use the Stryker Surgilav with multi-orifice tip at the high pressure setting.

2. For **low pressure** use the Stryker Surgilav with high flow trauma tip at the low pressure setting.

Zimmer Pulsavac Plus Pressure Settings:

1. For **high pressure** use the Zimmer Pulsavac Plus with shower tip at the high pressure setting.

2. For **low pressure** use the Zimmer Pulsavac Plus with shower tip at the low pressure setting.

FLOW #103 **Plate #003** **Visit #001**

Patient Study ID Number ☐☐ (Centre #) ☐☐☐☐ (Patient #) **Patient Initials** ☐☐ (F L) **Baseline Date:** ☐☐ (DD) ☐☐ (MM) 20☐☐ (YYYY)

BASELINE CHARACTERISTICS FORM (1 of 3) - FORM 3.1

1. Date of injury: Day ☐☐ Month ☐☐ Year 20☐☐

2. Date of hospital admission: Day ☐☐ Month ☐☐ Year 20☐☐

3. Sex: ☐ Male ☐ Female

4. Ethnicity: (check **one** only) ☐ Native ☐ Black ☐ White ☐ Asian ☐ Hispanic ☐ Other (specify): _____

5. Please specify the location of the **included fracture** (check **one** only) - Do NOT complete for excluded fractures.

Upper extremity:	**Left**	**Right**
Clavicle	☐	☐
Scapula	☐	☐
Proximal Humerus	☐	☐
Midshaft Humerus	☐	☐
Distal Humerus	☐	☐
Olecranon	☐	☐
Proximal Radius	☐	☐
Middle Radius	☐	☐
Distal Radius	☐	☐
Proximal Ulna	☐	☐
Middle Ulna	☐	☐
Distal Ulna	☐	☐
Other (specify below):	☐	☐

_____

Lower extremity:	**Left**	**Right**
Proximal Femur (Hip)	☐	☐
Middle Femur	☐	☐
Distal Femur	☐	☐
Patella	☐	☐
Proximal Tibia	☐	☐
Middle Tibia	☐	☐
Distal Tibia	☐	☐
Ankle (Plafond injury)	☐	☐
Ankle (Malleolus injury)	☐	☐
Talus	☐	☐
Calcaneus	☐	☐
Other (specify below):	☐	☐

_____

FLOW #103 **Plate #004** **Visit #001**

Patient Study ID Number ☐☐ ☐☐☐☐ **Patient Initials** ☐☐

Centre # **Patient #** **F L**

BASELINE CHARACTERISTICS FORM (2 of 3) - FORM 3.2

6. Are there additional fractures or injuries other than those included? (check **all** that apply)

- ☐ **None**
- ☐ Femoral fracture
- ☐ Pelvic fracture
- ☐ Spinal fracture
- ☐ Other lower extremity fracture (specify): _____
- ☐ Other upper extremity fracture (specify: _____
- ☐ Other lower extremity injury (contusion/laceration)
- ☐ Facial injury (contusion/laceration/fracture)
- ☐ Thoracic injury (contusion/laceration/fracture)
- ☐ Liver injury
- ☐ Bowel injury
- ☐ Splenic injury
- ☐ Other abdominal injury
- ☐ Other upper extremity injury
- ☐ Hemo/pneumothorax
- ☐ Closed head injury
- ☐ Urogenital injury
- ☐ Traumatic amputation
- ☐ Vascular injury
- ☐ Lung contusion
- ☐ Other injury (specify): _____

_____

7. Did this patient have any other open injuries (other than the randomized fracture) ? ☐ Yes ☐ No

8. Mechanism of injury: (chose **one** only)

- ☐ 1. Motor vehicle accident (**driver/passenger**)
- ☐ 2. Motor vehicle accident (**pedestrian**)
- ☐ 3. Motorcycle accident
- ☐ 4. ATV (4-wheeler, etc.)
- ☐ 5. Crush injury
- ☐ 6. Fall from standing
- ☐ 7. Fall from height
- ☐ 8. Twist
- ☐ 9. Direct trauma (penetrating)
- ☐ 10. Direct trauma (blunt)
- ☐ 11. Other _____

9. Is this patient diabetic?

- ☐ Yes → If **yes**, specify **one**: ☐ Insulin dependent ☐ Non-insulin dependent
- ☐ No

10. Is there a history of any of the following? (check **all** that apply)

- ☐ **None**
- ☐ Rheumatoid arthritis
- ☐ HIV*
- ☐ Kidney transplant*
- ☐ Hepatitis
- ☐ Systemic lupus erythematosus

***Please complete a protocol deviation form as this patient is ineligible.**

FLOW #103 **Plate #005** **Visit #001**

Patient Study ID Number ☐☐ (Centre #) ☐☐☐☐ (Patient #) **Patient Initials** ☐☐ (F L)

BASELINE CHARACTERISTICS FORM (3 of 3) - FORM 3.3

11. Does the patient use tobacco products? (Includes cigarettes, cigars, and chewing tobacco)

☐ No

☐ Yes → If **yes**, specify: How long ☐☐.☐ (years)

☐ Yes, quit → If **yes**, specify: Age began ☐☐ (years) Age quit ☐☐ (years)

12. Does the patient consume alcohol? If yes, please specify the amount on average the patient drinks per week.

☐ Yes → If **yes**, specify: Drinks per week ☐☐.☐

☐ No

13. Does the patient currently use recreational IV drugs?

☐ Yes

☐ No

14. Was the patient employed before this injury?

☐ Yes If yes, what is the patient's occupation? _____

☐ No If no → ☐ Retired ☐ Home-maker ☐ Other (please specify below)

☐ Doctor's Advice/ Disabled ☐ Student _____

15. Is this a work related injury?

☐ Yes ☐ No

16. Was this patient taking any of the following classifications of medications prior to injury? Please check all that apply.

☐ No (patient is **not** taking any of the following classes of medications)

☐ NSAIDS ☐ Analgesics: Opioid ☐ Anti-hypertension Medications

☐ General Cardiac Medications ☐ Pulmonary (Respiratory System) Medications ☐ Osteoporosis Medications

17. Did the patient receive preparation solution in the emergency room?

☐ Yes → Please specify ☐ Iodine ☐ Alcohol ☐ Chlorhexidine

☐ No ☐ Other (***please specify)*** _____

FLOW #103 **Plate #010** **Visit #001**

Patient Study ID Number Centre # Patient # **Patient Initials** F L

Check Follow-Up Visit:

- ☐ Peri-Operative
- ☐ 1 week
- ☐ 2 weeks
- ☐ 6 weeks
- ☐ 3 months
- ☐ 6 months
- ☐ 9 months
- ☐ 12 months
- ☐ Early W/D

ANTIBIOTICS LOG - FORM 4.1

*Please refax the **ENTIRE** Antibiotics Log if updated.

**Please only record antibiotics that are prescribed for the randomized fracture.

#	Antibiotic e.g. Ancef, Dose: 5, Unit: mg, Route: PO, Frequency: BID	Reason for Administration		Start Date / Stop Date
1	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20 YYYY Stop date: DD MM 20 YYYY
2	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20 YYYY Stop date: DD MM 20 YYYY
3	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20 YYYY Stop date: DD MM 20 YYYY
4	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20 YYYY Stop date: DD MM 20 YYYY
5	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20 YYYY Stop date: DD MM 20 YYYY
6	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20 YYYY Stop date: DD MM 20 YYYY

☐ **Check here if continued on another ANTIBIOTICS LOG**

FLOW #103 **Plate #011** **Visit #001**

Patient Study ID Number ☐☐ (Centre #) ☐☐☐☐ (Patient #) **Patient Initials** ☐☐ (F L)

Check Follow-Up Visit:

☐ Peri-Operative ☐ 3 months
☐ 1 week ☐ 6 months
☐ 2 weeks ☐ 9 months
☐ 6 weeks ☐ 12 months
☐ Early W/D

ANTIBIOTICS LOG - FORM 4.2

*Please refax the **ENTIRE** Antibiotics Log if updated.

**Please only record antibiotics that are prescribed for the randomized fracture.

#	Antibiotic e.g. Ancef, Dose: 5, Unit: mg, Route: PO, Frequency: BID	Reason for Administration		Start Date / Stop Date
1	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
2	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
3	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
4	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
5	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
6	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY

☐ **Check here if continued on another ANTIBIOTICS LOG**

FLOW #103 **Plate #012** **Visit #001**

Patient Study ID Number ☐☐ (Centre #) ☐☐☐☐ (Patient #) **Patient Initials** ☐☐ (F L)

Check Follow-Up Visit:

☐ Peri-Operative ☐ 3 months
☐ 1 week ☐ 6 months
☐ 2 weeks ☐ 9 months
☐ 6 weeks ☐ 12 months
☐ Early W/D

ANTIBIOTICS LOG - FORM 4.3

*Please refax the **ENTIRE** Antibiotics Log if updated.

**Please only record antibiotics that are prescribed for the randomized fracture.

#	Antibiotic e.g. Ancef, Dose: 5, Unit: mg, Route: PO, Frequency: BID	Reason for Administration		Start Date / Stop Date
1	Name Dose | Unit | Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
2	Name Dose | Unit | Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
3	Name Dose | Unit | Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
4	Name Dose | Unit | Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
5	Name Dose | Unit | Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
6	Name Dose | Unit | Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY

☐ **Check here if continued on another ANTIBIOTICS LOG**

FLOW #103 **Plate #013** **Visit #001**

Patient Study ID Number Centre # Patient # **Patient Initials** F L

Check Follow-Up Visit:

- ☐ Peri-Operative
- ☐ 1 week
- ☐ 2 weeks
- ☐ 6 weeks
- ☐ 3 months
- ☐ 6 months
- ☐ 9 months
- ☐ 12 months
- ☐ Early W/D

ANTIBIOTICS LOG - FORM 4.4

*Please refax the **ENTIRE** Antibiotics Log if updated.

**Please only record antibiotics that are prescribed for the randomized fracture.

#	Antibiotic e.g. Ancef, Dose: 5, Unit: mg, Route: PO, Frequency: BID	Reason for Administration		Start Date / Stop Date
1	Name Dose | Unit | Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
2	Name Dose | Unit | Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
3	Name Dose | Unit | Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
4	Name Dose | Unit | Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
5	Name Dose | Unit | Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
6	Name Dose | Unit | Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY

☐ **Check here if continued on another ANTIBIOTICS LOG**

FLOW #103 **Plate #014** **Visit #001**

Patient Study ID Number Centre # Patient # **Patient Initials** F L

Check Follow-Up Visit:

- ☐ Peri-Operative
- ☐ 1 week
- ☐ 2 weeks
- ☐ 6 weeks
- ☐ 3 months
- ☐ 6 months
- ☐ 9 months
- ☐ 12 months
- ☐ Early W/D

ANTIBIOTICS LOG - FORM 4.5

*Please refax the **ENTIRE** Antibiotics Log if updated.

**Please only record antibiotics that are prescribed for the randomized fracture.

#	Antibiotic e.g. Ancef, Dose: 5, Unit: mg, Route: PO, Frequency: BID	Reason for Administration		Start Date / Stop Date
1	Name Dose | Unit | Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20 YYYY Stop date: DD MM 20 YYYY
2	Name Dose | Unit | Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20 YYYY Stop date: DD MM 20 YYYY
3	Name Dose | Unit | Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20 YYYY Stop date: DD MM 20 YYYY
4	Name Dose | Unit | Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20 YYYY Stop date: DD MM 20 YYYY
5	Name Dose | Unit | Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20 YYYY Stop date: DD MM 20 YYYY
6	Name Dose | Unit | Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20 YYYY Stop date: DD MM 20 YYYY

☐ **Check here if continued on another ANTIBIOTICS LOG**

FLOW #103 **Plate #015** **Visit #001**

Patient Study ID Number ☐☐ (Centre #) ☐☐☐☐ (Patient #) **Patient Initials** ☐☐ (F L)

Check Follow-Up Visit:

☐ Peri-Operative ☐ 3 months
☐ 1 week ☐ 6 months
☐ 2 weeks ☐ 9 months
☐ 6 weeks ☐ 12 months
☐ Early W/D

ANTIBIOTICS LOG - FORM 4.6

*Please refax the **ENTIRE** Antibiotics Log if updated.

**Please only record antibiotics that are prescribed for the randomized fracture.

#	Antibiotic e.g. Ancef, Dose: 5, Unit: mg, Route: PO, Frequency: BID	Reason for Administration		Start Date / Stop Date
1	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
2	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
3	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
4	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
5	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
6	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY

☐ **Check here if continued on another ANTIBIOTICS LOG**

FLOW #103 Plate #016 Visit #001

Patient Study ID Number [ ][ ] Centre # [ ][ ][ ][ ] Patient # Patient Initials [ ][ ] F L

Check Follow-Up Visit:

- ☐ Peri-Operative
- ☐ 1 week
- ☐ 2 weeks
- ☐ 6 weeks
- ☐ 3 months
- ☐ 6 months
- ☐ 9 months
- ☐ 12 months
- ☐ Early W/D

ANTIBIOTICS LOG - FORM 4.7

*Please refax the **ENTIRE** Antibiotics Log if updated.

**Please only record antibiotics that are prescribed for the randomized fracture.

#	Antibiotic e.g. Ancef, Dose: 5, Unit: mg, Route: PO, Frequency: BID	Reason for Administration		Start Date / Stop Date
1	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
2	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
3	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
4	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
5	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
6	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY

☐ **Check here if continued on another ANTIBIOTICS LOG**

FLOW #103 **Plate #017** **Visit #001**

Patient Study ID Number [ ][ ] **Centre #** [ ][ ][ ][ ] **Patient #** **Patient Initials** [ ][ ] **F L**

Check Follow-Up Visit:

- ☐ Peri-Operative
- ☐ 1 week
- ☐ 2 weeks
- ☐ 6 weeks
- ☐ 3 months
- ☐ 6 months
- ☐ 9 months
- ☐ 12 months
- ☐ Early W/D

ANTIBIOTICS LOG - FORM 4.8

*Please refax the **ENTIRE** Antibiotics Log if updated.

**Please only record antibiotics that are prescribed for the randomized fracture.

#	Antibiotic e.g. Ancef, Dose: 5, Unit: mg, Route: PO, Frequency: BID	Reason for Administration		Start Date / Stop Date
1	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20 YYYY Stop date: DD MM 20 YYYY
2	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20 YYYY Stop date: DD MM 20 YYYY
3	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20 YYYY Stop date: DD MM 20 YYYY
4	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20 YYYY Stop date: DD MM 20 YYYY
5	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20 YYYY Stop date: DD MM 20 YYYY
6	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20 YYYY Stop date: DD MM 20 YYYY

☐ **Check here if continued on another ANTIBIOTICS LOG**

FLOW #103 **Plate #018** **Visit #001**

Patient Study ID Number ☐☐ (Centre #) ☐☐☐☐ (Patient #) **Patient Initials** ☐☐ (F L)

Check Follow-Up Visit:

☐ Peri-Operative ☐ 3 months
☐ 1 week ☐ 6 months
☐ 2 weeks ☐ 9 months
☐ 6 weeks ☐ 12 months
☐ Early W/D

ANTIBIOTICS LOG - FORM 4.9

*Please refax the **ENTIRE** Antibiotics Log if updated.

**Please only record antibiotics that are prescribed for the randomized fracture.

#	Antibiotic e.g. Ancef, Dose: 5, Unit: mg, Route: PO, Frequency: BID	Reason for Administration		Start Date / Stop Date
1	Name Dose | Unit | Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
2	Name Dose | Unit | Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
3	Name Dose | Unit | Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
4	Name Dose | Unit | Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
5	Name Dose | Unit | Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
6	Name Dose | Unit | Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY

☐ **Check here if continued on another ANTIBIOTICS LOG**

FLOW #103 **Plate #019** **Visit #001**

Patient Study ID Number ☐☐ (Centre #) ☐☐☐☐ (Patient #) **Patient Initials** ☐☐ (F L)

Check Follow-Up Visit:

☐ Peri-Operative ☐ 3 months
☐ 1 week ☐ 6 months
☐ 2 weeks ☐ 9 months
☐ 6 weeks ☐ 12 months
☐ Early W/D

ANTIBIOTICS LOG - FORM 4.10

*Please refax the **ENTIRE** Antibiotics Log if updated.

**Please only record antibiotics that are prescribed for the randomized fracture.

#	Antibiotic e.g. Ancef, Dose: 5, Unit: mg, Route: PO, Frequency: BID	Reason for Administration		Start Date / Stop Date
1	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
2	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
3	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
4	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
5	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
6	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY

☐ **Check here if continued on another ANTIBIOTICS LOG**

FLOW #103 **Plate #020** **Visit #001**

Patient Study ID Number Centre # Patient # **Patient Initials** F L

Check Follow-Up Visit:

- ☐ Peri-Operative
- ☐ 1 week
- ☐ 2 weeks
- ☐ 6 weeks
- ☐ 3 months
- ☐ 6 months
- ☐ 9 months
- ☐ 12 months
- ☐ Early W/D

ANTIBIOTICS LOG - FORM 4.11

*Please refax the **ENTIRE** Antibiotics Log if updated.

**Please only record antibiotics that are prescribed for the randomized fracture.

#	Antibiotic e.g. Ancef, Dose: 5, Unit: mg, Route: PO, Frequency: BID	Reason for Administration		Start Date / Stop Date
1	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20 YYYY Stop date: DD MM 20 YYYY
2	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20 YYYY Stop date: DD MM 20 YYYY
3	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20 YYYY Stop date: DD MM 20 YYYY
4	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20 YYYY Stop date: DD MM 20 YYYY
5	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20 YYYY Stop date: DD MM 20 YYYY
6	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20 YYYY Stop date: DD MM 20 YYYY

☐ **Check here if continued on another ANTIBIOTICS LOG**

FLOW #103 **Plate #021** **Visit #001**

Patient Study ID Number [ ][ ] **Centre #** [ ][ ][ ][ ] **Patient #** **Patient Initials** [ ][ ] **F L**

Check Follow-Up Visit:

- ☐ Peri-Operative
- ☐ 1 week
- ☐ 2 weeks
- ☐ 6 weeks
- ☐ 3 months
- ☐ 6 months
- ☐ 9 months
- ☐ 12 months
- ☐ Early W/D

ANTIBIOTICS LOG - FORM 4.12

*Please refax the **ENTIRE** Antibiotics Log if updated.

**Please only record antibiotics that are prescribed for the randomized fracture.

#	Antibiotic e.g. Ancef, Dose: 5, Unit: mg, Route: PO, Frequency: BID	Reason for Administration		Start Date / Stop Date
1	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20 YYYY Stop date: DD MM 20 YYYY
2	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20 YYYY Stop date: DD MM 20 YYYY
3	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20 YYYY Stop date: DD MM 20 YYYY
4	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20 YYYY Stop date: DD MM 20 YYYY
5	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20 YYYY Stop date: DD MM 20 YYYY
6	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20 YYYY Stop date: DD MM 20 YYYY

☐ **Check here if continued on another ANTIBIOTICS LOG**

FLOW #103 **Plate #022** **Visit #001**

Patient Study ID Number Centre # Patient # **Patient Initials** F L

Check Follow-Up Visit:

- ☐ Peri-Operative
- ☐ 1 week
- ☐ 2 weeks
- ☐ 6 weeks
- ☐ 3 months
- ☐ 6 months
- ☐ 9 months
- ☐ 12 months
- ☐ Early W/D

ANTIBIOTICS LOG - FORM 4.13

*Please refax the **ENTIRE** Antibiotics Log if updated.

**Please only record antibiotics that are prescribed for the randomized fracture.

#	Antibiotic e.g. Ancef, Dose: 5, Unit: mg, Route: PO, Frequency: BID	Reason for Administration		Start Date / Stop Date
1	Name Dose | Unit | Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20 YYYY Stop date: DD MM 20 YYYY
2	Name Dose | Unit | Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20 YYYY Stop date: DD MM 20 YYYY
3	Name Dose | Unit | Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20 YYYY Stop date: DD MM 20 YYYY
4	Name Dose | Unit | Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20 YYYY Stop date: DD MM 20 YYYY
5	Name Dose | Unit | Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20 YYYY Stop date: DD MM 20 YYYY
6	Name Dose | Unit | Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20 YYYY Stop date: DD MM 20 YYYY

☐ **Check here if continued on another ANTIBIOTICS LOG**

FLOW #103 **Plate #023** **Visit #001**

Patient Study ID Number ☐☐ (Centre #) ☐☐☐☐ (Patient #) **Patient Initials** ☐☐ (F L)

Check Follow-Up Visit:

☐ Peri-Operative ☐ 3 months
☐ 1 week ☐ 6 months
☐ 2 weeks ☐ 9 months
☐ 6 weeks ☐ 12 months
☐ Early W/D

ANTIBIOTICS LOG - FORM 4.14

*Please refax the **ENTIRE** Antibiotics Log if updated.

**Please only record antibiotics that are prescribed for the randomized fracture.

#	Antibiotic e.g. Ancef, Dose: 5, Unit: mg, Route: PO, Frequency: BID	Reason for Administration		Start Date / Stop Date
1	Name Dose | Unit | Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
2	Name Dose | Unit | Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
3	Name Dose | Unit | Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
4	Name Dose | Unit | Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
5	Name Dose | Unit | Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
6	Name Dose | Unit | Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY

☐ **Check here if continued on another ANTIBIOTICS LOG**

FLOW #103 **Plate #024** **Visit #001**

Patient Study ID Number Centre # Patient # **Patient Initials** F L

Check Follow-Up Visit:

- ☐ Peri-Operative
- ☐ 1 week
- ☐ 2 weeks
- ☐ 6 weeks
- ☐ 3 months
- ☐ 6 months
- ☐ 9 months
- ☐ 12 months
- ☐ Early W/D

ANTIBIOTICS LOG - FORM 4.15

*Please refax the **ENTIRE** Antibiotics Log if updated.

**Please only record antibiotics that are prescribed for the randomized fracture.

#	Antibiotic e.g. Ancef, Dose: 5, Unit: mg, Route: PO, Frequency: BID	Reason for Administration		Start Date / Stop Date
1	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20 YYYY Stop date: DD MM 20 YYYY
2	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20 YYYY Stop date: DD MM 20 YYYY
3	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20 YYYY Stop date: DD MM 20 YYYY
4	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20 YYYY Stop date: DD MM 20 YYYY
5	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20 YYYY Stop date: DD MM 20 YYYY
6	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20 YYYY Stop date: DD MM 20 YYYY

☐ **Check here if continued on another ANTIBIOTICS LOG**

FLOW #103 **Plate #025** **Visit #001**

Patient Study ID Number ☐☐ (Centre #) ☐☐☐☐ (Patient #) **Patient Initials** ☐☐ (F L)

Check Follow-Up Visit:

☐ Peri-Operative ☐ 3 months
☐ 1 week ☐ 6 months
☐ 2 weeks ☐ 9 months
☐ 6 weeks ☐ 12 months
☐ Early W/D

ANTIBIOTICS LOG - FORM 4.16

*Please refax the **ENTIRE** Antibiotics Log if updated.

**Please only record antibiotics that are prescribed for the randomized fracture.

#	Antibiotic e.g. Ancef, Dose: 5, Unit: mg, Route: PO, Frequency: BID	Reason for Administration		Start Date / Stop Date
1	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
2	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
3	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
4	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
5	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY
6	Name Dose / Unit / Route Frequency	☐ Prophylaxis ☐ Infection ☐ Other (specify below)	☐ Check if **Ongoing** ☐ Check if **Stopped** →	Start date: DD MM 20YY Stop date: DD MM 20YY

FLOW #103 **Plate #028** **Visit #001**

Patient Study ID Number ☐☐ ☐☐☐☐ **Patient Initials** ☐☐ **Date** ☐☐ ☐☐ 20☐☐

Centre # **Patient #** **F L** **DD** **MM** **YYYY**

FRACTURE CHARACTERISTICS FORM (1 of 1) - FORM 5.1

Characteristics of the fracture

1. Type of fracture (check all that apply):

☐ Comminuted ☐ Segmental ☐ Transverse ☐ Spiral ☐ Oblique

2. Involvement of joint: ☐ Intra-articular ☐ Extra-articular

3. Bone loss:

☐ Yes → If **yes**, specify ☐☐.☐ **cm**

☐ No

4. OTA classification of fractures ***(refer to booklet or see www.ota.org/compendium/compendium.html)***:

☐☐.☐☐.☐☐☐

Characteristics of the open wound:

5. Wound dimensions: Width: ☐☐☐.☐ **cm** Length: ☐☐☐.☐ **cm**

6. Location of wound (check **all** that apply): ☐ Anterior ☐ Posterior ☐ Lateral ☐ Medial

7. Is this a wound degloving injury: ☐ Yes ☐ No

8. Skin loss: ☐ Yes ☐ No

9. Muscle loss: ☐ Yes ☐ No

10. Degree of wound contamination: ☐ Mild ☐ Moderate ☐ Severe ***(examples of severe include contamination with clothes, grass, etc.)***

11. Were pre-operative cultures taken? ☐ Yes → Please complete a **Cultures Form 20.1**

☐ No

FLOW #103 **Plate #030** **Visit #001**

Patient Study ID Number ☐☐ (Centre #) ☐☐☐☐ (Patient #) **Patient Initials** ☐☐ (F L)

SURGICAL REPORT FORM (1 of 3) - FORM 6.1

1. Date of surgery : Day ☐☐ Month ☐☐ Year 2 0 ☐☐

2. Name of attending surgeon: _____ (Surname) _____ (Given name)

3. Who performed the majority of the surgery? (check **one** only) ☐ Surgeon ☐ Resident ☐ Fellow

Technical Issues:

4. Type of surgical preparation solution used (check **all** that apply):

☐ Iodine ☐ Alcohol
☐ Chlorhexidine ☐ Other (***please specify)*** _____

5. Type of fixation(s) used (check **all** that apply):

☐ Intramedullary Nail → If **yes**, specify **one**: ☐ Reamed ☐ Unreamed

☐ Plate and screws → If **yes**, check **all** that apply: ☐ Locked ☐ Non locked; ☐ Small incision, submuscular (MIPO) ☐ Traditional dissection (not MIPO)

☐ Screws only

☐ External fixator

☐ K-wire(s)

☐ Cerclage → If **yes**, specify **one**: ☐ Wire ☐ Cable ☐ Synthetic

☐ Other ***(please specify)*** _____

☐ No fixation at this time

6. Was bone grafting performed?

☐ No ☐ Yes → specify location: ☐ Cancellous ☐ Cortical (structural) ☐ Vascularized bone

Surgical Debridement:

7. How much skin was debrided? (check **one**)

☐ None
☐ Small amount (<1 cm^2)
☐ Moderate amount (1-5 cm^2)
☐ Large amount (>5 cm^2)

8. How much muscle was debrided? (check **one**)

☐ None
☐ Small amount (<1 cm^3)
☐ Moderate amount (1-5 cm^3)
☐ Large amount (>5 cm^3)

FLOW #103 **Plate #031** **Visit #001**

Patient Study ID Number ☐☐ (Centre #) ☐☐☐☐ (Patient #) **Patient Initials** ☐☐ (F L)

SURGICAL REPORT FORM (2 of 3) - FORM 6.2

Surgical Debridement Cont.:

9. How much fascial tissue was debrided? (check **one**)

- ☐ None
- ☐ Small amount (<1 cm^2)
- ☐ Moderate amount (1-5 cm^2)
- ☐ Large amount (>5 cm^2)

10. How much bone was debrided? (check **one**)

- ☐ None
- ☐ Small amount (<1 cm^3)
- ☐ Moderate amount (1-5 cm^3)
- ☐ Large amount (>5 cm^3)

Irrigation:

11. Irrigation pressure and device used for debridement and open wound management:

☐ High[1] →
- ☐ Stryker Surgilav with multi-orifice tip - high pressure setting
- ☐ Zimmer Pulsavac Plus with shower tip - high pressure setting
- ☐ Other[2] - Please specify: Manufacturer _____
  Device Name _____
  PSI _____

☐ Low[1] →
- ☐ Stryker Surgilav with high flow trauma tip - low pressure setting
- ☐ Zimmer Pulsavac Plus with shower tip - low pressure setting
- ☐ Other[2] - Please specify: Manufacturer _____
  Device Name _____
  PSI _____

☐ Gravity flow[1]

☐ Bulb syringe[3]

12. Irrigation solution additive[4]:

- ☐ Saline
- ☐ Castile Soap
- ☐ Bacitracin[5]
- ☐ Other[5] (***please specify)*** _____

Please complete a **Protocol Deviation Form 10.1** if any of the following occur:

1. The pressure differed from that to which patient was randomized.

2. A device other than the Stryker Surgilav or Zimmer Pulsavac Plus with tips and settings for high and low pressure as per protocol was used.

3. A bulb syringe was used.

4. The solution additive differed from that to which patient was randomized.

5. Solution additive other than saline or castile soap was used.

13. Amount of irrigation solution used[6]: ☐☐.☐ **Litres**

6. Less than 3L of solution was used for Type I open fracture.
Less than 6L of solution was used for Type II or Type III open fracture.

7. Type IIIC fracture was included.

14. Type of fracture **post-operatively**:

☐ Type I ☐ Type II ☐ Type IIIA ☐ Type IIIB ☐ Type IIIC[7]

FLOW #103 **Plate #032** **Visit #001**

Patient Study ID Number ☐☐ ☐☐☐☐ **Patient Initials** ☐☐

Centre # **Patient #** **F L**

SURGICAL REPORT FORM (3 of 3) - FORM 6.3

15. Was tourniquet used: ☐ Yes ☐ No

16. Cortical continuity following fixation:

☐ 0% ☐ 25% ☐ 50% ☐ 75% ☐ 100%

17. Size of post-operative fracture gap: ☐ < 1 cm ☐ 1-5 cm ☐ > 5 cm

18. Total operative time for affected limb: (hours) ☐☐☐ (minutes) ☐☐

19. Time to first incision from injury: ☐☐☐ ☐☐

20. Time to surgery from arrival at hospital: ☐☐☐ ☐☐

* if time to surgery is > **24 hours** from time of hospital arrival, complete a **Protocol Deviation Form**

21. If time to surgery from hospital arrival was > **6** hours please give reason for surgical delay (check **all** that apply):

☐ Operating room availability ☐ Post-operative bed availability

☐ Patient's condition ☐ Other (specify): _____

22. Were antibiotic beads or antibiotic osteobiologics used during the initial surgery?

☐ No ☐ Yes** → Please name the antibiotic(s): _____

↳ Specify the type: ☐ Cement ☐ Bio-absorbable ☐ Other: _____

23. Was the wound closed at the time of the initial procedure?

☐ Yes ☐ No

** If the antibiotic beads or osteobiologics are removed, please complete a **Follow-up Surgical Report Form 11.1-11.3**

24. Are there other additional procedures planned for the included fracture/wound?

☐ Yes → Please specify: _____

☐ No

25. Did any unexpected intraoperative events occur during this patient's surgery?

☐ Yes → Complete an **Adverse Event Form 12.1** for **each** separate adverse event.

☐ No

FLOW #103 Plate #060 Visit #001

Patient Study ID Number [ ][ ] Centre # [ ][ ][ ][ ] Patient # Patient Initials [ ][ ] F L

PERI-OPERATIVE FORM (1 of 1) - FORM 7.1

Section A: Antibiotics

1. Did the patient receive any antibiotics for the randomized fracture?

☐ Yes → Record **all** antibiotics on the **Antibiotics Log 4.1**

☐ No → Complete a **Protocol Deviation Form 10.1**

2. Were the appropriate antibiotics given according to the Antibiotic Protocol (see below)?

☐ Yes

☐ No → Complete a **Protocol Deviation Form 10.1**

ANTIBIOTIC PROTOCOL

Pre-operative I.V. antibiotics must be administered commencing on diagnosis. Post-operative, I.V. antibiotics must be administered for at least 24 hours post-surgery.

Specific antibiotics will be used at the discretion of the attending surgeon. The recommended guidelines will include: Cephalosporin (Ancef) I.V. for Grade I-II injuries, Cephalosporin (Ancef) I.V. and Aminoglycoside (Gentamycin) I.V. for Grade III injuries, and Cephalosporin (Ancef) I.V., Aminoglycoside (Gentamycin I.V.) and penicillin for gross contaminated injuries. For large open wounds (Type III), temporary local antibiotic administration will be permitted (bead pouch) until definitive wound closure. All antibiotics that are prescribed for the randomized fracture are to be recorded on the case report forms (CRFs).

Section B: Discharge Information

1. Date of hospital discharge: Day [ ][ ] Month [ ][ ] Year 2 0 [ ][ ]

2. Where is the patient being discharged to? (check **one** only)

☐ Home

☐ Rehabilitation facility

☐ Other (specify) _____

Section C: Wound Vac

1. Did the patient receive a wound vac during their inital hospitlization?

☐ Yes → Date of application: Day [ ][ ] Month [ ][ ] Year 2 0 [ ][ ]

Date of final removal: Day [ ][ ] Month [ ][ ] Year 2 0 [ ][ ]

☐ No

Follow Up Number: ☐ 1 week post/op ☐ 2 weeks post/op ☐ 6 weeks ☐ 3 months ☐ 6 months ☐ 9 months ☐ 12 months

FLOW #103 **Plate #070**

Patient Study ID Number ☐☐ (Centre #) ☐☐☐☐ (Patient #) **Patient Initials** ☐☐ (F L)

FOLLOW UP REPORT FORM (1 of 3) - FORM 8.1

1. Date of follow up: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

2. Does this follow up visit fall within the acceptable time window?

   ☐ No → Please specify why: _____

   ☐ Yes

3. Location: ☐ In Person ☐ Telephone **(only if patient is unable to return to clinic)**

4. **FOR EACH** of the following, please indicate if the interview was completed AND which version was administered:

	Interview Complete?			Version Administered?	
	Yes	**No**	**N/A**	**Self Admin**	**Interviewer Admin**
SF-12v2	☐	☐		☐	☐
EQ-5D (N.A. sites only)	☐	☐	☐	☐	☐
SPOC (week 1 & 6 only)	☐	☐	☐	☐	☐

5. Visit status:

   ☐ **Complete:** all required data collection forms and questionnaires completed

   ☐ **Partially** complete → Please specify _____

6. Are there any changes in the patient's antibiotics?

   ☐ Yes → Update and refax the entire **Antibiotics Log 4.1**. **Remember to check the correct visit number.**

   ☐ No

7. Has the patient had any re-operations and/or additional procedures on the randomized fracture since the last follow up?

   ☐ Yes → record **total** number of re-operations and/or additional procedures reported at this follow up for **the included fracture site** (this includes I&Ds and soft tissue procedures) ☐☐ → complete a separate **Follow Up Surgical Report Form 11.1-11.3 for each** additional procedure

   ☐ No

8. Has the patient had any infections* since the last follow up?

   ☐ Yes → record **total** number of infections reported at this follow up for **the included fracture site** ☐☐ → complete a separate **Infection Form 9.1-9.3** for each infection

   ☐ No

*Do ***not*** report the following conditions as SSI
[1] Stitch abscess (minimal inflammation & discharge confined to the points of suture penetration)
[2] Infected burn wound

Follow Up Number: ☐ 1 week post/op ☐ 2 weeks post/op ☐ 6 weeks ☐ 3 months ☐ 6 months ☐ 9 months ☐ 12 months

FLOW #103 **Plate #071**

Patient Study ID Number ☐☐ ☐☐☐☐ **Patient Initials** ☐☐

Centre # Patient # F L

FOLLOW UP REPORT FORM (2 of 3) - FORM 8.2

9. Has the patient had any cultures taken since the last follow up?

☐ Yes → record **total** number of cultures taken at this follow up for **the included fracture site** ☐☐ → complete a **Cultures Form 20.1**

☐ No

10. Has the patient had any wound healing problems since the last follow up?

☐ Yes → record **total** number of wound healing problems reported at this follow up for **the included fracture site** ☐☐ → complete a separate **Wound Healing Problem Form 19.1 for each** problem

☐ No

11. Was full closure of the wound obtained?

☐ Yes

☐ Yes, reported at a previous visit

☐ No

12. If full closure has not been obtained, what was the problem?

☐ Skin coverage ☐ Leaving wound to granulate secondarily

☐ Operation scheduled ☐ Other: _____

13. Has the wound healed (defined as complete epidermal closure)?

☐ Yes → First date the surgeon declares the wound healed: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

☐ Yes, reported at a previous visit

☐ No

☐ Not Sure → Please specify why: _____

14. Please record the date of the patient's most recent x-ray of the included fracture site:

Day ☐☐ Month ☐☐ Year 2 0 ☐☐

15. Has the fracture healed radiographically?

☐ Yes → Date of the first radiograph that shows complete fracture healing: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

☐ Yes, reported at a previous visit

☐ No

☐ Not Sure → Please specify why: _____

FLOW #103

Plate #072

Follow Up Number: ☐ 1 week post/op ☐ 2 weeks post/op ☐ 6 weeks ☐ 3 months ☐ 6 months ☐ 9 months ☐ 12 months

Patient Study ID Number ☐☐ ☐☐☐☐ (Centre # / Patient #)

Patient Initials ☐☐ (F L)

FOLLOW UP REPORT FORM (3 of 3) - FORM 8.3

16. Has the patient had any new adverse events, including **a nonunion / delayed union** since their last follow up visit?

☐ Yes → record **total** number of adverse events reported at this follow up including nonunion/delayed union ☐☐ → complete a separate **Adverse Event Form 12.1 for each** adverse event

☐ No

17. Has the patient been using stimulation modalities (i.e., ultrasound, electrical stimulation, etc.) on the included fracture to promote bone growth?

☐ Yes → Please specify _____

☐ No

18. Did the patient receive a wound vac?

☐ Yes → Date of application: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

☐ No Date of final removal: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

☐ Yes, reported at a previous visit

FOR 12 MONTH FOLLOW-UP ONLY:

19. Are there any planned re-operations for the included fracture after the 12-month follow-up?

☐ Yes → Please specify _____

☐ No

FLOW #103

Plate #090

Patient Study ID Number

Centre # | Patient #

Patient Initials

F L

Follow Up Number:

- ☐ 1 week post/op
- ☐ 2 weeks post/op
- ☐ 6 weeks
- ☐ 3 months
- ☐ 6 months
- ☐ 9 months
- ☐ 12 months
- ☐ 99 Early W/D

INFECTION FORM (1 of 3) - FORM 9.1

Notes

1. Report infection that involves both superficial and deep incision sites as deep incisional surgical site infections.
2. Report an organ/space SSI that drains through the incision as a deep incisional surgical site infection.

1. Date infection was diagnosed: ☐☐ DD ☐☐ MM 20☐☐ YYYY

2. Please specify the type of infection.

- ☐ Superficial Incisional Surgical Site Infection → **complete question 3a**
- ☐ Deep Incisional Surgical Site Infection → **complete question 3b**
- ☐ Organ/Space Surgical Site Infection → **complete question 3c**

3. Please provide details on the infection.

3. a) **Superficial Incisional Surgical Site Infection (SSI):**

Infection occurs within 6 weeks after the operation
and infection involves only skin or subcutaneous tissue of the incision
and at least ***one*** of the following:

- ☐ 1. Purulent drainage, with or without laboratory confirmation, from the superficial incision
- ☐ 2. Organism isolated from an aseptically obtained culture of fluid or tissue from the superficial incision
- ☐ 3. At least one of the following signs or symptoms of infection:
  - ☐ pain or tenderness
  - ☐ localized swelling
  - ☐ redness
  - ☐ heat
- ☐ 4. Diagnosis of superficial incisional SSI by the surgeon or attending physician

3. b) **Deep Incisional Surgical Site Infection:**

Infection occurs within 6 weeks after the operation if no implant is left in place or within 1 year if implant is in place and the infection appears to be related to the operation **and** infection involves deep soft tissue (e.g., fascial and muscle layers) of the incision **and** at least ***one*** of the following:

- ☐ 1. Purulent drainage from the deep incision but not from the organ/space component of the surgical site
- ☐ 2. A deep incision spontaneously dehisces or is deliberately opened by a surgeon when the patient has at least one of the following signs or symptoms:
  - ☐ fever (>38 degrees Celsius)
  - ☐ localized pain
  - ☐ or tenderness

  unless site is culture-negative
- ☐ 3. An abscess or other evidence of infection involving the deep incision is found on direct examination, during reoperation, or by histopathologic or radiologic examination.
- ☐ 4. Diagnosis of a deep incisional SSI by a surgeon or attending physician

FLOW #103 **Plate #091**

Patient Study ID Number Centre # Patient #

Patient Initials F L

Follow Up Number:
- ☐ 1 week post/op
- ☐ 2 weeks post/op
- ☐ 6 weeks
- ☐ 3 months
- ☐ 6 months
- ☐ 9 months
- ☐ 12 months
- ☐ 99 Early W/D

INFECTION FORM (2 of 3) - FORM 9.2

3. c) **Organ/Space Surgical Site Infection:**

Infection occurs within 6 weeks after the operation if no implant is left in place or within 1 year if implant is in place and the infection appears to be related to the operation
and
infection involves any part of the anatomy (e.g., organs or spaces), other than the incision, which was opened or manipulated during an operation
and
at least ***one*** of the following:

- ☐ 1. Purulent drainage from a drain that is placed through a stab wound into organ/space
- ☐ 2. Organism isolated from an aseptically obtained culture of fluid or tissue in the organ/space
- ☐ 3. An abscess or other evidence of infection involving the organ/space that is found on direct examination, during reoperation, or by histopathologic or radiologic examination.
- ☐ 4. Diagnosis of superficial incisional SSI by the surgeon or attending physician

4. Was the patient rehospitalized for the infection?

☐ Yes → Date of hospital admission: Day ☐☐ Month ☐☐ Year 20☐☐

☐ No Date of hospital discharge: Day ☐☐ Month ☐☐ Year 20☐☐

☐ N/A - infection occurred during initial hospitalization

5. How was the infection treated? (check **all** that apply)

- ☐ Antibiotics → **Please update and refax the entire Antibiotics Log 4.1**
- ☐ Operatively → **Please ensure that question 7 on the Follow Up Report Form 8.1-8.3 is filled out appropriately**
- ☐ Other: _____

6. Were cultures taken?

- ☐ Yes → Please complete a **Cultures Form 20.1**
- ☐ No

FLOW #103 **Plate #092**

Patient Study ID Number Centre # Patient #

Patient Initials F L

Follow Up Number:
- ☐ 1 week post/op
- ☐ 2 weeks post/op
- ☐ 6 weeks
- ☐ 3 months
- ☐ 6 months
- ☐ 9 months
- ☐ 12 months
- ☐ 99 Early W/D

INFECTION FORM (3 of 3) - FORM 9.3

7. Is this infection considered an serious adverse event (SAE) (fatal, immediately life threatening, permanent disability, hospitalization (repeat or prolonged))?

☐ Yes → **Please complete an SAE Form 21.1** ☐ No

8. Does the attending physician believe that the infection is directly related to the FLOW study (i.e., type of solution or pressure used)?

☐ Not related ☐ Possibly related ☐ Probably related ☐ Definitely related ☐ Unclassifiable

9. Outcome of infection:

☐ Resolved → **Please refax form when resolved.** → Date resolved/Date resolved with subsequent impairment: Day ☐☐ Month ☐☐ Year 20☐☐

☐ Resolved, with subsequent impairment → **Degree of impairment:** ☐ Mild ☐ Moderate ☐ Severe

☐ Ongoing → **Please update form when resolved.**

☐ Fatal → **Please complete an Early Withdrawal Form 14.1-14.3.**

10. Comments:

FLOW #103 Plate #093

Follow Up Number: ☐ 1 week post/op ☐ 6 months ☐ 2 weeks post/op ☐ 9 months ☐ 6 weeks ☐ 12 months ☐ 3 months ☐ 99 Early W/D

Patient Study ID Number ☐☐ (Centre #) ☐☐☐☐ (Patient #) Patient Initials ☐☐ (F L)

INFECTION FORM (1 of 3) - FORM 9.4

Notes
1. Report infection that involves both superficial and deep incision sites as deep incisional surgical site infections.
2. Report an organ/space SSI that drains through the incision as a deep incisional surgical site infection.

1. Date infection was diagnosed: ☐☐ (DD) ☐☐ (MM) 2 0 ☐☐ (YYYY)

2. Please specify the type of infection.

- ☐ Superficial Incisional Surgical Site Infection → **complete question 3a**
- ☐ Deep Incisional Surgical Site Infection → **complete question 3b**
- ☐ Organ/Space Surgical Site Infection → **complete question 3c**

3. Please provide details on the infection.

3. a) **Superficial Incisional Surgical Site Infection (SSI):**

Infection occurs within 6 weeks after the operation
and infection involves only skin or subcutaneous tissue of the incision
and at least ***one*** of the following:

- ☐ 1. Purulent drainage, with or without laboratory confirmation, from the superficial incision
- ☐ 2. Organism isolated from an aseptically obtained culture of fluid or tissue from the superficial incision
- ☐ 3. At least one of the following signs or symptoms of infection:
  - ☐ pain or tenderness ☐ localized swelling ☐ redness ☐ heat
- ☐ 4. Diagnosis of superficial incisional SSI by the surgeon or attending physician

3. b) **Deep Incisional Surgical Site Infection:**

Infection occurs within 6 weeks after the operation if no implant is left in place or within 1 year if implant is in place and the infection appears to be related to the operation **and** infection involves deep soft tissue (e.g., fascial and muscle layers) of the incision **and** at least ***one*** of the following:

- ☐ 1. Purulent drainage from the deep incision but not from the organ/space component of the surgical site
- ☐ 2. A deep incision spontaneously dehisces or is deliberately opened by a surgeon when the patient has at least one of the following signs or symptoms:
  - ☐ fever (>38 degrees Celsius)
  - ☐ localized pain
  - ☐ or tenderness

  unless site is culture-negative
- ☐ 3. An abscess or other evidence of infection involving the deep incision is found on direct examination, during reoperation, or by histopathologic or radiologic examination.
- ☐ 4. Diagnosis of a deep incisional SSI by a surgeon or attending physician

FLOW #103 **Plate #094**

Patient Study ID Number Centre # Patient #

Patient Initials F L

Follow Up Number:
- ☐ 1 week post/op
- ☐ 2 weeks post/op
- ☐ 6 weeks
- ☐ 3 months
- ☐ 6 months
- ☐ 9 months
- ☐ 12 months
- ☐ 99 Early W/D

INFECTION FORM (2 of 3) - FORM 9.5

3. c) **Organ/Space Surgical Site Infection:**

Infection occurs within 6 weeks after the operation if no implant is left in place or within 1 year if implant is in place and the infection appears to be related to the operation
and
infection involves any part of the anatomy (e.g., organs or spaces), other than the incision, which was opened or manipulated during an operation
and
at least ***one*** of the following:

- ☐ 1. Purulent drainage from a drain that is placed through a stab wound into organ/space
- ☐ 2. Organism isolated from an aseptically obtained culture of fluid or tissue in the organ/space
- ☐ 3. An abscess or other evidence of infection involving the organ/space that is found on direct examination, during reoperation, or by histopathologic or radiologic examination.
- ☐ 4. Diagnosis of superficial incisional SSI by the surgeon or attending physician

4. Was the patient rehospitalized for the infection?

☐ Yes → Date of hospital admission: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

☐ No Date of hospital discharge: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

☐ N/A - infection occurred during initial hospitalization

5. How was the infection treated? (check **all** that apply)

- ☐ Antibiotics → **Please update and refax the entire Antibiotics Log 4.1**
- ☐ Operatively → **Please ensure that question 7 on the Follow Up Report Form 8.1-8.3 is filled out appropriately**
- ☐ Other: _____

6. Were cultures taken?

- ☐ Yes → Please complete a **Cultures Form 20.1**
- ☐ No

FLOW #103 Plate #095

Follow Up Number: ☐ 1 week post/op ☐ 6 months ☐ 2 weeks post/op ☐ 9 months ☐ 6 weeks ☐ 12 months ☐ 3 months ☐ 99 Early W/D

Patient Study ID Number ☐☐ (Centre #) ☐☐☐☐ (Patient #) Patient Initials ☐☐ (F L)

INFECTION FORM (3 of 3) - FORM 9.6

7. Is this infection considered an serious adverse event (SAE) (fatal, immediately life threatening, permanent disability, hospitalization (repeat or prolonged))?

☐ Yes → **Please complete an SAE Form 21.1** ☐ No

8. Does the attending physician believe that the infection is directly related to the FLOW study (i.e., type of solution or pressure used)?

☐ Not related ☐ Possibly related ☐ Probably related ☐ Definitely related ☐ Unclassifiable

9. Outcome of infection:

☐ Resolved → **Please refax form when resolved.** → Date resolved/Date resolved with subsequent impairment: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

☐ Resolved, with subsequent impairment → **Degree of impairment:** ☐ Mild ☐ Moderate ☐ Severe

☐ Ongoing → **Please update form when resolved.**

☐ Fatal → **Please complete an Early Withdrawal Form 14.1-14.3.**

10. Comments:

FLOW #103 Plate #096

Follow Up Number: ☐ 1 week post/op ☐ 6 months ☐ 2 weeks post/op ☐ 9 months ☐ 6 weeks ☐ 12 months ☐ 3 months ☐ 99 Early W/D

Patient Study ID Number ☐☐ (Centre #) ☐☐☐☐ (Patient #) Patient Initials ☐☐ (F L)

INFECTION FORM (1 of 3) - FORM 9.7

Notes
1. Report infection that involves both superficial and deep incision sites as deep incisional surgical site infections.
2. Report an organ/space SSI that drains through the incision as a deep incisional surgical site infection.

1. Date infection was diagnosed: ☐☐ (DD) ☐☐ (MM) 2 0 ☐☐ (YYYY)

2. Please specify the type of infection.

☐ Superficial Incisional Surgical Site Infection → **complete question 3a**

☐ Deep Incisional Surgical Site Infection → **complete question 3b**

☐ Organ/Space Surgical Site Infection → **complete question 3c**

3. Please provide details on the infection.

3. a) **Superficial Incisional Surgical Site Infection (SSI):**

Infection occurs within 6 weeks after the operation
and infection involves only skin or subcutaneous tissue of the incision
and at least ***one*** of the following:

☐ 1. Purulent drainage, with or without laboratory confirmation, from the superficial incision

☐ 2. Organism isolated from an aseptically obtained culture of fluid or tissue from the superficial incision

☐ 3. At least one of the following signs or symptoms of infection:

☐ pain or tenderness ☐ localized swelling ☐ redness ☐ heat

☐ 4. Diagnosis of superficial incisional SSI by the surgeon or attending physician

3. b) **Deep Incisional Surgical Site Infection:**

Infection occurs within 6 weeks after the operation if no implant is left in place or within 1 year if implant is in place and the infection appears to be related to the operation **and** infection involves deep soft tissue (e.g., fascial and muscle layers) of the incision **and** at least ***one*** of the following:

☐ 1. Purulent drainage from the deep incision but not from the organ/space component of the surgical site

☐ 2. A deep incision spontaneously dehisces or is deliberately opened by a surgeon when the patient has at least one of the following signs or symptoms:

☐ fever (>38 degrees Celsius)

☐ localized pain

☐ or tenderness

unless site is culture-negative

☐ 3. An abscess or other evidence of infection involving the deep incision is found on direct examination, during reoperation, or by histopathologic or radiologic examination.

☐ 4. Diagnosis of a deep incisional SSI by a surgeon or attending physician

FLOW #103 **Plate #097**

Patient Study ID Number Centre # Patient #

Patient Initials F L

Follow Up Number:
- ☐ 1 week post/op
- ☐ 2 weeks post/op
- ☐ 6 weeks
- ☐ 3 months
- ☐ 6 months
- ☐ 9 months
- ☐ 12 months
- ☐ 99 Early W/D

INFECTION FORM (2 of 3) - FORM 9.8

3. c) **Organ/Space Surgical Site Infection:**

Infection occurs within 6 weeks after the operation if no implant is left in place or within 1 year if implant is in place and the infection appears to be related to the operation
and
infection involves any part of the anatomy (e.g., organs or spaces), other than the incision, which was opened or manipulated during an operation
and
at least ***one*** of the following:

- ☐ 1. Purulent drainage from a drain that is placed through a stab wound into organ/space
- ☐ 2. Organism isolated from an aseptically obtained culture of fluid or tissue in the organ/space
- ☐ 3. An abscess or other evidence of infection involving the organ/space that is found on direct examination, during reoperation, or by histopathologic or radiologic examination.
- ☐ 4. Diagnosis of superficial incisional SSI by the surgeon or attending physician

4. Was the patient rehospitalized for the infection?

☐ Yes → Date of hospital admission: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

☐ No Date of hospital discharge: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

☐ N/A - infection occurred during initial hospitalization

5. How was the infection treated? (check **all** that apply)

- ☐ Antibiotics → **Please update and refax the entire Antibiotics Log 4.1**
- ☐ Operatively → **Please ensure that question 7 on the Follow Up Report Form 8.1-8.3 is filled out appropriately**
- ☐ Other: _____

6. Were cultures taken?

- ☐ Yes → Please complete a **Cultures Form 20.1**
- ☐ No

FLOW #103 **Plate #098**

Patient Study ID Number Centre # Patient #

Patient Initials F L

Follow Up Number:
- ☐ 1 week post/op
- ☐ 2 weeks post/op
- ☐ 6 weeks
- ☐ 3 months
- ☐ 6 months
- ☐ 9 months
- ☐ 12 months
- ☐ 99 Early W/D

INFECTION FORM (3 of 3) - FORM 9.9

7. Is this infection considered an serious adverse event (SAE) (fatal, immediately life threatening, permanent disability, hospitalization (repeat or prolonged))?

☐ Yes → **Please complete an SAE Form 21.1** ☐ No

8. Does the attending physician believe that the infection is directly related to the FLOW study (i.e., type of solution or pressure used)?

☐ Not related ☐ Possibly related ☐ Probably related ☐ Definitely related ☐ Unclassifiable

9. Outcome of infection:

☐ Resolved → **Please refax form when resolved.** → Date resolved/Date resolved with subsequent impairment: Day ☐☐ Month ☐☐ Year 20☐☐

☐ Resolved, with subsequent impairment → **Degree of impairment:** ☐ Mild ☐ Moderate ☐ Severe

☐ Ongoing → **Please update form when resolved.**

☐ Fatal → **Please complete an Early Withdrawal Form 14.1-14.3.**

10. Comments:

Follow Up Number: ☐ Surgery ☐ 1 week post/op ☐ 2 weeks post/op ☐ 6 weeks ☐ 3 months ☐ 6 months ☐ 9 months ☐ 12 months ☐ 99 Early W/D

FLOW #103 **Plate #100**

Patient Study ID Number ☐☐ ☐☐☐☐ **Patient Initials** ☐☐

Centre # **Patient #** **F L**

PROTOCOL DEVIATION FORM (1 of 2) - FORM 10.1

Please answer 'Yes' or 'No' to all questions

1. Wrong pressure used?
   - ☐ Yes → If yes, please explain: _____
   - ☐ No _____
2. Wrong irrigation solution additive used?
   - ☐ Yes → If yes, please explain: _____
   - ☐ No _____
3. Bulb syringe used?
   - ☐ Yes → If yes, please explain: _____
   - ☐ No _____
4. Used less fluid than required (3L for type I and 6L for type II and III open fracture) ☐ **OR** wound **not** irrigated ☐ ?
   - ☐ Yes → If yes, please explain: _____
   - ☐ No _____
5. Device other than Stryker Surgilav or Zimmer Pulsavac Plus with tips and settings for high and low pressure as per protocol was used?
   - ☐ Yes → If yes, please explain: _____
   - ☐ No _____
6. Surgery delayed beyond 24 hours?
   - ☐ Yes → If yes, please explain: _____
   - ☐ No _____
7. No antibiotics given?
   - ☐ Yes → If yes, please explain: _____
   - ☐ No _____
8. Antibiotic protocol **not** followed?
   - ☐ Yes → If yes, please explain: _____
   - ☐ No _____

FLOW #103 Plate #101

Follow Up Number: ☐ Surgery ☐ 1 week post/op ☐ 2 weeks post/op ☐ 6 weeks ☐ 3 months ☐ 6 months ☐ 9 months ☐ 12 months ☐ 99 Early W/D

Patient Study ID Number ☐☐ (Centre #) ☐☐☐☐ (Patient #)

Patient Initials ☐☐ (F L)

PROTOCOL DEVIATION FORM (2 of 2) - FORM 10.2

9. Stratification error (initial judgment of fracture type was incorrect at time of randomization)?

☐ Yes → If yes, please explain: _____

☐ No _____

10. Type IIIC fracture was included?

☐ Yes → If yes, please explain: _____

☐ No _____

11. Ineligible patient was included (please follow patient as per protocol)?

☐ Yes → If yes, please explain: _____

☐ No _____

FLOW #103 Plate #105

Follow Up Number: ☐ 1 week post/op ☐ 6 months ☐ 2 weeks post/op ☐ 9 months ☐ 6 weeks ☐ 12 months ☐ 3 months ☐ 99 Early W/D

Patient Study ID Number ☐☐ ☐☐☐☐ Patient Initials ☐☐

Centre # Patient # F L

FOLLOW UP SURGICAL REPORT FORM: RE-OPERATIONS (1 of 3) - FORM 11.1

Please complete a separate form for each re-operation.

1. Date of re-operation or additional procedure: Day ☐☐ Month ☐☐ Year 20☐☐

2. Name of attending surgeon: _____ (Surname) _____ (Given name)

3. Was the re-operation planned at the time of the definitive treatment? ☐ Yes ☐ No ☐ Not Applicable (this is the definitive treatment)

4. Please specify type of re-operation(s) and/or additional procedure(s) on this specific date: (check **all** that apply)

- ☐ Fixation of fracture (specify) _____
- ☐ Irrigation and debridement ☐ Primary wound closure ☐ Removal of antibiotic beads or osteobiologics
- ☐ Fasciotomy ☐ Fasciotomy closure
- ☐ Wound flap (rotational or free) (specify) _____
- ☐ Skin graft (specify) _____
- ☐ Bone graft → specify location ☐ Cancellous ☐ Cortical (structural) ☐ Vascularized bone
- ☐ Implant exchange (specify) _____
- ☐ Removal of external fixation in OR ☐ Removal of external fixation in clinic
- ☐ Screw removal in OR ☐ Screw removal in clinic
- ☐ Other implant removal (specify) _____
- ☐ Amputation (specify) _____
- ☐ Other (specify) _____

5. Reason for re-operation: (Please check **all** that apply)

- ☐ Nonunion / Delayed union[1]
- ☐ Malunion[2]
- ☐ Infection (deep)*
- ☐ Infection (superficial)*
- ☐ Fracture gap
- ☐ Wound dehiscence*
- ☐ Definitive fixation
- ☐ Compartment syndrome
- ☐ Painful hardware / Patient discomfort
- ☐ Open wound
- ☐ Hardware failure (Specify)_____
- ☐ Other (Specify) _____
- ☐ Wound necrosis*

[1] a general guideline is failure of progression of fracture healing for at least 2 or 3 **successive** months with pain at the fracture site to palpation

[2] healing with an unsatisfactory alignment of the fracture, according to the attending surgeon's discretion

FLOW #103 **Plate #106**

Patient Study ID Number Centre # Patient #

Patient Initials F L

Follow Up Number: ☐ 1 week post/op ☐ 2 weeks post/op ☐ 6 weeks ☐ 3 months ☐ 6 months ☐ 9 months ☐ 12 months ☐ 99 Early W/D

FOLLOW UP SURGICAL REPORT FORM: RE-OPERATIONS (2 of 3) - FORM 11.2

6. Was irrigation and debridement done?

☐ Yes → complete Questions 7-13 ☐ No → skip to Question 14 on the next page

7. How much skin was debrided? (check **one**)

☐ None
☐ Small amount (<1 cm^2)
☐ Moderate amount (1-5 cm^2)
☐ Large amount (>5 cm^2)

8. How much muscle was debrided? (check **one**)

☐ None
☐ Small amount (<1 cm^3)
☐ Moderate amount (1-5 cm^3)
☐ Large amount (>5 cm^3)

9. How much fascial tissue was debrided? (check **one**)

☐ None
☐ Small amount (<1 cm^2)
☐ Moderate amount (1-5 cm^2)
☐ Large amount (>5 cm^2)

10. How much bone was debrided? (check **one**)

☐ None
☐ Small amount (<1 cm^3)
☐ Moderate amount (1-5 cm^3)
☐ Large amount (>5 cm^3)

11. Irrigation pressure and device used for debridement and open wound management:

☐ High[1] →
- ☐ Stryker Surgilav with multi-orifice tip - high pressure setting
- ☐ Zimmer Pulsavac Plus with shower tip - high pressure setting
- ☐ Other[2] - Please specify: Manufacturer _____
  Device Name _____
  PSI _____

☐ Low[1] →
- ☐ Stryker Surgilav with high flow trauma tip - low pressure setting
- ☐ Zimmer Pulsavac Plus with shower tip - low pressure setting
- ☐ Other[2] - Please specify: Manufacturer _____
  Device Name _____
  PSI _____

☐ Gravity flow[1]

☐ Bulb syringe[3]

12. Irrigation solution additive[4]:

☐ Saline
☐ Castile Soap
☐ Bacitracin[5]
☐ Other[5] (***please specify)*** _____

Please complete a **Protocol Deviation Form 10.1** if any of the following occur:

1. The pressure differed from that to which patient was randomized.

2. If a device other than the Stryker Surgilav or Zimmer Pulsavac Plus with tips and settings for high and low pressure as per protocol was used.

3. If a bulb syringe was used.

4. The solution additive differed from that to which patient was randomized.

5. Solution additive other than saline or castile soap was used.

FLOW #103 Plate #107

Follow Up Number: ☐ 1 week post/op ☐ 6 months ☐ 2 weeks post/op ☐ 9 months ☐ 6 weeks ☐ 12 months ☐ 3 months ☐ 99 Early W/D

Patient Study ID Number ☐☐ (Centre #) ☐☐☐☐ (Patient #) Patient Initials ☐☐ (F L)

FOLLOW UP SURGICAL REPORT FORM: RE-OPERATIONS (3 of 3) - FORM 11.3

13. Amount of irrigation solution used: ☐☐.☐ **Litres**

14. Was tourniquet used: ☐ Yes ☐ No

15. Cortical continuity following re-operation:

☐ 0% ☐ 25% ☐ 50% ☐ 75% ☐ 100%

16. Size of post-operative fracture gap: ☐ < 1 cm ☐ 1-5 cm ☐ > 5 cm

17. Was full closure of the wound obtained?

☐ Yes ☐ No ☐ N/A, previously closed

18. Were antibiotic beads or antibiotic osteobiologics used during the re-operation?

☐ No ☐ Yes → Please name the antibiotic(s): _____

↳ Specify the type: ☐ Cement ☐ Bio-absorbable ☐ Other: _____

19. Did any intraoperative adverse events occur during this patient's surgery?

☐ Yes → **Please complete an Adverse Event Form (12.1)**

☐ No

20. Was the patient rehospitalized?

☐ Yes → Date of hospital admission: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

☐ No Date of hospital discharge: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

☐ N/A - re-operation occurred during initial hospitalization

21. Are there other additional procedures planned for the included fracture/wound?

☐ Yes → Please specify: _____

☐ No

22. Is this re-operation considered an serious adverse event (SAE) (fatal, immediately life threatening, permanent disability, hospitalization (repeat or prolonged))?

☐ Yes → **Please complete an SAE Form 21.1** ☐ No

23. Does the attending physician believe that the re-operation is directly related to the FLOW study (i.e., type of solution or pressure used)?

☐ Not related ☐ Possibly related ☐ Probably related ☐ Definitely related ☐ Unclassifiable

FLOW #103 Plate #108

Follow Up Number: ☐ 1 week post/op ☐ 6 months ☐ 2 weeks post/op ☐ 9 months ☐ 6 weeks ☐ 12 months ☐ 3 months ☐ 99 Early W/D

Patient Study ID Number ☐☐ Centre # ☐☐☐☐ Patient #

Patient Initials ☐☐ F L

FOLLOW UP SURGICAL REPORT FORM: RE-OPERATIONS (1 of 3) - FORM 11.4

Please complete a separate form for each re-operation.

1. Date of re-operation or additional procedure: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

2. Name of attending surgeon: _____ Surname _____ Given name

3. Was the re-operation planned at the time of the definitive treatment? ☐ Yes ☐ No ☐ Not Applicable (this is the definitive treatment)

4. Please specify type of re-operation(s) and/or additional procedure(s) on this specific date: (check **all** that apply)

- ☐ Fixation of fracture (specify) _____
- ☐ Irrigation and debridement ☐ Primary wound closure ☐ Removal of antibiotic beads or osteobiologics
- ☐ Fasciotomy ☐ Fasciotomy closure
- ☐ Wound flap (rotational or free) (specify) _____
- ☐ Skin graft (specify) _____
- ☐ Bone graft → specify location ☐ Cancellous ☐ Cortical (structural) ☐ Vascularized bone
- ☐ Implant exchange (specify) _____
- ☐ Removal of external fixation in OR ☐ Removal of external fixation in clinic
- ☐ Screw removal in OR ☐ Screw removal in clinic
- ☐ Other implant removal (specify) _____
- ☐ Amputation (specify) _____
- ☐ Other (specify) _____

5. Reason for re-operation: (Please check **all** that apply)

- ☐ Nonunion / Delayed union[1]
- ☐ Malunion[2]
- ☐ Infection (deep)*
- ☐ Infection (superficial)*
- ☐ Fracture gap
- ☐ Wound dehiscence*
- ☐ Definitive fixation
- ☐ Compartment syndrome
- ☐ Painful hardware / Patient discomfort
- ☐ Open wound
- ☐ Hardware failure (Specify)_____
- ☐ Other (Specify) _____
- ☐ Wound necrosis*

[1]a general guideline is failure of progression of fracture healing for at least 2 or 3 **successive** months with pain at the fracture site to palpation

[2]healing with an unsatisfactory alignment of the fracture, according to the attending surgeon's discretion

FLOW #103 **Plate #109**

Patient Study ID Number Centre # Patient #

Patient Initials F L

Follow Up Number: ☐ 1 week post/op ☐ 2 weeks post/op ☐ 6 weeks ☐ 3 months ☐ 6 months ☐ 9 months ☐ 12 months ☐ 99 Early W/D

FOLLOW UP SURGICAL REPORT FORM: RE-OPERATIONS (2 of 3) - FORM 11.5

6. Was irrigation and debridement done?

☐ Yes → complete Questions 7-13 ☐ No → skip to Question 14 on the next page

7. How much skin was debrided? (check **one**)

☐ None
☐ Small amount (<1 cm^2)
☐ Moderate amount (1-5 cm^2)
☐ Large amount (>5 cm^2)

8. How much muscle was debrided? (check **one**)

☐ None
☐ Small amount (<1 cm^3)
☐ Moderate amount (1-5 cm^3)
☐ Large amount (>5 cm^3)

9. How much fascial tissue was debrided? (check **one**)

☐ None
☐ Small amount (<1 cm^2)
☐ Moderate amount (1-5 cm^2)
☐ Large amount (>5 cm^2)

10. How much bone was debrided? (check **one**)

☐ None
☐ Small amount (<1 cm^3)
☐ Moderate amount (1-5 cm^3)
☐ Large amount (>5 cm^3)

11. Irrigation pressure and device used for debridement and open wound management:

☐ High[1] →
- ☐ Stryker Surgilav with multi-orifice tip - high pressure setting
- ☐ Zimmer Pulsavac Plus with shower tip - high pressure setting
- ☐ Other[2] - Please specify: Manufacturer _____
  Device Name _____
  PSI _____

☐ Low[1] →
- ☐ Stryker Surgilav with high flow trauma tip - low pressure setting
- ☐ Zimmer Pulsavac Plus with shower tip - low pressure setting
- ☐ Other[2] - Please specify: Manufacturer _____
  Device Name _____
  PSI _____

☐ Gravity flow[1]

☐ Bulb syringe[3]

12. Irrigation solution additive[4]:

☐ Saline
☐ Castile Soap
☐ Bacitracin[5]
☐ Other[5] (***please specify)*** _____

Please complete a **Protocol Deviation Form 10.1** if any of the following occur:

1. The pressure differed from that to which patient was randomized.

2. If a device other than the Stryker Surgilav or Zimmer Pulsavac Plus with tips and settings for high and low pressure as per protocol was used.

3. If a bulb syringe was used.

4. The solution additive differed from that to which patient was randomized.

5. Solution additive other than saline or castile soap was used.

FLOW #103 Plate #110

Follow Up Number: ☐ 1 week post/op ☐ 6 months ☐ 2 weeks post/op ☐ 9 months ☐ 6 weeks ☐ 12 months ☐ 3 months ☐ 99 Early W/D

Patient Study ID Number ☐☐ ☐☐☐☐ Centre # Patient #

Patient Initials ☐☐ F L

FOLLOW UP SURGICAL REPORT FORM: RE-OPERATIONS (3 of 3) - FORM 11.6

13. Amount of irrigation solution used: ☐☐.☐ **Litres**

14. Was tourniquet used: ☐ Yes ☐ No

15. Cortical continuity following re-operation:

☐ 0% ☐ 25% ☐ 50% ☐ 75% ☐ 100%

16. Size of post-operative fracture gap: ☐ < 1 cm ☐ 1-5 cm ☐ > 5 cm

17. Was full closure of the wound obtained?

☐ Yes ☐ No ☐ N/A, previously closed

18. Were antibiotic beads or antibiotic osteobiologics used during the re-operation?

☐ No ☐ Yes → Please name the antibiotic(s): _____

↳ Specify the type: ☐ Cement ☐ Bio-absorbable ☐ Other: _____

19. Did any intraoperative adverse events occur during this patient's surgery?

☐ Yes → **Please complete an Adverse Event Form (12.1)**

☐ No

20. Was the patient rehospitalized?

☐ Yes → Date of hospital admission: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

☐ No Date of hospital discharge: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

☐ N/A - re-operation occurred during initial hospitalization

21. Are there other additional procedures planned for the included fracture/wound?

☐ Yes → Please specify: _____

☐ No

22. Is this re-operation considered an serious adverse event (SAE) (fatal, immediately life threatening, permanent disability, hospitalization (repeat or prolonged))?

☐ Yes → **Please complete an SAE Form 21.1** ☐ No

23. Does the attending physician believe that the re-operation is directly related to the FLOW study (i.e., type of solution or pressure used)?

☐ Not related ☐ Possibly related ☐ Probably related ☐ Definitely related ☐ Unclassifiable

FLOW #103 Plate #111

Follow Up Number: ☐ 1 week post/op ☐ 6 months ☐ 2 weeks post/op ☐ 9 months ☐ 6 weeks ☐ 12 months ☐ 3 months ☐ 99 Early W/D

Patient Study ID Number ☐☐ Centre # ☐☐☐☐ Patient #

Patient Initials ☐☐ F L

FOLLOW UP SURGICAL REPORT FORM: RE-OPERATIONS (1 of 3) - FORM 11.7

Please complete a separate form for each re-operation.

1. Date of re-operation or additional procedure: Day ☐☐ Month ☐☐ Year 20☐☐

2. Name of attending surgeon: _____ (Surname) _____ (Given name)

3. Was the re-operation planned at the time of the definitive treatment? ☐ Yes ☐ No ☐ Not Applicable (this is the definitive treatment)

4. Please specify type of re-operation(s) and/or additional procedure(s) on this specific date: (check **all** that apply)

- ☐ Fixation of fracture (specify) _____
- ☐ Irrigation and debridement ☐ Primary wound closure ☐ Removal of antibiotic beads or osteobiologics
- ☐ Fasciotomy ☐ Fasciotomy closure
- ☐ Wound flap (rotational or free) (specify) _____
- ☐ Skin graft (specify) _____
- ☐ Bone graft → specify location ☐ Cancellous ☐ Cortical (structural) ☐ Vascularized bone
- ☐ Implant exchange (specify) _____
- ☐ Removal of external fixation in OR ☐ Removal of external fixation in clinic
- ☐ Screw removal in OR ☐ Screw removal in clinic
- ☐ Other implant removal (specify) _____
- ☐ Amputation (specify) _____
- ☐ Other (specify) _____

5. Reason for re-operation: (Please check **all** that apply)

- ☐ Nonunion / Delayed union[1]
- ☐ Malunion[2]
- ☐ Infection (deep)*
- ☐ Infection (superficial)*
- ☐ Fracture gap
- ☐ Wound dehiscence*
- ☐ Definitive fixation
- ☐ Compartment syndrome
- ☐ Painful hardware / Patient discomfort
- ☐ Open wound
- ☐ Hardware failure (Specify)_____
- ☐ Other (Specify) _____
- ☐ Wound necrosis*

[1] a general guideline is failure of progression of fracture healing for at least 2 or 3 **successive** months with pain at the fracture site to palpation

[2] healing with an unsatisfactory alignment of the fracture, according to the attending surgeon's discretion

FLOW #103 Plate #112

Follow Up Number: ☐ 1 week post/op ☐ 6 months ☐ 2 weeks post/op ☐ 9 months ☐ 6 weeks ☐ 12 months ☐ 3 months ☐ 99 Early W/D

Patient Study ID Number ☐☐ Centre # ☐☐☐☐ Patient # Patient Initials ☐☐ F L

FOLLOW UP SURGICAL REPORT FORM: RE-OPERATIONS (2 of 3) - FORM 11.8

6. Was irrigation and debridement done?

☐ Yes → complete Questions 7-13 ☐ No → skip to Question 14 on the next page

7. How much skin was debrided? (check **one**)

☐ None
☐ Small amount (<1 cm^2)
☐ Moderate amount (1-5 cm^2)
☐ Large amount (>5 cm^2)

8. How much muscle was debrided? (check **one**)

☐ None
☐ Small amount (<1 cm^3)
☐ Moderate amount (1-5 cm^3)
☐ Large amount (>5 cm^3)

9. How much fascial tissue was debrided? (check **one**)

☐ None
☐ Small amount (<1 cm^2)
☐ Moderate amount (1-5 cm^2)
☐ Large amount (>5 cm^2)

10. How much bone was debrided? (check **one**)

☐ None
☐ Small amount (<1 cm^3)
☐ Moderate amount (1-5 cm^3)
☐ Large amount (>5 cm^3)

11. Irrigation pressure and device used for debridement and open wound management:

☐ High[1] →
- ☐ Stryker Surgilav with multi-orifice tip - high pressure setting
- ☐ Zimmer Pulsavac Plus with shower tip - high pressure setting
- ☐ Other[2] - Please specify: Manufacturer _____
  Device Name _____
  PSI _____

☐ Low[1] →
- ☐ Stryker Surgilav with high flow trauma tip - low pressure setting
- ☐ Zimmer Pulsavac Plus with shower tip - low pressure setting
- ☐ Other[2] - Please specify: Manufacturer _____
  Device Name _____
  PSI _____

☐ Gravity flow[1]

☐ Bulb syringe[3]

12. Irrigation solution additive[4]:

☐ Saline
☐ Castile Soap
☐ Bacitracin[5]
☐ Other[5] (***please specify)*** _____

Please complete a **Protocol Deviation Form 10.1** if any of the following occur:

1. The pressure differed from that to which patient was randomized.

2. If a device other than the Stryker Surgilav or Zimmer Pulsavac Plus with tips and settings for high and low pressure as per protocol was used.

3. If a bulb syringe was used.

4. The solution additive differed from that to which patient was randomized.

5. Solution additive other than saline or castile soap was used.

FLOW #103 Plate #113

Follow Up Number: ☐ 1 week post/op ☐ 6 months ☐ 2 weeks post/op ☐ 9 months ☐ 6 weeks ☐ 12 months ☐ 3 months ☐ 99 Early W/D

Patient Study ID Number ☐☐ ☐☐☐☐ Centre # Patient #

Patient Initials ☐☐ F L

FOLLOW UP SURGICAL REPORT FORM: RE-OPERATIONS (3 of 3) - FORM 11.9

13. Amount of irrigation solution used: ☐☐.☐ **Litres**

14. Was tourniquet used: ☐ Yes ☐ No

15. Cortical continuity following re-operation:

☐ 0% ☐ 25% ☐ 50% ☐ 75% ☐ 100%

16. Size of post-operative fracture gap: ☐ < 1 cm ☐ 1-5 cm ☐ > 5 cm

17. Was full closure of the wound obtained?

☐ Yes ☐ No ☐ N/A, previously closed

18. Were antibiotic beads or antibiotic osteobiologics used during the re-operation?

☐ No ☐ Yes → Please name the antibiotic(s): _____

↳ Specify the type: ☐ Cement ☐ Bio-absorbable ☐ Other: _____

19. Did any intraoperative adverse events occur during this patient's surgery?

☐ Yes → **Please complete an Adverse Event Form (12.1)**

☐ No

20. Was the patient rehospitalized?

☐ Yes → Date of hospital admission: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

☐ No Date of hospital discharge: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

☐ N/A - re-operation occurred during initial hospitalization

21. Are there other additional procedures planned for the included fracture/wound?

☐ Yes → Please specify: _____

☐ No

22. Is this re-operation considered an serious adverse event (SAE) (fatal, immediately life threatening, permanent disability, hospitalization (repeat or prolonged))?

☐ Yes → **Please complete an SAE Form 21.1** ☐ No

23. Does the attending physician believe that the re-operation is directly related to the FLOW study (i.e., type of solution or pressure used)?

☐ Not related ☐ Possibly related ☐ Probably related ☐ Definitely related ☐ Unclassifiable

Follow Up Number:
☐ 1 week post/op ☐ 6 months
☐ 2 weeks post/op ☐ 9 months
☐ 6 weeks ☐ 12 months
☐ 3 months ☐ 99 Early W/D

FLOW #103 **Plate #114**

Patient Study ID Number ☐☐ ☐☐☐☐ **Patient Initials** ☐☐
Centre # Patient # F L

FOLLOW UP SURGICAL REPORT FORM: RE-OPERATIONS (1 of 3) - FORM 11.10

Please complete a separate form for each re-operation.

1. Date of re-operation or additional procedure: Day ☐☐ Month ☐☐ Year 20☐☐

2. Name of attending surgeon: _____ (Surname) _____ (Given name)

3. Was the re-operation planned at the time of the definitive treatment? ☐ Yes ☐ No ☐ Not Applicable (this is the definitive treatment)

4. Please specify type of re-operation(s) and/or additional procedure(s) on this specific date: (check **all** that apply)
   - ☐ Fixation of fracture (specify) _____
   - ☐ Irrigation and debridement ☐ Primary wound closure ☐ Removal of antibiotic beads or osteobiologics
   - ☐ Fasciotomy ☐ Fasciotomy closure
   - ☐ Wound flap (rotational or free) (specify) _____
   - ☐ Skin graft (specify) _____
   - ☐ Bone graft (specify location →) ☐ Cancellous ☐ Cortical (structural) ☐ Vascularized bone
   - ☐ Implant exchange (specify) _____
   - ☐ Removal of external fixation in OR ☐ Removal of external fixation in clinic
   - ☐ Screw removal in OR ☐ Screw removal in clinic
   - ☐ Other implant removal (specify) _____
   - ☐ Amputation (specify) _____
   - ☐ Other (specify) _____

5. Reason for re-operation: (Please check **all** that apply)
   - ☐ Nonunion / Delayed union[1]
   - ☐ Malunion[2]
   - ☐ Infection (deep)*
   - ☐ Infection (superficial)*
   - ☐ Fracture gap
   - ☐ Wound dehiscence*
   - ☐ Definitive fixation
   - ☐ Compartment syndrome
   - ☐ Painful hardware / Patient discomfort
   - ☐ Open wound
   - ☐ Hardware failure (Specify) _____
   - ☐ Other (Specify) _____
   - ☐ Wound necrosis*

[1] a general guideline is failure of progression of fracture healing for at least 2 or 3 **successive** months with pain at the fracture site to palpation

[2] healing with an unsatisfactory alignment of the fracture, according to the attending surgeon's discretion

FLOW #103 **Plate #115**

Patient Study ID Number Centre # Patient #

Patient Initials F L

Follow Up Number:
- ☐ 1 week post/op
- ☐ 2 weeks post/op
- ☐ 6 weeks
- ☐ 3 months
- ☐ 6 months
- ☐ 9 months
- ☐ 12 months
- ☐ 99 Early W/D

FOLLOW UP SURGICAL REPORT FORM: RE-OPERATIONS (2 of 3) - FORM 11.11

6. Was irrigation and debridement done?

☐ Yes → complete Questions 7-13 ☐ No → skip to Question 14 on the next page

7. How much skin was debrided? (check **one**)
- ☐ None
- ☐ Small amount (<1 cm^2)
- ☐ Moderate amount (1-5 cm^2)
- ☐ Large amount (>5 cm^2)

8. How much muscle was debrided? (check **one**)
- ☐ None
- ☐ Small amount (<1 cm^3)
- ☐ Moderate amount (1-5 cm^3)
- ☐ Large amount (>5 cm^3)

9. How much fascial tissue was debrided? (check **one**)
- ☐ None
- ☐ Small amount (<1 cm^2)
- ☐ Moderate amount (1-5 cm^2)
- ☐ Large amount (>5 cm^2)

10. How much bone was debrided? (check **one**)
- ☐ None
- ☐ Small amount (<1 cm^3)
- ☐ Moderate amount (1-5 cm^3)
- ☐ Large amount (>5 cm^3)

11. Irrigation pressure and device used for debridement and open wound management:

☐ High[1] →
- ☐ Stryker Surgilav with multi-orifice tip - high pressure setting
- ☐ Zimmer Pulsavac Plus with shower tip - high pressure setting
- ☐ Other[2] - Please specify: Manufacturer _____
  Device Name _____
  PSI _____

☐ Low[1] →
- ☐ Stryker Surgilav with high flow trauma tip - low pressure setting
- ☐ Zimmer Pulsavac Plus with shower tip - low pressure setting
- ☐ Other[2] - Please specify: Manufacturer _____
  Device Name _____
  PSI _____

☐ Gravity flow[1]

☐ Bulb syringe[3]

12. Irrigation solution additive[4]:
- ☐ Saline
- ☐ Castile Soap
- ☐ Bacitracin[5]
- ☐ Other[5] (***please specify)*** _____

Please complete a **Protocol Deviation Form 10.1** if any of the following occur:

1. The pressure differed from that to which patient was randomized.

2. If a device other than the Stryker Surgilav or Zimmer Pulsavac Plus with tips and settings for high and low pressure as per protocol was used.

3. If a bulb syringe was used.

4. The solution additive differed from that to which patient was randomized.

5. Solution additive other than saline or castile soap was used.

FLOW #103 Plate #116

Follow Up Number: ☐ 1 week post/op ☐ 6 months ☐ 2 weeks post/op ☐ 9 months ☐ 6 weeks ☐ 12 months ☐ 3 months ☐ 99 Early W/D

Patient Study ID Number ☐☐ ☐☐☐☐ Centre # Patient #

Patient Initials ☐☐ F L

FOLLOW UP SURGICAL REPORT FORM: RE-OPERATIONS (3 of 3) - FORM 11.12

13. Amount of irrigation solution used: ☐☐.☐ **Litres**

14. Was tourniquet used: ☐ Yes ☐ No

15. Cortical continuity following re-operation:

☐ 0% ☐ 25% ☐ 50% ☐ 75% ☐ 100%

16. Size of post-operative fracture gap: ☐ < 1 cm ☐ 1-5 cm ☐ > 5 cm

17. Was full closure of the wound obtained?

☐ Yes ☐ No ☐ N/A, previously closed

18. Were antibiotic beads or antibiotic osteobiologics used during the re-operation?

☐ No ☐ Yes → Please name the antibiotic(s): _____

↳ Specify the type: ☐ Cement ☐ Bio-absorbable ☐ Other: _____

19. Did any intraoperative adverse events occur during this patient's surgery?

☐ Yes → **Please complete an Adverse Event Form (12.1)**

☐ No

20. Was the patient rehospitalized?

☐ Yes → Date of hospital admission: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

☐ No Date of hospital discharge: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

☐ N/A - re-operation occurred during initial hospitalization

21. Are there other additional procedures planned for the included fracture/wound?

☐ Yes → Please specify: _____

☐ No

22. Is this re-operation considered an serious adverse event (SAE) (fatal, immediately life threatening, permanent disability, hospitalization (repeat or prolonged))?

☐ Yes → **Please complete an SAE Form 21.1** ☐ No

23. Does the attending physician believe that the re-operation is directly related to the FLOW study (i.e., type of solution or pressure used)?

☐ Not related ☐ Possibly related ☐ Probably related ☐ Definitely related ☐ Unclassifiable

Follow Up Number:	☐ 1 week post/op	☐ 6 months	
	☐ 2 weeks post/op	☐ 9 months	
	☐ 6 weeks	☐ 12 months	
	☐ 3 months	☐ 99 Early W/D	

FLOW #103 **Plate #117**

Patient Study ID Number ☐☐ ☐☐☐☐ **Patient Initials** ☐☐

Centre # Patient # F L

FOLLOW UP SURGICAL REPORT FORM: RE-OPERATIONS (1 of 3) - FORM 11.13

Please complete a separate form for each re-operation.

1. Date of re-operation or additional procedure: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

2. Name of attending surgeon: _____ (Surname) _____ (Given name)

3. Was the re-operation planned at the time of the definitive treatment? ☐ Yes ☐ No ☐ Not Applicable (this is the definitive treatment)

4. Please specify type of re-operation(s) and/or additional procedure(s) on this specific date: (check **all** that apply)

- ☐ Fixation of fracture (specify) _____
- ☐ Irrigation and debridement ☐ Primary wound closure ☐ Removal of antibiotic beads or osteobiologics
- ☐ Fasciotomy ☐ Fasciotomy closure
- ☐ Wound flap (rotational or free) (specify) _____
- ☐ Skin graft (specify) _____
- ☐ Bone graft → specify location ☐ Cancellous ☐ Cortical (structural) ☐ Vascularized bone
- ☐ Implant exchange (specify) _____
- ☐ Removal of external fixation in OR ☐ Removal of external fixation in clinic
- ☐ Screw removal in OR ☐ Screw removal in clinic
- ☐ Other implant removal (specify) _____
- ☐ Amputation (specify) _____
- ☐ Other (specify) _____

5. Reason for re-operation: (Please check **all** that apply)

- ☐ Nonunion / Delayed union[1]
- ☐ Malunion[2]
- ☐ Infection (deep)*
- ☐ Infection (superficial)*
- ☐ Fracture gap
- ☐ Wound dehiscence*
- ☐ Definitive fixation
- ☐ Compartment syndrome
- ☐ Painful hardware / Patient discomfort
- ☐ Open wound
- ☐ Hardware failure (Specify)_____
- ☐ Other (Specify) _____
- ☐ Wound necrosis*

[1] a general guideline is failure of progression of fracture healing for at least 2 or 3 **successive** months with pain at the fracture site to palpation

[2] healing with an unsatisfactory alignment of the fracture, according to the attending surgeon's discretion

FLOW #103 Plate #118

Patient Study ID Number Centre # Patient # Patient Initials F L

Follow Up Number: ☐ 1 week post/op ☐ 2 weeks post/op ☐ 6 weeks ☐ 3 months ☐ 6 months ☐ 9 months ☐ 12 months ☐ 99 Early W/D

FOLLOW UP SURGICAL REPORT FORM: RE-OPERATIONS (2 of 3) - FORM 11.14

6. Was irrigation and debridement done?

☐ Yes → complete Questions 7-13 ☐ No → skip to Question 14 on the next page

7. How much skin was debrided? (check **one**)

☐ None
☐ Small amount (<1 cm^2)
☐ Moderate amount (1-5 cm^2)
☐ Large amount (>5 cm^2)

8. How much muscle was debrided? (check **one**)

☐ None
☐ Small amount (<1 cm^3)
☐ Moderate amount (1-5 cm^3)
☐ Large amount (>5 cm^3)

9. How much fascial tissue was debrided? (check **one**)

☐ None
☐ Small amount (<1 cm^2)
☐ Moderate amount (1-5 cm^2)
☐ Large amount (>5 cm^2)

10. How much bone was debrided? (check **one**)

☐ None
☐ Small amount (<1 cm^3)
☐ Moderate amount (1-5 cm^3)
☐ Large amount (>5 cm^3)

11. Irrigation pressure and device used for debridement and open wound management:

☐ High[1] →
- ☐ Stryker Surgilav with multi-orifice tip - high pressure setting
- ☐ Zimmer Pulsavac Plus with shower tip - high pressure setting
- ☐ Other[2] - Please specify: Manufacturer _____
  Device Name _____
  PSI _____

☐ Low[1] →
- ☐ Stryker Surgilav with high flow trauma tip - low pressure setting
- ☐ Zimmer Pulsavac Plus with shower tip - low pressure setting
- ☐ Other[2] - Please specify: Manufacturer _____
  Device Name _____
  PSI _____

☐ Gravity flow[1]

☐ Bulb syringe[3]

12. Irrigation solution additive[4]:

☐ Saline
☐ Castile Soap
☐ Bacitracin[5]
☐ Other[5] (***please specify)*** _____

Please complete a **Protocol Deviation Form 10.1** if any of the following occur:

1. The pressure differed from that to which patient was randomized.

2. If a device other than the Stryker Surgilav or Zimmer Pulsavac Plus with tips and settings for high and low pressure as per protocol was used.

3. If a bulb syringe was used.

4. The solution additive differed from that to which patient was randomized.

5. Solution additive other than saline or castile soap was used.

FLOW #103 Plate #119

Follow Up Number: ☐ 1 week post/op ☐ 6 months ☐ 2 weeks post/op ☐ 9 months ☐ 6 weeks ☐ 12 months ☐ 3 months ☐ 99 Early W/D

Patient Study ID Number ☐☐ ☐☐☐☐ Centre # Patient #

Patient Initials ☐☐ F L

FOLLOW UP SURGICAL REPORT FORM: RE-OPERATIONS (3 of 3) - FORM 11.15

13. Amount of irrigation solution used: ☐☐.☐ **Litres**

14. Was tourniquet used: ☐ Yes ☐ No

15. Cortical continuity following re-operation:

☐ 0% ☐ 25% ☐ 50% ☐ 75% ☐ 100%

16. Size of post-operative fracture gap: ☐ < 1 cm ☐ 1-5 cm ☐ > 5 cm

17. Was full closure of the wound obtained?

☐ Yes ☐ No ☐ N/A, previously closed

18. Were antibiotic beads or antibiotic osteobiologics used during the re-operation?

☐ No ☐ Yes → Please name the antibiotic(s): _____

↳ Specify the type: ☐ Cement ☐ Bio-absorbable ☐ Other: _____

19. Did any intraoperative adverse events occur during this patient's surgery?

☐ Yes → **Please complete an Adverse Event Form (12.1)**

☐ No

20. Was the patient rehospitalized?

☐ Yes → Date of hospital admission: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

☐ No Date of hospital discharge: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

☐ N/A - re-operation occurred during initial hospitalization

21. Are there other additional procedures planned for the included fracture/wound?

☐ Yes → Please specify: _____

☐ No

22. Is this re-operation considered an serious adverse event (SAE) (fatal, immediately life threatening, permanent disability, hospitalization (repeat or prolonged))?

☐ Yes → **Please complete an SAE Form 21.1** ☐ No

23. Does the attending physician believe that the re-operation is directly related to the FLOW study (i.e., type of solution or pressure used)?

☐ Not related ☐ Possibly related ☐ Probably related ☐ Definitely related ☐ Unclassifiable

FLOW #103 Plate #120

Follow Up Number: ☐ 1 week post/op ☐ 6 months ☐ 2 weeks post/op ☐ 9 months ☐ 6 weeks ☐ 12 months ☐ 3 months ☐ 99 Early W/D

Patient Study ID Number ☐☐ (Centre #) ☐☐☐☐ (Patient #) Patient Initials ☐☐ (F L)

FOLLOW UP SURGICAL REPORT FORM: RE-OPERATIONS (1 of 3) - FORM 11.16

Please complete a separate form for each re-operation.

1. Date of re-operation or additional procedure: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

2. Name of attending surgeon: _____ (Surname) _____ (Given name)

3. Was the re-operation planned at the time of the definitive treatment? ☐ Yes ☐ No ☐ Not Applicable (this is the definitive treatment)

4. Please specify type of re-operation(s) and/or additional procedure(s) on this specific date: (check **all** that apply)

- ☐ Fixation of fracture (specify) _____
- ☐ Irrigation and debridement ☐ Primary wound closure ☐ Removal of antibiotic beads or osteobiologics
- ☐ Fasciotomy ☐ Fasciotomy closure
- ☐ Wound flap (rotational or free) (specify) _____
- ☐ Skin graft (specify) _____
- ☐ Bone graft → specify location ☐ Cancellous ☐ Cortical (structural) ☐ Vascularized bone
- ☐ Implant exchange (specify) _____
- ☐ Removal of external fixation in OR ☐ Removal of external fixation in clinic
- ☐ Screw removal in OR ☐ Screw removal in clinic
- ☐ Other implant removal (specify) _____
- ☐ Amputation (specify) _____
- ☐ Other (specify) _____

5. Reason for re-operation: (Please check **all** that apply)

- ☐ Nonunion / Delayed union[1]
- ☐ Malunion[2]
- ☐ Infection (deep)*
- ☐ Infection (superficial)*
- ☐ Fracture gap
- ☐ Wound dehiscence*
- ☐ Definitive fixation
- ☐ Compartment syndrome
- ☐ Painful hardware / Patient discomfort
- ☐ Open wound
- ☐ Hardware failure (Specify)_____
- ☐ Other (Specify) _____
- ☐ Wound necrosis*

[1] a general guideline is failure of progression of fracture healing for at least 2 or 3 **successive** months with pain at the fracture site to palpation

[2] healing with an unsatisfactory alignment of the fracture, according to the attending surgeon's discretion

FLOW #103 **Plate #121**

Patient Study ID Number Centre # Patient #

Patient Initials F L

Follow Up Number:
- ☐ 1 week post/op
- ☐ 2 weeks post/op
- ☐ 6 weeks
- ☐ 3 months
- ☐ 6 months
- ☐ 9 months
- ☐ 12 months
- ☐ 99 Early W/D

FOLLOW UP SURGICAL REPORT FORM: RE-OPERATIONS (2 of 3) - FORM 11.17

6. Was irrigation and debridement done?

☐ Yes → complete Questions 7-13 ☐ No → skip to Question 14 on the next page

7. How much skin was debrided? (check **one**)
- ☐ None
- ☐ Small amount (<1 cm^2)
- ☐ Moderate amount (1-5 cm^2)
- ☐ Large amount (>5 cm^2)

8. How much muscle was debrided? (check **one**)
- ☐ None
- ☐ Small amount (<1 cm^3)
- ☐ Moderate amount (1-5 cm^3)
- ☐ Large amount (>5 cm^3)

9. How much fascial tissue was debrided? (check **one**)
- ☐ None
- ☐ Small amount (<1 cm^2)
- ☐ Moderate amount (1-5 cm^2)
- ☐ Large amount (>5 cm^2)

10. How much bone was debrided? (check **one**)
- ☐ None
- ☐ Small amount (<1 cm^3)
- ☐ Moderate amount (1-5 cm^3)
- ☐ Large amount (>5 cm^3)

11. Irrigation pressure and device used for debridement and open wound management:

☐ High[1] →
- ☐ Stryker Surgilav with multi-orifice tip - high pressure setting
- ☐ Zimmer Pulsavac Plus with shower tip - high pressure setting
- ☐ Other[2] - Please specify: Manufacturer _____
  Device Name _____
  PSI _____

☐ Low[1] →
- ☐ Stryker Surgilav with high flow trauma tip - low pressure setting
- ☐ Zimmer Pulsavac Plus with shower tip - low pressure setting
- ☐ Other[2] - Please specify: Manufacturer _____
  Device Name _____
  PSI _____

☐ Gravity flow[1]

☐ Bulb syringe[3]

12. Irrigation solution additive[4]:
- ☐ Saline
- ☐ Castile Soap
- ☐ Bacitracin[5]
- ☐ Other[5] (***please specify)*** _____

Please complete a **Protocol Deviation Form 10.1** if any of the following occur:

1. The pressure differed from that to which patient was randomized.

2. If a device other than the Stryker Surgilav or Zimmer Pulsavac Plus with tips and settings for high and low pressure as per protocol was used.

3. If a bulb syringe was used.

4. The solution additive differed from that to which patient was randomized.

5. Solution additive other than saline or castile soap was used.

FLOW #103 Plate #122

Follow Up Number: ☐ 1 week post/op ☐ 6 months ☐ 2 weeks post/op ☐ 9 months ☐ 6 weeks ☐ 12 months ☐ 3 months ☐ 99 Early W/D

Patient Study ID Number ☐☐ ☐☐☐☐ Centre # Patient #

Patient Initials ☐☐ F L

FOLLOW UP SURGICAL REPORT FORM: RE-OPERATIONS (3 of 3) - FORM 11.18

13. Amount of irrigation solution used: ☐☐.☐ **Litres**

14. Was tourniquet used: ☐ Yes ☐ No

15. Cortical continuity following re-operation:

☐ 0% ☐ 25% ☐ 50% ☐ 75% ☐ 100%

16. Size of post-operative fracture gap: ☐ < 1 cm ☐ 1-5 cm ☐ > 5 cm

17. Was full closure of the wound obtained?

☐ Yes ☐ No ☐ N/A, previously closed

18. Were antibiotic beads or antibiotic osteobiologics used during the re-operation?

☐ No ☐ Yes → Please name the antibiotic(s): _____

↳ Specify the type: ☐ Cement ☐ Bio-absorbable ☐ Other: _____

19. Did any intraoperative adverse events occur during this patient's surgery?

☐ Yes → **Please complete an Adverse Event Form (12.1)**

☐ No

20. Was the patient rehospitalized?

☐ Yes → Date of hospital admission: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

☐ No Date of hospital discharge: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

☐ N/A - re-operation occurred during initial hospitalization

21. Are there other additional procedures planned for the included fracture/wound?

☐ Yes → Please specify: _____

☐ No

22. Is this re-operation considered an serious adverse event (SAE) (fatal, immediately life threatening, permanent disability, hospitalization (repeat or prolonged))?

☐ Yes → **Please complete an SAE Form 21.1** ☐ No

23. Does the attending physician believe that the re-operation is directly related to the FLOW study (i.e., type of solution or pressure used)?

☐ Not related ☐ Possibly related ☐ Probably related ☐ Definitely related ☐ Unclassifiable

FLOW #103 Plate #123

Follow Up Number: ☐ 1 week post/op ☐ 6 months ☐ 2 weeks post/op ☐ 9 months ☐ 6 weeks ☐ 12 months ☐ 3 months ☐ 99 Early W/D

Patient Study ID Number ☐☐ (Centre #) ☐☐☐☐ (Patient #) Patient Initials ☐☐ (F L)

FOLLOW UP SURGICAL REPORT FORM: RE-OPERATIONS (1 of 3) - FORM 11.19

Please complete a separate form for each re-operation.

1. Date of re-operation or additional procedure: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

2. Name of attending surgeon: _____ (Surname) _____ (Given name)

3. Was the re-operation planned at the time of the definitive treatment? ☐ Yes ☐ No ☐ Not Applicable (this is the definitive treatment)

4. Please specify type of re-operation(s) and/or additional procedure(s) on this specific date: (check **all** that apply)

- ☐ Fixation of fracture (specify) _____
- ☐ Irrigation and debridement ☐ Primary wound closure ☐ Removal of antibiotic beads or osteobiologics
- ☐ Fasciotomy ☐ Fasciotomy closure
- ☐ Wound flap (rotational or free) (specify) _____
- ☐ Skin graft (specify) _____
- ☐ Bone graft (specify location →) ☐ Cancellous ☐ Cortical (structural) ☐ Vascularized bone
- ☐ Implant exchange (specify) _____
- ☐ Removal of external fixation in OR ☐ Removal of external fixation in clinic
- ☐ Screw removal in OR ☐ Screw removal in clinic
- ☐ Other implant removal (specify) _____
- ☐ Amputation (specify) _____
- ☐ Other (specify) _____

5. Reason for re-operation: (Please check **all** that apply)

- ☐ Nonunion / Delayed union[1]
- ☐ Malunion[2]
- ☐ Infection (deep)*
- ☐ Infection (superficial)*
- ☐ Fracture gap
- ☐ Wound dehiscence*
- ☐ Definitive fixation
- ☐ Compartment syndrome
- ☐ Painful hardware / Patient discomfort
- ☐ Open wound
- ☐ Hardware failure (Specify)_____
- ☐ Other (Specify) _____
- ☐ Wound necrosis*

[1] a general guideline is failure of progression of fracture healing for at least 2 or 3 **successive** months with pain at the fracture site to palpation

[2] healing with an unsatisfactory alignment of the fracture, according to the attending surgeon's discretion

Plate #124

FLOW #103

Patient Study ID Number Centre # Patient #

Patient Initials F L

Follow Up Number:
- ☐ 1 week post/op
- ☐ 2 weeks post/op
- ☐ 6 weeks
- ☐ 3 months
- ☐ 6 months
- ☐ 9 months
- ☐ 12 months
- ☐ 99 Early W/D

FOLLOW UP SURGICAL REPORT FORM: RE-OPERATIONS (2 of 3) - FORM 11.20

6. Was irrigation and debridement done?

☐ Yes → complete Questions 7-13 ☐ No → skip to Question 14 on the next page

7. How much skin was debrided? (check **one**)
- ☐ None
- ☐ Small amount (<1 cm^2)
- ☐ Moderate amount (1-5 cm^2)
- ☐ Large amount (>5 cm^2)

8. How much muscle was debrided? (check **one**)
- ☐ None
- ☐ Small amount (<1 cm^3)
- ☐ Moderate amount (1-5 cm^3)
- ☐ Large amount (>5 cm^3)

9. How much fascial tissue was debrided? (check **one**)
- ☐ None
- ☐ Small amount (<1 cm^2)
- ☐ Moderate amount (1-5 cm^2)
- ☐ Large amount (>5 cm^2)

10. How much bone was debrided? (check **one**)
- ☐ None
- ☐ Small amount (<1 cm^3)
- ☐ Moderate amount (1-5 cm^3)
- ☐ Large amount (>5 cm^3)

11. Irrigation pressure and device used for debridement and open wound management:

☐ High[1] →
- ☐ Stryker Surgilav with multi-orifice tip - high pressure setting
- ☐ Zimmer Pulsavac Plus with shower tip - high pressure setting
- ☐ Other[2] - Please specify: Manufacturer _____
  Device Name _____
  PSI _____

☐ Low[1] →
- ☐ Stryker Surgilav with high flow trauma tip - low pressure setting
- ☐ Zimmer Pulsavac Plus with shower tip - low pressure setting
- ☐ Other[2] - Please specify: Manufacturer _____
  Device Name _____
  PSI _____

☐ Gravity flow[1]

☐ Bulb syringe[3]

12. Irrigation solution additive[4]:
- ☐ Saline
- ☐ Castile Soap
- ☐ Bacitracin[5]
- ☐ Other[5] (***please specify)*** _____

Please complete a **Protocol Deviation Form 10.1** if any of the following occur:

1. The pressure differed from that to which patient was randomized.

2. If a device other than the Stryker Surgilav or Zimmer Pulsavac Plus with tips and settings for high and low pressure as per protocol was used.

3. If a bulb syringe was used.

4. The solution additive differed from that to which patient was randomized.

5. Solution additive other than saline or castile soap was used.

FLOW #103 Plate #125

Follow Up Number: ☐ 1 week post/op ☐ 2 weeks post/op ☐ 6 weeks ☐ 3 months ☐ 6 months ☐ 9 months ☐ 12 months ☐ 99 Early W/D

Patient Study ID Number ☐☐ (Centre #) ☐☐☐☐ (Patient #) Patient Initials ☐☐ (F L)

FOLLOW UP SURGICAL REPORT FORM: RE-OPERATIONS (3 of 3) - FORM 11.21

13. Amount of irrigation solution used: ☐☐.☐ **Litres**

14. Was tourniquet used: ☐ Yes ☐ No

15. Cortical continuity following re-operation:

☐ 0% ☐ 25% ☐ 50% ☐ 75% ☐ 100%

16. Size of post-operative fracture gap: ☐ < 1 cm ☐ 1-5 cm ☐ > 5 cm

17. Was full closure of the wound obtained?

☐ Yes ☐ No ☐ N/A, previously closed

18. Were antibiotic beads or antibiotic osteobiologics used during the re-operation?

☐ No ☐ Yes → Please name the antibiotic(s): _____

→ Specify the type: ☐ Cement ☐ Bio-absorbable ☐ Other: _____

19. Did any intraoperative adverse events occur during this patient's surgery?

☐ Yes → **Please complete an Adverse Event Form (12.1)**

☐ No

20. Was the patient rehospitalized?

☐ Yes → Date of hospital admission: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

☐ No Date of hospital discharge: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

☐ N/A - re-operation occurred during initial hospitalization

21. Are there other additional procedures planned for the included fracture/wound?

☐ Yes → Please specify: _____

☐ No

22. Is this re-operation considered an serious adverse event (SAE) (fatal, immediately life threatening, permanent disability, hospitalization (repeat or prolonged))?

☐ Yes → **Please complete an SAE Form 21.1** ☐ No

23. Does the attending physician believe that the re-operation is directly related to the FLOW study (i.e., type of solution or pressure used)?

☐ Not related ☐ Possibly related ☐ Probably related ☐ Definitely related ☐ Unclassifiable

FLOW #103 **Plate #150**

Patient Study ID Number Centre # Patient # **Patient Initials** F L

Follow Up Number:
- ☐ Surgery
- ☐ 1 week post/op
- ☐ 2 weeks post/op
- ☐ 6 weeks
- ☐ 3 months
- ☐ 6 months
- ☐ 9 months
- ☐ 12 months
- ☐ 99 Early W/D

ADVERSE EVENT FORM (1 of 1) - FORM 12.1

Please record all re-operations on Form 11.1-11.3. Even though re-ops are adverse events, you do NOT need to document them twice for this study. Please record all other adverse events on this form.

1. Date the adverse event was diagnosed: Day ☐☐ Month ☐☐ Year 20☐☐

2. Please specify the adverse event (check only one). If there are multiple adverse events, please complete a separate form for each adverse event.
   - ☐ Death → **Please complete an Early Withdrawal Form 14.1-14.3**
     → Cause: _____
   - ☐ Acute respiratory distress syndrome
   - ☐ Deep vein thrombosis
   - ☐ Nonunion
   - ☐ Delayed union
   - ☐ Sepsis
   - ☐ Hardware failure, specify location(s): _____
   - ☐ Pulmonary embolism
   - ☐ Operative adverse event, specify: _____
   - ☐ Pneumonia
   - ☐ Other: _____

3. Has the patient been rehospitalized for this adverse event?
   - ☐ Yes → Date of rehospitalization: Day ☐☐ Month ☐☐ Year 20☐☐
   - ☐ No — Date of hospital discharge: Day ☐☐ Month ☐☐ Year 20☐☐
   - ☐ N/A - adverse event occurred during initial hospitalization

   Reason for rehospitalization: _____

4. Is this adverse event considered either unexpected or a serious adverse event (fatal, immediate life threatening, permanent disability, hospitalization (repeat or prolonged))?
   - ☐ Yes → **Please complete an SAE Form 21.1**
   - ☐ No

5. Does the attending physician believe that the adverse event is directly related to the FLOW study (i.e., type of solution or pressure used)?
   - ☐ Not related
   - ☐ Possibly related
   - ☐ Probably related
   - ☐ Definitely related
   - ☐ Unclassifiable

6. Outcome of adverse event:
   - ☐ Resolved → **Please refax form when resolved.** → Date resolved/Date resolved with subsequent impairment: Day ☐☐ Month ☐☐ Year 20☐☐
   - ☐ Resolved, with subsequent impairment → **Degree of impairment:** ☐ Mild ☐ Moderate ☐ Severe
   - ☐ Ongoing → **Please update form when resolved.**
   - ☐ Fatal → **Please complete an Early Withdrawal Form 14.1-14.3.**

7. Please provide any additional information about the adverse event below:

_____

☐ Indicate here if you are reporting another adverse event. Please complete form 12.2.

Follow Up Number:
- ☐ Surgery
- ☐ 1 week post/op
- ☐ 2 weeks post/op
- ☐ 6 weeks
- ☐ 3 months
- ☐ 6 months
- ☐ 9 months
- ☐ 12 months
- ☐ 99 Early W/D

FLOW #103 **Plate #151**

Patient Study ID Number ☐☐ ☐☐☐☐ (Centre # / Patient #)

Patient Initials ☐☐ (F L)

ADVERSE EVENT FORM (1 of 1) - FORM 12.2

Please record all re-operations on Form 11.1-11.3. Even though re-ops are adverse events, you do NOT need to document them twice for this study. Please record all other adverse events on this form.

1. Date the adverse event was diagnosed: Day ☐☐ Month ☐☐ Year 20☐☐

2. Please specify the adverse event (check only one). If there are multiple adverse events, please complete a separate form for each adverse event.
   - ☐ Death → **Please complete an Early Withdrawal Form 14.1-14.3**
     → Cause: _____
   - ☐ Acute respiratory distress syndrome
   - ☐ Deep vein thrombosis
   - ☐ Nonunion
   - ☐ Delayed union
   - ☐ Sepsis
   - ☐ Hardware failure, specify location(s): _____
   - ☐ Pulmonary embolism
   - ☐ Operative adverse event, specify: _____
   - ☐ Pneumonia
   - ☐ Other: _____

3. Has the patient been rehospitalized for this adverse event?
   - ☐ Yes → Date of rehospitalization: Day ☐☐ Month ☐☐ Year 20☐☐
   - ☐ No — Date of hospital discharge: Day ☐☐ Month ☐☐ Year 20☐☐
   - ☐ N/A - adverse event occurred during initial hospitalization

   Reason for rehospitalization: _____

4. Is this adverse event considered either unexpected or a serious adverse event (fatal, immediate life threatening, permanent disability, hospitalization (repeat or prolonged))?
   - ☐ Yes → **Please complete an SAE Form 21.1**
   - ☐ No

5. Does the attending physician believe that the adverse event is directly related to the FLOW study (i.e., type of solution or pressure used)?
   - ☐ Not related
   - ☐ Possibly related
   - ☐ Probably related
   - ☐ Definitely related
   - ☐ Unclassifiable

6. Outcome of adverse event:
   - ☐ Resolved → **Please refax form when resolved.** → Date resolved/Date resolved with subsequent impairment: Day ☐☐ Month ☐☐ Year 20☐☐
   - ☐ Resolved, with subsequent impairment → **Degree of impairment:** ☐ Mild ☐ Moderate ☐ Severe
   - ☐ Ongoing → **Please update form when resolved.**
   - ☐ Fatal → **Please complete an Early Withdrawal Form 14.1-14.3.**

7. Please provide any additional information about the adverse event below:

_____

☐ Indicate here if you are reporting another adverse event. Please complete form 12.3.

FLOW #103 **Plate #152**

Patient Study ID Number Centre # Patient #

Patient Initials F L

Follow Up Number:
- ☐ Surgery
- ☐ 1 week post/op
- ☐ 2 weeks post/op
- ☐ 6 weeks
- ☐ 3 months
- ☐ 6 months
- ☐ 9 months
- ☐ 12 months
- ☐ 99 Early W/D

ADVERSE EVENT FORM (1 of 1) - FORM 12.3

Please record all re-operations on Form 11.1-11.3. Even though re-ops are adverse events, you do NOT need to document them twice for this study. Please record all other adverse events on this form.

1. Date the adverse event was diagnosed: Day ☐☐ Month ☐☐ Year 20☐☐

2. Please specify the adverse event (check only one). If there are multiple adverse events, please complete a separate form for each adverse event.
   - ☐ Death → **Please complete an Early Withdrawal Form 14.1-14.3**
     → Cause: _____
   - ☐ Acute respiratory distress syndrome
   - ☐ Deep vein thrombosis
   - ☐ Nonunion
   - ☐ Delayed union
   - ☐ Sepsis
   - ☐ Hardware failure, specify location(s): _____
   - ☐ Pulmonary embolism
   - ☐ Operative adverse event, specify: _____
   - ☐ Pneumonia
   - ☐ Other: _____

3. Has the patient been rehospitalized for this adverse event?
   - ☐ Yes → Date of rehospitalization: Day ☐☐ Month ☐☐ Year 20☐☐
   - ☐ No — Date of hospital discharge: Day ☐☐ Month ☐☐ Year 20☐☐
   - ☐ N/A - adverse event occurred during initial hospitalization

   Reason for rehospitalization: _____

4. Is this adverse event considered either unexpected or a serious adverse event (fatal, immediate life threatening, permanent disability, hospitalization (repeat or prolonged))?
   - ☐ Yes → **Please complete an SAE Form 21.1**
   - ☐ No

5. Does the attending physician believe that the adverse event is directly related to the FLOW study (i.e., type of solution or pressure used)?
   - ☐ Not related
   - ☐ Possibly related
   - ☐ Probably related
   - ☐ Definitely related
   - ☐ Unclassifiable

6. Outcome of adverse event:
   - ☐ Resolved → **Please refax form when resolved.** → Date resolved/Date resolved with subsequent impairment: Day ☐☐ Month ☐☐ Year 20☐☐
   - ☐ Resolved, with subsequent impairment → **Degree of impairment:** ☐ Mild ☐ Moderate ☐ Severe
   - ☐ Ongoing → **Please update form when resolved.**
   - ☐ Fatal → **Please complete an Early Withdrawal Form 14.1-14.3.**

7. Please provide any additional information about the adverse event below:

_____

☐ Indicate here if you are reporting another adverse event. Please complete form 12.4.

Follow Up Number:
- ☐ Surgery
- ☐ 1 week post/op
- ☐ 2 weeks post/op
- ☐ 6 weeks
- ☐ 3 months
- ☐ 6 months
- ☐ 9 months
- ☐ 12 months
- ☐ 99 Early W/D

FLOW #103 **Plate #153**

Patient Study ID Number ☐☐ ☐☐☐☐ **Patient Initials** ☐☐

Centre # Patient # F L

ADVERSE EVENT FORM (1 of 1) - FORM 12.4

Please record all re-operations on Form 11.1-11.3. Even though re-ops are adverse events, you do NOT need to document them twice for this study. Please record all other adverse events on this form.

1. Date the adverse event was diagnosed: Day ☐☐ Month ☐☐ Year 20☐☐

2. Please specify the adverse event (check only one). If there are multiple adverse events, please complete a separate form for each adverse event.
   - ☐ Death → **Please complete an Early Withdrawal Form 14.1-14.3**
     → Cause: _____
   - ☐ Acute respiratory distress syndrome
   - ☐ Deep vein thrombosis
   - ☐ Nonunion
   - ☐ Delayed union
   - ☐ Sepsis
   - ☐ Hardware failure, specify location(s): _____
   - ☐ Pulmonary embolism
   - ☐ Operative adverse event, specify: _____
   - ☐ Pneumonia
   - ☐ Other: _____

3. Has the patient been rehospitalized for this adverse event?
   - ☐ Yes → Date of rehospitalization: Day ☐☐ Month ☐☐ Year 20☐☐
     Reason for rehospitalization: _____
   - ☐ No — Date of hospital discharge: Day ☐☐ Month ☐☐ Year 20☐☐
   - ☐ N/A - adverse event occurred during initial hospitalization

4. Is this adverse event considered either unexpected or a serious adverse event (fatal, immediate life threatening, permanent disability, hospitalization (repeat or prolonged))?
   - ☐ Yes → **Please complete an SAE Form 21.1**
   - ☐ No

5. Does the attending physician believe that the adverse event is directly related to the FLOW study (i.e., type of solution or pressure used)?
   - ☐ Not related
   - ☐ Possibly related
   - ☐ Probably related
   - ☐ Definitely related
   - ☐ Unclassifiable

6. Outcome of adverse event:
   - ☐ Resolved → **Please refax form when resolved.** → Date resolved/Date resolved with subsequent impairment: Day ☐☐ Month ☐☐ Year 20☐☐
   - ☐ Resolved, with subsequent impairment → **Degree of impairment:** ☐ Mild ☐ Moderate ☐ Severe
   - ☐ Ongoing → **Please update form when resolved.**
   - ☐ Fatal → **Please complete an Early Withdrawal Form 14.1-14.3.**

7. Please provide any additional information about the adverse event below:

_____

☐ Indicate here if you are reporting another adverse event. Please complete form 12.5

FLOW #103 **Plate #154**

Patient Study ID Number Centre # Patient #

Patient Initials F L

Follow Up Number:
- ☐ Surgery
- ☐ 1 week post/op
- ☐ 2 weeks post/op
- ☐ 6 weeks
- ☐ 3 months
- ☐ 6 months
- ☐ 9 months
- ☐ 12 months
- ☐ 99 Early W/D

ADVERSE EVENT FORM (1 of 1) - FORM 12.5

Please record all re-operations on Form 11.1-11.3. Even though re-ops are adverse events, you do NOT need to document them twice for this study. Please record all other adverse events on this form.

1. Date the adverse event was diagnosed: Day ☐☐ Month ☐☐ Year 20☐☐

2. Please specify the adverse event (check only one). If there are multiple adverse events, please complete a separate form for each adverse event.
   - ☐ Death → **Please complete an Early Withdrawal Form 14.1-14.3**
     → Cause: _____
   - ☐ Acute respiratory distress syndrome
   - ☐ Deep vein thrombosis
   - ☐ Nonunion
   - ☐ Delayed union
   - ☐ Sepsis
   - ☐ Hardware failure, specify location(s): _____
   - ☐ Pulmonary embolism
   - ☐ Operative adverse event, specify: _____
   - ☐ Pneumonia
   - ☐ Other: _____

3. Has the patient been rehospitalized for this adverse event?
   - ☐ Yes → Date of rehospitalization: Day ☐☐ Month ☐☐ Year 20☐☐
   - ☐ No — Date of hospital discharge: Day ☐☐ Month ☐☐ Year 20☐☐
   - ☐ N/A - adverse event occurred during initial hospitalization

   Reason for rehospitalization: _____

4. Is this adverse event considered either unexpected or a serious adverse event (fatal, immediate life threatening, permanent disability, hospitalization (repeat or prolonged))?
   - ☐ Yes → **Please complete an SAE Form 21.1**
   - ☐ No

5. Does the attending physician believe that the adverse event is directly related to the FLOW study (i.e., type of solution or pressure used)?
   - ☐ Not related
   - ☐ Possibly related
   - ☐ Probably related
   - ☐ Definitely related
   - ☐ Unclassifiable

6. Outcome of adverse event:
   - ☐ Resolved → **Please refax form when resolved.** → Date resolved/Date resolved with subsequent impairment: Day ☐☐ Month ☐☐ Year 20☐☐
   - ☐ Resolved, with subsequent impairment → **Degree of impairment:** ☐ Mild ☐ Moderate ☐ Severe
   - ☐ Ongoing → **Please update form when resolved.**
   - ☐ Fatal → **Please complete an Early Withdrawal Form 14.1-14.3.**

7. Please provide any additional information about the adverse event below:

_____

FLOW #103 **Plate #160**

Patient Study ID Number ☐☐ ☐☐☐☐ **Patient Initials** ☐☐

Centre # **Patient #** **F** **L**

Follow Up Number:

☐ 1 week post/op ☐ 3 months

☐ 2 weeks post/op ☐ 6 months

☐ 6 weeks ☐ 9 months

☐ 12 months

MISSED FOLLOW UP FORM - FORM 13.1

1. Date form completed: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

2. Reason for missed follow up visit:

_____

_____

_____

* Please note that if the 12 month follow up visit is missed, you must complete an **Early Withdrawal Form 14.1-14.3.**

FLOW #103 **Plate #161** **Visit #099**

Patient Study ID Number [ ][ ] [ ][ ][ ][ ] **Patient Initials** [ ][ ]

Centre # **Patient #** **F L**

EARLY WITHDRAWAL FORM (1 of 3) - FORM 14.1

1. Date of withdrawal from study: Day [ ][ ] Month [ ][ ] Year [2][0][ ][ ]

2. Reason for withdrawal from study:

- ☐ Death → please complete an **Adverse Event Form 12.1**
- ☐ Unable to locate → ***please note that a patient is considered "unable to locate" only after all resources have been exhausted in trying to find the patient***
- ☐ Patient withdrew consent → please provide explanation under comments section below
- ☐ Randomized patient without consent
- ☐ Randomized a patient we cannot legally follow
- ☐ Patient improperly randomized
- ☐ Other → please specify: _____

Comments:

_____

_____

_____

3. Has the patient been to clinic or been contacted since their last follow-up visit before early withdrawal?

- ☐ Yes → **Please answer the questions below by referring to patient's chart or notes.**
- ☐ No → **Form is complete.**

4. Date of last visit: Day [ ][ ] Month [ ][ ] Year [2][0][ ][ ]

5. Are there any changes in the patient's antibiotics?

- ☐ Yes → Update and refax the entire **Antibiotics Log 4.1**. **Remember to check the correct visit number.**
- ☐ No

6. Has the patient had any re-operations and/or additional procedures on the randomized fracture since the last follow up?

- ☐ Yes → record **<u>total</u>** number of re-operations and/or additional procedures reported at this follow up for **<u>the included fracture site</u>** (this includes I&Ds and soft tissue procedures) [ ][ ] → complete a separate **Follow Up Surgical Report Form 11.1-11.3 for each** additional procedure
- ☐ No

FLOW #103 **Plate #162** **Visit #099**

Patient Study ID Number ☐☐ ☐☐☐☐ **Patient Initials** ☐☐

Centre # Patient # F L

EARLY WITHDRAWAL FORM (2 of 3) - FORM 14.2

7. Has the patient had any infections* since the last follow up?

☐ Yes → record **total** number of infections reported at this follow up for **the included fracture site** ☐☐ → complete a separate **Infection Form 9.1-9.3** for each infection

☐ No

*Do ***not*** report the following conditions as SSI
[1] Stitch abscess (minimal inflammation & discharge confined to the points of suture penetration)
[2] Infected burn wound

8. Has the patient had any cultures taken since the last follow up?

☐ Yes → record **total** number of cultures taken at this follow up for **the included fracture site** ☐☐ → complete a **Cultures Form 20.1**

☐ No

9. Has the patient had any wound healing problems since the last follow up?

☐ Yes → record **total** number of wound healing problems reported at this follow up for **the included fracture site** ☐☐ → complete a separate **Wound Healing Problem Form 19.1 for each** problem

☐ No

10. Was full closure of the wound obtained?

☐ Yes

☐ Yes, reported at a previous visit

☐ No

11. If full closure has not been obtained, what was the problem?

☐ Skin coverage ☐ Leaving wound to granulate secondarily

☐ Operation scheduled ☐ Other: _____

12. Has the wound healed (defined as complete epidermal closure)?

☐ Yes → First date the surgeon declares the wound healed: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

☐ Yes, reported at a previous visit

☐ No

☐ Not Sure → Please specify why: _____

13. Please record the date of the patient's most recent x-ray: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

FLOW #103 **Plate #163** **Visit #099**

Patient Study ID Number ☐☐ ☐☐☐☐ **Patient Initials** ☐☐

Centre # **Patient #** **F L**

EARLY WITHDRAWAL FORM (3 of 3) - FORM 14.3

14. Has the fracture healed radiographically ?

☐ Yes → Date of the first radiograph that shows complete fracture healing: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

☐ Yes, reported at a previous visit

☐ No

☐ Not Sure → Please specify why: _____

15. Has the patient had any new **Adverse Events**, including a **nonunion / delayed union** (defined as failure of progression of fracture healing for at least 2 or 3 **successive** months with pain at the fracture site to palpation) since their last follow up visit?

☐ Yes → record **total** number of adverse events reported at this follow up including nonunion/delayed union ☐☐ → complete a separate **Adverse Event Form 12.1 for each** adverse event

☐ No

16. Has the patient been using stimulation modalities (i.e., ultrasound, electrical stimulation, etc.) on this wound to promote bone growth?

☐ Yes

☐ No

17. Has the patient received a wound vac?

☐ Yes, reported at a previous visit

☐ Yes → Date of application: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

☐ No Date of final removal: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

18. Are there any planned re-operations for the included fracture?

☐ Yes → Please specify _____

☐ No

FLOW #103 Plate #200

Follow Up Number: ☐ 1 week post/op ☐ 3 months ☐ 2 weeks post/op ☐ 6 months ☐ 6 weeks ☐ 9 months ☐ 12 months

Patient Study ID Number ☐☐ Centre # ☐☐☐☐ Patient #

Patient Initials ☐☐ F L

Date form completed ☐☐ DD ☐☐ MM 20☐☐ YYYY

SF-12v2 SELF-ADMINISTERED FORM (1 of 2) - FORM 15.1

Your Health and Well-Being

This survey asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities. *Thank you for completing this survey!*

For each of the following questions, please mark an X in the one box that best describes your answer.

1. In general, would you say your health is:

☐ **Excellent** ☐ **Very Good** ☐ **Good** ☐ **Fair** ☐ **Poor**

2. The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

	Yes, Limited A Lot	Yes, Limited A Little	No, Not Limited At All
a) Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	☐	☐	☐
b) Climbing several flights of stairs	☐	☐	☐

3. During the past week, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a) Accomplished less than you would like	☐	☐	☐	☐	☐
b) Were limited in the kind of work or other activities	☐	☐	☐	☐	☐

continued on next page...

Follow Up Number: ☐ 1 week post/op ☐ 2 weeks post/op ☐ 6 weeks ☐ 3 months ☐ 6 months ☐ 9 months ☐ 12 months

FLOW #103 **Plate #201**

Patient Study ID Number ☐☐ ☐☐☐☐ **Patient Initials** ☐☐

Centre # **Patient #** **F L**

SF-12v2 SELF-ADMINISTERED FORM (2 of 2) - FORM 15.2

4. During the past week, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a) Accomplished less than you would like	☐	☐	☐	☐	☐
b) Did work or other activities less carefully than usual	☐	☐	☐	☐	☐

5. During the past week, how much did pain interfere with your normal work (including both work outside the home and housework)?

☐ **Not at all** ☐ **A little bit** ☐ **Moderately** ☐ **Quite a bit** ☐ **Extremely**

6. These questions are about how you feel and how things have been with you during the past week. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past week...

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a) Have you felt calm and peaceful?	☐	☐	☐	☐	☐
b) Did you have a lot of energy?	☐	☐	☐	☐	☐
c) Have you felt downhearted and depressed?	☐	☐	☐	☐	☐

7. During the past week, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting friends, relatives, etc.)?

☐ **All of the time** ☐ **Most of the time** ☐ **Some of the time** ☐ **A little of the time** ☐ **None of the time**

***Thank you for completing these questions*!**

FLOW #103 Plate #202

Patient Study ID Number ☐☐ Centre # ☐☐☐☐ Patient # Patient Initials ☐☐ F L

Follow Up Number: ☐ 1 week post/op ☐ 2 weeks post/op ☐ 6 weeks ☐ 3 months ☐ 6 months ☐ 9 months ☐ 12 months

Date form completed ☐☐ DD ☐☐ MM 20☐☐ YYYY

SF-12v2 INTERVIEW-ADMINISTERED FORM (1 of 4) - FORM 16.1

This first question is about your health in the past week. Please try to answer as accurately as you can.

1. In general, would you say your health is *[READ RESPONSE CHOICES]*
(Check off one box)

- ☐ Excellent
- ☐ Very Good
- ☐ Good
- ☐ Fair
- ☐ ***or*** Poor

Now I'm going to read a list of activities that you might do during a typical day. As I read each item, please tell me if your health now limits you a lot, limits you a little, or does not limit you at all in these activities.

2a. ...moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf. Does your health now limit you a lot, limit you a little, or not limit you at all? *[READ RESPONSE CHOICES ONLY IF NECESSARY]*

[IF RESPONDENT SAYS S/HE DOES NOT DO ACTIVITY, PROBE: Is that because of your health?]
(Check off one box)

- ☐ Yes, limited a lot
- ☐ Yes, limited a little
- ☐ No, not limited at all

2b. ...climbing several flights of stairs. Does your health now limit you a lot, limit you a little, or not limit you at all? *[READ RESPONSE CHOICES ONLY IF NECESSARY]*

[IF RESPONDENT SAYS S/HE DOES NOT DO ACTIVITY, PROBE: Is that because of your health?]
(Check off one box)

- ☐ Yes, limited a lot
- ☐ Yes, limited a little
- ☐ No, not limited at all

FLOW #103 Plate #203

Patient Study ID Number ☐☐ ☐☐☐☐ Centre # Patient #

Patient Initials ☐☐ F L

Follow Up Number: ☐ 1 week post/op ☐ 2 weeks post/op ☐ 6 weeks ☐ 3 months ☐ 6 months ☐ 9 months ☐ 12 months

SF-12v2 INTERVIEW-ADMINISTERED FORM (2 of 4) - FORM 16.2

The following two questions ask you about your physical health and your daily activities.

3a. During the past week, how much of the time have you accomplished less than you would like as a result of your physical health? ***[READ RESPONSE CHOICES]***
(Check off one box)

- ☐ All of the time
- ☐ Most of the time
- ☐ Some of the time
- ☐ A little of the time
- ☐ ***or*** None of the time

3b. During the past week, how much of the time were you limited in the kind of work or other regular daily activities you do as a result of your physical health? ***[READ RESPONSE CHOICES]***
(Check off one box)

- ☐ All of the time
- ☐ Most of the time
- ☐ Some of the time
- ☐ A little of the time
- ☐ ***or*** None of the time

The following two questions ask about your emotions and your daily activities.

4a. During the past week, how much of the time have you accomplished less than you would like as a result of any emotional problems, such as feeling depressed or anxious? ***[READ RESPONSE CHOICES]***
(Check off one box)

- ☐ All of the time
- ☐ Most of the time
- ☐ Some of the time
- ☐ A little of the time
- ☐ ***or*** None of the time

FLOW #103 Plate #204

Patient Study ID Number ☐☐ ☐☐☐☐ Centre # Patient #

Patient Initials ☐☐ F L

Follow Up Number: ☐ 1 week post/op ☐ 2 weeks post/op ☐ 6 weeks ☐ 3 months ☐ 6 months ☐ 9 months ☐ 12 months

SF-12v2 INTERVIEW-ADMINISTERED FORM (3 of 4) - FORM 16.3

4b. During the past week, how much of the time did you do work or other regular daily activities less carefully than usual as a result of any emotional problems, such as feeling depressed or anxious?
[READ RESPONSE CHOICES]
(Check off one box)

- ☐ All of the time
- ☐ Most of the time
- ☐ Some of the time
- ☐ A little of the time
- ☐ ***or*** None of the time

5. During the past week, how much did pain interfere with your normal work, including both work outside the home and housework? Did it interfere... *[READ RESPONSE CHOICES]*
(Check off one box)

- ☐ Not at all
- ☐ A little bit
- ☐ Moderately
- ☐ Quite a bit
- ☐ ***or*** Extremely

The next questions are about how you feel and how things have been with you during the past week.

As I read each statement, please give me the one answer that comes closest to the way you have been feeling; is it all of the time, most of the time, some of the time, a little of the time, or none of the time?

6a. How much of the time during the past week... have you felt calm and peaceful?
[READ RESPONSE CHOICES]
(Check off one box)

- ☐ All of the time
- ☐ Most of the time
- ☐ Some of the time
- ☐ A little of the time
- ☐ ***or*** None of the time

FLOW #103 Plate #205

Patient Study ID Number ☐☐ Centre # ☐☐☐☐ Patient # Patient Initials ☐☐ F L

Follow Up Number: ☐ 1 week post/op ☐ 2 weeks post/op ☐ 6 weeks ☐ 3 months ☐ 6 months ☐ 9 months ☐ 12 months

SF-12v2 INTERVIEW-ADMINISTERED FORM (4 of 4) - FORM 16.4

6b. How much of the time during the past week... did you have a lot of energy?
[READ RESPONSE CHOICES]
(Check off one box)

- ☐ All of the time
- ☐ Most of the time
- ☐ Some of the time
- ☐ A little of the time
- ☐ ***or*** None of the time

6c. How much of the time during the past week... have you felt downhearted and depressed?
[READ RESPONSE CHOICES ONLY IF NECESSARY]
(Check off one box)

- ☐ All of the time
- ☐ Most of the time
- ☐ Some of the time
- ☐ A little of the time
- ☐ ***or*** None of the time

7. During the past week, how much of the time has your physical health or emotional problems interfered with your social activities like visiting with friends or relatives, etc.? Has it interfered... *[READ RESPONSE CHOICES]*
(Check off one box)

- ☐ All of the time
- ☐ Most of the time
- ☐ Some of the time
- ☐ A little of the time
- ☐ ***or*** None of the time

FLOW #103 Plate #200

Follow Up Number: [X] 1 week post/op [ ] 2 weeks post/op [ ] 6 weeks [ ] 3 months [ ] 6 months [ ] 9 months [ ] 12 months

Patient Study ID Number: Centre # ____ Patient # ____

Patient Initials: F ____ L ____

Date form completed: DD ____ MM ____ YYYY 20__

SF-12v2 SELF-ADMINISTERED FORM (1 of 2) - FORM 15.1

Your Health and Well-Being

This survey asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities. ***Thank you for completing this survey!***

For each of the following questions, please mark an X in the one box that best describes your answer.

1. In general, before your injury, would you say your health was:

[ ] **Excellent** [ ] **Very Good** [ ] **Good** [ ] **Fair** [ ] **Poor**

2. The following questions are about activities you might do during a typical day. Before your injury, did your health limit you in these activities? If so, how much?

	Yes, Limited A Lot	Yes, Limited A Little	No, Not Limited At All
a) Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	[ ]	[ ]	[ ]
b) Climbing several flights of stairs	[ ]	[ ]	[ ]

3. Before your injury, how much of the time did you have any of the following problems with your work or other regular daily activities as a result of your physical health?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a) Accomplished less than you would like	[ ]	[ ]	[ ]	[ ]	[ ]
b) Were limited in the kind of work or other activities	[ ]	[ ]	[ ]	[ ]	[ ]

continued on next page...

FLOW #103 Plate #201

Patient Study ID Number: Centre # ☐☐ Patient # ☐☐☐☐

Patient Initials: F ☐ L ☐

Follow Up Number:
- ☒ 1 week post/op
- ☐ 2 weeks post/op
- ☐ 6 weeks
- ☐ 3 months
- ☐ 6 months
- ☐ 9 months
- ☐ 12 months

SF-12v2 SELF-ADMINISTERED FORM (2 of 2) - FORM 15.2

4. Before your injury, how much of the time did you have any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a) Accomplished less than you would like	☐	☐	☐	☐	☐
b) Did work or other activities less carefully than usual	☐	☐	☐	☐	☐

5. Before your injury, how much did pain interfere with your normal work (including both work outside the home and housework)?

☐ **Not at all** ☐ **A little bit** ☐ **Moderately** ☐ **Quite a bit** ☐ **Extremely**

6. These questions are about how you felt and how things had been with you before your injury. For each question, please give the one answer that comes closest to the way you had been feeling. How much of the time before your injury...

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a) Did you feel calm and peaceful?	☐	☐	☐	☐	☐
b) Did you have a lot of energy?	☐	☐	☐	☐	☐
c) Did you feel downhearted and depressed?	☐	☐	☐	☐	☐

7. Before your injury, how much of the time did your physical health or emotional problems interfere with your social activities (like visiting friends, relatives, etc.)?

☐ **All of the time** ☐ **Most of the time** ☐ **Some of the time** ☐ **A little of the time** ☐ **None of the time**

Thank you for completing these questions!

FLOW #103 Plate #202

Follow Up Number: [X] 1 week post/op [ ] 2 weeks post/op [ ] 6 weeks [ ] 3 months [ ] 6 months [ ] 9 months [ ] 12 months

Patient Study ID Number [ ][ ] Centre # [ ][ ][ ][ ] Patient # Patient Initials [ ][ ] F L

Date form completed [ ][ ] DD [ ][ ] MM 20[ ][ ] YYYY

SF-12v2 INTERVIEW-ADMINISTERED FORM (1 of 4) - FORM 16.1

This first question is about your health BEFORE YOUR INJURY. Please try to answer as accurately as you can.

1. In general, BEFORE YOUR INJURY, would you say your health was *[READ RESPONSE CHOICES]*
(Check off one box)

- [ ] Excellent
- [ ] Very Good
- [ ] Good
- [ ] Fair
- [ ] Poor

Now I'm going to read a list of activities that you might have done during a typical day. As I read each item, please tell me if your health limited you a lot, limited you a little, or did not limit you at all in these activities.

2a. ...moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf. BEFORE YOUR INJURY, did your health limit you a lot, limit you a little, or not limit you at all? *[READ RESPONSE CHOICES]*

[IF RESPONDENT SAYS HE/SHE DID NOT DO ACTIVITY, PROBE: Is that because of your health?]
(Check off one box)

- [ ] Yes, limited a lot
- [ ] Yes, limited a little
- [ ] No, not limited at all

2b. ...climbing several flights of stairs. BEFORE YOUR INJURY, did your health limit you a lot, limit you a little, or not limit you at all? *[READ RESPONSE CHOICES ONLY IF NECESSARY]*

[IF RESPONDENT SAYS HE/SHE DID NOT DO ACTIVITY, PROBE: Is that because of your health?]
(Check off one box)

- [ ] Yes, limited a lot
- [ ] Yes, limited a little
- [ ] No, not limited at all

FLOW #103 Plate #203

Patient Study ID Number ☐☐ Centre # ☐☐☐☐ Patient # Patient Initials ☐☐ F L

Follow Up Number: ☒ 1 week post/op ☐ 2 weeks post/op ☐ 6 weeks ☐ 3 months ☐ 6 months ☐ 9 months ☐ 12 months

SF-12v2 INTERVIEW-ADMINISTERED FORM (2 of 4) - FORM 16.2

The following two questions ask you about your physical health and your daily activities.

3a. BEFORE YOUR INJURY, how much of the time did you accomplish less than you would like as a result of your physical health? ***[READ RESPONSE CHOICES]***
(Check off one box)

- ☐ All of the time
- ☐ Most of the time
- ☐ Some of the time
- ☐ A little of the time
- ☐ ***or*** None of the time

3b. BEFORE YOUR INJURY, how much of the time were you limited in the kind of work or other regular daily activities you did as a result of your physical health? ***[READ RESPONSE CHOICES]***
(Check off one box)

- ☐ All of the time
- ☐ Most of the time
- ☐ Some of the time
- ☐ A little of the time
- ☐ ***or*** None of the time

The following two questions ask about your emotions and your daily activities.

4a. BEFORE YOUR INJURY, how much of the time did you accomplish less than you would like as a result of any emotional problems, such as feeling depressed or anxious? ***[READ RESPONSE CHOICES]***
(Check off one box)

- ☐ All of the time
- ☐ Most of the time
- ☐ Some of the time
- ☐ A little of the time
- ☐ ***or*** None of the time

FLOW #103 Plate #204

Patient Study ID Number: Centre # ____ Patient # ____ Patient Initials: F ____ L ____

Follow Up Number: [X] 1 week post/op [ ] 2 weeks post/op [ ] 6 weeks [ ] 3 months [ ] 6 months [ ] 9 months [ ] 12 months

SF-12v2 INTERVIEW-ADMINISTERED FORM (3 of 4) - FORM 16.3

4b. BEFORE YOUR INJURY, how much of the time did you do work or other regular daily activities less carefully than usual as a result of any emotional problems, such as feeling depressed or anxious?
[READ RESPONSE CHOICES]
(Check off one box)

- [ ] All of the time
- [ ] Most of the time
- [ ] Some of the time
- [ ] A little of the time
- [ ] ***or*** None of the time

5. BEFORE YOUR INJURY, how much did pain interfere with your normal work, including both work outside the home and housework? Did it interfere... *[READ RESPONSE CHOICES]*
(Check off one box)

- [ ] Not at all
- [ ] A little bit
- [ ] Moderately
- [ ] Quite a bit
- [ ] ***or*** Extremely

The next questions are about how you felt and how things had been with you BEFORE YOUR INJURY.

As I read each statement, please give me the one answer that comes closest to the way you had been feeling; is it all of the time, most of the time, some of the time, a little of the time, or none of the time?

6a. How much of the time BEFORE YOUR INJURY... did you feel calm and peaceful?
[READ RESPONSE CHOICES]
(Check off one box)

- [ ] All of the time
- [ ] Most of the time
- [ ] Some of the time
- [ ] A little of the time
- [ ] ***or*** None of the time

FLOW #103 Plate #205

Follow Up Number: [X] 1 week post/op [ ] 2 weeks post/op [ ] 6 weeks [ ] 3 months [ ] 6 months [ ] 9 months [ ] 12 months

Patient Study ID Number [ ][ ] Centre # [ ][ ][ ][ ] Patient # Patient Initials [ ][ ] F L

SF-12v2 INTERVIEW-ADMINISTERED FORM (4 of 4) - FORM 16.4

6b. How much of the time BEFORE YOUR INJURY... did you have a lot of energy?
[READ RESPONSE CHOICES]
(Check off one box)

- [ ] All of the time
- [ ] Most of the time
- [ ] Some of the time
- [ ] A little of the time
- [ ] ***or*** None of the time

6c. How much of the time BEFORE YOUR INJURY... did you feel downhearted and depressed?
[READ RESPONSE CHOICES ONLY IF NECESSARY]
(Check off one box)

- [ ] All of the time
- [ ] Most of the time
- [ ] Some of the time
- [ ] A little of the time
- [ ] ***or*** None of the time

7. BEFORE YOUR INJURY, how much of the time did your physical health or emotional problems interfere with your social activities like visiting friends or relatives? Has it interfered... ***[READ RESPONSE CHOICES]***
(Check off one box)

- [ ] All of the time
- [ ] Most of the time
- [ ] Some of the time
- [ ] A little of the time
- [ ] ***or*** None of the time

FLOW #103 **Plate #210**

Patient Study ID Number Centre # Patient #

Patient Initials F L

Follow Up Number:
- ☐ 1 week post/op
- ☐ 2 weeks post/op
- ☐ 6 weeks
- ☐ 3 months
- ☐ 6 months
- ☐ 9 months
- ☐ 12 months

Date form completed DD MM 20 YYYY

EQ-5D SELF-ADMINISTERED FORM (1 of 2) - FORM 17.1

By placing an X in one box in each group below, please indicate which statements best describe your own state of health today.

1. Mobility

- ☐ I have no problems in walking about
- ☐ I have some problems in walking about
- ☐ I am confined to bed

2. Self-care

- ☐ I have no problems with self-care
- ☐ I have some problems washing or dressing myself
- ☐ I am unable to wash or dress myself

3. Usual Activities (e.g. work, study, housework, family or leisure activities)

- ☐ I have no problems with performing my usual activities
- ☐ I have some problems with performing my usual activities
- ☐ I am unable to perform my usual activities

4. Pain/Discomfort

- ☐ I have no pain or discomfort
- ☐ I have moderate pain or discomfort
- ☐ I have extreme pain or discomfort

5. Anxiety/Depression

- ☐ I am not anxious or depressed
- ☐ I am moderately anxious or depressed
- ☐ I am extremely anxious or depressed

FLOW #103 **Plate #211**

Patient Study ID Number Centre # Patient #

Patient Initials F L

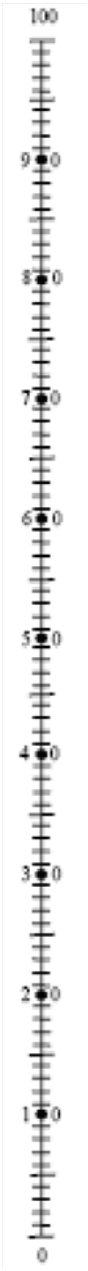
Follow Up Number:
- ☐ 1 week post/op
- ☐ 2 weeks post/op
- ☐ 6 weeks
- ☐ 3 months
- ☐ 6 months
- ☐ 9 months
- ☐ 12 months

EQ-5D SELF-ADMINISTERED FORM (2 of 2) - FORM 17.2

To help people say how good or bad their state of health is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.

We would like you to indicate on this scale how good or bad your health is today, in your opinion.
Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your state of health is today.

Best imaginable state of health



Worst imaginable state of health

Your own state of health TODAY

For administrative use only:

☐☐☐.☐

Place an 'x' in the box below if the EQ-5D Substudy Form (Form 17.3) was completed

☐

Follow Up Number: ☐ 1 week post/op ☐ 2 weeks post/op ☐ 6 weeks ☐ 3 months ☐ 6 months ☐ 9 months ☐ 12 months

FLOW #103 **Plate #212**

Patient Study ID Number ☐☐ ☐☐☐☐ **Patient Initials** ☐☐

Centre # **Patient #** **F L**

EQ-5D SELF-ADMINISTERED SUBSTUDY FORM (1 of 1) - FORM 17.3

By placing an X in one box in each group below, please indicate which statements best describe your own state of health today.

1. Mobility

- ☐ I have no problems in walking about
- ☐ I have slight problems in walking about
- ☐ I have moderate problems in walking about
- ☐ I have severe problems in walking about
- ☐ I am unable to walk about

2. Self-Care

- ☐ I have no problems washing or dressing myself
- ☐ I have slight problems washing or dressing myself
- ☐ I have moderate problems washing or dressing myself
- ☐ I have severe problems washing or dressing myself
- ☐ I am unable to wash or dress myself

3. Usual Activities (e.g. work, study, housework, family or leisure activities)

- ☐ I have no problems doing my usual activities
- ☐ I have slight problems doing my usual activities
- ☐ I have moderate problems doing my usual activities
- ☐ I have severe problems doing my usual activities
- ☐ I am unable to do my usual activities

4. Pain/Discomfort

- ☐ I have no pain or discomfort
- ☐ I have slight pain or discomfort
- ☐ I have moderate pain or discomfort
- ☐ I have severe pain or discomfort
- ☐ I have extreme pain or discomfort

5. Anxiety/Depression

- ☐ I am not anxious or depressed
- ☐ I am slightly anxious or depressed
- ☐ I am moderately anxious or depressed
- ☐ I am severely anxious or depressed
- ☐ I am extremely anxious or depressed

FLOW #103 Plate #210

Follow Up Number: [X] 1 week post/op [ ] 3 months [ ] 2 weeks post/op [ ] 6 months [ ] 6 weeks [ ] 9 months [ ] 12 months

Patient Study ID Number [ ][ ] Centre # [ ][ ][ ][ ] Patient # Patient Initials [ ][ ] F L

Date form completed [ ][ ] DD [ ][ ] MM 20[ ][ ] YYYY

EQ-5D SELF-ADMINISTERED FORM (1 of 2) - FORM 17.1

By placing an X in one box in each group below, please indicate which statements best describe your own state of health BEFORE YOUR INJURY.

1. Mobility (BEFORE YOUR INJURY)

- [ ] I had no problems in walking about
- [ ] I had some problems in walking about
- [ ] I was confined to bed

2. Self-care (BEFORE YOUR INJURY)

- [ ] I had no problems with self-care
- [ ] I had some problems washing or dressing myself
- [ ] I was unable to wash or dress myself

3. Usual Activities (e.g. work, study, housework, family or leisure activities) **(BEFORE YOUR INJURY)**

- [ ] I had no problems with performing my usual activities
- [ ] I had some problems with performing my usual activities
- [ ] I was unable to perform my usual activities

4. Pain/Discomfort (BEFORE YOUR INJURY)

- [ ] I had no pain or discomfort
- [ ] I had moderate pain or discomfort
- [ ] I had extreme pain or discomfort

5. Anxiety/Depression (BEFORE YOUR INJURY)

- [ ] I was not anxious or depressed
- [ ] I was moderately anxious or depressed
- [ ] I was extremely anxious or depressed

FLOW #103 **Plate #211**

Patient Study ID Number Centre # Patient #

Patient Initials F L

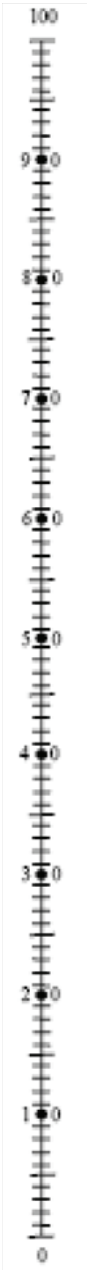
Follow Up Number:
- [x] 1 week post/op
- [ ] 2 weeks post/op
- [ ] 6 weeks
- [ ] 3 months
- [ ] 6 months
- [ ] 9 months
- [ ] 12 months

EQ-5D SELF-ADMINISTERED FORM (2 of 2) - FORM 17.2

To help people say how good or bad their state of health is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.

We would like you to indicate on this scale how good or bad your health was BEFORE YOUR INJURY, in your opinion. Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your state of health was BEFORE YOUR INJURY.

Best imaginable state of health



Worst imaginable state of health

Your own state of health BEFORE YOUR INJURY

For administrative use only:

□□□.□

Place an 'x' in the box below if the EQ-5D Substudy Form (Form 17.3) was completed

☐

Follow Up Number:
- [X] 1 week post/op
- [ ] 2 weeks post/op
- [ ] 6 weeks
- [ ] 3 months
- [ ] 6 months
- [ ] 9 months
- [ ] 12 months

FLOW #103 **Plate #212**

Patient Study ID Number [ ][ ] Centre # [ ][ ][ ][ ] Patient #

Patient Initials [ ][ ] F L

EQ-5D SELF-ADMINISTERED SUBSTUDY FORM (1 of 1) - FORM 17.3

By placing an X in one box in each group below, please indicate which statements best describe your own state of health BEFORE YOUR INJURY.

1. Mobility (BEFORE YOUR INJURY)
- [ ] I have no problems in walking about
- [ ] I have slight problems in walking about
- [ ] I have moderate problems in walking about
- [ ] I have severe problems in walking about
- [ ] I am unable to walk about

2. Self-Care (BEFORE YOUR INJURY)
- [ ] I have no problems washing or dressing myself
- [ ] I have slight problems washing or dressing myself
- [ ] I have moderate problems washing or dressing myself
- [ ] I have severe problems washing or dressing myself
- [ ] I am unable to wash or dress myself

3. Usual Activities (e.g. work, study, housework, family or leisure activities) **(BEFORE YOUR INJURY)**
- [ ] I have no problems doing my usual activities
- [ ] I have slight problems doing my usual activities
- [ ] I have moderate problems doing my usual activities
- [ ] I have severe problems doing my usual activities
- [ ] I am unable to do my usual activities

4. Pain/Discomfort (BEFORE YOUR INJURY)
- [ ] I have no pain or discomfort
- [ ] I have slight pain or discomfort
- [ ] I have moderate pain or discomfort
- [ ] I have severe pain or discomfort
- [ ] I have extreme pain or discomfort

5. Anxiety/Depression (BEFORE YOUR INJURY)
- [ ] I am not anxious or depressed
- [ ] I am slightly anxious or depressed
- [ ] I am moderately anxious or depressed
- [ ] I am severely anxious or depressed
- [ ] I am extremely anxious or depressed

FLOW #103 Plate #213

Follow Up Number: [X] 1 week post/op [ ] 2 weeks post/op [ ] 6 weeks [ ] 3 months [ ] 6 months [ ] 9 months [ ] 12 months

Patient Study ID Number [ ][ ] Centre # [ ][ ][ ][ ] Patient # Patient Initials [ ][ ] F L

EQ-5D INTERVIEW-ADMINISTERED FORM (1 of 3) - FORM 18.1

INTRODUCTION

We are trying to find out what you think about your health. I will first ask you a few brief and simple questions about your state of health **BEFORE YOUR INJURY.** I will then ask you to do a rather different task that involves rating your health on a measuring scale. I will explain the tasks fully as I go along but please interrupt me if you do not understand something or if things are not clear to you. Please also remember that there are no right or wrong answers. We are interested here only in your personal view.

First I am going to read out some questions. Each question has a choice of three answers. Please tell me which answer best describes your own state of health **BEFORE YOUR INJURY**.

Do not choose more than one answer in each group of questions.

(Note for administrator: It may be necessary to remind the respondent regularly that the time frame is before your injury.)

MOBILITY

First, I'd like to ask you about mobility.

Question 1: BEFORE YOUR INJURY, would you say you had...

- [ ] No problems in walking about?
- [ ] Some problems in walking about?
- [ ] Are you confined to bed?

So, would you say you had no problems in walking about, some problems in walking about or are you confined to bed?

(Note for administrator: mark the appropriate box on EQ-5D)

SELF-CARE

Next I'd like to ask you about self-care.

Question 2: BEFORE YOUR INJURY, would you say you had...

- [ ] No problems with self-care?
- [ ] Some problems washing or dressing yourself?
- [ ] Are you unable to wash or dress yourself?

So, would you say you had no problems with self-care, some problems washing or dressing yourself or are you unable to wash or dress yourself?

(Note for administrator: mark the appropriate box on EQ-5D)

FLOW #103 Plate #214

Follow Up Number: [X] 1 week post/op [ ] 3 months [ ] 2 weeks post/op [ ] 6 months [ ] 6 weeks [ ] 9 months [ ] 12 months

Patient Study ID Number [ ][ ] Centre # [ ][ ][ ][ ] Patient # Patient Initials [ ][ ] F L

EQ-5D INTERVIEW-ADMINISTERED FORM (2 of 3) - FORM 18.2

USUAL ACTIVITIES

Next I'd like to ask you about your usual activities, for example work, study, housework, family or leisure activities.

Questions 3: BEFORE YOUR INJURY, would you say you had...

- [ ] No problems with performing your usual activities?
- [ ] Some problems with performing your usual activities?
- [ ] Are you unable to perform your usual activities?

So, would you say you had no problems performing your usual activities, some problems performing your usual activities or are you unable to perform your usual activities?

(Note for administrator: mark the appropriate box on EQ-5D)

PAIN/DISCOMFORT

Next I'd like to ask you about pain or discomfort.

Question 4: BEFORE YOUR INJURY, would you say you had...

- [ ] No pain or discomfort?
- [ ] Moderate pain or discomfort?
- [ ] Extreme pain or discomfort?

So, would you say you had no pain or discomfort, moderate pain or discomfort, or extreme pain or discomfort?

(Note for administrator: mark the appropriate box on EQ-5D)

ANXIETY/DEPRESSION

Finally, I'd like to ask you about anxiety or depression.

Question 5: BEFORE YOUR INJURY, would you say you were...

- [ ] Not anxious or depressed?
- [ ] Moderately anxious or depressed?
- [ ] Extremely anxious or depressed?

So, would you say you were not anxious or depressed, moderately anxious or depressed, or extremely anxious or depressed?

(Note for administrator: mark the appropriate box on EQ-5D)

FLOW #103 Plate #215

Follow Up Number: [X] 1 week post/op [ ] 2 weeks post/op [ ] 6 weeks [ ] 3 months [ ] 6 months [ ] 9 months [ ] 12 months

Patient Study ID Number [ ][ ] Centre # [ ][ ][ ][ ] Patient # Patient Initials [ ][ ] F L

EQ-5D INTERVIEW-ADMINISTERED FORM (3 of 3) - FORM 18.3

(Note for administrator: If possible, it might be useful to send a visual aid (i.e. the EQ VAS) before the telephone call so that they can have this in front of them when completing the task).

I would now like to ask you to do a rather different task.

To help you say how good or bad your state of health was BEFORE YOUR INJURY, I'd like you to try to picture in your mind a scale that looks rather like a thermometer. Can you do that? The best state you can imagine is marked 100 (one hundred) at the top of the scale and the worst state you can imagine is marked 0 (zero) at the bottom.

I would now like you to tell me the point on this scale where you would put your own state of health BEFORE YOUR INJURY.

[ ][ ][ ].[ ]

Thank you for taking the time to answer these questions.

FLOW #103 Plate #213

Follow Up Number: ☐ 1 week post/op ☐ 2 weeks post/op ☐ 6 weeks ☐ 3 months ☐ 6 months ☐ 9 months ☐ 12 months

Patient Study ID Number ☐☐ ☐☐☐☐ Centre # Patient #

Patient Initials ☐☐ F L

EQ-5D INTERVIEW-ADMINISTERED FORM (1 of 3) - FORM 18.1

INTRODUCTION

We are trying to find out what you think about your health. I will first ask you a few brief and simple questions about your own state of health **today**. I will then ask you to do a rather different task that involves rating your health on a measuring scale. I will explain the tasks fully as I go along but please interrupt me if you do not understand something or if things are not clear to you. Please also remember that there are no right or wrong answers. We are interested here only in your personal view.

First I am going to read out some questions. Each question has a choice of three answers. Please tell me which answer best describes your own state of health **today**.

Do not choose more than one answer in each group of questions.

(Note for administrator: It may be necessary to remind the respondent regularly that the time frame is today.)

MOBILITY

First, I'd like to ask you about mobility.

Question 1: Would you say you have...

- ☐ No problems in walking about?
- ☐ Some problems in walking about?
- ☐ Are you confined to bed?

So, would you say you have no problems in walking about, some problems in walking about or are you confined to bed?

(Note for administrator: mark the appropriate box on EQ-5D)

SELF-CARE

Next I'd like to ask you about self-care.

Question 2: Would you say you have...

- ☐ No problems with self-care?
- ☐ Some problems washing or dressing yourself?
- ☐ Are you unable to wash or dress yourself?

So, would you say you have no problems with self-care, some problems washing or dressing yourself or are you unable to wash or dress yourself?

(Note for administrator: mark the appropriate box on EQ-5D)

FLOW #103 Plate #214

Follow Up Number: ☐ 1 week post/op ☐ 2 weeks post/op ☐ 6 weeks ☐ 3 months ☐ 6 months ☐ 9 months ☐ 12 months

Patient Study ID Number ☐☐ ☐☐☐☐ Centre # Patient #

Patient Initials ☐☐ F L

EQ-5D INTERVIEW-ADMINISTERED FORM (2 of 3) - FORM 18.2

USUAL ACTIVITIES

Next I'd like to ask you about your usual activities, for example work, study, housework, family or leisure activities.

Questions 3: Would you say you have...

- ☐ No problems with performing your usual activities?
- ☐ Some problems with performing your usual activities?
- ☐ Are you unable to perform your usual activities?

So, would you say you have no problems performing your usual activities, some problems performing your usual activities or are you unable to perform your usual activities?

(Note for administrator: mark the appropriate box on EQ-5D)

PAIN/DISCOMFORT

Next I'd like to ask you about pain or discomfort.

Question 4: Would you say you have...

- ☐ No pain or discomfort?
- ☐ Moderate pain or discomfort?
- ☐ Extreme pain or discomfort?

So, would you say you have no pain or discomfort, moderate pain or discomfort, or extreme pain or discomfort?

(Note for administrator: mark the appropriate box on EQ-5D)

ANXIETY/DEPRESSION

Finally, I'd like to ask you about anxiety or depression.

Question 5: Would you say you are...

- ☐ Not anxious or depressed?
- ☐ Moderately anxious or depressed?
- ☐ Extremely anxious or depressed?

So, would you say you are not anxious or depressed, moderately anxious or depressed, or extremely anxious or depressed?

(Note for administrator: mark the appropriate box on EQ-5D)

FLOW #103 Plate #215

Follow Up Number: ☐ 1 week post/op ☐ 3 months ☐ 2 weeks post/op ☐ 6 months ☐ 6 weeks ☐ 9 months ☐ 12 months

Patient Study ID Number ☐☐ ☐☐☐☐ Centre # Patient #

Patient Initials ☐☐ F L

EQ-5D INTERVIEW-ADMINISTERED FORM (3 of 3) - FORM 18.3

(Note for administrator: If possible, it might be useful to send a visual aid (i.e. the EQ VAS) before the telephone call so that they can have this in front of them when completing the task).

I would now like to ask you to do a rather different task.

To help you say how good or bad your state of health is, I'd like you to try to picture in your mind a scale that looks rather like a thermometer. Can you do that? The best state you can imagine is marked 100 (one hundred) at the top of the scale and the worst state you can imagine is marked 0 (zero) at the bottom.

I would now like you to tell me the point on this scale where you would put your own state of health today.

☐☐☐.☐

Thank you for taking the time to answer these questions.

FLOW #103 Plate #180

Follow Up Number: ☐ 1 week post/op ☐ 6 months ☐ 2 weeks post/op ☐ 9 months ☐ 6 weeks ☐ 12 months ☐ 3 months ☐ 99 Early W/D

Patient Study ID Number: ☐☐ (Centre #) ☐☐☐☐ (Patient #)

Patient Initials: ☐☐ (F L)

WOUND HEALING PROBLEM FORM (1 of 1) - FORM 19.1

1. Date wound healing problem was diagnosed: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

2. What was the wound healing problem?
   - ☐ Dehiscence of suture line
   - ☐ Death of a flap or graft
   - ☐ Failure of closure to heal
   - ☐ Wound grew larger over time
   - ☐ Failed granulation
   - ☐ Development of necrosis
   - ☐ Other: _____

3. How was the wound healing problem treated? (check **all** that apply)
   - ☐ Antibiotics → **Please update and refax the entire Antibiotics Log 4.1.**
   - ☐ Operatively → **Please complete a Follow Up Surgical Report Form 11.1-11.3.**
   - ☐ Other: _____

4. Outcome of wound healing problem:
   - ☐ Resolved → **Please refax form when resolved.** → Date resolved/Date resolved with subsequent impairment: Day ☐☐ Month ☐☐ Year 2 0 ☐☐
   - ☐ Resolved, with subsequent impairment → **Degree of impairment:** ☐ Mild ☐ Moderate ☐ Severe
   - ☐ Ongoing → **Please update form when resolved.**
   - ☐ Fatal → **Please complete an Early Withdrawal Form 14.1-14.3.**

5. Was the patient rehospitalized for this problem?
   - ☐ Yes → Date of hospital admission: Day ☐☐ Month ☐☐ Year 2 0 ☐☐
   - ☐ No — Date of hospital discharge: Day ☐☐ Month ☐☐ Year 2 0 ☐☐
   - ☐ N/A - wound healing problem occurred during initial hospitalization

6. Is this adverse event considered either unexpected or a serious adverse event (fatal, immediate life threatening, permanent disability, hospitalization (repeat or prolonged))?
   - ☐ Yes → **Please complete an SAE Form 21.1**
   - ☐ No

7. Does the attending physician believe that the wound healing problem is directly related to the FLOW study (i.e., type of solution or pressure used)?
   - ☐ Not related
   - ☐ Possibly related
   - ☐ Probably related
   - ☐ Definitely related
   - ☐ Unclassifiable

☐ Indicate here if you require another page. Please complete form 19.2

Follow Up Number: ☐ 1 week post/op ☐ 2 weeks post/op ☐ 6 weeks ☐ 3 months ☐ 6 months ☐ 9 months ☐ 12 months ☐ 99 Early W/D

FLOW #103 **Plate #181**

Patient Study ID Number ☐☐ (Centre #) ☐☐☐☐ (Patient #) **Patient Initials** ☐☐ (F L)

WOUND HEALING PROBLEM FORM (1 of 1) - FORM 19.2

1. Date wound healing problem was diagnosed: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

2. What was the wound healing problem?
   - ☐ Dehiscence of suture line
   - ☐ Death of a flap or graft
   - ☐ Failure of closure to heal
   - ☐ Wound grew larger over time
   - ☐ Failed granulation
   - ☐ Development of necrosis
   - ☐ Other: _____

3. How was the wound healing problem treated? (check **all** that apply)
   - ☐ Antibiotics → **Please update and refax the entire Antibiotics Log 4.1.**
   - ☐ Operatively → **Please complete a Follow Up Surgical Report Form 11.1-11.3.**
   - ☐ Other: _____

4. Outcome of wound healing problem:
   - ☐ Resolved → **Please refax form when resolved.** → Date resolved/Date resolved with subsequent impairment: Day ☐☐ Month ☐☐ Year 2 0 ☐☐
   - ☐ Resolved, with subsequent impairment → **Degree of impairment:** ☐ Mild ☐ Moderate ☐ Severe
   - ☐ Ongoing → **Please update form when resolved.**
   - ☐ Fatal → **Please complete an Early Withdrawal Form 14.1-14.3.**

5. Was the patient rehospitalized for this problem?
   - ☐ Yes → Date of hospital admission: Day ☐☐ Month ☐☐ Year 2 0 ☐☐
   - ☐ No → Date of hospital discharge: Day ☐☐ Month ☐☐ Year 2 0 ☐☐
   - ☐ N/A - wound healing problem occurred during initial hospitalization

6. Is this adverse event considered either unexpected or a serious adverse event (fatal, immediate life threatening, permanent disability, hospitalization (repeat or prolonged))?
   - ☐ Yes → **Please complete an SAE Form 21.1**
   - ☐ No

7. Does the attending physician believe that the wound healing problem is directly related to the FLOW study (i.e., type of solution or pressure used)?
   - ☐ Not related
   - ☐ Possibly related
   - ☐ Probably related
   - ☐ Definitely related
   - ☐ Unclassifiable

☐ Indicate here if you require another page. Please complete form 19.3

FLOW #103 Plate #182

Follow Up Number: ☐ 1 week post/op ☐ 6 months ☐ 2 weeks post/op ☐ 9 months ☐ 6 weeks ☐ 12 months ☐ 3 months ☐ 99 Early W/D

Patient Study ID Number ☐☐ (Centre #) ☐☐☐☐ (Patient #) Patient Initials ☐☐ (F L)

WOUND HEALING PROBLEM FORM (1 of 1) - FORM 19.3

1. Date wound healing problem was diagnosed: Day ☐☐ Month ☐☐ Year 20☐☐

2. What was the wound healing problem?
   - ☐ Dehiscence of suture line
   - ☐ Death of a flap or graft
   - ☐ Failure of closure to heal
   - ☐ Wound grew larger over time
   - ☐ Failed granulation
   - ☐ Development of necrosis
   - ☐ Other: _____

3. How was the wound healing problem treated? (check **all** that apply)
   - ☐ Antibiotics → **Please update and refax the entire Antibiotics Log 4.1.**
   - ☐ Operatively → **Please complete a Follow Up Surgical Report Form 11.1-11.3.**
   - ☐ Other: _____

4. Outcome of wound healing problem:
   - ☐ Resolved → **Please refax form when resolved.** → Date resolved/Date resolved with subsequent impairment: Day ☐☐ Month ☐☐ Year 20☐☐
   - ☐ Resolved, with subsequent impairment → **Degree of impairment:** ☐ Mild ☐ Moderate ☐ Severe
   - ☐ Ongoing → **Please update form when resolved.**
   - ☐ Fatal → **Please complete an Early Withdrawal Form 14.1-14.3.**

5. Was the patient rehospitalized for this problem?
   - ☐ Yes → Date of hospital admission: Day ☐☐ Month ☐☐ Year 20☐☐
   - ☐ No → Date of hospital discharge: Day ☐☐ Month ☐☐ Year 20☐☐
   - ☐ N/A - wound healing problem occurred during initial hospitalization

6. Is this adverse event considered either unexpected or a serious adverse event (fatal, immediate life threatening, permanent disability, hospitalization (repeat or prolonged))?
   - ☐ Yes → **Please complete an SAE Form 21.1**
   - ☐ No

7. Does the attending physician believe that the wound healing problem is directly related to the FLOW study (i.e., type of solution or pressure used)?
   - ☐ Not related
   - ☐ Possibly related
   - ☐ Probably related
   - ☐ Definitely related
   - ☐ Unclassifiable

☐ Indicate here if you require another page. Please complete form 19.4

Follow Up Number: ☐ 1 week post/op ☐ 2 weeks post/op ☐ 6 weeks ☐ 3 months ☐ 6 months ☐ 9 months ☐ 12 months ☐ 99 Early W/D

FLOW #103 **Plate #183**

Patient Study ID Number ☐☐ (Centre #) ☐☐☐☐ (Patient #) **Patient Initials** ☐☐ (F L)

WOUND HEALING PROBLEM FORM (1 of 1) - FORM 19.4

1. Date wound healing problem was diagnosed: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

2. What was the wound healing problem?
   - ☐ Dehiscence of suture line
   - ☐ Death of a flap or graft
   - ☐ Failure of closure to heal
   - ☐ Wound grew larger over time
   - ☐ Failed granulation
   - ☐ Development of necrosis
   - ☐ Other: _____

3. How was the wound healing problem treated? (check **all** that apply)
   - ☐ Antibiotics → **Please update and refax the entire Antibiotics Log 4.1.**
   - ☐ Operatively → **Please complete a Follow Up Surgical Report Form 11.1-11.3.**
   - ☐ Other: _____

4. Outcome of wound healing problem:
   - ☐ Resolved → **Please refax form when resolved.** → Date resolved/Date resolved with subsequent impairment: Day ☐☐ Month ☐☐ Year 2 0 ☐☐
   - ☐ Resolved, with subsequent impairment → **Degree of impairment:** ☐ Mild ☐ Moderate ☐ Severe
   - ☐ Ongoing → **Please update form when resolved.**
   - ☐ Fatal → **Please complete an Early Withdrawal Form 14.1-14.3.**

5. Was the patient rehospitalized for this problem?
   - ☐ Yes → Date of hospital admission: Day ☐☐ Month ☐☐ Year 2 0 ☐☐
   - ☐ No → Date of hospital discharge: Day ☐☐ Month ☐☐ Year 2 0 ☐☐
   - ☐ N/A - wound healing problem occurred during initial hospitalization

6. Is this adverse event considered either unexpected or a serious adverse event (fatal, immediate life threatening, permanent disability, hospitalization (repeat or prolonged))?
   - ☐ Yes → **Please complete an SAE Form 21.1**
   - ☐ No

7. Does the attending physician believe that the wound healing problem is directly related to the FLOW study (i.e., type of solution or pressure used)?
   - ☐ Not related
   - ☐ Possibly related
   - ☐ Probably related
   - ☐ Definitely related
   - ☐ Unclassifiable

☐ Indicate here if you require another page. Please complete form 19.5

FLOW #103 **Plate #184**

Patient Study ID Number ☐☐ (Centre #) ☐☐☐☐ (Patient #) **Patient Initials** ☐☐ (F L)

Follow Up Number:
☐ 1 week post/op ☐ 6 months
☐ 2 weeks post/op ☐ 9 months
☐ 6 weeks ☐ 12 months
☐ 3 months ☐ 99 Early W/D

WOUND HEALING PROBLEM FORM (1 of 1) - FORM 19.5

1. Date wound healing problem was diagnosed: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

2. What was the wound healing problem?
   - ☐ Dehiscence of suture line
   - ☐ Death of a flap or graft
   - ☐ Failure of closure to heal
   - ☐ Other: _____
   - ☐ Wound grew larger over time
   - ☐ Failed granulation
   - ☐ Development of necrosis

3. How was the wound healing problem treated? (check **all** that apply)
   - ☐ Antibiotics → **Please update and refax the entire Antibiotics Log 4.1.**
   - ☐ Operatively → **Please complete a Follow Up Surgical Report Form 11.1-11.3.**
   - ☐ Other: _____

4. Outcome of wound healing problem:
   - ☐ Resolved → **Please refax form when resolved.** → Date resolved/Date resolved with subsequent impairment: Day ☐☐ Month ☐☐ Year 2 0 ☐☐
   - ☐ Resolved, with subsequent impairment → **Degree of impairment:** ☐ Mild ☐ Moderate ☐ Severe
   - ☐ Ongoing → **Please update form when resolved.**
   - ☐ Fatal → **Please complete an Early Withdrawal Form 14.1-14.3.**

5. Was the patient rehospitalized for this problem?
   - ☐ Yes → Date of hospital admission: Day ☐☐ Month ☐☐ Year 2 0 ☐☐
   - ☐ No → Date of hospital discharge: Day ☐☐ Month ☐☐ Year 2 0 ☐☐
   - ☐ N/A - wound healing problem occurred during initial hospitalization

6. Is this adverse event considered either unexpected or a serious adverse event (fatal, immediate life threatening, permanent disability, hospitalization (repeat or prolonged))?
   - ☐ Yes → **Please complete an SAE Form 21.1**
   - ☐ No

7. Does the attending physician believe that the wound healing problem is directly related to the FLOW study (i.e., type of solution or pressure used)?
   - ☐ Not related
   - ☐ Possibly related
   - ☐ Probably related
   - ☐ Definitely related
   - ☐ Unclassifiable

FLOW #103 Plate #190

Patient Study ID Number: Centre # ☐☐ Patient # ☐☐☐☐

Patient Initials: F ☐ L ☐

Follow Up Number:
☐ Baseline ☐ 3 months
☐ 1 week post/op ☐ 6 months
☐ 2 weeks post/op ☐ 9 months
☐ 6 weeks ☐ 12 months
☐ 99 Early W/D

CULTURES FORM (1 of 1) - FORM 20.1

#	Before Initial I & D	Date	Results	If positive, please specify the organism(s)
1	☐ Yes ☐ No	Day ☐☐ Month ☐☐ Year 2 0 ☐☐	☐ Positive ☐ Negative	_____ _____ _____
2	☐ Yes ☐ No	Day ☐☐ Month ☐☐ Year 2 0 ☐☐	☐ Positive ☐ Negative	_____ _____ _____
3	☐ Yes ☐ No	Day ☐☐ Month ☐☐ Year 2 0 ☐☐	☐ Positive ☐ Negative	_____ _____ _____
4	☐ Yes ☐ No	Day ☐☐ Month ☐☐ Year 2 0 ☐☐	☐ Positive ☐ Negative	_____ _____ _____
5	☐ Yes ☐ No	Day ☐☐ Month ☐☐ Year 2 0 ☐☐	☐ Positive ☐ Negative	_____ _____ _____
6	☐ Yes ☐ No	Day ☐☐ Month ☐☐ Year 2 0 ☐☐	☐ Positive ☐ Negative	_____ _____ _____

☐ Indicate here if you require another page. Please complete form 20.2.

FLOW #103 Plate #191

Patient Study ID Number: Centre # ☐☐ Patient # ☐☐☐☐ Patient Initials: F ☐ L ☐

Follow Up Number:
☐ Baseline ☐ 3 months
☐ 1 week post/op ☐ 6 months
☐ 2 weeks post/op ☐ 9 months
☐ 6 weeks ☐ 12 months
☐ 99 Early W/D

CULTURES FORM (1 of 1) - FORM 20.2

#	Before Initial I & D	Date	Results	If positive, please specify the organism(s)
7	☐ Yes ☐ No	Day ☐☐ Month ☐☐ Year 2 0 ☐☐	☐ Positive ☐ Negative	
8	☐ Yes ☐ No	Day ☐☐ Month ☐☐ Year 2 0 ☐☐	☐ Positive ☐ Negative	
9	☐ Yes ☐ No	Day ☐☐ Month ☐☐ Year 2 0 ☐☐	☐ Positive ☐ Negative	
10	☐ Yes ☐ No	Day ☐☐ Month ☐☐ Year 2 0 ☐☐	☐ Positive ☐ Negative	
11	☐ Yes ☐ No	Day ☐☐ Month ☐☐ Year 2 0 ☐☐	☐ Positive ☐ Negative	
12	☐ Yes ☐ No	Day ☐☐ Month ☐☐ Year 2 0 ☐☐	☐ Positive ☐ Negative	

☐ Indicate here if you require another page. Please complete form 20.3.

FLOW #103 Plate #192

Patient Study ID Number: Centre # ☐☐ Patient # ☐☐☐☐ Patient Initials: F ☐ L ☐

Follow Up Number:
☐ Baseline ☐ 3 months
☐ 1 week post/op ☐ 6 months
☐ 2 weeks post/op ☐ 9 months
☐ 6 weeks ☐ 12 months
☐ 99 Early W/D

CULTURES FORM (1 of 1) - FORM 20.3

#	Before Initial I & D	Date	Results	If positive, please specify the organism(s)
13	☐ Yes ☐ No	Day ☐☐ Month ☐☐ Year 2 0 ☐☐	☐ Positive ☐ Negative	
14	☐ Yes ☐ No	Day ☐☐ Month ☐☐ Year 2 0 ☐☐	☐ Positive ☐ Negative	
15	☐ Yes ☐ No	Day ☐☐ Month ☐☐ Year 2 0 ☐☐	☐ Positive ☐ Negative	
16	☐ Yes ☐ No	Day ☐☐ Month ☐☐ Year 2 0 ☐☐	☐ Positive ☐ Negative	
17	☐ Yes ☐ No	Day ☐☐ Month ☐☐ Year 2 0 ☐☐	☐ Positive ☐ Negative	
18	☐ Yes ☐ No	Day ☐☐ Month ☐☐ Year 2 0 ☐☐	☐ Positive ☐ Negative	

☐ Indicate here if you require another page. Please complete form 20.3.

FLOW #103 Plate #193

Patient Study ID Number: Centre # ☐☐ Patient # ☐☐☐☐ Patient Initials: F ☐ L ☐

Follow Up Number:
☐ Baseline ☐ 3 months
☐ 1 week post/op ☐ 6 months
☐ 2 weeks post/op ☐ 9 months
☐ 6 weeks ☐ 12 months
☐ 99 Early W/D

CULTURES FORM (1 of 1) - FORM 20.4

#	Before Initial I & D	Date	Results	If positive, please specify the organism(s)
19	☐ Yes ☐ No	Day ☐☐ Month ☐☐ Year 2 0 ☐☐	☐ Positive ☐ Negative	
20	☐ Yes ☐ No	Day ☐☐ Month ☐☐ Year 2 0 ☐☐	☐ Positive ☐ Negative	
21	☐ Yes ☐ No	Day ☐☐ Month ☐☐ Year 2 0 ☐☐	☐ Positive ☐ Negative	
22	☐ Yes ☐ No	Day ☐☐ Month ☐☐ Year 2 0 ☐☐	☐ Positive ☐ Negative	
23	☐ Yes ☐ No	Day ☐☐ Month ☐☐ Year 2 0 ☐☐	☐ Positive ☐ Negative	
24	☐ Yes ☐ No	Day ☐☐ Month ☐☐ Year 2 0 ☐☐	☐ Positive ☐ Negative	

☐ Indicate here if you require another page. Please complete form 20.5.

FLOW #103 Plate #194

Patient Study ID Number: Centre # ☐☐ Patient # ☐☐☐☐ Patient Initials: F ☐ L ☐

Follow Up Number:
☐ Baseline ☐ 3 months
☐ 1 week post/op ☐ 6 months
☐ 2 weeks post/op ☐ 9 months
☐ 6 weeks ☐ 12 months
☐ 99 Early W/D

CULTURES FORM (1 of 1) - FORM 20.5

#	Before Initial I & D	Date	Results	If positive, please specify the organism(s)
25	☐ Yes ☐ No	Day ☐☐ Month ☐☐ Year 2 0 ☐☐	☐ Positive ☐ Negative	
26	☐ Yes ☐ No	Day ☐☐ Month ☐☐ Year 2 0 ☐☐	☐ Positive ☐ Negative	
27	☐ Yes ☐ No	Day ☐☐ Month ☐☐ Year 2 0 ☐☐	☐ Positive ☐ Negative	
28	☐ Yes ☐ No	Day ☐☐ Month ☐☐ Year 2 0 ☐☐	☐ Positive ☐ Negative	
29	☐ Yes ☐ No	Day ☐☐ Month ☐☐ Year 2 0 ☐☐	☐ Positive ☐ Negative	
30	☐ Yes ☐ No	Day ☐☐ Month ☐☐ Year 2 0 ☐☐	☐ Positive ☐ Negative	

Follow Up Number:
- ☐ Surgery
- ☐ 1 week post/op
- ☐ 2 weeks post/op
- ☐ 6 weeks
- ☐ 3 months
- ☐ 6 months
- ☐ 9 months
- ☐ 12 months
- ☐ 99 Early W/D

FLOW #103 **Plate #140**

Patient Study ID Number ☐☐ ☐☐☐☐ **Patient Initials** ☐☐

Centre # **Patient #** **F L**

SERIOUS ADVERSE EVENT FORM (1 of 1) - FORM 21.1

Please record all unexpected or serious adverse events (SAE) (fatal, immediately life threatening, permanent disability, hospitalization (repeat or prolonged))on the Serious Adverse Event Form.

1. Date the serious adverse event was diagnosed: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

2. What is the seriousness of the adverse event?

- ☐ Fatal → **Please complete an Early Withdrawal Form 14.1-14.3**
- ☐ Life threatening
- ☐ Hospitalization (initial or prolonged)
- ☐ Disability
- ☐ Other: _____

3. Pertinent medical history, including medication use: _____

4. Actions taken or anticipated actions in response to this unanticipated problem: _____

5. Date reported to IRB/REB: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

6. Are any actions required by the IRB/REB?

- ☐ Yes (specify) _____
- ☐ No

7. Details of physician submitting report:

_____
Name

_____
Title

_____
Telephone Number

☐ Indicate here if you require another page. Please complete form 21.2.

Follow Up Number:
- ☐ Surgery
- ☐ 1 week post/op
- ☐ 2 weeks post/op
- ☐ 6 weeks
- ☐ 3 months
- ☐ 6 months
- ☐ 9 months
- ☐ 12 months
- ☐ 99 Early W/D

FLOW #103 **Plate #141**

Patient Study ID Number ☐☐ ☐☐☐☐ **Patient Initials** ☐☐

Centre # **Patient #** **F L**

SERIOUS ADVERSE EVENT FORM (1 of 1) - FORM 21.2

Please record all unexpected or serious adverse events (SAE) (fatal, immediately life threatening, permanent disability, hospitalization (repeat or prolonged))on the Serious Adverse Event Form.

1. Date the serious adverse event was diagnosed: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

2. What is the seriousness of the adverse event?

- ☐ Fatal → **Please complete an Early Withdrawal Form 14.1-14.3**
- ☐ Life threatening
- ☐ Hospitalization (initial or prolonged)
- ☐ Disability
- ☐ Other: _____

3. Pertinent medical history, including medication use: _____

4. Actions taken or anticipated actions in response to this unanticipated problem: _____

5. Date reported to IRB/REB: Day ☐☐ Month ☐☐ Year 2 0 ☐☐

6. Are any actions required by the IRB/REB?

- ☐ Yes (specify)_____
- ☐ No

7. Details of physician submitting report:

_____
Name

_____
Title

_____
Telephone Number

☐ Indicate here if you require another page. Please complete form 21.3.

FLOW #103 **Plate #142**

Patient Study ID Number Centre # Patient #

Patient Initials F L

Follow Up Number:

- ☐ Surgery
- ☐ 1 week post/op
- ☐ 2 weeks post/op
- ☐ 6 weeks
- ☐ 3 months
- ☐ 6 months
- ☐ 9 months
- ☐ 12 months
- ☐ 99 Early W/D

SERIOUS ADVERSE EVENT FORM (1 of 1) - FORM 21.3

Please record all unexpected or serious adverse events (SAE) (fatal, immediately life threatening, permanent disability, hospitalization (repeat or prolonged))on the Serious Adverse Event Form.

1. Date the serious adverse event was diagnosed: Day Month Year 2 0

2. What is the seriousness of the adverse event?

- ☐ Fatal → **Please complete an Early Withdrawal Form 14.1-14.3**
- ☐ Life threatening
- ☐ Hospitalization (initial or prolonged)
- ☐ Disability
- ☐ Other: _____

3. Pertinent medical history, including medication use: _____

4. Actions taken or anticipated actions in response to this unanticipated problem: _____

5. Date reported to IRB/REB: Day Month Year 2 0

6. Are any actions required by the IRB/REB?

- ☐ Yes (specify) _____
- ☐ No

7. Details of physician submitting report:

_____
Name

_____
Title

_____
Telephone Number

FLOW #103 Plate #220

Follow Up Number: ☐ 1 week post/op ☐ 3 months ☐ 2 weeks post/op ☐ 6 months ☐ 6 weeks ☐ 9 months ☐ 12 months

Patient Study ID Number ☐☐ ☐☐☐☐ Centre # Patient #

Patient Initials ☐☐ F L

SOMATIC PRE-OCCUPATION AND COPING (SPOC) QUESTIONNAIRE (1 of 4) - FORM 22.1

Please answer all questions by marking the box above the answer that you think most applies to you. Place an "X" in one box only.

1. How often have you experienced pain in the past week?

☐ All of the time ☐ Most of the time ☐ A good bit of the time ☐ Some of the time ☐ A little of the time ☐ Hardly any of the time ☐ None of the time

2. How often have you experienced fatigue in the past week?

☐ All of the time ☐ Most of the time ☐ A good bit of the time ☐ Some of the time ☐ A little of the time ☐ Hardly any of the time ☐ None of the time

3. How often have you experienced stiff joints in the past week?

☐ All of the time ☐ Most of the time ☐ A good bit of the time ☐ Some of the time ☐ A little of the time ☐ Hardly any of the time ☐ None of the time

4. How often have you experienced problems with sleep in the past week?

☐ All of the time ☐ Most of the time ☐ A good bit of the time ☐ Some of the time ☐ A little of the time ☐ Hardly any of the time ☐ None of the time

5. How often have you experienced balance problems in the past week?

☐ All of the time ☐ Most of the time ☐ A good bit of the time ☐ Some of the time ☐ A little of the time ☐ Hardly any of the time ☐ None of the time

6. How often have you experienced loss of strength in the past week?

☐ All of the time ☐ Most of the time ☐ A good bit of the time ☐ Some of the time ☐ A little of the time ☐ Hardly any of the time ☐ None of the time

FLOW #103 Plate #221

Follow Up Number: ☐ 1 week post/op ☐ 3 months ☐ 2 weeks post/op ☐ 6 months ☐ 6 weeks ☐ 9 months ☐ 12 months

Patient Study ID Number ☐☐ (Centre #) ☐☐☐☐ (Patient #)

Patient Initials ☐☐ (F L)

SOMATIC PRE-OCCUPATION AND COPING (SPOC) QUESTIONNAIRE (2 of 4) - FORM 22.2

Please answer all questions by marking the box above the answer that you think most applies to you. Place an "X" in one box only.

7. The symptoms due to my injury will last a short time.

☐ Completely agree ☐ Strongly agree ☐ Agree ☐ Uncertain ☐ Disagree ☐ Strongly disagree ☐ Completely disagree

8. The symptoms due to my injury will improve with time.

☐ Completely agree ☐ Strongly agree ☐ Agree ☐ Uncertain ☐ Disagree ☐ Strongly disagree ☐ Completely disagree

9. There is a lot that I can do to control my injury-related symptoms.

☐ Completely agree ☐ Strongly agree ☐ Agree ☐ Uncertain ☐ Disagree ☐ Strongly disagree ☐ Completely disagree

10. My treatment will be effective in curing my injury, and the related symptoms.

☐ Completely agree ☐ Strongly agree ☐ Agree ☐ Uncertain ☐ Disagree ☐ Strongly disagree ☐ Completely disagree

11. Do you need to rest more?

☐ All of the time ☐ Most of the time ☐ A good bit of the time ☐ Some of the time ☐ A little of the time ☐ Hardly any of the time ☐ None of the time

12. Do you have problems starting things?

☐ All of the time ☐ Most of the time ☐ A good bit of the time ☐ Some of the time ☐ A little of the time ☐ Hardly any of the time ☐ None of the time

13. Do you have less strength in your muscles?

☐ All of the time ☐ Most of the time ☐ A good bit of the time ☐ Some of the time ☐ A little of the time ☐ Hardly any of the time ☐ None of the time

FLOW #103

Plate #222

Follow Up Number: ☐ 1 week post/op ☐ 2 weeks post/op ☐ 6 weeks ☐ 3 months ☐ 6 months ☐ 9 months ☐ 12 months

Patient Study ID Number ☐☐ (Centre #) ☐☐☐☐ (Patient #)

Patient Initials ☐☐ (F L)

SOMATIC PRE-OCCUPATION AND COPING (SPOC) QUESTIONNAIRE (3 of 4) - FORM 22.3

Please answer all questions by marking the box above the answer that you think most applies to you. Place an "X" in one box only.

14. Do you have difficulty concentrating?

☐ All of the time ☐ Most of the time ☐ A good bit of the time ☐ Some of the time ☐ A little of the time ☐ Hardly any of the time ☐ None of the time

15. Is your memory poor?

☐ All of the time ☐ Most of the time ☐ A good bit of the time ☐ Some of the time ☐ A little of the time ☐ Hardly any of the time ☐ None of the time

16. Do your muscles hurt at rest?

☐ All of the time ☐ Most of the time ☐ A good bit of the time ☐ Some of the time ☐ A little of the time ☐ Hardly any of the time ☐ None of the time

17. Do your muscles hurt after exercise?

☐ All of the time ☐ Most of the time ☐ A good bit of the time ☐ Some of the time ☐ A little of the time ☐ Hardly any of the time ☐ None of the time

18. Have you lost much sleep over worry in the past week?

☐ All of the time ☐ Most of the time ☐ A good bit of the time ☐ Some of the time ☐ A little of the time ☐ Hardly any of the time ☐ None of the time

19. Have you felt under constant strain in the past week?

☐ All of the time ☐ Most of the time ☐ A good bit of the time ☐ Some of the time ☐ A little of the time ☐ Hardly any of the time ☐ None of the time

20. Have you felt you couldn't overcome your difficulties in the past week?

☐ All of the time ☐ Most of the time ☐ A good bit of the time ☐ Some of the time ☐ A little of the time ☐ Hardly any of the time ☐ None of the time

FLOW #103 Plate #223

Follow Up Number: ☐ 1 week post/op ☐ 3 months ☐ 2 weeks post/op ☐ 6 months ☐ 6 weeks ☐ 9 months ☐ 12 months

Patient Study ID Number ☐☐ ☐☐☐☐ Centre # Patient #

Patient Initials ☐☐ F L

SOMATIC PRE-OCCUPATION AND COPING (SPOC) QUESTIONNAIRE (4 of 4) - FORM 22.4

Please answer all questions by marking the box above the answer that you think most applies to you. Place an "X" in one box only.

21. Have you been thinking of yourself as a worthless person in the past week?

☐ All of the time ☐ Most of the time ☐ A good bit of the time ☐ Some of the time ☐ A little of the time ☐ Hardly any of the time ☐ None of the time

22. Have you been feeling reasonably happy, all things considered in the past week?

☐ All of the time ☐ Most of the time ☐ A good bit of the time ☐ Some of the time ☐ A little of the time ☐ Hardly any of the time ☐ None of the time

23. Have you been feeling low in energy or slowed down in the past week?

☐ All of the time ☐ Most of the time ☐ A good bit of the time ☐ Some of the time ☐ A little of the time ☐ Hardly any of the time ☐ None of the time

24. Have you felt pains in your lower back in the past week?

☐ All of the time ☐ Most of the time ☐ A good bit of the time ☐ Some of the time ☐ A little of the time ☐ Hardly any of the time ☐ None of the time

25. Have you experienced hot or cold spells in the past week?

☐ All of the time ☐ Most of the time ☐ A good bit of the time ☐ Some of the time ☐ A little of the time ☐ Hardly any of the time ☐ None of the time

26. Have you been feeling weak in parts of your body in the past week?

☐ All of the time ☐ Most of the time ☐ A good bit of the time ☐ Some of the time ☐ A little of the time ☐ Hardly any of the time ☐ None of the time

27. Have you experienced heavy feelings in your arms or legs in the past week?

☐ All of the time ☐ Most of the time ☐ A good bit of the time ☐ Some of the time ☐ A little of the time ☐ Hardly any of the time ☐ None of the time