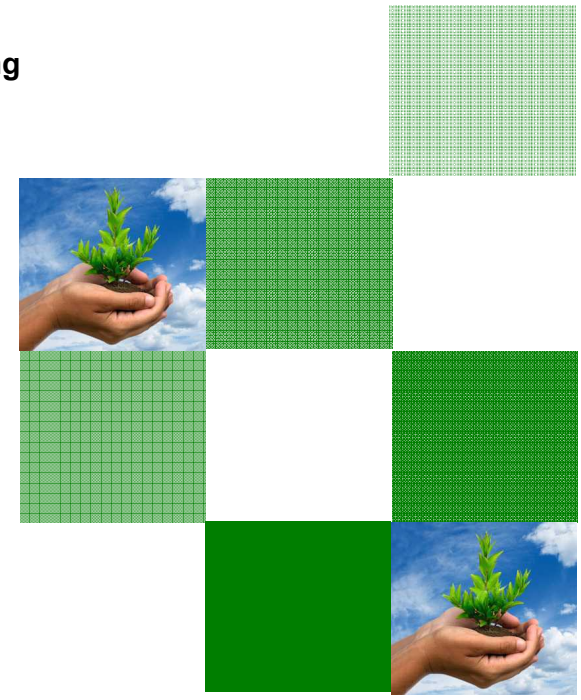
CLINICAL INVESTIGATION PLAN (CIP)

INVESTIGATIONAL DEVICE:

Mepilex Border Post-Op Ag

INVESTIGATION TITLE:

A single center, open, non-controlled investigation to evaluate the performance of a flexible, self-adherent absorbent silver dressing coated with a soft silicone layer after elective primary total hip or knee arthroplasty



CO-ORDINATING INVESTIGATOR:

Dr. Steven Myerthall

Center for Orthopedic Research and Education, Inc. d/b/a The CORE Institute

18444 N. 25th Avenue

Suite 320

Phoenix, Arizona 85023

MÖLNLYCKE CLINICAL STUDY MANAGER:

Tina Kjellén

Mölnlycke Health Care

P.O Box 130 80

402 52 Gothenburg, Sweden

Phone: +46 31 722 30 98

CLINICAL INVESTIGATION PLAN (CIP) SYNOPSIS

INVESTIGATION TITLE:

A single center, open, non-controlled investigation to evaluate the performance of a flexible, self-adherent absorbent silver dressing coated with a soft silicone layer after elective primary total hip or knee arthroplasty

Objectives

This investigation is undertaken to investigate the performance of a self-adhesive absorbent post-operative silver dressing coated with a soft silicone layer in subjects undergoing elective primary total hip or knee arthroplasty

The primary objective and outcome variable are shown in the table below::

Primary objective	Primary outcome variable
To evaluate the skin damage under the dressing from operation day to last visit	Damage to the incision and surrounding skin from operation day to last visit in terms of: - Blistering - Redness - Maceration

The secondary objectives and outcome variables are shown in the table below:

Secondary objective	Secondary outcome variable
To evaluate performance of the dressing from operation day to last visit	- Leakage - Shower ability - Dressing sticks to the staples/wound closure strips/sutures - Bleeding caused by the dressing removal - Dressing wear time (days) - Number of dressing changes - Residuals of the dressing material in the wound or surrounding skin - Dressing capacity of handling blood
To evaluate comfort, conformability and acceptability of the dressing from operation day to last visit	Nurse/Investigator evaluation - Ease of application of the dressing - Ease of removal of the dressing

	- Conformation to the body contours - Overall experience (only at the last visit) Subject evaluation - Comfort when wearing the dressing - Ease of mobility - Overall experience of the dressing (only at the last visit)
To evaluate pain at dressing removal from operation day to last visit	- Millimeter reading on visual analogue scales (VAS) filled in by subject

The safety objective and outcome variables are shown in the table below:

Safety objective	**Safety outcome variable**
To evaluate safety of Mepilex Border Post-Op Ag by assessment of device deficiencies and adverse events, non-serious and serious, rated for causality	- Incidence of AE/ADE/SAE/SADE/DD - Incidence of AE/ADE/SAE/SADE/DD leading to withdrawal

Overall Design
This descriptive, prospective, non-controlled clinical investigation will be conducted on approximately 20 enrolled subjects at one site in the US.

The target subjects are male or female, 18 years and older, undergoing elective primary hip or knee arthroplasty with a possibility to participate in a follow-up visit 7 days after surgery. Subjects will consecutively be allocated to a subject ID. The subjects will be followed 1-3 days after surgery and scheduled for a follow-up visit 7 days after surgery.

Study Period
Estimated date of first subject enrolled Q1 2017
Estimated date of last subject completed Q2 2017

Estimated date of end of clinical investigation (database lock) is Q2 2017

Inclusion Criteria
For inclusion in the investigation, the subjects must fulfill all of the below criteria prior to enrollment:

Screening Phase:

1. Age ≥18 years
2. Available for a follow-up visit including dressing change 7 days after surgery
3. Plan for elective primary hip or knee arthroplasty
4. Plan for incision size ≤18 cm
5. Provision of informed consent i.e. subject must be able to understand and sign the Patient Information and Consent Form

Enrollment Phase (Day of surgery)::

6. Undergoing elective primary hip or knee arthroplasty

Exclusion Criteria
Subjects who meet any of the below criteria will be excluded from the investigation:

Screening Phase:

1. Known allergy/hypersensitivity to any of the components of the dressing
2. Multi-trauma
3. Undergoing arthroplasty due to tumor
4. Previous incision at the same knee or same side of the hip
5. Wound at the surgical site prior to surgery
6. Neurological deficit of operated side (hemiplegia, etc.)
7. Documented skin disease at time of enrollment, as judged by the investigator
8. Previously enrolled in the present investigation
9. Inclusion in other ongoing investigations at present that would preclude the subject from participating in this investigation as judged by the investigator
10. Involvement in the planning and conduct of the clinical investigation (applies to all MHC staff, investigational site staff and third party vendor)

Enrollment Phase (Day of surgery):

11. Dressing size does not fit the incision size (>18 cm)
12. Complications that would increase wound risks if investigational dressing is applied

Schedule of Assessment

Day	Baseline (screening visit)	**Day 0 Day of surgery**	Day 1 1st post-op day	Day 2 2nd post-op day[a]	Day 3 3rd post-op day[a]	Unscheduled visit[b]	Day 7 7th post-op day	Termination
Visit window/days	-21 to 0	0	0	0	0	0	-2 to 0[c]	0
Visit (number)	1	2	3	4	5	Unscheduled	6	Termination
Inclusion/ Exclusion Criteria	✓	✓						
Informed Consent	✓							
Subject ID	✓							
Subject demography	✓							
Skin status at incision site	✓							
Medical /Surgical history	✓							
Type of surgery		✓						
Surgical incision condition		✓	✓	✓	✓	✓	✓	
Performance of the dressing		✓	✓	✓	✓	✓	✓	
Dressing log[d]		✓	(✓)	(✓)	(✓)	✓	✓	
Medication Log	✓	✓	✓	✓	✓	✓	✓	
Pain assessment[e]			(✓)	(✓)	(✓)	✓	✓	
Photos[f]		✓	✓	✓	✓	✓	✓	
Nurse/investigator evaluation[g]		✓	✓	✓	✓	✓	✓	
Subject evaluation[h]			✓	✓	✓	✓	✓	
Reason for termination								✓
AE/ADE/SAE/SADE/DD	✓	✓	✓	✓	✓	✓	✓	

a Information will be collected at Day 3 only if the subject is still at the hospital and hasn´t been discharged

b If the dressing is changed prior to post-op day 7 and outside scheduled visits, an unscheduled visit will be performed.

c When possible, visit 6 should be scheduled to post-op day 7. When not possible due to weekends, post-op day 5 or post-op day 6 could be scheduled.

d Dressing application/change/removal will be documented in the Dressing log. Ability to stay on (curl up at edges and partial/complete detachment) will also be collected

e Pain assessment at dressing removal (VAS). If a dressing change is deemed necessary prior to visit 6, pain assessment should be collected

f Photos should be taken at visit 2 (at the incision before application of the dressing, at dressing after application of the dressing) and if the dressing is changed at visit 3-6 (at the dressing before removal of the dressing, at the incision after removal of the dressing and at dressing (side facing the incision) , if signs of infection and if there in an unscheduled visit

g The nurse or the investigator will give their assessment concerning the treatment

h The nurse or the investigator will collect the subject´s experience via interview

If the subject is discharged prior to post-op day 2 , visit 4 and 5 will not be performed.

An occurrence of an AE/ADE/SAE/SADE/DD can be documented via photos at any time. Photos shall include a sticker marked with subject ID and visit number/date within the photograph. All photos will be checked (inspected) by Mölnlycke Health Care (MHC) personnel.

Details regarding variables to be collected are to be found in Appendix C.

Investigational Device

Mepilex Border Post-Op Ag is a soft silicone foam dressing that absorbs exudates, maintains a moist wound healing environment and has antimicrobial properties. The investigational device is a line extension under current Mepilex Border Ag 510(k) clearance (K100029).

Mepilex Border Post-Op Ag consists of a Safetac® soft silicone wound contact layer, an absorbent polyurethane foam pad containing a silver compound and activated carbon, a layer with super absorbent polyacrylate fibers, a non-woven and a vapor permeable waterproof film. The silicone layer is covered with a polyethylene release film which is in three parts with grip edges for easy application.
The dressing is sterilized in ethylene oxide (EO). Further details can be found in appendix D.

For this clinical investigation, Mepilex Border Post-Op Ag will be available in the following size:

Device (cm)	Wound pad (cm)	Border (cm)
10x25	5x20	2.5

No comparator will be used in this investigation.

TABLE OF CONTENTS

LIST OF APPENDICES

Appendix A F-449 Clinical Investigation Plan Appendix A, Core Signatures

Appendix B F-173 Patient Information and Consent Forms

Appendix C F-542 All variables to be obtained during the Investigation

Appendix D Instructions for Use

Appendix E Guide for Digital Photography

LIST OF ABBREVIATIONS

ADE	**Adverse Device Effect**
AE	**Adverse Event**
CA	**Competent Authority**
CIP	**Clinical Investigation Plan**
CRF	**Case Report Form**
CRM	**Clinical Research Manager**
DD	**Device Deficiency**
GCP	**Good Clinical Practice**
ICF	**Informed Consent Form**
IRB	**Institutional Review Board**
MHC	**Mölnlycke Health Care**
PI	**Principal Investigator**
PJI	**Periprosthetic Joint Infection**
SAE	**Serious Adverse Event**
SADE	**Serious Adverse Device Effect**
SSI	**Surgical Site Infection**
THR/THA	**Total Hip replacement/Total Hip Arthroplasty**
TJA	**Total Joint Arthroplasty**
TKR/TKA	**Total Knee Replacement/Total Knee Arthroplasty**

1. INTRODUCTION

Total joint arthroplasty is a safe and effective procedure improving the quality of life and restoring function to patients with arthritis of the hip and knee. Although its general success is beyond dispute, postoperative complications such as periprosthetic joint infection (PJI) still occur[1].

Most surgical wounds heal rapidly without complications; however some can become infected. Such infections occur when microorganisms are introduced through the surgical incision as a result of bacteria or fungi migration from the patient´s skin or gastrointestinal tract, direct transfer from surgical instruments, equipment or hands of healthcare workers or via airborne route.[2]

Every time the dressing needs to be changed, there is an increased risk of the wound becoming exposed to contamination. The evidence for optimal choice of dressing is based on chronic wounds and not surgical wounds,[2] However, in 2014, an International Consensus Meeting on Periprosthetic Joint Infection was held at which delegates from various disciplines worldwide participated and came to a consensus that an occlusive dressing after total joint arthroplasty (TJA) should be used.[3] Occlusive dressings protect the wound from both pathogenic invasion and further trauma. They act as barriers and prevent the entry of outside pathogens that might infect the wound and delay healing. Since they conform to the body's contours, they are more likely to remain in place and offer protection from further trauma as well. They move as the body moves, making them less susceptible to shearing and tearing during the daily activities.[4]

NICE (2008) guidelines on the prevention and treatment of surgical site infection and the DH (2007) High Impact Intervention care bundle recommend that dressings applied in operating theatre should remain in situ for at least 48 hours before removal to prevent the entry of microorganisms and promote healing. Dressings should be removed before this time only if there is excessive leakage from the dressing. Nurses should ensure that any signs and symptoms of infection in patients are discussed with surgeons responsible for the care of these patients to ensure timely and appropriate treatment.[2]

Other post-operative complications are blistering and pain at dressing removal. Pain at dressing removal is a frequent complaint heard from patients who have their wounds dressed with gauze dressings that have dried into their wound. Dressings that do not cause skin damage upon removal are now available. The World Union of Wound Healing Societies initiative, ‘‘Principles of Best Practice: Minimising Pain at Dressing-Related Procedures: Implementation of Pain Relieving Strategies’’, recommends that clinicians use dressings that minimize trauma/pain during application and removal.[5]
Even blisters lead to increased pain, delayed healing and increased susceptibility to wound infection as the integrity of the skin has been breached. Blistering occurs when the dermis becomes separated from the epidermis, which is invariably the result of continued abrasion. The deep, finger-like projections of epidermal tissue holding the epidermis and dermis together are weakened, allowing the two skin layers to separate. The incidence of wound blisters has been reported in the literature of between 6-24%.[6]

When developing postoperative wound complications and surgical site infections this can increase recovery times, hospital stay costs and morbidity rates.[7]

In a prospective randomized controlled study, three types of dressings (Mepore Pro, Mepilex Border Surgical Size and Hypafix Transparent) were compared in 150 consecutive subjects admitted for hip surgery with regard to prevalence of tape blisters. The blister prevalence was significantly lower for the Mepilex Border group (4%), than for the Mepore Pro group (51%, $p<0.01$) and Hypafix group (61%, $p<0.01$). The total number of dressings used during the hospital stay were also significantly lower for the Mepilex Border group compared to the Mepore Pro and Hypafix group ($p<0.01$). The conclusion was that the dressing with a silicone adhesive (Mepilex Border) significantly reduced the prevalence of blisters following hip surgery.[8]

In another open, prospective Post Market Clinical Follow-Up Study (MxB Po 01), Mepilex Border Post-Op was used in 49 patients and a standard dressing in 11 patients.
The results indicated that Mepilex Border Post-Op with the high absorption capacity, flexible wound pad, broader border and the skin friendly Safetac®Technology led to good stay on ability (7 days), no blisters, no skin stripping, almost no pain at dressing removal, no dressing related infections and no hypersensitive reaction.[13]

Mepilex Border Ag is a conformable self-adherent silver dressing in the Mepilex Border assortment. Several investigations have been conducted showing that Mepilex Border Ag minimizes trauma to the wound bed and surrounding skin upon dressing removal, has good exudate management,[9,10] reduce the number of microorganisms,[10,11,12] minimizes pain to the patient during dressing removal, minimizes the risk of maceration and is easy to handle.[9,10,11,12] The adhesive is Safetac®Technology (silicon), a unique and patented adhesive technology that minimizes pain to patients and trauma to wounds and the surrounding skin. Mepilex Border Post-Op Ag is an upgraded version of the Mepilex Border Ag and will be evaluated in this investigation.

The overall rationale for this investigation is to evaluate the clinical performance potential for Mepilex Border Post-Op Ag in the ability to minimize the risk of skin related post-operative wound complications such as blistering, maceration and redness at the incision and surrounding skin.

1.1 Risk/benefit Assessment

Incorrect dressing selection may leads to increased rates of blistering and wound discharge. This, in turn, may translate into additional costs caused by the need for more dressing changes and a prolonged hospital stay.[6]

Previous investigations have shown that Mepilex Border Ag with the adhesive Safetac® Technology is effective and skin friendly. [9,10] Since the Mepilex Border Post-Op Ag is an upgraded version of Mepilex Border Ag the performance will be further looked at in this investigation. It is believed that these upgrades will give both the hospital staff and the subject an even better experience and satisfaction when it comes to application, conformation to the body contours and ability to stay on.
Site staff will be trained on how to use the investigational device and subjects will be closely monitored during the investigation. Adverse events (AEs), Adverse Device Effects (ADEs) Serious Adverse Events (SAE), and Device Deficiencies (DD) will be registered throughout the investigation. The investigation will also be subjected to IRB review and approval before any subjects are included.

2. OBJECTIVES

This investigation is undertaken to investigate the performance of a self-adhesive absorbent post-operative silver dressing coated with a soft silicone layer in subjects undergoing elective, primary, total hip or knee arthroplasty.

The primary objective and outcome variable are shown in the table below:

Primary objective	Primary outcome variable
To evaluate the skin damage under the dressing from operation day to last visit	Damage to the incision and surrounding skin from operation day to last visit in terms of: - Blistering - Redness - Maceration

The secondary objectives and outcome variables are shown in the table below:

Secondary objective	Secondary outcome variable
To evaluate performance of the dressing from operation day to last visit	- Leakage - Shower ability - Dressing sticks to the staples/sutures - Bleeding caused by the dressing removal - Dressing wear time (days) - Number of dressing changes - Residuals of the dressing material in the wound or surrounding skin - Dressing capacity of handling blood
To evaluate comfort, conformability and acceptability of the dressing from operation day to last visit	Nurse/investigator evaluation - Ease of application of the dressing - Ease of removal of the dressing - Conformation to the body contours - Overall experience (only at the last visit) Subject evaluation - Comfort when wearing the dressing - Ease of mobility - Overall experience of the dressing (only at the last visit)
To evaluate pain at dressing removal from operation day to last visit	- Millimeter reading on visual analogue scales (VAS) filled in by subject

The safety objective and outcome variables are shown in the table below:

Safety objective	Safety outcome variable
To evaluate safety of the dressing by assessment of device deficiencies and adverse events, non-serious and serious, rated for causality	- Incidence of AE/ADE/SAE/SADE/DD - Incidence of AE/ADE/SAE/SADE/DD leading to withdrawal

3. CLINICAL INVESTIGATOR(S) AND INVESTIGATION ADMINISTRATIVE STRUCTURE

3.1 Staff at Investigation site(s)

Name and address of the PI at the investigation site is to be found in Appendix A.

3.2 Mölnlycke Investigation Personnel

Role in the investigation	Name	Contact information
Clinical Research Manager	Tina Kjellén	Mölnlycke Health Care AB Byfogdegatan 1 SE-415 05 Göteborg, SWEDEN Phone: +46 31 722 30 98 E-mail: tina.kjellen@molnlycke.com
Clinical Research Manager	David Pham	Molnlycke Health Care US, LLC 5550 Peachtree Parkway Suite 500 Norcross, GA 30092 USA Phone: +1 905 829 1502 E-mail: david.pham@molnlycke.com
Clinical Research Administrator	Annika Rydström	Mölnlycke Health Care AB Byfogdegatan 1 SE-415 05 Göteborg, SWEDEN Phone: +46 31 722 3000 E-mail: annika.rydstrom@molnlycke.com
Clinical Data Manager	Henrik Ahlbom	Mölnlycke Health Care AB Byfogdegatan 1 SE-415 05 Göteborg, SWEDEN

		Phone: +46 31 722 3000 E-mail: henrik.ahlbom@molnlycke.com
Biostatistician	Henrik Ahlbom	Mölnlycke Health Care AB Byfogdegatan 1 SE-415 05 Göteborg, SWEDEN Phone: +46 31 722 3000 E-mail: henrik.ahlbom@molnlycke.com
Global Clinical Research Director	Markus Wittebo	Mölnlycke Health Care AB Byfogdegatan 1 SE-415 05 Göteborg, SWEDEN Phone: +46 31 722 3000 E-mail: markus.wittebo@molnlycke.com

3.3 Other Participants

Role in the investigation	Contact information
eCRF activities	Pharma Consulting Group AB Kungsängsvägen 19 SE-753 23 Uppsala Sweden Phone: +46 18 430 3100

4. INVESTIGATION PLAN AND PROCEDURES

4.1 Overall Design

This single center, open, non-controlled investigation will be conducted at one site , US.

Approximately 20 male or female subjects, 18 years or older, with a planned elective primary total hip or knee replacement will be recruited in this investigation. The primary purpose is to investigate if there is any skin damage under the dressing from operation day to last visit. Performance of the dressing as well as comfort, conformability, acceptability and pain at dressing removal will also be followed-up until post-op day 7. Subjects at site number 01 are usually sent home on post-op day two or three but this investigation will include a follow-up visit on post-op day 7 when the dressing is removed and the incision and incision site are inspected before termination. If it is not possible to schedule a visit at post-op day 7 due to weekends, it is ok to schedule a visit for post-op day 5 or 6. Post-op day 7 is however the day to strive for.

4.2 Procedures and Assessments

The investigational device shall be used only in this investigation and according to the Clinical Investigation Plan (CIP). The devices are for single use only and must be used according to instructions for use (Appendix D).

Following Institutional Review Board (IRB) approval and before any investigation related procedure, potential subjects will be asked to sign a written informed consent form (ICF). The subjects will be given sufficient time for the information to be read and understood. The subject

will be approached and given the chance to ask any questions that have arisen after reading the ICF. After obtaining the subject´s written informed consent and verifying that the subject fulfills all inclusion and none of the exclusion criteria, the subject will participate in a screening visit and be allocated a subject ID. The screening visit will obtain information about the subject's medical/surgical history, concomitant medication, and factors pertaining to the scheduled surgical procedure. Only subjects who fulfill all inclusion and none of the exclusion criteria and are found eligible by the investigator, will be enrolled in the investigation. The subject ID (unique identification code) will be recorded in the site's all relevant investigation documentation pertaining to that individual.

If a subject is judged to be ineligible for enrollment, the primary reason of ineligibility will be documented and the subject will be considered as a screening failure. Ineligible subjects will receive the standard of care at the facility and no investigational documentation will be collected for these subjects.

4.2.1 Schedule of Assessment

All variables to be obtained during the Investigation are to be found 4.6.1, 4.6.2, 4.6.3 and

in Appendix C.

Schedule of Assessment

Day	Baseline (screening visit)	**Day 0 Day of surgery**	Day 1 1st post-op day	Day 2 2nd post-op day[a]	Day 3 3rd post-op day[a]	Unscheduled visit[b]	Day 7 7th post-op day	Termination
Visit window/days	-21 to 0	0	0	0	0	0	-2 to 0[c]	0
Visit (number)	1	2	3	4	5	Unscheduled	6	Termination
Inclusion/ Exclusion Criteria	✓	✓						
Informed Consent	✓							
Subject ID	✓							
Subject demography	✓							
Skin status at incision site	✓							
Medical /Surgical history	✓							
Type of surgery		✓						
Surgical incision condition		✓	✓	✓	✓	✓	✓	
Performance of the dressing		✓	✓	✓	✓	✓	✓	
Dressing log[d]		✓	(✓)	(✓)	(✓)	✓	✓	

Day	Baseline (screening visit)	**Day 0 Day of surgery**	Day 1 1st post-op day	Day 2 2nd post-op day[a]	Day 3 3rd post-op day[a]	Unscheduled visit[b]	Day 7 7th post-op day	Termination
Medication Log	✓	✓	✓	✓	✓	✓	✓	
Pain assessment[e]			(✓)	(✓)	(✓)	✓	✓	
Photos[f]		✓	✓	✓	✓	✓	✓	
Nurse/investigator evaluation[g]		✓	✓	✓	✓	✓	✓	
Subject evaluation[h]			✓	✓	✓	✓	✓	
Reason for termination								✓
AE/ADE/SAE/SADE/DD	✓	✓	✓	✓	✓	✓	✓	

a Information will be collected at Day 3 only if the subject is still at the hospital and hasn´t been discharged

b If the dressing is changed prior to post-op day 7 and outside scheduled visits, an unscheduled visit will be performed.

c When possible, visit 6 should be scheduled to post-op day 7. When not possible due to weekends, post-op day 5 or post-op day 6 could be scheduled.

d Dressing application/change/removal will be documented in the Dressing log. Ability to stay on (curl up at edges and partial/complete detachment) will also be collected

e Pain assessment at dressing removal (VAS). If a dressing change is deemed necessary prior to visit 6, pain assessment should be collected

f Photos should be taken at visit 2 (at the incision before application of the dressing, at dressing after application of the dressing) and if the dressing is changed at visit 3-6 (at the dressing before removal of the dressing, at the incision after removal of the dressing and at dressing (side facing the incision) , if signs of infection and if there in an unscheduled visit

g The nurse or the investigator will give their assessment concerning the treatment

h The nurse or the investigator will collect the subject´s experience via interview

4.3 Selection of Population for Investigation

4.3.1 Inclusion Criteria

For inclusion in the investigation, the subjects must fulfill all of the below criteria prior to enrollment:

Screening Phase:

1. Age ≥18 years
2. Available for a follow-up visit including dressing change 7 days after surgery
3. Plan for elective primary hip or knee arthroplasty
4. Plan for incision size ≤18 cm
5. Provision of informed consent i.e. subject must be able to understand and sign the Patient Information and Consent Form

Enrollment Phase (Day of surgery)::

6. Undergoing elective primary arthroplasty of the hip or knee.

4.3.2 Exclusion Criteria

Subjects who meet any of the below criteria will be excluded from the investigation:

Screening Phase:

1. Known allergy/hypersensitivity to any of the components of the dressing
2. Multi-trauma
3. Undergoing arthroplasty due to tumor
4. Previous incision at the same knee or same side of the hip
5. Wound at the surgical site prior to surgery
6. Neurological deficit of operated side (hemiplegia, etc.)
7. Documented skin disease at time of enrollment, as judged by the investigator
8. Previously enrolled in the present investigation
9. Inclusion in other ongoing investigations at present that would preclude the subject from participating in this investigation as judged by the investigator
10. Involvement in the planning and conduct of the clinical investigation (applies to all MHC staff, investigational site staff and third party vendor)

Enrollment Phase (Day of surgery):

11. Dressing size does not fit the incision area (>18 cm)
12. Complications that would increase wound risks if investigational dressing is applied

4.3.3 Withdrawal of Subjects from Treatment or Assessment

Subjects are free to discontinue participation in the investigation at any time, and without prejudice to further treatment. Subjects who discontinue the investigation should always be asked about the reason(s) for their discontinuation and about the presence of any Adverse Event/Adverse Device Effect or Device Deficiency and, if possible, be assessed by an investigator. Adverse Event/Adverse Device Effect should be followed up.

Subjects may be withdrawn from investigation treatment and assessments at any time, at the discretion of the investigator.

Incorrectly enrolled subjects will be withdrawn from further investigation treatment and assessments. A subject may, however, continue the investigation under special circumstances (i.e. if continuation of investigation treatment or follow-up actions are necessary for the subject's safety and well-being, or if only a follow-up period remains, and the continuation of the investigation is not expected to be associated with any risk or discomfort for the subject)

4.4 Investigational Device

4.4.1 Summary description of the Investigational Device(s)

Mepilex Border Post-Op Ag is a soft silicone foam dressing that absorbs exudates, maintains a moist wound healing environment and has antimicrobial properties. The investigational device is a line extension under current Mepilex Border Ag 510(k) clearance (K100029).

Mepilex Border Post-Op Ag consists of a Safetac® soft silicone wound contact layer, an absorbent polyurethane foam pad containing a silver compound and activated carbon, a layer with super absorbent polyacrylate fibers, a non-woven and a vapor permeable waterproof film. The silicone layer is covered with a polyethylene release film which is in three parts with grip edges for easy application.
The dressing is sterilized in ethylene oxide (EO). Further details can be found in appendix D.

For more information regarding the investigational device, instructions for use and precautions, please see Appendix D - Instructions for use.

For this clinical investigation, Mepilex Border Post-Op Ag will be available in the following size

Device (cm)	Wound pad (cm)	Border (cm)
10x25	5x20	2.5

4.4.2 Labelling

MHC will provide the investigational medical devices to the investigation site for free. Labelling of the investigational medical device will be performed in accordance with Good Manufacturing Practice (GMP). The labels will be produced in the local language and in accordance with local regulations for the US. The medical device will be marked with the following text:

Mepilex Border Post-Op Ag
Study Code: MxB Po Ag 01
“CAUTION - Investigational Device. Limited by Federal (or United States) law to investigational use."

4.4.3 Accountability

The investigational devices will not be distributed to the investigation site until all agreements between the investigator and MHC are finalized and IRB approval has been obtained. All investigational devices must be kept in a secure place under appropriate storage conditions.

Use of investigational devices will be logged in a separate accountability form stored in the Investigator Site File and be reviewed at each monitoring visit. The investigational devices may only be used in this clinical investigation and according to the CIP.

The principal investigator or an authorized designee shall keep records documenting the receipt, use, return and disposal of the investigational devices.

Unused products are accounted for and returned to MHC for destruction, or destroyed locally upon agreement with and approval from MHC.

Applicable documents are the “Certificate of Delivery of Investigational Device/Material”, the “Accountability Form” and the “Certificate of Return and Destruction of Investigation Product”.

4.4.4 Storage conditions

Investigational medical devices are to be handled and stored safely, properly and in agreement with the given storage instructions. Mepilex Border Post-Op Ag should be stored in dry conditions and protected from direct sunlight. A description of the appropriate storage and shipment conditions are specified on the investigational medical device label and in the instructions for use documentation (IFU), Appendix D**.**

4.4.5 Method of Assigning Subjects to Treatment Groups

The investigation is an open, non-controlled investigation and hence, all subjects who fulfill all inclusion and none of the exclusion criteria will be enrolled to the investigation.

If a subject discontinues from the investigation, the subject ID will not be reused and the subject will not be allowed to re-enter the investigation.

4.5 Concomitant Treatments

Medication, which is considered necessary for the subject's safety and well-being, may be given at the discretion of the investigator. All concomitant medication and relevant treatment must be recorded in the appropriate section of the Case Report Form (CRF).

Only antiseptics, anticoagulants, antibiotics and analgesics as well as skin related medication and those related to medical/surgical history and AEs are to be collected and reported in the Medication log.

4.6 Performance and Safety

4.6.1 Subject Characteristics

The following subject characteristics (demographics) will be recorded in the eCRF:

- Date of birth (dd-mm-yyyy)
- Gender (f/m)
- Weight (kg)
- Height (cm)
- BMI
- Medical History
- Surgical History
- Skin Status at Incision (type of skin (normal, dry, flaky, oily, moist, other)
- Type of Surgery (primary hip or knee arthroplasty, length of incision and type of incision closure)
- Surgical incision condition (compression over the incision)
- Drainage used (N/Y)
- Drainage placed (outside the dressing border, under the dressing border)
- Exudate level

- Exudate nature
- Signs of local/systemic infection and systemic antibiotic given for the local/systematic infection

4.6.2 Performance Measurements and Variables

Primary objective	Outcome variable	Method
To evaluate the skin damage from operation day to last visit	Damage to the incision and surrounding skin (blistering, redness, maceration)	Nurse or investigator assessment.

Secondary objective	Outcome variable	Method
To evaluate performance of the dressing from operation day to last visit	a. Incidence of Leakage	a. Nurse or investigator assessment (N/Y)
	b. Shower ability	b. Nurse or investigator assessment (NA/N/Y)
	c. Dressing sticks to the staples/wound closure strips/sutures	c. Nurse or investigator assessment (N/Y)
	d. Bleeding at dressing removal	d. Nurse or investigator assessment (N/Y)
	e. Dressing wear time	e. Nurse or investigator assessment (days)
	f. Number of dressing changes	f. Nurse or investigator assessment (Dressing log)
	g. Residuals of the dressing material in the wound or surrounding skin	g. Nurse or investigator assessment (N/Y)
	h. Dressing capacity of handling blood	h. Nurse or investigator assessment (N/Y)
To evaluate comfort, conformability and acceptability of the dressing from operation day to last visit	i. Ease of application of the dressing	i-m. Nurse/investigator evaluation (NA/ Poor/ Good/ Very Good/ Excellent)
	j. Ease of removal of the dressing	

	k. Conformation to the body contours l. Overall experience m. Comfort when wearing the dressing n. Ease of mobility o. Overall experience of the dressing	n-o. Subject evaluation (NA/ Poor/ Good/ Very Good/ Excellent)
To evaluate pain at dressing removal from operation day to last visit	Pain	Millimeter reading on visual analogue scales (VAS) filled in by subject. The results will be transferred to the eCRF by the staff at the investigation site

4.6.3 Safety Measurements and Variables

Adverse Event (AE)/Adverse Device Effect (ADE), Serious Adverse Event (SAE)/Serious Adverse Device Effect (SADE) and Device Deficiencies (DD). The definition of AE, ADE, SAE, SADE and DD and procedures for reporting SAE and SADE and DD that could have led to a SADE are presented in section 8 of this CIP. All AE, ADE, SAE, SADE and DD must also be recorded in the appropriate section of the CRF. It is of utmost importance that all staff involved in the investigation is familiar with the content of section 8. It is the responsibility of the Principal Investigator to ensure this.

4.6.4 Anticipated ADEs

The following events have been identified as anticipated effects in the Product Risk Management Record:

- Wound dry out
- Maceration
- Infection
- Pain and discomfort
- Skin irritation

The conclusion of the Product Risk Management Record is as following:

Based on the risk management record it can be concluded that for Mepilex Border Post-Op Ag products, there are no unacceptable risks of harm to the subject, the user nor third party involved in this device when used under normal conditions and for its intended use.

4.7 Data Quality Assurance

4.7.1 Monitoring, Audits and Inspections

During the investigation, the monitor will have regular contacts with the investigation site. These contacts will include visits to confirm that the facilities remain adequate to specified standards and that the investigation site team is carrying out the procedure stated in the clinical investigation plan and supports the investigator. All data must be accurately recorded in the CRF. Source data verification (a comparison of data in the CRF with the subject's hospital/practice and other records at the investigation site) with direct access to records will also be performed.

The monitor or other Mölnlycke Health Care (MHC) personnel will be available between visits if the investigator or other staff at the site needs information and/or advice.

Authorized representatives of MHC and/or a Competent Authority (CA) and/or the Institutional Review Board (IRB) may visit the investigation site to perform audits/inspections, including source data verification.

4.7.2 Training of Staff

The Principal Investigator will ensure that appropriate training relevant to the investigation is given to the medical, nursing and other staff at the site involved and that new information of relevance to the performance of this investigation is forwarded to the staff involved.

Before the first subject is entered into the investigation, Mölnlycke Health Care personnel will conduct a site initiation visit. The purpose of the visit is to provide training to the involved site personnel including, but not limited to the following items:

- Clinical investigation plan (CIP) and execution thereof
- Use of the investigational device
- Use of the eCRF system
- Study Equipment to be used
- Maintenance of Investigator Site File (ISF)

The staff at the investigational site will sign a confirmation document that they are trained in how to use the investigational device. Only trained staff (who has received delegation from the PI) will be allowed to apply and remove the dressings for a given subject..

4.7.3 Data Management

The Data Management process includes all activities related to data handling regarding:

- Set-up of eCRF and database
- Specification of on-line checks
- Data entry / Data editing
- Export of data from Viedoc to SAS
- Creation of post-entry checks and listings
- Reconciliation of Serious Adverse Event (SAE), Serious Adverse Device Effect (SADE), Adverse Devise Effect (ADE) and Device Deficiency (DD)

- Clean-file process including execution of post-entry checks and listings
- Post clean-file tasks

Pharma Consulting Group will build and set up Viedoc, a web based electronic CRF system that will be used to capture data in this investigation. The eCRF system complies with FDA Title 21 CRF part 11 (ER/ES) requirement.

eCRF training will be given to appropriate personnel before/at initiation of the investigation site(s).

Data entry will be done by investigators and other authorized personnel at the site(s). When entering data, on-line checks are incorporated in Viedoc for consistency and validation. Pharma Consulting Group will support with a helpdesk function taking care of system user questions regarding Viedoc.

When data has been entered authorized personnel at MHC can immediately view the data, send queries if necessary and lock eCRF pages when they have been validated.

Photos will be uploaded in Viedoc and are marked with the subject ID. Uploaded photos shall not contain any information that can reveal the identity of the subject. All uploaded photos will be reviewed by personnel at MHC and stored in the company database. All data entered in Viedoc will be encrypted. The physical database will be stored in Sweden.

Programs for post-entry checks and data listings will be created and executed for validation of data.

Completeness will be checked by authorized personnel at MHC so that there are no unexplainable empty fields in Viedoc. This is done in order to prevent that data being overlooked by personnel entering the data.

A clean-file meeting will be held prior to database lock. All decisions on the evaluability of the data from each individual subject for the statistical analysis must be made and documented before locking the database. Readable copies of the eCRF data will be archived in the Investigator Site File (ISF) at the investigation site after clean file.

Data will be retained for at least 10 years after investigation closure.

4.8 Statistical Methods and Determination of Sample Size

4.8.1 Statistical Evaluation

Presentation of the data
The results from this open, non-controlled clinical investigation will be presented with descriptive statistics. No hypothesis testing is planned for this investigation.
Data listings will be prepared for all data. Certain data will be collated into summary tables and figures. Those summary tables and figures will be integrated into the body of the investigation report.

Populations for analysis
Safety population
The population for the assessment of safety will include all enrolled subjects who provide at least the baseline visit.

ITT population
The Intention to Treat (ITT) population will include all subjects to at least one post-enrolment treatment.

PP population
The Per Protocol (PP) population will include all subjects without significant protocol violations. Subjects identified as protocol violators will be documented and agreed upon before declaration of clean-file.

Baseline characteristics
All variables measured at baseline will be summarized for the ITT- and PP population using appropriate summary statistics.

Performance and safety measurement
All endpoints will be summarized as above and by visit. The result from the CRF will be summarized appropriately for all evaluable subjects.
The number of subjects reporting one or more adverse events during the course of the investigation will be summarized using frequency counts.

4.8.2 Determination of Sample Size

This is a descriptive investigation and the number of subjects have been chosen to be able to find explorative trends.

4.9 Changes to the Clinical Investigation Plan

No change in the investigation procedure will be effected without the mutual agreement of the Principal Investigator and MHC.

An amendment to the Investigation Plan may require notification or approval from IRB before implementation. Local requirements must be followed.

MHC will distribute clinical investigation plan amendments to the Principal Investigator who is responsible for the distribution of these documents to the IRB and staff involved at his/her site.

5. STATEMENTS OF COMPLIANCE

5.1 Ethics

5.1.1 Ethics review

The final clinical investigation plan, including the final version of the Patient Information and Consent Form, must be approved or given a favorable opinion in writing by an IRB before enrollment of any subject into the investigation. The Principal Investigator is responsible for informing the IRB of any amendment to the investigation plan as per local requirements.

5.1.2 Ethical Conduct of the Investigation

The investigation will be performed in accordance with the ethical principles that have their origin in the most recent version of the Declaration of Helsinki, and with applicable regulatory requirements. Patients, who are close colleagues, associates, or family members of, or in any way dependent on the sponsor or the investigator, will not be included in this investigation.

5.1.3 Patient Information and Consent Form

The Principal Investigator will ensure that the subject is given full and adequate oral and written information about the nature, purpose, possible risks and benefits of the investigation. Subjects must also be notified that they are free to discontinue participation in the investigation at any time. The subject should be given the opportunity to ask questions and time for consideration.

The subject's signed informed consent has to be obtained before conducting any investigation related procedures. The original must be filed by the Principal Investigator. A copy of the Patient Information including the signed Consent Form should be given to the subject.

A sample of the Patient Information and Consent Form is enclosed (Appendix B). If modifications are made according to local requirements, the new version must be approved by MHC.

5.2 Regulatory and standards

5.2.1 Regulatory review

If applicable, the final clinical investigation plan, including the final version of the Patient Information and Consent Form, must be approved or given a favorable opinion in writing by a CA before enrollment of any subject into the investigation. MHC is responsible for informing the CA of any amendment to the investigation plan as per local requirements.

5.2.2 Standards and other

The most recent version of ISO 14155 is followed in addition to national regulations, 21 CFR 50 Protection of Human Subjects, 21 CFR 56 Institutional Review Boards and 21 CFR 54 Financial Disclosure.

5.2.3 Subject Data Protection

The written Patient Information explains that the data will be stored in a computer database, maintaining confidentiality in accordance with national data legislation and that authorized representatives of MHC and/or IRB, require direct access to those parts of the hospital/practice records relevant to the investigation, including medical history, for verification of data. All data computerized by MHC will be identified by subject ID only.

5.3 SUBJECT PROTECTION PROCEDURES

5.3.1 Procedures in Case of Medical Emergency

The Principal Investigator is responsible for ensuring that procedures and expertise are available to cope with medical emergencies during the investigation.

5.3.2 Insurance

Mölnlycke Health Care AB has product liability insurance, which also covers test products.

6. INVESTIGATION TIMETABLE AND TERMINATION

Investigation start: Q1 2017

Inclusion completed: Q2 2017

Last subject out: Q2 2017

The investigation could be prematurely discontinued if the investigation site is unable to fulfill the inclusion period according to the Clinical Investigation Agreement.

7. LITERATURE REVIEW AND REFERENCES

1. Parvizi J, Pawasarat IM, Azzam KA, et al. Periprosthetic joint infection: the economic impact of methicillin-resistant infections. JOA 2010;25(6 Sup):103.

2. Harrington P (2014) Prevention of surgical site infection. Nursing Standard. 28, 48, 50-58. Date of submission: March 7 2014; date of acceptance: April 28 2014.

3. Elie Ghanem, E., Heppert, V. et al., Wound Managment. J Orthop Res 32: 108–S119, 2014

4. Rheinecker,s., Wound Management: The Occlusive Dressing. J Athl Train. 1995 Jun; 30(2): 143-144, 146

5. Baranoski S, Ayello EA., Wound dressings: an evolving art and science. Adv Skin Wound Care. 2012 Feb;25(2):87-92

6. Cosker, T., Elsayed, S., Gupta, S. et al. Choice of dressing has a major impact on blistering and healing outcomes in orthopaedic patients. J Wound Care 2005; 14: 1, 27-29.

7. Tustanowski, J. Effect of dressing choice on outcomes after hip and knee arthroplasty: a literature review. J Wound Care 2009; 18: 11, 449-454.

8. Côte M, Provost J, Denault A, Pelet S. 2010. Presentation on 66th Annual Meeting of Canadian Orthopedic Association: Reduction of tape blisters after hip surgery; A prospective evaluation of three kinds of bandages.

9. Davis, D. Use of an antimicrobial Soft Silicone Borded Foam Dressing as an Adjunctive Treatment with a Single Layer Bioengineered Dermal Tissue, Poster at SAWC 2012

10. Davies, P. Mepilex® Border Ag: A Global In-Market Evaluation (Former Follow-up of the intended use of Mepilex Border Ag), 2013

11. Latenser, B. Open multi-centre investigation to evaluate signs and symptoms of local inflammation/infection on chronic ulcers and partial thickness burns when using Mepilex Border Ag as an anti-microbial wound dressing. MxB Ag 01, 2012

12. Huss, F. An open, non-controlled, post-marketing investigation evaluating the experience of using a self-adherent antimicrobial soft silicone, silver containing, foam dressing, Mepilex Border Ag, in second degree burns MxB Ag, 2011

13. Zarghooni K., Lohmann C., Bredow N., Oppermann A., Krueger B., Wenk J., Meyer H. Effect of a modern dressing compared to a standard dressing on outcome after primary hip and knee arthroplasty, prospective non randomised study. Poster EWMA 2015

8. DEFINITIONS AND PROCEDURES FOR REPORTING OF ADVERSE EVENT, ADVERSE DEVICE EFFECT, SERIOUS ADVERSE EVENT, SERIOUS ADVERSE DEVICE EFFECT AND DEVICE DEFICIENCY

Definitions:

Device Deficiency (DD)
Inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance.

Note:

- Device Deficiencies include malfunctions, use errors, and inadequate labelling.

All Device Deficiencies that might have led to a Serious Adverse Device Effect shall be reported in accordance with Serious Adverse Event reporting procedures, as specified below.

Adverse Event (AE)
Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device

Note:

- This definition includes events related to the investigational medical device or the comparator.
- This definition includes events related to the procedures involved.
- For users or other persons, this definition is restricted to events related to investigational medical devices.

Adverse Device Effect (ADE)
Adverse Event related to the use of an investigational medical device

Note:

- This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, or operation, or any malfunction of the investigational medical device.
- This definition includes any event resulting from use error or from intentional misuse of the investigational medical device.

Serious Adverse Event (SAE)
Adverse Event that:

a) led to death,

b) led to a serious deterioration in the health of the subject, that either resulted in

1) a life-threatening illness or injury, or

2) a permanent impairment of a body structure or a body function, or

3) in-patient hospitalization or prolonged hospitalization or,

4) medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function.

c) led to foetal distress, foetal death or a congenital abnormality or birth defect.

Note:
Planned hospitalization for a pre-existing condition, or a procedure required by the CIP, without serious deterioration in health, is not considered a serious adverse event.

Serious Adverse Device Effect (SADE)

Adverse Device Effect that has resulted in any of the consequences characteristic of a Serious Adverse Event.

PROCEDURES FOR SAE AND/OR SADE REPORTING OR REPORTING OF DD THAT COULD HAVE LED TO A SADE

The investigator must inform Mölnlycke Health Care (MHC), within 1 calender day of awareness of the event. When a SAE/SADE has been entered into the eCRF by the investigator /authorised site staff, the eCRF system will automatically generate a report to: Clinical_Investigations_Event_Reporting@molnlycke.com.

In case of problem with the eCRF, a paper based version of the SAE/SADE report form (available in the Investigator Site File) shall be used and sent by email to: Clinical_Investigations_Event_Reporting@molnlycke.com.

All SAEs/SADEs that occurs during the Clinical Investigation shall be reported, whether or not they are considered causally related to the investigational device.

Device Deficiencies that might have led to SADE if either a) suitable action had not been taken, b) if intervention had not been made, or c) if circumstances had been less fortunate must be reported as a SADE.

The investigator is responsible for informing the EC/IRB and/or the Competent Authority of the SAE/SADE as per local requirements.

PROCEDURES FOR DD REPORTING

All DD shall be reported to MHC as soon as possible, without unjustified delay . If the DD might have led to a SADE the reporting requirements for SADE described above must be followed. DDs can be either subject related or non-subject related depending on if the investigational device was used by a subject or not. Separate forms are used for subject related and non-

subject related DDs. When a subject related DD has been entered into the eCRF by the investigator /authorised site staff, the eCRF system will automatically generate a report to: Clinical_Investigations_Event_Reporting@molnlycke.

Non-subject related DDs are reported using the paper based report form located in the Investigator Site File. The completed form shall be sent by email to Clinical_Investigations_Event_Reporting@molnlycke.com

Causality Assessment

The relationship between the use of the investigational device and the occurrence of each AE/SAE shall be assessed by the investigator and the sponsor and classified as investigational device related or not related to investigational device.

Investigation Code MxB Po Ag 01Final Version CIP Approval date 2016-11-15

Amendment Final Version Amendment Approval date 2016-11-21

CLINICAL INVESTIGATION PLAN (CIP) Central AMENDMENT no 1

Substantial

INVESTIGATIONAL DEVICE:

Mepilex Border Post-Op Ag

INVESTIGATION TITLE:

A single center, open, non-controlled investigation to evaluate the performance of a flexible, self-adherent absorbent silver dressing coated with a soft silicone layer after elective primary total hip or knee arthroplasty

SITES AFFECTED BY THE AMENDMENT:

The amendment affect all in the study

THE CLINICAL INVESTIGATION PLAN (CIP) IS TO BE AMENDED AS FOLLOWS:

Section and page in the Clinical Investigation Plan (CIP):

CIP section: Synopsis / Overall Design

CIP page: 3

From:
This descriptive, prospective, non-controlled clinical investigation will be conducted on approximately 20 enrolled subjects at one site in the US.
The target subjects are male or female, 18 years and older, undergoing elective primary hip or knee arthroplasty with a possibility to participate in a follow-up visit 7 days after surgery. Subjects will consecutively be allocated to a subject ID. ~~The subjects will be followed 1-3 days after surgery and scheduled for a follow-up visit 7 days after surgery.~~

To:
This descriptive, prospective, non-controlled clinical investigation will be conducted on approximately 20 enrolled subjects at one site in the US.

The target subjects are male or female, 18 years and older, undergoing elective primary hip or knee arthroplasty with a possibility to participate in a follow-up visit 7 days after surgery. Subjects will consecutively be allocated to a subject ID.
Subjects at site number 01 are usually sent home on post-op day one (1) or two (2). If the subject are sent home post-op day two (2) this investigation will include a telephone follow-up on post-op day two (2), clinic visit on post-op day three (3) and a follow-up visit on post-op day 7 when the dressing is removed and the incision and incision site are inspected before termination. If the dressing is changed prior to post-op day 7 and outside scheduled visits, an unscheduled visit will be performed.

CIP section: Synopsis / Schedule of Assessment & 4.2.1 **Schedule of Assessment**

CIP page: 5 & 15

From:

Day	Baseline (screening visit)	**Day 0 Day of surgery**	Day 1 1st post - op day	Day 2 2nd post-op day[a]	Day 3 3rd post-op day[a]	Unscheduled visit[b]	Day 7 7th post-op day	Termination
Visit window/days	-21 to 0	0	0	0	0	0	-2 to 0[c]	0
Visit (number)	1	2	3	4	5	Unscheduled	6	Termination

Investigation Code MxB Po Ag 01Final Version CIP Approval date 2016-11-15

Amendment Final Version Amendment Approval date 2016-11-21

Day	Baseline (screening visit)	**Day 0 Day of surgery**	Day 1 1st post - op day	Day 2 2nd post-op day[a]	Day 3 3rd post-op day[a]	Unscheduled visit[b]	Day 7 7th post-op day	Termination
Inclusion/ Exclusion Criteria	✓	✓						
Informed Consent	✓							
Subject ID	✓							
Subject demography	✓							
Skin status at incision site	~~✓~~							
Medical /Surgical history	✓							
Type of surgery		✓						
Surgical incision condition		✓	✓	✓	✓	✓	✓	
Performance of the dressing		✓	✓	✓	✓	✓	✓	
Dressing log[d]		✓	(✓)	(✓)	(✓)	✓	✓	
Medication Log	✓	✓	✓	✓	✓	✓	✓	
Pain assessment[e]			(✓)	(✓)	(✓)	✓	✓	
Photos[f]		✓	✓	✓	✓	✓	✓	
Nurse/investigator evaluation[g]		✓	✓	✓	✓	✓	✓	
Subject evaluation[h]			✓	✓	✓	✓	✓	
Reason for termination								✓
AE/ADE/SAE/SADE/DD	✓	✓	✓	✓	✓	✓	✓	

a Information will be collected at Day 3 only if the subject is still at the hospital and hasn´t been discharged

b If the dressing is changed prior to post-op day 7 and outside scheduled visits, an unscheduled visit will be performed.

c When possible, visit 6 should be scheduled to post-op day 7. When not possible due to weekends, post-op day 5 or post-op day 6 could be scheduled.

d Dressing application/change/removal will be documented in the Dressing log. Ability to stay on (curl up at edges and partial/complete detachment) will also be collected

e Pain assessment at dressing removal (VAS). If a dressing change is deemed necessary prior to visit 6, pain assessment should be collected

f Photos should be taken at visit 2 (at the incision before application of the dressing, at dressing after application of the dressing) and if the dressing is changed at visit 3-6 (at the dressing before removal of the dressing, at the incision after removal of the dressing and at dressing (side facing the incision) , if signs of infection and if there in an unscheduled visit

g The nurse or the investigator will give their assessment concerning the treatment

h The nurse or the investigator will collect the subject´s experience via interview

To:

Day	Baseline (screening visit)	**Day 0 Day of surgery**	Day 1 1st post - op day	Day 2 2nd post-op day[a]	Day 2 2nd post-op Telephone Follow-Up i	Day 3 3rd post-op day[a]	Un-scheduled visit[b]	Day 7 7th post-op day	Term-ination
Visit window/days	-21 to 0	0	0	0	0	0	0	-2 to 0[c]	0
Visit (number)	1	2	3	4	4	5	Un-scheduled	6	Term-ination
Inclusion/ Exclusion Criteria	✓	✓							
Informed Consent	✓								
Subject ID	✓								
Subject demography	✓								
Skin status at incision site		✓							
Medical /Surgical history	✓								
Type of surgery		✓							
Surgical incision condition		✓	✓	✓		✓	✓	✓	
Performance of the dressing		✓	✓	✓		✓	✓	✓	
Dressing log[d]		✓	(✓)	(✓)		(✓)	✓	✓	
Medication Log	✓	✓	✓	✓	✓	✓	✓	✓	
Pain assessment[e]			(✓)	(✓)		(✓)	✓	✓	
Photos[f]		✓	✓	✓		✓	✓	✓	
Nurse/investigator evaluation[g]		✓	✓	✓		✓	✓	✓	
Subject evaluation[h]			✓	✓		✓	✓	✓	
Reason for termination									✓
AE/ADE/SAE/SADE/DD	✓	✓	✓	✓	✓	✓	✓	✓	

a Information will be collected at Day 3 only if the subject is still at the hospital and hasn´t been discharged

b If the dressing is changed prior to post-op day 7 and outside scheduled visits, an unscheduled visit will be performed.

c When possible, visit 6 should be scheduled to post-op day 7. When not possible due to weekends, post-op day 5 or post-op day 6 could be scheduled.

d Dressing application/change/removal will be documented in the Dressing log. Ability to stay on (curl up at edges and partial/complete detachment) will also be collected

e Pain assessment at dressing removal (VAS). If a dressing change is deemed necessary prior to visit 6, pain assessment should be collected

f Photos should be taken at visit 2 (at the incision before application of the dressing, at dressing after application of the dressing) and if the dressing is changed at visit 3-6 (at the dressing before removal of the dressing, at the incision after removal of the dressing and at dressing (side facing the incision) , if signs of infection and if there in an unscheduled visit

g The nurse or the investigator will give their assessment concerning the treatment

h The nurse or the investigator will collect the subject´s experience via interview

i Telephone Follow-Up

CIP section: 4.1 Overall Design
CIP page: 14

From:
This single center, open, non-controlled investigation will be conducted at one site in the US.

Approximately 20 male or female subjects, 18 years or older, with a planned elective primary total hip or knee replacement will be recruited in this investigation. The primary purpose is to investigate if there is any skin damage under the dressing from operation day to last visit. Performance of the dressing as well as comfort, conformability, acceptability and pain at dressing removal will also be followed-up until post-op day 7. ~~Subjects at site number 01 are usually sent home on post-op day two or three but this investigation will include a follow-up visit on post-op day 7 when the dressing is removed and the incision and incision site are inspected before termination.~~ If it is not possible to schedule a visit at post-op day 7 due to weekends, it is ok to schedule a visit for post-op day 5 or 6. Post-op day 7 is however the day to strive for.

To:
This single center, open, non-controlled investigation will be conducted at one site in the US.

Approximately 20 male or female subjects, 18 years or older, with a planned elective primary total hip or knee replacement will be recruited in this investigation. The primary purpose is to investigate if there is any skin damage under the dressing from operation day to last visit. Performance of the dressing as well as comfort, conformability, acceptability and pain at dressing removal will also be followed-up until post-op day 7. Subjects at site number 01 are usually sent home on post-op day one (1) or two (2). If the subject are sent home post-op day two (2) this investigation will include a telephone follow-up on post-op day two (2), clinic visit on post-op day three (3) and a follow-up visit on post-op day 7 when the dressing is removed and the incision and incision site are inspected before termination. If the dressing is changed prior to post-op day 7 and outside scheduled visits, an unscheduled visit will be performed.
If it is not possible to schedule a visit at post-op day 7 due to weekends, it is ok to schedule a visit for post-op day 5 or 6. Post-op day 7 is however the day to strive for.

CIP section: 4.1 Labelling
CIP page: 18

From:
MHC will provide the investigational medical devices to the investigation site for free. Labelling of the investigational medical device will be performed in accordance with Good Manufacturing Practice (GMP). The labels will be produced in the local language and in accordance with local regulations for the US. The medical device will be marked with the following text:

Mepilex Border Post-Op Ag
Study Code: MxB Po Ag 01

~~"CAUTION - Investigational Device. Limited by Federal (or United States) law to investigational use."~~

To:
MHC will provide the investigational medical devices to the investigation site for free. Labelling of the investigational medical device will be performed in accordance with Good Manufacturing Practice (GMP). The labels will be produced in the local language and in accordance with local regulations for the US. The medical device will be marked with the following text:

Mepilex Border Post-Op Ag
Study Code: MxB Po Ag 01
Investigational Device - Not for Resale

REASON FOR MAKING THE AMENDMENT:

Reason for making the amendment:

According to standard of care on site no 01. Subjects are usually sent home on post-op day one (1) and not post-op day three (3). The clinical investigation plan was updated to fit the standard of care on site no 01.

Correcting typing errors: discrepancies between the label specification and labelling section in the clinical investigation plan.

ACTIONS TO BE TAKEN:

Investigator at the site will be provided with the amendment and signature will be collected.

The Amendment will be sent to the IRB for approval according to local procedures.

Title: CIP Amendment No 02

Investigation Code MxB Po Ag 01Final Version CIP Approval date 2016-11-15

Amendment Final Version Amendment Approval date 2017-01-20

CLINICAL INVESTIGATION PLAN (CIP) Central AMENDMENT no 2

Substantial

INVESTIGATIONAL DEVICE:

Mepilex Border Post-Op Ag

INVESTIGATION TITLE:

A single center, open, non-controlled investigation to evaluate the performance of a flexible, self-adherent absorbent silver dressing coated with a soft silicone layer after elective primary total hip or knee arthroplasty

SITES AFFECTED BY THE AMENDMENT:

The amendment affect all in the study

Title: CIP Amendment No 02

Investigation Code MxB Po Ag 01Final Version CIP Approval date 2016-11-15

Amendment Final Version Amendment Approval date 2017-01-20

THE CLINICAL INVESTIGATION PLAN (CIP) IS TO BE AMENDED AS FOLLOWS:

Section and page in the Clinical Investigation Plan (CIP):

CIP section: Synopsis / Overall Design

CIP page: 3

From:

Subjects at site number 01 are usually sent home on post-op day one (1) or two (2). If the subject are sent home post-op day two (2) this investigation will include a telephone follow-up on post-op day two (2), clinic visit on post-op day three (3) and a follow-up visit on post-op day 7 when the dressing is removed and the incision and incision site are inspected before termination. If the dressing is changed prior to post-op day 7 and outside scheduled visits, an unscheduled visit will be performed

To:

Subjects at site number 01 are usually sent home on post-op day one (1) or two (2). If the subject are sent home post-op day two (2) this investigation will include a telephone follow-up on post-op day two (2), clinic visit on post-op day three (3) (+ 1 day) and a follow-up visit on post-op day 7 when the dressing is removed and the incision and incision site are inspected before termination. If the dressing is changed prior to post-op day 7 and outside scheduled visits, an unscheduled visit will be performed

CIP section: 4.1 Overall Design

CIP page: 14

From:

This single center, open, non-controlled investigation will be conducted at one site in the US.

Approximately 20 male or female subjects, 18 years or older, with a planned elective primary total hip or knee replacement will be recruited in this investigation. The primary purpose is to investigate if there is any skin damage under the dressing from operation day to last visit. Performance of the dressing as well as comfort, conformability, acceptability and pain at dressing removal will also be followed-up until post-op day 7. Subjects at site number 01 are usually sent home on post-op day one (1) or two (2). If the subject are sent home post-op day two (2) this investigation will include a telephone follow-up on post-op day two (2), clinic visit on post-op day three (3) and a follow-up visit on post-op day 7 when the dressing is removed and the incision and incision site are inspected before termination. If the dressing is changed prior to post-op day 7 and outside scheduled visits, an unscheduled visit will be performed.
If it is not possible to schedule a visit at post-op day 7 due to weekends, it is ok to schedule a visit for post-op day 5 or 6. Post-op day 7 is however the day to strive for.

Title: CIP Amendment No 02

Investigation Code MxB Po Ag 01Final Version CIP Approval date 2016-11-15

Amendment Final Version Amendment Approval date 2017-01-20

To:

This single center, open, non-controlled investigation will be conducted at one site in the US.

Approximately 20 male or female subjects, 18 years or older, with a planned elective primary total hip or knee replacement will be recruited in this investigation. The primary purpose is to investigate if there is any skin damage under the dressing from operation day to last visit. Performance of the dressing as well as comfort, conformability, acceptability and pain at dressing removal will also be followed-up until post-op day 7. Subjects at site number 01 are usually sent home on post-op day one (1) or two (2). If the subject are sent home post-op day two (2) this investigation will include a telephone follow-up on post-op day two (2), clinic visit on post-op day three (3) (+1 day) and a follow-up visit on post-op day 7 when the dressing is removed and the incision and incision site are inspected before termination. If the dressing is changed prior to post-op day 7 and outside scheduled visits, an unscheduled visit will be performed.
If it is not possible to schedule a visit at post-op day 7 due to weekends, it is ok to schedule a visit for post-op day 5 or 6. Post-op day 7 is however the day to strive for.

CIP section: Synopsis / Schedule of Assessment & 4.2.1 Schedule of Assessment

CIP page: 5 & 15

From:

Day	Baseline (screening visit)	Day 0 Day of surgery	Day 1 1st post - op day	Day 2 2nd post-op day[a]	Day 2 2nd post-op Telephone Follow-Up i	Day 3 3rd post-op day[a]	Un-scheduled visit[b]	Day 7 7th post-op day	Term-ination
Visit window/days	-21 to 0	0	0	0	0	~~0~~	0	-2 to 0[c]	0
Visit (number)	1	2	3	4	4	5	Un-scheduled	6	Term-ination
Inclusion/ Exclusion Criteria	✓	✓							
Informed Consent	✓								
Subject ID	✓								
Subject demography	✓								
Skin status at incision site		✓							
Medical /Surgical history	✓								
Type of surgery		✓							
Surgical incision condition		✓	✓	✓		✓	✓	✓	
Performance of the dressing		✓	✓	✓		✓	✓	✓	
Dressing log[d]		✓	(✓)	(✓)		(✓)	✓	✓	

Title: CIP Amendment No 02

Investigation Code MxB Po Ag 01Final Version CIP Approval date 2016-11-15

Amendment Final Version Amendment Approval date 2017-01-20

Day	Baseline (screening visit)	Day 0 Day of surgery	Day 1 1st post - op day	Day 2 2nd post-op day[a]	Day 2 2nd post-op Telephone Follow-Up i	Day 3 3rd post-op day[a]	Un-scheduled visit[b]	Day 7 7th post-op day	Term-ination
Medication Log	✓	✓	✓	✓	✓	✓	✓	✓	
Pain assessment[e]			(✓)	(✓)		(✓)	✓	✓	
Photos[f]		✓	✓	✓		✓	✓	✓	
Nurse/investigator evaluation[g]		✓	✓	✓		✓	✓	✓	
Subject evaluation[h]			✓	✓		✓	✓	✓	
Reason for termination									✓
AE/ADE/SAE/SADE/DD	✓	✓	✓	✓	✓	✓	✓	✓	

a Information will be collected at Day 3 only if the subject is still at the hospital and hasn´t been discharged

b If the dressing is changed prior to post-op day 7 and outside scheduled visits, an unscheduled visit will be performed.

c When possible, visit 6 should be scheduled to post-op day 7. When not possible due to weekends, post-op day 5 or post-op day 6 could be scheduled.

d Dressing application/change/removal will be documented in the Dressing log. Ability to stay on (curl up at edges and partial/complete detachment) will also be collected

e Pain assessment at dressing removal (VAS). If a dressing change is deemed necessary prior to visit 6, pain assessment should be collected

f Photos should be taken at visit 2 (at the incision before application of the dressing, at dressing after application of the dressing) and if the dressing is changed at visit 3-6 (at the dressing before removal of the dressing, at the incision after removal of the dressing and at dressing (side facing the incision) , if signs of infection and if there in an unscheduled visit

g The ~~nurse or the investigator~~ will give their assessment concerning the treatment

h The ~~nurse or the investigator~~ will collect the subject´s experience via interview

To:

Day	Baseline (screening visit)	Day 0 Day of surgery	Day 1 1st post - op day	Day 2 2nd post-op day[a]	Day 2 2nd post-op Telephone Follow-Up i	Day 3 3rd post-op day[a]	Un-scheduled visit[b]	Day 7 7th post-op day	Term-ination
Visit window/days	-21 to 0	0	0	0	0	+1	0	-2 to 0[c]	0
Visit (number)	1	2	3	4	4	5	Un-scheduled	6	Term-ination
Inclusion/ Exclusion Criteria	✓	✓							
Informed Consent	✓								
Subject ID	✓								
Subject demography	✓								
Skin status at incision site		✓							
Medical /Surgical history	✓								

Title: CIP Amendment No 02

Investigation Code MxB Po Ag 01Final Version CIP Approval date 2016-11-15

Amendment Final Version Amendment Approval date 2017-01-20

Day	Baseline (screening visit)	Day 0 Day of surgery	Day 1 1st post - op day	Day 2 2nd post-op day[a]	Day 2 2nd post-op Telephone Follow-Up i	Day 3 3rd post-op day[a]	Un-scheduled visit[b]	Day 7 7th post-op day	Term-ination
Type of surgery		✓							
Surgical incision condition		✓	✓	✓		✓	✓	✓	
Performance of the dressing		✓	✓	✓		✓	✓	✓	
Dressing log[d]		✓	(✓)	(✓)		(✓)	✓	✓	
Medication Log	✓	✓	✓	✓	✓	✓	✓	✓	
Pain assessment[e]			(✓)	(✓)		(✓)	✓	✓	
Photos[f]		✓	✓	✓		✓	✓	✓	
Nurse/investigator evaluation[g]		✓	✓	✓		✓	✓	✓	
Subject evaluation[h]			✓	✓		✓	✓	✓	
Reason for termination									✓
AE/ADE/SAE/SADE/DD	✓	✓	✓	✓	✓	✓	✓	✓	

a Information will be collected at Day 3 only if the subject is still at the hospital and hasn´t been discharged

b If the dressing is changed prior to post-op day 7 and outside scheduled visits, an unscheduled visit will be performed.

c When possible, visit 6 should be scheduled to post-op day 7. When not possible due to weekends, post-op day 5 or post-op day 6 could be scheduled.

d Dressing application/change/removal will be documented in the Dressing log. Ability to stay on (curl up at edges and partial/complete detachment) will also be collected

e Pain assessment at dressing removal (VAS). If a dressing change is deemed necessary prior to visit 6, pain assessment should be collected

f Photos should be taken at visit 2 (at the incision before application of the dressing, at dressing after application of the dressing) and if the dressing is changed at visit 3-6 (at the dressing before removal of the dressing, at the incision after removal of the dressing and at dressing (side facing the incision) , if signs of infection and if there in an unscheduled visit

g The research staff will give their assessment concerning the treatment

h The research staff will collect the subject´s experience via interview

i Telephone Follow-Up

Title: CIP Amendment No 02

Investigation Code MxB Po Ag 01Final Version CIP Approval date 2016-11-15

Amendment Final Version Amendment Approval date 2017-01-20

REASON FOR MAKING THE AMENDMENT:

Reason for making the amendment:

According to standard of care on site no 01, the surgeries are usually performed Monday and Thursdays, to add a visit window of one day on post-op day three (3), will avoid the need to return for a follow-up to the clinic during the weekend. The clinical investigation plan was updated to fit the standard of care on site no 01, the recruitment has not started.

ACTIONS TO BE TAKEN:

Investigator at the site will be provided with the amendment and signature will be collected.

The Amendment will be sent to the IRB for approval according to local procedures.

Title: CIP Non-substantial amendment 01

Investigation Code	**MxB Po Ag 01Final Version**	**CIP Approval date**	**2016-11-15**
Amendment Final Version		**Amendment Approval date**	**2016-12-01**

CLINICAL INVESTIGATION PLAN (CIP) Central AMENDMENT no 2

Non Substantial

INVESTIGATIONAL DEVICE:

Mepilex Border Post-Op Ag

INVESTIGATION TITLE:

A single center, open, non-controlled investigation to evaluate the performance of a flexible, self-adherent absorbent silver dressing coated with a soft silicone layer after elective primary total hip or knee arthroplasty

SITES AFFECTED BY THE AMENDMENT:

The amendment affect all in the study

THE CLINICAL INVESTIGATION PLAN (CIP) IS TO BE AMENDED AS FOLLOWS:

Section and page in the Clinical Investigation Plan:

CIP section: Synopsis / Schedule of Assessment & 4.2.1 **Schedule of Assessment**

CIP page: 5 & 15

From:

Day	Baseline (screening visit)	**Day 0 Day of surgery**	Day 1 1st post - op day	Day 2 2nd post-op day[a]	Day 2 2nd post-op Telephone Follow-Up i	Day 3 3rd post-op day[a]	Un-scheduled visit[b]	Day 7 7th post-op day	Term-ination
Visit window/days	-21 to 0	0	0	0	0	0	0	-2 to 0[c]	0
Visit (number)	1	2	3	4	4	5	Un-scheduled	6	Term-ination
Inclusion/ Exclusion Criteria	✓	✓							
Informed Consent	✓								
Subject ID	✓								
Subject demography	✓								
Skin status at incision site		✓							
Medical /Surgical history	✓								
Type of surgery		✓							
Surgical incision condition		✓	✓	✓		✓	✓	✓	
Performance of the dressing		✓	✓	✓		✓	✓	✓	
Dressing log[d]		✓	(✓)	(✓)		(✓)	✓	✓	
Medication Log	✓	✓	✓	✓	✓	✓	✓	✓	
Pain assessment[e]			(✓)	(✓)		(✓)	✓	✓	
Photos[f]		✓	✓	✓		✓	✓	✓	
Nurse/investigator evaluation[g]		✓	✓	✓		✓	✓	✓	
Subject evaluation[h]			✓	✓		✓	✓	✓	
Reason for termination									✓
AE/ADE/SAE/SADE/DD	✓	✓	✓	✓	✓	✓	✓	✓	

a Information will be collected at Day 3 ~~only if the subject is still at the hospital and hasn´t been discharged~~

b If the dressing is changed prior to post-op day 7 and outside scheduled visits, an unscheduled visit will be performed.

c When possible, visit 6 should be scheduled to post-op day 7. When not possible due to weekends, post-op day 5 or post-op day 6 could be scheduled.

d Dressing application/change/removal will be documented in the Dressing log. Ability to stay on (curl up at edges and partial/complete detachment) will also be collected

e Pain assessment at dressing removal (VAS). If a dressing change is deemed necessary prior to visit 6, pain assessment should be collected

f Photos should be taken at visit 2 (at the incision before application of the dressing, at dressing after application of the dressing) and if the dressing is changed at visit 3-6 (at the dressing before removal of the dressing, at the incision after removal of the dressing and at dressing (side facing the incision) , if signs of infection and if there in an unscheduled visit

g The nurse or the investigator will give their assessment concerning the treatment

h The nurse or the investigator will collect the subject´s experience via interview

i Telephone Follow-Up

To:

Day	Baseline (screening visit)	**Day 0 Day of surgery**	Day 1 1st post - op day	Day 2 2nd post-op day[a]	Day 2 2nd post-op Telephone Follow-Up i	Day 3 3rd post-op day[a]	Un-scheduled visit[b]	Day 7 7th post-op day	Term-ination
Visit window/days	-21 to 0	0	0	0	0	0	0	-2 to 0[c]	0
Visit (number)	1	2	3	4	4	5	Un-scheduled	6	Term-ination
Inclusion/ Exclusion Criteria	✓	✓							
Informed Consent	✓								
Subject ID	✓								
Subject demography	✓								
Skin status at incision site		✓							
Medical /Surgical history	✓								
Type of surgery		✓							
Surgical incision condition		✓	✓	✓		✓	✓	✓	
Performance of the dressing		✓	✓	✓		✓	✓	✓	
Dressing log[d]		✓	(✓)	(✓)		(✓)	✓	✓	
Medication Log	✓	✓	✓	✓	✓	✓	✓	✓	
Pain assessment[e]			(✓)	(✓)		(✓)	✓	✓	
Photos[f]		✓	✓	✓		✓	✓	✓	
Nurse/investigator evaluation[g]		✓	✓	✓		✓	✓	✓	

Day	Baseline (screening visit)	**Day 0 Day of surgery**	Day 1 1st post - op day	Day 2 2nd post-op day[a]	Day 2 2nd post-op Telephone Follow-Up i	Day 3 3rd post-op day[a]	Un-scheduled visit[b]	Day 7 7th post-op day	Term-ination
Subject evaluation[h]			✓	✓		✓	✓	✓	
Reason for termination									✓
AE/ADE/SAE/SADE/DD	✓	✓	✓	✓	✓	✓	✓	✓	

a Information will be collected at Day 3 at the hospital or as outpatient visit

b If the dressing is changed prior to post-op day 7 and outside scheduled visits, an unscheduled visit will be performed.

c When possible, visit 6 should be scheduled to post-op day 7. When not possible due to weekends, post-op day 5 or post-op day 6 could be scheduled.

d Dressing application/change/removal will be documented in the Dressing log. Ability to stay on (curl up at edges and partial/complete detachment) will also be collected

e Pain assessment at dressing removal (VAS). If a dressing change is deemed necessary prior to visit 6, pain assessment should be collected

f Photos should be taken at visit 2 (at the incision before application of the dressing, at dressing after application of the dressing) and if the dressing is changed at visit 3-6 (at the dressing before removal of the dressing, at the incision after removal of the dressing and at dressing (side facing the incision) , if signs of infection and if there in an unscheduled visit

g The nurse or the investigator will give their assessment concerning the treatment

h The nurse or the investigator will collect the subject´s experience via interview

i Telephone Follow-Up

REASON FOR MAKING THE AMENDMENT:

Typing error, inconsistency between Overall Design and Scheduled of Assessment in the CIP body.

ACTIONS TO BE TAKEN:

Protocol updated with the corrections.