MÉXICO

Department of Medical Benefits
Education Unit. Research and Health Policies
Coordination of Health Research

***2015. Year of Generalissimo José María Morelos y Pavón*.**

19 June 2015

Ref 09-B5-61-2800/201500/**1751**

Dr AVILA JIMENEZ LAURA
Auxiliary Medical Coordination for Health Research in Morelos
Morelos

I hereby inform you that protocol entitled: **ASSESSMENT OF EFFECTIVENESS AND SAFETY OF THE USE OF TISSUPOR® 3D EMBROIDERY DRESSINGS FOR WOUNDS IN PATIENTS WITH NEUROPATHIC ULCERATION ON THE DIABETIC FOOT** was submitted for the analysis of this National Commission for Scientific Research.

Procedures proposed in the protocol meet requirements of current standards, according to the opinions of the members of the Ethics and Science Commission. An **AUTHORISED** expert opinion has been issued, with record number: R-2015-785-058.

In accordance with current legislation, you shall inform this Commission in January and July of each year about the development of the project you are in charge of. This expert opinion has a validity period of only one year. Therefore, if necessary, you will be asked to request another authorisation to the Research Ethics Commission of the National Commission for Scientific Research at the end of the term.

Regards,

Dr Fabio Salamanca Gómez
Chairman
National Commission for Scientific Research

Remarks Annex:

JMMA/ iah. F-CNIC-2015-55

MEXICAN SOCIAL SECURITY INSTITUTE
DEPARTMENT OF MEDICAL BENEFITS
Coordination of Health Research

"Follow-up technical report for research protocols in collaboration with the pharmaceutical industry"

I. Identification information of the Researcher in charge:

Name	ÁVILA	JIMÉNEZ	LAURA
	Paternal surname	Maternal surname	Name(s)
Adscription:	Auxiliary Medical Coordinator for Health Research		Morelos Borough
	Service	Medical Care Facility or Research Centre Facility or Unit	

Address of the adscription: Boulevard Benito Juárez No. 18, Col. Centro, Cuernavaca Morelos

Email(s): laura.avilaj@imss.gob.mx

Phone, extension and institutional network No.: 777 3295100 ext. 51142 / 777 3187632

II. Research Protocol Information:

Title: "ASSESSMENT OF EFFECTIVENESS AND SAFETY OF THE USE OF TISSUPOR® 3D EMBROIDERY DRESSINGS FOR WOUNDS IN PATIENTS WITH NEUROPATHIC ULCERATION ON THE DIABETIC FOOT"

Pharmaceutical Laboratory or CRO: INTERSUIMEX S.A. DE C.V.

Record number of the National Centre for Scientific Research: _____

Authorisation date: 19 / 06 / 15

III. Co-operation Agreement:

Folio: _____

Date of signature: _____

Term or validity: (in months) 24 months

(IT MUST BE A PERIOD OF UP TO FOUR YEARS; AN AMENDING AGREEMENT SHALL BE REQUESTED OTHERWISE)

Financing percentage: 1) 70/30% [X] 2) Other [ ] _____ (specify) 3) Not applicable [ ]

Number of patients intended to include: 57

Number of consultations intended to be granted per patient: 4

Protocol start date: [ ][ ][ ]

Protocol end date: [ ][ ][ ]

Full name of the facility/facilities where the research protocol shall be carried out:
Hospital General Regional con Medicina Familiar No 1 "Lic. Ignacio García Téllez"
Hospital General de Zona con Medicina Familiar No. 5
Hospital General de Zona con Medicina Familiar No 7

Is the research protocol a multi-centre study? NO [ ] YES [XX]

How many care facilities participate?

a) Number 3 b) Unknown _____

Password 2850-009-001

MEXICAN SOCIAL SECURITY INSTITUTE
DEPARTMENT OF MEDICAL BENEFITS

Coordination of Health Research

IV. Research Protocol Follow-up. Semester being informed about:

First ☐ Second ☐ Third ☐ Fourth ☐

Another semester (mark the number) ☐ Authorisation date: ☐☐☐

Number of	In this period	Since the start of the study
Patients enrolled		
Consultations granted		

FUNDING BALANCE TO THIS DATE $ Date:

COMPENSATION AMOUNTS:

Do you get compensation in the protocol you are reporting?	**NO**	**YES X**	Monthly amount: **$ 8,000.00**

Do you get compensation for other research protocols related to the Pharmaceutical Industry?	**NO X**	**YES**

Specify the record number of the National Centre for Scientific Research (Centro Nacional de Investigaciones Científicas, CNIC) of other protocols you get compensation for.

1) Total monthly amount of the compensation:

2) $

V. Adverse effects on patients during this period:

Adverse effects are related to the study drug	NO	YES
Adverse effects were reported to the CNIC	NO	YES (date)

VI. If the study has concluded within the co-operation agreement terms:

Study end date: ☐☐☐

Remarks, comments, or pending issues:

Report drafting date ☐☐☐

PhD in Sciences LAURA ÁVILA JIMÉNEZ
Name and signature of the researcher in charge

VII. Information to be completed only by the Coordination of Health Research

Number of	In this period	Since the start of the study	Initial expectations	Goal achieved	Percentage
Patients enrolled					
Consultations granted					

Password 2850-009-001

Department of Medical Benefits
Education Unit. Research and Health Policies
Coordination of Health Research
National Commission for Scientific Research

07 March 2016

Ref. 09-B5-61-2800/201600/**0744**

Dr LAURA AVILA JIMÉNEZ
Auxiliary Medical Coordination for Health Research in Morelos
Cuernavaca, Morelos

Regarding your request to examine the documents of the project, **ASSESSMENT OF EFFECTIVENESS AND SAFETY OF THE USE OF TISSUPOR® 3D EMBROIDERY DRESSINGS FOR WOUNDS IN PATIENTS WITH NEUROPATHIC ULCERATION ON THE DIABETIC FOOT**, I hereby inform you that the Research Ethics Committee **CONBIOÉTICA09CEI01520130424**, accepts the document entitled "Technical Summary of Protocol Assessment of Effectiveness and Safety of the Use of Tissupor® 3D Embroidery Dressings for Wounds in Patients with Neuropathic Ulceration on the Diabetic Foot" in its first version dated 25 February 2016.

This study shall be carried out by Dr Laura Ávila Jiménez as main researcher in charge, of Hospital General Regional - MF - No. 1, Cuernavaca, Morelos.

Regards,

Dr Fabio Salamanca Gómez
Legal Representative
National Commission for Health Research
Centro Médico Nacional Siglo XXI
Record COFEPRIS CEI 12 CEI 09 006 14
Record COFEPRIS CI 13 CI 09 015 213
Record COFEPRIS CB 13 CB 09 015 214

Dr Niels Agustín H. Wachcr Rodarte
Chairman of the Research Ethics Committee
Coordination of Health Research
Centro Médico Nacional Siglo XXI

ASSESSMENT OF EFFECTIVENESS AND SAFETY OF THE USE OF TISSUPOR® 3D EMBROIDERY DRESSINGS FOR WOUNDS IN PATIENTS WITH NEUROPATHIC ULCERATION ON THE DIABETIC FOOT

Researcher in charge:
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Spanish	*English*
Coordinación de Investigación en Salud	*Coordination of Health Research*
Comité de Ética en Investigación	*Research Ethics Committee*
CONBIOÉTICA09CE101520138()424	*CONBIOÉTICA09CE101520138()424*
Aprobado	*APPROVED*

ASSESSMENT OF EFFECTIVENESS AND SAFETY OF THE USE OF TISSUPOR® 3D EMBROIDERY DRESSINGS FOR WOUNDS IN PATIENTS WITH NEUROPATHIC ULCERATION ON THE DIABETIC FOOT.

Avila-Jiménez, Laura[1]; Cedillo-Flores, Marco Antonio[2]; Romero-Ramirez, Anita[3].

1. Auxiliary Medical Coordination for Health Research, Headquarters of Medical Benefits Services, Morelos Borough. 2. Hospital General de Zona con Medicina Familiar No. 5, Zacatepec, Morelos. 3. Coordination of Planning and Institutional Liaison, Headquarters of Medical Benefits Services, Morelos Borough.

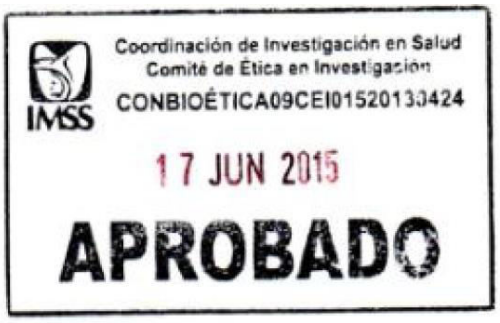
SUMMARY

Introduction: Being the ulceration of the diabetic foot the most common complication of DM, with a prevalence of four to ten percent among patients with DM, the challenge for society and health systems is immense due to the economic cost and the loss of quality of life for patients suffering from diabetes and their families, as well as for the significant resources they need in the public health system for their care.

Dressings used after wound excision are designed to keep the wound clean and free from contamination, as well as to enhance its healing. In particular, the action mechanism of the TISSUPOR® 3D EMBROIDERY dressing is to trigger a mechanical stimulus that allows an ordered structure for granulation, and it enhances angiogenesis by means of a mechanic stimulation of the wound bed, but there are no studies whatsoever reaching a conclusion regarding their effectiveness and safety.

Purpose: To assess the effectiveness and safety of the use of TISSUPOR® 3D EMBROIDERY dressings for wounds in patients with ulceration on the diabetic foot.

Materials and methods: The project shall be conducted in three hospitals of Morelos borough of the National Commission for Scientific Research of the Mexican Social Security Institute (Instituto Mexicano de Seguridad Social, IMSS), where there are outpatient care, hospitalisation, urgent care, and diagnostic auxiliaries services. A randomised double-blind controlled clinical trial shall be carried out. Patients shall be recruited according to eligibility criteria. Patients to be included shall have diagnostics of Diabetes Mellitus type 2 recorded on the clinical file, be aged 18-80, with full-thickness ulceration on the foot, of at least two weeks before they are admitted to the study, with a Wagner 1 or 2 classification, and shall have provided



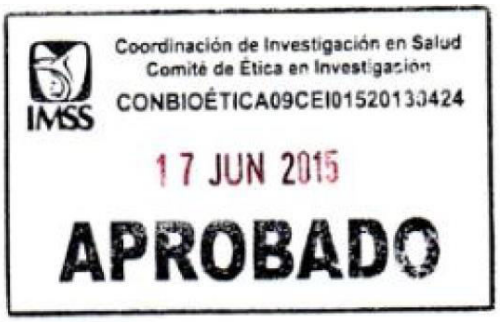
written informed consent. Patients excluded shall be those having ulcerations in epithelisation phase, deep ulceration with abscess, acute osteitis or joint sepsis, localised gangrene (forefoot or heel), extensive gangrene or serious infection. Patients who lack availability to continue with the treatment shall be removed from the project. After getting the informed consent form, patients selected in HGR MF1 and HGZ MF5 (n=57) shall constitute the intervention arm (use of TISSUPOR® 3D EMBROIDERY dressings for wounds), and patients selected in HGZ MF7 (n=57) shall constitute the control arm (local treatment proposed by clinical guide based on evidence for the treatment of the diabetic foot).
The main event is the measurement of the effectiveness of the use of TISSUPOR® 3D EMBROIDERY dressings for wounds, operationalised as a reduction of the ulcer area, where a reduction of 24% after 12 weeks of the size of the ulcer to 4 weeks by means of a digitalised assessment of the print obtained in triplicate by a trained and standardised observer.

The procedure to record the wound surface area (WSA) shall be the following:
In each visit, and before the placement of the dressing, a transparent and sterilised film shall be placed (transparent Visitrak of 2 layers) over the wound, and the perimeter of the ulcer shall be traced with a permanent marker. Each ulcer shall be measured three times in order to ensure measurement reliability. The tracing shall be digitalised by means of an A4 G-Note 7100 digitizer tablet using a wireless mouse, and a high precision wireless pointer pencil (KYE systems, Corp, China); the digitalised tracing shall be exported to a specialised computer program (Photoshop C4me) to calculate the wound surface area.
The percentage of the reduction of the surface area of the ulcer shall be calculated with this equation:

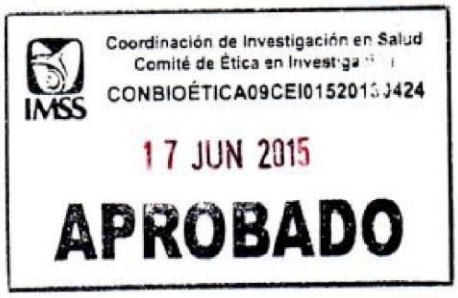
WSA % = [initial WSA (cm^2) - WSA (cm^2) during week 1] X 100

WSA: wound surface area

The percentage of wounds that have been completely closed shall be identified in each measurement (once every 8 calendar days, when the dressing will be replaced, and during the healing of day 8 in patients of the arm subjected to local treatment proposed by the clinical guideline based on evidence for the treatment of the diabetic foot). It shall be classified as a complete closure only if there is total re-epithelialisation with absence of drainage.
Dichotomous categorical variable: 0 = No effectiveness; 1 = Effectiveness



Descriptive statistical analysis shall be performed using the calculation of measures central tendency and dispersion measures. For bivariate analysis, proportions inference with a value of α=0.05 shall be used. A multiple regression is stated as an analysis alternative that would allow to be adjusted for the effect potential confounding factors. An alternative analysis shall also be performed for longitudinal data. The Kappa ratio shall be estimated to examine and quantify the intra-observer agreement among observers, who shall assess the reduction percentage of the ulcer. Besides, a Wilcoxon test shall be used to assess changes between baseline and final values, as well as to differentiate the groups. All analyses shall be carried out using the principle of intent to treat. This protocol shall be submitted for the assessment of the National Commission for Scientific Research of IMSS.

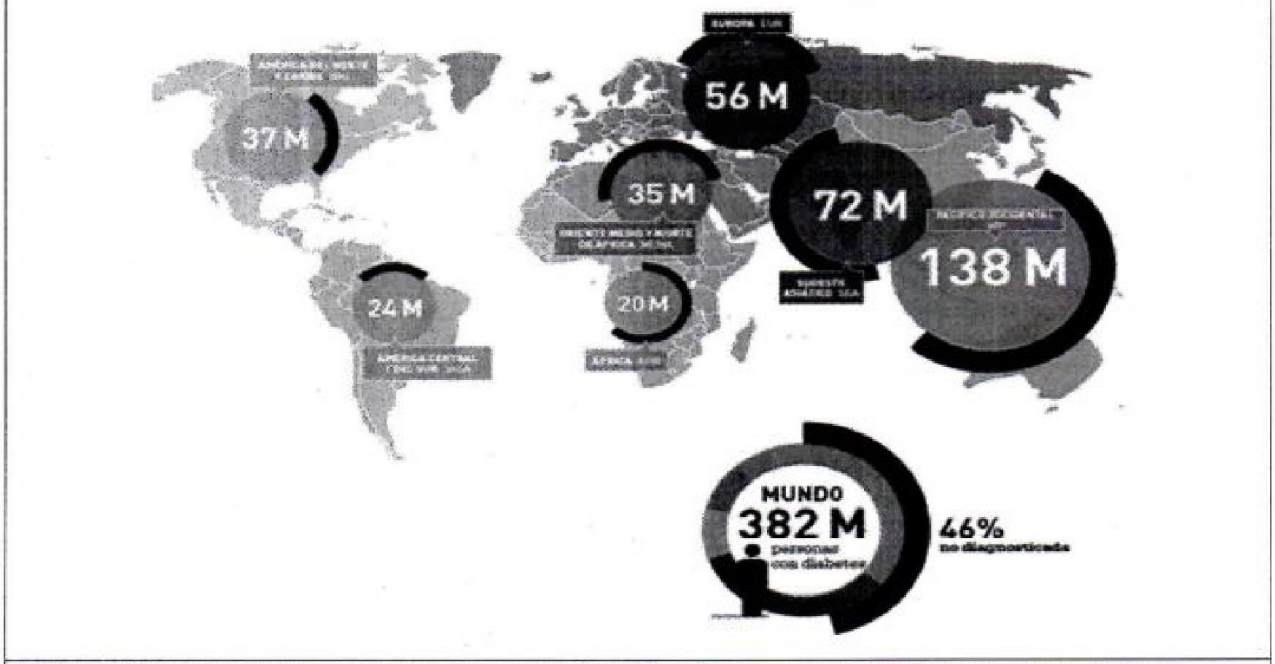


THEORETICAL FRAMEWORK

Diabetes mellitus is one of the most frequent noncommunicable diseases (NCDs) in the world. It is the fourth or fifth cause of death in most World Bank high-income economies, and there is sound evidence that it has epidemic dimensions in several economically developing countries and with recent industrialisation. [1, 2]

The increase in the prevalence of Diabetes Mellitus (DM) and its complications poses a global public health issue and with financial impact for healthcare centres. [3] The most recent calculations of the International Diabetes Federation (IDF) indicate that 8.3% of adults (382 million people) have diabetes, and the number of people with the disease will increase in over 592 millions in less than 25 years (Image 1). [1]

Figura 1. Número de personas con diabetes por Región de la FID, 2013.



Fuente: International Diabetes Federation, *Atlas de la Diabetes* FID, Editor. 2014, FID: Brussels, Belgium.

Spanish	*English*
MUNDO	*WORLD*
FIGURA 1 Numero de persona con diabetes por región de la FID, 2013	*IMAGE 1 Number of people with diabetes per region of the IDF, 2013*
Fuente: International Diabetes Federation. Atlas de la Diabetes FID, Editor, 2014 Brussels, Belgium	*Source: International Diabetes Federation. IDF Diabetes Atlas, Editor, 2014 Brussels, Belgium*

Estimated prevalence of DM in Mexico was 5.7% in 2000, 7% in 2006, and 9.1% in 2012. The trend in the prevalence of DM2 shows an increase of 59.6%. [4] Given that diabetes has multiple causes, and that during its initial stage it does not produce symptoms, when it is identified late and not properly treated, it causes serious health complications, such as heart attack, blindness, kidney failure, amputation of the lower extremities and premature death. [2]

It has been estimated that life expectancy of people with diabetes is reduced 5 to 10 years. [5] In Mexico, the average age of people who died due to diabetes in 2010 was 66.7 years old, which suggests a reduction of 10 years. [2]

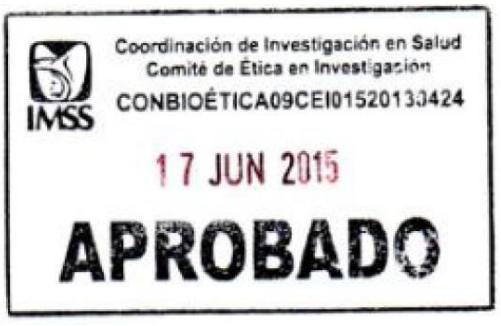
The challenge for society and health systems is immense due to the economic cost and the loss of quality of life for patients suffering from diabetes and their families, as well as for the significant resources they need in the public health system for their care. [6] In Mexico, exiting estimations are very variable with healthcare cost calculation per patient ranging from 700 to 3200 dollars annually, [7] which means 5% to 14% of the expenditure in health allocated to the treatment of this disease and its complications, an investment that is directly related to the mortality rate due to this cause, according to the International Diabetes Federation. [1]

DIABETIC FOOT

Infection of the diabetic foot is the most common infection of the soft tissue related to DM, which may only be caused by nerve disease, ischemia, ischemia and nerve disease combined, or ischemia combined with infection [B], where peripheral nerve disease, macroangiopathy, and vascular disease play key roles in the complication of diabetes. Infection of the diabetic foot is almost ten times more frequent than in non-diabetic patients; up to 25% of people with diabetes will develop ulcerations on the foot during their life, and, of all those people, more than half of them will be infected, increasing in some cases the risk of amputation. [9, 10]

The definition proposed by consensus of the International Working Group on the Diabetic Foot (IWGDF), taken from the WHO, the diabetic foot is the infection and destruction of deep tissues related to neurological alterations and several levels of peripheral vascular disease in the lower extremity. [11]

The most common complications of the DM are the diabetic foot ulcers (DFUs), with a prevalence of four to ten percent among patients with DM. [10, 12] In Mexico, the percentage of diabetic people with ulcers in the leg or feet is 7.15%, which increases depending on the diagnostic time, that ranges from a year up to over 12 years, being 2.21 and 12.44 respectively (Chart 1). [4] There are several factors



that predispose DFU in DM patients, infections, traumas, long evolution of diabetes, poor glucose control, use of footwear unsuitable for nerve disease and peripheral vascular disease. [13]

Chart 1. Percentage (95% CI) of diabetic people with ulcers in legs or feet according to diagnostic time. Mexico, NHANES 2012.

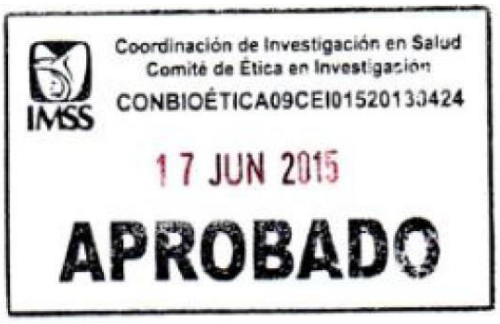
Features	All	One year or less	Over 1 year and up to 5 years	Over 5 years and up to 12 years	Over 12 years
Ulcers in legs or feet	7.15	2.21	4.63	7.60	12.44
	(5.87-8.43)	(1.09-3.33)	(2.78-6.47)	(5.30-9.90)	(8.88-16.00)

Source: Gutiérrez JP, Rivera DJ, Shamah LT, Villalpando HS, Franco A, Cuevas NL, Romero MM, Hernández AM. National Health and Nutrition Examination Survey 2012. National Results. Cuernavaca, Mexico: National Public Health Institute, 2012.

Vascular or ischemic disease may lead to ulceration and significantly delay wound healing. Neuropathic ulcers are located on the sole surface, while ischemic ulcerations are frequently located on the margins of the foot, on toes joints and tips or under foot nails. [14] Consensus of the IWGDF defines a superficial ulcer a wound of the entire thickness of the skin, which does not reach the subcutaneous tissue, and deep ulcer as a wound of the entire thickness of the skin, which reaches the subcutaneous tissue, and may affect the muscle, tendon, bone, and joints. [9]

The DFU starts with a mild trauma, which is subsequently infected and may advance to cellulitis, necrosis of the soft tissue, and extend to the bone. Between 25% and 50% of these infections lead to a minor amputation, and among 10% and 40% to a major amputation. [9, 15] In addition to severe morbidity posed by DFU, it generates prolonged hospitalisations, and social and psychological problems for the patients and their families since besides from the foot pathology in diabetic patients, it causes loss of productivity in patients. [15]

Winkley and collaborators, in a study carried out in Germany in 2007 documented that DFU severity is an independent factor linked to amputation (3.18 RH, 95% CI 1.53-6.59). [16] Morbach and collaborators in 2012 reported, as significant predictor for DM patients mortality, age (1.08 RH, 95% CI 1.06-1.10), male



gender (1.65 RH, 95% CI 1.18-2.32), and peripheral artery disease (1.44 RH, 95% CI 1.05-1.98). However, age (1.05 RH, 95% CI 1.01-1.10), and peripheral artery disease (35.34 RH, 95% CI 4.81-259.79) were significant predictors of major amputations. [17] Mortality subsequent to amputation varies from 13% to 40% on year after the amputation, 35% to 65% three years after the amputation, and 39% to 80% five years after the amputation. [10]

DFU may not lead to limb amputation. Due to the significant economic and medical burden to healthcare system and quality of life of the family, early therapeutic interventions are essential for patients with DFU. [8]

CLASSIFICATION OF THE DIABETIC FOOT

Due to the variety of causes that may lead to the development of the diabetic foot, it is important to have a classification system for ulcers in order to standardise different definitions, and allow the assessment of the clinical course, and outcomes of different treatments. [13] To that end, several classifications globally accepted have been created: Wagner, Texas, PEDIS, Saint Elian. [18, 19]

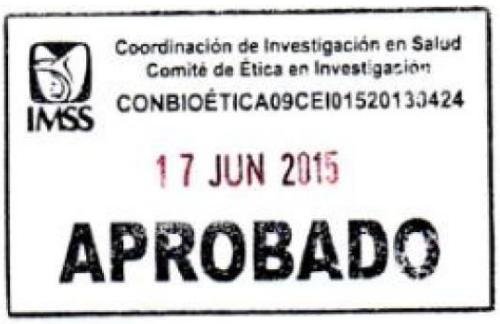
Wagner classification [19, 20] is based on depth, presence of acute osteitis or gangrene, and the extension of tissue necrosis. However, this classification does not include two essential parameters: ischemia and infection.

Wagner Classification

Grade	Features
Grade 0	Absence of ulcer. Foot at risk (deformity, hyperkeratosis)
Grade 1	Superficial ulcer
Grade 2	Deep ulcer penetrating into tendon or joint capsule
Grade 3	Deep ulcer with abscess, acute osteitis, or septic arthritis
Grade 4	Localised gangrene (forefoot or heel)
Grade 5	Extensive gangrene

TREATMENT ACCORDING TO WAGNER CLASSIFICATION

Grades 1 and 2: Patients who may be treated in first degree on an outpatient basis, with advanced healings, use of dressings with hydrogel or hydrocolloids, as appropriate, decompressing ulceration areas.



It is important to inform the patient, remove calluses, debride hyperkeratosis, and use antibiotics.

Grades 3 and 4: Patients who must be treated in second and third degree of care, hospitalised, and treated aggressively. Surgical cleaning, debridement and minor amputations, as appropriate, use of systemic antibiotics. It is intended to go back to second degree and then to follow its treatment in first degree, provided that there is no indication of revascularisation.

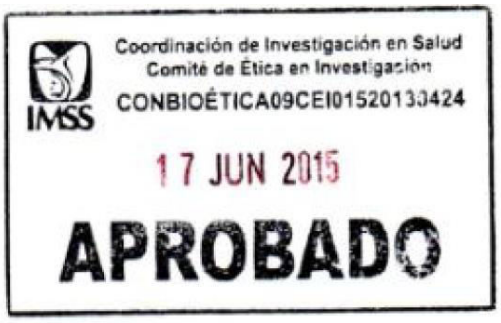
Grade 5: In general, it is a health (surgical) emergency, a "foot appendicitis", so these patients must be treated aggressively by a multidisciplinary team in third degree of care, adapting biochemical parameters and practising a healing amputation as soon as possible, adding a systemic antibiotics treatment.

Saint Elian wound classification is a diagnostic-therapeutic system that allows to assess ulcers evolution and the impact of treatment according to wound severity. [21] It takes into account 10 factors that play a part in wound severity and healing progress of the diabetic foot.

LOCAL TREATMENT OF THE DIABETIC FOOT

Local treatment of the DFU, as well as the selection of the technique to address it and the debridement process shall depend on a variety of factors, including aetiology, morphological features and clinical presentation of the ulcer. When infection involves superficial layers, local treatment with cleaning and mechanic debridement is usually enough. However, the presence of severe infection requires surgical debridement. It is indicated for deep abscess, necrotising fasciitis, gas phlegmone and compartment syndrome. In the absence of ischemia, debridement shall be extensive in order to remove most of the necrotic tissue possible. If there is ischemia, abscess drainage removal of necrotic tissue must be carried out after revascularisation procedures.[22]

Debridement allows to have a proper bed to start wound healing; however, natural barriers protecting the limb are removed. For that reason, there are current therapies based on growth factor or recombinant platelet growth factor, which stimulates chemotaxis and mitosis of neutrophils, fibroblasts, monocytes, and other components, which contribute to wound healing in 43% cases, compared to 35% treated with placebo gel.



Other growth factors are: endothelial growth factor, fibroblasts and keratinocytes growth factor, autologous plasma patches, among others, which have controversial results. [20]

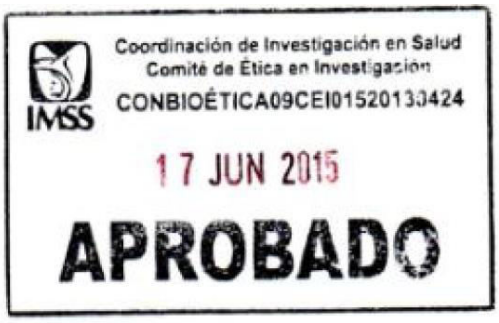
Tissue patches created by means of bioengineering have been extremely useful in venous ulcers healing of the diabetic foot. These patches have essential components to foster substrate and accelerate wound healing and angiogenesis. [20]

Dressings used for medical debridement are designed to keep the wound clean and free from contamination, while they also stimulate wound healing. [19, 22] In particular, the action mechanism of the TISSUPOR® 3D EMBROIDERY dressing is to trigger a mechanical stimulus of the wound bed that allows an ordered structure for granulation by enhancing angiogenesis. [20]

WOUND TREATMENT WITH NEW TECHNOLOGIES

Wound treatment constitutes one of the most innovative applications of medical devices technology. The foundation of the latest breakthroughs in wound care has been built over advances in polymer technology during the last three decades. New and unique materials have been developed to provide properties with significant technical and clinical benefits. These new products have been made possible for wound care thanks to the convergence of three interrelated fields: (1) more complete understanding of underlying principles of recovery processes for skin wounds, (2) new polymers and elastomers for the manufacturing of protective dressings, and (3) advances in breathable adhesive technology. [23]

New-generation medical textiles are a field of greater significance with important expansion in wound treatment. There are indeed new products with enhanced properties using advanced technologies, and which are at the core of research, being highly technical, technological, functional, and efficient. The main features of fibres and bandages as products to treat wounds include bacteriostatic, antiviral, fungistatic, non-toxic, absorbent, non-allergic, breathable, haemostatic, biocompatible, and manipulable features to incorporate medication. Several advantages over traditional materials is that they have modified products, or products mixed on a basis of alginate fibres, chitin/chitosan, collagen, ferulate, and carbon.



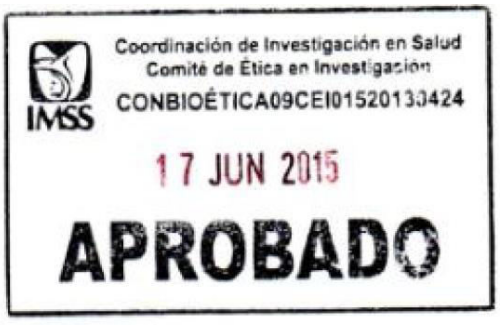
Textile structures used for modern bandages or dressings come in several varieties: splinter, threading, fabric, non-fabric, knitted, crocheted, braided, embroidery, composite materials. For wound care, materials such as hydrogels, grid (tissue engineering), films, hydrocolloids, and foams are also used. There are also specialty additives which may be introduced in advanced dressings in order to absorb smells, provide antibacterial properties and painkillers, and reduce irritation. Due to their unique properties, such as contact area with the volume of the surface, the thin film, the diameter of the fibre on nano scale, porosity, and light weight, these are used for wound care. [24]

Chitin and its deacetylated by-product, chitosan, are non-toxic biopolymers, with antibacterial action, biodegradable and biocompatible. Thanks to these properties, they are widely used for biomedical applications, such as scaffolds in tissue engineering, drug administration, dressings for wounds, separation membranes and antibacterial coating, stent linings, and sensors. [25]

The new generation of smart textiles is represented by fibres, threading, knitting, and other resulting products which have special mechanic, chemic, electrical and thermal isolation properties. This is an innovation field that broadens the scope of textile products, designed to meet specific needs, with the aid of different technologies and products according to required properties, such as personal protection, safety, and health. [26]

TISSUPOR® 3D EMBROIDERY DRESSING FEATURES

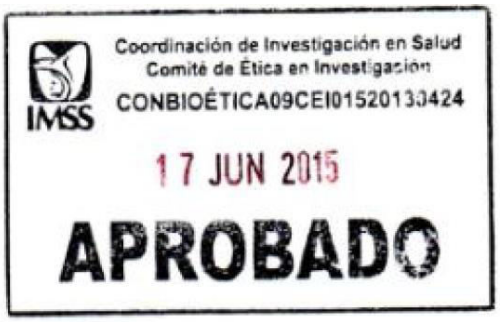
Directed morphologically induced angiogenesis: Proliferation of capillary vessels is produced by means of directed angiogenesis. The three-dimensional superficial structure of TISSUPOR® 3D EMBROIDERY dressings has specific openings of pores of 10 µm to 3 mm, which enhances internal growth of cells and capillaries, while stimulating the creation of granulation tissue, creating a network of blood vessels around a ceramic cell carrier.



Mechanical stimulation of the wound bed: The angiogenesis model previously described requires a mechanic stimulation of the wound bed by means of the stitched three-dimensional material.

Combination of dry and humid treatment: The hydrophobic structure of the dressing allows to perform a dry treatment of wounds having mild to severe exudation.

Directed induction of the bleeding during the replacement of bandages: The grid cause bleeding in the wound bed in order to create a colonisation process over the surface of the stitched material, which shall encourage proliferation of small to very small blood vessels.



JUSTIFICATION

Being the ulceration of the diabetic foot the most common complication of DM, with a prevalence of four to ten percent among patients with DM, [10, 12] the challenge for society and health systems is immense due to the economic cost and the loss of quality of life for patients suffering from diabetes and their families, as well as for the significant resources they need in the public health system for their care. [6]

In Morelos borough, in 2013, nearly 1040 first-degree consultations were granted for medical care of patients with non- insulin-dependent diabetes mellitus, with peripheral circulatory complications (E115, according to CIE-10), that at certain point will be classified as diabetic foot and evolve into an ulcer of the diabetic foot. So far, local treatment of the diabetic foot ulcer in IMSS does not have alternative use for dressings. TISSUPOR® 3D EMBROIDERY dressings has a feature that triggers a mechanic stimulus that allows an ordered structure for granulation, enhances angiogenesis, which would reduce time to shorten the wound surface area, reducing the risk of minor or major amputation.

It is for this reason that this clinical trial shall be performed to provide grounds to use dressings for wounds in patients with diabetic foot ulcers. The use of these dressings is necessary for these patients since traditional treatment has not been proven to be effective in all cases.

RESEARCH QUESTION

What is the effectiveness and safety of the use of TISSUPOR® 3D EMBROIDERY dressings for wounds in patients with diabetic foot ulcers compared to the standard use of sterilised gauzes in the treatment of the diabetic foot?

PURPOSE

GENERAL PURPOSE

To assess the effectiveness and safety of the use of TISSUPOR® 3D EMBROIDERY dressings for wounds in patients with ulceration on the diabetic foot.

SPECIFIC PURPOSES

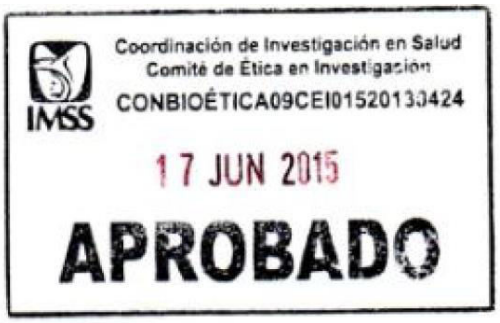
To assess the effectiveness and safety of the use of TISSUPOR® 3D EMBROIDERY dressings for wounds in the volume and size of the diabetic foot ulcer, compared to the standard use of sterilised gauzes in the treatment of the diabetic foot.

To assess the effectiveness of the use of TISSUPOR® 3D EMBROIDERY dressings for wounds in the percentage of granulation tissue, necrotic tissue and presence of exudation, compared to the standard use of sterilised gauzes in the treatment of the diabetic foot.

To assess the effectiveness of the use of TISSUPOR® 3D EMBROIDERY dressings for wounds in the full healing time of the wound, compared to the standard use of sterilised gauzes in the treatment of the diabetic foot.

HYPOTHESIS

Treatment of diabetic foot ulcers shows higher effectiveness using TISSUPOR® 3D EMBROIDERY dressings for wounds compared to the standard use of sterilised gauzes in the treatment of the diabetic foot.



METHODOLOGY

Research location:

The clinical trial shall be carried out in the healing area of HGR MF No. 1, of HGZ MF5 y of HGZ MF7 of the IMSS in Cuernavaca, Morelos. These hospitals deal with legitimate beneficiaries of the state of Morelos and surrounding municipalities; they have outpatient consultation, hospitalisation, urgent care, and different diagnostic assistants. The subjects of the study shall join through outpatient consultation, and shall be channelled by the treating doctor.

Design:

Clinical trial: An innovative therapeutic manoeuvre shall be implemented in patients with diabetic foot ulcers, which shall be monitored by the researcher.

Randomised: For the random allocation of subjects to the treatment arm.

Double-blind: For blindness in the application and assessment of manoeuvres. There will be 3 levels of blinding operation of the experimental manoeuvre since the patient, the person assessing its effects, and the person performing the statistical analysis shall not know the treatment being provided.

Controlled: For the existence of a control arm. Outcome variables obtained in the experimental arm treated with TISSUPOR® 3D EMBROIDERY shall be compared to those of the control arm subjected to standard treatment with sterilised gauze.

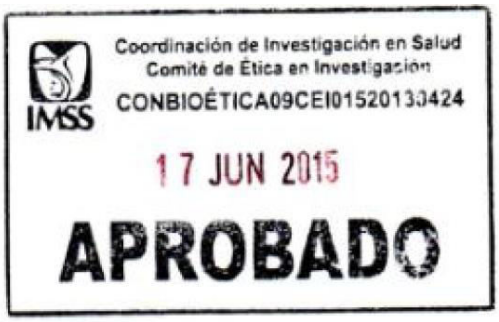
Longitudinal: For the measurement of the phenomena in time. Several measurements of the outcome variables shall be performed throughout the study.

Prospective: For the temporal direction of the study phenomena, from the cause to the effect.

Non-paired: Two independent arms shall be created, one for each designated treatment. Data statistical inference shall be of non-paired samples.

Study Arms:

Features of the Experimental Arm:



It shall be made up of patients with clinical diagnostic of diabetes mellitus type 2, and with presence of diabetic foot ulcer in the sole, who shall be randomly allocated to experimental treatment with TISSUPOR® 3D EMBROIDERY dressings.

Features of the Control Arm:

It shall be made up of patients with clinical diagnostic of diabetes mellitus type 2, and with presence of diabetic foot ulcer in the sole, who shall be randomly allocated to control treatment with sterilised gauze.

Screening Criteria

Inclusion: Patients with diagnostic of diabetes mellitus type 2 recorded on the clinical file. Aged 18 to 80. Presence of ulcer of the foot of entire thickness, of at least two weeks of duration before they are admitted to the study, with a 1 or 2 Wagner classification. They must have submitted a written informed consent form.

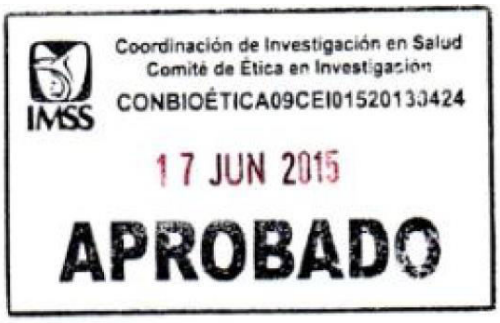
***Exclusion*:** Patients with ulcers in epithelisation phase. Deep ulcers with abscess, acute osteitis or joint sepsis, localised gangrene (forefoot or heel), extensive gangrene or serious infection.

***Removal*:** Patients who lack availability to continue with the treatment.

Variables specification:

Intervention Variable

Experimental treatment: TISSUPOR® 3D EMBROIDERY dressing, which is made up of: three-dimensional, hydrophobic material of polyamide/polyester (inner side), polyester fabric to provide space, layer of viscose wool to absorb wound secretions, and polyester printed fabric (outer side).
The evaluating, trained, and standardised general practitioner of the project shall perform the following healing technique:
a) Diabetic foot ulcer cleaning with dry and sterilised gauze, and removal of dead tissue.



b) Scarification with scalpel with a superficial grid over the entire wound.
c) Placement of the TISSUPOR® 3D EMBROIDERY dressing covering the entire ulcer, with compressive gauzes and bandages of 10 cm.
d) The patients shall be scheduled to have their dressings removed after 8 calendar days, and the next appointment is scheduled to complete 4 consecutive appointments.
Dichotomous nominal variable. Scale: 0 = Absence; 1 = Presence.

Control treatment: Treatment with sterilised gauze. The evaluating, trained, and standardised general practitioner of the project shall perform the following healing technique:

a) Diabetic foot ulcer cleaning with saline solution and iodopovidone with dry and sterilised gauze, and removal of dead tissue.
c) Placement of the sterilised gauze covering the entire ulcer, with compressive gauzes and bandages of 10 cm.
d) Wound cleaning shall be daily, with sterilised gauze replacement, for a month.
Dichotomous nominal variable. Scale: 0 = Absence; 1 = Presence.

Outcome Variables

Primary Event

Therapeutic effectiveness, assessed with a VISITRAK wound evaluating system that allows measurement of wound dimensions (area, length, width and depth) generating a record, which will enable to calculate the percentage change of the wound areas measured before. It shall be deemed therapeutic effectiveness with VISITRAK when the subject reduces 24% of the wound or more compared to the baseline assessment. [27]

The procedure to record the wound surface area (WSA) shall be the following:
In each visit, and before the placement of the dressing, a transparent and sterilised film shall be placed (transparent Visitrak of 2 layers) over the wound, and the perimeter of the ulcer shall be traced with a permanent marker. Each ulcer shall be measured three times in order to ensure measurement reliability. The tracing shall be digitalised by means of an A4 G-Note 7100 digitizer tablet using a wireless mouse, and a high precision wireless pointer pencil (KYE systems, Corp, China); the digitalised tracing shall be exported to a specialised computer program (Photoshop C4me) to calculate the wound surface area.

The percentage of the reduction of the surface area of the ulcer shall be calculated with this equation:

WSA % = [initial WSA (cm^2) - WSA (cm^2) during week 1] X 100

WSA: wound surface area

The percentage of wounds that have been completely closed shall be identified in each measurement (once every 8 calendar days, when the dressing will be replaced, and during the healing of day 8 in patients of the arm subjected to local treatment proposed by the clinical guideline based on evidence for the treatment of the diabetic foot). It shall be classified as a complete closure only if there is total re-epithelialisation with absence of drainage.

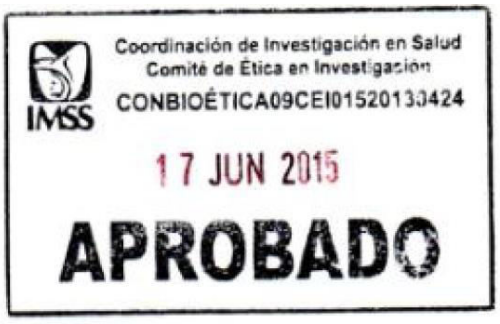
Dichotomous categorical variable: 0 = No effectiveness; 1 = Effectiveness

Secondary Event

Therapeutic safety: It corresponds to the absence of deterioration of the wound condition or surface and/or deep infection data, in patients with the use of TISSUPOR® 3D EMBROIDERY dressings for wounds compared to patients of the control arm using a sterile gauze, and which is attributable to the use of the dressing. 0 = No safety; 1 = Safety.

Demographic Variables

- Gender: It corresponds to the gender of subjects participating in the study. It shall be obtained from the aggregate appearing after the number of enrolment to the IMSS. Dichotomous variable. Scale: 1 = Female; 2 = Male.
- Age: It corresponds to the age of subjects at the moment of the study. It shall be calculated from the aggregate appearing after the number of enrolment to the IMSS, and the date of birth. Continuous quantitative variable. Scale: Sequential numbering from 18 to 60.
- Occupation: It corresponds to the activity or profession of the study subject. Nominal categorical variable. Scale: 0 = unemployed; 1 = domestic work; 2 = farmer; 3 = blue-collar worker; 4 = employee; 5 = professional; 6 = Other; 9 = no answer.



- Education: It correspond to the highest degree of education of official recognition attained by the study subject. Nominal categorical variable. Scale: 0 = illiterate; 01 = elementary education; 02 = medium-higher level; 03 = graduate; 04 = postgraduate; 99 = no answer.

- Marital status: It corresponds to the marital status of the subject at the moment of the study. Nominal categorical variable. Scale: 1 = single; 2 = married; 3 = consensual union; 4 = divorced; 5 = widow(er); 6 = divorced; 7 = others; 99 = no answer.

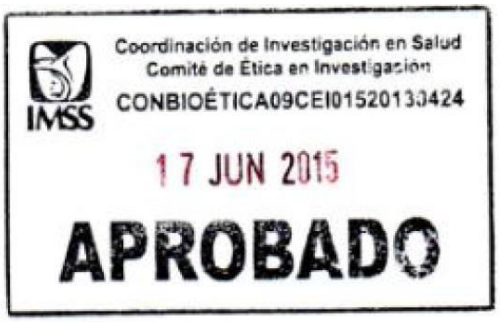
Potentially Confounding Factors

Variables such as time of evolution of diabetes, evolution of the diabetic foot, pharmacological and non-pharmacological treatment, nutritional condition, personal pathological history, smoking habit, and glucose control are deemed potentially confounding since they may affect both the genesis of the disease and the therapeutic outcome. In order to determine whether they are confounding variables or not, a stratified analysis shall be performed with the proposed categorised variables.

***Research description*:** Participants of this clinical trial shall be recruited from those who meet the eligibility criteria, and treated by Family Medicine and/or Outpatient Consultation of Angiology of Hospital General Regional con Medicina Familiar No. 1 (HGR MF1) in Cuernavaca; Family Medicine and/or General Surgery of Hospital General de Zona con Medicina Familiar No. 5 (HGZ MF5) in Zacatepec; and Hospital General de Zona con Medicina Familiar No. 7 (HGZ MF7) in Cuautla, Morelos, with DFU diagnosis.

Patients selected in HGR MF1, HGZ MF5, and HGZ MF7 shall be randomised to constitute the intervention arm (use of TISSUPOR® 3D EMBROIDERY dressings for wounds), the control arm (which shall only use standard treatment with sterilised gauze). [20]

During the enrolment process, an *ad hoc* questionnaire shall be included, previously organized to document family history, personal pathological history, age, gender, smoking habit, time of evolution of diabetes, time of evolution of the diabetic foot, pharmacological and non-pharmacological treatments the patient may have been administered.



A pre-participation evaluation shall be performed by a trained general practitioner by means of a directed physical exploration and diagnosis. This approach shall include questioning and general physical exploration, apart from a directed examination of lower extremities, which is based on a dermatological, neurologic, vascular, and musculoskeletal assessment.

The dermatological exploration shall include inspection of the skin of the legs and feet on their dorsal, sole, medial, lateral, and posterior sides. It includes skin appearance, oedema, onychopathies, toes alignment disorder, structural disorders, and temperature.

The neurological exploration shall be performed to inspect whether there is dysesthesia, pins and needles, hyperaesthesia, and by means of the Semmes-Weinstein monofilament test, which is deemed as a reliable and simple method that allows a fast assessment.

The vascular exploration is assessed through the presence or absence of tibial, popliteal, and femoral pulses.

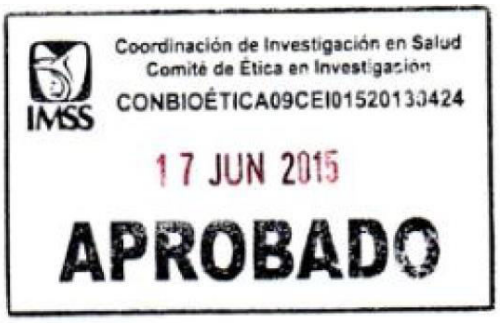
The osteomioarticular exploration shall assess foot shape, reduction of the sole arch, claw toes or hammertoes, hyperkeratosis in pressure points and general osteoarticular deformities.

It is carried out to clinically determine whether it is a neuropathic, ischemic, neuro-ischemic, ulcerated or ulcerated and infected diabetic foot. After that, Wagner classification of the diabetic foot shall be used, which is classified in the following manner:

Grade 0: with no high risk ulcer in the foot.

Grade 1: ulcer extended to all skin layers, but not reaching other tissues.

Grade 2: deep ulcer, penetrating ligaments and muscles, but not reaching the bone, nor provoking the formation of abscesses.



Grade 3: ulcer with cellulitis or formation of abscess and subsequent acute osteitis.

Grade 4: localised gangrene.

Grade 5: extensive gangrene affecting the entire foot.

And with all this data, participants shall be selected according to eligibility criteria. At least 20 participants are intended to be recruited, who, after being selected to participate in the study, shall be requested to provide their authorisation to participate by means of an informed consent form. Once the informed consent form has been obtained, depending on the corresponding hospital, the subject shall be included in the control arm or in the intervention arm. The start of the intervention shall be continuous as they are being recruited.

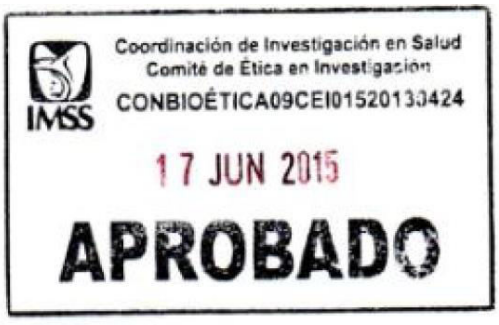
During the study, safety analysis shall be performed in order to identify known and unexpected adverse effects related to the use of TISSUPOR® 3D EMBROIDERY dressings for wounds.

Sample Size

The calculation of the sample size shall be performed according to the formula proposed by Argimon [28] in order to compare two proportions, where a reduction of 24% of the ulcer size after 4 weeks of treatment shall be considered as the success value.

$$n= \frac{\left[Z\alpha\sqrt{\left[2\bullet P\bullet(1-P)\right]}+Z\beta\sqrt{\left[P1\bullet(1-P1)+P2\bullet(1-P2)\right]}\right]^2}{(P1-P2)^2}$$

n=	**57**	**Subjects required per arm**
Zα	1.96	Z value corresponding to set alpha risk
P	0.66	Weighted average of proportions P1 and P2
Zβ	0.842	Z value corresponding to beta risk
P1	0.5	Value of proportion supposed to exist in the reference arm
P2	0.24	Value of proportion supposed to exist in the study arm
P2-P1	0.25	Minimum value of the difference intended to be identified (qualitative variable)



Information Collection

Medical history: During screening for recruitment, questions related to medical history of participants shall be asked, including diseases, use of medication, complications directly related to comorbidities.

Sociodemographic information: In the recruitment process, participants will be given a questionnaire, which shall collect sociodemographic information about marital status, years of schooling, occupation, date of birth and place of residence.

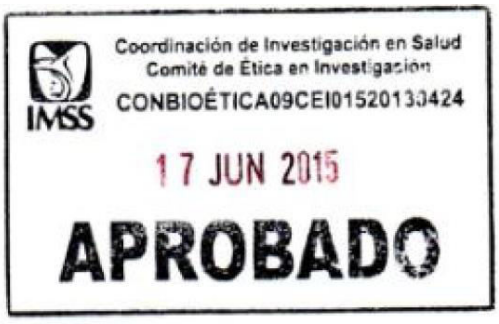
Anthropometric and ulcer measurements: Weight and size of participants. Measurements shall be taken according to the technique recommended by Lohman's Anthropometric Standardization Reference Manual. Measurements shall be obtained by trained and standardised personnel hired for the project according to the method described by Habitch.

Randomisation and Blinding

Participants who successfully complete the screening period shall be randomised with standard treatment added to the use of TISSUPOR® 3D Embroidery, or just standard treatment for a patient with diabetic foot ulcer, according to the random sequences by means of a free statistical software called "random number generator no repeats" in *NOSETUP.org* (Image 2).

Given the features of the intervention proposed, the blinding strategy shall consist in not communicating the person in charge of the statistical analysis (different from the researcher in charge), nor the participants, which of the analysed arms shall correspond to the intervention or control arm.

Participant's screening shall be performed by the researcher in charge. The random allocation sequence and the allocation of participants to the arm of standard treatment added to the use of TISSUPOR® 3D Embroidery dressings or to the arm of only standard treatment shall be performed by a biostatistician.



Statistical Analysis

A data cleaning analysis shall be performed in order to identify inconsistent, non-plausible or out of scope values. After that, information shall be summarised in frequencies (or percentages) for categorical variables and in means (with their standard deviations) for continuous variables. Chi-square test (or Fisher's exact test, if appropriate) and T test for two samples, shall be used to compare differences between the arms, both for categorical and continuous variables, respectively. Even the randomisation process is expected to eliminate possible initial differences between the arms to be compared, a multiple regression is stated as an analysis alternative that would allow to be adjusted for the effect potential confounding factors. An alternative analysis shall also be performed for longitudinal data. All analyses shall be carried out using the principle of intent to treat.

The Kappa ratio shall be estimated to examine and quantify the intra-observer agreement among observers, who shall assess the reduction percentage of the ulcer. Besides, a Wilcoxon test shall be used to assess changes between baseline and final values, as well as to differentiate the groups. STATA v. 12 statistical software shall be used.

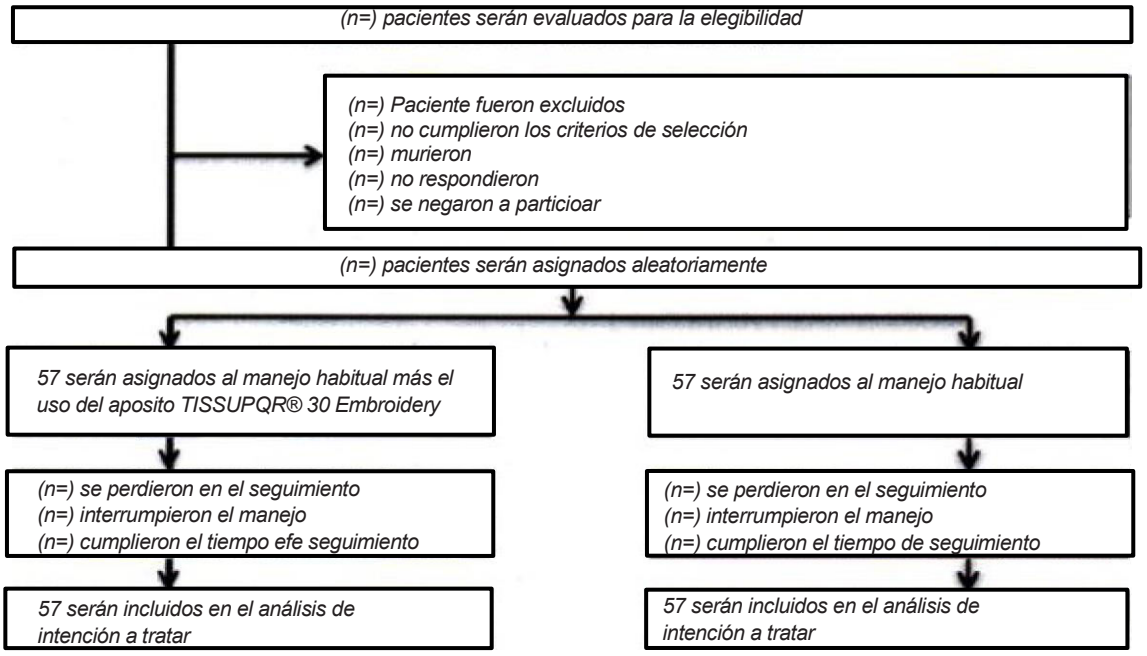


Image 2. Study flow chart

Spanish	*English*
(n=) pacientes serán evaluados para la elegibilidad	*(n=) patients who shall be assessed for eligibility*
(n=) Paciente fueron excluidos	*(n=) Patients who were excluded*
(n=) no cumplieron los criterios de selección	*(n=) did not meet screening criteria*
(n=) murieron	*(n=) died*
(n=) no respondieron	*(n=) did not answer*
(n=) se negaron a particioar	*(n=) refused to participate*

Spanish	*English*
(n=) pacientes serán asignados aleatoriamente	*(n=) patients who shall be randomly appointed*
57 serán asignados al manejo habitual más el uso del aposito TISSUPQR® 30 Embroidery	*57 shall be allocated to standard treatment coupled with the use of TISSUPOR® 3D EMBROIDERY*
(n=) se perdieron en el seguimiento	*(n=) lost during follow-up*
(n=) interrumpieron el manejo	*(n=) interrupted the treatment*
(n=) cumplieron el tiempo efe seguimiento	*(n=) completed follow-up*
57 serán incluidos en el análisis de intención a tratar	*57 shall be included in the analysis of intent for treatment*
57 serán asignados al manejo habitual	*57 shall be allocated to standard treatment*
(n=) se perdieron en el seguimient	*(n=) lost during follow-up*
(n=) interrumpieron el manejo	*(n=) interrupted the treatment*
(n=) cumplieron el tiempo de seguimiento	*(n=) completed follow-up*
(n=) pacientes serán evaluados para la elegibilidad	*(n=) patients who shall be assessed for eligibility*

Quality Assurance

The validity of the inferences created by this study depends on the accuracy of the methods and procedures used. For that reason, activities directed to ensure data quality before their collection are proposed, aiming at keeping and monitoring data quality throughout data collection.

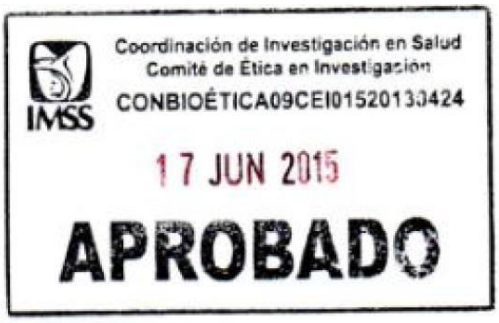
The assessment of the wound is critical in the monitoring of treatment effectiveness of all wounds. In a research, the use of the same technique is the only way to monitor closing events. If the area of the wound will be used as main event, it is essential that all measurements are accurate and consistent.

It is important that for the study, the same technique to measure the wound, and that observers are standardised, in order to reach comparisons. The use of a “ruler” to measure the wound surface area will underestimate the measurement. For that reason, measurement using a sterilised, digitalised film, and assessed through a computer program in triplicate, in order to assess intra-observer variability.

Ethical Aspects

The implementation of this clinical trial shall be performed complying with the current legislation of our country, in strict accordance with the Second Title of the General Health Act regarding health research: “Ethical Aspects of Research on Human Subjects”, in particular in chapter 2 [39] and the current Helsinki Statement.

Protection of rights and wellbeing of the patients in this study as subjects for research shall also abide by Good Clinical Practice (GCP), [30] created and continuously improved by the International Conference on Harmonisation (ICH).



The inclusion of participants in the study shall be carried out with prior informed consent form, conducted according to minimum standards and considering national an international current legislation.

Information collected as part of this study is strictly confidential. Information that may be used to identify patient(s) (name, phone and address) shall be saved confidentially. Personal data shall be saved separately from the questionnaires to keep confidentiality of the clinical tests results. Personal date and results shall be safeguarded in the Auxiliary Medical Coordination for Health Research. Only the research team of the IMSS shall have access to that information.

Only the IMSS research team in charge will know which patients are participating in the study. No one shall have access to the patient's information.

When results of this study are published or presented in conferences, no information that may reveal the identity of any patient shall be disclosed. Identity shall be protected and kept confidential. In order to protect the identity, name, and any other information that may be used to identify any of the patients shall not be linked to files information and study results. Information shall be saved in secure databases which are password protected.

All the information shall be destroyed seven years after the completion of the study.

Any adverse effect (expected or unexpected) shall be solved in a prompt and dedicated manner by the expert medical personnel of the hospital the patient comes from.

The implementation of this clinical trial includes the use of treatment that requires informed consent forms, and compliance with the provisions set by the Belmont Declaration shall be monitored at all times.

Discomfort or risks associated with clinical assessment procedures (weight, size, waistline, blood pressure measurement, among others) or healing procedures are the same as those of a medical consultation.
In some occasions, the procedure to clean the ulcer wound may cause pain or discomfort. The risks a foot ulcer may pose to the patient may include local infection, deep infection, bone infection, which, in the event it is not promptly treated, may lead to an amputation in order to avoid fatal complication, such as a systemic infection and/or death. Therefore, if any of the

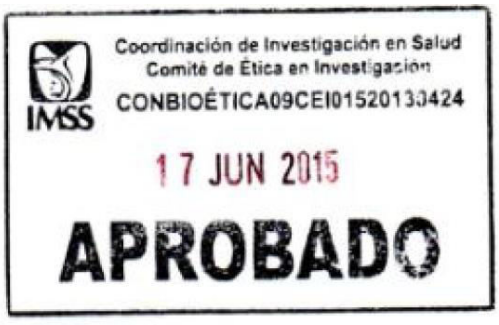
participants were to suffer any complication due to the participation in this trial, that patient shall get the proper treatment and follow-up in the IMSS by specialised personnel.

Participants shall not obtain any payment for their participation in this study, nor will this participation involve any expense on their part. They may not obtain a direct benefit, but there shall be knowledge breakthrough. A possible benefit from their participation in this study is that the results of clinical tests we will perform shall provide them with information about their health condition. They will also benefit from foot ulcer treatment with strict monitoring performed by specialised personnel.

During the study, patients shall be informed about any new finding (whether positive or not) that is important for their decision to participate or continue to participate in this study; for example, if there were changes in the risks or benefits resulting from their participation in this research, or if there were new treatment alternatives that may change their opinion over their participation in this study.

Patients will be guaranteed the necessary amount of dressings they are allocated, as well as any other necessary item to deal with their current health status or with any problem that may arise throughout the study. Besides, once the study finishes, in the event the ulcer has not closed yet, they will continue to be treated with those gauzes studied up to the moment when the wound closes.

Risk probabilities and possible benefits have been thoroughly assessed, and it is estimated that they may have a positive balance for patients. As this new technology is being evaluated, it is possible that the patient may not obtain an immediate personal benefit, but it is estimated that society as a whole shall benefit from the results.



Resources and Feasibility

The three hospitals of Morelos borough have the necessary infrastructure for the supervision, execution and monitoring of the clinical trial. There are also clinical researchers to supervise the project; one of the associated researchers is responsible for the development of the debridement technique, and shall train the rest of the observer team.

TISSUPOR® 3D EMBROIDERY dressings for wounds, as well as healing material (bandages, gauzes, scalpel blades, surgical gloves, isodine) shall be donated by the SWISSGLOBUS AG company through the importer company called INTERSUIMEX S.A. de C.V. Semmes-Weinstein monofilaments of 10 g. Three A4 G-Note 7100 digitizer tablet using a wireless mouse, and a high precision wireless pointer pencil (*KYE systems, Corp, China*); computer program (Photoshop C4me) to calculate the wound surface area. The project funding shall be at the expense of company SWISSGLOBUS AG.

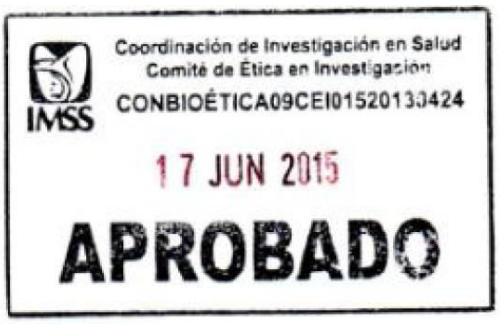
Biosafety Aspects

The three healthcare centres that participate shall be responsible for the handling and disposal of biological waste resulting from the implementation of this clinical trial under standard procedure for handling biohazardous and infectious waste in hospitals.

Activities Schedule

ACTIVITY	MONTHS	M1	M2	M3	M4	M5	M6	M7	M8	M9	M10	M11	M12-M18	
Literature review		X	X	X	X	X	X	X	X	X	X	X	X	X
Assessment of the clinical trial protocol before the Review Committee					X	X	X							
Integration of databases of contact information of patients with ulceration on the diabetic foot					X	X	X	X	X	X				
Beginning of recruitment							X	X	X	X	X	X		
WEEK 1 Assessment and treatment							X	X	X	X	X	X		
WEEK 2 Assessment and treatment							X	X	X	X	X	X		
WEEK 3 Assessment and treatment							X	X	X	X	X	X		
WEEK 4 Assessment and treatment							X	X	X	X	X	X		
Quality assurance							X	X	X	X	X	X		
Intermediate analysis of general assessment							X	X	X	X	X	X		
Statistical analysis													X	
Drafting of the clinical trial final report													X	X
Dissemination of outcomes														X

M: months



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INTERSUIMEX, S.A deC.V.
Avenida 10 de Abril No 1013, C.P. 06170,
Cuernavaca, Morelos.

153300410D0026/2016
163300ES450270/2016
Mexico City, Mexico, 31 March 2016

3. Technical summary of the protocol called "Assessment of Effectiveness and Safety of the Use of Tissupor® 3D Embroidery Dressings for Wounds in Patients with Neuropathic Ulceration of the Diabetic Foot", in its first version dated 25 February 2016.

Receipt of the following documents is acknowledged; therefore, said documentation shall be only submitted through annual partial report:

1. Document of: Research Project, State of the IMSS, Morelos Borough, version accepted on 26 May 2015.

Main purpose To assess the effectiveness and safety of the use of Tissupor® 3D Embroidery dressings for wounds in patients with ulceration on the diabetic foot. To assess the effectiveness and safety of the use of Tissupor® 3D Embroidery dressings for wounds in the volume and size of the diabetic foot ulcer, compared to the regular use of sterilised gauzes in the treatment of the diabetic foot.

Design of the study Randomised clinical trial. Phase II, with control arm.

Treatment arm(s)		***Procedure***	***Treatment duration per subject***
G1	*Tissupor® 3D Embroidery*	*Cleaning of the ulcer and placement of the dressing covering the entire ulcer, with compressive gauzes and bandages of 10 cm.*	*Dressing replacement after 8 days*
G2	*Standard treatment*	*Cleaning with saline solution and iodopovidone with sterilised gauze. Placement of the sterilised gauze covering the entire ulcer, with compressive bandages of 10 cm.*	*Daily cleaning with sterilised gauze replacement, for a month.*

Sample Size 114 subjects are expected to be included in the research, aged 18 to 80 in Mexico.

Tests or procedures involved in the study: dermatological, neurological, vascular and musculoskeletal assessment, planimetric measurement of ulcers (Silhouette Star camera).

Biological samples collected shall not be used for permanent or immortal cell lines.

The list of supplies included in the authorisation request are only deemed for knowledge, and not for authorisation.

We insist on the commitment to submit the reports of suspected adverse events and reactions to the National Pharmacovigilance Centre.

This Sanitary Authorisation Commission shall be informed about the conclusion of the study, including highlights and findings.

You must record the supplementary information of your research through a platform of the National Clinical Trials Register (Registro Nacional de Ensayos Clínicos, RNEC) on section "Research on Human Subjects" available on the website of the Federal Commission for the Protection against Sanitary Risks (Comisión Federal para la Protección contra Riesgos Sanitarios, COFEPRIS) within 5 business days from the receipt hereof.

SANITARY AUTHORISATION COMMISSION

LMR/ERS

JUAN CARLOS GALLAGA SOLÓRZANO

INTERSUIMEX S.A. de C.V.
Avenida 10 de Abril No 1013, C.P. 06170,
Cuernavaca, Morelos.

153300410D0026/2016
163300ES450270/2016
Mexico City, Mexico, 31 March 2016

Regarding the request with entry No. 153300410D0026, dated 21 December 2015, and free motion with entry No. 163300ES450270, dated 22 March 2016, received at the Integral Service Centre (Centro Integral de Servicios, CIS), the following notification is submitted, based on articles 4, paragraph 4, 8, 14, and 16 of the Political Constitution of the United Mexican States; 17, 39, sections XV, XXI, and XXIV of the Organic Law of the Federal Public Administration; 1, 2, 3, and 15 of the Federal Law on Administrative Procedures; 1 and 3, sections I, XXII, and XXV; 4, section III; 13, part A, sections IX and X; 17 bis, section IV; 102, 194, last paragraph; 194 bis, 204, 262, 315, 316, 317, 317 bis, 317 bis 1, 318, and 319 of Title Fourteenth; 368 and 371 of the General Health Law; 1, 2, subsection C, section X, and 36 of the Internal Regulations of the Secretariat of Health; 1, 2, 3, 4, 5, 6, 7, 13, 14, 16, 21, 22, 62, 64, 67, 73, 98 and 116, section VI of the Regulation of the General Health Law regarding Health Research; 1, 155, 156, and 184 of the Regulation on Health Inputs; 1, 3, sections I, subsection b, VI, VII, and XII, 4, section II, subsection c, and 14, section I of the Federal Commission for the Protection against Sanitary Risks, as well as articles 7, 8, 9, 10, and 11 of the AGREEMENT containing the proceedings and services, as well as formats that the Secretariat of Health applies through the Federal Commission for the Protection against Sanitary Risks, recorded in the Federal Record of Proceedings and Services of the Federal Regulatory Improvement Commission, published on the Official Gazette on 01 July 2013.

The following research protocol is authorised to be implemented:

Title	"Assessment of the effectiveness and safety of the use of Tissupor® 3D Embroidery dressings for wounds in patients with ulceration on the diabetic foot"
Protocol No.	2015-78S-058
Sponsor	SWISSGLOBUS AG

Locations:

1. **Hospital General Regional C/M.F. No. 1**
   Address: Av Plan de Ayala No. 1201, Cuernavaca, Morelos
   Medical emergencies: Hospital General Regional C/M.F, No. 1
   Address: Av Plan de Ayala No. 1201, Cuernavaca, Morelos

2. **Hospital General de Zona con Medicina Familiar No. 5**
   Address: Blvd. Lázaro Cárdenas S/N. C.P. 62780, Zacatepec de Hidalgo, Morelos.
   Medical emergencies: Hospital General de Zona con Medicina Familiar No. 5
   Address: Blvd Lázaro Cárdenas S/N,C.P. 62780, Zacatepec de Hidalgo, Morelos.

Principal investigator: Dr Laura Ávila Jiménez.
Researchers Ethics Committee
(Comité de Ética de Investigadores, CEI): Mexican Social Security Institute, Coordination of Health Research
Address: Av Cuauhtémoc # 330. C. P. 06720 Meneo. Federal District
Approved by Dr Niels Wacher Rodarte. Chairman of the Committee
Date: 09 October 2015, 09 December 2015, and 07 March 2016.

Research Committee
(Comité de Investigación, CI): Centro Médico Nacional Siglo XXI
Address: Av Cuauhtémoc # 330. C. P. 06720 Meneo. Federal District
Approved by Dr Fabio Abdel Salamanca Gómez, Chairman of the Committee
Date: 09 October 2015, 09 December 2015, and 07 March 2016.

Documents authorised by the aforementioned hospitals in accordance with the CEI and CI expert opinion:

1 Informed Consent Form to participate in the research protocols, version accepted on 26 May 2015.
2 Protocol "Assessment of the effectiveness and safety of the use of Tissupor® 3D Embroidery dressings for wounds in patients with ulceration on the diabetic foot", version accepted on 17 June 2015.

ZACATEPEC, MOR. 18 JULY 2016

DR LAURA AVILA JIMENEZ

RESEARCHER IN CHARGE

CUERNAVACA, MORELOS

AS AN ASSOCIATE RESEARCHER IN THE RESEARCH PROTOCOL: **"ASSESSMENT OF EFFECTIVENESS AND SAFETY OF THE USE OF TISSUPOR® 3D EMBROIDERY DRESSINGS FOR WOUNDS IN PATIENTS WITH NEUROPATHIC ULCERATION ON THE DIABETIC FOOT",** IN RESPONSE TO YOUR INSTRUCTIONS, I HEREBY ATTACH THE REPORT ON DEVELOPMENT PROGRESS OF THE AFOREMENTIONED STUDY, WITH RECORD DATE ON 30 JUNE OF THE CURRENT YEAR, TAKING AS SUPPORT THE MEASUREMENT SOFTWARE IMPLEMENTED CALLED SilhouetteCentral, WITH THE IMAGE CAPTURING EQUIPMENT SilhouetteStar. AT THE TIME OF THE RECORD.

DATA USED FOR THE ASSESSMENT RESULTED FROM SOFTWARE DATA PROCESSING, WITH PLANIMETRIC MEASUREMENT OF EACH ULCER INDIVIDUALLY, AND FOR THE MATHEMATICAL AND STATISTICAL CALCULATION OF THE STATA v12 SYSTEM.

ANALYSIS WERE CONDUCTED IN ACCORDANCE WITH THE AUTHORISED PROTOCOL, COMPLYING WITH RESEARCH REGULATION, AND FOLLOWING YOUR INSTRUCTIONS STRICTLY, WITH VERIFIABLE DATA IN THE COMPUTER PROGRAM PROCURED FOR THIS END

WITH PROPER PARTICIPATION FROM THE MEDICAL PERSONNEL HIRED AND TRAINED, RELIABILITY IS HIGH AND SECURE, THEREFORE, IT IS IMPORTANT TO MENTION THAT THE PROGRAMMED GOAL OF A 24% PROGRESS IN RECOVERY OF ULCERS IN THE INTERVENTION ARM WAS SUCCESSFULLY EXCEEDED, AS IT IS RECORDED IN THE DOCUMENT SUBMITTED FOR YOUR ANALYSIS, SUPPLEMENTATIONS, AND APPROVAL.

HAVING NOTHING FURTHER TO ADD, I SEND YOU MY KIND

REGARDS,

DR. MARCO ANTONIO CEDILLO FLORES
ASSOCIATE RESEARCHER AND CLINICAL COORDINATOR,
AFTERNOON SHIFTS AT HOSPITAL
GENERAL DE ZONA CON MEDICINA FAMILIAR NO. 5
ZACATEPEC, MORELOS

IMSS DELEGACIÓN MORELOS
RECIBIDO
- 1 AGO. 2016
COORD. DE PLANEACION Y ENLACE INSTITUCIONAL
ANEXO:
HORA:

WITH COPY TO GENERAL DIRECTOR.- HOSPITAL BUILDING.- OFFICE OF THE DIRECTION.

Spanish	*English*
COORD: DE PLANEACION Y ENLACE INSTITUCIONAL	*COORDINATION OF PLANNING AND INSTITUTIONAL LIAISON*
DELEGACIÓN MORELOS	*MORELOS BOROUGH*

CÉDULA 2520382

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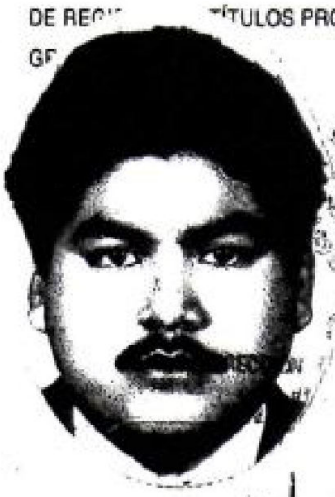

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SECRETARÍA DE EDUCACIÓN PÚBLICA

DIRECCIÓN GENERAL DE PROFESIONES

2520382

EN VIRTUD DE QUE MARCO ANTONIO CEDILLO FLORES CUMPLIÓ CON LOS REQUISITOS EXIGIDOS POR LA LEY REGLAMENTARIA DEL ARTÍCULO 5o. CONSTITUCIONAL EN MATERIA DE PROFESIONES Y SU REGLAMENTO SE LE EXPIDE LA PRESENTE

CÉDULA

CON EFECTOS DE PATENTE PARA EJERCER LA PROFESIÓN DE

MEDICO CIRUJANO Y PARTERO

MEXICO, D.F. A 12 DE AGO DE 1997

DIRECTOR GENERAL DE PROFESIONES

LIC. DIANA CECILIA ORTEGA AMIEVA

Spanish	*English*
CEDULA	*CARD No.*
25200382	*25200382*
TITULO REGISTRADO FOJAS 008-33	*DEGREE LE RECORDED ON REGISTER 008-33*
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SECRETARIA DE EDUCACION PUBLICA	*SECRETARY OF PUBLIC EDUCATION*
DIRECCION GENERAL DE PROFESIONES	*GENERAL DIRECTION OF PROFESSIONS*
2520382	*2520382*
EN VIRTUD DE QUE MARCO ANTONIO CEDILLO FLORES	*SINCE MARCO ANTONIO CEDILLO FLORES*
CUMPLIO CON LOS REQUISISTOS EXIGIDOS POR LA LEY REGLAMENTARIA DEL ARTICULO 5° CONSTITUCIONAL EN MATERIA DE PROFESIONES Y SU REGLAMENTO SE LE EXPIDE LA PRESENTE	*MET THE REQUIREMENTS MANDATED BY THE LEGISLATION OF CONSTITUTIONAL ARTICLE 5 ON PROFESSIONALS AND ITS REGULATION, IT IS HEREBY ISSUED HIS*
CEDULA	*PROFESSIONAL CARD*
CON EFECTOS DE PATENTE PARA EJERCER LA PROFESIÓN DE	*ACTING AS PATENT TO CARRY OUT THE PROFFESSION OF*
**MEDICO CIRUJANO Y PARTERO*	**GENERAL PRACTITIONER*
MEXICO D.F A 12 DE AGO DE 1997	*MEXICO, FEDERAL DISTRICT, 12 AUGUST 1997*
DIRECTOR GENERAL DE PROFESIONES	*GENERAL DIRECTOR OF PROFESSIONS*
LIC. DIANA CICILIA ORTEGA AMIEVA	*LIC. DIANA CECILIA ORTEGA AMIEVA*
FIRMA DEL INTERESADO	*INTERESTED PARTY'S SIGNATURE*

ANNEX 10

Shortened CURRICULUM VITAE (CV)

Name: MARCO
Middle name: ANTONIO
Surname: CEDILLO FLORES
Profession: GENERAL PRACTITIONER
Name of the affiliation facility: MEXICAN SOCIAL SECURITY INSTITUTE

Address: CALLE DEL SABINO, NUMBER 14, RANCHO NUEVO NEIGHBOURHOOD
City: YAUTEPEC
Postal code: 62730
State/Region/Province: MORELOS
Country: MEXICO
Phone: 01735-3943686
Fax: 01736-3943686
Email: centroqxmasson@prodigy,net.mx
Name of the study location
(if different): CUERNAVACA, MORELOS, MEXICO

EDUCATION		
University	**Degree**	**Year of completion**
INSTITUTO POLITÉCNICO NACIONAL	**GENERAL PRACTITIONER**	**1993**
MEDICAL EDUCATION		
University	**Degree**	**Year of completion**
INSTITUTO POLITÉCNICO NACIONAL	**GENERAL PRACTITIONER**	**1993**
BENEMÉRITA UNIVERSIDAD AUTÓNOMA DE PUEBLA	**MAJOR IN GENERAL SURGERY**	**2002**

PROFESSIONAL EXPERTISE/OTHER RELATED TRAINING		
Institution	**Medical field**	**Year of completion**
RE-CERTIFIED BY THE MEXICAN COUNCIL OF GENERAL SURGERY	**GENERAL SURGERY**	**2002/VALID UP TO 2018. FOLIO 02121**
MEXICAN SOCIAL SECURITY INSTITUTE ZACATEPEC, MORELOS, MEXICO	**CLINICAL MEDICAL COORDINATOR**	**2014 /VALID**

Professional licence number: 3509794 (PROFESSIONAL CARD NUMBER)
State/Region/Province: MORELOS, MEXICO
Expiration date: VALID
Research area(s) of interest:
Clinical study phases: ☐ I ■ II ☐ III ☐ IV

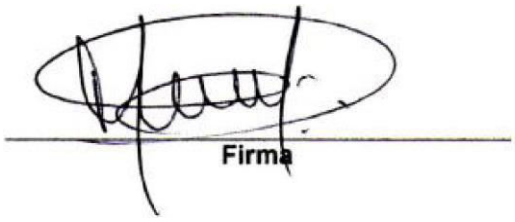
List below your most recent clinical research:

Therapy area:	Study type	Phase:	Completed:	Ongoing
ASSESSMENT OF EFFECTIVENESS AND SAFETY OF THE USE OF TISSUPOR® 3D EMBROIDERY DRESSINGS FOR WOUNDS IN PATIENTS WITH NEUROPATHIC ULCERATION ON THE DIABETIC FOOT	**Industry****	**II**		**XX**
	Started by researcher			
	Academic			
	None			

Training documents on Good Clinical Practices (GCP) (course provider/year of completion):

NOVEMBER 2015

By signing this document, I hereby acknowledge that the information provided in this shortened CV is accurate, and informs about my current job and my qualifications:



Firma

27/NOVIEMBRE/2015.

Fecha

Spanish	*English*
firma	*Signature*
fecha	*Date*
noviembre	*27 November 2015*

MEXICO
Government of the Republic

MORELOS BOROUGH
HEADQUARTERS OF MEDICAL BENEFITS SERVICES
COORDINATION OF PLANNING AND INSTITUTIONAL LIAISON
AUXILIARY MEDICAL COORDINATION FOR HEALTH RESEARCH
IMSS

REF: 18-90-01-280110-060/2016

DATE: 4 AUGUST 2016

DR FABIO SALAMANCA GÓMEZ
HEALTH RESEARCH COORDINATOR
4th FLOOR. BLOQUE B, UNIDAD DE CONGRESOS
NATIONAL MEDICAL CENTRE
AV. CUAUHTEMOC 330, COL. DOCTORES
C.P. 06725 MEXICO D.F.

Dear Dr Salamanca: I do hereby submit the preliminary analysis of protocol entitled: ASSESSMENT OF EFFECTIVENESS AND SAFETY OF THE USE OF TISSUPOR® 3D EMBROIDERY DRESSINGS FOR WOUNDS IN PATIENTS WITH NEUROPATHIC ULCERATION ON THE DIABETIC FOOT, duly recorded on the National Commission for Scientific Research under number R-2015-785-058, that is being developed in Morelos borough.

Due to the significance of findings identified and recorded on the annexed document entitled “Core Document for Expert Opinion”, we consider it is highly important to subject them to consideration every time that findings exceed the percentage proposed in the study hypothesis.

I thank you for your attention

REGARDS,
“SOCIAL SECURITY AND SOLIDARITY”

DR LAURA AVILA JIMÉNEZ
Researcher in charge of the Project
Auxiliary Medical Coordinator for Health Research
Associate Researcher “A”

DC. LAJ

INSTITUTO MEXICANO DEL SEGURO SOCIAL
DIRECCION DE PRESTACIONES MEDICAS
UNIDAD DE EDUCACION INVESTIGACION Y POLITICA DE SALUD
RECIBIDO
05 AGO 2016
10:07
COORDINACION DE INVESTIGACION EN SALUD

CORE DOCUMENT FOR EXPERT OPINION

1. STUDY NAME

ASSESSMENT OF EFFECTIVENESS AND SAFETY OF THE USE OF TISSUPOR® 3D EMBROIDERY DRESSINGS FOR WOUNDS IN PATIENTS WITH NEUROPATHIC ULCERATION ON THE DIABETIC FOOT.

2. RESEARCHERS

RESEARCHER IN CHARGE:
DR IN SCIENCES, LAURA ÁVILA JIMÉNEZ
AUXILIARY MEDICAL COORDINATOR FOR HEALTH RESEARCH
COORDINATION OF PLANNING AND INSTITUTIONAL LIAISON
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ASSOCIATE RESEARCHERS:
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DR ANITA ROMERO RAMÍREZ
COORDINATOR OF PLANNING AND INSTITUTIONAL LIAISON
HEADQUARTERS OF MEDICAL BENEFITS SERVICES
MORELOS BOROUGH
CUERNAVACA, MORELOS
LICENCE: 10657215
PHONE: 777 3 18 76 32
EMAIL: ANITA.ROMERO@IMSS.GOB.MX

1. MEDICAL FACILITIES PARTICIPATING

- Hospital General Regional No. Uno.- AV. Plan de Ayala esq. Av. Central S/N, Col. Ricardo Flores Magón, CP 62460, Cuernavaca, Morelos.

- Hospital General de Zona con Medicina Familiar no. 5; Av. Lázaro Cárdenas S/N. Col. Galeana CP 62780, Zacatepec, Morelos.

2. OPERATIONAL PROCEDURE BASED ON THE ACTIVITIES SCHEDULE PROPOSED ON THE AUTHORISED PROTOCOL

SCHEDULED

ACTIVITY	MONTHS	M1	M2	M3	M4	M5	M6	M7	M8	M9	M10	M11	M12-M18	
Literature review		x	x	x	x	x	x	x	x	x	x	x	x	x
Assessment of the clinical trial protocol before the review committee					x	x	x							
Integration of databases of contact information of patients with ulceration on the diabetic foot					x	x	x	x	x	x				
Start of recruitment							x	x	x	x	x	x		
WEEK 1 assessment and treatment							x	x	x	x	x	x		
WEEK 2 assessment and treatment							x	x	x	x	x	x		
WEEK 3 assessment and treatment							x	x	x	x	x	x		
WEEK 4 assessment and treatment							x	x	x	x	x	x		
Quality assurance							x	x	x	x	x	x		
Intermediate analysis of general assessment							x	x	x	x	x	x		
Statistical analysis													x	
Drafting of the clinical trial final report													x	x
Dissemination of outcomes														x

M: MONTHS

ACTIVITIES PERFORMED UP TO EXPERT OPINION DATE

	MONTHS				
ACTIVITY	M1	M2	M3	M4	
TRAINING	X	X	X	X	
START OF RECRUITMENT		X	X	X	
WEEK 1 ASSESSMENT AND TREATMENT		X	X	X	
WEEK 2 ASSESSMENT AND TREATMENT		X	X	X	
WEEK 3 ASSESSMENT AND TREATMENT		X	X	X	
WEEK 4 ASSESSMENT AND TREATMENT		X	X	X	
QUALITY ASSURANCE		X	X	X	
INTERMEDIATE ANALYSIS OF GENERAL ASSESSMENT		X	X	X	
STATISTICAL ANALYSIS				X	

A) TRAINING

IT WAS PERFORMED IN FOUR AREAS:

I. - TRAINING TO DOCTORS HIRED TO CARRY OUT HEALINGS (6 PROFESSIONALS IN TOTAL) ON COMPUTER EQUIPMENT USE WITH DATA RECORDING SOFTWARE AND MEASUREMENT CAMERA.

II. - TRAINING ON THE USE OF FITTED DEBRIDEMENT TECHNIQUE DEVELOPED FOR THE USE OF THE DRESSING SUBJECT MATTER OF THIS STUDY.

III. - HANDLING OF SCREENING DOCUMENTS, DATA RECORDING, INFORMED CONSENT, AND INTEGRATION OF FILES.

IV. - BASIC KNOWLEDGE OF THE PRODUCT, STUDY PURPOSE, AND TECHNICAL MANUAL, DESIGN, AND APPLICATION OF THE PRODUCT.

B) RECRUITMENT

I. REGARDING THE PROCEDURE AND AFOREMENTIONED STANDARDS TO CARRY OUT PRODUCTS STUDIES IN COLLABORATION WITH THE IMSS, AND REGARDING THE PROGRAM SET IN THE AUTHORISED PROTOCOL, THE RECRUITMENT OF BENEFICIARY PATIENTS DIAGNOSED WITH DIABETES MELLITUS TYPE 2 REGISTERED ON THEIR CLINICAL FILES WERE RECRUITED, OF AT LEAST TWO WEEKS BEFORE THEY ARE ADMITTED TO THE STUDY, WITH A 1 OR 2 WAGNER CLASSIFICATION.

FOR THE STUDY PROCEDURE, THE TWO ARMS WERE INCLUDED:

CONTROL ARM

A.- PATIENTS FOR STANDARD TREATMENT, AT HOSPITAL GENERAL REGIONAL CON MEDICINA FAMILIAR NO. 1, (HGR MF1) IN CUERNAVACA, MORELOS.

INTERVENTION ARM

A.- PATIENTS AFFILIATED TO HOSPITAL GENERAL DE ZONA CON MEDICINA FAMILIAR NO. 5 (HGZ MF5) IN ZACATEPEC, MORELOS.

IN THIS ARM, THE DATA AND MEASUREMENT RECORDING PROCEDURE WAS PERFORMED WITH TWO CAMERAS (SILHOUETTESTAR) AND TWO COMPUTER EQUIPMENT (ASSUS) IN ORDER TO RECORD DATA SENT VIA INTERNET TO THE SOFTWARE MANAGEMENT CENTRAL IN NEW ZEALAND. RECORDS OF CAMERA 1 IDENTIFIED TO MONITOR ARM AS ZACATEPEC, AS HGZ MF1 , AND RECORDS OF CAMERA 2 IDENTIFIED AS HGZ MF1A.

DATA FROM BOTH GROUPS (OF THE THREE CHAMBERS IN LINE) WERE PLACED IN A PIECE OF EQUIPMENT USED AS “CENTRAL” IN THE OFFICE CONDITIONED FOR THAT PURPOSE IN THE BUILDING OF BOROUGH OF THE IMSS IN CUERNAVACA, MORELOS.

II. EXCLUSION: PATIENTS EXCLUDED WERE THOSE ULCERS CLASSIFIED AS WAGNER 3, AND/OR IN EPITHELISATION PHASE, JOINT SEPSIS, LOCALISED GANGRENE (FOREFOOT OR HEEL), EXTENSIVE GANGRENE, SERIOUS INFECTION, IN THEIR DIAGNOSTIC, INCLUDING THOSE WITH ANGIOLOGY PROBLEMS WHICH POSED A RECOVERY ISSUE FOR THIS CAUSE. BESIDES, ALL PATIENTS WITH ULCERATION DIAGNOSED AS VARICOSE WERE EXCLUDED.

THIS PROCEDURE WAS COMPLETED WHEN THE NUMBER OF ULCERS SET FOR THE STUDY WERE REACHED, OBTAINING UP TO THE ASSESSMENT DATE (30 JUNE 2016) 56 ULCERS IN 29 PATIENTS RECRUITED FOR THE CONTROL ARM IN HOSPITAL GENERAL REGIONAL NUM. 1 AND 92 ULCERS IN 44 PATIENTS RECRUITED FOR THE INTERVENTION ARM.

FOR THE ASSESSMENT, THE NUMBER OF PATIENTS RECRUITED IN THE INTERVENTION ARM, COMPOSED BY AFFILIATES TO AL HOSPITAL REGIONAL DE ZONA CON MEDICINA FAMILIAR No. 5 IN ZACATEPEC, WAS MADE UP ACCORDING TO THE FOLLOWING CHARTS.

III. ANALYSIS OF THE CONSTITUTED ARMS

A) CONTROL ARM

FOR THE ANALYSIS OF PATIENTS PARTICIPATING IN THE CONTROL ARM, 29 PATIENTS WERE RECRUITED, WHO SIGNED AN INFORMED CONSENT FORM. IN THIS ARM, A TOTAL OF 56 ULCERS WERE ASSESSED, DIAGNOSED WAGNER 1 AND WAGNER 2.

CONTROL ARM
HOSPITAL GENERAL REGIONAL CON MEDICINA FAMILIAR NO. 1

ADSCRIPTION	40-45	46-50	51-55	56-60	61-65	66-70	71-75	76-82
HGR MF1	0	0	1	2	2	0	2	3
HGR MF1	0	0	1	5	2	2	0	0
HGR MF1	0	1	0	3	2	2		1
	0	1	2	10	6	4	2	4

	0	1	2	10	6	4	2	4
%	0.00	3.45	6.90	34.48	20.69	13.79	6.90	13.79
					65.52			34.48

- 16 MEN 55.17%
- 13 WOMEN 44.83%

B) INTERVENTION ARM
FOR THE ANALYSIS OF PATIENTS PARTICIPATING IN THE INTERVENTION ARM AND ASSESSMENT OF **TISSUPOR® 3D EMBROIDERY** DRESSINGS FOR WOUNDS, 44 PATIENTS WERE RECRUITED, WHO SIGNED AN INFORMED CONSENT FORM. IN THIS ARM, A TOTAL OF 59 ULCERS WERE ASSESSED, DIAGNOSED WAGNER 1 AND WAGNER 2.

INTERVENTION ARM
HOSPITAL GENERAL DE ZONA CON MEDICINA FAMILIAR NUM. 5

ADSCRIPTION	40-45	46-50	51-55	56-60	61-65	66-70	71-75	76-78
HGZ MF5	0	0	3	2	3	1	0	1
HGZ MF5	1	0	1	2	3	2	0	1
HGZ MF5	1	3	2	0	2			
	2	3	6	4	8	3	0	2
HGZ MF5A	1	2	1	0	4	0	2	0
HGZ MF5A	2	1	0	2	0	1		
	3	3	1	2	4	1	2	0

	5	6	7	6	12	4	2	2
%	11.36	13.64	15.91	13.64	27.27	9.09	4.55	4.55
					81.82			18.18

NOTE: HGZ MF= CAMERA ONE HGZ MF5A = CAMERA TWO

- 29 MEN 65.90%
- 15 WOMEN 34.10%

C) BEHAVIOUR OF ARMS ACCORDING TO AGE RANGE

CONTROL ARM

- IN THE CONTROL ARM, THE AGE RANGE SET WAS 46-82 YEARS.
- THE HIGHEST PERCENTAGE APPEARED IN THE RANGE OF 56-60 YEARS, WITH 35.71%
- THE HIGHEST CONCENTRATION APPEARED IN THE RANGE OF 46-65 YEARS, WITH 64.29%

INTERVENTION ARM

- IN THE INTERVENTION ARM, THE AGE RANGE SET WAS 41-78 YEARS.
- THE HIGHEST PERCENTAGE APPEARED IN THE RANGE OF 61-65 YEARS, WITH 27.27%
- THE HIGHEST CONCENTRATION APPEARED IN THE RANGE OF 40-65 YEARS, WITH 81.82%

IV ANALYSIS OF THE SYSTEM IMPLEMENTED FOR MEASUREMENT

THE IRREGULAR SHAPE OF ULCERS REQUIRE AN ADVANCED SYSTEMS FOR ITS MEASUREMENT THAT ALLOWS SETTING TWO IMPORTANT PARAMETERS TO KNOW THEIR VOLUME IN CM3, SPECIFIED FOR THE MEASUREMENT OF THE WOUND AREA AND ITS DEPTH.

THE MEASUREMENT OF THE IRREGULAR AREA REQUIRES DATA OF THE SHAPE OF THE ULCER USING INFORMATION COLLECTED FROM:

- WOUND OR ULCER LONGITUDE
- ULCER WIDTH
- MEASUREMENT OF 2 AXES CROSSING IN THE MIDDLE OF THE ULCER, AND WHICH HAVE AS MEASUREMENT LIMIT THE POLYGON OR MARKED PERIMETER ON THE MARGIN OF THE OPENING, I.E. UP TO THE EPITHELISATION MARGIN.

THE INTERNAL SURVEYING OF THE ULCER IS SET ACCORDING TO THE MEASURE OF THE CONCAVITY ESTIMATED USING THE AXES TO OBTAIN:

- MAXIMUM DEPTH
- AVERAGE DEPTH

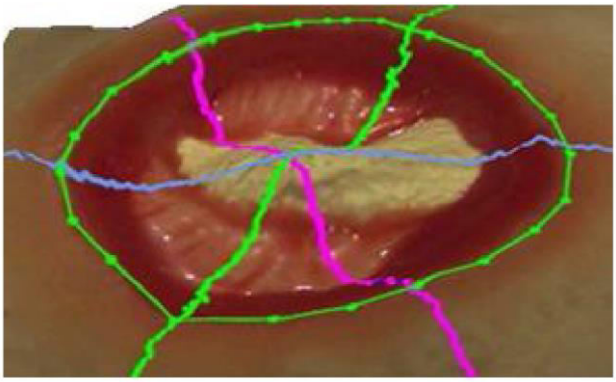
ULCERS IN SOME AREAS TEND TO HAVE CERTAIN CONVEXITY, SUCH AS THOSE ON THE TOES AND HEEL, AND VARIANTS MAY MAKE THE DEPTH MEASUREMENT BE ESTIMATED IN MILLIMETRES.

EQUATION

WSA % = [INITIAL WSA (CM^2) - WSA (CM^2) DURING WEEK 1] X 100
WSA: WOUND SURFACE ARE IT WAS SET IN ORDER TO MAKE AN ASSESSMENT BASED ON

THE MEASUREMENT OF EACH ULCER USING THE TRANSPARENT FILM KNOWN AS VISITRAK, AND RECORDED ON A MEASUREMENT TABLE, WHERE THE AREA IS SET IN CMS2, AND ITS PROGRESS EVERY 8 DAYS OF HEALING.

IN SEARCH FOR A MORE EXACT ALTERNATIVE, THE GROUP OF INVESTIGATORS REQUESTED THE COMPANY TO REPLACE THE MEASUREMENT EQUIPMENT USING VISITRAK FOR THAT ONE OF SILHOUETTESTAR CAMERA WITH SILHOUETTECENTRAL SOFTWARE, WHICH PERFORMS MEASUREMENT REDUCING SCOPE FOR HUMAN ERROR, AND MAKING THE ULCERATION MEASUREMENT MORE OBJECTIVE.

SILOUETTESTAR CAMERA IMAGE	MARKING IMAGE
	

THE CAMERA TAKES A PHOTOGRAPH WITH THE AID OF A LASER MARKER OF THE AXES, AND SENDS THE IMAGE TO A COMPUTER SYSTEM, AND, OVER THE DIGITALISED IMAGE, IT MARKS A DOTTED PERIMETER OF THE ULCER. THEN, IT SENDS IT TO THE SYSTEM. THE ONLINE SOFTWARE CONNECTED TO A CENTRAL BASE IN NEW ZEALAND PROCESSES DATA AND GENERATES THE ENTIRE MEASUREMENT.

IN THE SYSTEM, TWO IMAGES ARE INCLUDED FOR EACH HEALING:

IMAGE A.- BEFORE HEALING
IMAGE B.- AFTER HEALING

BESIDES, IN THE RECORD, ERRORS RELATED TO WRITING AND DETERMINATION OF THE EXACT LOCATION OF THE ULCER WITH INDIVIDUAL MEASUREMENT WERE REMOVED, OR JUST PLACING THE IMAGE FOR THE MOST REPRESENTATIVE IMAGE, OR THE ONE OF LARGER VOLUME, SINCE SOME PATIENTS HAD MORE THAN ONE ULCER IN THE SAME LIMB, OR DIFFERENT ONES IN EACH FOOT. THE IDENTIFICATION AND MARKING WERE PERFORMED IN THE SCREENING DOCUMENT INCLUDED IN EACH FILE OF PARTICIPANT PATIENTS.

THE SOFTWARE PERFORMS THE PROCESSING OF DATA REGISTERED IN THE SYSTEM INSTALLED IN EACH COMPUTER EQUIPMENT, AND IN ORDER TO REACH A MORE OBJECTIVE MONITORING, DOCTORS WHO ASSISTED THE CONTROL ARM (HGR MF1) WERE EQUIPPED WITH AN ASSUS LAPTOP, AND A CAMERA (SILHOUETTESTAR), WHICH IS CONNECTED TO THE SOFTWARE INSTALLED (SILHOUETTECENTRAL) AND THE IMAGE TAKEN IS SENT TO THE EQUIPMENT DISPLAY, WHERE THE PERIMETER MARKING IS PERFORMED, AND SENT FOR ITS PROCESSING: DOCTORS TREATING THE INTERVENTION ARM (HGZ MF5) ALSO HAD TWO ASSUS LAPTOPS, AND ONE CAMERA EACH (HGZ MF5 AND HGZ MF5A).

CONTROL OF THE DATA FROM BOTH GROUPS WAS PERFORMED AT A CENTRAL FACILITY NETWORKED AND OPERATED BY THE RESEARCHER IN CHARGE, TO WHICH OPERATING DOCTORS HAD NO ACCESS. CENTRAL EQUIPMENT IS AN ASSEMBLED FIXED COMPUTER (MARC GYGABYTE GA-Z97XSLI S. 1150: WITH HP 27”IPS LED MONITOR; 1 EAGLE WARRIOR MOUSE, GAMINGMOUSE G13 MODEL). 1 EAGLE WARRIOR KEYBOARD, GAMINGKEYBOARD G78 MODEL).

EACH IMAGE, DATA AND PROCESS IS SENT TO THE CENTRAL IN NEW ZEALAND AFTER ITS STORAGE AND SUBMISSION, WHICH ALSO KEEPS A STRICT CONTROL THAT DOES NOT ALLOW, AFTER THIS PROCESS, ANY KIND OF MANOEUVRING BY ANY OPERATOR, NOR BY THE RESEARCHERS GROUP; IT KEEPS DATA BACKUP, AND SENDS THEM BACK THROUGH THE SYSTEM TO THE CENTRAL IN MEXICO FOR THE RESEARCH GROUP TO HAVE AT THEIR DISPOSAL, AND SENDS THE SAME DATA TO THE PARTICIPATING COMPANY, FOR IT TO ANALYSE THE BEHAVIOUR OF THE PRODUCT IN THE TRIAL.

WITH THE AFOREMENTIONED DATA, AND ACCORDING TO THE RESEARCH PROTOCOL, CALCULATIONS TO RULE A PROGRESS HIGHER THAN 24% ARE SET, ESTABLISHED BY MEASUREMENT RECORDS OF SILHOUETTECENTRAL SYSTEM.

IN AN ANALYSIS OF 44 PATIENTS REGISTERED BETWEEN 1 MAY 2016 AND 30 JUNE 2016, 68 ULCERS WERE REGISTERED, OF A TOTAL OF 57 TO BE TREATED. THIS INCREASE WAS DUE TO THE FACT THAT THERE WERE PATIENTS WITH 2, 3, AND UP TO 7 ULCERS.

FOR THE EFFECTS OF TREATMENT AND ASSESSMENT, IT IS DETERMINED THAT THE PURPOSE OF RECORDING PROJECTED ULCERATIONS HAS BEEN MET.

IN THIS ANALYSIS, (ANNEXED IN AN EXCEL TABLE), CALCULATING WITH RECORD DATE ON 30 JUNE, AND ESTIMATING PROGRESSION TO TREATMENT NUMBER FOUR, A 34.46% OF RECOVERY PERFORMANCE OF THE VOLUME WAS OBTAINED, COMPARED TO THE ULCER AREA MEASUREMENT, AND -3.43% COMPARED TO THE VOLUME, WITH AN AREA/VOLUME RATION OF 31.02% OF GENERAL AVERAGE SINCE IN THE TOPOGRAPHY OF THE ULCER, ALL OF THEM HAVING CONVEXITY SHOW MEASUREMENT OF “0”.

V. GENERALISED ANALYSIS AND CONCLUSIONS

ALL THE ULCERS, ALL THE PATIENTS
SILHOUETTECENTRAL DATABASE

THE TOTAL COUNT FOR THE STUDY WAS 148 ULCERS.

- 29 PATIENTS, 16 MEN (55.17%) AND 13 WOMEN (44.83%) WITH 56 ULCERS IN THE CONTROL ARM AT HOSPITAL GENERAL DE ZONA CON MEDICINA FAMILIAR No. 1 IN CUERNAVACA.
- 44 PATIENTS, 29 MEN (65.90%) AND 15 WOMEN (34.10%) WITH 92 ULCERS IN THE INTERVENTION ARM AT HOSPITAL GENERAL DE ZONA CON MEDICINA FAMILIAR No. 5 IN ZACATEPEC. IN THIS HOSPITAL, UP TO THE RECORD DATE FOR THE ASSESSMENT, 990 HEALINGS WERE COUNTED IN ALL PATIENTS.

IN FACILITY HGR MF1 OF CUERNAVACA, THE AVERAGE OF HEALINGS FOR WAGNER 1 AND WAGNER 2 PATIENTS WAS 12.25 AND 12.76 RESPECTIVELY. FOR PATIENTS TREATED IN HGZ MF5 OF ZACATEPEC WITH TISSUPOR® 3D EMBROIDERY DRESSINGS WITH WAGNER 1 AND WAGNER 2 CLASSIFICATION WAS 5.06 AND 6 HEALINGS ON AVERAGE, RESPECTIVELY (TABLE 1). IN OTHER WORDS, PATIENTS TREATED IN THE MEDICAL FACILITY OF ZACATEPEC, REQUIRED AT LEAST 50% LESS HEALINGS COMPARED TO THOSE OF THE MEDICAL FACILITY IN CUERNAVACA, WHO HAD STANDARD TREATMENT.

WHILE CONDUCTING THE MEAN DIFFERENCE ANALYSIS COMPARED TO THE % OF REDUCTION OF THE AREA, IT WAS OBSERVED THAT OF THE LEVENE TEST, THE P VALUE IS SIGNIFICANT, AND IT IS ASSUMED THAT THERE ARE DIFFERENT VARIANCES. THUS, THE STATISTICAL RESULT OF THE TEST IS t=-3.860, AND THE ASSOCIATED P VALUE IS 0.00. THEREFORE, THERE IS A DIFFERENCE IN BOTH FACILITIES WHERE PATIENTS WERE TREATED, AND MEANS ARE 95% DIFFERENT. IN THE CASE OF ZACATEPEC, THE MEANS IS MORE THAN DOUBLE THAN IN CUERNAVACA, WITH A P VALUE OF 0.000 (TABLES 2 AND 3). LIKEWISE, IT WAS OBSERVED THAT THERE WERE DIFFERENCES ACCORDING TO GENDER IN THE TREATMENT RESPONSE OF MEN (P 0.000) (STATA 12.0).

THESE RESULTS ALLOW US TO CONCLUDE THAT PATIENTS IN ZACATEPEC TREATED WITH TISSUPOR® 3D EMBROIDERY DRESSINGS HAD MORE PERCENTAGE OF REDUCTION AREA COMPARED TO PATIENTS IN CUERNAVACA, WHO HAD STANDARD TREATMENT (CONTROL ARM). THIS IS STATISTICALLY SIGNIFICANT, EVEN WITH FOLLOW-UP LOSSES AND PATIENTS WHO ABANDONED THE TREATMENT (< 30%). THEREFORE, IT IS IMPORTANT TO CONSIDER TREATMENT WITH TISSUPOR® 3D EMBROIDERY DRESSINGS TO IMPROVE THE PROGNOSIS OF PATIENTS WITH DIABETIC FOOT, AND TO AVOID AMPUTATIONS OF THE EXTREMITY BEING COMPROMISED. LIKEWISE, IT WOULD BE IMPORTANT TO CARRY OUT ANOTHER RESEARCH MEASURING THE COST-BENEFIT IMPACT, SINCE IN THIS RESEARCH, IT WAS FOUND THAT THE NUMBER OF HEALINGS DECREASES IN MORE THAN 50% OF PATIENTS IN ZACATEPEC MEDICAL FACILITY TREATED WITH TISSUPOR® 3D EMBROIDERY DRESSINGS COMPARED TO

PATIENTS WHO RECEIVED STANDARD TREATMENT IN THE CONTROL ARM (HGR MF1). THIS HAS IMPLICATIONS, NOT ONLY IN THE SUBSTANTIAL COST SAVING IN HEALING MATERIAL, BUT ALSO IN THE NEED TO PRESCRIBE TREATMENT WITH MULTIPLE ANTIBIOTICS SINCE, IN THE CASE OF PATIENTS TREATED WITH TISSUPOR® 3D EMBROIDERY DRESSINGS (PETRULYTE S, 2008), THE USE OF ANTIBIOTICS IS DISPENSED WITH, PRIORITISING TOPIC TREATMENT. IN ADDITION, THIS CREATES SAVINGS IN THE NUMBER OF TRANSPORT COSTS FOR PATIENTS TO HAVE THEIR HEALINGS CARRIED OUT, OR THOSE THE OUTPATIENT FACILITY NEEDS TO CARRY OUT HEALINGS AT THE PATIENT'S ADDRESS. THIS ALSO CREATES SAVINGS IN WORKER-HOURS, FUEL, AND EVEN BURNOUT OF THE PRIMARY CAREGIVER TAKING CARE OF THE PATIENT AT HOME.

ON THE OTHER HAND, FROM THE CLINICAL PERSPECTIVE, IT WAS OBSERVED IN THE ARM THAT BELONGED TO PATIENTS TREATED AT THE FACILITY IN ZACATEPEC, CLASSIFIED AS WAGNER 1, AND WHO WERE TREATED WITH THE DRESSING, THAT THEY SHOWED FASTER EVOLUTION TO WOUND HEALING COMPARED TO SUBJECTS IN CUERNAVACA FACILITY, WHO RECEIVED CONVENTIONAL TREATMENT. THIS HAS BEEN BASED ON RESULTS OBTAINED, FOR EXAMPLE: ON 7 PATIENTS WHO WERE DISCHARGED FOR HEALING OF WAGNER 1 ULCERS. IN THE CASE OF PATIENTS IN CUERNAVACA FACILITY, IT WAS OBSERVED THAT THEY SHOWED A SLOWER EVOLUTION TO WOUND HEALING, AND THEY REQUIRE CLOSER MONITORING SINCE THEY CAN EASILY RELAPSE. IT MUST BE STATED THAT IT ESSENTIALLY DEPENDS ON THE PATIENT'S REST. IT WAS ALSO FOUND THAT THEY DO NOT GET EASILY INFECTED. AS REGARDS HEALING, IT DOES NOT NEED TO BE AGGRESSIVE.

AS REGARDS WAGNER 2 CLASSIFICATION PATIENTS, IT WAS FOUND THAT THEY MAY EASILY EVOLVE TO WAGNER 3. IN THIS SENSE, THE KEY TO SUCCESS IN THIS PATIENTS IS TO IMPROVE HEALING TECHNIQUE ON THE BASIS OF DEBRIDEMENT. LIKEWISE, HUMIDITY KEEPS THE WOUND IN GOOD CONDITION. AGGRESSIVE HEALINGS WITH DEBRIDEMENT MAKE THE WOUND EVOLVE FASTER TO WOUND HEALING.

IT WAS DETERMINED THAT KEEPING PROLONGED SUPPORT OVER THE WOUND EVOLVES QUICKLY TO NECROSIS. SOME EVOLVE FASTER FROM THE INFLAMMATORY PHASE TO THE PROLIFERATION PHASE. WITHIN THE PROLIFERATION PHASE ITSELF, EVOLVING FROM ANGIOGENESIS TO GRANULATION IS FASTER, THAN FROM GRANULATION TO RE-EPITHELISATION. THAT MENTIONED BEFORE IS GREATLY DETERMINED BY OPTIMUM METABOLIC CONTROL.

IN CASES OBSERVED IN THE ZACATEPEC FACILITY WITH THE USE OF THE DRESSING, IT WAS OBSERVED THAT IN VERY SMALL ULCERS, IT WAS DIFFICULT TO PLACE THE DRESSING, AND THIS INCREASES WITH UNSUITABLE FOOTWEAR, INCREASING THE RISK IT MOVES OUTSIDE THE ULCER. FOR THIS REASON, THE USE OF PROPER FOOTWEAR IS IMPORTANT FOR THE DIABETIC FOOT.

IN SUMMARY, IT IS ASSUMED THAT THE DIABETIC FOOT IN ITS ADVANCED STAGES (WAGNER 2, 3, AND 4) (MARTÍNEZ DE JESÚS, ET AL, 2012) IS ONE OF THE MOST SEVERE COMPLICATIONS FOR PATIENTS WITH DM2, SINCE IT CREATES FUNCTIONAL DEPENDENCE AND PROGRESSIVE AND PERMANENT DISABILITY (INCLUDING PREMATURE DEATH) (INTERNATIONAL DIABETES FEDERATION, 2014), COUPLED WITH LOST PRODUCTIVE LIFE YEARS, WHICH HAS IMPLICATIONS FOR THE HEALTHCARE SYSTEM, SOCIETY, AND ESSENTIALLY FOR THE FAMILY. THIS CREATES A SIGNIFICANT BURDEN FOR THE PRIMARY CAREGIVER, WHO IS GENERALLY THE WIFE OR THE CLOSEST SON/DAUGHTER. IT IS WORTH RECALLING THAT CHRONIC PATIENTS REQUIRE CHRONIC CARE. HOWEVER, OVER TIME, THIS SUPPORT PROVIDED BY THE FAMILY TENDS TO LEAD TO BURNOUT. THEREFORE, INNOVATIONS RELATED TO THE DIABETIC FOOT TREATMENT IS KEY TO KEEP THE MOBILITY OF PATIENTS SUFFERING FROM THESE COMPLEX CONDITIONS IN AN ERA OF LIMITED RESOURCES, WHERE CHRONICAL DISEASES AND THEIR COMPLICATIONS HAVE OVERWHELMED INSTITUTIONS (WONG R, ET AL, 2012).

TABLE 1. NUMBER OF HEALINGS PER ULCER ACCORDING TO CARE FACILITY			
CUERNAVACA FACILITY (AVERAGE OF HEALINGS PER ULCER WITH STANDARD TREATMENT)		ZACATEPEC FACILITY (AVERAGE OF HEALINGS PER ULCER WITH NON-STANDARD TREATMENT/DRESSINGS)	
WAGNER 1	WAGNER 2	WAGNER 1	WAGNER 2
12.25	12.76	5.06	6

TABLE 2. AREA REDUCTION %

	MEDICAL FACILITIES	N	MEAN	STD DEVIATION	STANDARD ERROR OF THE MEAN
AREA REDUCTION (%)	CUERNAVACA	56	0.120	0.2283	0.0305
	ZACATEPEC	92	0.308	0.3633	0.0379

Table 3. Area reduction % - Independent samples test

		Levene test for equality of variances		T Test for equality of means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean difference	Std. error difference	95% confidence interval Lower	95% confidence interval Upper
reduction area (%)	Equal variance assumed	37.428	0.000	-3.470	146	0.001	-0.1877	0.0541	-0.2947	-0.0808
	Equal variance not assumed			-3.860	145.824	0.000	-0.1877	0.0486	-0.2839	-0.0916

VI. SOCIO-ECONOMIC ANALYSIS OF THE STUDY

PERCENTAGES HIGHER THAN 80% OF SICK PEOPLE WITHIN AN AGE RANGE OF 40-65 SIGNIFICANTLY AFFECT THE ECONOMY OF THE PATIENT'S FAMILY IN A REDUCTION OF THE PRODUCTIVE RHYTHM, TENDENCY TO INCREASE MEDICAL LEAVES OF ABSENCE AND MEDICAL LEAVES OF THE PATIENTS; AND THIS GREATLY DAMAGE THE ECONOMY OF THEIR FAMILIES, BEING COMPANIES THOSE WHICH ARE AFFECTED THE MOST.
THE IMPACT OF THE PARTIAL OR TOTAL LOSS OF LIMBS DUE TO AMPUTATION DAMAGES THE SOCIAL STABILITY OF THE FAMILY, IT HAS NEGATIVE EFFECTS SINCE IT IS CONSIDERED AS THE CAUSE OF OTHER TYPES OF PROBLEMS THAT APPEAR WITHIN A COMPANY AND FAMILY TOO.

THE PURPOSE IS TO ABIDE BY EVERYTHING SET IN THE PROTOCOL, AND TO PROVIDE A POSITIVE EXPERT OPINION SINCE RESULTS ARE VERY SATISFACTORY. AND HOWEVER, THERE ARE PATIENTS IN THE CONTROL ARM, WHO SHOW HIGHLY NEGATIVE ADVANCES COMPARED TO THOSE OF THE INTERVENTION ARM. THIS INDICATES THAT FOR THEIR WELLBEING, AND METING ALL NORMATIVE AND ETHICAL PROCEDURES OF THE RESEARCH ARM, A "POSITIVE" EXPERT OPINION IS PROVIDED IN ORDER TO BE INCLUDED IN THE TREATMENT FOR THE CONTROL ARM IMMEDIATELY.

ZACATEPEC, MORELOS, 29 SEPTEMBER 2016

DR LAURA AVILA JIMENEZ
RESEARCHER IN CHARGE
CUERNAVACA, MORELOS

CARRYING ON WITH THE ASSESSMENT PROCESS OF **TISSUPOR® 3D EMBROIDERY** DRESSINGS, I HEREBY ATTACH THE SECOND ASSESSMENT REPORT OF THE STUDY WITH RECORD DATE ON 23 SEPTEMBER 2016, HAVING AS SUPPORT THE MEASUREMENT PROGRAM IMPLEMENTED, SilhouetleCentral SOFTWARE, WITH EQUIPMENT SilhouetleStar TO TAKE IMAGES, AS WELL AS DATABASES OF DOCTORS DESIGNATED PER ARM, BOTH INTERVENTION AND CONTROL.

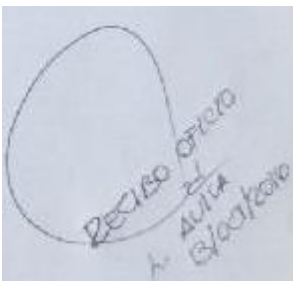
IN THE SAME WAY AS IN THE PREVIOUS REPORT, ALL THE VALUES USED FOR THE ASSESSMENT RESULTED FROM SOFTWARE DATA PROCESSING, WITH PLANIMETRIC MEASUREMENT OF EACH ULCER INDIVIDUALLY, AND FOR THE MATHEMATICAL AND STATISTICAL CALCULATION OF THE STATA v12 SYSTEM.

ANALYSIS WERE PERFORMED ACCORDING TO THE AUTHORISED PROTOCOL, COMPLYING WITH RESEARCH REGULATION, AND FOLLOWING YOUR INSTRUCTIONS STRICTLY, WITH VERIFIABLE DATA IN THE COMPUTER PROGRAM PROCURED FOR THIS END

REGARDING THE FULFILMENT OF THE STIPULATED TARGET FOR ALL PATIENTS OF 72% AFTER 12 WEEKS, 65.93% WAS REACHED AFTER 11 WEEKS IN THE INTERVENTION ARM, WHILE IN THE CONTROL ARM, THERE WAS A -17.27% PROGRESS; THEREFORE, WE CAN STATE THAT THE TARGET WAS SUCCESSFULLY FULFILLED ACCORDING TO THE AUTHORISED PROTOCOL, AS IT IS RECORDED IN THE DOCUMENT SENT FOR YOUR ANALYSIS AND APPROVAL.

HAVING NOTHING FURTHER TO ADD, I SEND YOU MY KIND

REGARDS,



DR MARCO ANTONIO CEDILLO FLORES

ASSOCIATE RESEARCHER AND CLINICAL
COORDINATOR , AFTERNOON SHIFTS AT
HOSPITAL GENERAL DE ZONA CON MEDICINA
FAMILIAR NO. 5 ZACATEPEC, MORELOS

WITH COPY TO GENERAL DIRECTOR.- HOSPITAL BUILDING.- OFFICE OF THE DIRECTION.

Spanish	***English***
Recibo oficio	*Acknowledgement of receipt*

MEXICO
Government of the Republic

MORELOS BOROUGH
HEADQUARTERS OF MEDICAL BENEFITS SERVICES
COORDINATION OF PLANNING AND INSTITUTIONAL LIAISON
AUXILIARY MEDICAL COORDINATION
FOR HEALTH RESEARCH
IMSS

REF: 18-90-01-280110-636/2016

DATE: 25 OCTOBER 2016

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NATIONAL MEDICAL CENTRE
AV. CUAUHTEMOC 330, COL. DOCTORES
C.P. 06725 MEXICO D.F.

Dear Dr Salamanca: I do hereby submit the final analysis of protocol entitled: ASSESSMENT OF EFFECTIVENESS AND SAFETY OF THE USE OF TISSUPOR® 3D EMBROIDERY DRESSINGS FOR WOUNDS IN PATIENTS WITH NEUROPATHIC ULCERATION ON THE DIABETIC FOOT, duly recorded on the National Commission for Scientific Research under number R-2015-785-058, that was developed in Morelos borough.

Due to the significance of findings identified and recorded on the annexed document entitled "Core Document for Expert Opinion", we consider it is highly important to subject them to consideration, and for the possible integration to the next meeting of the Group for the Application of Successful Research Results (Grupo para la Aplicación de Resultados Exitosos de la Investigación, CAREI) every time that findings exceed the percentage proposed in the study hypothesis.

I thank you for your attention

REGARDS,
SOCIAL SECURITY AND SOLIDARITY

DR LAURA AVILA JIMENEZ
Researcher in charge of the Project
Auxiliary Medical Coordinator for Health Research
Associate Researcher "A"

DC LAJ

INSTITUTO MEXICANO DEL SEGURO SOCIAL
RECIBIDO
26 OCT 2016
14:07
COORDINACION DE INVESTIGACION EN SALUD
Recibí cuadernillo

Spanish	*English*
Recibí cuadernillo	*I received the booklet*

CORE DOCUMENT FOR EXPERT OPINION

3 STUDY NAME

ASSESSMENT OF EFFECTIVENESS AND SAFETY OF THE USE OF TISSUPOR® 3D EMBROIDERY DRESSINGS FOR WOUNDS IN PATIENTS WITH NEUROPATHIC ULCERATION ON THE DIABETIC FOOT.

4 RESEARCHERS

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3 MEDICAL FACILITIES PARTICIPATING

- Hospital General Regional No. Uno.- AV. Plan de Ayala esq. Av. Central S/N, Col. Ricardo Flores Magón, CP 62460, Cuernavaca, Morelos.

- Hospital General de Zona con Medicina Familiar no. 5; Av. Lázaro Cárdenas S/N. Col. Galeana CP 62780, Zacatepec, Morelos.

4 OPERATIONAL PROCEDURE BASED ON THE ACTIVITIES SCHEDULE PROPOSED ON THE AUTHORISED PROTOCOL

SCHEDULED

ACTIVITY	MONTHS	M1	M2	M3	M4	M5	M6	M7	M8	M9	M10	M11	M12-M18	
Literature review		**x**	**x**	**x**	**x**	**x**	**x**	**x**	**x**	**x**	**x**	**x**	**x**	**x**
Assessment of the clinical trial protocol before the review committee					**x**	**x**	**x**							
Integration of databases of contact information of patients with ulceration on the diabetic foot					**x**	**x**	**x**	**x**	**x**	**x**				
Start of recruitment							**x**	**x**	**x**	**x**	**x**	**x**		
WEEK 1 assessment and treatment							**x**	**x**	**x**	**x**	**x**	**x**		
WEEK 2 assessment and treatment							**x**	**x**	**x**	**x**	**x**	**x**		
WEEK 3 assessment and treatment							**x**	**x**	**x**	**x**	**x**	**x**		
WEEK 4 assessment and treatment							**x**	**x**	**x**	**x**	**x**	**x**		
Quality assurance							**x**	**x**	**x**	**x**	**x**	**x**		
Intermediate analysis of general assessment							**x**	**x**	**x**	**x**	**x**	**x**		
Statistical analysis													**x**	
Drafting of the clinical trial final report													**x**	**x**
Dissemination of outcomes														**x**

M: MONTHS

ACTIVITIES PERFORMED BEFORE STARTING THE STUDY, PATIENT LEVEL

ACTIVITY	**MONTHS**	**M1**	**M2**	**M3**	**M4**	**M5**
Literature review		x	x	x	x	x
Assessment of the clinical trial protocol before the review committee					x	x
Integration of databases of contact information of patients with ulceration on the diabetic foot					x	x

ACTIVITIES PERFORMED UP TO FIRST EXPERT OPINION

	MONTHS				
ACTIVITY	M1	M2	M3	M4	
TRAINING	X	X	X	X	
START OF RECRUITMENT		X	X	X	
WEEK 1 ASSESSMENT AND TREATMENT		X	X	X	
WEEK 2 ASSESSMENT AND TREATMENT		X	X	X	
WEEK 3 ASSESSMENT AND TREATMENT		X	X	X	
WEEK 4 ASSESSMENT AND TREATMENT		X	X	X	
QUALITY ASSURANCE		X	X	X	
INTERMEDIATE ANALYSIS OF GENERAL ASSESSMENT		X	X	X	
STATISTICAL ANALYSIS				X	

ACTIVITIES PERFORMED UP TO SECOND EXPERT OPINION

	MONTHS						
ACTIVITY	M5	M6	M7	M8	M9	M10	M11
TRAINING	X	X	X	X			
START OF RECRUITMENT		X	X	X	X	X	
WEEK 1 ASSESSMENT AND TREATMENT		X	X	X	X	X	
WEEK 2 ASSESSMENT AND TREATMENT		X	X	X	X	X	
WEEK 3 ASSESSMENT AND TREATMENT		X	X	X	X	X	
WEEK 4 ASSESSMENT AND TREATMENT		X	X	X	X	X	
QUALITY ASSURANCE		X	X	X			
INTERMEDIATE ANALYSIS OF GENERAL (1ST) ASSESSMENT		X	X	X			
STATISTICAL ANALYSIS				X			
INTERMEDIATE ANALYSIS OF GENERAL (2ND) ASSESSMENT					X	X	
DRAFTING OF THE CLINICAL TRIAL FINAL REPORT							**X**
STATISTICAL ANALYSIS							**X**

C. TRAINING

IT WAS PERFORMED IN FOUR AREAS:

I.- TRAINING TO DOCTORS HIRED TO CARRY OUT HEALINGS (6 PROFESSIONALS IN TOTAL) ON COMPUTER EQUIPMENT USE WITH DATA RECORDING SOFTWARE AND MEASUREMENT CAMERA.

II.- TRAINING ON THE USE OF FITTED DEBRIDEMENT TECHNIQUE DEVELOPED FOR THE USE OF THE DRESSING SUBJECT MATTER OF THIS STUDY.

III.- HANDLING OF SCREENING DOCUMENTS, DATA RECORDING, INFORMED CONSENT, AND INTEGRATION OF FILES.

IV.-BASIC KNOWLEDGE OF THE PRODUCT, STUDY PURPOSE, AND TECHNICAL MANUAL, DESIGN, AND APPLICATION OF THE PRODUCT.

D. RECRUITMENT

VII. REGARDING THE PROCEDURE AND AFOREMENTIONED STANDARDS TO CARRY OUT PRODUCTS STUDIES IN COLLABORATION WITH THE IMSS, AND REGARDING THE PROGRAM SET IN THE AUTHORISED PROTOCOL, THE RECRUITMENT OF BENEFICIARY PATIENTS DIAGNOSED WITH DIABETES MELLITUS TYPE 2 REGISTERED ON THEIR CLINICAL FILES WERE RECRUITED, OF AT LEAST TWO WEEKS BEFORE THEY ARE ADMITTED TO THE STUDY, WITH A 1 OR 2 WAGNER CLASSIFICATION.
THREE WORK TEAMS WERE CREATED, EACH ONE DESIGNATED TO CONDUCT THE RECRUITMENT OF A GROUP OF PATIENTS ACCORDING TO THE HOSPITALS THAT PARTICIPATED.

EACH WORK TEAM WAS INTEGRATED BY: TWO DOCTORS, A CAMERA, AND COMPUTER EQUIPMENT TO TAKE IMAGES AND CONDUCT RECORDS ON THE PROGRAM'S DATABASES.

ARM I.- PATIENTS RECRUITED AT HOSPITAL GENERAL REGIONAL CON MEDICINA FAMILIAR NO. ONE, IDENTIFIED AS HGR MF1, IN CUERNAVACA, MORELOS.

ARM II.- PATIENTS RECRUITED AT HOSPITAL GENERAL DE ZONA CON MEDICINA FAMILIAR NO. FIVE, IDENTIFIED AS HGZ MF5, IN ZACATEPEC, MORELOS.

ARM III.- PATIENTS RECRUITED AT HOSPITAL GENERAL DE ZONA CON MEDICINA FAMILIAR NO. FIVE, IDENTIFIED AS HGZ MF5, IN ZACATEPEC, MORELOS (OF THE EAST REGION OF THE STATE), DIFFERENTIATED WITH LETTER "A".

RESULTS AND/OR RECRUITMENT BEHAVIOUR:

PERIOD: IT HAS BEEN SET NATURALLY SINCE 02 MAY UP TO WEEK OF 1-2 SEPTEMBER IN THE ARM OF THE HOSPITAL GENERAL REGIONAL DE CUERNAVACA, MORELOS.

CONTROL ARM - HOSPITAL GENERAL REGIONAL CON MEDICINA FAMILIAR NO. 1

	WEEKS MARKED IN THE PERIOD																								
	MAY					JUNE					JULY						AUGUST					SEPTEMBER			
	2-6	9-13	16-20	23-27	30-31	1-3	6-10	13-17	20-24	27-30	1	4-8	11-15	18-22	25-29	31	1-5	8-12	15-19	22-26	29-31	1-2	5-9	12-16	19-23
FEM.	7	1	1	2	0	0	0	0	0	0	1	1	0	0	1	0	0	1							
MALE	8	1	0	1	0	0	1	1	4	0	0	0	0	1	3	0	1	3	0	0	2	2			
T	15	2	1i	3	0	0	1	1	4	0	1	1	0	1	4	0	1	4	0	0	2	2			
CUM	15	17	18	21	21	21	22	23	27	27	28	29	29	30	34	34	35	39	39	39	41	43			

THE PERIOD SET NATURALLY IN THE ARM OF THE HOSPITAL GENERAL DE ZONA CON MEDICINA FAMILIAR NO. 5 IN ZACATEPEC, MORELOS, RECORD IN THE FIRST ARM (ARM II) FROM 02 MAY TO THE PERIOD OF THE WEEK OF 15-19 AUGUST; AND ARM iii WAS SET NATURALLY FROM 02 MAY TO 02 SEPTEMBER.

INTERVENTION ARM - HOSPITAL GENERAL DE ZONA CON MEDICINA FAMILIAR NO. 5

	WEEKS MARKED IN THE PERIOD																								
	MAY					JUNE					JULY						AUGUST					SEPTEMBER			
	2-6	9-13	16-20	23-27	30-31	1-3	6-10	13-17	20-24	27-30	1	4-8	11-15	18-22	25-29	31	1-5	8-12	15-19	22-26	29-31	1-2	5-9	12-16	19-23
FEM.	1	3	2	2	0	0	1	1	0	0	0	0	0	0	1	0	2	0	1						
MALE	7	1	2	2	0	0	2	1	1	1	1	2	0	0	1										
T	8	4	4	4	0	0	3	2	1	1	1	2	0	0	2	0	2	0	1						
CUM	8	12	16	20	20	20	23	25	26	27	28	30	30	30	32	32	34	34	35						

HOSPITAL GENERAL DE ZONA CON MEDICINA FAMILIAR NO 5 ARM "A"

FEM.	1	1	0	2	1	0	1	1	0	0	0	0	0	2	0	0	1	0	0	2	0	1			
MALE	2	0	2	0	1	1	0	1	2	0	0	0	0	0	0	0	0	0	1	0	0	0			
T	3	1	2	2	2	1	1	2	2	0	0	0	0	2	0	0	1	0	1	2	0	1			
CUM	3	4	6	8	10	11	12	14	16	16	16	16	16	18	18	18	19	19	20	22	22	23			

SUM OF GROUPS HGZ MF5 AND HGZ MF5A

T	11	5	6	6	2	1	4	4	3	1	1	2	0	2	2	0	3	0	2	2	0	1			
CUM	11	16	22	28	30	31	35	39	42	43	44	46	46	48	50	50	53	53	55	57	57	58			

FOR THE STUDY PROCEDURE, TWO ARMS WERE INCLUDED: CONTROL ARM AND INTERVENTION ARM

CONTROL ARM

A.- PATIENTS FOR STANDARD TREATMENT, AT HOSPITAL GENERAL REGIONAL CON MEDICINA FAMILIAR NO. 1, (HGR MF1) IN CUERNAVACA, MORELOS. .

BEHAVIOUR ACCORDING TO AGE

CONTROL ARM, HOSPITAL GENERAL REGIONAL NO. 1 CUERNAVACA, MORELOS.

NO.	SUBJECT	GENDER	AGE	25-30	31-35	36-40	41-45	46-50	51-55	56-60	61-65	66-70	71-75	76-80	81-85
1	000005	FEMALE	61								1				
2	000006	FEMALE	53						1						
3	000010	FEMALE	46					1							
4	000011	FEMALE	80											1	
5	000014	FEMALE	60							1					
6	000017	FEMALE	72										1		
7	000019	FEMALE	79											1	
8	000061	FEMALE	71										1		
9	000063	FEMALE	82												1
10	000064	FEMALE	57							1					
11	000065	FEMALE	69									1			
12	000072	FEMALE	60							1					
13	000073	FEMALE	55						1						
14	000075	FEMALE	48					1							
15	000080	FEMALE	46					1							
16	000001	MALE	58							1					
17	000004	MALE	60							1					
18	000008	MALE	69									1			
19	000012	MALE	56							1					
20	000013	MALE	61								1				
21	000015	MALE	57							1					
22	000016	MALE	61								1				
23	000018	MALE	59							1					
24	000020	MALE	62								1				
25	000062	MALE	59							1					
26	000066	MALE	75										1		
27	000067	MALE	67									1			
28	000068	MALE	63								1				
29	000069	MALE	56							1					
30	000070	MALE	76											1	
31	000071	MALE	66									1			
32	000074	MALE	64								1				
33	000076	MALE	69									1			
34	000077	MALE	43				1								
35	000078	MALE	56							1					
36	000079	MALE	56							1					
37	000101	MALE	27	1											
38	000102	MALE	61								1				
39	000103	MALE	72										1		
40	000104	MALE	61								1				
41	000105	MALE	50					1							
42	000106	MALE	55						1						
43	000107	MALE	59							1					
			T	**1**	**0**	**0**	**1**	**4**	**3**	**13**	**8**	**5**	**4**	**3**	**1**
			%	2.33	0.00	0.00	2.33	9.30	6.98	30.23	18.60	11.63	9.30	6.98	2.33

INTERVENTION ARM

A. - PATIENTS AFFILIATED TO HOSPITAL GENERAL DE ZONA CON MEDICINA FAMILIAR NO. 5, (HGZ MF5) IN ZACATEPEC, MORELOS.

IN THIS ARM, THE DATA AND MEASUREMENT RECORDING PROCEDURE WAS PERFORMED WITH TWO CAMERAS (SILHOUETTESTAR) AND TWO COMPUTER EQUIPMENT (ASSUS) IN ORDER TO RECORD DATA SENT VIA INTERNET TO THE SOFTWARE MANAGEMENT CENTRAL IN NEW ZEALAND. RECORDS OF CAMERA 1 IDENTIFIED TO MONITOR ARM AS ZACATEPEC, AS HGZ MF5 , AND RECORDS OF CAMERA 2 IDENTIFIED AS HGZ MF5A.

BEHAVIOUR ACCORDING TO AGE

INTERVENTION ARM - HOSPITAL GENERAL DE ZONA CON MEDICINA FAMILIAR NO. 5, ZACATEPEC, MORELOS. (TWO ARMS)

NO.	SUBJECT	GENDER	AGE	25-30	31-35	36-40	41-45	46-50	51-55	56-60	61-65	66-70	71-75	76-80	71-85
1	000041	FEMALE	46					1							
2	000045	FEMALE	64								1				
3	000048	FEMALE	71										1		
4	000049	FEMALE	50					1							
5	000050	FEMALE	73										1		
6	000053	FEMALE	58							1					
7	000054	FEMALE	67									1			
8	000058	FEMALE	65								1				
9	000059	FEMALE	50					1							
10	000060	FEMALE	58							1					
11	000092	FEMALE	76											1	
12	000093	FEMALE	78											1	
13	000094	FEMALE	33		1										
14	000042	MALE	65								1				
15	000043	MALE	45				1								
16	000046	MALE	43				1								
17	000047	MALE	41				1								
18	000051	MALE	54						1						
19	000052	MALE	49					1							
20	000055	MALE	56							1					
21	000056	MALE	64								1				
22	000057	MALE	62								1				
23	000091	MALE	50					1							
			ST	**0**	**1**	**0**	**3**	**5**	**1**	**3**	**5**	**1**	**2**	**2**	**0**
			%	0.00	4.35	0.00	13.04	21.74	4.35	13.04	21.74	4.35	8.70	8.70	0

IN THIS ARM, IT IS OBSERVED THAT THE HIGHEST PERCENTAGE OF PATIENTS IS BETWEEN THE AGE RANGE 46-50, AND THE AGE RANGE 61-65, AND THE HIGHEST RANGE IS LOCATED BETWEEN 46 TO 65 YEARS OLD.

INTERVENTION ARM IN HGZ MF5

NO.	SUBJECT	GENDER	AGE	25-30	31-35	36-40	41-45	46-50	51-55	56-60	61-65	66-70	71-75	76-80	71-85
1	000026	FEMALE	78											1	
2	000028	FEMALE	65								1				
3	000030	FEMALE	65								1				
4	000031	FEMALE	64								1				
5	000035	FEMALE	70									1			
6	000036	FEMALE	70									1			
7	000037	FEMALE	62								1				
8	000082	FEMALE	50					1							
9	000083	FEMALE	51						1						
10	000091	FEMALE	79											1	
11	000092	FEMALE	59							1					
12	000093	FEMALE	65								1				
13	000094	FEMALE	60							1					
14	NOT APPLICABLE	FEMALE	69									1			
15	000021	MALE	61								1				
16	000022	MALE	51						1						
17	000023	MALE	51						1						
18	000024	MALE	74										1		
19	000025	MALE	44				1								
20	000027	MALE	76											1	
21	000029	MALE	65								1				
22	000032	MALE	66									1			
23	000033	MALE	67									1			
24	000034	MALE	57							1					
25	000038	MALE	68									1			
26	000039	MALE	51						1						
27	000040	MALE	59							1					
28	000081	MALE	63								1				
29	000084	MALE	54						1						
30	000085	MALE	63								1				
31	000086	MALE	58							1					
32	000087	MALE	58							1					
33	000088	MALE	69									1			
34	000089	MALE	48					1							
35	000090	MALE	52						1						
			ST	0	0	0	1	2	6	6	9	7	1	3	
			%	0.00	0.00	0.00	2.86	5.71	17.14	17.14	25.71	20.00	2.86	8.57	

58	0	1	0	4	7	7	9	14	8	3	5
100	0	1.72	0	6.9	12.1	12.1	15.5	24.1	13.8	5.17	8.62

DATA FROM BOTH GROUPS (OF THE THREE CHAMBERS IN LINE) WERE PLACED IN A PIECE OF EQUIPMENT USED AS “CENTRAL” IN THE OFFICE CONDITIONED FOR THAT PURPOSE IN THE BUILDING OF BOROUGH OF THE IMSS IN CUERNAVACA, MORELOS.

II. EXCLUSION: PATIENTS EXCLUDED WERE THOSE ULCERS CLASSIFIED AS WAGNER 3, AND/OR IN EPITHELISATION PHASE, JOINT SEPSIS, LOCALISED GANGRENE (FOREFOOT OR HEEL), EXTENSIVE GANGRENE, SERIOUS INFECTION, IN THEIR DIAGNOSTIC, INCLUDING THOSE WITH ANGIOLOGY PROBLEMS WHICH POSED A RECOVERY ISSUE FOR THIS CAUSE. BESIDES, ALL PATIENTS WITH ULCERATION DIAGNOSED AS VARICOSE WERE EXCLUDED.
THIS PROCEDURE WAS COMPLETED WHEN THE NUMBER OF ULCERS SET FOR THE STUDY WERE REACHED, OBTAINING UP TO THE FIRST ASSESSMENT DATE (30 JUNE 2016) 56 ULCERS IN 29 PATIENTS RECRUITED FOR THE CONTROL ARM IN HOSPITAL GENERAL REGIONAL NO. 1 AND 92 ULCERS IN 44 PATIENTS RECRUITED FOR THE INTERVENTION ARM.

STARTING THE SECOND ASSESSMENT PERIOD, FALSE IMAGES WERE IDENTIFIED IN THE SYSTEM IN BOTH ARMS. BESIDES, AFTER AN ASSESSMENT, THEY WERE RULED NON-VIABLE ULCERS, BEING DEEMED EXCLUDED, “CLEANING THE TAKE”, AND ALL OF THEM WERE CLASSIFIED AS “EXERCISE”, THAT THE SYSTEM DEEMS “TRAINING” SINCE THE CONTROL OF THE CAMERA IS RECORDED BY PHOTOGRAPH, AND IT CREATES RECORDS IN THE SOFTWARE.

AFTER THE SECOND EVALUATION, THE ARMS WERE MADE UP IN THE FOLLOWING WAY:

ARM	MEDICAL FACILITY	NUMBER OF PATIENTS
CONTROL	HOSPITAL GENERAL REGIONAL CON MEDICINA FAMILIAR NO. UNO IN CUERNAVACA, MORELOS	43
	WOMEN	15
	MEN	28

*

ARM	MEDICAL FACILITY	NUMBER OF PATIENTS
INTERVENTION HGZ MF5	HOSPITAL GENERAL DE ZONA CON MEDICINA FAMILIAR NO. CINCO, ZACATEPEC, MORELOS	35
	WOMEN	14
	MEN	21
INTERVENTION HGZ MF5A	HOSPITAL GENERAL DE ZONA CON MEDICINA FAMILIAR NO. CINCO, ZACATEPEC, MORELOS	23
	WOMEN	13
	MEN	10
	TOTAL	**58**
	WOMEN	27
	MEN	31

VIII). ANALYSIS OF THE CONSTITUTED ARMS

A) CONTROL ARM

FOR THE ANALYSIS OF PATIENTS PARTICIPATING IN THE CONTROL ARM, 43 PATIENTS WERE RECRUITED, WHO SIGNED AN INFORMED CONSENT FORM. IN THIS ARM, A TOTAL OF 56 ULCERS WERE IDENTIFIED AND ASSESSED, DIAGNOSED WAGNER 1 AND WAGNER 2. AFTER THEIR CLASSIFICATION, AND BEING REMOVED THOSE TECHNICALLY NON-VIABLE, AND EXERCISE RECORDS, FOR THE FINAL ANALYSIS, THERE REMAINED: 43 PATIENTS WITH 52 ULCERS.

CONTROL ARM
HOSPITAL GENERAL REGIONAL CON MEDICINA FAMILIAR NO. 1

25-30	31-35	36-40	41-45	46-50	51-55	56-60	61-65	66-70	71-75	76-80	71-85
1	0	0	1	4	3	13	8	5	4	3	1
2.33	0.00	0.00	2.33	9.30	6.98	30.23	18.60	11.63	9.30	6.98	2.33

WOMEN

0	0	0	0	3	2	3	1	1	2	2	1

MEN

1	0	0	1	1	1	10	7	4	2	1	0

WOMEN	15	34.88%
MALE	28	65.12%
	43	100.00%

THE RANGE OBSERVED WAS 1, AND UP TO 3 ULCERS PER PATIENT, HIGHLIGHTING THAT THE DIFFERENCE BETWEEN THE NUMBER OF W1 AND W2 ULCERS IS11.2%, WHICH INDICATES THAT THOSE PATIENTS HAVE HAD PRIOR TREATMENT WITH NO POSITIVE EVOLUTION.

IN THE FOLLOWING CHART, THERE ARE RECORDS PER PATIENT AND ULCER CLASSIFICATION.

BEHAVIOUR PER GENDER, AMOUNT OF ULCERS AND GRADE
CONTROL ARM, HOSPITAL GENERAL REGIONAL NO. 1 CUERNAVACA, MORELOS.

NO.	SUBJECT	GENDER	AGE	1 ULCERS	2 ULCERS	3 ULCERS	4-9 ULCERS	T	W1	W2
1	000005	FEMALE	61		1			2	2	
2	000006	FEMALE	53	1				1	1	
3	000010	FEMALE	46	1				1		1
4	000011	FEMALE	80	1				1		1
5	000014	FEMALE	60	1				1	1	
6	000017	FEMALE	72	1				1		1
7	000019	FEMALE	79	1				1		1
8	000061	FEMALE	71	1				1	1	
9	000063	FEMALE	82	1				1		1
10	000064	FEMALE	57	1				1	1	
11	000065	FEMALE	69		1			2		2
12	000072	FEMALE	60		1			2	2	
13	000073	FEMALE	55	1				1	1	
14	000075	FEMALE	48	1				1	1	
15	000080	FEMALE	46	1				1	1	
16	000001	MALE	58	1				1	1	
17	000004	MALE	60	1				1		1
18	000008	MALE	69	1				1		1
19	000012	MALE	56	1				1		1
20	000013	MALE	61	1				1		1
21	000015	MALE	57	1				1	1	
22	000016	MALE	61	1				1	1	
23	000018	MALE	59	1				1		1
24	000020	MALE	62	1				1	1	
25	000062	MALE	59		1			2		2
26	000066	MALE	75	1				1		1
27	000067	MALE	67	1				1	1	
28	000068	MALE	63	1				1		1
29	000069	MALE	56	1				1		1
30	000070	MALE	76	1				1	1	
31	000071	MALE	66	1				1		1
32	000074	MALE	64			1		3	3	
33	000076	MALE	69		1			2	2	
34	000077	MALE	43		1			2		2
35	000078	MALE	56	1				1		1
36	000079	MALE	56		1			2		2
37	000101	MALE	27	1				1		1
38	000102	MALE	61	1				1		1
39	000103	MALE	72	1				1		1
40	000104	MALE	61	1				1		1
41	000105	MALE	50	1				1	1	
42	000106	MALE	55	1				1		1
43	000107	MALE	59	1				1		1
			T	35	7	1	0	52	23	29
			%	81.40	16.28	2.33	0	100	**44.2%**	**55.8%**

WOMEN	15	12	3	0	0
MEN	28	23	4	1	0
	43	35	7	1	0

11	7
12	22

ULCERS ACCORDING TO GENDER

WOMEN	34.6%	21.2%	13.5%
MEN	65.4%	23.1%	42.3%
	100.0%		

B) INTERVENTION ARM

FOR THE ANALYSIS OF PATIENTS PARTICIPATING IN THE INTERVENTION ARM AND ASSESSMENT OF **TISSUPOR® 3D EMBROIDERY** DRESSINGS FOR WOUNDS, 58 PATIENTS WERE RECRUITED, WHO SIGNED AN INFORMED CONSENT FORM. IN THIS ARM, A TOTAL OF 92 ULCERS WERE ASSESSED AND SUBJECTED TO CLASSIFICATION. THOSE NON-VIABLE WERE TECHNICALLY REMOVED, AS WELL AS EXERCISE RECORDS, REMAINING THE FOLLOWING FOR THE FINAL ANALYSIS: 58 PATIENTS WITH 91 ULCERS.

25-30	31-35	36-40	41-45	46-50	51-55	56-60	61-65	66-70	71-75	76-80	71-85
0	1	0	3	5	1	3	5	1	2	2	0
0	0	0	1	2	6	6	9	7	1	3	0
0	1	0	4	7	7	9	14	8	3	5	0
0.0%	1.7%	0.0%	6.9%	12.1%	12.1%	15.5%	24.1%	13.8%	5.2%	8.6%	0.0%

WOMEN

0	1	0	0	3	0	2	2	1	2	2	0
0	0	0	0	1	1	2	5	3	0	2	0
0	1	0	0	4	1	4	7	4	2	4	0

MEN

0	0	0	3	2	1	1	3	0	0	0	0
0	0	0	1	1	5	4	4	4	1	1	0
0	0	0	4	3	6	5	7	4	1	1	0

WOMEN	27	46.55%
MEN	31	53.45%
	58	100.00%

ARM OF HGZ MF5

ARM OF HGZ MF5A

IN THE FOLLOWING CHARTS, THE DISTRIBUTION OF PATIENTS AND THE NUMBER OF ULCERS CLASSIFIED AND ASSESSED, WITH THEIR W1 OR W2 GRADE PER PATIENT ARE DETAILED.

BEHAVIOUR PER GENDER, AMOUNT OF ULCERS AND GRADE

INTERVENTION ARM - HOSPITAL GENERAL DE ZONA CON MEDICINA FAMILIAR NO. 5, ZACATEPEC, MORELOS.

NO.	SUBJECT	GENDER	AGE	1 ULCERS	2 ULCERS	3 ULCERS	5 ULCERS	T	W1	W2
1	000041	FEMALE	46	1				1		1
2	000045	FEMALE	64	1				1	1	
3	000048	FEMALE	71				1	5		5
4	000049	FEMALE	50	1				1	1	
5	000050	FEMALE	73			1		3		3
6	000053	FEMALE	58			1		3	3	
7	000054	FEMALE	67	1				1	1	
8	000058	FEMALE	65		1			2		2
9	000059	FEMALE	50	1				1	1	
10	000060	FEMALE	58		1			2		2
11	000092	FEMALE	76		1			2		2
12	000093	FEMALE	78	1				1		1
13	000094	FEMALE	33	1				1	1	
14	000042	MALE	65	1				1		1
15	000043	MALE	45		1			2		2
16	000046	MALE	43		1			2		2
17	000047	MALE	41	1				1		1
18	000051	MALE	54	1				1		1
19	000052	MALE	49	1				1		1
20	000055	MALE	56	1				1		1
21	000056	MALE	64	1				1		1
22	000057	MALE	62	1				1	1	
23	000091	MALE	50	1				1		1
			ST	**15**	**5**	**2**	**1**	**36**	**9**	**27**
			%	65.22	21.74	8.70	4.35	100.00	**25.0%**	**75.0%**

THE RANGE BETWEEN THE NUMBER OF W1 AND W2 ULCERS IS: 50%, WHICH INDICATES A DEGREE OF HIGHER COMPLICATION IN THE INTERVENTION ARM (HGZ MF5A).

INTERVENTION ARM - HOSPITAL GENERAL DE ZONA CON MEDICINA FAMILIAR NO. 5, ZACATEPEC, MORELOS.

NO.	SUBJECT	GENDER	AGE	1 ULCER	2 ULCERS	3 ULCERS	9 ULCERS	T	W1	W2
1	000026	FEMALE	78	1				1	1	
2	000028	FEMALE	65			1		3	1	2
3	000030	FEMALE	65	1				1	1	
4	000031	FEMALE	64			1		3	2	1
5	000035	FEMALE	70	1				1	1	
6	000036	FEMALE	70	1				1	1	
7	000037	FEMALE	62	1				1	1	
8	000082	FEMALE	50	1				1	1	
9	000083	FEMALE	51		1			2	1	1
10	000091	FEMALE	79	1				1	1	
11	000092	FEMALE	59	1				1	1	
12	000093	FEMALE	65	1				1	1	
13	000094	FEMALE	60	1				1	1	
14	NO APLICA	FEMALE	69					0		
15	000021	MALE	61		1			2	2	
16	000022	MALE	51	1				1	1	
17	000023	MALE	51	1				1	1	
18	000024	MALE	74	1				1	1	
19	000025	MALE	44			1		3	1	2
20	000027	MALE	76	1				1	1	
21	000029	MALE	65	1				1	1	
22	000032	MALE	66		1			2	1	1
23	000033	MALE	67	1				1	1	
24	000034	MALE	57	1				1	1	
25	000038	MALE	68	1				1	1	
26	000039	MALE	51	1				1	1	
27	000040	MALE	59	1				1	1	
28	000081	MALE	63				1	9	9	
29	000084	MALE	54		1			2	2	
30	000085	MALE	63	1				1	1	
31	000086	MALE	58	1				1	1	
32	000087	MALE	58	1				1	1	
33	000088	MALE	69		1			2	2	
34	000089	MALE	48			1		3	3	
35	000090	MALE	52	1				1	1	
			ST	24	5	4	1	55	**48**	**7**
			%	70.59	14.71	11.76	2.94	100.00	**87.3%**	**12.7%**
			58	39	10	6	2	91	**57**	**34**
				68.421	17.544	10.526	3.5088	100.00	**63.7%**	**37.4%**
		WOMEN	26	17	4	4	1	42	22	20
		MEN	31	22	6	2	1	49	35	14
			57	39	10	6	2	91	57	34

ULCERS ACCORDING TO GENDER				
	WOMEN	46.2%	24.2%	22.0%
	MEN	53.8%	38.5%	15.4%
		100.0%		

C) BEHAVIOUR OF ARMS ACCORDING TO AGE RANGE

CONTROL ARM

- IN THE CONTROL ARM, THE AGE RANGE SET WAS 25.85 YEARS.
- THE HIGHEST PERCENTAGE APPEARED IN THE RANGE OF 56-60 YEARS, WITH 30.23%
- THE HIGHEST CONCENTRATION APPEARED IN THE RANGE OF 56-75 YEARS, WITH 69.77%

INTERVENTION ARM

- IN THE INTERVENTION ARM, THE AGE RANGE SET WAS 31-80 YEARS.
- THE HIGHEST PERCENTAGE APPEARED IN THE RANGE OF 61-65 YEARS, WITH 24.10%.
- THE HIGHEST CONCENTRATION APPEARED IN THE RANGE OF 46-70 YEARS, WITH 77.59%.

IV. ANALYSIS OF THE SYSTEM IMPLEMENTED FOR MEASUREMENT

THE IRREGULAR SHAPE OF ULCERS REQUIRE AN ADVANCED SYSTEMS FOR ITS MEASUREMENT THAT ALLOWS SETTING TWO IMPORTANT PARAMETERS TO KNOW THEIR VOLUME IN CM3, SPECIFIED FOR THE MEASUREMENT OF THE WOUND AREA AND ITS DEPTH.

THE MEASUREMENT OF THE IRREGULAR AREA REQUIRES DATA OF THE SHAPE OF THE ULCER USING INFORMATION COLLECTED FROM:

- WOUND OR ULCER LONGITUDE
- ULCER WIDTH
- MEASUREMENT OF 2 AXES CROSSING IN THE MIDDLE OF THE ULCER, AND WHICH HAVE AS MEASUREMENT LIMIT THE POLYGON OR MARKED PERIMETER ON THE MARGIN OF THE OPENING, I.E. UP TO THE EPITHELISATION MARGIN.

THE INTERNAL SURVEYING OF THE ULCER IS SET ACCORDING TO THE MEASURE OF THE CONCAVITY ESTIMATED USING THE AXES TO OBTAIN:

- MAXIMUM DEPTH
- AVERAGE DEPTH

ULCERS IN SOME AREAS TEND TO HAVE CERTAIN CONVEXITY, SUCH AS THOSE ON THE TOES AND HEEL, AND VARIANTS MAY MAKE THE DEPTH MEASUREMENT BE ESTIMATED IN MILLIMETRES.

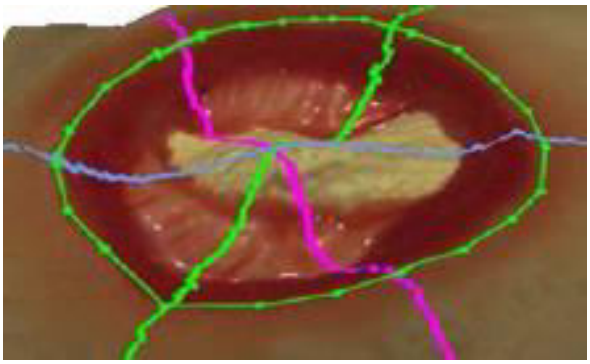
EQUATION

WSA % = [INITIAL WSA (CM^2) - WSA (CM^2) DURING WEEK 1] X 100

WSA: WOUND SURFACE AREA

THIS FORMULA WAS SET IN ORDER TO MAKE AN ASSESSMENT BASED ON THE MEASUREMENT OF EACH ULCER USING THE TRANSPARENT FILM KNOWN AS VISITRAK, AND RECORDED ON A MEASUREMENT TABLE, WHERE THE AREA IS SET IN CMS2, AND ITS PROGRESS EVERY 8 DAYS OF HEALING.

IN SEARCH FOR A MORE EXACT ALTERNATIVE, THE GROUP OF INVESTIGATORS REQUESTED THE COMPANY TO REPLACE THE MEASUREMENT EQUIPMENT USING VISITRAK FOR THAT ONE OF SILHOUETTESTAR CAMERA WITH SILHOUETTECENTRAL SOFTWARE, WHICH PERFORMS MEASUREMENT REDUCING SCOPE FOR HUMAN ERROR, AND MAKING THE ULCERATION MEASUREMENT MORE OBJECTIVE.

SILOUETTESTAR CAMERA IMAGE	MARKING IMAGE
	

THE CAMERA TAKES A PHOTOGRAPH WITH THE AID OF A LASER MARKER OF THE AXES, AND SENDS THE IMAGE TO A COMPUTER SYSTEM, AND, OVER THE DIGITALISED IMAGE, IT MARKS A DOTTED PERIMETER OF THE ULCER. THEN, IT SENDS IT TO THE SYSTEM. THE ONLINE SOFTWARE CONNECTED TO A CENTRAL BASE IN NEW ZEALAND PROCESSES DATA AND GENERATES THE ENTIRE MEASUREMENT.

IN THE SYSTEM, TWO IMAGES ARE INCLUDED FOR EACH HEALING:

IMAGE A.- BEFORE HEALING
IMAGE B.- AFTER HEALING

IN ORDER TO IDENTIFY IMAGES 2, 3, 4, 5, 6, 7, 8, AND 9 OF THE ULCERS OF THE SAME PATIENT, LETTERS C, E, G, I, K, M, O, AND Q ARE DESIGNATED BEFORE HEALING.

IN ORDER TO IDENTIFY IMAGES 2, 3, 4, 5, 6, 7, 8, AND 9 OF THE ULCERS OF THE SAME PATIENTS, LETTERS B, D, F, H, J, L, N, P, AND R ARE DESIGNATED AFTER HEALING. BESIDES, IN THE RECORD, ERRORS RELATED TO WRITING AND DETERMINATION OF THE EXACT LOCATION OF THE ULCER WITH INDIVIDUAL MEASUREMENT WERE REMOVED, OR JUST PLACING THE IMAGE FOR THE MOST REPRESENTATIVE IMAGE, OR THE ONE OF LARGER VOLUME, SINCE SOME PATIENTS HAD MORE THAN ONE ULCER IN THE SAME LIMB, OR DIFFERENT ONES IN EACH FOOT. THE IDENTIFICATION AND MARKING WERE PERFORMED IN THE SCREENING DOCUMENT INCLUDED IN EACH FILE OF PARTICIPANT PATIENTS.

THE SOFTWARE PERFORMS THE PROCESSING OF DATA REGISTERED IN THE SYSTEM INSTALLED IN EACH COMPUTER EQUIPMENT, AND IN ORDER TO REACH A MORE OBJECTIVE MONITORING, DOCTORS WHO ASSISTED THE CONTROL ARM (HGR MF1) WERE EQUIPPED WITH AN ASSUS LAPTOP, AND A CAMERA (SILHOUETTESTAR), WHICH IS CONNECTED TO THE SOFTWARE INSTALLED (SILHOUETTECENTRAL) AND THE IMAGE TAKEN IS SENT TO THE EQUIPMENT DISPLAY, WHERE THE PERIMETER MARKING IS PERFORMED, AND SENT FOR ITS PROCESSING: DOCTORS TREATING
TREATING THE INTERVENTION ARM (HGZ MF5) ALSO HAD TWO ASSUS LAPTOPS, AND ONE CAMERA EACH (HGZ MF5 AND HGZ MF5A).

CONTROL OF THE DATA FROM BOTH GROUPS WAS PERFORMED AT A CENTRAL FACILITY NETWORKED AND OPERATED BY THE RESEARCHER IN CHARGE, TO WHICH OPERATING DOCTORS HAD NO ACCESS. CENTRAL EQUIPMENT IS AN ASSEMBLED FIXED COMPUTER (MARC GYGABYTE GA-Z97XSLI S. 1150: WITH HP 27”IPS LED MONITOR; 1 EAGLE WARRIOR MOUSE, GAMINGMOUSE G13 MODEL), 1 EAGLE WARRIOR KEYBOARD, GAMINGKEYBOARD G78 MODEL).

EACH IMAGE, DATA AND PROCESS IS SENT TO THE CENTRAL IN NEW ZEALAND AFTER ITS STORAGE AND SUBMISSION, WHICH ALSO KEEPS A STRICT CONTROL THAT DOES NOT ALLOW, AFTER THIS PROCESS, ANY KIND OF MANOEUVRING BY ANY OPERATOR, NOR BY THE RESEARCHERS GROUP; IT KEEPS DATA BACKUP, AND SENDS THEM BACK THROUGH THE SYSTEM TO THE CENTRAL IN MEXICO FOR THE RESEARCH GROUP TO HAVE AT THEIR DISPOSAL, AND SENDS THE SAME DATA TO THE PARTICIPATING COMPANY, FOR IT TO ANALYSE THE BEHAVIOUR OF THE PRODUCT IN THE TRIAL.
WITH THE AFOREMENTIONED DATA, AND ACCORDING TO THE RESEARCH PROTOCOL, CALCULATIONS TO RULE A PROGRESS HIGHER THAN 24% ARE SET, ESTABLISHED BY MEASUREMENT RECORDS OF SILHOUETTECENTRAL SYSTEM.
IN AN ANALYSIS OF 44 PATIENTS REGISTERED BETWEEN 1 MAY 2016 AND 02 SEPTEMBER, 92 ULCERS WERE REGISTERED FOR THE INTERVENTION ARM, AND 56 FOR THE CONTROL ARM. AFTER THEIR CLASSIFICATION, ALL THOSE THAT DID NOT CLASSIFY FOR THE TRIAL WERE MOVED, AS SET IN THE STUDY PROTOCOL, IN ORDER TO DEFINE A NUMBER OF:

91 ULCERS IN THE INTERVENTION ARM AND
52 ULCERS IN THE CONTROL ARM.

OF A TOTAL OF 57 TO BE TREATED PER ARM, WE CAN STATE THAT THE CONTROL ARM WAS FULFILLED IN 91.23%.

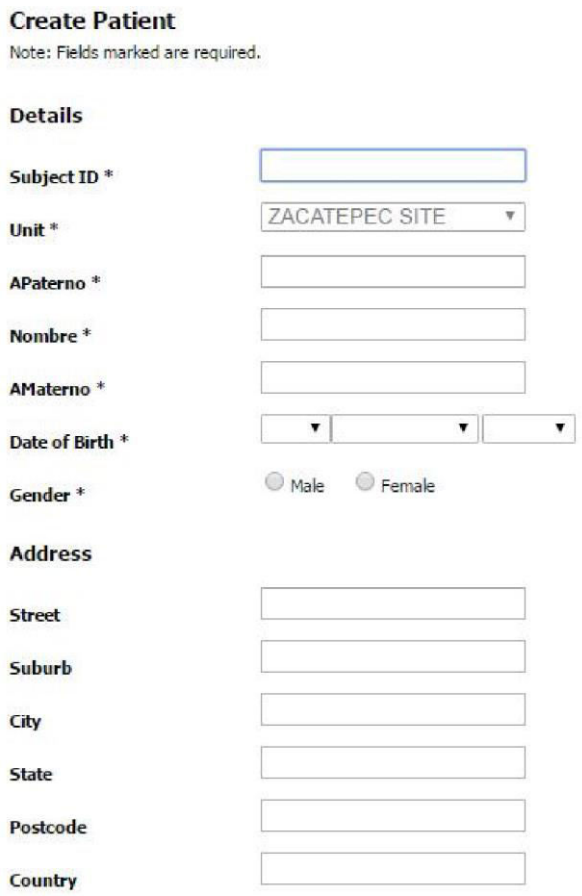
WHILE IN THE INTERVENTION ARM, 157.89% WAS FULFILLED. THIS INCREASE WAS DUE TO THE FACT THAT THERE WERE PATIENTS WITH 2, 3, 5, AND UP TO 9 ULCERS.

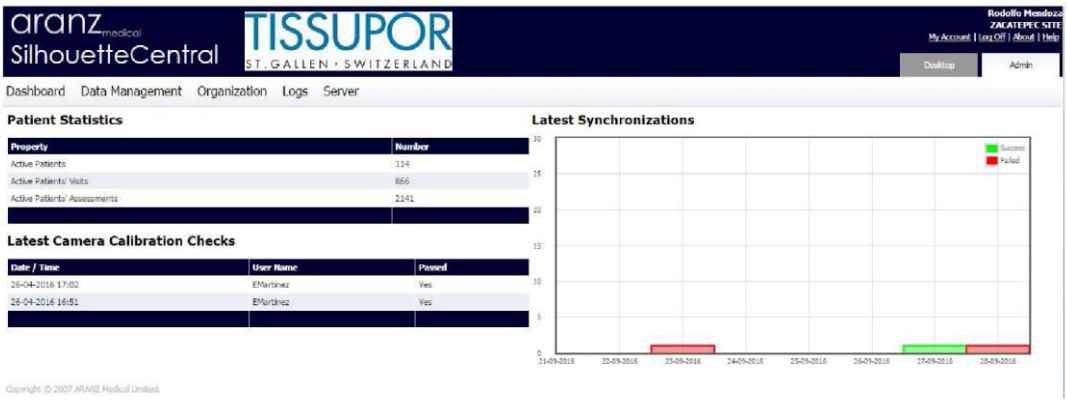
FOR THE EFFECTS OF TREATMENT AND ASSESSMENT, IT IS DETERMINED THAT THE PURPOSE OF RECORDING PROJECTED ULCERATIONS HAS BEEN MET.

IN THE THOROUGH ANALYSIS, ALL MATHEMATICAL CALCULATIONS WERE CARRIED OUT WITH SILHOUETTECENTRAL SOFTWARE, THE SAME ONE CREATING DATABASES IN EXCEL, FOR WHICH THERE IS NO NEED TO USE ANY OTHER TYPE OF CALCULATION AND MEASUREMENT.

DETAILS OF SILHOUETTECENTRAL PROGRAM

IT IS DESIGNED TO COLLECT DATA PER PATIENT.





IT ALSO COLLECTS DATA AND RECORDS. THE SOFTWARE STARTS CALCULATING AND CREATING GRAPHICS INDIVIDUALLY; EACH GRAPHIC HAS ACCURATE MEASUREMENT, THE SAME ONE THAT IS TRANSFERRED TO BE ANALYSED IN A DATABASE THAT CAN BE DOWNLOADED IN EXCEL.

TABLE DIVIDED IN THREE BASIC SEGMENTS:

1. PATIENT DATA
2. DATA REGARDING THE ULCER'S AREA, PERIMETER, DEPTH, LENGTH, AND WIDTH.
3. ACCURACY DATA OF THE AXIS MARKED WITH THE CAMERA LASER

TO EACH PHOTOGRAPH, THE PROGRAM AUTOMATICALLY RECORDS THE DATE, AND IT COMPLETES INFORMATION OF THE EQUIPMENT OPERATORS, REGISTERING INFORMATION, EVENTS, AND IMPORTANT NOTES.

Paternal S.	**Name**	**Maternal S.**	**Address**
RIVERA	CANDELARIA	SERRANO	NAVOLATO
ROMAN	MARIA DEL CARMEN	JIMENEZ	VENUSTIANO
CORTINA	VIRGINIA	CASTRO	VICENTE GUERRERO
VALENCIA	SIXTA	DELGADO	DURANGOSN
ALVEAR	CARMEN	ZUNIGA	AVENIDA *20* DE
PEREZ	ESTELA	SOTELO	LORENZO VAZQUEZ

Subject ID	Gender	Anatomical Site	Assessment Date	Assessment#	Image Date
000021	Male	Left Foot, Solé;	03-05-2016 11: 19	1	03-05-2016 11:19
000021	Male	Left Foot, Solé;	09-05-2016 10:59	2	09-05-2016 10:59
000021	Male	Left Foot, Solé;	17-05-2016 10:41	3	17-05-2016 10:41
000021	Male	Left Foot, Solé;	23-05-2016 10:5B	4	23-05-2016 10:53
000021	Male	Left Foot, Solé;	31-05-2016 10:56	5	31-05-2016 10:56

Assessment #	Wound	Area (cm²)	Area Reduction (%)	Perimeter (mm)	Max Depth (mm)	Mean Depth (mm)	Volume (cm³)	Length (mm)	Width (mm)
1	A	0.4	0.0%	27	10	2	0.1	10	4
1	A	0.8	0.0%	43	10	3	0.2	19	6
1	A	0.3	0.0%	21	2	0	0.0	8	5
1	A	1.2	0.0%	59	2	0	0.1	21	10
1	A	1.3	0.0%	38	1	0	0.0	14	12
1	A	3.3	0.0%	83	3	1	0.2	28	21

ADDITIONALLY, AND EVERY TIME RESEARCHERS WANT, IT DOWNLOADS A PDF PER ULCER, INCLUDING: DATES, CALCULATIONS AND BEHAVIOUR, APART FROM THE PHOTOGRAPH OF THE ULCER BEING MEASURED.

TISSUPOR ST. GALLEN · SWITZERLAND

Wound Assessment Report

Single Assessment, Single Wound

JESUS C ALBINO — ***Assessment 19-07-2016***

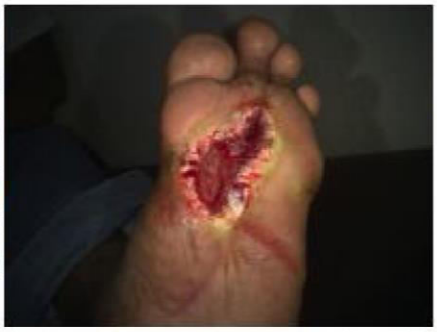
Subject ID 000023 — **Date of Birth** 03-01-1965

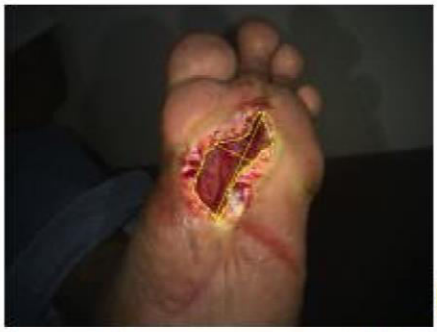
Left Foot, Sole; DESPUES DE LA CURACION: Wound B — Status: Open

Assessment Summary

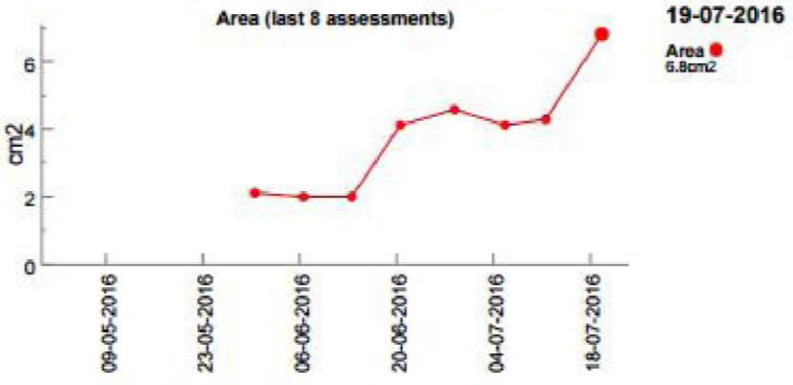
Area: 6.8cm2 **Area Reduction:** -188.6% **Perimeter:** 126mm **Length:** 48mm
Width: 19mm **Max Depth:** 5mm **Mean Depth:** 1mm **Volume:** 0.6cm3

Image taken 19-07-2016 12:10:55
Area 6.8cm2
Perimeter 126mm
Max. Depth 5mm
Mean Depth 1mm
Volume 0.6cm3





Length/Width
L: 48mm
W: 19mm



19-07-2016
Area 6.8cm2

IN THIS ANALYSIS, THE PROGRESS TO ULCER RECOVERY IS THE FOLLOWING **OVERVIEW OF THE STUDY BEHAVIOUR IN THE CONTROL ARM**

HOSPITAL GENERAL REGIONAL CON MEDICINA FAMILIAR NO. 1, CUERNAVACA, MORELOS

	NO. PATIENT	DATE ASSESSMENT	NUMBER OF HEALING	ULCER	AREA CM2	REDUCT/AREA %	PERIMETER MM	DEPTH		VOL CM3	LONG MM	WIDTH MM
								MAXIMUM	MEAN			
1	000001	06-07-2016 08:11	10	A	0.2	18.3%	20	1	0	0.0	6	5
2	000004	29-08-2016 08:36	18	A	17.9	-15.1%	170	3	0	0.8	60	44
3	000005	31-05-2016 10:44	5	A	0.4	54.1%	23	2	0	0.0	8	7
	000005	31-05-2016 10:45	3	C	2.8	-394.2%	61	3	0	0.1	21	20
4	000006	22-08-2016 08:38	17	A	0.2	42.3%	15	0	0	0.0	5	4
5	000008	29-08-2016 09:00	16	A	4.4	-808.5%	82	3	0	0.1	32	16
6	000010	01-08-2016 08:38	14	A	0.0	100.0%	0				0	0
7	000011	02-08-2016 12:09	14	A	7.6	33.7%	106	2	0	0.0	40	26
8	000012	16-05-2016 13:42	2	A	6.3	60.2%	160	37	2	1.1	40	19
9	000013	27-05-2016 12:22	5	A	3.3	9.6%	66	2	0	0.0	23	19
10	000014	23-06-2016 10:22	8	A								
11	000015	28-06-2016 09:37	8	A								
12	000016	04-07-2016 12:32	10	A								
13	000017	30-08-2016 12:26	18	A	0.8	86.0%	35	2	1	0.0	12	10
14	000018	02-09-2016 12:02	18	A	5.6	59.1%	114	2	0	0.0	43	23
15	000019	26-08-2016 11:17	13	A	34.0	-3.0%	270	2	0	0.0	96	49
16	000020	31-08-2016 11:04	14	A	0.0	95.4%	7	0	0	0.0	3	1
17	000061	15-06-2016 12:20	6	A								
18	000062	01-09-2016 09:20	15	A	2.9	80.5%	68	2	0	0.0	27	15
	000062	01-09-2016 09:20	15	C	0.0	99.8%	11				6	0
19	000063	30-08-2016 14:15	15	A	2.1	72.4%	66	0	0	0.0	24	13
20	000064	30-08-2016 12:01	15	A	0.0	93.5%	3				1	1
21	000065	16-06-2016 10:15	3	C	3.1	0.5%	64	1	0	0.0	25	14
22	000066	01-09-2016 10:54	11	A	2.2	92.0%	97	2	0	0.1	36	11
23	000067	14-07-2016 09:19	5	A	0.0	100.0%	0				0	0
24	000068	17-08-2016 11:15	9	A	0.7	9.8%	33	2	1	0.0	12	7
25	000069	05-07-2016 11:36	2	A	4.1	-7.0%	76	3	1	0.5	27	20
26	000070	29-07-2016 12:30	4	A	4.4	-1564.7%	77	3	0	0.1	26	25
27	000071	01-07-2016 10:01	2	A	3.5	-9.2%	102	10	3	1.0	36	13
28	000072	26-08-2016 08:28	9	A	0.0	100.0%	0				0	0
	000072	05-08-2016 08:25	5	C	0.0	100.0%	0				0	0
29	000073	26-07-2016 12:06	3	A	0.0	100.0%	0				0	0
30	000074	31-08-2016 11:27	6	A	1.1	-2.1%	43	2	0	0.0	15	12
	000074	31-08-2016 11:27	6	C	0.2	60.4%	15	1	0	0.0	5	4
	000074	08-08-2016 12:55	4	E	0.0	100.0%	0				0	0
31	000075	29-08-2016 09:07	6	A	0.1	82.8%	10	1	0	0.0	4	2
32	000076	17-08-2016 12:49	4	A	0.0	100.0%	0				0	0
	000076	17-08-2016 12:50	4	C	0.0	100.0%	0				0	0
33	000077	01-09-2016 09:03	6	A	0.7	57.3%	37	2	0	0.0	17	5
	000077	01-09-2016 09:03	6	C	0.9	61.5%	35	3	0	0.0	12	10
34	000078	02-09-2016 08:13	6	A	0.9	61.2%	54	2	0	0.0	22	11
35	000079	02-09-2016 09:07	4	A	2.2	70.4%	94	2	0	0.1	34	15
	000079	02-09-2016 09:08	4	C	11.1	-26.1%	173	5	1	1.7	74	22
36	000080	22-08-2016 08:32	3	A	0.0	100.0%	0				0	0
37	000101	30-08-2016 12:14	4	A	2.0	-89.2%	57	2	1	0.2	20	15
38	000102	30-08-2016 13:43	4	A	1.4	-46.4%	43	3	1	0.1	14	13
39	000103	02-09-2016 09:55	3	A	18.0	22.1%	156	3	1	1.3	54	47
40	000104	29-08-2016 09:31	1	A	41.7	0.0%	263	26	1	5.2	100	80
41	000105	29-08-2016 12:39	1	A	1.0	0.0%	52	6	1	0.1	18	12
42	000106	02-09-2016 13:19	1	A	5.9	0.0%	93	2	0	0.1	34	25
43	000107	02-09-2016 12:40	1	A	7.6	0.0%	205	4	1	0.7	48	30
			386			-742.5%						
			9			**-17.27%**	AVERAGE PROGRESS PER PATIENT					

OVERVIEW OF THE STUDY BEHAVIOUR IN THE INTERVENTION ARM

HOSPITAL GENERAL DE ZONA CON MEDICINA FAMILIAR NO. 5, ZACATEPEC, MORELOS.

	NO. PATIENT	DATE ASSESSMENT	NUMBER OF HEALING	ULCER	AREA CM2	REDUCT/AREA %	PERIMETER MM	DEPTH MAXIMUM	DEPTH MEAN	VOL CM3	LONG MM	WIDTH MM
1	000041	22-06-2016 10:11	8	A	0.0	100.0%	0				0	0
2	000042	06-09-2016 10:31	19	A	2.9	75.4%	69	2	1	0.3	24	18
3	000043	08-06-2016 11:10	6	A	0.9	68.9%	37	4	1	0.1	15	8
	000043	08-06-2016 11:11	1	C	0.9	0.0%	36	0	0	0.0	13	10
4	000045	25-05-2016 10:17	3	A	0.0	90.9%	5	1	0	0.0	2	1
5	000046	20-09-2016 10:51	19	A	3.4	76.0%	80	3	1	0.4	29	15
6	000047	06-09-2016 10:20	17	A	3.0	85.0%	76	1	0	0.1	27	18
7	000048	12-09-2016 11:16	17	A	0.0	100.0%	0				0	0
	000048	06-09-2016 11:31	16	C	0.0	100.0%	0				0	0
	000048	22-09-2016 10:33	12	E	1.2	-89.3%	44	2	1	0.1	14	11
	000048	22-09-2016 10:34	7	G	0.5	70.5%	26	1	0	0.0	9	8
	000048	22-09-2016 10:36	2	I	0.1	59.4%	11	1	0	0.0	4	4
8	000049	30-06-2016 09:59	6	A	0.2	94.7%	18	0	0	0.0	6	5
9	000050	20-09-2016 10:30	17	A	11.9	-164.8%	145	4	1	0.7	46	44
	000050	20-09-2016 10:41	17	C	11.3	-150.4%	156	5	1	1.1	47	44
	000050	20-09-2016 10:30	17	E	0.0	97.4%	6	0	0	0.0	2	2
10	000051	03-08-2016 11:05	10	A	1.5	12.2%	44	1	0	0.0	15	14
11	000052	14-09-2016 09:45	16	A	0.0	100.0%	0				0	0
12	000053	23-06-2016 09:51	3	A	0.0	100.0%	0				0	0
	000053	07-07-2016 09:53	5	C	0.0	100.0%	0				0	0
	000053	30-06-2016 10:32	1	E								
13	000054	20-07-2016 09:47	6	A	2.7	-16.3%	60	1	0	0.0	22	17
14	000055	27-06-2016 10:15	2	A	7.0	-77.1%	117	6	1	0.9	44	21
15	000056	20-09-2016 10:21	15	A	0.0	100.0%	0				0	0
16	000057	07-09-2016 08:44	12	A	0.0	100.0%	0				0	0
17	000058	25-07-2016 11:39	2	A	0.0	100.0%	0				0	0
	000058	09-08-2016 08:26	4	C	0.0	100.0%	0				0	0
18	000059	04-08-2016 10:23	3	A	0.0	100.0%	0				0	0
19	000060	21-09-2016 09:10	8	A	0.0	100.0%	0				0	0
	000060	18-08-2016 09:43	3	C	0.0	100.0%	0				0	0
20	000091	22-08-2016 11:19	2	A	7.9	6.2%	102	1	0	0.0	35	29
21	000092	21-09-2016 09:31	5	A	0.2	-33.5%	16	0	0	0.0	6	4
	000092	06-09-2016 11:02	3	C	0.0	100.0%	0				0	0
22	000093	21-09-2016 09:56	5	A	0.3	84.3%	23	1	0	0.0	10	4
23	000094	14-09-2016 13:00	3	A	0.0	100.0%	0				0	0
			292			1789.3%						
			13			77.8%	AVERAGE PROGRESS PER PATIENT					

1	000021	29-08-2016 12:02	18	A	0.2	97.4%	16				7	3
	000021	31-05-2016 10:56	5	C	0.6	21.0%	28	1	0	0.0	11	7
2	000022	09-06-2016 09:53	6	A								
3	000023	19-07-2016 11:52	12	A	3.6	-52.4%	114	6	2	0.7	43	15
4	000024	15-06-2016 11:31	7	A	0.2	73.7%	16				6	4
5	000025	20-06-2016 10:36	8	A								
	000025	11-07-2016 13:57	9	C	0.7	47.5%	30	1	0	0.0	11	7
	000025	27-06-2016 14:15	1	E	41.4	0.0%	268	8	1	2.4	100	50
6	000026	24-05-2016 13:51	1	A	0.4	0.0%	27	10	2	0.1	10	4
7	000027	22-06-2016 09:26	8	A	0.0	98.5%	4				2	1
8	000028	24-05-2016 12:57	4	A	0.4	48.1%	33				14	2
	000028	24-05-2016 12:57	4	C	14.3	13.3%	158	3	0	0.5	56	37
	000028	14-09-2016 08:55	14	E	23.1	49.6%	195	3	0	0.0	64	49
9	000029	21-07-2016 11:15	11	A	2.8	58.4%	76	1	0	0.0	26	21
10	000030	06-06-2016 08:28	5	A	0.3	13.5%	18	0	0	0.0	7	5
11	000031	25-05-2016 11:39	3	A	0.0	99.9%	1				1	0
	000031	27-07-2016 10:17	12	C	0.0	99.8%	2				1	1
	000031	02-09-2016 11:41	13	E	2.8	-110.3%	62	3	0	0.0	25	12
12	000032	01-08-2016 11:37	13	A	0.1	93.9%	12	1	0	0.0	5	3
	000032	05-09-2016 11:21	18	C	0.8	97.7%	34	1	0	0.0	13	9
13	000033	14-09-2016 12:13	17	A	5.9	-19.1%	114	4	0	0.3	49	16
14	000034	13-06-2016 11:06	5	A								
15	000035	27-05-2016 12:06	3	A	0.4	70.3%	23	0	0	0.0	8	7
16	000036	25-08-2016 12:47	14	A	0.4	88.9%	25	2	1	0.0	7	6
17	000037	27-06-2016 11:28	6	A	1.0	64.8%	52	0	0	0.0	24	8
18	000038	16-06-2016 10:38	4	A	0.2	30.9%	14	0	0	0.0	5	4
19	000039	14-09-2016 09:57	16	A	0.2	-29.0%	18	2	0	0.0	6	5
20	000040	06-06-2016 14:04	1	A	0.5	0.0%	25	1	1	0.0	10	7
21	000081	28-06-2016 11:35	4	A	0.0	70.6%	6				3	2
	000081	12-07-2016 08:37	6	C	0.1	69.9%	16				8	3
	000081	14-06-2016 11:38	2	E	0.1	86.7%	9	0	0	0.0	4	2
	000081	21-06-2016 11:25	3	G	0.1	30.3%	15	0	0	0.0	7	2
	000081	21-06-2016 11:25	3	I	0.0	77.3%	9				3	2
	000081	21-06-2016 11:26	3	K	0.0	84.6%	9				4	1
	000081	19-07-2016 10:28	7	M	0.0	97.9%	8	0	0	0.0	3	2
	000081	05-07-2016 11:10	5	O	0.1	81.1%	25	1	0	0.0	11	2
	000081	14-06-2016 11:47	2	Q	0.0	3.6%	7	0	0	0.0	3	2
22	000082	15-06-2016 12:24	2	A								
23	000083	01-08-2016 09:33	8	A	0.1	92.7%	15	1	0	0.0	6	4
	000083	12-09-2016 11:01	14	C	4.1	55.1%	94	2	0	0.1	33	20
24	000084	16-06-2016 11:33	1	A	6.2	0.0%	97	2	0	0.0	32	27
	000084	16-06-2016 11:33	1	C	0.4	0.0%	25	1	0	0.0	10	5
25	000085	12-09-2016 11:48	13	A	7.5	14.8%	98	0	0	0.0	37	21
26	000086	16-08-2016 09:04	7	A	0.0	99.9%	3				2	0
27	000087	01-07-2016 10:58	1	A	8.8	0.0%	168	3	1	0.8	75	17
28	000088	08-09-2016 12:06	9	A	0.4	21.5%	24	2	1	0.0	9	7
	000088	08-09-2016 12:06	9	C	0.1	95.4%	15				5	5
29	000089	14-09-2016 11:54	11	A	2.0	-130.2%	52	1	0	0.0	21	11
	000089	18-08-2016 11:19	7	C	0.0	99.3%	5	0	0	0.0	2	2
	000089	18-08-2016 11:19	7	E	0.2	60.4%	26	3	1	0.0	13	2
30	000090	14-09-2016 09:30	8	A	0.2	-3.8%	17	1	0	0.0	7	4
31	000091	05-08-2016 08:28	2	A	0.5	9.9%	24	1	0	0.0	9	7
32	000092	10-08-2016 11:59	2	A	0.4	-103.6%	24	0	0	0.0	9	6
33	000093	12-09-2016 11:33	7	A	0.4	65.8%	25	4	1	0.0	9	7
34	000094	14-09-2016 13:01	5	A	0.0	98.8%	6	0	0	0.0	2	2
35	NO APLICA	19-05-2016 11:12	1	A	1.4	0.0%	46	0	0	0.0	16	13
			388			2034.6%						
			11			58.13%						

AVERAGE PROGRESS PER PATIENT

FINAL BEHAVIOUR:

TOTAL	680	3823.9%	
HEALING/PATIENT	**11.72**	**65.93%**	GENERAL AVERAGE PROGRESS/PATIENT

GENERAL PROGNOSIS:	IF 11.72 HEALINGS IS = 65.93% THEN IN AN AVERAGE OF 16 HEALINGS/ULCER (65.93%/11.72)*16 = **89.97%**

WITH THIS PERCENTAGE, AND GIVEN THAT THE RECRUITMENT PERIOD WAS EXTENDED TO SEPTEMBER, PROGRESS RECORDS ARE HIGHLY SATISFACTORY COMPARED TO THE TREATMENT RECEIVED BY THE CONTROL ARM.

IX. GENERALISED ANALYSIS

IN THE PREPARATION OF THE STUDY ENTITLED **ASSESSMENT OF EFFECTIVENESS AND SAFETY OF THE USE OF TISSUPOR® 3D EMBROIDERY DRESSINGS FOR WOUNDS IN PATIENTS WITH NEUROPATHIC ULCERATION ON THE DIABETIC FOOT**,

THREE COMPONENTS WERE PROPERLY INTRODUCED:

- THE STUDY DRESSING
- THE DEBRIDEMENT TECHNIQUE INTEGRATED WITH THE USE OF THE DRESSING
- THE MEASUREMENT TECHNIQUE

AFTER THE SECOND ASSESSMENT, THE STUDY IS DEEMED HIGHLY POSITIVE AND SATISFACTORY, AND THE DEBRIDEMENT TECHNIQUE IMPLEMENTED IN ULCER TREATMENT WITH THE USE OF DRESSINGS IS SUITABLE, AND IT IS WORTH MAKING IT AVAILABLE FOR THE INSTITUTION TO BE PRACTISED IN ALL MEDICAL FACILITIES OF THE COUNTRY DEALING WITH ULCERS OF THE DIABETIC FOOT.

THE TECHNOLOGY USED BOTH TO TAKE THE IMAGES AND TO PROCESS DATA IS HIGHLY OBJECTIVE AND RELIABLE, SINCE DATA PROCESSING MAY NOT BE INFLUENCED BY THE OPERATOR OR RESEARCHER.

DATA PROCESSED AND CALCULATIONS OBTAINED ARE THE PRODUCT OF A PROPER HANDLING OF EQUIPMENT AND THE QUALITY OF PROGRAMS. THEREFORE, THAT IS CONSIDERED SUPPLEMENTARY AND VALUABLE FOR THE STUDY SINCE IT HAS ALLOWED THE PROCESSING TO BE MORE OBJECTIVE AND RELIABLE.

IN THE PROPOSITION OF THE SECOND ASSESSMENT, AFTER BEING PROPOSED, ONCE THE MINIMUM TARGET AVERAGE WAS ACHIEVED, WITH THE NUMBER OF ULCERS PROGRAMMED IN 8, THE SCOPE WAS 48%, AND IT WAS OBTAINED (CALCULATING THE PERCENTAGE REACHED AND OVER 8 WEEKS, ACCORDING TO TREATMENTS EACH WEEK = ONE TREATMENT).

REGARDING THE COMPARATIVE ANALYSIS WITH THE RESULTS OBTAINED IN THE CONTROL ARM, WHICH HAD ADVANCE ON THE SAME DATE OF THIS ANALYSIS, -17.27% ADVANCE IN THE RECOVERY OF ULCERS TREATED WITH THE STANDARD METHOD WAS OBTAINED.

WE CONCLUDE THAT THE STUDY TO ASSESS THE EFFICIENCY OF THE DRESSING BEING STUDIED HAS SUCCEEDED.

X. SOCIO-ECONOMIC ANALYSIS OF THE STUDY

IN THIS ASSESSMENT, THE CONNECTION TO THE AGE OF PATIENTS RECRUITED IN THE PERIOD BETWEEN 46-70 YEARS OLD IS CLEARER, AND A 77.6% HAS BEEN SET. AND, IF WE CONSIDER THE INITIAL RANGE OF 40 YEARS, THIS PERCENTAGE EXCEEDS 80% OF PEOPLE WITH THE DISEASE.

WITH STANDARD TREATMENT, PATIENT CARE CREATES A NUMBER OF INTERVENTIONS ON THE ULCER THAT RANGE FROM USING MEDICAL PRODUCTS, AND EVEN ALTERNATIVE PRODUCTS, THAT IN GENERAL PROLONG THE RECOVERY PERIOD OF THE ULCER, AND IN SOME CASES, PATIENT'S HISTORY INDICATES THAT ON AVERAGE, THEY TAKE MORE THAN SIX MONTHS.

AN AVERAGE SET AT 9 VISITS PER PATIENT TO ANY OF THE CLINICS, IF HE/SHE IS A PATIENT TREATED WITH THE STANDARD METHOD AT AN INSTITUTION, AND WHO WILL HAVE A PROGRESS OF LESS THAN -17.27%, INDICATES THAT THE PATIENT WILL HAVE TO LOOK FOR ANOTHER ALTERNATIVE, OR ELSE SPEND MORE TIME IN THIS TYPE OF TREATMENT, AND IN THE WORST CASE SCENARIO, IT WILL EVOLVE TO WAGNER 3, AND BE AT RISK OF PARTIAL AMPUTATION OF THE LIMB BEING COMPROMISED.

IN THIS LONG CARE PERIOD, THE ECONOMY OF THE PATIENTS' FAMILIES IS AFFECTED WITH THE RESULTING MEDICAL EXPENSES, THE REDUCTION OF THE PRODUCTIVE RHYTHM, AND TIME DEPENDENCY OF A FAMILY MEMBER.

FOR COMPANIES, IT IS WORTH MENTIONING THAT LEAVES OF ABSENCE AND MEDICAL LEAVES NOTABLY DAMAGE THE PRODUCTIVITY AND ECONOMY, WHICH IN TURN IMPACTS NEGATIVELY ON THE COUNTRY.

THE PSYCHOLOGICAL DAMAGE IN PATIENTS AND FAMILY MEMBERS DUE TO THE PARTIAL OR TOTAL LOSS OF THE EXTREMITIES FOR THE AMPUTATION HAS A NEGATIVE IMPACT, TRIGGERING OTHER TYPES OF PROBLEMS.

AFTER THE SECOND AND LAST ASSESSMENT OF THE CLINICAL TRIAL, THE COMPARATIVE PROGRESS BETWEEN THE CONTROL ARM AND THE INTERVENTION ARM INDICATE THAT THE LATTER HAS BEEN SATISFACTORY, AND THAT IT IS NECESSARY TO IMPLEMENT THE TREATMENT IN THE CONTROL ARM IN THE SAME WAY, AS SET IN THE COMMITMENTS OF THE INSTITUTION AND THE COMPANY.

LIKEWISE, IT IS NECESSARY TO CONDUCT OTHER STATISTICAL ANALYSIS AND PROMOTE THIS TREATMENT IN THE REST OF THE MEDICAL FACILITIES.

VII CONCLUSIONS

The total count for the study was 101 subjects, 43 subjects in HGR MF1 (Cuernavaca) and 58 subjects in HGZ MF5 (Zacatepec); 28 men and 15 women in HGR MF1 (Cuernavaca), and 31 men and 27 women in HGZ MF5 (Zacatepec).

The total number of ulcers was 143. Of patients at the HGR MF1 facility in Cuernavaca, there were 52 ulcers, of which 23 were Wagner 1 and 29 were Wagner 2. Of patients at the HGZ MF5 facility in Zacatepec, there were 91 ulcers, of which 57 were Wagner 1 and 34 were Wagner 2.

1485 healing were performed in all patients. At HGR MFI facility in Cuernavaca, the average of healings for Wagner 1 and Wagner 2 patients was 26.63 and 24.92 respectively. At HGZ MF5 facility in Zacatepec with Tissupor® 3D Embroidery dressings, the average of healings for Wagner 1 and Wagner 2 patients was 11.0 and 11.72 respectively.

In a generalised analysis, with all the values and all the patients, while conducting the mean difference analysis compared to the % of reduction of the area, it was observed that of the Levene test, the P value is significant, and it is assumed that there are different variances. Thus, the statistical result of the test is t=-3.860, and the associated P value is 0.00. Therefore, there is a difference on both facilities where patients were treated, and means are 95% different. Likewise, it was observed that there were differences according to gender in the treatment response of men (P 0.000) (Stata 12.0).

These results allow us to conclude that patients in HGZ MF5 of Zacatepec treated with Tissupor® 3D Embroidery dressings had more percentage of reduction area compared to patients in Cuernavaca, who had standard treatment (control arm). This is statistically significant, even with follow-up losses and patients who abandoned the treatment (< 30%). Therefore, it is important to consider treatment with Tissupor® 3D Embroidery dressings to improve the prognosis of patients with diabetic foot, and to avoid amputations of the extremity being compromised. Likewise, it would be important to carry out another research measuring the cost-benefit impact, since in this research, it was found that the number of healings decreases in more than 50% of patients in Zacatepec medical facility treated with Tissupor® 3D Embroidery dressings compared to patients who received standard treatment in the medical facility of Cuernavaca. This has implications, not only in the substantial cost saving in healing material, but also in the need to prescribe treatment with multiple antibiotics since, in the case of patients treated with Tissupor® 3D Embroidery dressings (Petrulyte s, 2008), the use of antibiotics is dispensed with, prioritising topic treatment.

In addition, this creates savings in the number of transport costs for patients to have their healings carried out, or those the outpatient facility needs to carry out healings at the patient's address. this also creates savings in worker-hours, fuel, and even burnout of the primary caregiver taking care of the patient at home.

On the other hand, it was observed from the clinical perspective that patients treated in HGZ MF5 in Zacatepec, classified as Wagner 1, and who received treatment with the dressing showed a faster evolution towards wound healing compared to subjects treated in HGR MF1 in Cuernavaca, who received standard treatment. This has been based on results obtained, for example: on 7 patients who were discharged for healing of Wagner 1 ulcers. In the case of patients in HGR MF1 in Cuernavaca, it was observed that they showed a slower evolution to wound healing, and they require closer monitoring since they can easily relapse. It must be stated that it essentially depends on the patient's rest. It was also found that they do not get easily infected. As regards healing, it does not need to be aggressive.

As regards Wagner 2 classification patients, it was found that they may easily evolve to Wagner 3. In this sense, the key to success in this patients is debridement. Likewise, humidity keeps the wound in good condition. Aggressive healings with debridement make the wound evolve faster to wound healing. It was determined that keeping prolonged support over the wound evolves quickly to necrosis. Some evolve faster from the inflammatory phase to the proliferation phase. Within the proliferation phase itself, evolving from angiogenesis to granulation is faster, than from granulation to re-epithelisation. That mentioned before is greatly determined by optimum metabolic control.

In cases observed in HGZ MF5, Zacatepec, with the use of the dressing, it was observed that in very small ulcers, it was difficult to place the dressing, and this increases with unsuitable footwear, increasing the risk it moves outside the ulcer. For this reason, the use of proper footwear is important for the diabetic foot.

In summary, it is assumed that the diabetic foot in its advanced stages (Wagner 2, 3, and 4) (Martínez de Jesús, et al, 2012) is one of the most severe complications for patients with DM2, since it creates functional dependence and progressive and permanent disability (including premature death) (International Diabetes Federation, 2014), coupled with lost productive life years, which has implications for the healthcare system, society, and essentially for the family. This creates a significant burden for the primary caregiver, who is generally the wife or the closest son/daughter. It is worth recalling that chronic patients require chronic care. However, over time, this support provided by the family tends to lead to burnout. Therefore, innovations related to the diabetic foot treatment is key to keep the mobility of patients suffering from these complex conditions in an era of limited resources, where chronical diseases and their complications have overwhelmed institutions (Wong R., et al, 2012).

TABLE 1. NUMBER OF HEALINGS PER ULCER ACCORDING TO CARE FACILITY			
CUERNAVACA FACILITY HGR MF1 (AVERAGE OF HEALINGS PER ULCER WITH STANDARD TREATMENT)		ZACATEPEC FACILITY HGZ MF5 (AVERAGE OF HEALINGS PER ULCER WITH NON-STANDARD TREATMENT/DRESSINGS)	
WAGNER 1	WAGNER 2	WAGNER 1	WAGNER 2
26.63	24.92	11	11.72

Table 2. Area reduction %

	Medical Facilities	N	MEAN	STD DEVIATION	STANDARD ERROR OF THE MEAN
Reduction area (%)	CUERNAVACA	56	0.120	0.2283	0.0305
	ZACATEPEC	91	0.308	0.3633	0.0379

Table 3. Area reduction % - Independent samples test

		Levene test for equality of variances		T Test for equality of means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean difference	Std. error difference	95% confidence interval	
									Lower	Upper
reduction area (%)	Equal variance assumed	37.428	0.000	-3.470	146	0.001	-0.1877	0.0541	-0.2947	-0.0808
	Equal variance not assumed			-3.860	145.824	0.000	-0.1877	0.0486	-0.2839	-0.0916

REF 18-90-01-280100-459/2017

DATE: 28 APRIL 2017

PROF. RODOLFO MENDOZA CRUZ
GENERAL DIRECTOR OF INTERSUIMEX
AV 10 DE ABRIL NO 1013, COL. GRANJAS
CUERNAVACA, MORELOS
CP 62460

Dear Professor Mendoza, in response to your letter dated 26 April, I hereby submit the **final analysis** of the protocol entitled ASSESSMENT OF EFFECTIVENESS AND SAFETY OF THE USE OF TISSUPOR® 3D EMBROIDERY DRESSINGS FOR WOUNDS IN PATIENTS WITH NEUROPATHIC ULCERATION ON THE DIABETIC FOOT, duly recorded on the National Commission for Scientific Research under number R-2015-785*058, that is being developed in Morelos borough. We have completed the recruitment process and analysis of the information of the project.

I thank you for your attention

REGARDS,
SOCIAL SECURITY AND SOLIDARITY

DR LAURA AVILA JIMENEZ
Researcher in charge of the Project
Auxiliary Medical Coordinator for Health Research
Associate Researcher “A”

DC. LAJ

With copy to Dr Fabio Abel Salamanca Gómez, as information
With copy to Dr Eusebio Pérez Flores, as information
With copy to Lic. Paola Álvarez Cabello, FIS , as information

ANNEX 1. Final Document

Spanish	***English***
Recibo apra su despacho	*Acknowledged receipt*

HOW THE PROGRAM IMPORTS MEASUREMENT RECORDS TO THE DATABASE

	A	B	C	D	E	F	G	H	I
1	APaterı	Nombre	AMaterr	Address	Subject ID	Unit	Date of Birth	Gender	Anatomical Site
2	Zárraga	José Luis	Castillo	8 Norte Manzana N.	000001	CUERNAVACA SITE	06-11-1958	Male	Right Toe, Big; Plantar
22	Reyes	Erasto	Vázquez	Jacarandas N. 4	000004	CUERNAVACA SITE	28-03-1956	Male	Right Foot, Heel
58	Romero	Margarita	Martínez	Del Ferrocarril N. 51 Int	000005	CUERNAVACA SITE	26-01-1955	Female	Left Foot, Sole
74	Pérez	Gema	Álvarez	U. Hab La Joya Ed 13	000006	CUERNAVACA SITE	11-04-1963	Female	Left Foot, Sole
108	Sánchez	José	Delgado	Begonia N.108	000008	CUERNAVACA SITE	10-03-1947	Male	Right Foot, Sole; A Nivel De 1er
140	Valdivia	María	Terrones	Prolongacion Durando	000010	CUERNAVACA SITE	06-08-1970	Female	Right Foot, Medial
168	Duarte	María Marta	Amezcua	av vicente suarez	000011	CUERNAVACA SITE	18-04-1936	Female	Left Foot, Heel
196	Ortega	Gonzalo	Suárez	Tulipanes N.5	000012	CUERNAVACA SITE	08-01-1960	Male	Right Foot, Dorsum; Y Plantar En Region
197	Ortega	Gonzalo	Suárez	Tulipanes N.5	000012	CUERNAVACA SITE	08-01-1960	Male	Right Foot, Dorsum; Y Plantar En Region
198	Ortega	Gonzalo	Suárez	Tulipanes N.5	000012	CUERNAVACA SITE	08-01-1960	Male	Right Foot, Dorsum; POSTERIOR A
199	Ortega	Gonzalo	Suárez	Tulipanes N.5	000012	CUERNAVACA SITE	08-01-1960	Male	Right Foot, Dorsum; POSTERIOR A
200	Oliveros	Augusto	Moreno	Francisco Leyva N 95	000013	CUERNAVACA SITE	15-03-1955	Male	Left Toe, Big
205	Oliveros	Augusto	Moreno	Francisco Leyva N 95	000013	CUERNAVACA SITE	15-03-1955	Male	Left Toe, Big; POSTERIOR A CURACIÓN
210	Ortíz	Lidia	Arredondo	Topacio N 93	000014	CUERNAVACA SITE	11-10-1956	Female	Right Toe, Forth; Interdigital Entre 4to Y
218	Ortíz	Lidia	Arredondo	Topacio N 93	000014	CUERNAVACA SITE	11-10-1956	Female	Right Toe, Forth; POSTERIOR A CURACIÓN
226	García	Fernando	Gama	Andador 410 Lote 13 U.	000015	CUERNAVACA SITE	27-06-1959	Male	Right Foot, Sole
234	García	Fernando	Gama	Andador 410 Lote 13 U.	000015	CUERNAVACA SITE	27-06-1959	Male	Right Foot, Sole; POSTERIOR A CURACIÓN
242	Arroyo	Gonzalo	Cruz	palmas SN esq la	000016	CUERNAVACA SITE	10-05-1955	Male	Left Foot, Sole
252	Arroyo	Gonzalo	Cruz	palmas SN esq la	000016	CUERNAVACA SITE	10-05-1955	Male	Left Foot, Sole; POSTERIOR A CURACIÓN
262	Sandoval	Aurora	.	pino suarez N. 107	000017	CUERNAVACA SITE	29-06-1944	Female	Left Toe, Big
280	Sandoval	Aurora	.	pino suarez N. 107	000017	CUERNAVACA SITE	29-06-1944	Female	Left Toe, Big; POSTERIOR A CURACIÓN

Spanish	***English***
APaterno	Paternal S.
8 Norte Manzana N	8 Norte Manzana N
Jacarandas	Jacarandas
Del ferrocaril N .51 Int	Del Ferrocaril N .51 Int
U Hab La joya ed 13	U. Hab La Joya ed 13
Begonia n 108	Begonia N. 108
Prolongacion Durando	Prolongacion Durando
Av Vicente suarez	Av Vicente Suarez
Tulipanes N S	Tulipanes N.5
Francisco Leyva N 95	Francisco Leyva N. 95
Topacio N93	Topacio N. 93
Andador 410 Lote 13 U	Andador 410 Lote 13 U
Palmas SN esq la	Palmas SN esq la
Pino suarez N 107	Pino Suarez N. 107
Cuernavaca Site	Cuernavaca Site
Male	Male
Female	Female
Rig toe, big, planter	Rig toe, big; plantar
Right foot, heeñ	Right foot, heel
Left foot, sole	Left foot, sole
Right foot sole; a nível de 1er	Right foot sole; at 1st level
Right foot mesial	Right foot, medial
Left foot, heel	Left foot, heel
Right foot, dorsum; y plantar em region	Right foot, dorsum; and plantar in region
Right foot Dorsum, POSTERIOR A	Right foot, dorsum, AFTER
Left Toe, Big	Left toe, big
Left toe; Big POSTERIOR A CURACION	Left toe, big; AFTER HEALING
Right toe, forth, interdigital Entre 4 Y	Right toe, forth, interdigital between 4th and
Right toe, forth, POSTERIOR A CURACION	Right toe, forth, AFTER HEALING
Right Foot, sole	Right Foot, sole
Right foot, sole; POSTERIOR A CURACION	Right foot, sole; AFTER HEALING
Left toe big	Left toe, big
Left toe big Posterior a Curacion	Left toe, big; after healing
Nombre	Name
AMaterno	Maternal S.
Address	Address
Subjet id	Subject ID
Unit	Unit
Date of Birth	Date of Birth
Gender	Gender
Anatomical Site	Anatomical Site

	E	J	K	L	M	N	O	P	Q	R	S	T
1	Subject ID	Assessment Date	Assessment #	Wound	Area (cm^2)	Area Reduction (%)	Perimeter (mm)	Max Depth (mm)	Mean Depth (mm)	Volume (cm^3)	Length (mm)	Width (mm)
2	000001	02-05-2016 11:29	1	A	0.2	0.0%	20	1	0	0.0	8	5
22	000004	02-05-2016 09:22	1	A	15.6	0.0%	157	2	0	0.3	53	38
58	000005	03-05-2016 08:47	1	A	0.9	0.0%	35	0	0	0.0	12	10
74	000006	02-05-2016 08:20	1	A	0.4	0.0%	27	1	0	0.0	10	6
108	000008	05-05-2016 08:46	1	A	0.5	0.0%	28	1	0	0.0	12	6
140	000010	02-05-2016 10:15	1	A	14.3	0.0%	259	3	0	0.1	96	42
168	000011	02-05-2016 14:15	1	A	11.5	0.0%	124	1	0	0.0	47	34
196	000012	02-05-2016 09:42	1	A	15.8	0.0%	215	27	5	7.8	60	31
197	000012	16-05-2016 13:42	2	A	6.3	60.2%	160	37	2	1.1	40	19
198	000012	02-05-2016 09:42	1	B	13.4	0.0%	188	18	4	5.4	52	29
199	000012	16-05-2016 13:42	2	B	6.5	51.5%	171	21	2	1.1	39	17
200	000013	03-05-2016 11:18	1	A	3.6	0.0%	69	4	0	0.0	26	21
205	000013	03-05-2016 11:23	1	B	3.6	0.0%	68	1	0	0.0	24	19
210	000014	05-05-2016 08:29	1	A	1.8	0.0%	55	7	2	0.4	17	12
218	000014	05-05-2016 08:32	1	B	1.6	0.0%	54	6	1	0.2	17	11
226	000015	04-05-2016 11:01	1	A	2.2	0.0%	55	0	0	0.0	20	14
234	000015	04-05-2016 11:05	1	B	2.2	0.0%	56	0	0	0.0	19	15
242	000016	02-05-2016 13:19	1	A	1.2	0.0%	51	2	0	0.0	18	12
252	000016	02-05-2016 13:23	1	B	1.2	0.0%	49	0	0	0.0	19	12
262	000017	04-05-2016 12:36	1	A	5.5	0.0%	83	0	0	0.0	27	25

THE PATIENTS' RECORDS ARE LOCATED IN THE DATABASE OF THE LIAISON BETWEEN TISSUPOR COMPANY AND THE MEXICAN SOCIAL SECURITY INSTITUTE, (INSTITUTO MEXICANO DEL SEGURO SOCIAL, IMSS), MEXICO.