TEST FACILITY

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SPONSOR

Geoff Daly
Analytica Ltd
85 Brandl Street Eight Mile Plains
Brisbane, Queensland, 4113
Australia

STUDY TITLE

ISO Intracutaneous Study - Extract

TEST ARTICLE NAME

Analytica AutoStart 150mL Burette

TEST ARTICLE IDENTIFICATION

Lot: 20080909

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Summary

The potential of the test article, Analytica AutoStart 150mL Burette, Lot: 20080909, to cause irritation following intradermal injection in rabbits was evaluated based on the International Organization for Standardization 10993-10: Biological Evaluation of Medical Devices, Part 10: Tests for Irritation and Delayed-Type Hypersensitivity. The test article was extracted in 0.9% sodium chloride USP solution (SC). A 0.2 mL dose of the appropriate test article extract was injected by the intracutaneous route into five separate sites on the right side of the back of each of two rabbits. Similarly, the control was injected on the left side of the back of each rabbit. The injection sites were observed immediately after injection. Observations for erythema and edema were conducted at 24, 48, and 72 hours after injection.

Under the conditions of this study, there was no erythema and no edema from the SC test extract injected intracutaneously into rabbits. The SC test article extract met the requirements of the test since the difference between the test extract and control mean score was 1.0 or less.

Study and Supervisory Personnel:

Molly F. Corvo, B.S.
Mark S. Werth
Michelle R. Horner, B.S.
Shelli L. Petterle, A.A., B.A.
Colleen M. Stevenson, A.A.
Mark J. Menzel, RVT, A.A.S.
Natasha N. Norris, B.S.
Lesia M. Wasio, B.S.
Nathan L. Alt, B.S.
Carrie A. Fetter
Don R. Pohl, B.S.
Melissa A. Cadaret, B.A., M.S.

Approved by:

Jolee Bartrom 10-15-08

Jolee Bartrom, B.S.
Study Director

Date Completed

Statement of GLP Compliance

This study was conducted in accordance with the provisions of the FDA Good Laboratory Practice (GLP) Regulations (21 CFR, Part 58).

There were no deviations from the protocol, standard operating procedures or the GLP Regulations which were judged to have had any significant impact on the validity or interpretation of the data.

All laboratory data has been accurately recorded and verified, as indicated by the signature below.

Study Director: Jolee Bartrom — Jolee Bartrom, B.S. — 10-15-08 — Date

1. Introduction

Purpose
The test article identified below was extracted and the extract was evaluated to determine whether leachables extracted from the material would cause local dermal irritant effects following injection into rabbit skin.

Testing Guidelines
The study was conducted based on the International Organization for Standardization 10993-10: Biological Evaluation of Medical Devices, Part 10: Tests for Irritation and Delayed-Type Hypersensitivity and the United States Pharmacopeia, National Formulary, General Chapter <88>, Biological Reactivity Tests, In Vivo.

Dates

Test Article Receipt:	September 15, 2008.
Treatment Start Date:	September 25, 2008
Observations Concluded Date:	September 28, 2008

GLP Compliance
The study initiated by protocol signature on September 15, 2008, was conducted in accordance with the provisions of the FDA Good Laboratory Practice (GLP) Regulations, 21 CFR 58. A Statement of Quality Assurance Activities was issued with this report.

Duplication of Experimental Work
By signature on the protocol, the sponsor confirmed that the conduct of this study did not unnecessarily duplicate previous experiments.

2. Materials

The test article provided by the sponsor was identified and handled as follows:

Test Article Name:	Analytica AutoStart 150mL Burette
Test Article Identification:	Lot: 20080909
Stability Testing:	In progress (per sponsor)
Expiration Date:	Stable for duration of intended testing (per sponsor)
Strength, Purity and Composition	Strength: Not applicable as there are no active ingredients are used to formulate a concentration; Purity: Not applicable, because the test article is a multi-component device with no active ingredients; Composition: See Appendix 2.
Physical Description of the Test Article:	Single-use, sterile, medical device. Predominantly transparent PVC and white ABS.
Storage Conditions:	Room Temperature
Extraction Vehicle/Control:	0.9% sodium chloride USP solution (SC)
Control Article Stability Testing:	Marketed product stability characterized by its labeling.
Control Article Strength, Purity and Composition:	SC: Strength: Not applicable, no active components in the formulation; Purity: Meets requirements of USP Sodium Chloride for Injection and is certified as USP Grade. 0.9% NaCl ± 5.0% of label claim, balance is water; Composition: CAS #: 7647-14-5 Sodium Chloride/Water CAS #: 7732-18-5.

Extraction Procedure: One device was filled to capacity with a total of 160 ml of the vehicle. The device was sealed as necessary to avoid loss of the vehicle during extraction. The test article and the control blank (extraction vehicle without the test article) were subjected to the extraction conditions as described below.

Extraction Ratio	Sample Amount	Volume of Vehicle	Extraction Condition
NA	NA	160 mL	50°C for 72 hours

The extracts were agitated during extraction.
NA = Not Applicable

Condition of Extracts:

Vehicle	Treatment Group	Condition of Extract
SC	Test	clear with particulates
	Control	clear

3. Test System

Test System

Species:	Rabbit (*Oryctolagus cuniculus*)
Breed:	New Zealand White
Source:	Myrtle's Rabbitry, Inc.
Sex:	Male
Body Weight Range:	2.5 kg to 2.6 kg at selection
Age:	Young adult
Acclimation Period:	Minimum 5 days
Number of Animals:	Two
Identification Method:	Ear tag

Justification of Test System
The intracutaneous injection test in rabbits is specified in the current ISO testing standards and has been used historically to evaluate biomaterial extracts.

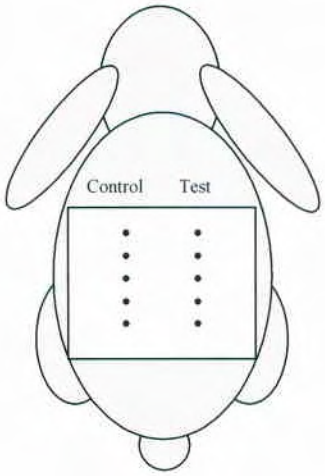
4. Animal Management

Husbandry:	Conditions conformed to Standard Operating Procedures that are based on the "*Guide for the Care and Use of Laboratory Animals*."
Food:	A commercially available rabbit feed was provided daily.
Water:	Potable water was provided *ad libitum* through species appropriate water containers or delivered through an automatic watering system.
Contaminants:	Reasonably expected contaminants in feed or water supplies did not have the potential to influence the outcome of this test.
Housing:	Animals were individually housed in stainless steel suspended cages identified by a card indicating the lab number, animal number, test code, sex, and date dosed.
Environment:	The animal housing room temperature and relative humidity was monitored daily. The recommended temperature range for the room was 61-72°F and 30-70% for relative humidity. There were no significant temperature or relative humidity excursions that adversely affected the health of the animals. The light cycle was controlled using an automatic timer (12 hours light, 12 hours dark).
Accreditation:	NAMSA is an AAALAC International accredited facility and is registered with the United States Department of Agriculture. Additionally, NAMSA maintains an approved Animal Welfare Assurance on file with the National Institutes of Health, Office for Laboratory Animal Welfare.
Personnel:	Associates involved were appropriately qualified and trained.

Selection:	Only healthy, previously unused, thin-skinned animals free of mechanical irritation or trauma that could interfere with the test were selected.
Sedation, Analgesia or Anesthesia:	Sedation, analgesia or anesthesia was not necessary during the routine course of this procedure.
Veterinary Care:	In the unlikely event that an animal became injured, ill, or moribund, care was conducted in accordance with current veterinary medical practice. If warranted for humane reasons, euthanasia was conducted in accordance with the current report of the American Veterinary Medical Association's Guidelines on Euthanasia. The objective of the study was given due consideration in any decision and the study sponsor was advised.
IACUC:	This procedure has been approved by NAMSA Institutional Animal Care and Use Committees (IACUC), and is reviewed at least annually by the same committees. Any significant changes to this procedure were approved by the IACUC prior to conduct.

5. Method

Within a 4 to 18 hour period before treatment, each rabbit was clipped free of fur from the back and both sides of the spinal column to yield a sufficient injection area. A 0.2 mL dose of the test article extract was injected by the intracutaneous route into five separate sites on the right side of the back of each rabbit. Similarly, the control was injected on the left side of the back of each rabbit. Injections were spaced approximately 2 cm apart.



The appearance of each injection site was noted immediately after injection. The animals were returned to their respective cages following the procedure.

Observations for erythema and edema were conducted at 24, 48, and 72 hours after injection. Reactions were scored on a 0 to 4 basis. Any reaction at the injection sites was also noted. The reactions were evaluated according to the following subjective rating scale:

Score	Erythema (ER)	Edema (ED)
0	No erythema	No edema
1	Very slight erythema (barely perceptible)	Very slight edema (barely perceptible)
2	Well-defined erythema	Well-defined edema (edges of area well-defined by definite raising)
3	Moderate erythema	Moderate edema (raised approximately 1 mm)
4	Severe erythema (beet redness) to eschar formation preventing grading of erythema	Severe edema (raised more than 1 mm, and extending beyond exposure area)

6. Evaluation and Statistical Analysis

The mean erythema and edema scores for the test and control extracts for each animal at each scoring interval were calculated. All mean erythema and edema scores for the test and control extracts were totaled and divided by 12 (2 animals x 3 grading periods x 2 grading categories) to determine the overall mean score for the test extract and control. The difference between the overall mean score of the test and control extracts was calculated by subtracting the overall mean score for the control from the overall mean score for the test extract.

The requirements of the test were met if the difference between the test extract mean score and control mean score was 1.0 or less.

7. Results

All animals appeared normal throughout the study. Results of scores for individual rabbits appear in Appendix 1. All injection sites appeared normal immediately following injection. The overall mean difference for the extract is summarized below:

Extract	Overall Test Group Mean	Overall Control Group Mean	Overall Mean Difference (Test – Control)
SC	0.0	0.0	0.0

8. Conclusion

Under the conditions of this study, there was no erythema and no edema from the SC test extract injected intracutaneously into rabbits. The SC test article extract met the requirements of the test since the difference between the test extract and control mean score was 1.0 or less.

Results and conclusions apply only to the test article tested. Any extrapolation of these data to other samples is the sponsor's responsibility. All procedures were conducted in conformance with good manufacturing practices and certified to ISO 13485:2003.

9. Quality Assurance

Inspections were conducted at intervals adequate to assure the integrity of the study in conformance with 21 CFR 58.35(b)(3). The final report was reviewed for conformance to Section 58.185, Subpart J, of the GLP Regulations. A Statement of Quality Assurance Activities was issued with the report.

10. Proposed Dates

The study dates were finalized by the study director following receipt of the sponsor approved protocol and appropriate material for the study. Initiation of the study was the date on which the study director signed the GLP protocol. Projected dates for starting the study (first treatment) and for the completion of the study (final report release) were provided to the sponsor (or representative of the sponsor).

11. Records

All raw data pertaining to this study and a copy of the final report are to be retained in designated NAMSA archive files.

12. References

21 CFR 58 (GLP Regulations).

Code of Federal Regulations (CFR), Title 9, Parts 1-199, Animal Welfare Act (2007).

Office of Laboratory Animal Welfare (OLAW), Public Health Service Policy on Humane Care and Use of Laboratory Animals.

National Research Council, *Guide for the Care and Use of Laboratory Animals*, Washington, DC: National Academy Press, 1996.

International Organization for Standardization (ISO) 10993-2, Biological Evaluation of Medical Devices - Part 2: Animal Welfare Requirements (2006).

International Organization for Standardization (ISO) 10993-10, Biological Evaluation of Medical Devices - Part 10: Tests For Irritation And Delayed-Type Hypersensitivity (2002).

United States Pharmacopeia 31, National Formulary 26 (USP), General Chapter <88> Biological Reactivity Tests, In Vivo (2008).

13. Protocol Changes

Any necessary changes to the protocol after sponsor approval or study initiation were documented and approved by the study director as protocol amendments. Copies were distributed to the sponsor, the raw data file, and the NAMSA Quality Assurance department.

Appendix 1 - ISO Intracutaneous Observations

Extract	Animal Number	Gender	Body Weight (kg)	Scoring Interval											
				24 Hours				48 Hours				72 Hours			
				Test		Control		Test		Control		Test		Control	
				ER	ED	ER	ED	ER	ED	ER	ED	ER	ED	ER	ED
SC	60487	Male	2.6	0	0	0	0	0	0	0	0	0	0	0	0
				0	0	0	0	0	0	0	0	0	0	0	0
				0	0	0	0	0	0	0	0	0	0	0	0
				0	0	0	0	0	0	0	0	0	0	0	0
				0	0	0	0	0	0	0	0	0	0	0	0
Mean Score				0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
SC	60488	Male	2.5	0	0	0	0	0	0	0	0	0	0	0	0
				0	0	0	0	0	0	0	0	0	0	0	0
				0	0	0	0	0	0	0	0	0	0	0	0
				0	0	0	0	0	0	0	0	0	0	0	0
				0	0	0	0	0	0	0	0	0	0	0	0
Mean Score				0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

ER = Erythema
ED = Edema

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GLP SAMPLE SUBMISSION FORM

*Annotates a required field

08T-48695

Materials List

This listing comprises 'wet' parts only, i.e. parts that come into contact with IV fluid during normal use.

Part Number and Name	*Material*
ALT002-0110 Dual-Outlet Spike	White ABS, Manufacturer: Chi Mei Corporation, Taiwan, Product Code: PA-757
ALT002-0113 Top Cap	
ALT002-0129 Alignment Piece	
ALT002-0118 Dropper Support	
ALT002-0117 Float Guide	
ALT002-0116 Float Body	
ALT002-0128 Float Bottom	
ALT002-0131 Bottom Cap	
ALT002-0120 Upper Dropper Tube	ASTM 304 S30400 Stainless steel tubing
ALT002-0119 Lower Dropper Tube	
ALT002-0166 Spike Cap	PVC – Taizhou Boren Plastic Products Co, Ltd. China – Grade MT-2
ALT002-0114 Spike Port	– Note: contains DEHP
ALT002-0121 Inlet Tube	
ALT002-0122 Bypass Tube	
ALT002-0130 Central Tube	
ALT002-0115 Extruded Main Chamber	
ALT002-0041 Float Seal	Silicone Rubber - Wacker Elastosil R 401/20
ALT002-0096 Glue	99.5% Cyclohexanone ($C_6H_{10}O$) glue/solvent (cured/dry) - Jiangsu Tengxing chemical
ALT002-0159 Swabbable Needle-free injection Port	OEM – Halkey-Roberts part # 245204024 Polycarbonate: Clear polycarbonate Makrolon RX1805-451118 Silicone: Silicone 40 durometer, blue; Elastosil LR 3003140, OT color K-75238 Blue
ALT002-0105 Air Vent subassembly.	OEM – PVC + hydrophobic filter. Both materials with predicate use.

Geoff Daly, Operations Manager, Analytica Ltd
AUTHORIZED BY SPONSOR

9 SEPT 2008
DATE

NAMSA STUDY DIRECTOR

9-15-08
DATE

REV091107

Statement of Quality Assurance Activities

Phase Inspected	Auditor	Date
Scoring	V. D. Gnepper	September 26, 2008
Study Data Inspection	S. M. Pellitieri	October 2, 2008
Final Report Review	D. S. Dunn	October 15, 2008

Reports to Management and Study Director(s)	Date
Periodic Status Report	October 10, 2008

This study will be included in the next periodic status report as completed.

Based on a review of this study, it has been concluded that this report accurately describes the methods and standard operating procedures, and that the reported results accurately reflect the raw data of the study. This study has been reviewed in accordance with the provisions of the FDA Good Laboratory Practice Regulations (21 CFR, Part 58).

QA Representative: Debra S Dunn 10-15-08

Debra S. Dunn
Auditor, Quality Assurance

Date

NAMSA

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08T_48893
26068_001 26068

*Annotates a required field

SPONSOR FINAL REPORT WILL BE ADDRESSED AND MAILED TO

ANALYTICA LTD — Geoff Daly
COMPANY NAME* — **ATTN***
85 Brandl St, Eight Mile Plains
ADDRESS*
Brisbane — QLD — 4113
CITY* — **STATE*** — **ZIP***
AUSTRALIA
COUNTRY*
+61 (7) 3278-1950
PHONE*
+61 (7) 3259-8313
FAX*
GDALY@ANALYTICAMEDICAL.COM
E-MAIL*

INVOICE INFORMATION
As Above
BILLING ADDRESS (include Company Name if different from mailed to)*

7233
PURCHASE ORDER NUMBER*

COST ESTIMATE AND PROPOSAL NUMBER

☐ VISA ☐ MasterCard ☐ American Exp.
CARD HOLDER NAME

CREDIT CARD NUMBER — **EXPIRATION DATE**
+61 (7) 3295-0507 — As Above
ACCOUNTS PAYABLE PHONE* — **ACCOUNTS PAYABLE FAX***

Analytica AutoStart 150mL Burette
TEST ARTICLE NAME *USE EXACT WORDING DESIRED ON FINAL REPORT* * +
As per GMDN code 12159 - Intravenous administration set, general-purpose

INTENDED CLINICAL USE OF TEST ARTICLE:*

☐ BATCH ☐ CODE ☑ LOT 20080909.
CHECK ONE — **IDENTIFICATION NUMBER***

CONTROL ARTICLE NAME*

☐ BATCH ☐ CODE ☐ LOT
CHECK ONE — **IDENTIFICATION NUMBER***
NAMSA recommends only one lot, batch, or code per test article submission.

QUANTITY SUBMITTED:* 25 units total (includes non-GLP test units)
(please specify quantities for each lot/batch/code provided)
Single-use, sterile, medical device. Predominantly transparent PVC and white ABS
PHYSICAL DESCRIPTION OF TEST ARTICLE (Chemical/Material type/Color)*

TEST ARTICLE IS CATEGORIZED AS BEING A (check all that apply):* +
X MEDICAL DEVICE ☐ BIOLOGIC ☐ TISSUE
☐ PHARMACEUTICAL ☐ CHEMICAL ☐ OTHER

+ A detailed composition list and current MSDS sheet must accompany any chemical or biologic test article. A certificate of testing or reprocessing must be submitted for any human tissue derived sample or clinically used medical device

TEST ARTICLE BEING SUBMITTED IS:*
X STERILIZED ☐ NOT STERILIZED
☐ **NAMSA TO STERILIZE BY**: ☐ EO (additional charge) ☐ STEAM

Mixtures of test or control articles with carriers require analysis to demonstrate proper concentration, homogeneity, and stability.*
☐ Sponsor will provide analytical methods; or
☐ Sponsor will perform analysis on representative aliquots provided by NAMSA

STORAGE CONDITIONS*
X ROOM TEMPERATURE ☐ REFRIGERATION ☐ FREEZER
☐ OTHER:

① competed by JBloll on 9-15-08
JBloll 9-15-08

TEST AND CONTROL ARTICLE CHARACTERIZATION: The sponsor assures the above test article has been characterized for identity, strength, purity, and composition as required by FDA Good Laboratory Practice Regulations of 21 CFR Part 58.105. Stability testing is the responsibility of the sponsor and is subject to FDA audit. Characterization and stability information are also required for control articles. Please check the statement(s) applicable to the test and control articles for both Stability and Characterization sections below.

Test Article	Control Article	Stability (Choose One)
X	☐	Stability testing is in progress, article is stable for duration of intended testing.
☐	☐	Stability testing is complete and on file with sponsor. Expiration date (test): Expiration date (control):
☐	☐	Marketed product stability characterized by its labeling.

Test Article	Control Article	Characterization (if not applicable state clearly the reason why)
① ☒	☐	Strength: N/A: No active ingredients are used to formulate a concentration
① ☒	☐	Purity: N/A because test article is a multi-component device with no active ingredients JBloll 9-15-08
X	☐	Composition: Refer attached materials list

If requesting to return sample, please check the courier and include your:
☐ UPS ☐ Federal Express ☐ Other: _____ Account Number: _____

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UPS linhai univer start

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F 419 666 2954

08T-48695

Materials List

This listing comprises 'wet' parts only, i.e. parts that come into contact with IV fluid during normal use.

Part Number and Name	*Material*
ALT002-0110 Dual-Outlet Spike	White ABS, Manufacturer: Chi Mei Corporation, Taiwan, Product Code: PA-757
ALT002-0113 Top Cap	
ALT002-0129 Alignment Piece	
ALT002-0118 Dropper Support	
ALT002-0117 Float Guide	
ALT002-0116 Float Body	
ALT002-0128 Float Bottom	
ALT002-0131 Bottom Cap	
ALT002-0120 Upper Dropper Tube	ASTM 304 S30400 Stainless steel tubing
ALT002-0119 Lower Dropper Tube	
ALT002-0166 Spike Cap	PVC – Taizhou Boren Plastic Products Co, Ltd. China – Grade MT-2 – Note: contains DEHP
ALT002-0114 Spike Port	
ALT002-0121 Inlet Tube	
ALT002-0122 Bypass Tube	
ALT002-0130 Central Tube	
ALT002-0115 Extruded Main Chamber	
ALT002-0041 Float Seal	Silicone Rubber - Wacker Elastosil R 401/20
ALT002-0096 Glue	99.5% Cyclohexanone ($C_6H_{10}O$) glue/solvent (cured/dry) - Jiangsu Tengxing chemical
ALT002-0159 Swabbable Needle-free injection Port	OEM – Halkey-Roberts part # 245204024 Polycarbonate: Clear polycarbonate Makrolon RX1805-451118 Silicone: Silicone 40 durometer, blue; Elastosil LR 3003140, OT color K-75238 Blue
ALT002-0105 Air Vent subassembly.	OEM – PVC + hydrophobic filter. Both materials with predicate use.

Geoff Daly, Operations Manager, Analytica Ltd
AUTHORIZED BY SPONSOR — DATE 9 SEPT 2008

NAMSA STUDY DIRECTOR — DATE 9-15-08

GLP PROTOCOL

TEST FACILITY:

NAMSA
6750 Wales Road
Northwood, OH 43619

SPONSOR:

Geoff Daly
Analytica Ltd
Eight Mile Plains
Brisbane, Queensland 4113
Australia

STUDY TITLE:

ISO Intracutaneous Study, Extract

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Approvals

Sponsor Representative (Sponsor):	Geoff Daly, Operations Manager Analytica Ltd.
Date Approved:	Thursday, 4th September 2008
Study Director (NAMSA):	
Date Initiated:	9-15-08

1. Introduction

Purpose
The purpose of this study is to evaluate the local dermal irritant effects of leachables extracted from the test article following intracutaneous injection in rabbits. This study will be based on the requirements of the International Organization for Standardization 10993: Biological Evaluation of Medical Devices, Part 10: Tests for Irritation and Delayed-Type Hypersensitivity.

GLP Compliance
Good Laboratory Practice – This nonclinical laboratory study will be conducted in accordance with the United States Food and Drug Administration Good Laboratory Practice Regulations, 21 CFR Part 58.

Duplication of Experimental Work
By signature on this protocol, the sponsor confirms that the conduct of this study does not unnecessarily duplicate previous experiments.

2. Materials

Test Article
The sponsor will submit the test article to be evaluated. Detailed information about the test article will be provided by the sponsor on the NAMSA Sample Submission Form or on a similar attachment to the protocol.

Preparation
The following is to be completed by the sponsor or study director. Further instructions may be attached to the protocol. The sample will be prepared as follows:

Ratio of test article to extraction vehicle (select one):

___ Material thickness less than 0.5 mm - ratio of 120 cm^2:20 ml
___ Material thickness greater than or equal to 0.5 mm - ratio of 60 cm^2:20 ml
___ Irregularly shaped objects and/or sponsor option - ratio of 4 g:20 ml
X Other (explain): Fill Device Wet internal surface area = approx 41127 mm^2, Fluid volume = 170mL total (tubes and chambers)

dB 10/11 9-16-08

completed by sponsor dB 10/11 9-15-08

Test Article Preparation Instructions:
Refer to attached product labelling (file: ALT002-0082-200807232018.pdf). Open the air vent (item "E"). Open clamps C and D. Fill main chamber to approximately half way and close off clamps. With thumb and forefinger squeeze the pvc spike port (the small chamber to the right of label "G" in the diagram) until approximately almost full. Fluid will enter the chamber via the canula. Reopen the clamps and allow the fluid to flood the chamber. Close the vent(E). The item can now be exposed to the extraction conditions. To remove the extraction vehicle, open the air vent, and either puncture the diaphragm at the spike port (H), AND/OR the clamps opened and the device turned upside down, AND/OR the device may be punctured or otherwise destroyed or opened.

Extraction Vehicle (select all that apply):

X 0.9% sodium chloride USP solution (SC)
___ Alcohol in saline 1:20 solution (AS)
___ Polyethylene glycol 400 (PEG)*
___ Vegetable oil
___ Other (specify):_____

Extraction Conditions (select one):

___ 37°C, 72 hours
X 50°C, 72 hours
___ 70°C, 24 hours
___ 121°C, 1 hour
___ Other (specify):_____

NOTE: Due to the known pH of these vehicles, the pH of the test article extracts will not be determined.

*If PEG is used, the PEG test extract and control will be diluted with saline to provide 120 mg of PEG/ml.

Disposition of Test/Control Article (select one):

X Discard ___ Return unused article ___ Return unused and used article

completed by Sponsor dB 10/19-15-08

Special Laboratory Instructions:
No special instructions from Sponsor

Control Article
Controls (extraction vehicle without test material) will be prepared in the same way and at the same time as the test extracts.

3. Test System

Test System

Species:	Rabbit (*Oryctolagus cuniculus*)
Breed:	New Zealand White
Source:	Single USDA licensed supplier
Sex:	No particular gender is prescribed in this test
Body Weight Range:	2.0 kg or greater at selection
Age:	Young adults
Acclimation Period:	Minimum 5 days
Number of Animals:	Two per extract or pair of extracts
Identification Method:	Ear tag

Justification of Test System
The intracutaneous injection test in rabbits is specified in the current ISO testing standards and has been used historically to evaluate biomaterial extracts.

4. Animal Management

Husbandry:	Conditions will conform to Standard Operating Procedures that are based on the "Guide for the Care and Use of Laboratory Animals."
Food:	A commercially available rabbit feed will be provided daily.
Water:	Potable water will be provided *ad libitum* through species appropriate water containers or delivered through an automatic watering system.
Contaminants:	Reasonably expected contaminants in feed or water supplies should not have the potential to influence the outcome of this test.
Housing:	Animals will be individually housed in stainless steel suspended cages identified by a card indicating the lab number, animal number, test code, sex, and date dosed.
Environment:	The room temperature will be monitored daily. The recommended temperature range for the room is 61-72°F. The room humidity will be monitored daily. The humidity range for the room is 30-70%. The light cycle will be controlled using an automatic timer (12 hours light, 12 hours dark).
Accreditation:	NAMSA is an AAALAC International accredited facility and is registered with the United States Department of Agriculture. Additionally, NAMSA maintains an approved Animal Welfare Assurance on file with the National Institutes of Health, Office for Laboratory Animal Welfare.
Personnel:	Associates involved will be appropriately qualified and trained.
Selection:	Only healthy, thin-skinned animals free of mechanical irritation or trauma that could interfere with the test will be selected. To reduce the number of animals used for testing, and to comply with the directives of the NAMSA Institutional Animal Care and Use Committee (IACUC), rabbits on this study may have been used previously in an unrelated test model. Any previously evaluated test or control articles did not cause a response in the animals. Complete history of animal usage is traceable in laboratory records. Animals used for previous evaluations will be identified in the report.

Sedation, Analgesia or Anesthesia: It has been determined that the use of sedation, analgesia or anesthesia will not be necessary during the routine course of this procedure.

Veterinary Care: In the unlikely event that an animal should become injured, ill, or moribund, care will be conducted in accordance with current veterinary medical practice. If warranted for humane reasons, euthanasia will be conducted in accordance with the current report of the American Veterinary Medical Association's Panel on Euthanasia. The objective of the study will be given due consideration in any decision and the study sponsor will be advised.

IACUC: This protocol has been approved by NAMSA IACUC, and is reviewed at least annually by the same committees. Any significant changes to this protocol must be approved by the IACUC prior to conduct.

5. Method

Within a 4 to 18 hour period before treatment, each rabbit will be clipped free of fur from the back and both sides of the spinal column to yield a sufficient injection area. If necessary, swab the skin lightly with 35% IPA and allow to dry prior to injection. Due to concern with the crowding and subsequent obscuring of injection sites, the test and control sites will not be cranial and caudal on the same side of the back as defined in the ISO standards. A 0.2 ml dose of the appropriate test article extract will be injected by the intracutaneous route into five separate sites on the right side of the back of each rabbit. Similarly, the corresponding control will be injected on the left side of the back of each rabbit. No more than two test extracts and the corresponding controls will be injected into each animal. Injections will be about 2 cm apart. The appearance of the injection sites will be noted immediately after injection.

Observations for erythema and edema will be noted for each injection site at 24 , 48 and 72 hours after injection. Wipe the skin lightly with 35% IPA as necessary to facilitate scoring of the injection sites. Reactions will be scored on a 0 to 4 basis. Other adverse changes at the injection sites will also be noted. After the test is completed, all animals will be handled in accordance with IACUC approved NAMSA procedures. The reactions will be evaluated according to the subjective rating scale as shown below:

SCORE	ERYTHEMA (ER)	EDEMA (ED)
0	No erythema	No edema
1	Very slight erythema (barely perceptible)	Very slight edema (barely perceptible)
2	Well-defined erythema	Well-defined edema (edges of area well-defined by definite raising)
3	Moderate erythema	Moderate edema (raised approximately 1 mm)
4	Severe erythema (beet redness) to eschar formation preventing grading of erythema	Severe edema (raised more than 1 mm, and extending beyond exposure area)

6. Evaluation and Statistical Analysis

No statistical analysis of the data will be performed. Calculate the mean erythema and edema scores for the test and control extracts for each animal at each scoring interval. Separately total all mean erythema and edema scores for the test and control extracts and divide by 12 (2 animals x 3 grading periods x 2 grading categories) to determine the overall mean score for the test extract and corresponding control. Calculate the difference between the overall mean score of the test and corresponding control extracts by subtracting the overall mean score for the control from the overall mean score for the test extract.

The requirements of the test are met if the difference between the test extract mean score and corresponding control mean score is 1.0 or less. If the interval difference between test and control is greater than 1.0 at any interval, repeat the test in three additional animals. The requirements of the test are met if the difference between the test extract and the corresponding control mean score is 1.0 or less.

7. Report

The final report will include a description of the methods employed, individual dermal scores for each test and control injection site, and the assessment of the results.

8. Quality Assurance

Inspections will be conducted at intervals adequate to assure the integrity of the study in conformance with 21 CFR 58.35(b)(3). The final report will also be reviewed for conformance to Section 58.185, Subpart J, of the GLP Regulations. A Statement of Quality Assurance Activities will be provided with the final report.

9. Proposed Dates

The study dates will be finalized by the study director following receipt of the sponsor-approved protocol and appropriate material for the study. Initiation of the study will be the date on which the study director signs the GLP protocol. Projected dates for starting the study (first treatment) and for the completion of the study (final report release) will be provided to the sponsor (or representative of the sponsor).

10. Records

Test article and control preparation data, dates of relevant activities (such as the study initiation and completion), the appearance of each injection site immediately after injection, individual dermal scores at 24, 48, and 72 hours.

All raw data pertaining to this study and a copy of the final report will be retained in designated NAMSA archive files.

11. References

Code of Federal Regulations (CFR), Title 21, Part 58, Good Laboratory Practice for Nonclinical Laboratory Studies (2007).

Code of Federal Regulations (CFR), Title 9, Parts 1-199, Animal Welfare Act (2007).

Office of Laboratory Animal Welfare (OLAW), Public Health Service Policy on Humane Care and Use of Laboratory Animals.

Guide for the Care and Use of Laboratory Animals, Institute for Laboratory Animal Research, National Academy of Sciences (Washington: National Academy Press, 1996).

International Organization for Standardization (ISO) 10993-10, (2002) Biological Evaluation of Medical Devices - Part 10: Tests For Irritation And Delayed-Type Hypersensitivity (2002).

United States Pharmacopeia 30, National Formulary 25 (USP), General Chapter <88> Biological Reactivity Tests, In Vivo (2007).

12. Protocol Changes

Any necessary changes to the protocol after sponsor approval or study initiation will be documented and approved by the study director as protocol amendments. Copies will be distributed to the sponsor, the raw data file, and the NAMSA Quality Assurance department.

To 08T_48893_09

NAMSA™
Ensuring Medical Device Safety and Compliance™
2261 Tracy Road, Northwood, OH 43619-1397
419.666.9455

DATE 9-22-08 SUBJECT

MESSAGE

Test article preparation instructions state to fill device with 170 mL of fluid. Test article is unable to hold that amount of fluid and will be filled to capacity and documented appropriately.

SIGNED UMW1022 9-22-08

DATE OF REPLY

REPLY

SIGNED

THIS COPY FOR PERSON ADDRESSED

NAMSA

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September 17, 2008

Geoff Daly
Analytica Ltd
85 Brandl StreetEight Mile Plains
Brisbane, Queensland, 4113
Australia

PROTOCOL AMENDMENT I

Test Article: Analytica AutoStart 150mL Burette

Identification: Lot: 20080909

NAMSA Submission ID.: 08T_48893

We have received appropriate test article and approved protocol(s) for the program to be conducted in accordance with the Good Laboratory Practice (GLP) Regulations on the material described above. Below is a projected schedule for the work to be performed.

NAMSA Code	NAMSA Lab Number	Study	Estimated Start Date:	Estimated Report Release Date:
V0014_130	08T_48893_02	Cytotoxicity Study Using the ISO Elution Method - 1X MEM Extract	October 1, 2008	October 9, 2008
TI261_300	08T_48893_03	ISO Maximization Sensitization Study - Extract - 0.9% SC Extract	September 27, 2008	November 19, 2008
TI251_800	08T_48893_04	ISO Intracutaneous Study - Extract - 0.9% SC Extract	September 21, 2008	October 15, 2008
T0625_500	08T_48893_05	ISO Systemic Toxicity Study - Extract - 0.9% SC Extract	September 22, 2008	October 15, 2008
V0607_100	08T_48893_06	ASTM Hemolysis - CMF-PBS Extract	October 16, 2008	October 20, 2008

Jolee Bartrom, B.S.
Study Director

9-17-08
Date

cc: QA (NAMSA)
Sponsor

NAMSA

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October 8, 2008

Geoff Daly
Analytica Ltd
85 Brandl Street, Eight Mile Plains
Brisbane, Queensland, 4113
Australia

REVISED*
PROTOCOL AMENDMENT I

Test Article: Analytica AutoStart 150mL Burette

Identification: Lot: 20080909

NAMSA Submission ID.: 08T_48893

We have received appropriate test article and approved protocol(s) for the program to be conducted in accordance with the Good Laboratory Practice (GLP) Regulations on the material described above. Below is a projected schedule for the work to be performed.

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V0607_100	08T_48893_06	ASTM Hemolysis - CMF-PBS Extract	October 16, 2008	October 20, 2008

*This amendment has been revised to correct the sponsor's address.

Jolee Bartrom

Jolee Bartrom, B.S.
Study Director

10-8-08

Date

cc: QA (NAMSA)
Sponsor

NAMSA

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September 23, 2008

Geoff Daly
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85 Brandl StreetEight Mile Plains
Brisbane, Queensland, 4113
Australia

PROTOCOL AMENDMENT II

Test Article: Analytica AutoStart 150mL Burette

Identification: Lot: 20080909

NAMSA Submission ID.: 08T_48893

NAMSA Code	NAMSA Lab Number	Study
TI251_800	08T_48893_04	ISO Intracutaneous Study - Extract - 0.9% SC Extract

This amendment was written to provide additional instructions regarding the Test Article Preparation section of the study protocol:

- The test article is unable to hold 170 ml of fluid. The test article should be filled to capacity and the volume utilized should be recorded.

Reason for Change: The test article preparation section was incorrect.

Jolee Bartrom, B.S.
Study Director

9-23-08
Date

cc: QA (NAMSA)
Sponsor