TEST FACILITY

NAMSA
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419.666.9455

SPONSOR

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

STUDY TITLE

ISO Systemic Toxicity Study – Extract

TEST ARTICLE NAME

Analytica AutoStart 150mL Burette

TEST ARTICLE IDENTIFICATION

Lot: 20080909

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Summary

The test article, Analytica AutoStart 150mL Burette, Lot: 20080909, was evaluated for systemic toxicity in mice in accordance with the International Organization for Standardization 10993-11: Biological Evaluation of Medical Devices, Part 11: Tests for Systemic Toxicity. The test article was extracted in 0.9% sodium chloride USP solution. A single dose of the test article extract was injected into a group of five mice. Similarly, a separate group of five mice was dosed with the blank vehicle. The animals were observed for signs of systemic toxicity immediately after injection and at 4, 24, 48 and 72 hours after injection.

Under the conditions of this study, there was no mortality or evidence of systemic toxicity from the extracts. The test article extracts met the requirements of the study.

Study and Supervisory Personnel:

Molly F. Corvo, B.S.
Anthony J. Campagna, B.S.
Carrie A. Fetter
Shelli L. Petterle, A.A., B.A.
Natasha N. Norris, B.S.
Mark S. Werth
Laura A. Breitigan, B.S.
Don R. Pohl, B.S.
Colleen M. Stevenson, A.A.

Approved by:

Jolee Bartrom

Jolee Bartrom, B.S.
Study Director

10-15-08
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 10-15-08

Jolee Bartrom, B.S. Date

1. Introduction

Purpose
The test article identified below was extracted and the extract was evaluated to determine whether leachables extracted from the test article would cause systemic toxicity following injection into mice.

Testing Guidelines
The study was conducted based on the International Organization for Standardization 10993-11: Biological Evaluation of Medical Devices, Part 11: Tests for Systemic Toxicity.

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:	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:	Mouse (*Mus musculus*)
Strain:	Hla®: (ICR) CVF®
Source:	Hilltop Lab Animals, Inc.
Sex:	Male
Body Weight Range:	20 grams to 23 grams at injection
Age:	Approximately 4 weeks of age at injection
Acclimation Period:	Minimum 1 day
Number of Animals:	Ten
Identification Method:	Ear Punch

Justification of Test System
Mice have historically been used to evaluate biomaterial extracts. The use of albino mice injected with a single intravenous (IV) or intraperitoneal (IP) dose of test article extract or control blank is specified in the current ISO standard for evaluation of medical plastics.

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 rodent 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 housed in groups of five in stainless steel suspended cages or polycarbonate shoebox cages identified by a card indicating the lab number, animal numbers, test code, sex, animal code and date dosed.
Environment:	The animal housing room temperature and relative humidity was monitored daily. The recommended temperature range for the room was 64-79°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 animals 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

Prior to dosing, the mice were individually identified, weighed and arbitrarily assigned to a treatment group as shown below:

Extract	Treatment Group	Number of Animals	Sex	Dose	Route of Administration
SC	Test	5	Male	50 mL/kg	Intravenous
	Control	5	Male	50 mL/kg	Intravenous

A single dose of the test article extract was injected into the designated group of mice. The control blank was similarly injected into the separate group of designated control mice. Mice were observed for any adverse clinical reactions immediately after injection. The animals were then returned to their cages. The animals were observed for signs of systemic reactions at 4, 24, 48 and 72 hours after injection. The animals were weighed daily for three days after dosing. Any animal found dead was subjected to a gross necropsy of the viscera. After the test was completed, all animals were euthanized according to IACUC approved NAMSA procedure.

6. Evaluation and Statistical Analysis

Mean body weight data were summarized at each interval for each treatment group. If during the observation period, none of the mice treated with the test extract exhibited a significantly greater reaction than the control mice, the test article met the requirements. If two or more mice died, or if abnormal behavior such as convulsions or prostration occurred in two or more mice, or if body weight loss greater than 2 grams occurred in three or more mice, the test article did not meet the test requirements.

7. Results

Clinical Observations
All animals appeared clinically normal throughout the study. The clinical observations are presented in Table 1 in the appendix.

Mortality Rate Data
There was no mortality during the study. The mortality rate data are presented in Table 2 in the appendix.

Body Weight
Body weight data were acceptable and equivalent between the corresponding test and control treatment groups. Body weight data are presented in Table 3 in the appendix.

8. Conclusion

Under the conditions of this study, there was no mortality or evidence of systemic toxicity from the extracts. The test article extracts met the requirements of the study

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 retained in designated NAMSA archive files.

12. References

21 CFR 58 (GLP Regulations).

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) 10993-11, Biological Evaluation of Medical Devices – Part 11: Tests for Systemic Toxicity (2006).

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

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 - Systemic Toxicity Observations - SC Extract

Table 1: Clinical Observations

Extract	Treatment Group	Animal Number	Observation				
			Immediate	4 Hours	24 Hours	48 Hours	72 Hours
SC	Test Extract	6	Appeared Normal	Appeared Normal	Appeared Normal	Appeared Normal	Appeared Normal
		7	Appeared Normal	Appeared Normal	Appeared Normal	Appeared Normal	Appeared Normal
		8	Appeared Normal	Appeared Normal	Appeared Normal	Appeared Normal	Appeared Normal
		9	Appeared Normal	Appeared Normal	Appeared Normal	Appeared Normal	Appeared Normal
		10	Appeared Normal	Appeared Normal	Appeared Normal	Appeared Normal	Appeared Normal
	Control Extract	1	Appeared Normal	Appeared Normal	Appeared Normal	Appeared Normal	Appeared Normal
		2	Appeared Normal	Appeared Normal	Appeared Normal	Appeared Normal	Appeared Normal
		3	Appeared Normal	Appeared Normal	Appeared Normal	Appeared Normal	Appeared Normal
		4	Appeared Normal	Appeared Normal	Appeared Normal	Appeared Normal	Appeared Normal
		5	Appeared Normal	Appeared Normal	Appeared Normal	Appeared Normal	Appeared Normal

Table 2: Mortality Rate Data

Extract	Treatment Group	Number Dead/Number Tested
SC	Test Extract	0/5
	Control Blank	0/5

Table 3: Body Weight Data

Extract	Treatment Group	Animal Number	Weight (g)			
			Day 0	Day 1	Day 2	Day 3
SC	Test Extract	6	23	23	23	24
		7	23	24	24	25
		8	20	21	22	23
		9	22	21	22	23
		10	23	24	25	26
	Control Blank	1	21	22	22	23
		2	21	22	22	22
		3	23	24	24	25
		4	22	22	23	24
		5	23	23	23	23

Appendix 2 – Composition

NAMSA

GLP SAMPLE SUBMISSION FORM

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*Annotates a required field

08T-48893

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 — DATE 9 Sept 2008.

NAMSA STUDY DIRECTOR — DATE 9-15-08

REV091107

Statement of Quality Assurance Activities

Phase Inspected	Auditor	Date
Body Weight/ Observations	L. M. Byrd	September 26, 2008
Study Data Review	S. M. Pellitieri	October 2, 2008
Final Report Review	K. J. Evener	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: Karen J. Evener — 10-15-08

Karen J. Evener, B.E.
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***	
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COUNTRY*	
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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 JBOll on 9-15-08
JBOll 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 JBOll 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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UM 9.15.08

NAMSA

PEOPLE SCIENCE SOLUTIONS

*Annotates a required field

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08T-48093

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 Systemic Toxicity 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 acute systemic toxicity of leachables extracted from the test article following a single intravenous or intraperitoneal injection in mice. This study will be conducted in accordance with the method recommended by the International Organization for Standardization (ISO) 10993: Biological evaluation of medical devices, Part 11: Tests for systemic toxicity.

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)

completed by Biott dB1011 9-15-08 per sponsor dB1011 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)*
X Vegetable oil completed by dB1011 per sponsor on 9-15-08
___ Other (specify): ___ dB1011 9-15-08

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 reagent control will be diluted with saline to obtain 200 mg of PEG/ml.

① Not applicable dB1011 9-15-08

Disposition of Test Article (select one):

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

completed by Sponsor dB 9/1 9-15-08

Special Laboratory Instructions:

No special instructions from Sponsor

Control Article

Blank 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:	Mouse (*Mus musculus*)
Strain:	Outbred albino
Source:	NAMSA approved supplier
Sex:	No particular gender is prescribed for this test
Body Weight Range:	17-23 grams at injection
Age:	No particular age is prescribed for this test
Acclimation Period:	Minimum 1 day
Number of Animals:	Five per extract and control
Identification Method:	Ear punch

Justification of Test System

Mice have historically been used to evaluate biomaterial extracts. The use of albino mice injected with a single intravenous (IV) or intraperitoneal (IP) dose of test article extract or control blank have been suggested by ISO for evaluation of medical plastics.

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 rodent 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 housed in groups of five in stainless steel suspended cages or polycarbonate shoebox cages identified by a card indicating the lab number, animal numbers, test code, sex, animal code and date injected.
Environment:	The room temperature will be monitored daily. The recommended temperature range for the room is 64-79°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, previously unused animals will be selected.

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 Institutional Animal Care and Use Committees (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

Prior to dosing, the mice will be identified and weighed. Five animals will each be injected with the appropriate test extract at a dose of 50 ml/kg (SC, AS, vegetable oil) or 10 g/kg (PEG). Five mice will be similarly injected with the corresponding extraction vehicles. The SC and AS will be injected intravenously via the lateral tail vein while the PEG and vegetable oil will be injected intraperitoneally.

Mice will be observed for adverse reactions immediately after dosing, and at 4, 24, 48 and 72 hours after injection. The animals will be weighed daily for three days after dosing. Any animal found dead will be subjected to a gross necropsy of the viscera. After the test is completed, all animals will be handled in accordance with IACUC approved NAMSA procedures.

6. Evaluation and Statistical Analysis

No statistical analysis of the data will be performed. If during the observation period none of the mice treated with the test extract show a significantly greater reaction than the corresponding control mice, then the test sample meets the test requirements. If two or more mice die, or if abnormal behavior such as convulsions or prostration occurs in two or more mice, or if body weight loss greater than 2 grams occurs in three or more mice, the test sample does not meet the test requirements.

If any mice treated with the test extract show only slight signs of toxicity and not more than one mouse shows gross signs of toxicity or dies, a ten mouse retest may be required. If all ten mice treated with the test extract on the repeat test show no significant reaction greater than the ten control mice, then the test sample meets the current test requirements.

7. Report

The final report will include a description of the methods employed, individual body weights, and any observations.

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 preparation, dates of relevant activities (such as the study initiation and completion), initial and final body weights, and observations will be recorded.

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

11. References

21 CFR 58 (GLP Regulations).

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

ISO 10993-11 (2006) Biological evaluation of medical devices – Part 11: Tests for systemic toxicity.

OLAW, Public Health Service Policy on Humane Care and Use of Laboratory Animals (NIH Publication).

12. Protocol Changes

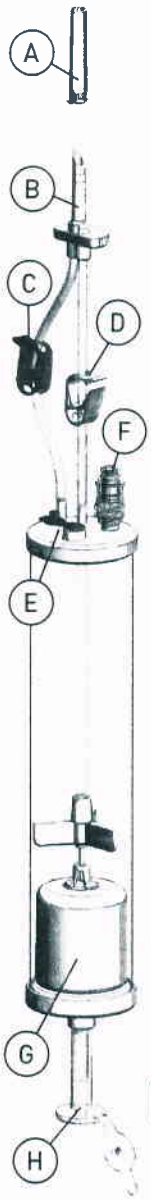
Any necessary changes to the protocol after sponsor approval or study initiation will be documented and approved by the study director as protocol amendments. Copies will be distributed to the sponsor, the raw data file, and the NAMSA Quality Assurance department.

OPEN

ANALYTICA

AutoStart®

STERILE SINGLE-USE 150 mL BURETTE



Setting Up

1. Close the WHITE On/Off clamp (D), and BLUE bypass clamp (C).

2. Open filtered vent (E). NOTE: This vent should be left open during normal use.

3. Remove the spike cap (A)

4. Puncture solution container with spike (B).

5. Open WHITE on/off clamp (D). Fluid will begin to fill the chamber and will be stopped by the float (G).

6. Open the spike port cap (H).

7. Connect an infusion line to the spike port (H).

8. Prime the system according to the infusion line instructions.

• The device is now ready for use.

Medication Delivery

1. Open and shut the BLUE bypass Clamp (C) to fill the Burette with infusion fluid.

2. Add medication via injection site (F) as per hospital protcol.

• The Autostart float (G) will automatically return the device to continuous infusion mode once the medication has been delivered.

⚠ Important Notes

• The float (G) shuts off flow once the fluid reservoir is empty. This shutoff is not for long-term use.

• Replace device every 24 hours or per hospital protocol.

• Sterile whilst packaging intact. Do not use if packaging is damaged or if protective caps are not in place.

• Gravity feed only.

• Use aseptic technique.

• WARNING: Air in infusion line may cause embolism

STERILE EO

NON-PYROGENIC
NON-TOXIC
LATEX FREE

CE 0123

Manufacturer: Zhejiang Lingyang Medical Apparatus Co. Ltd. Baishuiyang, Linhai City Province CHINA www.ly-medical.com LY

TGA Sponsor. Analytica Ltd. 85 Brandl St. Eight Mile Plains, Brisbane, 4113 AUSTRALIA www.**AutoStartBurette**.com

ALT002-0082-v1

REF 0080

LOT

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September 17, 2008

Geoff Daly
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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

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REVISED*
PROTOCOL AMENDMENT I

Test Article: Analytica AutoStart 150mL Burette

Identification: Lot: 20080909

NAMSA Submission ID.: 08T_48893

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*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