CiToxLAB
Safety and Health Research Laboratories

TOXICOLOGY SERVICES

General toxicology:
- Rodents
- Non-rodents: dogs, NHPs and minipigs

Infusion
Inhalation
Dermal
Ocular
Immunotoxicology
Reproductive toxicology **including minipigs and NHPs**
Carcinogenicity studies **also in rasH2 and *p53+/-* mice**
Genetic toxicology: **ICH compliant package**
In vitro toxicology: **BCOP, MUSST, DPRA, Photo 3T3, Episkin™**
Agrochemical / Chemical / REACH
QSAR
Physical chemistry
Ecotoxicology: **wide range of test species**

SAFETY PHARMACOLOGY

CV telemetry / ECG / BP
Jacketed External Telemetry (JET) / ECG / BP
Respiratory / plethysmography / JET telemetry
CNS / EEG
Early safety pharmacology

DMPK AND BIOMARKERS

Radiolabelled DMPK: **in all species**
Bioanalysis LC-MS/MS, GC-MS/MS, LC-ICP/MS, ELISA, RIA
Toxicogenomics, miRNA: **Affymetrix™ / Accredited service provider**
Immunology: **10-color flow cytometer, Luminex, Mesoscale**

SPECIALIZED EXPERTISES

Juvenile studies **including minipigs**
Fertility studies **in rodents and NHPs**
Radiation safety and efficacy studies
Tissue Cross Reactivity: **human and animal tissue banks**
Gene therapy vector biodistribution **via qPCR**
ES cell testing: **devTOX™ and cardioTOX™** (with Stemina)
Lead optimization and predictive toxicology services: **Leadscreen™**

CiToxLAB GROUP COMPANIES

CiToxLAB in France
+33 (0)2 32 29 26 26
contact.france@citoxlab.com
B.P. 563 - 27005 Evreux Cedex, France

CiToxLAB in North-America
+1 888 353 2240
contact.northamerica@citoxlab.com
445, Armand-Frappier Blvd,
Laval, Quebec, H7V 4B3, Canada

CiToxLAB in Denmark
+45 56 86 15 00
contact.scantox@citoxlab.com
Hestehavevej 36A, Ejby,
DK-4623 Lille Skensved, Denmark

CiToxLAB in Hungary
+ 36 88 545-300
contact.hungary@citoxlab.com
Veszprém, Szabadságpuszta,
8200, Hungary

Atlanbio
+33 (0)2 51 10 01 00
atlanbio@atlanbio.com
www.atlanbio.com
1 Rue Graham Bell - Z.I de Brais
B.P 40309,
44605 Saint Nazaire Cedex, France

ALSO REPRESENTED BY

Media Services Ltd
+81 3 3666 9915
citoxlab@mediaservices-jp.com
Fuji 16 Bldg 7F
1-11-2 Nihonbashi Kayabacho,
Chuo-ku, Tokyo 103-0025, Japan

Croen Research Inc.
+82 31 888 9390
customerservice@croen.co.kr
Advanced Institutes of Convergence
Technology - B-6th Fl., 864-1, lui-dong,
Yeongtong-gu, Suwon-si - Gyeonggi-do,
443-270, Korea

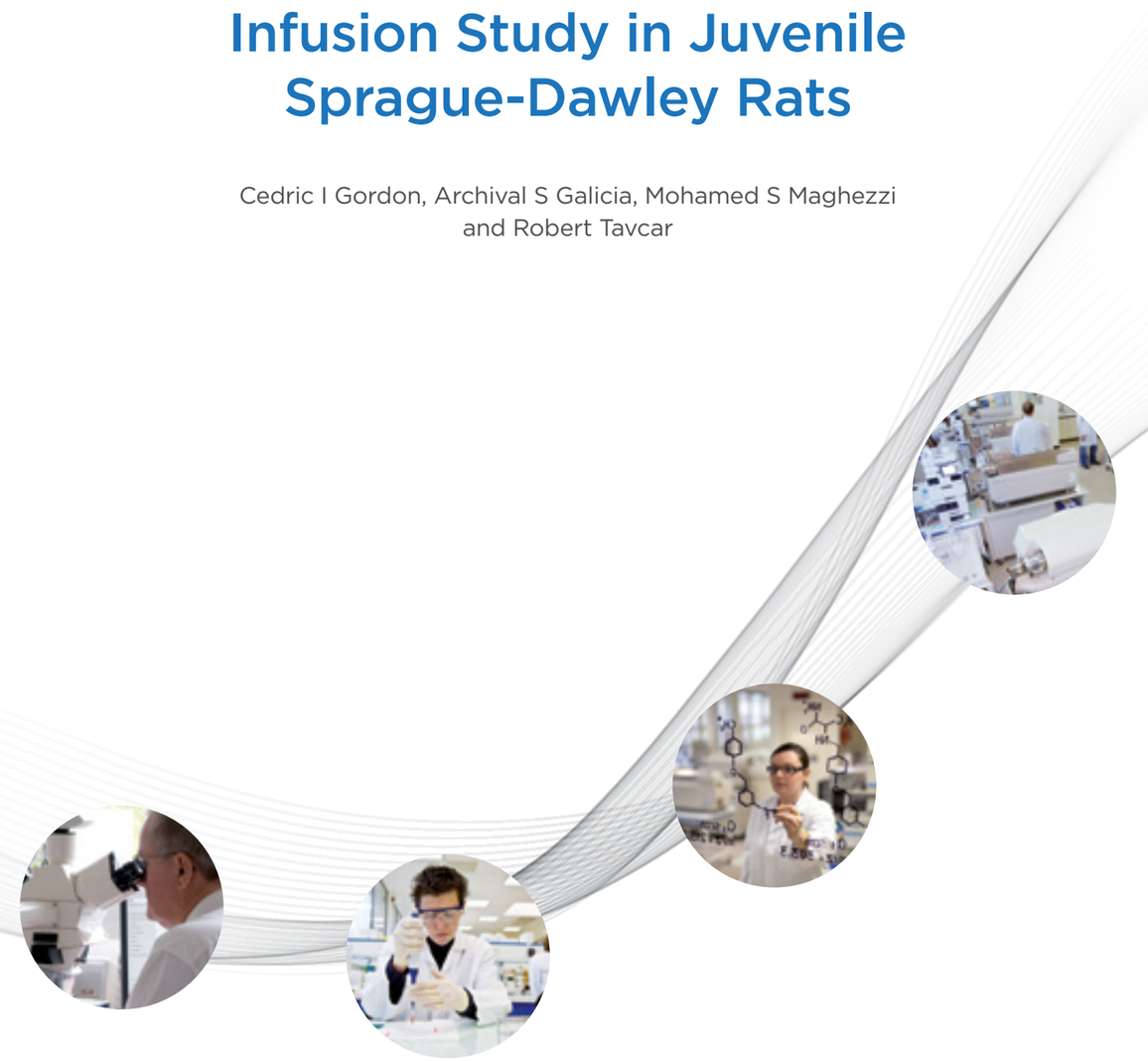
PARTNER COMPANY

Stemina
+1 608 204 0104
info@stemina.com
www.stemina.com
504 South Rosa Road,
Suite 150 Madison,
Wisconsin 53719, USA

CiToxLAB
Safety and Health Research Laboratories

A Qualification Intravenous Infusion Study in Juvenile Sprague-Dawley Rats

Cedric I Gordon, Archival S Galicia, Mohamed S Maghezzi and Robert Tavcar



aaalac INTERNATIONAL
GLP CERTIFIED
atlanbio BIOANALYSIS EXPERTISE
Stemina

www.citoxlab.com

A Qualification Intravenous Infusion Study in Juvenile Sprague-Dawley Rats

Cedric I Gordon, Archival S Galicia, Mohamed S Maghezzi and Robert Tavcar

CiToxLAB North America, 445 Armand-Frappier Blvd. Laval, (Quebec), Canada, H7V 4B3

INTRODUCTION AND OBJECTIVE

The ability to administer drugs intravenously to neonatal rats is critical for the assessment of non-clinical development of many pharmaceuticals. The objective of this study was to qualify procedures for continuous intravenous infusion of saline via a surgically implanted catheter following surgical procedures to neonatal Sprague Dawley rats starting on Day 21 post partum for 35 days (to day 57 *post partum*).

METHODS

Rat pups were 13-15 days at arrival and 21 days old at the start of treatment. Body weights ranged from 53.9 to 71.6g for males and 51.6 to 71.7g for females at the start of treatment. Dose levels of any anesthetics, antibiotics, analgesics and other such study plan-mandated treatments employed in the surgical preparation of the animals were in accordance with the facility's standard operating procedures. Weanling rat pups underwent surgery on Day 21 post partum (PPD21) and a medical grade catheter was surgically implanted so the tip of the catheter was located in the vena cava at approximately the level of the kidneys. The catheter was secured in place and exteriorized at the nape of the neck through a subcutaneous tunnel from the inguinal area to the dorso-cervical area.

Following recovery from surgery, the animals were placed into 2 groups of 10 animals per/sex with a third (non-operated) group consisting of 5 animals/sex were used as controls. Animals received 0.9% saline at a rate of 0.2 or 0.4 mL/hour via an infusion pump. Body weights and food consumption were recorded weekly throughout the period, until necropsy. Blood samples were collected for clinical pathology (hematology, clinical chemistry and coagulation) at necropsy and the animals were given a gross and microscopic examination.

RESULTS

Body weights were significantly reduced from PPD 28 to 56 for males dosed at 0.2 and 0.4 mL/hr and for females from PPD 35 to 42, with marked reduction at days 49 and 56 in comparison to the animals that did not undergo surgical procedures (control). Body weights for females dosed at 0.4 mL/hr were lower than those dosed at 0.2 mL/hr from PPD 35 to 56.

Food consumption was reduced for males and females at 0.2 and 0.4 mL/hr throughout the dosing period.

There was a decrease in mean platelet and PCT values at 0.2 and 0.4 mL/hr for females that attained statistical significance and increases of red cell distribution count and hemoglobin distribution width for both 0.2 and 0.4 mL/hr that were statistically significant for either or both dose rates for females. There was a significant increase in activated partial thromboplastin time for females at 0.2 and 0.4 mL/hr in comparison to the controls that was not observed in male animals. Urea increased for males and females at 0.2 and 0.4 mL/hr and total protein and albumin decrease for males and/or females at 0.2 and 0.4 mL/hr in comparison to the controls.

CONCLUSION

The qualification of the surgical procedures at weaning and the daily administration of saline at dose rates of 0.2 or 0.4 mL/hr by continuous intravenous (IV) infusion via a surgically implanted catheter in male and female Sprague-Dawley rats starting from Day 21 to 57 post partum when compared to animals of similar age with no surgical procedures was acceptable and proven viable.

ACKNOWLEDGEMENT

The authors would like to acknowledge the help of Sonia Laframboise, Julius Haruna and all participating staff especially Johanne Cadieux and the report and production group.

Figure 1

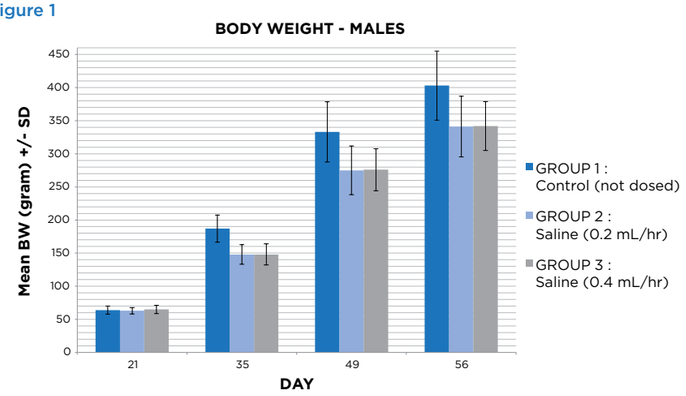


Figure 2

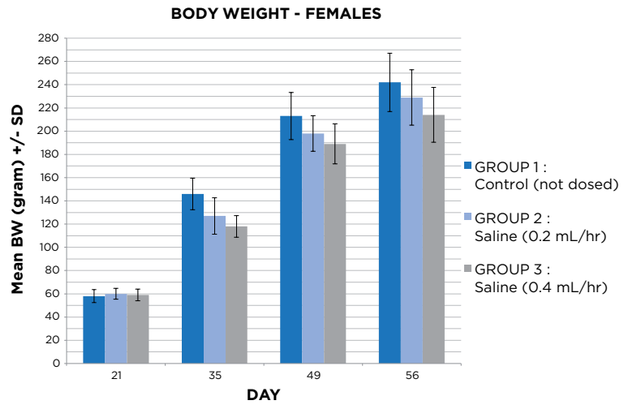


Figure 3

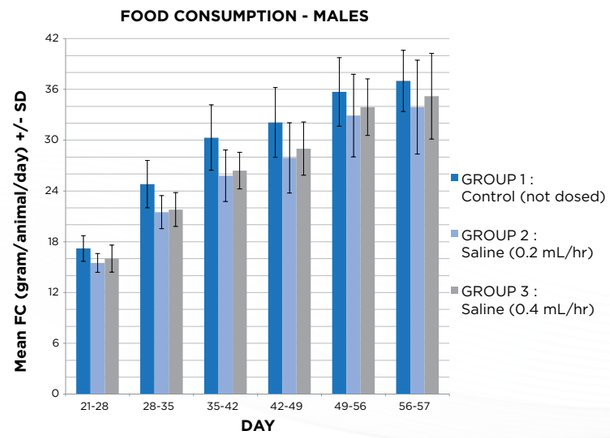


Figure 4

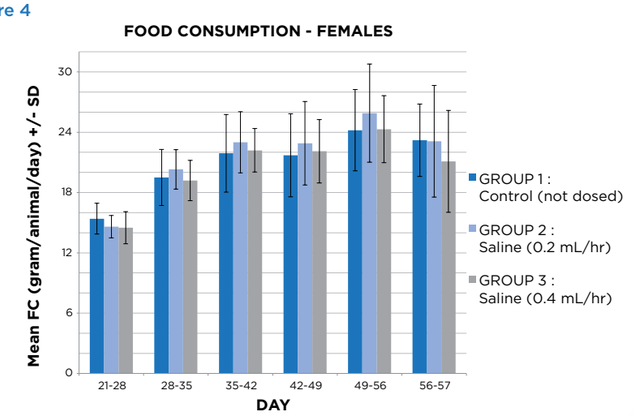


Figure 5

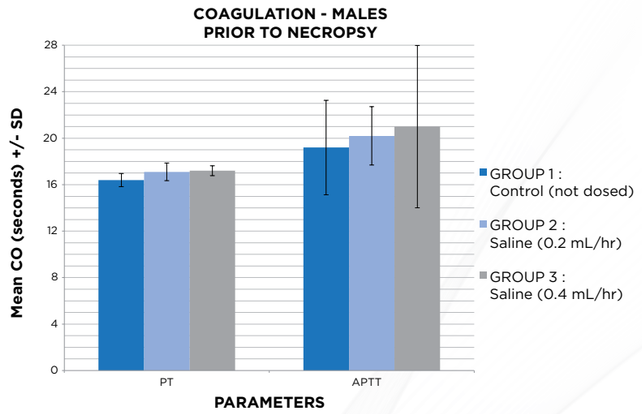


Figure 6