FINAL REPORT

FY20-110

IACUC # FY20-117I
Proposal # 2020-432
Test Article: L0880

Efficacy of Calcium Glycerophosphate (CGP) against SARS-CoV-2 in a Syrian hamster model

Sponsor:

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Pleasantville, NJ 08232

Test Facility:

Lovelace Biomedical
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Courier Address and Location of Laboratory:
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Study Initiation: 30Nov2020 **Study In-Life Completion:** 05Dec2020

STUDY DIRECTOR SIGNATURE

Study Director

08 Mar 2021

Date

EXECUTIVE SUMMARY

The purpose of this study was to test the efficacy of calcium glycerophosphate (CGP) as a therapeutic agent against SARS-CoV2 in a Syrian hamster model. CGP was dosed by intranasal administration (IN) twice daily starting one day prior to viral inoculation (Day -1) until one day prior to terminal procedures (Day 4). Viral inoculation consisted of dosing animals intranasally (IN) with $8x10^4$ $TCID_{50}$ in 200 µL on Day 0. A control group received the same treatments, with sterile water replacing CGP. Thirty-two (32) animals were included in each of the two groups and all animals were euthanized for terminal endpoints on Day 5.

In-life data collection and metrics of efficacy included twice daily observations, daily body weights, and nasal swabs for detection of both genomic and subgenomic viral RNA by RT-qPCR on Day 1, 3, and 5 post-infection. Terminal collections to gauge efficacy included lung weights, reported as a percent of body weight, and pulmonary tissue collection for detection of genomic and subgenomic RNA by RT-qPCR. Pulmonary tissue was also collected and stored for potential future live virus quantification (i.e. $TCID_{50}$). Lung tissue and nasal tissue were also fixed in 10% neutral buffered formalin and stored for potential future analysis by histopathology. $TCID_{50}$ assays and histopathology are not included in this analysis and report.

Twice daily observations: Three animals in the control group, Group 1, had observations of a hunched posture or slow movement post viral inoculation. No Group 2 animals had clinical observation calls.

Body Weight: Animals in both groups lost slightly more than 15% body weight. There was no significant difference between groups.

Nasal Swab RT-qPCR: There was no difference in amplification of genomic RNA from nasal swabs between groups on any of the days of collection. There was a slight decrease in subgenomic RNA in Group 2 CGP treatment) compared to Group 1 (water control) on Days 3 and 5. This difference was significant on Day 3.

Lung Weight: Lung weights in both groups, expressed as a percent of body weight, suggested moderate to severe inflammation. There was a slight, but significant increase in lung weights of CPG-treated animals when compared to controls.

Pulmonary tissue RT-qPCR: Genomic and subgenomic RNA levels in the lungs of both groups were similar.

Overall, CGP administered IN twice daily did not appear to offer substantial advantages over water dosed in the same way. CGP may have slightly increased pulmonary inflammation as evidenced by an increase in lung weight in these animals when compared to controls. While there was no evidence that CGP administration positively affected the lungs or the animals systemically, there may have been a local effect in the nasal cavity as evidenced by reduction in subgenomic viral RNA at Days 3 and 5. Subgenomic RNA is thought to represent a subset of viral RNA that is more representative of replicating virus as opposed to non-replicating virus or virus that was administered at inoculation. Data here may suggest that CGP could have a slight, local, viral replication inhibitory effect where it was administered, the nasal cavity.

It is important to point out that we dosed animals in this study at $8x10^4$ $TCID_{50}$/animal. This dose level is consistent with other studies that Lovelace has run to date (n=20+), and with what others are publishing. This dose was purposeful, as it has been an appropriate inoculation to cause clinical disease, multiple measurable outcomes both in life and at terminal, and has proven to be reliable in showing statistically significant differences in control and treatment groups when the test article shows efficacy against SARS-CoV-2. However, this dose is likely several orders of magnitude higher than what a hamster, or human, would pick up as an environmental infection. It is likely that this "supraphysiological" infectious dose may be a very harsh hit on the hamster from day of inoculation. Such a harsh hit may mask the effects of any test article that has subtler efficacy against SARS-CoV-2 infection and COVID19 symptoms. A test article with "subtle efficacy" may still be beneficial as a prophylaxis or treatment against SARS-CoV-2, but not show this efficacy in a model such as the one run here. Moving forward, CGP may be a good candidate to test in a SARS-CoV-2 model where animals are infected with a viral inoculum more similar to what may be expected to be picked up from the environment, which may be around 100-1000$TCID_{50}$/animal.

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LIST OF ACRONYMS/ABBREVIATIONS

AAALAC	Association for Assessment and Accreditation of Laboratory Animal Care
AMS	Animal Management System
AVE	Average
BID	Twice Daily
BSC	Biosafety Cabinet
BSL3	Biosafety Level 3
C	Celcius
CGP	Calcium Glycerophosphate
CFR	Code of Federal Regulations
CRL	Charles River Laboratories
FDA	Food and Drug Administration
g	Gram
GLP	Good Laboratory Practice
IACUC	Institutional Animal Care and Use Committee
IM	Intramuscular
IN	Intranasal
IP	Intraperitoneal
IU	International Unit
L	Liter
LBRI	Lovelace Biomedical Research Institute
mg	milligram
mL	milliliter
µL	microliter
mm	millimeter
N	Animal Number
N gene	Nucleocapsid Phosphoprotein Gene
NIH	National Institute of Health
n/a	Not Applicable
PBS	Phosphate Buffered Saline
PO	Oral Gavage
RT-qPCR	Real-time quantitative polymerase chain reaction
SD	Standard Deviation
SOPs	Standard Operation Procedures
TA	Test Article
$TCID_{50}$	Median Tissue Culture Infectious Dose
UTMB	University of Texas Medical Branch

1 OBJECTIVE

The objective of this study was to test calcium glycerophosphate (CGP) as a therapeutic against SARS-CoV-2 in a Syrian hamster model. To do this, CGP was administered to the nasal cavity of hamsters up to twice daily, starting at one day prior to viral inoculation (i.e. Day -1) and continuing until animal sacrifice (i.e. Day 5). Clinical observations and viral burden, in comparison with a control group, was used to determine the metrics of test article (TA) efficacy.

2 COMPLIANCE

This study was not conducted in accordance with 21 CFR Part 58 (Good Laboratory Practices for Non-Clinical Laboratory Studies) and is not intended to fulfill formal regulatory requirements consistent with Investigational New Drug Applications or other FDA regulatory submissions. However, the principles of the regulations were followed including documentation and protocol and SOP adherence.

This study complies with all applicable sections of the Final Rules of the Animal Welfare Act regulations (9 CFR Parts 1, 2, and 3), as well as the *Guide for the Care and Use of Laboratory Animals* (2011). Lovelace Biomedical is fully accredited by the Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC).

3 KEY PERSONNEL

Study Director and Veterinary Support:	Adam Werts, DVM, PhD, DACLAM Email: awerts@lovelacebiomedical.org Phone: 505-348-9668
Attending Veterinarian:	Meghan Vermillion, DVM, PhD, DACLAM Email: mvermillion@lovelacebiomedical.org Phone: 505-348-9749
Contributing Scientist - Microbiology/PCR:	Bryan Gullick, PhD Email: bgullick@lovelacebiomedical.org Phone: 505-348-8522
Contributing Scientist-Virology:	Ariel Arndt, PhD Email: aarndt@lovelacebiomedical.org
Sponsor Representatives:	Alan E. Kligerman, CEO, AkPharma Inc. Email: akligerman@akpharma.com Phone: 609/645-5100 x101

4 MATERIALS AND METHODS

4.1 Challenge Agent

Identity:	SARS-CoV-2
Description	SARS-CoV-2, isolate USA-WA1/2020
Supplier/ Manufacturer :	Isolate sourced from BEI Resources and propagated in Vero E6 African Green Monkey kidney cells (BEI, catalog #N596) at the University of Texas Medical Branch (UTMB).
Lot :	TVP23156 WA1/2020 E6_P1 03Sep2020; stock titer of 5.51E+06 TCID50/mL
Storage Conditions:	Virus was stored in a biosafety level 3 (BSL3) compliant facility. Viral stocks were stored at -80ºC ±10ºC.

4.2 Test Article

All Test Articles (TA) and Sponsor-supplied vehicles were characterized by the Sponsor or designee. The Sponsor ensured that documentation on the identity (suppler/manufacturer), batch number and/or lot number, uniformity, and stability for the test articles are provided for inclusion in the Final Report.

Identity:	Calcium Glycerophosphate (CGP)
Description:	A generally recognized as safe (GRAS) food ingredient and nutrient supplement; A non-selective phosphatase inhibitor that has been shown to prevent cytokine-induced loss of epithelial integrity in cultured cells.
Supplier/Manufacturer:	Givaudan-Lavirotte, 58 Rue Paul Cazeneuve, 69008 Lyon, France
Lot :	1900002518; Sample No. 15799 (Avantis Distr.)
Storage Conditions:	Dry, cool, room temperature, no sunlight

4.3 Diluent and Control Article

Identity:	Sterile distilled water

4.4 Test System

Species Strain:	Hamster, Syrian (*Mesocricetus auratus*)
Age of Animals:	6-8 weeks
Weight of Animals:	Weight at randomization: 113.3-140.9g
Number on Study/Sex:	Males. 64 on study, 6 spares. 70 total.

Unused spares were conveyed to another institutional animal care and use committee (IACUC)-approved protocol on or after Study Day 0 (challenge day).

Source: Charles River Laboratories (CRL).

4.5 Experimental Design and Execution

Complete details are included in in the study protocol (Appendix A). In brief, after the quarantine period and prior to treatment initiation, all hamsters were randomly assigned to treatment groups per the study design below.

Table 1. Experimental Design

Group	Group Description[1]	Number of Animals	Inoculation (Day 0)	Clinical Readouts	Endpoints and readouts
1	Control (Distilled Water) Dosed 2x daily starting at Day -1	32	200ul of virus diluted to 4E+05TCID$_{50}$/mL	Starting at Day -3: Daily body weights; twice daily observations; nasal swabs for RT-qPCR on Day 1, 3, and 5.	Viral burden on lung. One genomic RT-qPCR and subgenomic RT-qPCR per animal. Tissue collected and stored for potential virology assessment. Fixing and holding right lungs and skulls for potential future histopathology
2	CGP Dosed 2x daily starting at Day -1	32			

[1]Dosing was intranasal (IN) and occur twice daily from Day -1 through Day 4. On the day of inoculation (Day 0), viral inoculation occurred in the a.m. instead of TA dosing.

5 RESULTS

5.1 Compliance

The approved study protocol, amendments, and a single memo are shown in Appendix A. There were no deviations on study. The single memo covered pH adjustments to the TA and is summarized as follows: A 3.75% CGP suspension was made by adding 4.5g of CGP to 115.5mL of sterile water. pH of this suspension when fully mixed read 11.27, much higher than expected based on communication with the sponsor. To bring the pH down to a physiologically compatible range, ~8-10 drops of 10N HCl was added. The resulting pH was 7.34. This solution was used on study.

5.2 Animal Husbandry and Environmental Conditions

Complete details are included in the study folder. Environmental conditions, monitored through the duration of the study, were within the windows described in the study protocol.

5.3 Challenge Formulation and Administration

Challenge material was prepared from frozen stocks. Challenge material was used within 4 hours of preparation. One aliquot of the prepared challenge material was withheld for future titer

verification by $TCID_{50}$. $TCID_{50}$ assays are currently under optimization and have not been run on this study. Once optimization is complete, challenge material samples will be run following the most recent version of SOP BSF-1907 *Determination of Median Tissue Culture Infectious Dose ($TCID_{50}$) for Viral Samples.*

5.4 Intranasal Instillation (Virus)

Animals were anaesthetized with ketamine and xylazine per SOP ACS-0423, Small Animal Anesthesia, and instillations were performed in accordance with SOP TXP-0559 Respiratory Instillation in Rodents for this procedure. Animals had the challenge agent delivered via IN instillation at a volume of 100 µL/naris, 200 µL/animal.

5.5 Intranasal dosing of TA

Intranasal (IN) dosing followed SOP TXP-0559 Respiratory Instillation in Rodents. Dosing occurred 2x daily from Day -1 through Day 4, with the exception of only one dose on Day 0. See Table 1. Briefly, CGP was made up at 3.75% in sterile distilled water, and animals were dosed at 150µL per animal, split between each naris at 75µL/naris. Dosing was recorded in the study files.

5.6 Clinical Observations and Survival

Detailed observations were performed twice a day (a.m. and p.m.), with special attention to normal behavior per SOP TXP-1532, Pharmacologic and Toxicologic Observations of Experimental Animals starting 3 days prior to the day of challenge (i.e. Day -3) and continuing until the end of the study. Only minor clinical observations were noted, in Group 1 (i.e. 1027 hunched starting at day 1, 1030 hunched starting at day 3, 1012 slow starting at day 4), and no clinical observations were noted in Group 2. Full observations are included in Appendix C. All animals survived until scheduled euthanasia.

5.7 Bodyweights

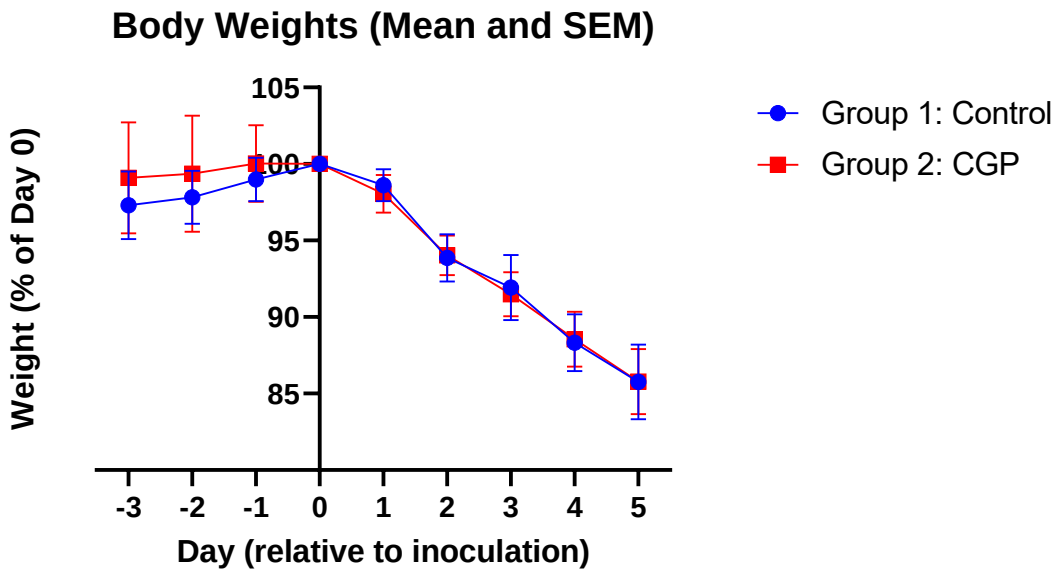
A pre-study weight of all animals was collected for randomization. The animals were also weighed once daily in the a.m. beginning on Study Day -3 and continuing until the end of the study. Weights were acquired following SOP TXP-1924, Procedure for Recording Temperatures and Weighing Animals and Tissues in the Provantis System. Average group body weights are shown in Table 2 and Figure 1.

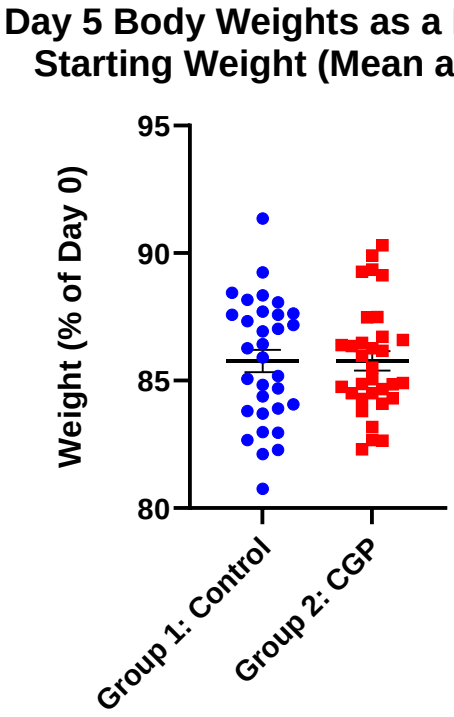
Individual body weights are included in Appendix D.

Table 2. Bodyweight Summary

	Group:	1	2
Day -5	**Ave**	127.28	127.42
	SD	*7.23*	*7.13*
Day -3	**Ave**	127.61	127.94
	SD	*7.21*	*7.10*
Day -2	**Ave**	128.31	128.29
	SD	*7.36*	*7.39*
Day -1	**Ave**	129.84	129.20
	SD	*7.50*	*7.52*
Day 0	**Ave**	131.7	129.20
	SD	*8.05*	*7.46*
Day 1	**Ave**	129.39	126.70
	SD	*7.89*	*7.76*
Day 2	**Ave**	157.88	121.50
	SD	*196.67*	*7.64*
Day 3	**Ave**	120.62	118.23
	SD	7.89	7.49
Day 4	**Ave**	115.90	114.41
	SD	7.50	7.28
Day 5	**Ave**	112.46	119.93
	SD	*19.92*	*7.25*

Figure 1. Hamster Change in Bodyweight





	Group 1: Control	Group 2: CGP
Number of values	32	32
Minimum	80.75	82.30
Maximum	91.36	90.31
Range	10.61	8.008
Mean	85.77	85.78
Std. Deviation	2.443	2.131
Std. Error of Mean	0.4319	0.3767

On average, animals in each group lost slightly over 14% body weight by 5 days post-inoculation. There was no significant difference between groups that received CPG or water control.

5.8 Euthanasia and Necropsy

At scheduled euthanasia, animals were euthanized by intraperitoneal injection of an overdose of a barbiturate-based sedative following SOP ACS-0334, Euthanasia of Small Animals.

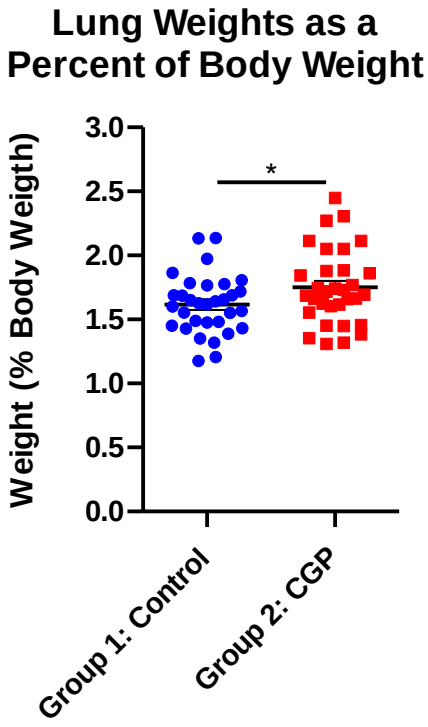
Scheduled necropsies included a terminal bodyweight, whole lung weight, sample collection and processing. Gross necropsy observations of the lung were recorded in Provantis using consistent descriptive terminology to document location(s), size, shape, color, consistency, and number of any lesions and are reported in Table 3. Overall, gross pathology calls between lungs were similar.

Table 3. Gross Pathology Call on Lungs

Percent lung discolored, red	Group 1	Group 2
0%; normal	1	3
1-25%	2	0
26-50%	5	4
51-75%	23	17
76-100%	1	8

Weights of lungs were also recorded at necropsy. In general, a healthy, uninfected Syrian hamster should have lung weights of approximately 0.45-0.6% of body weight. An increase in lung weight as a percentage of body weight is an indicator of cellular infiltrates and edema; inflammation secondary to SARS-CoV-2. Weights as a percent of body weight above 1.2% are consistent with moderate to severe pulmonary inflammation. Both groups averaged above 1.5% lung weight as a percent of body weight, suggesting severe inflammation in both. The group treated with CGP had a slightly, and significantly higher increase in weight gain suggesting the CGP may have contributed to pulmonary inflammation in this model (Figure 2).

Figure 2. Lung Weights



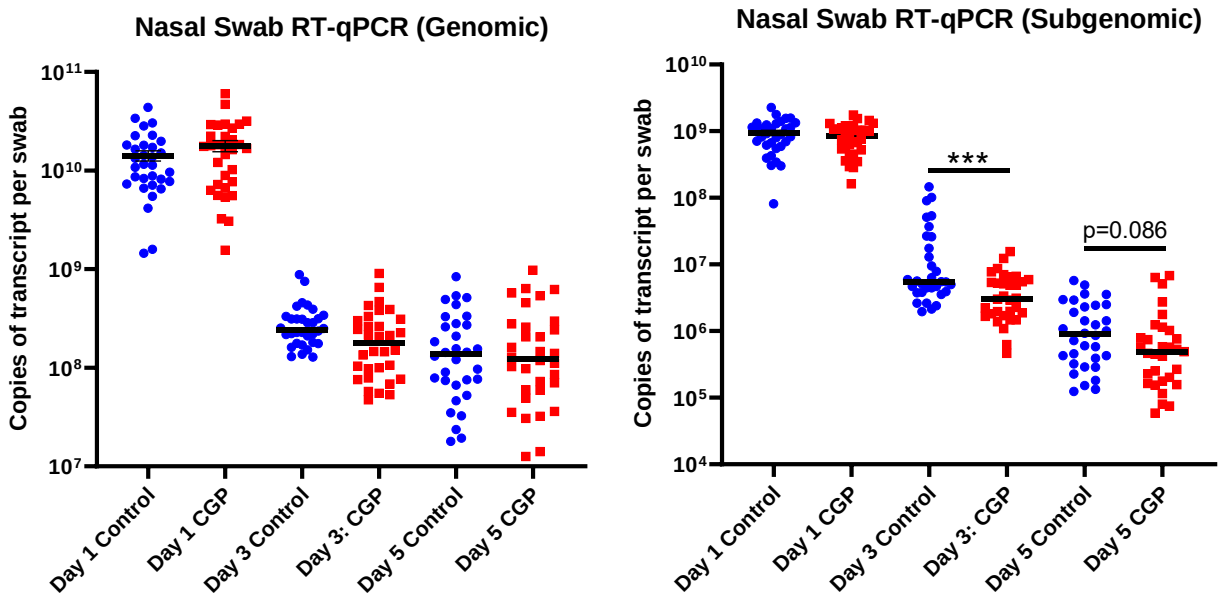
	Group 1: Control	Group 2: CGP
Number of values	32	32
Minimum	1.176	1.310
Maximum	2.136	2.449
Range	0.9596	1.139
Mean	1.615	1.750
Std. Deviation	0.2273	0.2916
Std. Error of Mean	0.04018	0.05155

Table Analyzed	Lung Weights
Column B	Group 2: CGP
vs.	vs.
Column A	Group 1: Control
Unpaired t test	
P value	0.0431
P value summary	*
Significantly different (P < 0.05)?	Yes
One- or two-tailed P value?	Two-tailed
t, df	t=2.066, df=62
How big is the difference?	
Mean of column A	1.615
Mean of column B	1.750
Difference between means (B - A) ± SEM	0.1350 ± 0.06536
95% confidence interval	0.004350 to 0.2657
R squared (eta squared)	0.06438
F test to compare variances	
F, DFn, Dfd	1.646, 31, 31
P value	0.1710
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	32
Sample size, column B	32

5.9 Tissue and Sample Processing for PCR

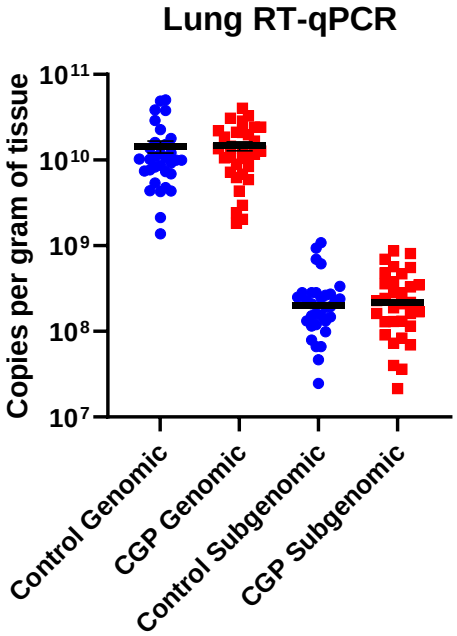
Nasal swabs were collected into Trizol on study Days 1, 3, and 5 and stored at -80ºC. Pulmonary tissue samples from the right lung were collected at necropsy, frozen at -80ºC, and then homogenized Trizol using a TissueLyser. RNA from swabs and tissue was extracted using a QIAGEN RNeasy Kit following manufacturer's instructions. Nucleic acids were then amplified and quantified. Genomic RT-qPCR represents amplification of the nucleocapsid phosphoprotein gene (N gene) and Subgenomic RT-qPCR represents amplification of the envelope small membrane protein gene (E gene). Results are presented in Figure 3 and Figure 4, with raw data in Appendix E.

Figure 3. RT-PCR Analysis of Nasal Swabs



There was no difference between groups in the amount of genomic RNA collected on nasal swabs on any of the days tested. There was a slight, but significant reduction in genomic RNA in Group 2, the CGP group, on Day 3. This trend in reduction was also present on Day 5, but did not quite reach significance. Statistics were run on log transformed data and represent One Way ANOVA tests with Sidak's Multiple Comparison test between groups. *** $p<0.001$.

Figure 4. RT-PCR Analysis of Lung Tissue



There were no statistical differences between groups in either genomic or subgenomic RNA collected from lung tissue at necropsy.

6 CONCLUSION

The objective of this study was to test calcium glycerophosphate (CGP) as a therapeutic against SARS-CoV-2 in a Syrian hamster model. CGP was administered twice daily starting one day pre-viral inoculation (Day -1) through Day 4. A control group received the same dosing regimen but with water instead of CGP. During the in life portion of the study, animals were weighed daily, received twice daily clinical observations, and had nasal swabs collected for viral RNA quantification on study Days 1, 3 and 5. On terminal Day 5, animals were euthanized, lung weights were taken, and pulmonary tissue was collected for RT-qPCR analysis. Pulmonary tissue was also collected and stored for future virology endpoints (e.g. TCID50), and lung and nasal tissue was collected and fixed for potential future histopathology. These endpoints are beyond the scope of this report.

Overall, CGP showed minimal to no signs consistent with efficacy against SARS-CoV-2. Animals in Groups 1 (control, water) and 2 CGP showed similar body weight loss, lung weight gain, and pulmonary viral titers by RT-qPCR. Lung weight data suggested that CGP may have made pulmonary inflammation slightly worse than the water control.

Nasal swabs on Group 2 animals on Days 3 and 5 did show a slight decrease in subgenomic RNA compared to Group 1. While amplification of genomic RNA will detect all intact viral RNA, including the inoculum, subgenomic RNA amplification is thought to be more specific for replicating virus. Thus, a slight reduction in subgenomic in the nasal swabs on Days 3 and 5 suggests that CGP may have had a small, localized effect at reducing viral replication at the site of administration. Follow up nasal histopathology might help to determine if this translates to a reduction of pathology at that site.

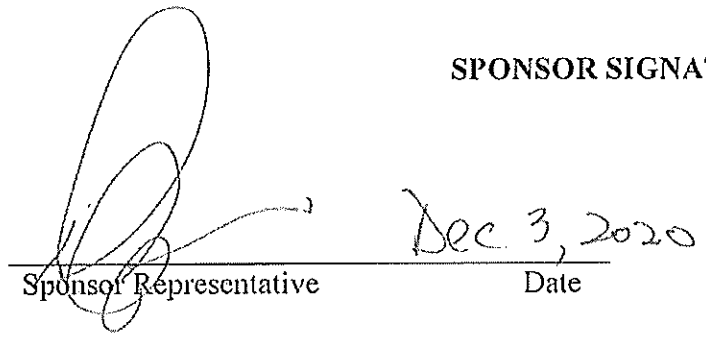
Appendix A. Approved Protocol, Amendments, and Memos

LOVELACE
BIOMEDICAL

PROTOCOL

Study Title:	SARS-CoV-2 Efficacy of Calcium Glycerophosphate (CGP) in a Syrian hamster model
Lovelace Protocol Number:	Study Protocol: FY20-110 IACUC # FY20-1171 Proposal # 2020-432 Test Article: L0880
Sponsor:	AkPharma Inc P.O. Box 111 Pleasantville, NJ 08232
Test Facility:	Lovelace Biomedical 2425 Ridgecrest Drive SE Albuquerque, NM 87108 Courier Address and location of Laboratory: Bldg 9217, Area Y Kirtland Air Force Base Albuquerque, NM 87115
Study Director:	Adam Werts, DVM, PhD, DACLAM
Sponsor Representative:	Alan Kligerman
Version	03

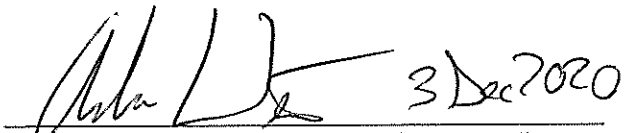
SPONSOR SIGNATURE



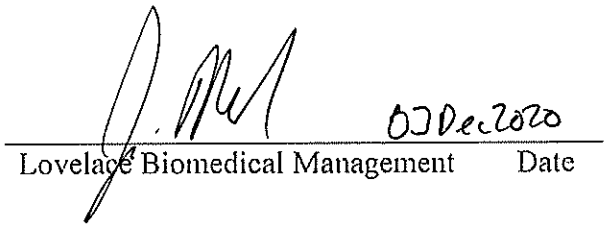
Dec 3, 2020

Sponsor Representative Date

LOVELACE BIOMEDICAL SIGNATURES



Lovelace Biomedical Study Director Date



Lovelace Biomedical Management Date

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1 OBJECTIVE

The objective of this study is to test calcium glycerophosphate (CGP) as a therapeutic against SARS-CoV-2 in a Syrian hamster model. To do this, CGP will be administered to the nasal cavity of hamsters up to twice daily, starting at one day prior to viral inoculation and continuing until animal sacrifice (i.e. Day 5). Clinical observations and viral burden, in comparison with a control group, will be used a metrics of test article (TA) efficacy.

2 JUSTIFICATION

In the current pandemic of the coronavirus SARS-CoV-2 it is imperative to identify effective treatments against this virus as rapidly as possible. Prior to use in humans, potential therapeutic efficacy needs to be shown in germane animal models. One model that has shown to be permissive to SARS-CoV-2 infection, and demonstrates mild-to-moderate disease is the Syrian hamster. The studies proposed here take advantage of this hamster model and will be used to evaluate the efficacy of CGP treatment designed to reduce viral loads and consequent disease burden.

3 REGULATORY COMPLIANCE

This study will not be conducted in strict accordance with U.S. FDA 21 CFR Part 58 (Good Laboratory Practices for Nonclinical Laboratory Studies, GLP). This is a preliminary study and is not intended to fulfill formal regulatory requirements consistent with Investigational New Drug Applications or other regulatory submissions.

This study will comply with all applicable sections of the Final Rules of the Animal Welfare Act regulations (9 CFR Parts 1, 2, and 3) and Guide for the Care and Use of Laboratory Animals—National Academy Press, Washington D.C. 2011 (the Guide). The study will be performed in LB's animal research facilities, which are fully accredited by the Association for the Assessment and Accreditation of Laboratory Animal Care (AAALAC).

Standard operating procedures (SOPs) and Study Specific Procedures (SSPs), if any, will be followed. All SSPs generated during the conduct of this study will be included in the Study File.

4 KEY STUDY PERSONNEL

Changes in the Study Director, if any, will be added by amendment. Any additional key study personnel changes or additions will be identified in the final report.

Study Director and Veterinary Support:	Adam Werts, DVM, PhD, DACLAM Email: awerts@lovelacebiomedical.org Phone: 505-348-9668
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Contributing Scientist - Microbiology/PCR:	Bryan Gullick, PhD Email: bgullick@lovelacebiomedical.org Phone: 505-348-8522
Contributing Scientist-Virology:	Ariel Arndt, PhD Email: aarndt@lovelacebiomedical.org
Sponsor Representatives:	Alan Kligeman Email: aekligerman@akpharma.com Phone: 609/645-5100 x101

5 PATHOGEN

5.1 SARS-CoV-2

Description:	SARS-CoV-2, isolate USA-WA1/2020
Infectious Titer of Stock:	Stock diluted to approximately 4E+05$TCID_{50}$/mL; to be recorded in all relevant paperwork and included in the final report. Viral sequencing data will be provided to the sponsor when available.
Supplier/Manufacturer:	Isolate sourced from BEI Resources and propagated in Vero E6 African Green Monkey kidney cells (BEI, catalog #N596) at the University of Texas Medical Branch (UTMB).
Lot:	To be documented in the data file and the final report.
Storage Conditions:	Virus will be stored in a biosafety level 3 (BSL3) compliant facility. Viral stocks will be stored at -80°C ±10°C.
Handling Precautions:	All manipulations with this agent will be performed under BSL3 compliance. Any manipulations or procedures that would expose the agent to the environment will be performed in a certified biosafety cabinet (BSC), or equivalent.

6 TEST ARTICLE

All Test Articles (TA) and Sponsor-supplied vehicles will be characterized by the Sponsor or designee. The Sponsor will ensure that documentation on the identity (suppler/manufacturer), batch number and/or lot number, uniformity, and stability for the test articles are provided for inclusion in the Final Report.

6.1 Test Article

Identity:	Calcium Glycerophosphate (CGP)
Description:	A generally recognized as safe (GRAS) food ingredient and nutrient supplement; A non-selective phosphatase inhibitor that has been shown to prevent cytokine-induced loss of epithelial integrity in cultured cells.
Supplier/Manufacturer:	Givaudan-Lavirotte, 58 Rue Paul Cazeneuve, 69008 Lyon, France
Lot :	1900002518; Sample No. 15799 (Avantis Distr.)
Storage Conditions:	dry, cool, room temperature, no sunlight
Solution Preparation:	Dilute in sterile distilled water, record pH. Store at room temperature or refrigerated for up to 30 days. Ship unused CGP back to the sponsor at the end of the study.

6.2 Diluent and Control Article

Identity:	Sterile distilled water
Description:	Any commercial source
Supplier/Manufacturer:	Any commercial source
Lot:	Any commercial source
Storage Conditions:	Room Temperature
Injection solution preparation:	Used to create sterile Test Article solution

7 TEST SYSTEM

Species Strain:	Hamster, Syrian (*Mesocricetus auratus*)
Target Age of Animals:	6-10 weeks
Target Weight of Animals:	110-180g
Number on Study/Sex:	Males. 64 on study, 6 spares. 70 total. Spares, if not used, will be humanely euthanized or conveyed to another institutional animal care and use committee (IACUC)-approved protocol on or after Study Day 0 (challenge day).
Source:	Charles River Laboratories (CRL).
Identification:	Animals will be uniquely identified as per SOP ACS-1385, Rodent and Rabbit Identification by cage card. Animal cages will be labeled at a minimum with study number, name of Study Director, and study ID.
Randomization:	Animals will be assigned to groups using Provantis with a stratified (body weight) randomization procedure. Animals will be placed in groups so that animals with the most similar body weights will be included on study.

8 ANIMAL HUSBANDRY

Housing: Animals will be single or pair housed with husbandry performed

according to SOP ACS-0075, Rodent Husbandry and Manual Restraint, in appropriate caging. Cage changes will not occur in the ABSL3 facility.

Quarantine Period: The animals will be quarantined per SOP, which is at least 7 days prior to study start.

Food: Envigo Diet (Envigo, Indianapolis, IN), restricted diet, once daily. Each batch of feed is analyzed per SOP ACG-0571, Analysis of Water and Feed Consumed by Animals and will be used within the manufacturer's designated shelf-life. The Study Director will review the feed analyses documentation and copies of the analyses will be included in the study files.

Water: Filtered municipal water (serial filters at 5, 1, and 0.2 μm pore size), unlimited access. Water is analyzed at least annually per SOP ACG-0571, Analysis of Water and Feed Consumed by Animals. The Study Director will review the water analyses documentation, and copies of the analyses will be included in the study files.

Enrichment: Enrichment will be Provided per SOP ACG-1951, Behavioral Management and Enrichment for All Animals House at Lovelace. Hamsters will receive, when appropriate, environmental stimulation such as, but not limited to, Plexiglas tubes, nylabones, bells, etc. Food enrichment, especially in the case of sustained inappetence, may be provided with prior approval by the Study Director.

Environmental Conditions: The targeted conditions for animal room environment and photoperiod are as follows:

Temperature, 18-26°C

Humidity, 30-70%

Light Cycle, 12:12 hour light:dark cycle (which may be interrupted for study activities).

Excursions that may have an impact on the study will be reviewed by the Study Director and noted if they are considered to affect the study. Light, humidity, and temperature excursions are defined as a sustained reading that falls out of range for more than 3 hours. Other excursions will be dealt with on a case-by-case basis.

9 EXPERIMENTAL DESIGN

Table 1: Experimental Design

Group	Group Description[1]	Number of Animals	Inoculation (Day 0)	Clinical Readouts	Endpoints and readouts
1	Control (Distilled Water) Dosed 2x daily starting at Day -1	32	200ul of virus at approximately 4E+05TCID$_{50}$/mL	Starting at Day -3: Daily body weights; twice daily observations; nasal swabs for RT-qPCR on Day 1, 3, and 5. Photos of 3 representative animals/group prior to inoculation and on each of the days of nasal swabs	Viral burden on lung. One genomic RT-qPCR and subgenomic RT-qPCR per animal. Tissue collected and stored for potential virology assessment (added by amendment)
2	CGP Dosed 2x daily starting at Day -1	32			

[1]Dosing will be intranasal (IN) and occur twice daily between approximately 7:00a.m. and 10:00 a.m. and 4:00p.m. and 7:00p.m each day from Day -1 through Day 4. On the day of inoculation (Day 0), viral inoculation will occur in the a.m. instead of TA dosing.

10 VIRAL CHALLENGE AND TA DOSING

10.1 Preparation of Challenge Material; TCID$_{50}$ assay

Challenge material will be prepared from frozen stocks by quickly thawing the appropriate number of vials at 37°C. Once thawed, challenge material in separate vials will be combined and held on wet ice until challenge. Challenge material will be used within 4 hours of preparation which will be defined as the completion of any dilutions and beginning of storage onto wet ice. One aliquot of the prepared challenge material will be withheld for titer verification by TCID$_{50}$ and processed post-challenge. TCID$_{50}$ assays will be run according to SOP BSF-1907 *Determination of Median Tissue Culture Infectious Dose (TCID$_{50}$) for Viral Samples*, using Vero E6 cells in a 96-well format. Stock virus of known concentration and blank media will serve as positive and negative controls, respectively. At assay completion, cells will be formalin fixed and stained, and plates will be stored according to Study Director discretion. The TCID$_{50}$ titer will be calculated according to the Reed-Muench method. Achieved dosing levels will be determined and included in the final report.

10.2 Intranasal Instillation (Virus)

Animals in Table 2 will have the challenge agent delivered via IN instillation. Animals will receive a volume of 100 µL/nares, 200 µL/animal. Animals will be anaesthetized with ketamine and xylazine per SOP ACS-0423, Small Animal Anesthesia, and instillations will be performed in accordance with SOP TXP-0559 Respiratory Instillation in Rodents for this procedure.

10.3 Intranasal dosing of TA

Intranasal (IN) dosing will follow SOP TXP-0559 Respiratory Instillation in Rodents. Dosing will occur 2x daily from Day -1 through Day 4, with the exception of only one dose on Day 0. See Table 1. Briefly, CGP will be made up at 3.75% in sterile distilled water (e.g. 3.75g CGP in 96.25 mL water), and animals will be dosed at 150µL per animal, split between each naris at 75µL/naris. All volumes will be recorded, with deviations ≥10% noted.

11 OBSERVATIONS, MEASUREMENTS AND IN-LIFE DATA COLLECTION

Data Documentation Note: Whenever possible, a validated computerized data acquisition system [e.g., Provantis™ or Animal Management System (AMS) software] will be used for data acquisition and recording. Hand recording of data will be performed when required. Excursions in refrigerators', freezers', and incubators' temperature may be expected due to use; excursions lasting >3 hours will be assessed for study impact by the Study Director or designee.

11.1 Clinical Observations

Detailed observations will be performed twice a day (a.m. and p.m.), with special attention to normal behavior per SOP TXP-1532, Pharmacologic and Toxicologic Observations of Experimental Animals starting 3 days prior to the day of challenge (i.e. Day -3) and continuing until the end of the study, or until moribund or found dead. In the event that an animal is found to have severe clinical signs, additional observations will be added by study director discretion. Detailed observations may be tailored to assessing respiratory distress, neurological symptoms, provoked and unprovoked behavior, appearance/posture, and gastrointestinal/urogenital abnormalities. Activity, posture, nasal discharge, respiratory characteristics, ocular discharge, inappetence/ anorexia, stool characteristics, seizures, or other abnormality will be noted as they appear during clinical observations of the animals. Additional observations may be added at the discretion of the study director or designee.

11.2 Body Weights

A pre-study weight of all animals will be collected for randomization (no more than 4-7 days prior to Study Day 0). The animals will also be weighed once daily in the a.m. beginning on Study Day -3 and continuing until the end of the study, or until scheduled euthanasia, declared moribund or found dead per SOP TXP-1924, Procedure for Recording Temperatures and Weighing Animals and Tissues in the Provantis System. The interval and frequency may be changed by the Study Director or designee based on health assessment of the animals.

12 PATHOLOGY

12.1 Moribund/Euthanasia Criteria

Animals found moribund will be euthanized per SOP ACS-0334, Euthanasia of Small Animals. Moribund/Euthanasia criteria are outlined below. Euthanasia decisions will be made by the Study Director, and/or the Clinical Veterinarian, or designee. Moribund animals will be defined as those demonstrating more than one of the following:

- Severe respiratory distress, e.g. severe dyspnea (difficult and/or labored breathing, gasping)
- Reluctance to move when stimulated to do so (e.g. unresponsiveness to touch or external stimuli)
- 25% or greater body weight loss when compared to the highest recorded body weight for that animal

Animals that are approaching moribund status but may not meet the stated criteria—those whose survival to the next scheduled observation session is questionable—will be reported to the Study Director or designee and veterinary consultation may be requested.

12.2 Euthanasia

At scheduled euthanasia or in cases of morbidity, animals will be euthanized by intraperitoneal injection of an overdose of a barbiturate-based sedative following SOP ACS-0334, Euthanasia of Small Animals. Necropsy will be performed on animals for either unscheduled or scheduled euthanasia.

12.3 Necropsy

A complete necropsy will be performed on all animals found dead or euthanized on or after Day -1 due to morbidity to determine the cause of death (SOP BSF-1488, Necropsy Procedure for Animals Infected with Biohazardous Agents).

Should unexpected deaths occur before Day -1, the animal will have gross examination to determine cause of death (if possible); however, the carcass will be discarded with no tissue or weights obtained unless recommended by the Study Pathologist or Study Director.

Moribund animals subjected to unscheduled euthanasia or animals that are found dead will be necropsied as soon as possible but in no case will the initiation of the necropsy be later than 18 hours after euthanasia is performed or being found dead. If animal carcasses must be held longer than 1 hour before necropsy begins, they will be refrigerated. A gross examination will be completed on all animals moribund or found dead. Liver, heart, brain, kidney, lung and any lesioned tissues will be fixed in 10% NBF and held for possible future evaluation. In addition, if autolysis has not significantly affected the samples, moribund and found dead animals will have the samples in **Table 3** collected. The Study Director or Veterinary Pathologist in concert the necropsy technicians will determine if autolysis has affected sample quality. Should this occur the carcass will be disposed of with no collections and will be noted in the study file. Found dead and moribund animals will not have organ weights collected.

Scheduled necropsies will include a terminal bodyweight, whole lung weight, sample collection and processing according to **Table 3**. Gross necropsy observations of the lung will be recorded in Provantis using consistent descriptive terminology to document location(s), size, shape, color,

consistency, and number. Gross observations will include a severity grade for pneumonia based on a 5 point scale: none, minimal, mild, moderate, marked correlating to 0, 1-25, 26-50, 51-75, and 76-100% affected, respectively. Photographs may be used to document tissues and unusual or characteristic lesions of the lung or for other reasons at the discretion of the necropsy technician, Study Pathologist, or Study Director. Additional tissues may be collected upon the recommendation of the Study Pathologist or Study Director.

Table 3: Tissue and Sample Collection for Study 1

Organ	Organ Weight	Genomic RT-qPCR (Target weight ~50-75mg)	Virology (collect and hold) (Target weight ~100-200mg)	Histopathology
Whole animal	X			
Lung	X			
a) Left lobe		X	X	
b) Right Lungs				Instill with 10% NBF, trim, embed and store. Histopathology can be added by amendment.
Skull/nasal cavity				Fix in 10% NBF and hold. Histopathology can be added by amendment

12.4 Reverse Transcription Quantitative PCR (genomic and subgenomic RT-qPCR)

Left lung tissue samples, approximately 50-75 mg will be homogenized in Trizol using a TissueLyser. Samples will be centrifuged at 4000 x *g* for 5 minutes, and supernatants will be saved for RNA extraction. RNA will be isolated from all samples using the QIAGEN RNeasy Kit or equivalent, according to the manufacturer's instructions.

Genomic RT-qPCR:

SARS-CoV-2 viral RNA will be quantified by a RT-qPCR assay targeting the SARS CoV-2 nucleocapsid phosphoprotein gene (N gene). Genome copies per mL or g equivalents will be calculated from a standard curve generated from RNA standards of known copy concentration (to be documented in the study files). All samples will be run in triplicate.

The SARS CoV-2 N gene primers and probe sequences are as follows:

SARS CoV-2 Forward: 5' TTACAAACATTGGCCGCAAA 3'
SARS CoV-2 Reverse: 5' GCGCGACATTCCGAAGAA 3'
SARS CoV-2 Probe: 6FAM-ACAATTTGCCCCCAGCGCTTCAG-BHQ-1

Amplification and detection will be performed using a suitable real-time thermal cycler under the following cycling conditions: 50 °C for 5 minutes, 95 °C for 20 seconds and 40 cycles of 95 °C for 3 seconds, and 60 °C for 30 seconds.

Subgenomic RT-qPCR:

Quantification of sgmRNA content will be by a RT-qPCR assay targeting the subgenomic RNA of SARS CoV-2 around the E-gene using the common leader of the virus. Genome copies per mL or g equivalents will be calculated relative to a standard curve generated from E-gene plasmid

standards of known copy concentration (to be documented in the study files). All samples will be run in triplicate.

The SARS CoV-2 sgmRNA primers and probe sequences are as follows:

Forward Primer: sgLeadSARSCoV2-F: 5'-CGATCTCTTGTAGATCTGTTCTC-3'
Reverse Primer: E_Sarbeco_R: 5'- ATATTGCAGCAGTACGCACACA-3'
Probe: E_Sarbeco_P1: 6FAM-ACACTAGCCATCCTTACTGCGCTTCG-BHQ-1

The primers used for generation of the E-gene calibration curve are as follows:

Forward Primer: E_Sarbeco_F: 5'-ACAGGTACGTTAATAGTTAATAGCGT-3'
Reverse Primer: E_Sarbeco_R: 5'- ATATTGCAGCAGTACGCACACA-3'
Probe: E_Sarbeco_P1: 6FAM-ACACTAGCCATCCTTACTGCGCTTCG-BHQ-1

Amplification and detection will be performed using a suitable real-time thermal cycler under the following cycling conditions: 50 °C for 5 minutes, 95 °C for 20 seconds and 40 cycles of 95 °C for 3 seconds, and 60 °C for 30 seconds.

13 RECORDS TO BE MAINTAINED

Specimens shall be identified by test system, study, nature, and date of collection. All raw data and records that would be required to reconstruct the study will be maintained at Lovelace for a minimum of one year.

Records retained shall include but not be limited to:

- Test Materials:
  - Test material receipt storage, usage, and disposition
  - Dosing and Chemistry data
- Facility:
  - Animal room temperature and humidity
  - Water analyses
  - Feed identification, analyses, and usage
  - Animal care records
  - Medical records
- In-Life Phase:
  - Animal receipt and disposition
  - Quarantine observation, health assessment, and release
  - Animal randomization
- In-Life Phase (continued):
  - Body weights
  - Treatment
  - Animal observations
  - Sample collection
  - Necropsy recordings
  - Micro and Virology
  - Data analysis
  - Photos

14 PROTOCOL CHANGES/DEVIATIONS

If any change to the approved protocol is required, the change and the reason for it, will be put in writing in the form of a protocol revision and will be signed by the Sponsor, Study Director and Lovelace Management.

Deviations from the Study Protocol, and Standard Operating Procedures will be promptly reported to the Study Director. The Study Director notes in the study file the nature of the deviation, the effect on the study, and corrective action taken, if any.

15 TIMELINE AND REPORTING

In-Life: 2 weeks
Preliminary PCR (polymerase chain reaction, genomic and subgenomic RT-qPCR): 3-4 weeks post in-life
Data summary: Updated data presented in PowerPoint as data is available; this data will include all relevant statistical analysis.
Final Deliverable: Approximately 8 weeks post sample analysis completion; this will include complete data analysis.

16 VERSION HISTORY AND CHANGE SUMMARY

Version	Approval Date	Summary of Changes (including sections)	Justification for Changes
1	29Oct2020	Original Signed Protocol	
2	20Nov2020	1) Changed viral dosing from maximum titer to 4E+05TCID50/mL. Sections 5 and 9 2) Clarified photos taken and PCR assays (Table 1, section 9)	1) We have routinely used this dose with hamster studies and shown good results. Current viral stocks are much higher than several months ago. Using these risks overwhelming the system and covering up any effect of the TA. 2) Made text more clear
3		3) Removed sentence about not collecting blood from moribund animals from section 12.3 4) Added collection and fixing of skulls to Table 3 in section 12.3.	3) Blood is not being collected from any animal 4) The test article is being administered via the intranasal route. Saving fixed skulls will allow for histopathology of the nasal cavity if added by amendment.

TO: Study File Study Number: FY20-110

FROM: Adam Werts

DATE: 25Nov2020

SUBJECT: TA formulatoin and dosing changes

From: Werts, Adam
Sent: Wednesday, November 25, 2020 1:58 PM
To: 'Alan E Kligerman' <aekligerman@akpharma.com>
Cc: Kathy Jamison <kjamison@akpharma.com>; Weis, Margaret <Margaret.Weis@ttuhsc.edu>
Subject: RE: COA FOR THE MATERIAL THAT LOVELACE IS NOW USING FOR THE HAMSTERS

Thank you Alan, I will include this CoA in the Report.

I also wanted to summarize and document for the final report the changes we made today:

1) pH
a. 3.75% CGP was made by adding 4.5g of CGP to 115.5mL of water. pH of the water alone was measured at 6.83. pH of the CGP solution was measured at 11.27. A second batch of CPG solution was made up using the same recipe above to confirm that the reading was accurate. This second solution had a pH of 11.30. The second solution was read on another pH meter and the result showed 11.25. After discussing the potential issues of repeat dosing of a highly alkaline solution to the nares of hamsters with Alan, it was agreed that we would lower the pH to a more physiological range. A member of our formulations group added approximately 8-10 drops of 10N HCl to the solution and the pH was reduced to 7.34. This is the solution that will be used to dose all animals on study.
2) CGP dosing
a. The solution, as made, is a suspension with a significant amount of CGP settling out over several minutes. All technicians dosing animals on study have been notified that the suspension needs agitation and visual verification of homogeneity before dosing each animal.

I've reserved an aliquot of the suspension that we will be using for dosing. I plan to ship that back to you with the remaining CGP powder once the study has completed.

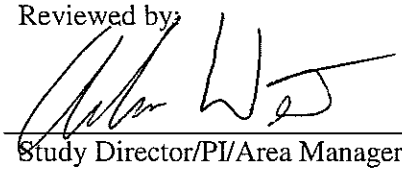
Please let me know if you have any questions or concerns.

Adam Werts, DVM, PhD, Dipl. ACLAM
Veterinary Research Scientist
awerts@lrri.org

Office: (505) 348-9668
Cell: (919) 428-0735

Lovelace Biomedical • 2425 Ridgecrest Dr. SE •
Albuquerque • NM • 87108 • USA

Reviewed by:



Study Director/PI/Area Manager* Signature

25Nov2020

Date

*Area Manager Signature if non-study specific

Appendix B. Test Article Documentation

ISALTIS
GIVAUDAN-LAVIROTTE

GIVAUDAN-LAVIROTTE
56 RUE PAUL CAZENEUVE
69008 LYON - FRANCE

Tel: +33 (0)4 78 61 55 00 Fax: +33 (0)4 78 61 55 94
Siret: 95550921100012 - TVA: FR38955509211

RW1034
LOT: 15799
EXP. 01/21
Qty: 48 x 25 kg

Product code : 30130J	**Report issue :** 17/10/2019
Product : GIVOCAL	**Batch :** 1900002518
Quality : F.C.C.	

Certificate of analysis

Characteristics	Process	Standards	Results
Appearance	MI-LAB-016-6.1	fine white powder	conforms
Identification	MI-LAB-016-6.2	conforms	conforms
Assay ($C_3H_7O_6PCa$ dry basis)	MI-LAB-016-6.23	98.0 - 100.5 %	100.4 %
Alkalinity (ml 0,1N H_2SO_4 /g)	MI-LAB-016-6.6	max. 1.5 ml	1.1 ml
Lead	MI-LAB-016-6.10	max. 0,00030 %	conforms
Loss on drying (4 H at 150°C)	MI-LAB-016-6.21	max. 12.0 %	11.2 %
Cadmium	MI-LAB-016-6.12	max. 0.00010 %	conforms
Mercury	MI-LAB-016-6.13	max. 0.00001 %	conforms
Arsenic	MI-LAB-016-6.11	max. 0.0002 %	conforms
Total aerobic germs	MI-LAB-016-6.27	max. 1000 /g	10 /g
Yeasts - moulds	MI-LAB-016-6.28	max. 100 /g	10 /g
.....	-		
F.C.C. Quality (according to last version)	-		
.....	-		

Manufacturing date : 02/10/2019

Re-test date : 01/10/2022

Quality control laboratory
Approved and signed certificate of analysis

REMARKS: This is a computer generated certificate and requires therefore no signature.
IMPORTANT: Certificate for the use of your quality control laboratory.

Appendix C. Clinical Observations

Clinical Observations - Clinical Observations - Animals by Time

20-110 - SARS-CoV-2 Efficacy of Calcium Glycerophosphate in a Syrian hamster model

Grp1 Cntrl Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		-3	-2	-1	0	1	2	3
1001	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
1002	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
1003	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
1004	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
1005	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
1006	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
1007	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
1008	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
1009	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
1010	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
1011	Normal	X	X	X	X	X	X	X

X=Present

Clinical Observations - Clinical Observations - Animals by Time

20-110 - SARS-CoV-2 Efficacy of Calcium Glycerophosphate in a Syrian hamster model

Grp1 Cntrl Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		-3	-2	-1	0	1	2	3
1011	Scheduled Euthanasia	.	.	.	.	.	.	.
1012	Normal	X	X	X	X	X	.	.
	Scheduled Euthanasia	.	.	.	.	.	.	.
	Appearance: Rough Hair Coat	.	.	.	.	.	X	X
	Activity	.	.	.	.	.	.	.
1013	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
1014	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
1015	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
1016	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
1017	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
1018	Normal	X	X	X	X	X	X	.
	Scheduled Euthanasia	.	.	.	.	.	.	.
	Appearance: Rough Hair Coat	.	.	.	.	.	.	X
1019	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
1020	Normal	X	X	X	X	X	X	X

X=Present

Clinical Observations - Clinical Observations - Animals by Time

20-110 - SARS-CoV-2 Efficacy of Calcium Glycerophosphate in a Syrian hamster model

Grp1 Cntrl Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		-3	-2	-1	0	1	2	3
1020	Scheduled Euthanasia	.	.	.	.	.	.	.
1021	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
1022	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
1023	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
1024	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
1025	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
1026	Normal	X	X	X	X	X	.	.
	Scheduled Euthanasia	.	.	.	.	.	.	.
	Appearance: Rough Hair Coat	.	.	.	.	.	X	X
1027	Normal	X	X	X	X	.	.	.
	Scheduled Euthanasia	.	.	.	.	.	.	.
	Appearance: Posture	.	.	.	.	?Hun	?Hun	?Hun
1028	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
1029	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.

X=Present; ?Hun=Hunched

Clinical Observations - Clinical Observations - Animals by Time

20-110 - SARS-CoV-2 Efficacy of Calcium Glycerophosphate in a Syrian hamster model

Grp1 Cntrl Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		-3	-2	-1	0	1	2	3
1030	Normal	X	X	X	X	X	X	.
	Scheduled Euthanasia	.	.	.	.	.	.	.
	Appearance: Posture	.	.	.	.	.	.	?Hun
1031	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
1032	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.

X=Present; ?Hun=Hunched

Clinical Observations - Clinical Observations - Animals by Time

20-110 - SARS-CoV-2 Efficacy of Calcium Glycerophosphate in a Syrian hamster model

Grp1 Cntrl Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		4	5					
1001	Normal	X	.					
	Scheduled Euthanasia	.	X					
1002	Normal	X	.					
	Scheduled Euthanasia	.	X					
1003	Normal	X	.					
	Scheduled Euthanasia	.	X					
1004	Normal	X	.					
	Scheduled Euthanasia	.	X					
1005	Normal	X	.					
	Scheduled Euthanasia	.	X					
1006	Normal	X	.					
	Scheduled Euthanasia	.	X					
1007	Normal	X	.					
	Scheduled Euthanasia	.	X					
1008	Normal	X	.					
	Scheduled Euthanasia	.	X					
1009	Normal	X	.					
	Scheduled Euthanasia	.	X					
1010	Normal	X	.					
	Scheduled Euthanasia	.	X					
1011	Normal	X	.					

X=Present

Clinical Observations - Clinical Observations - Animals by Time

20-110 - SARS-CoV-2 Efficacy of Calcium Glycerophosphate in a Syrian hamster model

Grp1 Cntrl Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		4	5					
1011	Scheduled Euthanasia	.	X					
1012	Normal	.	.					
	Scheduled Euthanasia	.	X					
	Appearance: Rough Hair Coat	X	.					
	Activity	Slow	.					
1013	Normal	X	.					
	Scheduled Euthanasia	.	X					
1014	Normal	X	.					
	Scheduled Euthanasia	.	X					
1015	Normal	X	.					
	Scheduled Euthanasia	.	X					
1016	Normal	X	.					
	Scheduled Euthanasia	.	X					
1017	Normal	X	.					
	Scheduled Euthanasia	.	X					
1018	Normal	.	.					
	Scheduled Euthanasia	.	X					
	Appearance: Rough Hair Coat	X	.					
1019	Normal	X	.					
	Scheduled Euthanasia	.	X					
1020	Normal	X	.					

X=Present; Slow=Slow To Move

Clinical Observations - Clinical Observations - Animals by Time

20-110 - SARS-CoV-2 Efficacy of Calcium Glycerophosphate in a Syrian hamster model

Grp1 Cntrl Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		4	5					
1020	Scheduled Euthanasia	.	X					
1021	Normal	X	.					
	Scheduled Euthanasia	.	X					
1022	Normal	X	.					
	Scheduled Euthanasia	.	X					
1023	Normal	X	.					
	Scheduled Euthanasia	.	X					
1024	Normal	X	.					
	Scheduled Euthanasia	.	X					
1025	Normal	X	.					
	Scheduled Euthanasia	.	X					
1026	Normal	.	.					
	Scheduled Euthanasia	.	X					
	Appearance: Rough Hair Coat	X	.					
1027	Normal	.	.					
	Scheduled Euthanasia	.	X					
	Appearance: Posture	?Hun	.					
1028	Normal	X	.					
	Scheduled Euthanasia	.	X					
1029	Normal	X	.					
	Scheduled Euthanasia	.	X					

X=Present; ?Hun=Hunched

Clinical Observations - Clinical Observations - Animals by Time

20-110 - SARS-CoV-2 Efficacy of Calcium Glycerophosphate in a Syrian hamster model

Grp1 Cntrl Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		4	5					
1030	Normal	.	.					
	Scheduled Euthanasia	.	X					
	Appearance: Posture	?Hun	.					
1031	Normal	X	.					
	Scheduled Euthanasia	.	X					
1032	Normal	X	.					
	Scheduled Euthanasia	.	X					

X=Present; ?Hun=Hunched

Clinical Observations - Clinical Observations - Animals by Time

20-110 - SARS-CoV-2 Efficacy of Calcium Glycerophosphate in a Syrian hamster model

Grp2 CGP Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		-3	-2	-1	0	1	2	3
2001	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
2002	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
2003	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
2004	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
2005	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
2006	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
2007	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
2008	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
2009	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
2010	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
2011	Normal	X	X	X	X	X	X	X

X=Present

Clinical Observations - Clinical Observations - Animals by Time

20-110 - SARS-CoV-2 Efficacy of Calcium Glycerophosphate in a Syrian hamster model

Grp2 CGP Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		-3	-2	-1	0	1	2	3
2011	Scheduled Euthanasia	.	.	.	.	.	.	.
2012	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
2013	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
2014	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
2015	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
2016	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
2017	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
2018	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
2019	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
2020	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
2021	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.

X=Present

Clinical Observations - Clinical Observations - Animals by Time

20-110 - SARS-CoV-2 Efficacy of Calcium Glycerophosphate in a Syrian hamster model

Grp2 CGP Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		-3	-2	-1	0	1	2	3
2022	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
2023	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
2024	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
2025	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
2026	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
2027	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
2028	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
2029	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
2030	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
2031	Normal	X	X	X	X	X	X	X
	Scheduled Euthanasia	.	.	.	.	.	.	.
2032	Normal	X	X	X	X	X	X	X

X=Present

Clinical Observations - Clinical Observations - Animals by Time

20-110 - SARS-CoV-2 Efficacy of Calcium Glycerophosphate in a Syrian hamster model

Grp2 CGP Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		-3	-2	-1	0	1	2	3
2032	Scheduled Euthanasia	.	.	.	.	.	.	.

Clinical Observations - Clinical Observations - Animals by Time

20-110 - SARS-CoV-2 Efficacy of Calcium Glycerophosphate in a Syrian hamster model

Grp2 CGP Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		4	5					
2001	Normal	X	.					
	Scheduled Euthanasia	.	X					
2002	Normal	X	.					
	Scheduled Euthanasia	.	X					
2003	Normal	X	.					
	Scheduled Euthanasia	.	X					
2004	Normal	X	.					
	Scheduled Euthanasia	.	X					
2005	Normal	X	.					
	Scheduled Euthanasia	.	X					
2006	Normal	X	.					
	Scheduled Euthanasia	.	X					
2007	Normal	X	.					
	Scheduled Euthanasia	.	X					
2008	Normal	X	.					
	Scheduled Euthanasia	.	X					
2009	Normal	X	.					
	Scheduled Euthanasia	.	X					
2010	Normal	X	.					
	Scheduled Euthanasia	.	X					
2011	Normal	X	.					

X=Present

Clinical Observations - Clinical Observations - Animals by Time

20-110 - SARS-CoV-2 Efficacy of Calcium Glycerophosphate in a Syrian hamster model

Grp2 CGP Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		4	5					
2011	Scheduled Euthanasia	.	X					
2012	Normal	X	.					
	Scheduled Euthanasia	.	X					
2013	Normal	X	.					
	Scheduled Euthanasia	.	X					
2014	Normal	X	.					
	Scheduled Euthanasia	.	X					
2015	Normal	X	.					
	Scheduled Euthanasia	.	X					
2016	Normal	X	.					
	Scheduled Euthanasia	.	X					
2017	Normal	X	.					
	Scheduled Euthanasia	.	X					
2018	Normal	X	.					
	Scheduled Euthanasia	.	X					
2019	Normal	X	.					
	Scheduled Euthanasia	.	X					
2020	Normal	X	.					
	Scheduled Euthanasia	.	X					
2021	Normal	X	.					
	Scheduled Euthanasia	.	X					

X=Present

Clinical Observations - Clinical Observations - Animals by Time

20-110 - SARS-CoV-2 Efficacy of Calcium Glycerophosphate in a Syrian hamster model

Grp2 CGP Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		4	5					
2022	Normal	X	.					
	Scheduled Euthanasia	.	X					
2023	Normal	X	.					
	Scheduled Euthanasia	.	X					
2024	Normal	X	.					
	Scheduled Euthanasia	.	X					
2025	Normal	X	.					
	Scheduled Euthanasia	.	X					
2026	Normal	X	.					
	Scheduled Euthanasia	.	X					
2027	Normal	X	.					
	Scheduled Euthanasia	.	X					
2028	Normal	X	.					
	Scheduled Euthanasia	.	X					
2029	Normal	X	.					
	Scheduled Euthanasia	.	X					
2030	Normal	X	.					
	Scheduled Euthanasia	.	X					
2031	Normal	X	.					
	Scheduled Euthanasia	.	X					
2032	Normal	X	.					

X=Present

Clinical Observations - Clinical Observations - Animals by Time

20-110 - SARS-CoV-2 Efficacy of Calcium Glycerophosphate in a Syrian hamster model

Grp2 CGP Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		4	5					
2032	Scheduled Euthanasia	.	X					

X=Present

Appendix D. Body Weights and Lung Weights

Generalized Results - Animals by Mixed Parameter / Time

20-110 - SARS-CoV-2 Efficacy of Calcium Glycerophosphate in a Syrian hamster model

Sex: Male Day(s) Relative to Start Date

Grp1 Cntrl	Body weights						
	Weight on day (g)	Weight on day (g)	Weight on day (g)	Weight on day (g)	Weight on day (g)	Weight on day (g)	Weight on day (g)
	-5	-3	-2	-1	0	1	2
1001	139.4	139.9	140.1	140.7	143.7	141	136.7
1002	127.8	128.8	130.1	133.4	135.4	130.7	124.6
1003	123.4	125.1	126.5	129.2	130.5	130.7	123.9
1004	113.3	113.7	114.9	115.8	116.7	116.9	110.2
1005	127.5	128.7	130.0	131.7	132.8	130.8	123.2
1006	132.0	131.3	133.3	132.2	132.4	131.1	125.3
1007	135.0	134.4	133.9	137.6	138.5	136.6	129.9
1008	119.7	118.8	118.5	119.8	119.2	116.6	112.8
1009	140.8	143.2	144.0	147.6	147	148.4	140.7
1010	123.1	126.7	126.2	128.9	130.3	127.4	1234.80 E[a]
1011	138.3	137.4	139.4	141.2	144.6	142.7	136
1012	125.0	123.5	122.1	124.3	125.1	122.3	117.3
1013	114.8	116.0	118.5	119.4	121.7	121.8	119
1014	136.1	132.2	134.5	137.3	139.2	137.9	134.5
1015	122.8	125.9	128.2	128.1	129.4	129.3	123.2
1016	120.5	120.0	119.2	120.8	120.7	118.9	112.3

E = Exclude

[a] [FC:Weight value is inconsistent with other body weight results. Apparent error in reporting.]

Generalized Results - Animals by Mixed Parameter / Time

20-110 - SARS-CoV-2 Efficacy of Calcium Glycerophosphate in a Syrian hamster model

Sex: Male Day(s) Relative to Start Date

Grp1 Cntrl	Body weights		
	Weight on day (g)	Weight on day (g)	Weight on day (g)
	3	4	5
1001	135.7	128.7	129.030
1002	123.8	119.1	11.234
1003	123.3	117.4	117.287
1004	109.7	103.4	103.86
1005	122.6	115.2	114.639
1006	124.8	120.4	119.730
1007	128.7	122.2	120.814
1008	112.3	107.5	108.426
1009	140.4	137.7	137.299
1010	123.4	116.1	116.269
1011	135.8	128.7	125.663
1012	117.4	110.2	108.959
1013	113.4	109.1	110.518
1014	126	120.7	122.581
1015	122.5	115.4	116.329
1016	110.3	108.1	108.404

Generalized Results - Animals by Mixed Parameter / Time

20-110 - SARS-CoV-2 Efficacy of Calcium Glycerophosphate in a Syrian hamster model

Sex: Male Day(s) Relative to Start Date

Grp1 Cntrl	Body weights						
	Weight on day (g)	Weight on day (g)	Weight on day (g)	Weight on day (g)	Weight on day (g)	Weight on day (g)	Weight on day (g)
	-5	-3	-2	-1	0	1	2
1017	127.0	129.1	129.1	130.3	131.7	129.6	124.6
1018	129.1	130.5	129.7	129.7	124.4	122.9	117.5
1019	120.7	122.6	123.5	123.7	128.8	127.2	122.8
1020	122.2	123.8	124.6	125.6	126.2	125	118.9
1021	126.0	124.1	123.0	125.6	126.1	123.6	117.9
1022	132.7	130.9	130.6	131.4	132.3	129.1	123.8
1023	139.5	141.1	141.7	141.6	143.6	141	133.7
1024	134.1	134.8	136.4	137.4	142.8	137.9	130.8
1025	130.2	127.6	130.4	134.4	136.6	134.9	124
1026	125.2	125.5	124.3	125.4	125.7	124.3	119.6
1027	121.6	123.1	123.6	125.6	129.1	125.6	118.3
1028	123.8	120.6	120.8	120.6	121.7	121.1	112.8
1029	118.1	119.5	120.7	124.2	124.8	123.6	114.7
1030	124.9	123.2	123.9	125.6	126.3	122.9	116.7
1031	133.8	136.3	136.9	137.2	139.9	136.9	129.5

Generalized Results - Animals by Mixed Parameter / Time

20-110 - SARS-CoV-2 Efficacy of Calcium Glycerophosphate in a Syrian hamster model

Sex: Male Day(s) Relative to Start Date

Grp1 Cntrl	Body weights		
	Weight on day (g)	Weight on day (g)	Weight on day (g)
	3	4	5
1017	120.1	116.7	115.177
1018	115.2	112.0	112.563
1019	118.4	113.6	111.689
1020	115.1	111.8	111.873
1021	114.1	112.0	112.754
1022	121.5	118.6	121.935
1023	129.2	123.7	122.134
1024	127.3	122.4	120.506
1025	119.8	115.9	117.348
1026	117	113.0	115.172
1027	114.3	110.5	109.022
1028	109	104.6	103.601
1029	111.7	108.2	107.710
1030	113.2	109.3	107.813
1031	125.6	122.4	124.971

Generalized Results - Animals by Mixed Parameter / Time

20-110 - SARS-CoV-2 Efficacy of Calcium Glycerophosphate in a Syrian hamster model

Sex: Male Day(s) Relative to Start Date

Grp1 Cntrl	Body weights						
	Weight on day (g)	Weight on day (g)	Weight on day (g)	Weight on day (g)	Weight on day (g)	Weight on day (g)	Weight on day (g)
	-5	-3	-2	-1	0	1	2
1032	124.60	125.2	127.2	128.7	131.7	131.7	122.2
Mean	127.281	127.609	128.306	129.844	131.216	129.388	123.142
SD	7.228	7.210	7.360	7.502	8.050	7.893	7.812
N	32	32	32	32	32	32	31

Generalized Results - Animals by Mixed Parameter / Time

20-110 - SARS-CoV-2 Efficacy of Calcium Glycerophosphate in a Syrian hamster model

Sex: Male Day(s) Relative to Start Date

Grp1 Cntrl	Body weights		
	Weight on day (g)	Weight on day (g)	Weight on day (g)
	3	4	5
1032	118.3	114.1	113.371
Mean	120.622	115.897	112.459
SD	7.892	7.498	19.917
N	32	32	32

Generalized Results - Animals by Mixed Parameter / Time

20-110 - SARS-CoV-2 Efficacy of Calcium Glycerophosphate in a Syrian hamster model

Sex: Male Day(s) Relative to Start Date

Grp2 CGP	Body weights						
	Weight on day (g)	Weight on day (g)	Weight on day (g)	Weight on day (g)	Weight on day (g)	Weight on day (g)	Weight on day (g)
	-5	-3	-2	-1	0	1	2
2001	120.2	120.8	120.0	121.8	122.4	121.6	117.5
2002	128.2	132.2	132.2	134.9	132.8	129.7	123.7
2003	122.3	123.1	124.6	125.9	125.6	123.6	118.1
2004	135.8	137.5	138.0	140.4	139.9	139	135.3
2005	117.9	120.0	120.3	122.3	124	120.6	114.6
2006	133.2	134.5	135.5	136.8	135.8	133.3	126.7
2007	124.0	125.8	126.651	125.1	125.8	123	119.5
2008	136.4	138.3	139.0	141.3	141.3	140.2	134.6
2009	125.1	127.5	127.8	128.2	129.6	125.2	119.9
2010	132.7	131.7	131.3	129.3	129.4	125.9	119.4
2011	125.7	126.8	126.1	126.8	127.7	125.2	119.4
2012	127.3	127.3	128.4	126.8	128.4	125.8	121.2
2013	129.3	128.4	129.1	132.5	133	130	125.2
2014	116.2	118.0	118.2	119.5	119.1	117.3	111.5
2015	134.6	134.7	134.3	134.5	134.8	133.2	128.4
2016	121.9	122.9	122.9	124.3	124.3	121	116.1

Generalized Results - Animals by Mixed Parameter / Time

20-110 - SARS-CoV-2 Efficacy of Calcium Glycerophosphate in a Syrian hamster model

Sex: Male Day(s) Relative to Start Date

Grp2 CGP	Body weights		
	Weight on day (g)	Weight on day (g)	Weight on day (g)
	3	4	5
2001	113.6	109.2	109.143
2002	120.9	116	115.695
2003	115.1	113.0	114.955
2004	132.2	128.5	127.880
2005	111.3	107.4	107.786
2006	123.7	119.0	120.318
2007	117.7	114.8	116.611
2008	131.1	126.7	125.353
2009	115.6	110.8	109.664
2010	115.5	112.2	109.948
2011	115.8	111.2	110.385
2012	118.8	116.5	117.736
2013	124.1	122.4	122.567
2014	108.6	104.0	103.383
2015	124	120.9	119.411
2016	112	108.7	108.534

Generalized Results - Animals by Mixed Parameter / Time

20-110 - SARS-CoV-2 Efficacy of Calcium Glycerophosphate in a Syrian hamster model

Sex: Male Day(s) Relative to Start Date

Grp2 CGP	Body weights						
	Weight on day (g)	Weight on day (g)	Weight on day (g)	Weight on day (g)	Weight on day (g)	Weight on day (g)	Weight on day (g)
	-5	-3	-2	-1	0	1	2
2017	114.7	113.4	114.5	118.2	118.3	117.8	112.4
2018	124.2	122.9	121.7	122.7	121.7	118.3	113.3
2019	121.6	122.1	122.4	122.5	117.8	116.9	112.2
2020	139.4	142.3	144.9	145.9	145.8	143.1	138.8
2021	140.9	139.4	140.5	124.9	127	124	119
2022	122.9	124.1	124.1	124.6	126.4	126.1	120.2
2023	123.3	123.1	124.3	141.0	139.7	141.4	135.6
2024	139.7	139.1	139.0	140.0	142.4	140.9	133.5
2025	120.4	122.8	123.1	121.8	122.6	116.9	112.4
2026	121.6	120.5	119.8	121.8	123.1	120.7	115.2
2027	138.2	136.2	136.1	137.3	136.3	129.6	126.5
2028	128.5	129.50	129.7	132.6	129.4	125.7	120.3
2029	124.6	124.0	124.1	122.6	122.6	119.2	114.4
2030	133.3	133.3	135.3	136.6	124.8	123.3	118.8
2031	126.0	126.3	124.6	125.7	136.4	133.6	126.6

Generalized Results - Animals by Mixed Parameter / Time

20-110 - SARS-CoV-2 Efficacy of Calcium Glycerophosphate in a Syrian hamster model

Sex: Male Day(s) Relative to Start Date

Grp2 CGP	Body weights		
	Weight on day (g)	Weight on day (g)	Weight on day (g)
	3	4	5
2017	110.3	107.5	105.309
2018	110.6	107.2	107.64
2019	108.5	104.5	102.850
2020	134.5	129.2	127.669
2021	116.1	111.5	110.527
2022	117.3	114.5	112.048
2023	131.3	126.9	125.218
2024	130.5	125.5	125.698
2025	111.1	107.2	107.054
2026	111.6	107.7	107.711
2027	123.3	117.7	115.675
2028	115.7	111.7	110.635
2029	110.8	107.1	106.601
2030	115.8	112.9	112.19
2031	122.8	118.5	117.999

Generalized Results - Animals by Mixed Parameter / Time

20-110 - SARS-CoV-2 Efficacy of Calcium Glycerophosphate in a Syrian hamster model

Sex: Male Day(s) Relative to Start Date

Grp2 CGP	Body weights						
	Weight on day (g)	Weight on day (g)	Weight on day (g)	Weight on day (g)	Weight on day (g)	Weight on day (g)	Weight on day (g)
	-5	-3	-2	-1	0	1	2
2032	127.4	125.5	126.7	125.9	126.1	122.4	117.8
Mean	127.422	127.938	128.286	129.203	129.197	126.703	121.503
SD	7.134	7.104	7.390	7.519	7.456	7.763	7.637
N	32	32	32	32	32	32	32

Generalized Results - Animals by Mixed Parameter / Time

20-110 - SARS-CoV-2 Efficacy of Calcium Glycerophosphate in a Syrian hamster model

Sex: Male Day(s) Relative to Start Date

Grp2 CGP	Body weights		
	Weight on day (g)	Weight on day (g)	Weight on day (g)
	3	4	5
2032	113.2	110.2	111.677
Mean	118.231	114.409	113.933
SD	7.489	7.275	7.248
N	32	32	32

Generalized Results - Animals by Parameter - Fixed Time

20-110 - SARS-CoV-2 Efficacy of Calcium Glycerophosphate in a Syrian hamster model

Sex: Male Day(s): -9999 → 9999 Relative to Start Date

Grp1 Cntrl	Organ Weigh Lung(s) (g)
1001	1.508
1002	1.155
1003	1.156
1004	1.561
1005	1.418
1006	1.224
1007	1.383
1008	1.195
1009	1.103
1010	1.469
1011	1.252
1012	1.370
1013	1.315
1014	1.517
1015	1.030
1016	1.367
1017	1.438
1018	1.571

Generalized Results - Animals by Parameter - Fixed Time

20-110 - SARS-CoV-2 Efficacy of Calcium Glycerophosphate in a Syrian hamster model

Sex: Male Day(s): -9999 → 9999 Relative to Start Date

Grp1 Cntrl	Organ Weigh Lung(s) (g)
1019	1.398
1020	1.277
1021	1.263
1022	1.403
1023	1.361
1024	1.533
1025	1.298
1026	1.387
1027	1.356
1028	1.468
1029	1.199
1030	1.771
1031	1.862
1032	1.654
Mean	1.383
SD	0.184
N	32

Generalized Results - Animals by Parameter - Fixed Time

20-110 - SARS-CoV-2 Efficacy of Calcium Glycerophosphate in a Syrian hamster model

Sex: Male Day(s): -9999 → 9999 Relative to Start Date

Grp2 CGP	Organ Weigh Lung(s) (g)
2001	1.390
2002	1.231
2003	1.481
2004	1.831
2005	1.558
2006	1.496
2007	1.183
2008	1.405
2009	1.531
2010	2.024
2011	1.585
2012	1.209
2013	1.453
2014	1.781
2015	1.341
2016	1.175
2017	1.252
2018	1.475

Generalized Results - Animals by Parameter - Fixed Time

20-110 - SARS-CoV-2 Efficacy of Calcium Glycerophosphate in a Syrian hamster model

Sex: Male Day(s): -9999 → 9999 Relative to Start Date

Grp2 CGP	Organ Weigh Lung(s) (g)
2019	1.410
2020	1.488
2021	1.497
2022	1.257
2023	1.528
2024	1.822
2025	1.437
2026	1.435
2027	1.906
2028	1.562
2029	1.401
2030	1.154
2031	1.915
2032	1.719
Mean	1.498
SD	0.231
N	32

Appendix E. RT-qPCR Raw Data

Sample ID	Copies/Swab N2	Copies/Swab sgm
1001 Nasal Swab D1	1.81E+10	1.24E+09
1002 Nasal Swab D1	1.33E+10	8.21E+08
1003 Nasal Swab D1	1.51E+10	6.68E+08
1004 Nasal Swab D1	2.84E+10	1.14E+09
1005 Nasal Swab D1	3.04E+10	1.57E+09
1006 Nasal Swab D1	1.72E+10	8.00E+08
1007 Nasal Swab D1	7.29E+09	3.02E+08
1008 Nasal Swab D1	9.64E+09	5.52E+08
1009 Nasal Swab D1	1.45E+09	3.44E+08
1010 Nasal Swab D1	1.08E+10	6.99E+08
1011 Nasal Swab D1	8.18E+09	4.27E+08
1012 Nasal Swab D1	1.38E+10	8.26E+08
1013 Nasal Swab D1	4.38E+10	2.26E+09
1014 Nasal Swab D1	1.98E+10	1.33E+09
1015 Nasal Swab D1	2.25E+10	1.08E+09
1016 Nasal Swab D1	1.16E+10	6.14E+08
1017 Nasal Swab D1	1.13E+10	8.99E+08
1018 Nasal Swab D1	5.49E+09	7.08E+08
1019 Nasal Swab D1	1.42E+10	9.16E+08
1020 Nasal Swab D1	6.63E+09	1.77E+09
1021 Nasal Swab D1	8.33E+09	5.92E+08
1022 Nasal Swab D1	8.64E+09	1.32E+09
1023 Nasal Swab D1	2.28E+10	1.13E+09
1024 Nasal Swab D1	1.65E+10	9.81E+08
1025 Nasal Swab D1	3.39E+10	1.40E+09
1026 Nasal Swab D1	4.15E+09	3.05E+08
1027 Nasal Swab D1	7.11E+09	1.09E+09
1028 Nasal Swab D1	7.77E+09	1.10E+09
1029 Nasal Swab D1	8.81E+09	1.56E+09
1030 Nasal Swab D1	1.82E+10	1.29E+09
1031 Nasal Swab D1	1.59E+09	8.10E+07
1032 Nasal Swab D1	6.50E+09	3.95E+08
2001 Nasal Swab D1	1.21E+10	6.90E+08
2002 Nasal Swab D1	1.02E+10	3.56E+08
2003 Nasal Swab D1	6.65E+09	3.48E+08
2004 Nasal Swab D1	5.57E+09	7.40E+08
2005 Nasal Swab D1	1.56E+09	2.94E+08
2006 Nasal Swab D1	6.30E+09	1.31E+09
2007 Nasal Swab D1	1.83E+10	5.56E+08
2008 Nasal Swab D1	2.96E+10	1.03E+09
2009 Nasal Swab D1	2.93E+10	1.03E+09
2010 Nasal Swab D1	1.67E+10	5.42E+08
2011 Nasal Swab D1	3.07E+09	2.85E+08
2012 Nasal Swab D1	7.70E+09	1.07E+09
2013 Nasal Swab D1	1.63E+10	1.45E+09
2014 Nasal Swab D1	5.38E+09	8.47E+08
2015 Nasal Swab D1	2.70E+10	1.22E+09
2016 Nasal Swab D1	1.84E+10	7.56E+08
2017 Nasal Swab D1	1.79E+10	9.97E+08
2018 Nasal Swab D1	1.79E+10	6.29E+08
2019 Nasal Swab D1	8.91E+09	4.53E+08
2020 Nasal Swab D1	5.60E+09	5.23E+08
2021 Nasal Swab D1	1.76E+10	1.03E+09
2022 Nasal Swab D1	3.18E+10	1.17E+09
2023 Nasal Swab D1	4.68E+10	1.55E+09
2024 Nasal Swab D1	6.03E+10	1.75E+09
2025 Nasal Swab D1	2.06E+10	1.07E+09
2026 Nasal Swab D1	3.23E+09	1.62E+08
2027 Nasal Swab D1	7.22E+09	3.97E+08
2028 Nasal Swab D1	1.45E+10	6.75E+08
2029 Nasal Swab D1	2.22E+10	8.99E+08
2030 Nasal Swab D1	2.96E+10	1.20E+09
2031 Nasal Swab D1	2.89E+10	1.30E+09
2032 Nasal Swab D1	2.23E+10	1.12E+09
Limit of Quantification	1.25E+03	1.25E+03

Sample ID	Copies/Swab N2	Copies/Swab sgm
1001 Nasal Swab D3	1.81E+08	2.66E+07
1002 Nasal Swab D3	1.52E+08	5.37E+07
1003 Nasal Swab D3	2.50E+08	9.05E+07
1004 Nasal Swab D3	4.20E+08	3.68E+07
1005 Nasal Swab D3	2.22E+08	4.69E+06
1006 Nasal Swab D3	1.76E+08	2.63E+06
1007 Nasal Swab D3	3.10E+08	5.10E+06
1008 Nasal Swab D3	4.57E+08	9.52E+06
1009 Nasal Swab D3	2.86E+08	5.11E+07
1010 Nasal Swab D3	3.41E+08	1.01E+08
1011 Nasal Swab D3	3.31E+08	1.46E+08
1012 Nasal Swab D3	2.28E+08	2.61E+07
1013 Nasal Swab D3	2.10E+08	5.50E+06
1014 Nasal Swab D3	1.77E+08	2.39E+06
1015 Nasal Swab D3	2.21E+08	3.92E+06
1016 Nasal Swab D3	3.12E+08	4.44E+06
1017 Nasal Swab D3	8.79E+08	1.29E+07
1018 Nasal Swab D3	2.28E+08	4.97E+06
1019 Nasal Swab D3	3.92E+08	5.94E+06
1020 Nasal Swab D3	1.30E+08	2.62E+06
1021 Nasal Swab D3	2.17E+08	4.67E+06
1022 Nasal Swab D3	1.37E+08	3.74E+06
1023 Nasal Swab D3	2.36E+08	2.14E+06
1024 Nasal Swab D3	3.14E+08	4.44E+06
1025 Nasal Swab D3	4.32E+08	3.80E+06
1026 Nasal Swab D3	7.54E+08	1.75E+07
1027 Nasal Swab D3	1.28E+08	6.33E+06
1028 Nasal Swab D3	2.87E+08	5.46E+06
1029 Nasal Swab D3	1.61E+08	1.95E+06
1030 Nasal Swab D3	2.53E+08	7.85E+06
1031 Nasal Swab D3	1.70E+08	5.63E+06
1032 Nasal Swab D3	3.13E+08	3.54E+06
2001 Nasal Swab D3	4.69E+08	8.67E+06
2002 Nasal Swab D3	9.79E+07	2.26E+06
2003 Nasal Swab D3	5.50E+07	1.47E+06
2004 Nasal Swab D3	1.51E+08	3.35E+06
2005 Nasal Swab D3	1.45E+08	2.91E+06
2006 Nasal Swab D3	2.15E+08	6.65E+06
2007 Nasal Swab D3	1.00E+08	1.95E+06
2008 Nasal Swab D3	3.01E+08	5.25E+06
2009 Nasal Swab D3	9.03E+08	1.56E+07
2010 Nasal Swab D3	2.12E+08	5.36E+06
2011 Nasal Swab D3	3.32E+08	5.51E+06
2012 Nasal Swab D3	5.34E+07	6.27E+05
2013 Nasal Swab D3	6.84E+07	1.09E+06
2014 Nasal Swab D3	4.73E+07	4.63E+05
2015 Nasal Swab D3	1.04E+08	1.97E+06
2016 Nasal Swab D3	2.63E+08	3.10E+06
2017 Nasal Swab D3	5.76E+07	1.38E+06
2018 Nasal Swab D3	7.57E+07	1.71E+06
2019 Nasal Swab D3	1.35E+08	3.00E+06
2020 Nasal Swab D3	2.63E+08	4.89E+06
2021 Nasal Swab D3	6.55E+08	1.23E+07
2022 Nasal Swab D3	1.06E+08	1.82E+06
2023 Nasal Swab D3	7.66E+07	1.88E+06
2024 Nasal Swab D3	7.88E+07	1.66E+06
2025 Nasal Swab D3	1.46E+08	1.47E+06
2026 Nasal Swab D3	3.81E+08	7.02E+06
2027 Nasal Swab D3	2.45E+08	5.13E+06
2028 Nasal Swab D3	3.91E+08	5.90E+06
2029 Nasal Swab D3	2.08E+08	2.22E+06
2030 Nasal Swab D3	4.28E+08	4.86E+06
2031 Nasal Swab D3	2.27E+08	6.50E+06
2032 Nasal Swab D3	3.11E+08	7.72E+06
Limit of Quantification	1.25E+03	1.25E+03

Sample ID	Copies/Swab N2	Copies/Swab sgm
1001 Nasal Swab D5	5.23E+07	2.90E+05
1002 Nasal Swab D5	2.36E+07	2.27E+05
1003 Nasal Swab D5	3.49E+07	2.87E+05
1004 Nasal Swab D5	5.14E+08	3.59E+06
1005 Nasal Swab D5	1.84E+08	1.91E+06
1006 Nasal Swab D5	1.55E+08	9.22E+05
1007 Nasal Swab D5	9.66E+07	5.82E+05
1008 Nasal Swab D5	7.43E+07	8.62E+05
1009 Nasal Swab D5	7.55E+07	4.57E+05
1010 Nasal Swab D5	3.33E+08	2.43E+06
1011 Nasal Swab D5	8.38E+08	5.72E+06
1012 Nasal Swab D5	4.94E+08	4.91E+06
1013 Nasal Swab D5	6.66E+07	4.27E+05
1014 Nasal Swab D5	1.21E+08	6.01E+05
1015 Nasal Swab D5	1.44E+08	7.21E+05
1016 Nasal Swab D5	5.36E+08	3.53E+06
1017 Nasal Swab D5	1.31E+08	1.08E+06
1018 Nasal Swab D5	2.60E+08	1.42E+06
1019 Nasal Swab D5	1.56E+08	1.00E+06
1020 Nasal Swab D5	3.25E+07	1.52E+05
1021 Nasal Swab D5	7.65E+07	4.27E+05
1022 Nasal Swab D5	4.62E+07	1.82E+05
1023 Nasal Swab D5	7.88E+07	3.22E+05
1024 Nasal Swab D5	1.43E+08	1.24E+06
1025 Nasal Swab D5	9.03E+07	3.91E+05
1026 Nasal Swab D5	2.09E+08	1.42E+06
1027 Nasal Swab D5	2.72E+08	2.97E+06
1028 Nasal Swab D5	3.29E+08	2.50E+06
1029 Nasal Swab D5	1.93E+07	1.24E+05
1030 Nasal Swab D5	4.37E+08	2.30E+06
1031 Nasal Swab D5	1.79E+07	1.33E+05
1032 Nasal Swab D5	2.80E+08	2.92E+06
2001 Nasal Swab D5	6.23E+08	5.09E+06
2002 Nasal Swab D5	3.07E+07	1.55E+05
2003 Nasal Swab D5	1.41E+07	BQL
2004 Nasal Swab D5	1.03E+08	7.97E+04
2005 Nasal Swab D5	1.40E+08	4.91E+05
2006 Nasal Swab D5	5.72E+08	2.74E+06
2007 Nasal Swab D5	3.53E+07	1.15E+05
2008 Nasal Swab D5	2.42E+08	1.02E+06
2009 Nasal Swab D5	1.46E+08	5.82E+05
2010 Nasal Swab D5	3.60E+07	2.29E+05
2011 Nasal Swab D5	2.06E+08	5.77E+05
2012 Nasal Swab D5	1.11E+08	1.64E+05
2013 Nasal Swab D5	5.91E+07	2.02E+05
2014 Nasal Swab D5	7.02E+07	2.66E+05
2015 Nasal Swab D5	2.59E+08	5.33E+05
2016 Nasal Swab D5	2.79E+08	1.24E+06
2017 Nasal Swab D5	3.22E+07	1.57E+05
2018 Nasal Swab D5	5.36E+08	6.36E+06
2019 Nasal Swab D5	4.91E+07	2.52E+05
2020 Nasal Swab D5	1.28E+08	7.63E+05
2021 Nasal Swab D5	1.18E+08	4.48E+05
2022 Nasal Swab D5	1.26E+07	5.87E+04
2023 Nasal Swab D5	1.61E+08	5.71E+05
2024 Nasal Swab D5	5.97E+07	1.77E+05
2025 Nasal Swab D5	7.27E+07	7.48E+04
2026 Nasal Swab D5	9.78E+08	6.81E+06
2027 Nasal Swab D5	6.37E+08	7.41E+05
2028 Nasal Swab D5	2.06E+08	7.94E+05
2029 Nasal Swab D5	4.57E+08	1.77E+06
2030 Nasal Swab D5	9.81E+07	4.21E+05
2031 Nasal Swab D5	8.55E+07	4.62E+05
2032 Nasal Swab D5	2.97E+08	1.14E+06
Limit of Quantification	1.25E+03	1.25E+03

Sample ID	Copies/g Tissue N2	Copies/g Tissue sgm
1001 Lung	9.95E+09	2.26E+08
1002 Lung	4.39E+09	6.65E+07
1003 Lung	7.67E+09	1.94E+08
1004 Lung	2.90E+10	2.64E+08
1005 Lung	3.80E+10	6.94E+08
1006 Lung	4.77E+09	9.88E+07
1007 Lung	9.20E+09	1.53E+08
1008 Lung	5.38E+09	1.15E+08
1009 Lung	2.13E+09	4.67E+07
1010 Lung	1.07E+10	2.84E+08
1011 Lung	1.00E+10	1.52E+08
1012 Lung	1.02E+10	2.09E+08
1013 Lung	6.88E+09	1.62E+08
1014 Lung	3.86E+10	6.15E+08
1015 Lung	8.65E+09	2.45E+08
1016 Lung	1.52E+10	2.26E+08
1017 Lung	8.26E+09	1.32E+08
1018 Lung	4.34E+09	7.90E+07
1019 Lung	4.89E+10	1.08E+09
1020 Lung	7.31E+09	1.32E+08
1021 Lung	1.19E+10	1.47E+08
1022 Lung	1.37E+10	2.82E+08
1023 Lung	1.22E+10	2.84E+08
1024 Lung	7.44E+09	1.20E+08
1025 Lung	4.29E+09	6.63E+07
1026 Lung	1.03E+10	1.91E+08
1027 Lung	5.05E+10	9.35E+08
1028 Lung	2.27E+10	3.36E+08
1029 Lung	1.60E+10	2.50E+08
1030 Lung	1.79E+10	2.73E+08
1031 Lung	1.37E+09	2.46E+07
1032 Lung	1.09E+10	2.39E+08
2001 Lung	4.03E+10	5.67E+08
2002 Lung	4.35E+09	8.33E+07
2003 Lung	2.04E+09	3.99E+07
2004 Lung	1.06E+10	2.18E+08
2005 Lung	8.41E+09	1.30E+08
2006 Lung	3.28E+10	6.94E+08
2007 Lung	2.43E+10	8.67E+08
2008 Lung	7.24E+09	1.61E+08
2009 Lung	1.45E+10	2.83E+08
2010 Lung	3.08E+10	8.09E+08
2011 Lung	1.04E+10	1.29E+08
2012 Lung	2.19E+10	5.56E+08
2013 Lung	1.83E+09	2.14E+07
2014 Lung	1.27E+10	3.31E+08
2015 Lung	6.25E+09	1.89E+08
2016 Lung	2.43E+10	4.81E+08
2017 Lung	1.38E+10	2.42E+08
2018 Lung	2.11E+10	3.47E+08
2019 Lung	1.17E+10	1.31E+08
2020 Lung	8.97E+09	9.08E+07
2021 Lung	2.86E+10	4.71E+08
2022 Lung	5.93E+09	7.30E+07
2023 Lung	1.14E+10	1.69E+08
2024 Lung	2.43E+09	3.63E+07
2025 Lung	2.09E+10	2.80E+08
2026 Lung	1.86E+10	2.28E+08
2027 Lung	6.82E+09	1.15E+08
2028 Lung	1.66E+10	2.10E+08
2029 Lung	1.08E+10	1.62E+08
2030 Lung	2.96E+09	6.97E+07
2031 Lung	1.35E+10	3.78E+08
2032 Lung	1.97E+10	3.60E+08
Limit of Quantification	1.95E+04	1.95E+04