AVIPure® AAV2 Affinity Resin

Regulatory Support File

AVITIDE | A REPLIGEN COMPANY

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INSPIRING ADVANCES IN BIOPROCESSING

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Abbreviations

AAV	Adeno-associated virus
ASTM	American society for testing and materials
BSE	Bovine spongiform encephalopathy
C	Celsius
CFU	Colony-forming unit
cm	Centimeter
DMF	*N,N*-dimethylformamide
DMAP	4-(dimethylamino) pyridine
DSC	*N,N'*-disuccinimidyl carbonate
EDA	Ethylenediamine
EU	Endotoxin units
FTIR	Fourier transform infrared spectroscopy
HEPA	High efficiency particulate air (filter)
HDPE	High density polyethylene
HP-SEC	High performance size-exclusion chromatography
hr	Hour
HVAC	Heating, ventilation, and air conditioning
LAL	Limulus amebocyte lysate
LOD	Limit of detection
LOQ	Limit of quantitation
µm	Micrometer
µmol	Micromole
µS	Microsecond
mL	Milliliter
mg	Milligram
NaOH	Sodium hydroxide
NHS	*N*-hydroxysuccinimide
PET	Polyethylene terephthalate
ppm	Parts per million
RODI	Reverse osmosis deionized water
SDS	Safety data sheet
TAMC	Total aerobic microbial count
TOC	Total organic carbon
TSE	Transmissible spongiform encephalopathy
TYM	Total yeasts and molds
UPLC	Ultra performance liquid chromatography

1. Introduction

The purpose of this document is to provide customers in filings for regulatory approval of drug substances produced using AVIPure® AAV2 Affinity Resin as a process aid in the purification process. Requests for audits or additional information can be directed to Avitide at LBN-quality@repligen.com.

Safety notices:

- For laboratory and manufacturing production use only
- Not for administration to humans
- The safety data sheet (SDS) is included as an attachment in Section 7 and describes that the product is shipped in an aqueous 2% benzyl alcohol, a bacteriostatic agent. It is flushed from the resin during equilibration and preparation for use.
- Follow all local regulations for safe disposal

2. Manufacturing information

2.1 Introduction: Manufacturing

AVIPure® AAV2 Affinity Resin is manufactured by Avitide, LLC, a Repligen company, located at 16 Cavendish Ct, Lebanon, NH 03766. This resin was first manufactured as a commercially supplied product in 2021. The resin is comprised of a recombinant protein conjugated to an agarose bead.

2.2 Quality Management System

Commercially supplied resins are manufactured under Avitide's ISO 9001 certified quality management system. Certification is provided by Bureau Veritas and was first awarded in August 2017. Certification renewal was achieved in 2020. The current certificate can be accessed from the by contacting LBN-quality@repligen.com and the certificate is shown in Section 7. Documents and records are maintained electronically.

2.2.1 Process Change Control

Manufacturing process changes are governed by the Avitide change management procedures.

2.2.2 Product Storage Control

Product is stored in temperature-controlled units. All units are monitored, and an alarm cascade notifies responsible personnel by email and text message of any excursions.

2.2.3 Calibration Control

Equipment and monitoring devices are controlled through the Avitide equipment management process. Each piece of equipment is uniquely identified and has a preventive maintenance and/or calibration schedule as necessary.

2.3 Business continuity

In order to avoid disruptions to supply to customers of AVIPure® AAV2 Affinity Resin, wherever possible, Avitide avoids the use of sole source suppliers and has qualified both primary and secondary suppliers of critical materials. Additionally, Avitide plans for supply chain disruptions by maintaining adequate stock of critical materials to meet forecasted production needs.

2.4 Facilities

Avitide facilities are designed for controlled storage and flow of materials. Material storage areas at -80 °C, -20 °C, 5 °C, and ambient conditions are available with both quarantine and released sections.

2.4.1 Clean room

Resins are manufactured in a controlled environment with its own heating, ventilation, and air conditioning (HVAC) system. Air quality is maintained by 100% HEPA filtered air, which is tested to ISO Class 8 specifications for non-viable particulates. Routine environmental monitoring is performed to check for viable contamination. The clean room is a secure area and access is restricted to authorized personnel only. Personnel entering the clean room adhere to gowning and personnel/material flow procedures at all times.

2.4.2 Purified water

USP purified grade II water for use in resin production is generated in-house from a Reverse Osmosis/Deionization (RODI) plant. The RODI system is fully automated and provides high quality water in a continuously circulating loop. The water system design performance specifications are ASTM Type I Reagent Grade Water supplemented with extra specifications to address low endotoxin and bioburden requirements. The complete specifications are shown in Table 1. Water quality is routinely monitored by Avitide Quality Control.

Table 1. Purified water specifications

Criteria	Specification
Conductivity	1.3 µS/cm
LAL	< 0.25 EU/mL
TOC	0.5 ppm

2.4.3 Waste disposal

Waste disposal is handled by a contracted third-party organization in accordance with state and local regulations.

2.5 Process description

The process involves coupling a ligand that contains a single cysteine residue with a bromoacetyl functionalized resin. The preparation of the bromoacetyl functionalized resin is a three-step process:

1. NHS activation of the base bead.
2. Conjugating ethylenediamine spacer.
3. Functionalization of the free amine of ethylenediamine with bromoacetic acid.

The initial step is NHS activation of the base bead. This chemistry is based on the following publication:

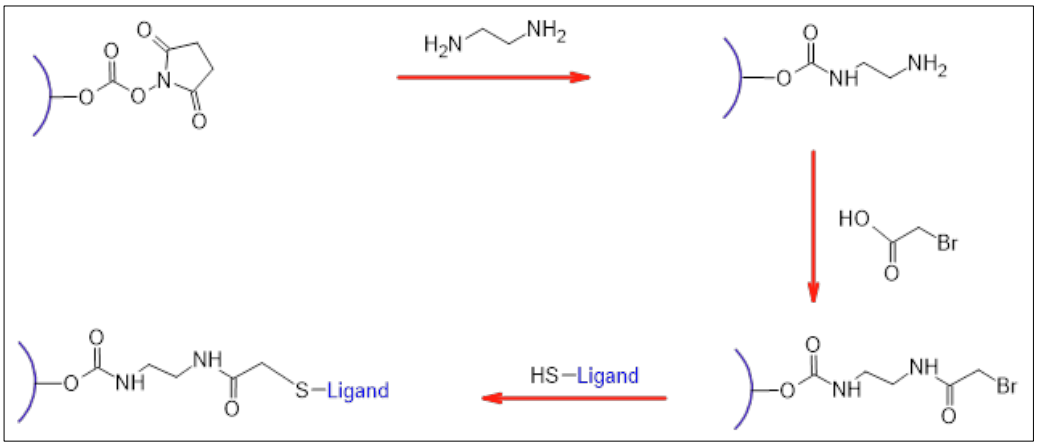
Wilchek, M., Miron, T. Activation of Sepharose with *N,N'*-disuccinimidyl carbonate. Appl Biochem Biotechnol 11, 191–193 (1985) https://doi.org/10.1007/BF02798475

The chemistry involves activation of hydroxyl groups forming an intermediate reactive carbonate ester.

In the second step an ethylenediamine linker generates a carbamate bond of the linker to the bead and a free amine at the other end of the linker (Figure 1).

In the third step bromoacetic acid is conjugated to the free amine of the linker. Lastly, the free thiol of the cysteine contained within the ligand is reacted with the bromoacetyl group, which has high reactivity and high specificity towards the thiol over amine groups.

Figure 1. Reaction overview for the activation of resin and coupling of thiol ligands, beginning with the NHS activated resin



The entire production process takes place in a closed system. Cross-linked agarose resin stored in 20% ethanol is loaded into a reactor. The aqueous supernatant is replaced with dry dimethylformamide (DMF). Once moisture content is confirmed to be sufficiently low, the resin is activated. The activation level is confirmed, then the conjugation solution containing the recombinant ligand is added to effect conjugation. The conjugation is confirmed to be complete, then the resin is washed to remove residual activation and conjugation solutions. Once complete, the resin is put into 2% benzyl alcohol and removed from the reactor into bottles ahead of release by Quality Assurance.

3. Product information

Table 2. Product specifications

Criteria	Specification
Total bioburden	Sum of TAMC and TYM: ≤ 100 CFU/mL
Visual inspection	White to off-white slurry
Resin characterization	FTIR spectrum matches library reference
Ligand confirmation	Ligand identity confirmed
Resin specificity	Target binds

3.1 Product description

AVIPure® AAV2 Affinity Resin is a cross-linked agarose resin conjugated with a recombinant protein ligand for bind and elute purification of adeno-associated virus particles (AAV2) directly from clarified culture fluid. List of product attributes shown in Table 3.

Table 3. Product attributes of AVIPure® AAV2 Affinity Resin

Category	Description
Base matrix	Cross-linked agarose, spherical
Particle size (d_{50v})[1]	50 µm
Ligand	Protein (recombinant)
Coupling chemistry	Thiol
Binding capacity	>2 x 10^{14} vp/mL_{res} of chromatography medium, depending on composition of feed stock, at 1 min residence time
Buffer compatibility	Stable to all commonly used aqueous buffers, including 8 M urea, 6 M guanidine hydrochloride, ethylene glycol, and detergents
Solvent compatibility	Water, alcohol (0 - 20% v/v), acetonitrile, 1–2 M acetic acid, other common organic solvents
pH stability	1 - 13
Cleaning-in-place stability	0.1 M NaOH
Pressure/flow[2]	3 bar at >300 cm/hr
Temperature stability	2 - 40 °C
Delivery conditions	2% benzyl alcohol
Storage	2 - 8 °C, 2% benzyl alcohol; do not freeze

[1] Median particle size of cumulative volume distribution.
[2] In a 2.6 x 20 cm column pressure packed at 4 bar.

3.1.1 Ligand description

The AVIPure® AAV2 Affinity Resin ligand is produced by E. coli fermentation and purified by cation exchange. The concentration, identity, purity, percent active binding sites by conjugation efficiency, and endotoxin level of the ligand is confirmed prior to conjugation. Required testing and specifications are shown below in Table 4.

Table 4. Ligand testing and specifications

Method	Test	Specification
SOP-00090	Absorbance at λ=280 nm	Report
ANM-00034	Purity by UPLC	Report; ≥90% is typical
SOP-ANA-042	Monomeric purity by HP-SEC	Report; ≥95% is typical
ANM-00317	Endotoxin	≤1 EU/mg
SOP-00362	Molecular weight by LC/MS	Mass confirmed
SOP CNJ-010	Small scale determination of conjugation efficiency	Report; conjugation efficiency ~80% is typical. Report amount of ligand required to achieve target on-resin ligand density.

3.2 Materials and reagents

Table 5. Materials used in the production of AVIPure® AAV2 Affinity Resin

Material Name	Step(s) where used
Highly cross-linked agarose beads	Starting material; base resin
Dimethylformamide (DMF)	Dewatering, activation
N,N'-Disuccinimidyl carbonate (DSC)	Activation
4-(Dimethylamino) pyridine (DMAP)	Activation
Bromoacetic acid	Activation
Ethylenediamine (EDA)	Activation
2-(N-Morpholino) ethanesulfonic acid monohydrate (MES)	Activation
3-(3-Dimethylaminopropyl)-1-ethyl-carbodiimide hydrochloride (EDC.HCl)	Activation
Boric acid	Conjugation, post-conjugation washing
Recombinant protein ligand	Starting material; conjugation
Thioglycerol	Post-conjugation blocking
Sodium hydroxide (NaOH, aqueous)	Conjugation, post-conjugation washing
Benzyl alcohol	Down packing, storage
Purified water	Aqueous buffer preparation
PET containers with HDPE caps	Bulk product temporary storage
HDPE containers	Final product storage

Materials used in the resin production process are listed in the table above along with the process step where they are used.

Materials are held at the conditions recommended by the supplier. All raw materials are assessed for risk of transmissible spongiform encephalopathy (TSE/BSE). Where animal-derived components are used in final packaging materials (colorant of caps), sourcing and handling is in accordance with European guidance document EMEA/410/01 version 3 on animal derivatives entitled "Note for guidance on minimizing the risk of transmitting animal spongiform encephalopathy agents via human and veterinary medicinal products" and risk of BSE/TSE transmission is negligible.

3.3 Base beads

The agarose base bead is a major constituent of the affinity resin and is described in detail in this section. AVIPure® AAV2 Affinity Resin is produced using Praesto Jetted A50 intermediate 2 agarose beads manufactured by Purolite®.

3.3.1 Description

Agarose is an inert polysaccharide which forms hydrophilic and high strength gels at low concentrations. Agarose beads are small spherical and porous particles manufactured from agarose. The resin is very hydrophilic, resulting in very low non-specific interactions, and its microporous structure confers a great internal surface area providing a very high binding capability when the beads are activated. These chromatographic resin beads have been commonly used in commercial manufacturing for many years.

Purolite Praesto Jetted A50 resin is composed of agarose beads chemically crosslinked to improve their mechanical strength. This material is provided as an aqueous suspension using 20% ethanol as preservative.

3.3.2 Statement of Origins

Purolite Praesto Jetted A50 resin is manufactured from naturally derived agarose and produced without the use of specific risk materials as defined in European Commission Decision 97/534/EC.

The manufacturing process does not use any ingredient or risk material from animal origin. The resin is therefore considered free from Transmissible Animal Spongiform Encephalopathy (TSE/BSE).

3.4 Technical specifications

3.4.1 Raw materials

Certificates of analysis are received and reviewed for all raw materials used in production. Additional analyses performed on materials prior to release are shown in Table 6.

Table 6. Analysis performed on materials prior to use in production of AVIPure® AAV2 Affinity Resin

Material name	Analysis for release
Highly cross-linked agarose beads	Particle size Exclusion limit Appearance Endotoxin content Hydraulic performance
Dimethylformamide (DMF)	Water content Amine content Identity and purity Appearance
N,N'-Disuccinimidyl carbonate (DSC)	Water content Molar activation level Appearance
4-(Dimethylamino) pyridine (DMAP)	Identity and purity Appearance
Bromoacetic acid	Appearance
Ethylenediamine (EDA)	Identity and purity Appearance
2-(N-Morpholino) ethanesulfonic acid monohydrate (MES)	Appearance
3-(3-Dimethylaminopropyl)-1-ethyl-carbodiimide hydrochloride (EDC.HCl)	Identity Appearance
Boric acid	Appearance
Recombinant protein ligand	Concentration Identity confirmation Monomerity Purity Conjugation efficiency Endotoxin content
Thioglycerol	Identity Appearance
Sodium hydroxide (NaOH, aqueous)	Appearance
Benzyl alcohol	Water content Identity and purity Appearance
Purified water	Resistivity Total organic content (TOC) Endotoxin

3.4.2 In process testing

Table 7. In process testing of AVIPure® AAV2 Affinity Resin

Step	Parameter verified
Resin de-watering	Water content
Resin NHS activation	NHS activation level
Resin bromoacetyl activation	Bromoacetyl activation level
Conjugation	On-resin ligand density
Down packing from reactor	Slurry resin ratio

3.4.3 Final product

Table 8. Final product specifications for AVIPure® AAV2 Affinity Resin

Parameter	Specification
Total bioburden	Sum of TAMC and TYM ≤100 CFU/mL
Ligand confirmation	Ligand identity confirmed
Resin characterization	FTIR spectrum matches library reference
Visual inspection	White to off-white particulate suspension
Resin Specificity	Target binds

3.4.4 Overview of analytical methods

3.4.4.1 Hydraulic performance

Resin is packed in a 1.5 x 35 cm column to a 17 cm bed height. Deionized water is flowed across the bed at increasing flow rates to the defined maximum to confirm no bed collapse as indicated by a pressure greater than 75 psi (5 bar).

3.4.4.2 Particle size

Particle size is measured using a Coulter Counter Multisizer 3 particle size analyzer. As the Coulter method does not allow for direct measurement of porous materials such as resins and will underestimate size as a result of the porosity, the output from the Multisizer is correlated to an accurate size range determined by contracted analysis of resins of various sizes using laser diffraction.

The standard deviation and relative standard deviation of this method are 1.3 µm and 1.5%, respectively.

3.4.4.3 NHS activation level

Resin activation level is measured by treating activated resin with ammonium hydroxide and measuring the resulting free N-hydroxy succinimide (NHS) by UV-Vis. From the weight of the resin used for the assay, the activation level of the resin can be determined.

The standard deviation and relative standard deviation of this method are 0.40 µmol/g and 1.5%, respectively.

3.4.4.4 Bromoacetyl activation level

Bromoacetyl activation level is measured by treating the resin with thioglycerol and measuring the concentration of bromide ion that is released using ion chromatography. The activation level is determined based on the weight of resin used in the assay.

The standard deviation and relative standard deviation of this method are 0.23 µmol/g and 1.79%, respectively.

3.4.4.5 Ligand density

After the UPLC system to be used has been demonstrated to be suitable based on replicate injection peak area and retention time relative standard deviation values of ≤2.0%, the peak area of the conjugation solution, and all wash solutions are determined. Incorporating the size of the washes and the peak area, the conjugation efficiency is determined as a percentage. This percentage is then multiplied by the initial ligand concentration to determine on resin ligand density.

The LOD and LOQ of this method are 0.02 and 0.065 µg, respectively. The standard deviation and relative standard deviation are 0.024 mg/mL and 2.4%, respectively.

3.4.4.6 FTIR

Resin is analyzed by FTIR by removing the supernatant from the resin and comparing the sample against standard spectra.

3.4.4.7 Bioburden

Bioburden testing for total aerobic microbial count and total yeasts and moles is performed per USP <61> Microbial Enumeration by a site accredited to ISO/IEC 17025:2017.

3.4.4.8 Appearance

Appearance testing is performed by inspecting a set amount of resin in a clear container.

4. Production and performance consistency

The production process results in consistent production of AVIPure® AAV2 Affinity Resin. Methods for activation level and ligand density are described in Section 3.4.4.5. Across three large scale batches, ligand density levels were achieved with 3.1% RSD. The FTIR traces of the three resins agreed with the reference spectra established during transfer to commercial production. Dynamic binding capacity as measured by 10% breakthrough was demonstrated to be >2 x 10^{14} vp/mL_{resin} for each of the three batches.

5. Stability

5.1 Resin stability

5.1.1 Storage stability

Accelerated short term stability studies have been initiated at 40 °C supporting a 3- year retest date. Results are presented in Table 9 below. For these studies a control sample was held at 4 °C until the test date. The stability samples were placed into storage at decreasing intervals (e.g., two months from the test date, then one month from the test date) and all samples tested on the test date. Samples were packed into 0.18 mL columns and challenged with 5 x 10^{12} vp/mL purified AAV2 capsids with a 1-minute residence time. Binding capacity (10% breakthrough) was measured using commercially available AAV2 PROGEN ELISA Kits.

A long-term stability study of AVIPure® AAV2 Affinity Resin held at recommended storage condition of 4 °C has been commenced and will run for 3 years. When complete the report will be made available to users upon request.

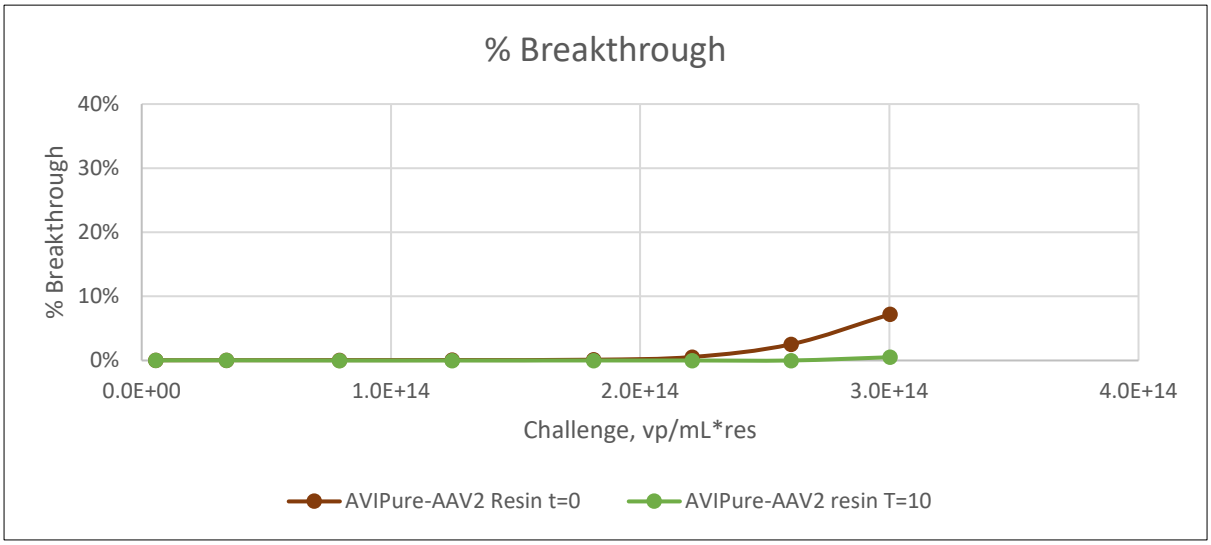
Table 9. Accelerated stability study at 40 °C.

Condition	Storage time	Capacity
40 °C in 2% benzyl alcohol	12 weeks	4.2 x 10^{14} vp/mL_{resin}
40 °C in 2% benzyl alcohol	18 weeks	3.7 x 10^{14} vp/mL_{resin}
Control: 4 °C in 2% benzyl alcohol	20 weeks	4.1 x 10^{14} vp/mL_{resin}

5.1.2 Resin lifetime

Initial studies into NaOH stability showed stability of AVIPure® AAV2 Affinity Resin. Resin was incubated in 0.5 M NaOH for 10 hours, with performance being measured at T=0 and T=10 hour timepoints. See Figure 2.

Figure 2. Breakthrough curves of AVIPure® AAV2 resin before and after 10 hours of exposure to 0.5 M NaOH



6. Product safety

The primary constituents of AVIPure® AAV2 Affinity Resin are the agarose bead and the protein ligand.

Benzyl alcohol added as a preservative is addressed in the SDS. It is used only as a bacteriostatic agent and is flushed from the resin during equilibration and preparation for use. Residual solvents and reagents used in the manufacturing process are addressed below.

6.1 Agarose bead

The SDS for Purolite® A50 base bead is included in Attachment 7.3.

6.2 Protein ligand

Ligand toxicity was evaluated by single dose intravenous administration in Wistar rats with a 14-day observation period. Ten Wistar rats were acclimated for five days prior to the study. A slow bolus dose of 10 mg/kg was administered intravenously over a 1-minute period on the first day of the study to each animal. Daily clinical observations were performed.

All results were normal with no abnormal findings at gross necropsy. The ligand was tolerated by all animals in the study. The protein ligand is nontoxic.

6.3 Residual solvents and reagents

Table 10. Residual solvent and reagents material

Material name	Amount detected
Dimethylformamide (DMF)	Testing pending*; theoretical value in final product is <0.05 ppm
N,N'-disuccinimidyl carbonate (DSC) as N-hydroxysuccinimide (NHS)	<14 ppm (LOD)
4-(Dimethylamino)pyridine (DMAP)	<0.4 ppm (LOD)

*Upon completion of testing, report will be available upon user's request.

7. Attachments

7.1 Attachment 1: AVIPure® AAV2 Safety Data Sheet

7.2 Attachment 2: ISO 9001 Certificate

7.3 Attachment 3: SDS for Purolite® Praesto Jetted A50 Intermediate 2

7.4 Attachment 4: BSE/TSE Statement for AVIPure® AAV2

7.5 Attachment 5: REACH Statement for AVIPure® AAV2

7.6 Attachment 6: RoHS Statement for AVIPure® AAV2

7.7 Attachment 7: AVIPure® AAV2 Ligand Toxicity Report

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REPLIGEN

AVIPure® - AAV Affinity Resins

Safety Data Sheet

According To Federal Register / Vol. 77, No. 58 / Monday, March 26, 2012 / Rules And Regulations
Date of Issue: 01/12/2022 Version: 1.0

SECTION 1: IDENTIFICATION

1.1. Product Identifier

Product Form: Mixture

Product Name: AVIPure® - AAV Affinity Resins

Synonyms:

AVIPure® - AAV2 (100AAV2)

AVIPure® - AAV8 (100AAV8)

AVIPure® - AAV9 (100AAV9)

1.2. Intended Use of the Product

Use of the Substance/Mixture: For research use only. Not for use in diagnostics procedures

1.3. Name, Address, and Telephone of the Responsible Party

Company

Repligen Corporation
16 Cavendish Ct, Suite 151
Lebanon, NH 03766
USA
+1 603-965-2100
customerserviceUS@repligen.com

1.4. Emergency Telephone Number

Emergency Number : ChemTel LLC
(800)255-3924 (North America)
+1 (813)248-0585 (International)

SECTION 2: HAZARDS IDENTIFICATION

2.1. Classification of the Substance or Mixture

GHS-US Classification

Not classified

2.2. Label Elements

GHS-US Labeling

No labeling applicable according to 29 CFR 1910.1200.

2.3. Other Hazards

Exposure may aggravate pre-existing eye, skin, or respiratory conditions.

2.4. Unknown Acute Toxicity (GHS-US)

No data available

SECTION 3: COMPOSITION/INFORMATION ON INGREDIENTS

3.1. Substance

Not applicable

3.2. Mixture

Name	Synonyms	Product Identifier	%	GHS US classification
Benzyl alcohol	Benzenecarbinol / Benzenemethanol / Methanol, phenyl- / Phenylmethanol / Phenylmethyl alcohol / BENZYL ALCOHOL / .alpha.-Hydroxytoluene / Benzylalcohol	(CAS-No.) 100-51-6	0.1 – 1	Flam. Liq. 4, H227 Acute Tox. 4 (Oral), H302 Acute Tox. 4 (Inhalation:dust,mist), H332 Eye Irrit. 2A, H319 Aquatic Acute 2, H401

Full text of H-phrases: see section 16

The specific chemical identity and/or exact percentage of composition have been withheld as a trade secret [29 CFR 1910.1200].

SECTION 4: FIRST AID MEASURES

4.1. Description of First-aid Measures

First-aid Measures General: Never give anything by mouth to an unconscious person. If you feel unwell, seek medical advice (show the label where possible). If product is biologically contaminated, follow all institutional protocols concerning the potential release of pathogens.

First-aid Measures After Inhalation: When symptoms occur: go into open air and ventilate suspected area. Obtain medical attention if breathing difficulty persists.

First-aid Measures After Skin Contact: Remove contaminated clothing. Drench affected area with water for at least 5 minutes. Obtain medical attention if irritation develops or persists.

First-aid Measures After Eye Contact: Rinse cautiously with water for at least 5 minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Obtain medical attention if irritation develops or persists.

First-aid Measures After Ingestion: Rinse mouth. Do NOT induce vomiting. Obtain medical attention.

4.2. Most Important Symptoms and Effects Both Acute and Delayed

Symptoms/Injuries: Not expected to present a significant hazard under anticipated conditions of normal use.

Symptoms/Injuries After Inhalation: Prolonged exposure may cause irritation.

Symptoms/Injuries After Skin Contact: Prolonged exposure may cause skin irritation.

Symptoms/Injuries After Eye Contact: May cause slight irritation to eyes.

Symptoms/Injuries After Ingestion: Ingestion may cause adverse effects.

Chronic Symptoms: None expected under normal conditions of use.

4.3. Indication of Any Immediate Medical Attention and Special Treatment Needed

If exposed or concerned, get medical advice and attention. If medical advice is needed, have product container or label at hand.

SECTION 5: FIRE-FIGHTING MEASURES

5.1. Extinguishing Media

Suitable Extinguishing Media: Water spray, fog, carbon dioxide (CO_2), alcohol-resistant foam, or dry chemical.

Unsuitable Extinguishing Media: Do not use a heavy water stream. Use of heavy stream of water may spread fire.

5.2. Special Hazards Arising From the Substance or Mixture

Fire Hazard: Not considered flammable but may burn at high temperatures.

Explosion Hazard: Product is not explosive.

Reactivity: Hazardous reactions will not occur under normal conditions.

5.3. Advice for Firefighters

Precautionary Measures Fire: Exercise caution when fighting any chemical fire.

Firefighting Instructions: Use water spray or fog for cooling exposed containers.

Protection During Firefighting: Do not enter fire area without proper protective equipment, including respiratory protection.

Hazardous Combustion Products: Carbon oxides (CO, CO_2).

SECTION 6: ACCIDENTAL RELEASE MEASURES

6.1. Personal Precautions, Protective Equipment and Emergency Procedures

General Measures: Avoid prolonged contact with eyes, skin and clothing. Avoid breathing (vapor, mist, spray).

6.1.1. For Non-Emergency Personnel

Protective Equipment: Use appropriate personal protective equipment (PPE).

Emergency Procedures: Evacuate unnecessary personnel.

6.1.2. For Emergency Personnel

Protective Equipment: Equip cleanup crew with proper protection.

Emergency Procedures: Upon arrival at the scene, a first responder is expected to recognize the presence of dangerous goods, protect oneself and the public, secure the area, and call for the assistance of trained personnel as soon as conditions permit. Ventilate area.

6.2. Environmental Precautions

Prevent entry to sewers and public waters.

6.3. Methods and Materials for Containment and Cleaning Up

For Containment: Contain any spills with dikes or absorbents to prevent migration and entry into sewers or streams.

Methods for Cleaning Up: Clean up spills immediately and dispose of waste safely. Transfer spilled material to a suitable container for disposal. Contact competent authorities after a spill.

6.4. Reference to Other Sections

See Section 8 for exposure controls and personal protection and Section 13 for disposal considerations.

SECTION 7: HANDLING AND STORAGE

7.1. Precautions for Safe Handling

Precautions for Safe Handling: Wash hands and other exposed areas with mild soap and water before eating, drinking or smoking and when leaving work. Avoid prolonged contact with eyes, skin and clothing. Avoid breathing vapors, mist, spray. If product is biologically contaminated, follow all institutional protocols concerning the potential release of pathogens.

Hygiene Measures: Handle in accordance with good industrial hygiene and safety procedures.

7.2. Conditions for Safe Storage, Including Any Incompatibilities

Technical Measures: Comply with applicable regulations.

Storage Conditions: Keep container closed when not in use. Store in a dry, cool place. Keep/Store away from direct sunlight, extremely high or low temperatures and incompatible materials.

Incompatible Materials: Strong acids, strong bases, strong oxidizers.

7.3. Specific End Use(s)

For research use only. Not for use in diagnostics procedures

SECTION 8: EXPOSURE CONTROLS/PERSONAL PROTECTION

8.1. Control Parameters

For substances listed in section 3 that are not listed here, there are no established exposure limits from the manufacturer, supplier, importer, or the appropriate advisory agency including: ACGIH (TLV), AIHA (WEEL), NIOSH (REL), or OSHA (PEL).

Benzyl alcohol (100-51-6)		
USA AIHA	WEEL TWA [ppm]	10 ppm

8.2. Exposure Controls

Appropriate Engineering Controls : Suitable eye/body wash equipment should be available in the vicinity of any potential exposure. Ensure adequate ventilation, especially in confined areas. Ensure all national/local regulations are observed.

Personal Protective Equipment : Gloves. Protective clothing. Protective goggles.

Materials for Protective Clothing : Chemically resistant materials and fabrics.

Hand Protection : Wear protective gloves.

Eye and Face Protection : Chemical safety goggles.

Skin and Body Protection : Wear suitable protective clothing.

Respiratory Protection : If exposure limits are exceeded or irritation is experienced, approved respiratory protection should be worn. In case of inadequate ventilation, oxygen deficient atmosphere, or where exposure levels are not known wear approved respiratory protection.

Other Information : When using, do not eat, drink or smoke.

SECTION 9: PHYSICAL AND CHEMICAL PROPERTIES

9.1. Information on Basic Physical and Chemical Properties

Physical State	: Liquid
Appearance	: Liquid
Odor	: No data available
Odor Threshold	: No data available
pH	: No data available
Evaporation Rate	: No data available
Melting Point	: No data available
Freezing Point	: No data available
Boiling Point	: No data available
Flash Point	: No data available
Auto-ignition Temperature	: No data available
Decomposition Temperature	: No data available
Flammability (solid, gas)	: Not applicable
Vapor Pressure	: No data available
Relative Vapor Density at 20°C	: No data available
Relative Density	: No data available
Solubility	: No data available
Partition Coefficient: N-Octanol/Water	: No data available
Viscosity	: No data available

9.2. Other Information

No additional information available

SECTION 10: STABILITY AND REACTIVITY

10.1. Reactivity

Hazardous reactions will not occur under normal conditions.

10.2. Chemical Stability
Stable under recommended handling and storage conditions (see section 7).

10.3. Possibility of Hazardous Reactions
Hazardous polymerization will not occur.

10.4. Conditions to Avoid
Direct sunlight, extremely high or low temperatures, and incompatible materials.

10.5. Incompatible Materials
Strong acids, strong bases, strong oxidizers.

10.6. Hazardous Decomposition Products
None expected under normal conditions of use.

SECTION 11: TOXICOLOGICAL INFORMATION

11.1. Information on Toxicological Effects
Acute Toxicity (Oral): Not classified (Based on available data, the classification criteria are not met)
Acute Toxicity (Dermal): Not classified (Based on available data, the classification criteria are not met)
Acute Toxicity (Inhalation): Not classified (Based on available data, the classification criteria are not met)

Benzyl alcohol (100-51-6)	
LD50 Oral Rat	1230 mg/kg
LD50 Dermal Rabbit	> 2000 mg/kg
LC50 Inhalation Rat	> 4.178 mg/l/4h
ATE (Dust/Mist)	1.50 mg/l/4h

Skin Corrosion/Irritation: Not classified (Based on available data, the classification criteria are not met)
Serious Eye Damage/Irritation: Not classified (Based on available data, the classification criteria are not met)
Respiratory or Skin Sensitization: Not classified (Based on available data, the classification criteria are not met)
Germ Cell Mutagenicity: Not classified (Based on available data, the classification criteria are not met)
Carcinogenicity: Not classified (Based on available data, the classification criteria are not met)
Reproductive Toxicity: Not classified (Based on available data, the classification criteria are not met)
Specific Target Organ Toxicity (Single Exposure): Not classified (Based on available data, the classification criteria are not met)
Specific Target Organ Toxicity (Repeated Exposure): Not classified (Based on available data, the classification criteria are not met)
Aspiration Hazard: Not classified (Based on available data, the classification criteria are not met)
Symptoms/Injuries After Inhalation: Prolonged exposure may cause irritation.
Symptoms/Injuries After Skin Contact: Prolonged exposure may cause skin irritation.
Symptoms/Injuries After Eye Contact: May cause slight irritation to eyes.
Symptoms/Injuries After Ingestion: Ingestion may cause adverse effects.
Chronic Symptoms: None expected under normal conditions of use.

SECTION 12: ECOLOGICAL INFORMATION

12.1. Toxicity
Ecology - General : Not classified.

Benzyl alcohol (100-51-6)	
LC50 Fish 1	460 mg/l (Exposure time: 96 h - Species: Pimephales promelas [static])
LC50 Fish 2	10 mg/l (Exposure time: 96 h - Species: Lepomis macrochirus [static])
NOEC Chronic Crustacea	51 mg/l

12.2. Persistence and Degradability

AVIPure® - AAV Affinity Resins	
Persistence and Degradability	Not established.

12.3. Bioaccumulative Potential

AVIPure® - AAV Affinity Resins	
Bioaccumulative Potential	Not established.

Benzyl alcohol (100-51-6)	
Partition coefficient n-octanol/water (Log Pow)	1.1

12.4. Mobility in Soil
No additional information available

AVIPure® - AAV Affinity Resins

Safety Data Sheet

12.5. Other Adverse Effects

Other Information : Avoid release to the environment.

SECTION 13: DISPOSAL CONSIDERATIONS

13.1. Waste Treatment Methods

Waste Disposal Recommendations: Dispose of contents/container in accordance with local, regional, national, and international regulations.

Ecology - Waste Materials: Avoid release to the environment.

SECTION 14: TRANSPORT INFORMATION

The shipping description(s) stated herein were prepared in accordance with certain assumptions at the time the SDS was authored, and can vary based on a number of variables that may or may not have been known at the time the SDS was issued.

14.1. In Accordance with DOT

Not regulated for transport

14.2. In Accordance with IMDG

Not regulated for transport

14.3. In Accordance with IATA

Not regulated for transport

SECTION 15: REGULATORY INFORMATION

15.1. US Federal Regulations

Benzyl alcohol (100-51-6)
Listed on the United States TSCA (Toxic Substances Control Act) inventory - Status: Active

15.2. US State Regulations

Benzyl alcohol (100-51-6)
U.S. - Pennsylvania - RTK (Right to Know) List
U.S. - Massachusetts - Right To Know List

SECTION 16: OTHER INFORMATION, INCLUDING DATE OF PREPARATION OR LAST REVISION

Date of Preparation or Latest Revision : 01/12/2022

Other Information : This document has been prepared in accordance with the SDS requirements of the OSHA Hazard Communication Standard 29 CFR 1910.1200

GHS Full Text Phrases:

Acute Tox. 4 (Inhalation:dust,mist)	Acute toxicity (inhalation:dust,mist) Category 4
Acute Tox. 4 (Oral)	Acute toxicity (oral) Category 4
Aquatic Acute 2	Hazardous to the aquatic environment - Acute Hazard Category 2
Comb. Dust	Combustible Dust
Eye Irrit. 2A	Serious eye damage/eye irritation Category 2A
Flam. Liq. 4	Flammable liquids Category 4
H227	Combustible liquid
H302	Harmful if swallowed
H319	Causes serious eye irritation
H332	Harmful if inhaled
H401	Toxic to aquatic life

This information is based on our current knowledge and is intended to describe the product for the purposes of health, safety and environmental requirements only. It should not therefore be construed as guaranteeing any specific property of the product.

SDS US (GHS HazCom)

Bureau Veritas Certification

Avitide, Inc.

16 Cavendish Ct, Lebanon, NH 03766 USA

Bureau Veritas Certification Holding SAS – UK Branch certifies that the Management System of the above organisation has been audited and found to be in accordance with the requirements of the management system standards detailed below

ISO 9001:2015

Scope of certification

DESIGN AND MANUFACTURE OF AFFINITY PURIFICATION RESINS

Original Cycle Start Date:	18-August-2017
Expiry date of previous cycle:	17-August-2020
Certification / Recertification Audit date:	02-July-2020
Certification / Recertification cycle start date:	18-August-2020
Subject to the continued satisfactory operation of the organization's Management System, this certificate expires on:	17-August-2023

Certificate No. : US014403 Version: 1 Issue Date: 23-July-2020

UKAS MANAGEMENT SYSTEMS

0008

Certification Body Address: 5th Floor, 66 Prescot Street, London, E1 8HG, United Kingdom

Local Office: 16800 Greenspoint Park Drive, Suite 300S, Houston, TX 77060, USA

Further clarifications regarding the scope of this certificate and the applicability of the management system requirements may be obtained by consulting the organisation.
To check this certificate validity please call: +(800) 937-9311

SAFETY DATA SHEET

SECTION 1: Identification of the substance/mixture and of the company/undertaking

1.1. Product identifier

Trade name or designation of the mixture	Praesto® Jetted A50 Int2
Registration number	-
Synonyms	None.
Product number	PR00559
Issue date	20-July-2020
Version number	01
Revision date	-
Supersedes date	-

1.2. Relevant identified uses of the substance or mixture and uses advised against

Identified uses	Ion Exchange, Adsorbent, and/or Catalyst.
Uses advised against	None known.

1.3. Details of the supplier of the safety data sheet

Supplier	Purolite Ltd. Llantrisant Business Park Llantrisant, Wales, UK CF72 8LF
Telephone	+44 1443 229334
Fax	+44 1443 227073
Manufacturer	Purolite Ltd. Llantrisant Business Park Llantrisant, Wales, UK CF72 8LF
Telephone	+44 1443 229334
Fax	+44 1443 227073
1.4 Emergency telephone number	+1 866 387 7344 +1 760 602 8703

SECTION 2: Hazards identification

2.1. Classification of the substance or mixture

The mixture has been assessed and/or tested for its physical, health and environmental hazards and the following classification applies.

Classification according to Regulation (EC) No 1272/2008 as amended

Physical hazards

Flammable liquids	Category 3	H226 - Flammable liquid and vapour.

Hazard summary May be ignited by heat, sparks or flames. Occupational exposure to the substance or mixture may cause adverse health effects.

2.2. Label elements

Label according to Regulation (EC) No. 1272/2008 as amended

Contains: Ethanol

Hazard pictograms

Signal word Warning

Hazard statements

H226 Flammable liquid and vapour.

Precautionary statements

Prevention

P210	Keep away from heat/sparks/open flames/hot surfaces. - No smoking.
P280	Wear protective gloves/protective clothing/eye protection/face protection.

Response

P303 + P361 + P353	IF ON SKIN (or hair): Remove/Take off immediately all contaminated clothing. Rinse skin with water/shower.
P370 + P378	In case of fire: Use appropriate media to extinguish.

Storage

P403 + P235	Store in a well-ventilated place. Keep cool.

Disposal

P501	Dispose of contents/container in accordance with local/regional/national/international regulations.

Supplemental label information None.

2.3. Other hazards This mixture does not contain substances assessed to be vPvB / PBT according to Regulation (EC) No 1907/2006, Annex XIII.

SECTION 3: Composition/information on ingredients

3.2. Mixtures

General information

Chemical name	%	CAS-No. / EC No.	REACH Registration No.	Index No.	Notes
Ethanol	20	64-17-5 200-578-6	-	603-002-00-5	
Classification: Flam. Liq. 2;H225, Eye Irrit. 2;H319					
Agarose	2 - 6	9012-36-6 232-731-8	-	-	
Classification: -					
Water	74 - 78	7732-18-5 231-791-2	-	-	
Classification: -					

Composition comments All concentrations are in percent by weight unless ingredient is a gas. Gas concentrations are in percent by volume. The full text for all H-statements is displayed in section 16.

SECTION 4: First aid measures

General information Take off all contaminated clothing immediately. Ensure that medical personnel are aware of the material(s) involved, and take precautions to protect themselves. Wash contaminated clothing before reuse.

4.1. Description of first aid measures

Inhalation Move to fresh air. Call a physician if symptoms develop or persist.

Skin contact Take off immediately all contaminated clothing. Rinse skin with water/shower. Get medical attention if irritation develops and persists.

Eye contact Immediately flush eyes with plenty of water for at least 15 minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Get medical attention if irritation develops and persists.

Ingestion Rinse mouth. Get medical attention if symptoms occur.

4.2. Most important symptoms and effects, both acute and delayed Headache. Coughing.

4.3. Indication of any immediate medical attention and special treatment needed Provide general supportive measures and treat symptomatically. Thermal burns: Flush with water immediately. While flushing, remove clothes which do not adhere to affected area. Call an ambulance. Continue flushing during transport to hospital. Keep victim under observation. Symptoms may be delayed.

SECTION 5: Firefighting measures

General fire hazards Flammable liquid and vapour.

5.1. Extinguishing media

Suitable extinguishing media Water fog. Alcohol resistant foam. Dry chemical powder. Carbon dioxide (CO2).

Unsuitable extinguishing media Do not use water jet as an extinguisher, as this will spread the fire.

5.2. Special hazards arising from the substance or mixture Vapours may form explosive mixtures with air. Vapours may travel considerable distance to a source of ignition and flash back. During fire, gases hazardous to health may be formed.

5.3. Advice for firefighters

Special protective equipment for firefighters	Self-contained breathing apparatus and full protective clothing must be worn in case of fire.
Special fire fighting procedures	In case of fire and/or explosion do not breathe fumes. Move containers from fire area if you can do so without risk.
Specific methods	Use standard firefighting procedures and consider the hazards of other involved materials.

SECTION 6: Accidental release measures

6.1. Personal precautions, protective equipment and emergency procedures

For non-emergency personnel	Keep unnecessary personnel away. Keep people away from and upwind of spill/leak. Eliminate all ignition sources (no smoking, flares, sparks, or flames in immediate area). Wear appropriate protective equipment and clothing during clean-up. Do not touch damaged containers or spilled material unless wearing appropriate protective clothing. Ventilate closed spaces before entering them. Local authorities should be advised if significant spillages cannot be contained.
For emergency responders	Keep unnecessary personnel away. Wear appropriate protective equipment and clothing during clean-up. Use personal protection recommended in Section 8 of the SDS.
6.2. Environmental precautions	Avoid discharge into drains, water courses or onto the ground.
6.3. Methods and material for containment and cleaning up	Eliminate all ignition sources (no smoking, flares, sparks, or flames in immediate area). Keep combustibles (wood, paper, oil etc) away from spilled material. Take precautionary measures against static discharge. Use only non-sparking tools. The product is immiscible with water and will spread on the water surface. Large Spills: Stop the flow of material, if this is without risk. Dike the spilled material, where this is possible. Use a non-combustible material like vermiculite, sand or earth to soak up the product and place into a container for later disposal. Following product recovery, flush area with water. Small Spills: Absorb with earth, sand or other non-combustible material and transfer to containers for later disposal. Clean surface thoroughly to remove residual contamination. Never return spills to original containers for re-use.
6.4. Reference to other sections	For personal protection, see section 8 of the SDS. For waste disposal, see section 13 of the SDS.

SECTION 7: Handling and storage

7.1. Precautions for safe handling	Do not handle, store or open near an open flame, sources of heat or sources of ignition. Protect material from direct sunlight. When using do not smoke. Explosion-proof general and local exhaust ventilation. Take precautionary measures against static discharges. All equipment used when handling the product must be grounded. Use non-sparking tools and explosion-proof equipment. Avoid contact with eyes. Avoid prolonged exposure. Wear appropriate personal protective equipment. Observe good industrial hygiene practices.
7.2. Conditions for safe storage, including any incompatibilities	Keep away from heat, sparks and open flame. Prevent electrostatic charge build-up by using common bonding and grounding techniques. Store in a cool, dry place out of direct sunlight. Store in tightly closed container. Store in a well-ventilated place. Keep in an area equipped with sprinklers. Store away from incompatible materials (see section 10 of the SDS).
7.3. Specific end use(s)	Ion Exchange, Adsorbent, and/or Catalyst.

SECTION 8: Exposure controls/personal protection

8.1. Control parameters

Occupational exposure limits

UK. EH40 Workplace Exposure Limits (WELs)

Components	Type	Value
Ethanol (CAS 64-17-5)	TWA	1920 mg/m3
		1000 ppm

Biological limit values	No biological exposure limits noted for the ingredient(s).
Recommended monitoring procedures	Follow standard monitoring procedures.
Derived no effect levels (DNELs)	Not available.
Predicted no effect concentrations (PNECs)	Not available.

8.2. Exposure controls

Appropriate engineering controls	Explosion-proof general and local exhaust ventilation. Good general ventilation should be used. Ventilation rates should be matched to conditions. If applicable, use process enclosures, local exhaust ventilation, or other engineering controls to maintain airborne levels below recommended exposure limits. If exposure limits have not been established, maintain airborne levels to an acceptable level. Provide eyewash station.

Individual protection measures, such as personal protective equipment

General information	Use personal protective equipment as required. Personal protection equipment should be chosen according to the CEN standards and in discussion with the supplier of the personal protective equipment.
Eye/face protection	Wear safety glasses with side shields (or goggles). Eye protection should meet standard EN 166.
Skin protection	
- Hand protection	Protective gloves should be worn to prevent skin contact. SPECIFIC RECOMMENDATIONS. Breakthrough time: > 10 min (EN 374-3 Class 1). Suitable gloves can be recommended by the glove supplier.
- Other	Wear suitable protective clothing.
Respiratory protection	If engineering controls do not maintain airborne concentrations below recommended exposure limits (where applicable) or to an acceptable level (in countries where exposure limits have not been established), an approved respirator must be worn.
Thermal hazards	Wear appropriate thermal protective clothing, when necessary.
Hygiene measures	When using do not smoke. Always observe good personal hygiene measures, such as washing after handling the material and before eating, drinking, and/or smoking. Routinely wash work clothing and protective equipment to remove contaminants.
Environmental exposure controls	Emissions from ventilation or work process equipment should be checked to ensure they comply with the requirements of environmental protection legislation. Fume scrubbers, filters or engineering modifications to the process equipment may be necessary to reduce emissions to acceptable levels.

SECTION 9: Physical and chemical properties

9.1. Information on basic physical and chemical properties

Appearance	
Physical state	Liquid.
Form	Slurry.
Colour	White to off-white.
Odour	Sweetish. Slight alcohol.
Odour threshold	Not available.
pH	Neutral.
Melting point/freezing point	Not available.
Initial boiling point and boiling range	Not available.
Flash point	38.0 - 43.0 °C (100.4 - 109.4 °F) Closed cup
Evaporation rate	Not available.
Flammability (solid, gas)	Not applicable.
Upper/lower flammability or explosive limits	
Flammability limit - lower (%)	Not available.
Flammability limit - upper (%)	Not available.
Vapour pressure	Not available.
Vapour density	Not available.
Relative density	Not available.
Solubility(ies)	Insoluble in water.
Partition coefficient (n-octanol/water)	Not available.
Auto-ignition temperature	Not available.
Decomposition temperature	Not available.
Viscosity	Not available.
Explosive properties	Not explosive.
Oxidising properties	Not oxidising.
9.2. Other information	No relevant additional information available.

SECTION 10: Stability and reactivity

10.1. Reactivity The product is stable and non-reactive under normal conditions of use, storage and transport.

10.2. Chemical stability Material is stable under normal conditions.

10.3. Possibility of hazardous reactions No dangerous reaction known under conditions of normal use.

10.4. Conditions to avoid Avoid heat, sparks, open flames and other ignition sources. Avoid temperatures exceeding the flash point. Contact with incompatible materials.

10.5. Incompatible materials Strong oxidising agents.

10.6. Hazardous decomposition products Carbon oxides.

SECTION 11: Toxicological information

General information Occupational exposure to the substance or mixture may cause adverse effects.

Information on likely routes of exposure

Inhalation In high concentrations, vapours are narcotic and may cause headache, fatigue, dizziness and nausea.

Skin contact Frequent or prolonged contact may defat and dry the skin, leading to discomfort and dermatitis.

Eye contact Direct contact with eyes may cause temporary irritation.

Ingestion May cause discomfort if swallowed. However, ingestion is not likely to be a primary route of occupational exposure.

Symptoms Headache. Coughing.

11.1. Information on toxicological effects

Acute toxicity Not expected to be acutely toxic.

Components	Species	Test Results
Ethanol (CAS 64-17-5)		
Acute		
Inhalation		
LC50	Mouse	60000 ppm, 60 minutes
	Rat	115.9 - 133.8 mg/l, 4 hours
		82.1 - 92.6 mg/l, 6 hours
Oral		
LD50	Mouse	8300 mg/kg
	Rat	7800 - 22500 ml/kg
		1187 - 15010 mg/kg

Skin corrosion/irritation Due to partial or complete lack of data the classification is not possible.

Serious eye damage/eye irritation Direct contact with eyes may cause temporary irritation.

Respiratory sensitisation Due to partial or complete lack of data the classification is not possible.

Skin sensitisation Due to partial or complete lack of data the classification is not possible.

Germ cell mutagenicity Due to partial or complete lack of data the classification is not possible.

Carcinogenicity Due to partial or complete lack of data the classification is not possible.

Reproductive toxicity Due to partial or complete lack of data the classification is not possible.

Specific target organ toxicity - single exposure Due to partial or complete lack of data the classification is not possible.

Specific target organ toxicity - repeated exposure Due to partial or complete lack of data the classification is not possible.

Aspiration hazard Not an aspiration hazard.

Mixture versus substance information No information available.

Other information No other specific acute or chronic health impact noted.

SECTION 12: Ecological information

12.1. Toxicity Based on available data, the classification criteria are not met for hazardous to the aquatic environment.

Components		Species	Test Results
Ethanol (CAS 64-17-5)			
Aquatic			
Algae	EC50	Algae	675 - 22000 mg/l, 96 hours
			275 mg/l, 72 hours
Acute			
Crustacea	EC50	Aquatic Invertebrates	10000 mg/l, 24 hours
			10000 mg/l, 48 hours
	LC50	Aquatic Invertebrates	5012 mg/l, 48 hours
Fish	EC50	Fish	12700 - 12900 mg/l, 96 hours
	LC50	Fish	14200 - 15400 mg/l, 96 hours
Chronic			
Fish	NOEC	Fish	250 - 1000 mg/l, 120 hours

12.2. Persistence and degradability No data is available on the degradability of this product.

12.3. Bioaccumulative potential

Partition coefficient n-octanol/water (log Kow)

Ethanol (CAS 64-17-5) -0.31

Bioconcentration factor (BCF) Not available.

12.4. Mobility in soil The product is insoluble in water.

12.5. Results of PBT and vPvB assessment This mixture does not contain substances assessed to be vPvB / PBT according to Regulation (EC) No 1907/2006, Annex XIII.

12.6. Other adverse effects The product contains volatile organic compounds which have a photochemical ozone creation potential.

SECTION 13: Disposal considerations

13.1. Waste treatment methods

Residual waste Dispose of in accordance with local regulations. Empty containers or liners may retain some product residues. This material and its container must be disposed of in a safe manner (see: Disposal instructions).

Contaminated packaging Since emptied containers may retain product residue, follow label warnings even after container is emptied. Empty containers should be taken to an approved waste handling site for recycling or disposal.

EU waste code The Waste code should be assigned in discussion between the user, the producer and the waste disposal company.

Disposal methods/information Collect and reclaim or dispose in sealed containers at licensed waste disposal site. Dispose of contents/container in accordance with local/regional/national/international regulations.

Special precautions Dispose in accordance with all applicable regulations.

SECTION 14: Transport information

ADR

14.1. - 14.6.: Not regulated as dangerous goods.

RID

14.1. - 14.6.: Not regulated as dangerous goods.

ADN

14.1. - 14.6.: Not regulated as dangerous goods.

IATA

14.1. - 14.6.: Not regulated as dangerous goods.

IMDG

14.1. - 14.6.: Not regulated as dangerous goods.

14.7. Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code Not established.

SECTION 15: Regulatory information

15.1. Safety, health and environmental regulations/legislation specific for the substance or mixture

EU regulations

Regulation (EC) No. 1005/2009 on substances that deplete the ozone layer, Annex I and II, as amended

Not listed.

Regulation (EU) 2019/1021 On persistent organic pollutants (recast), as amended

Not listed.

Regulation (EU) No. 649/2012 concerning the export and import of dangerous chemicals, Annex I, Part 1 as amended

Not listed.

Regulation (EU) No. 649/2012 concerning the export and import of dangerous chemicals, Annex I, Part 2 as amended

Not listed.

Regulation (EU) No. 649/2012 concerning the export and import of dangerous chemicals, Annex I, Part 3 as amended

Not listed.

Regulation (EU) No. 649/2012 concerning the export and import of dangerous chemicals, Annex V as amended

Not listed.

Regulation (EC) No. 166/2006 Annex II Pollutant Release and Transfer Registry, as amended

Not listed.

Regulation (EC) No. 1907/2006, REACH Article 59(10) Candidate List as currently published by ECHA

Not listed.

Authorisations

Regulation (EC) No. 1907/2006, REACH Annex XIV Substances subject to authorisation, as amended

Not listed.

Restrictions on use

Regulation (EC) No. 1907/2006, REACH Annex XVII Substances subject to restriction on marketing and use as amended

Ethanol (CAS 64-17-5)

Directive 2004/37/EC: on the protection of workers from the risks related to exposure to carcinogens and mutagens at work, as amended.

Not listed.

Other EU regulations

Directive 2012/18/EU on major accident hazards involving dangerous substances, as amended

Not listed.

Other regulations	The product is classified and labelled in accordance with Regulation (EC) 1272/2008 (CLP Regulation) as amended. This Safety Data Sheet complies with the requirements of Regulation (EC) No 1907/2006, as amended.
National regulations	Follow national regulation for work with chemical agents in accordance with Directive 98/24/EC, as amended. Directive 2012/18/EU on major accident hazards involving dangerous substances: P5c
15.2. Chemical safety assessment	No Chemical Safety Assessment has been carried out.

SECTION 16: Other information

List of abbreviations

TWA: Time Weighted Average Value.
PBT: Persistent, bioaccumulative and toxic.
vPvB: Very Persistent and very Bioaccumulative.
DNEL: Derived No-Effect Level.
PNEC: Predicted No-Effect Concentration.
LD50: Lethal Dose, 50%.
LC50: Lethal Concentration, 50%.
NOEC: No observed effect concentration.
ADR: European Agreement Concerning the International Carriage of Dangerous Goods by Road.
RID: Regulations concerning the International Carriage of Dangerous Goods by Rail.
ADN: European Agreement Concerning the International Carriage of Dangerous Goods by Inland Waterways.
IATA: International Air Transport Association.
IMDG Code: International Maritime Dangerous Goods Code.
MARPOL: International Convention for the Prevention of Pollution from Ships.

References	ECHA CHEM
Information on evaluation method leading to the classification of mixture	The classification for health and environmental hazards is derived by a combination of calculation methods and test data, if available.
Full text of any H-statements not written out in full under Sections 2 to 15	H225 Highly flammable liquid and vapour. H319 Causes serious eye irritation.
Training information	Follow training instructions when handling this material.

Disclaimer

The information provided in this safety data sheet is based on current knowledge about the product and current legal requirements and standards. It relates specifically to health, safety and environmental requirements and standards, may not identify all hazards associated with the product or its uses or misuses, does not signify any warranty with regard to the properties of the product, and only applies when the product is used for the purposes indicated in section 1. This product is not sold as suitable for other purposes and such other usage may cause risks not mentioned in this safety data sheet.

AVITIDE | A REPLIGEN COMPANY

Repligen Corporation
41 Seyon Street
Building 1, Suite 100
Waltham, MA 02453, USA
+1-781-250-0111
www.repligen.com
January 21, 2022

To whom it may concern,

Avitide LLC, a Repligen Company, manufactures AVIPure® – AAV2 Resins in the United States of America using materials sourced from qualified suppliers. Wherever possible, materials used in production of commercial resins from Avitide Manufacturing are free from human or animal-derived components, thereby minimizing risk of transmission of bovine or transmissible spongiform encephalopathy (BSE/TSE) agents in those products.

Where animal-derived components are used in raw materials, process aids, or final packaging materials, sourcing and handling is in accordance with European guidance document EMEA/410/01 version 3 on animal derivatives entitled “Note for guidance on minimizing the risk of transmitting animal spongiform encephalopathy agents via human and veterinary medicinal products” and risk of BSE/TSE transmission is negligible.

Sincerely,

Brittany Crocco
Director of Quality
Avitide LLC, a Repligen Company

Repligen Corporation
41 Seyon Street
Building 1, Suite 100
Waltham, MA 02453
+1-781-250-0111

REACH and CA Proposition 65 Assessment

From

Brittany Crocco
Director of Quality, Avitide LLC, a Repligen Company

Date

January 24, 2022

RE

REACH and CA Proposition 65 Assessment

Introduction

This memo intends to summarize the regulatory assessment activities for the following criteria for AVIPure® – AAV Affinity Resins.

Table 1: AVIPure® – AAV Affinity Resin regulatory assessments

Assessment	Acceptance criteria
REACH	Product must be REACH compliant and registered if applicable
Prop 65	Product must be Prop-65 compliant and registered if applicable

REACH

The AVIPure® – AAV Affinity Resins (AVIPure® – AAV2, AVIPure® – AAV8, and AVIPure® – AAV9) are comprised of two components: the custom affinity ligand and an agarose resin bead. The affinity ligand for each product is exempted from the registration requirements due to production volumes not exceeding one metric ton. The resin bead is exempt from registration due to its polymer classification. The vendor has confirmed the monomers have been registered by the appropriate suppliers; see attachment 1.

The dry weight of each AVIPure® – AAV Affinity Resin product is not projected to exceed one metric ton annually, so the final resin product is also exempt from registration.

No substances of very high concern are expected to be present in the final AVIPure® – AAV Affinity Resin products at levels that exceed the established limits. Dimethylformamide (DMF) is used early in the production process. Extensive washing of the resin in subsequent steps removes DMF to calculated levels of < 0.5 ppm.

REACH compliance assessment is ongoing with Assent Compliance.

Proposition 65

The California Proposition 65 assessment has been initiated and is in process with Intertek per quote Qu-01234593-0.

Conclusion

Compliance assessments are in process. Although the assessments are still ongoing, it has been determined that REACH registration is not required.

Attachments

Attachment 1 - General Statement of Compliance with REACH (Purolite)

Mark Price
Corporate QA & Regulatory
Affairs Manager
Llantrisant Business Park,
Llantrisant, South Wales.
CF72 8LF, UK
Telephone +44 1443 229 334
Mobile +44 7824 553 419
mark.price@purolite.com

3 September 2019

Statement of Compliance with REACH

Classification of Ion Exchange Resins and Synthetic Adsorbents
Under REACH, ion exchange resins and polymeric adsorbents are considered "polymers" (ref. Title I, Article 3.5) and "polymers" are exempt from Title II - Registration and Title VI - Evaluation (ref. Title I, Article 2.9). However, monomers and reactants used in their manufacture are subject to registration.

Registration of Monomers and Reactants for Purolite Ion Exchange Resins Manufactured in Europe
All monomers and reactants used in the manufacture of Purolite ion exchange resins and adsorbents are purchased only from REACH compliant suppliers. This means that all monomers and reactants were pre-registered prior to the closure date of December 1st, 2008 and full registration is now complete.

Registration of Monomers and Reactants for Purolite Ion Exchange Resins Imported into Europe
, Llantrisant, U.K, has been formally appointed the "Only Representative" application and the implementation of REACH for all Purolite products imported into the EU. Purolite Ltd., acting as the O.R., successfully pre-registered all REACH relevant substances (monomers and reactants over 2% w/w) in the imported polymers and ensured that the same substances were fully registered by the relevant deadlines.

Brexit Update
In order to prepare for any eventuality resulting from the Brexit situation, Purolite, supported by our long-term consultants, are in the process of transferring all current registrations to our Purolite S.R.L site located in Romania (Str. Aleea Uzinei, Nr. 11,505 700, Victoria, Jud. Brasov, Romania. This move will ensure there is no disruption in supply of Purolite products and we are fully compliant with EU requirements.

Substances of Very High Concern
Purolite ion exchange resins and synthetic adsorbents have SVHC's concentration limits below the legal limits for substances of Very High Concern and are compliant with the Candidate List of the Substances of Very High Concern. The candidate list can be found at http://echa.europa.eu/candidate-list-table

M. A. P. Price.

Mark Price
Corporate QA & Regulatory Affairs Manager

AVITIDE | A REPLIGEN COMPANY

Repligen Corporation
41 Seyon Street
Building 1, Suite 100
Waltham, MA 02453, USA
+1-781-250-0111
www.repligen.com
April 18th, 2022

Under EU Directive 2015/863 from 31 March 2015, maximum concentration values by weight of certain substances have been established as shown below:

Lead, 0.1%

Mercury, 0.1%

Cadmium, 0.01%

Hexavalent chromium, 0.1%

Polybrominated biphenyls (PBB), 0.1%

Polybrominated biphenyl ethers (PBDE), 0.1%

Bis(2-ehtylhexyl) phythalate (DEHP), 0.1%

Butyl benzyl phthalate (BBP), 0.1%

Dibutyl phthalate (DBP). 0.1%

Diisobutyl phthalate (DIBP), 0.1%

Products manufactured by Avitide are in compliance with EU Directive 2105/863. Avitide does not intentionally add any of the listed substances to its products

Signed:

James Hendrickx
Senior Manager, Quality
Avitide LLC, a Repligen Company

TOXIKON
RIGHT. FROM THE START.℠

FINAL NON-GLP REPORT: 21-03949-N2

TOLERABILITY OF SMP-00082 FOLLOWING SINGLE DOSE INTRAVENOUS INJECTION IN WISTAR RATS

Test Article
SMP-00082

Final Report Date
3/23/2022

Study Director
Janel Kydd, Ph.D.

Sponsor
Avitide
16 Cavendish Court
Lebanon, NH 03766

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STUDY SUMMARY

The purpose of the study was to evaluate the tolerability of SMP-00082 following a single dose intravenous administration in Wistar rats with a fourteen (14) day observation period.

Ten (10) Wistar rats (5 males and 5 females) were acquired, acclimated for 5 days and assigned to study.

A slow bolus dose of 10 mg/kg test article was administered intravenously over a one-minute period on Day 1 of the study to all animals. Animals were observed for 14 days after test article administration.

Daily clinical observations and moribundity/mortality checks were performed (PADR220117002). Weekly body weights were recorded. Animals were humanely euthanized on Day 15 and a gross necropsy was performed.

SMP-00082 was tolerated by all animals in this study based on clinical observations and body weights.

STUDY DIRECTOR AND QUALITY ASSURANCE SIGNATURES AND VERIFICATION DATES

Study Information	
Protocol Number	p21–2019–00b
Study Director	Janel Kydd, Ph. D.
Study Supervisor	Jennifer Lopez, B.S.
Company	Toxikon Corporation

Verification Date(s)	
Test Article Receipt	10/28/2021
Project Log	10/31/2021
Study Initiation	11/8/2021
Study Completion	3/23/2022

Teresa Lescinskas, B.S.
Quality Assurance

3/23/22
Date

Janel Kydd, Ph.D.
Study Director

3/23/22
Date

1.0 PURPOSE

The purpose of the study was to evaluate the tolerability of SMP-00082 following a single dose intravenous administration in Wistar rats with a fourteen (14) day observation period.

2.0 REFERENCES

The study was based upon the following references:

- ISO/IEC 17025, 2017, General Requirements for the Competence of Testing and Calibration Laboratories.
- Sponsor Specifications.

3.0 COMPLIANCE

The data and report generated from this Non-GLP report should not be used to support applications for research or marketing permits for products regulated by the FDA. Compliance to 21 CFR part 58 Good Laboratory Practice (GLP) is required for data/reports intended for regulatory submission to assure the quality and integrity of safety data. The Sponsor is responsible for informing the Test Facility and the Study Director if the data are for any regulatory submission purpose. It was the Sponsor's responsibility to request GLP compliance prior to study initiation. Although this study was Non-GLP, this was conducted according to the accredited Quality System in effect at Toxikon, including ISO/IEC 17025, 2017, General Requirements for the Competence of Testing and Calibration Laboratories.

4.0 IDENTIFICATION OF TEST AND CONTROL ARTICLES

The Sponsor supplied the following information on a Test Requisition Form or other correspondence, wherever applicable (excluding confidential or trade secret information).

4.1 Test Article:

Name: SMP-00082

CAS/Code Number: Not Supplied by Sponsor (N/S)

Lot/Batch Number: NL-93

Physical State: N/S

Color: N/S

Expiration Date: N/S

Density: N/S

Stability: N/S

Sterility: N/S

Sterilization Conditions: N/S

Storage Condition: -20 ± 4 ℃

Safety Precautions: Standard Toxikon Laboratory Safety Precautions

Intended Use: Raw material

5.0 IDENTIFICATION OF TEST SYSTEM

5.1 Animals Used in the Study:

Number and Species: ten (10) Wistar rats (*Rattus norvegicus*)

Sex: 5 male and 5 female (females were non-pregnant and nulliparous)

Weight/Age Range: 261.7 – 424.5 grams / 8-9 weeks old (adult)
weighed to the nearest 0.1 g

Health Status: healthy, not used in other experimental procedures

Animal Purchase: Hilltop Lab Animals, Inc. (Scottdale, PA)

Animal Identification: ear tag

Acclimation: minimum 5 days, under same conditions as for the actual test

Animal Selection: selected from larger pool and examined to ensure lack of adverse clinical signs

5.2 Animal Care and Maintenance:

Animal Room Target Temperature: 70 ± 5 °F

Animal Room Target Relative Humidity: 30-70%

Air Exchanges per Hour: a minimum of 10 changes per hour

Lights: 12-hour light/dark cycle, full spectrum fluorescent lights

Housing: single housed

Cages: polycarbonate

Bedding: Hardwood Chips used as contact bedding, ScottPharma Solutions (Marlborough, MA)

Animal Rations: Teklad 2020X Rodent Diet, Envigo (Madison, WI), *ad libitum*

Water: tap water, *ad libitum*

There were no known contaminants present in the feed, water, or bedding expected to interfere with the test data.

The laboratory and animal rooms are maintained as limited-access facilities.

6.0 JUSTIFICATION OF TEST SYSTEM AND ROUTE OF ADMINISTRATION

6.1 Justification of Test System:

Rats were used in this study because they have historically been used in tolerability studies and the guidelines have no-alternative (non-animal) methods. The number of animals used in this study was the minimum number of animals that would allow proper evaluation of the data.

6.2 Route of Administration:

The test article was administered intravenously (IV) as a slow bolus for approximately one minute. This route of administration was selected per Sponsor request since it is the intended route of human exposure.

7.0 EXPERIMENTAL DESIGN AND DOSAGE

7.1 Preparation of Test Article:

The test article, SMP-00082, was provided as a frozen liquid by the Sponsor. The content of the vial was thawed at ambient temperature for 2 hours and homogenized using a vortexer prior to administration. The composition and purity of the test article was the responsibility of the Sponsor. No further preparation was needed.

7.2 Pre-Dose Procedure:

7.2.1 Animal Assignment:

Animals were acquired and assigned to this study (Table 1).

7.2.2 Clinical Observations:

Clinical observations were conducted on Day -1.

7.2.3 Body Weights:

All animals were weighed on Day -1.

7.3 Dose Administration:

Test article was administered intravenously as a slow bolus for approximately a1-minute period. The first day of dosing was designated as Day 1.

TABLE 1:
Animal Assignment

Group	Article	Number of Animals	Dosing	Dose Route	Dose (mL/kg)	Dose Volume (mL/kg)	Dose Concentration (mg/mL)
1	SMP-00082	10 (5 M and 5 F)	Once on Day 1	IV	10 mg/kg	10 mL/kg	1

M = Males; F = Females; IV = Intravenous

7.4 Post-Dose Procedure:

7.4.1 Clinical Observation:

Animals were observed daily for clinical signs of toxicity. Findings were recorded as they were observed. Clinical observations included, but were not limited to, changes in the skin, fur, eyes and mucous membranes, respiratory system, circulatory system, autonomic central nervous system, somatomotor activity, locomotor activity, and behavioral pattern.

7.4.2 Moribundity/Mortality:

The animals were also observed once daily for moribundity/mortality, at a separate time from the clinical observations (PADR220117002).

7.4.3 Body Weight:

Weekly body weights were measured for all animals.

7.4.4 Euthanasia and Gross Necropsy:

All surviving animals were humanely euthanized via carbon dioxide inhalation at the end of their in-life portion (Day 15) and gross necropsy was performed. The gross necropsy observations included examination of the external surface of the body, all orifices, and the cranial, thoracic, and abdominal cavities and their contents. Gross lesions and abnormalities were noted.

8.0 EVALUATION CRITERIA

8.1 Evaluation of Animal Data:

Evaluation was limited to reporting tabulated data as body weights and clinical observations. Tolerability was assessed by clinical observations and body weights. No statistical analysis was performed.

8.2 Control of Bias Statement:

The study as designed employed methodology to minimize uncertainty of measurement and to control bias for data collection and analysis, which included but was not limited to: system suitability assessment and method controls such as replicates.

9.0 RESULTS

9.1 Clinical Observation:

All clinical observations were normal.

9.2 Moribundity/Mortality:

There were no incidences of moribundity or mortality.

9.3 Body Weight:

All animals gained weight throughout the course of the study.

9.4 Euthanasia and Gross Necropsy:

There were no abnormal findings at gross necropsy.

10.0 CONCLUSION

SMP-00082 was tolerated by all animals in this study based on clinical observations and body weights.

11.0 RECORDS

- Original raw data will be archived by Toxikon Corporation.
- A copy of the final report and any report amendments will be archived by Toxikon Corporation.
- The original final report and a copy of the protocol and any protocol amendments or deviations will be forwarded to the Sponsor.
- The test article will be disposed by Toxikon.
- Test article retention upon study completion is the responsibility of the Sponsor.

12.0 CONFIDENTIALITY AGREEMENT

Per corporate policy, confidentiality shall be maintained in general, and in specific accordance with any relevant agreement specifically executed between Toxikon and the Sponsor.

13.0 ANIMAL WELFARE STATEMENT

The Sponsor assured that, to the best of their knowledge, this study did not unnecessarily duplicate previous testing and that there were no non-animal alternatives acceptable for the evaluation of the test article as defined by the protocol.

No evidence of pain and distress was reported to the Veterinarian and Study Director.

Toxikon strictly adhered to the following standards in maintaining the animal care and use program:

United States Department of Agriculture (USDA), Animal and Plant Health Inspection Service, 9 CFR Ch. 1 Subchapter A-Animal Welfare.

“Guide for the Care and Use of Laboratory Animals,” National Research Council, 2011.

Office for Laboratory Animal Welfare (OLAW), “Public Health Service Policy on Humane Care and Use of Laboratory Animals,” Health Research Extension Act of 1985 (Public Law 99–158 November 20, 1985), Revised 2015.

ISO 10993–2, 2006, Biological Evaluation of Medical Devices – Part 2: Animal Welfare Requirements.

AAALAC International accreditation.

14.0 UNFORESEEN CIRCUMSTANCES

Any unforeseen circumstances were documented in the raw data. However, no unforeseen circumstances that affected the integrity of the study were noted.

15.0 PROTOCOL AMENDMENTS AND DEVIATIONS

Original protocol and any protocol amendments/deviations are in Attachment C.

APPENDIX I:
Software Systems

Software	Use	21 CFR Part 11 Status	Publisher/ Vendor	Location
Adobe Acrobat 8, 9, and 10 Professional	Document preparation	Not Applicable	Adobe Systems, Inc.	San José, CA
Matrix Gemini 5.3.19	Laboratory Information Management System	Compliant	Autoscribe Limited	Reading, UK
MS Office 2010 Small Business Suite and MS Office 2013 Professional Suite and higher	Business software (suite includes Word, Excel, PowerPoint, Outlook, Publisher, Office tools)	Not Applicable	Microsoft Corporation	Redmond, WA
Provantis 10	Module-based data collection and analysis SaaS application for toxicology studies.	Compliant	Instem	Conshohocken, PA
Rees Scientific Centron Presidio 3.0	Automated Environmental Monitoring	Compliant	Rees Scientific	Trenton, NJ
TMS Web 7	Document management for SOPs and training records management software system	Compliant	Quality Systems Integrators	Eagle, PA
Toxikon Protocol Manager 1.0	Protocol requisition application	Not Applicable	Toxikon Corporation	Bedford, MA

ATTACHMENT A:
Individual Animal Data

INDIVIDUAL ANIMAL DATA INDEX

Individual Clinical Observations
Toxikon Project #: 21-03949-N2
Tolerability of SMP-00082
Following Single Dose Intravenous Injection in Wistar Rats

Test Article 10mg/kg Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		-1	1	2	3	4	5	6
1001	Normal	X	X	X	X	X	X	X
	Sacrificed - terminal kill	.	.	.	.	.	.	.
1002	Normal	X	X	X	X	X	X	X
	Sacrificed - terminal kill	.	.	.	.	.	.	.
1003	Normal	X	X	X	X	X	X	X
	Sacrificed - terminal kill	.	.	.	.	.	.	.
1004	Normal	X	X	X	X	X	X	X
	Sacrificed - terminal kill	.	.	.	.	.	.	.
1005	Normal	X	X	X	X	X	X	X
	Sacrificed - terminal kill	.	.	.	.	.	.	.

X=Present

Individual Clinical Observations
Toxikon Project #: 21-03949-N2
Tolerability of SMP-00082
Following Single Dose Intravenous Injection in Wistar Rats

Test Article 10mg/kg Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		7	8	9	10	11	12	13
1001	Normal	X	X	X	X	X	X	X
	Sacrificed - terminal kill	.	.	.	.	.	.	.
1002	Normal	X	X	X	X	X	X	X
	Sacrificed - terminal kill	.	.	.	.	.	.	.
1003	Normal	X	X	X	X	X	X	X
	Sacrificed - terminal kill	.	.	.	.	.	.	.
1004	Normal	X	X	X	X	X	X	X
	Sacrificed - terminal kill	.	.	.	.	.	.	.
1005	Normal	X	X	X	X	X	X	X
	Sacrificed - terminal kill	.	.	.	.	.	.	.

X=Present

Individual Clinical Observations
Toxikon Project #: 21-03949-N2
Tolerability of SMP-00082
Following Single Dose Intravenous Injection in Wistar Rats

Test Article 10mg/kg Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		14	15					
1001	Normal	X	X					
	Sacrificed - terminal kill	.	K					
1002	Normal	X	X					
	Sacrificed - terminal kill	.	K					
1003	Normal	X	X					
	Sacrificed - terminal kill	.	K					
1004	Normal	X	X					
	Sacrificed - terminal kill	.	K					
1005	Normal	X	X					
	Sacrificed - terminal kill	.	K					

X=Present; K=Scheduled Removal

Individual Clinical Observations
Toxikon Project #: 21-03949-N2
Tolerability of SMP-00082
Following Single Dose Intravenous Injection in Wistar Rats

Test Article 10mg/kg Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		-1	1	2	3	4	5	6
1101	Normal	X	X	X	X	X	X	X
	Sacrificed - terminal kill	.	.	.	.	.	.	.
1102	Normal	X	X	X	X	X	X	X
	Sacrificed - terminal kill	.	.	.	.	.	.	.
1103	Normal	X	X	X	X	X	X	X
	Sacrificed - terminal kill	.	.	.	.	.	.	.
1104	Normal	X	X	X	X	X	X	X
	Sacrificed - terminal kill	.	.	.	.	.	.	.
1105	Normal	X	X	X	X	X	X	X
	Sacrificed - terminal kill	.	.	.	.	.	.	.

X=Present

Individual Clinical Observations
Toxikon Project #: 21-03949-N2
Tolerability of SMP-00082
Following Single Dose Intravenous Injection in Wistar Rats

Test Article 10mg/kg Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		7	8	9	10	11	12	13
1101	Normal	X	X	X	X	X	X	X
	Sacrificed - terminal kill	.	.	.	.	.	.	.
1102	Normal	X	X	X	X	X	X	X
	Sacrificed - terminal kill	.	.	.	.	.	.	.
1103	Normal	X	X	X	X	X	X	X
	Sacrificed - terminal kill	.	.	.	.	.	.	.
1104	Normal	X	X	X	X	X	X	X
	Sacrificed - terminal kill	.	.	.	.	.	.	.
1105	Normal	X	X	X	X	X	X	X
	Sacrificed - terminal kill	.	.	.	.	.	.	.

X=Present

Individual Clinical Observations
Toxikon Project #: 21-03949-N2
Tolerability of SMP-00082
Following Single Dose Intravenous Injection in Wistar Rats

Test Article 10mg/kg Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		14	15					
1101	Normal	X	X					
	Sacrificed - terminal kill	.	K					
1102	Normal	X	X					
	Sacrificed - terminal kill	.	K					
1103	Normal	X	X					
	Sacrificed - terminal kill	.	K					
1104	Normal	X	X					
	Sacrificed - terminal kill	.	K					
1105	Normal	X	X					
	Sacrificed - terminal kill	.	K					

X=Present; K=Scheduled Removal

Individual Clinical Observations
Toxikon Project #: 21-03949-N2
Tolerability of SMP-00082
Following Single Dose Intravenous Injection in Wistar Rats

Key Page

Group Information

Short Name	Long Name	Type	Report Headings		
1	SMP 00082	Dose	Test	Article	10mg/kg

Individual Body Weights and Body Weight Changes
Toxikon Project #: 21-03949-N2
Tolerability of SMP-00082
Following Single Dose Intravenous Injection in Wistar Rats

Sex: Male Day(s) Relative to Start Date

Test Article 10mg/kg	Body Weight (g)	Body Weight (g)	Body Weight (g)	BodyWeight Change	BodyWeight Change
	-1	5	12	-1 → 5	5 → 12
1001	424.5	439.9	465.9 >[1]	15.4	26.0
1002	423.6	449.1	483.9 >[1]	25.5	34.8
1003	396.1	425.8	457.1 >[1]	29.7	31.3
1004	379.9	406.7	442.7	26.8	36.0
1005	385.3	426.2	470.8 >[1]	40.9	44.6
Mean	401.88	429.54	464.08	27.66	34.54
SD	21.06	16.10	15.39	9.15	6.83
N	5	5	5	5	5

> = Out of range
[1] [RC:actual weight]

Individual Body Weights and Body Weight Changes
Toxikon Project #: 21-03949-N2
Tolerability of SMP-00082
Following Single Dose Intravenous Injection in Wistar Rats

Sex: Female Day(s) Relative to Start Date

Test Article 10mg/kg	Body Weight (g)	Body Weight (g)	Body Weight (g)	BodyWeight Change	BodyWeight Change
	-1	5	12	-1 → 5	5 → 12
1101	272.4	274.6	286.7	2.2	12.1
1102	265.3	269.5	282.2	4.2	12.7
1103	261.7	273.6	281.6	11.9	8.0
1104	285.2	296.6	311.6	11.4	15.0
1105	286.9	299.9	311.2	13.0	11.3
Mean	274.30	282.84	294.66	8.54	11.82
SD	11.41	14.24	15.41	4.96	2.54
N	5	5	5	5	5

Individual Body Weights and Body Weight Changes
Toxikon Project #: 21-03949-N2
Tolerability of SMP-00082
Following Single Dose Intravenous Injection in Wistar Rats

Comments and Markers

Page	Day	Group	Sex	Subject	Measurement	Type	Marker
	12	1	Male	1001	Body Weight	Out of Range	>
			Comment: actual weight				
	12	1	Male	1002	Body Weight	Out of Range	>
			Comment: actual weight				
	12	1	Male	1003	Body Weight	Out of Range	>
			Comment: actual weight				
	12	1	Male	1005	Body Weight	Out of Range	>
			Comment: actual weight				

Individual Body Weights and Body Weight Changes
Toxikon Project #: 21-03949-N2
Tolerability of SMP-00082
Following Single Dose Intravenous Injection in Wistar Rats

Key Page

Measurement Descriptions

Headings Used	Description
Body Weight	Bodyweight
BodyWeight Change	BodyWeight Change

Unit Descriptions

Headings Used	Description
g	g

Measurement/Statistics

Measurement	Descriptive
Body Weight	Mean
	Standard Deviation
	Count
BodyWeight Change	Mean
	Standard Deviation
	Count

Group Information

Short Name	Long Name	Type	Report Headings 1-4		
1	SMP 00082	Dose	Test	Article	10mg/kg

Individual Body Weights and Body Weight Changes
Toxikon Project #: 21-03949-N2
Tolerability of SMP-00082
Following Single Dose Intravenous Injection in Wistar Rats

Key Page

Comment Abbreviations

RC = Result Comment

ATTACHMENT B:
Certificate of Analysis

SAFETY DATA SHEET

16 Cavendish Ct
Lebanon NH 03766 USA

EMERGENCY TELEPHONE NO. (001)-603-965-2156

EMAIL: info@avitide.com

DATE: updated on 01Nov2021

SECTION 1 – IDENTIFICATION

Product Name: Custom affinity ligands, SMP-00082 and SMP-00070

Company:
Avitide, Inc.
16 Cavendish Court
Lebanon, NH 03766
1-603-965-2156

Emergency Response – Within the US: 1-800-424-9300
Emergency Response – Anywhere in the world: +1 703-741-5970

For research use only. Not for use in diagnostic procedures.

SECTION 2 – HAZARD(S) IDENTIFICATION

EMERGENCY OVERVIEW
Caution: The chemical, physical and toxicological properties of this product have not been thoroughly investigated. Exercise due care.
HMIS RATING HEALTH: 0 FLAMMABILITY: 0 REACTIVITY: 0

NFPA RATING HEALTH: 0 FLAMMABILITY: 0 REACTIVITY: 0
For additional information on toxicity, please refer to Section 11.

Signal Word
Warning
Hazard Statements

Precautionary Statements

PATHOGENICITY/INFECTIVITY: The product is considered non-pathogenic, non-infective and non-pyrogenic

SECTION 3 – COMPOSITION/ INFORMATION ON INGREDIENT

Chemical nature white amorphous solid

Substance Name	CAS #	SARA 313
Custom recombinant protein	None	N/A

Formula	Variable. Contains C, H, N, O, S.
Synonyms	N/A
Origin	Highly purified recombinant protein

SECTION 4 – FIRST AID MEASURES

ORAL EXPOSURE

If swallowed, wash out mouth with water provided person is conscious. Call a physician.

INHALATION EXPOSURE

If inhaled, remove to fresh air. If breathing becomes difficult, call a physician.

DERMAL EXPOSURE

In case of contact, immediately wash skin with soap and copious amounts of water. Call a physician.

EYE EXPOSURE

In case of contact with eyes, flush with copious amounts of water for at least 15 minutes. Assure adequate flushing by separating the eyelids with fingers. Call a physician.

SECTION 5 – FIRE FIGHTING MEASURES

FLASH POINT N/A AUTOIGNITION TEMP N/A FLAMMABILITY N/A

EXTINGUISHING MEDIA Suitable: Water spray. Carbon dioxide, dry chemical powder, or appropriate foam.

FIREFIGHTING Protective Equipment: Wear self-contained breathing apparatus and protective clothing to prevent contact with skin and eyes. **Specific Hazard(s):** Emits toxic fumes under fire conditions.

SECTION 6 – ACCIDENTAL RELEASE MEASURES

PROCEDURE TO BE FOLLOWED IN CASE OF LEAK OR SPILL

Evacuate area.

PROCEDURE(S) OF PERSONAL PRECAUTION(S)

Wear respirator, chemical safety goggles, rubber boots and heavy rubber gloves.

METHODS FOR CLEANING UP

Sweep up, place in a bag and hold for waste disposal. Avoid raising dust. Ventilate area and wash spill site after material pickup is complete.

SECTION 7 – HANDLING AND STORAGE/SPECIAL PRECAUTIONS

HANDLING

User Exposure: Avoid inhalation. Avoid contact with eyes, skin and clothing. Avoid prolonged or repeated exposure.

STORAGE

Suitable: Keep tightly closed. Store at 4°C

SECTION 8 – EXPOSURE CONTROLS /PERSONAL PROTECTION

ENGINEERING CONTROLS: Safety shower and eye bath. Mechanical exhaust required.

PERSONAL PROTECTIVE EQUIPMENT: Respiratory: Wear dust mask, Hand: Protective gloves, Eye: Chemical safety goggles.

GENERAL HYGIENE MEASURES: Wash thoroughly after handling.

SECTION 9 – PHYSICAL AND CHEMICAL PROPERTIES

Physical state: Solid

Appearance: White amorphous solid

Flammability: No data available

Odor: No data available

Vapor pressure: No data available

Odor threshold: No data available

Vapor Density: No data available

pH: No data available

Relative Density: No data available

Melting/freezing point: No data available

Solubility: No data available

Initial boiling point/boiling range: No data available

Flash point: No data available

Evaporation Rate: No data available

Partition coefficient: No data available

Auto-ignition temperature: No data available

Decomposition temperature: No data available

Viscosity: No data available

SECTION 10 – STABILITY AND REACTIVITY

Reactivity: None known
Chemical Stability: Stable. Avoid strong acids, strong bases.
Hazardous decomposition products: Nature not known.
Hazardous polymerization: Hazardous polymerization will not occur.

SECTION 11 – TOXICOLOGICAL INFORMATION

Route of exposure: Skin contact: May cause skin irritation. Skin absorption: May be harmful. Eye contact: May cause eye irritation. Inhalation: May be harmful if inhaled. Material may be irritating to mucous membranes and upper respiratory tract. Ingestion: May be harmful if swallowed.
Conditions aggravated by exposure: The toxicological properties have not been thoroughly investigated.

SECTION 12 – ECOLOGICAL INFORMATION

No data available

SECTION 13 – DISPOSAL CONSIDERATIONS

Contact a licensed professional waste disposal service to dispose of this material. Dissolve or mix the material with a combustible solvent and burn in a chemical incinerator equipped with an afterburner and scrubber. **Observe all Federal, State and local environmental regulations.**

SECTION 14 – TRANSPORT INFORMATION

DOT
Proper Shipping Name: None
Non-Hazardous for Transport: This substance is considered to be non-hazardous for transport.

IATA
Non-Hazardous for Air Transport: Non-hazardous for air transport.

SECTION 15 – REGULATORY INFORMATION

DISCLAIMER: For R&D use only. Not for drug, household or other uses.
WARRANTY: The above information is believed to be correct but does not purport to be all inclusive and shall be used only as a guide. The information in this document is based on the present state of our knowledge and is applicable to the product with regard to appropriate safety precautions. It does not represent any guarantee of the properties of the product. Avitide, Inc., shall not be held liable for any damage resulting from handling or from contact with the above product. See reverse side of invoice or packing slip for additional terms and conditions of sale.

SECTION 16 – OTHER INFORMATION

The above information is believed to be correct but does not purport to be all inclusive and shall be used only as a guide.

Avitide, Inc. shall not be held liable for any damage resulting from handling or from contact with the above product

MATERIAL DETAILS:

Name:	[redacted]	Material ID:	SMP-00082
Hazards*:	N/A	Storage:	-20 °C long term, 5 °C short term

*Always consult the safety data sheet (SDS) prior to handling chemicals.

TESTING Lot NL-93

Method	Test	Specification	Result		
ANM-00034	Purity by UPLC*	Report; ≥90% is typical	Purity:	91.4	%
SOP ANA-042	Monomeric purity by HP-SEC*	Report; ≥95% is typical	% Monomeric:	94.2	%
ANM-00317	Endotoxin*	≤1 EU/mg	Reported:	<2.31	EU/mL
			Calculated*:	<0.29	EU/mg
SOP-00362	Molecular Weight by LC/MS	7410 or 7278* ± 5 Da	MW:	7279.0	Da
			Total amount of material required for one round of testing + 10%:	0.15	g

*See appendix.

ATTACHMENT C:
Protocol and Protocol Amendments/Deviations

TOXIKON
RIGHT. FROM THE START.℠

TOXIKON NON-GLP TEST PROTOCOL
CONFIDENTIAL PROPERTY OF TOXIKON

TOLERABILITY OF SMP-00082 FOLLOWING SINGLE DOSE INTRAVENOUS INJECTION IN WISTAR RATS

TOXIKON PROTOCOL NUMBER: p21-2019-00b

MANAGEMENT OF THE STUDY

Performing Laboratory
Toxikon Corporation
15 Wiggins Avenue
Bedford, MA 01730

Sponsor
Avitide
16 Cavendish Court
Lebanon, NH 03766

PROTOCOL SIGNATURES

Warren Kett

PRINT NAME

DocuSigned by:
Warren Kett
Signer Name: Warren Kett
Signing Reason: I acknowledge signing the protocol with this electronic signature
Signing Time: 11/8/2021 | 3:25:48 PM EST
408AC08E920A4E07B85834E2B6A65B1F

11/8/2021
Date

Sponsor's Representative Approval
Avitide
16 Cavendish Court
Lebanon, NH 03766

J. HELÈNE ANDERSSON
PRINT NAME

8 NOV 2021
Date

Quality Assurance Review
Toxikon Corporation
15 Wiggins Avenue
Bedford, MA 01730

Janet Kydd
PRINT NAME

11/8/2021
Date

Study Director Signature
Toxikon Corporation
15 Wiggins Avenue
Bedford, MA 01730

TABLE OF CONTENTS

TABLE OF CONTENTS (Cont.)

Table:

Appendix:

1.0 PURPOSE

The purpose of the study is to evaluate the tolerability of SMP-00082 following a single dose intravenous administration in Wistar rats with a fourteen (14) day observation period.

2.0 REFERENCES

The study will be based upon the following references:

- ISO/IEC 17025, 2017, General Requirements for the Competence of Testing and Calibration Laboratories.
- Sponsor Specifications.

3.0 COMPLIANCE

This study is Non-GLP and this status may not be accepted for a submission related to product safety or approval. Compliance to 21 CFR Part 58 Good Laboratory Practice (GLP) is required for data/reports intended for regulatory submission to assure the quality and integrity of safety data. The Sponsor is responsible for informing the Test Facility and the Study Director if the data is for any regulatory submission purpose. It is the Sponsor's responsibility to request GLP compliance prior to study initiation. Although this study is Non-GLP, this will be conducted according to the accredited Quality System in effect at Toxikon, including ISO/IEC 17025, 2017, General Requirements for the Competence of Testing and Calibration Laboratories.

4.0 IDENTIFICATION OF TEST AND CONTROL ARTICLES

The Sponsor will supply the following information on a Test Requisition Form or other correspondence, wherever applicable (excluding confidential or trade secret information).

4.1 Test Article:

Name: SMP-00082

CAS/Code Number: To Be Determined (TBD)

Lot/Batch Number: NL-93

Physical State: TBD

Color: TBD

Expiration Date: TBD

Density: TBD

Stability: TBD

Sterility: TBD

Sterilization Conditions: TBD

Storage Condition: -20 ± 4 °C

Safety Precautions: Standard Toxikon Laboratory Safety Precautions

Intended Use: Raw material

5.0 IDENTIFICATION OF TEST SYSTEM

5.1 Animals Used in the Study:

Number and Species: ten (10) Wistar rats

Sex: 5 male and 5 female

Weight/Age Range: at least 250 grams / 8-9 weeks old (adult)
weighed to the nearest 0.1 g

Health Status: healthy, not used in other experimental procedures

Animal Purchase: registered commercial breeder

Animal Identification: ear tag

Acclimation: minimum 5 days, under same conditions as for the actual test

Animal Selection: selected from larger pool and examined to ensure lack of adverse clinical signs

5.2 Animal Care and Maintenance:

Animal Room Target Temperature: 70 ± 5 °F

Animal Room Target Relative Humidity: 30-70%

Air Exchanges per Hour: a minimum of 10 changes per hour

Lights: 12-hour light/dark cycle, full spectrum fluorescent lights; the light/dark cycle maybe interrupted for study related activities

Housing: single housed

Cages: polycarbonate or PET plastic

Bedding: laboratory grade bedding (contact)

Animal Rations: commercial rodent ration, *ad libitum*

Water: tap water, *ad libitum*

There will be no known contaminants present in the feed, water, or bedding expected to interfere with the test data.

The laboratory and animal rooms are maintained as limited-access facilities.

6.0 JUSTIFICATION OF TEST SYSTEM AND ROUTE OF ADMINISTRATION

6.1 Justification of Test System:

Rats will be used in this study because they have historically been used in tolerability studies and the guidelines have no-alternative (non-animal) methods. The number of animals used in this study is the minimum number of animals that will allow proper evaluation of the data.

6.2 Route of Administration:

The test article will be administered intravenously (IV) as a slow bolus for approximately one minute. This route of administration was selected per Sponsor request since this is the intended route of human exposure.

7.0 EXPERIMENTAL DESIGN AND DOSAGE

7.1 Preparation of Test Article:

The test article, SMP-00082, will be provided as a frozen liquid by the Sponsor. The content of the vial will be thawed overnight at 4 ± 2 °C (or ambient temperature for 2 hours) and homogenized using a vortexer prior to administration. The composition and purity of the test article will be the responsibility of the Sponsor. No further preparation will be needed.

7.2 Pre-Dose Procedure:

7.2.1 Animal Assignment:

Animals will be acquired and assigned to this study (Table 1).

7.2.2 Clinical Observations:

Clinical observations will be conducted on Day -1 or prior to dose administration on Day 1.

7.2.3 Body Weights:

All animals will be weighed on Day -1 or prior to dose administration on Day 1.

7.3 Dose Administration:

Test article will be administered intravenously as a slow bolus for approximately a 1-minute period. The first day of dosing will be designated as Day 1.

TABLE 1:
Animal Assignment

Group	Article	Number of Animals	Dosing	Dose Route	Dose (mg/kg)	Dose Volume (mL/kg)	Dose Concentration (mg/mL)
1	SMP-00082	10 (5 M and 5 F)	Once on Day 1	IV	10 mg/kg	10 mL/kg	1

M = Males; F= Females; IV = Intravenous

7.4 Post-Dose Procedure:

7.4.1 Clinical Observation:

Animals will be observed daily for clinical signs of toxicity. Findings will be recorded as they are observed. Clinical observations include, but are not limited to, changes in the skin, fur, eyes and mucous membranes, respiratory system, circulatory system, autonomic central nervous system, somatomotor activity, locomotor activity, and behavioral pattern.

7.4.2 Moribundity/ Mortality:

The animals will also be observed once daily for moribundity/mortality, at a separate time from the clinical observations. Animals whose condition make it unlikely that they will survive until the next observation, based upon the criteria established by the Study Director in concert with the veterinary staff, will be humanely euthanized immediately and may be necropsied. The Sponsor's representative will be notified. If an animal is removed from the study due to non-test article related circumstances, it may be replaced at the discretion of the Study Director. The incident will be noted in the study record and final report.

7.4.3 Body Weight:

Weekly body weights will be measured for all animals.

7.4.4 Euthanasia and Gross Necropsy:

All surviving animals will be humanely euthanized via carbon dioxide inhalation at the end of their in-life portion (Day 15) and gross necropsy will be performed. The gross necropsy observations will include examination of the external surface of the body, all orifices, and the cranial, thoracic, and abdominal cavities and their contents. Gross lesions and abnormalities will be noted.

8.0 EVALUATION CRITERIA

8.1 Evaluation of Animal Data:

Evaluation will be limited to reporting tabulated data as body weights and clinical observations. Tolerability will be assessed by clinical observations and body weights. No statistical analysis will be performed.

8.2 Control of Bias Statement:

The study as designed employs methodology to minimize uncertainty of measurement and to control bias for data collection and analysis, which includes but is not limited to: control data (retrospective, concurrent, or prospective), system suitability assessment, randomization, method controls such as blanks and replicates, or others as required by the specific study or guideline. Methods employed will be specified in the final report.

9.0 RECORDS

- Original raw data will be archived by Toxikon Corporation.
- A copy of the final report and any report amendments will be archived by Toxikon Corporation.
- The original final report and a copy of the protocol and any protocol amendments or deviations will be forwarded to the Sponsor.
- All used and unused test article will be handled as specified on the Test Requisition Form. If not indicated on the Test Requisition Form, all remaining test article will be disposed.
- Test article retention upon study completion is the responsibility of the Sponsor.

10.0 CONFIDENTIALITY AGREEMENT

Per corporate policy, confidentiality will be maintained in general, and in specific accordance with any relevant agreement specifically executed between Toxikon and the Sponsor.

11.0 ANIMAL WELFARE STATEMENT

The Sponsor assures that, to the best of their knowledge, this study does not unnecessarily duplicate previous testing and that there are no non-animal alternatives acceptable for the evaluation of the test article as defined by the protocol.

Evidence of pain and distress will be immediately reported to the Veterinarian and/or Study Director, who will make a decision, independently or in concert with the Sponsor, to terminate the study or to continue with or without appropriate analgesics. In toxicity studies, animals cannot be administered analgesics since they would interfere with the toxicity determination. Animals may be immediately euthanized. In other studies, one or more analgesics may be administered to reduce pain and distress. The Institutional Official (IO) and the Institutional Animal Care and Use Committee (IACUC) bases this policy upon Toxikon's Standard Operating Procedures and animal care and welfare standards as governed.

Toxikon strictly adheres to the following standards, where applicable, in maintaining the animal care and use program:

United States Department of Agriculture (USDA), Animal and Plant Health Inspection Service, 9 CFR Ch. 1, Subchapter A-Animal Welfare.

"Guide for the Care and Use of Laboratory Animals," National Research Council, 2011.

Office for Laboratory Animal Welfare (OLAW), "Public Health Service Policy on Humane Care and Use of Laboratory Animals," Health Research Extension Act of 1985 (Public Law 99-158 November 20, 1985), revised 2015.

ISO 10993-2, 2006, Biological Evaluation of Medical Devices - Part 2: Animal Welfare Requirements.

AAALAC International accreditation.

12.0 UNFORESEEN CIRCUMSTANCES

All unforeseen circumstances will be documented in the raw data. Any unforeseen circumstances that affect the integrity of the study will be discussed in the final report.

13.0 PROTOCOL AMENDMENTS/DEVIATIONS

All changes to the approved protocol and the reason for the changes will be documented in writing, signed by the Study Director, dated, and maintained with the protocol. A Protocol Amendment (PA) or a Protocol Deviation (PD) will be generated as closely as possible to the time of the change. The document will be created and signed by the Study Director and sent to the Sponsor. Sponsor's signature will be required for amendments (PA) to indicate approval of the amendment. Acknowledgement of notification of deviations is preferred and may be with a signature or other form of documentation.

APPENDIX I:
Software Systems

The following are the proposed software systems to be used during the conduct of this study. The actual systems used, as well as 21 CFR Part 11 compliance if applicable, will be documented in the final report.

Software	Use	Publisher/ Vendor	Location
Adobe Acrobat 8, 9, and 10 Professional	Document preparation	Adobe Systems, Inc.	San José, CA
Matrix Gemini 5.3.19	Laboratory Information Management System	Autoscribe Limited	Reading, UK
MS Office 2010 Small Business Suite and MS Office 2013 Professional Suite and higher	Business software (suite includes Word, Excel, PowerPoint, Outlook, Publisher, Office tools)	Microsoft Corporation	Redmond, WA
Provantis 10.1	Module–based data collection and analysis SaaS application for toxicology studies.	Instem	Conshohocken, PA
Rees Scientific Centron Presidio 3.0	Automated Environmental Monitoring	Rees Scientific	Trenton, NJ
TMS Web 7	Document management for SOPs and training records management software system	Quality Systems Integrators	Eagle, PA
Toxikon Protocol Manager 1.0	Protocol requisition application	Toxikon Corporation	Bedford, MA

DocuSign

Certificate Of Completion

Envelope Id: CA29DE9265074F7EA41C4296C7847C4A
Status: Completed
Subject: Please DocuSign: Toxikon protocol p21-2019-00b_v01.pdf
Source Envelope:
Document Pages: 10
Signatures: 1
Envelope Originator:
Certificate Pages: 5
Initials: 0
Andrew Matthews
AutoNav: Enabled
andrew.matthews@toxikon.com
EnvelopeId Stamping: Disabled
IP Address: 204.14.66.98
Time Zone: (UTC-05:00) Eastern Time (US & Canada)

Record Tracking

Status: Original
11/8/2021 3:19:05 PM
Holder: Andrew Matthews
andrew.matthews@toxikon.com
Location: DocuSign

Signer Events	Signature	Timestamp
Warren Kett warren.kett@avitide.com Security Level: Email, Account Authentication (Required)	Warren Kett Signature Adoption: Pre-selected Style Signature ID: 408AC08E-920A-4E07-B858-34E2B6A65B1F Using IP Address: 64.223.250.67 With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I acknowledge signing the protocol with this electronic signature	Sent: 11/8/2021 3:20:36 PM Viewed: 11/8/2021 3:25:02 PM Signed: 11/8/2021 3:25:53 PM
Electronic Record and Signature Disclosure: Accepted: 11/8/2021 3:23:06 PM ID: d5bbf336-35b4-4e09-a283-d163e9c28ada		

In Person Signer Events	Signature	Timestamp

Editor Delivery Events	Status	Timestamp

Agent Delivery Events	Status	Timestamp

Intermediary Delivery Events	Status	Timestamp

Certified Delivery Events	Status	Timestamp

Carbon Copy Events	Status	Timestamp
Janel Kydd janel.kydd@toxikon.com Security Level: Email, Account Authentication (Required)	COPIED	Sent: 11/8/2021 3:20:37 PM
Electronic Record and Signature Disclosure: Not Offered via DocuSign		

Witness Events	Signature	Timestamp

Notary Events	Signature	Timestamp

Envelope Summary Events	Status	Timestamps
Envelope Sent	Hashed/Encrypted	11/8/2021 3:20:37 PM

Envelope Summary Events	Status	Timestamps
Certified Delivered	Security Checked	11/8/2021 3:25:02 PM
Signing Complete	Security Checked	11/8/2021 3:25:53 PM
Completed	Security Checked	11/8/2021 3:25:53 PM

Payment Events	Status	Timestamps

Electronic Record and Signature Disclosure

ELECTRONIC RECORD AND SIGNATURE DISCLOSURE

From time to time, Toxikon Corporation - Part 11 (we, us or Company) may be required by law to provide to you certain written notices or disclosures. Described below are the terms and conditions for providing to you such notices and disclosures electronically through the DocuSign system. Please read the information below carefully and thoroughly, and if you can access this information electronically to your satisfaction and agree to this Electronic Record and Signature Disclosure (ERSD), please confirm your agreement by selecting the check-box next to 'I agree to use electronic records and signatures' before clicking 'CONTINUE' within the DocuSign system.

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Withdrawing your consent

If you decide to receive notices and disclosures from us electronically, you may at any time change your mind and tell us that thereafter you want to receive required notices and disclosures only in paper format. How you must inform us of your decision to receive future notices and disclosure in paper format and withdraw your consent to receive notices and disclosures electronically is described below.

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If you elect to receive required notices and disclosures only in paper format, it will slow the speed at which we can complete certain steps in transactions with you and delivering services to you because we will need first to send the required notices or disclosures to you in paper format, and then wait until we receive back from you your acknowledgment of your receipt of such paper notices or disclosures. Further, you will no longer be able to use the DocuSign system to receive required notices and consents electronically from us or to sign electronically documents from us.

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Unless you tell us otherwise in accordance with the procedures described herein, we will provide electronically to you through the DocuSign system all required notices, disclosures, authorizations, acknowledgements, and other documents that are required to be provided or made available to you during the course of our relationship with you. To reduce the chance of you inadvertently not receiving any notice or disclosure, we prefer to provide all of the required notices and disclosures to you by the same method and to the same address that you have given us. Thus, you can receive all the disclosures and notices electronically or in paper format through the paper mail delivery system. If you do not agree with this process, please let us know as described below. Please also see the paragraph immediately above that describes the consequences of your electing not to receive delivery of the notices and disclosures electronically from us.

How to contact Toxikon Corporation - Part 11:

You may contact us to let us know of your changes as to how we may contact you electronically, to request paper copies of certain information from us, and to withdraw your prior consent to receive notices and disclosures electronically as follows:
To contact us by email send messages to: gensales@toxikon.com

To advise Toxikon Corporation - Part 11 of your new email address

To let us know of a change in your email address where we should send notices and disclosures electronically to you, you must send an email message to us at gensales@toxikon.com and in the body of such request you must state: your previous email address, your new email address. We do not require any other information from you to change your email address.

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To request delivery from us of paper copies of the notices and disclosures previously provided by us to you electronically, you must send us an email to gensales@toxikon.com and in the body of such request you must state your email address, full name, mailing address, and telephone number. We will bill you for any fees at that time, if any.

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To inform us that you no longer wish to receive future notices and disclosures in electronic format you may:

i. decline to sign a document from within your signing session, and on the subsequent page, select the check-box indicating you wish to withdraw your consent, or you may;

ii. send us an email to gensales@toxikon.com and in the body of such request you must state your email, full name, mailing address, and telephone number. We do not need any other information from you to withdraw consent.. The consequences of your withdrawing consent for online documents will be that transactions may take a longer time to process..

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PROTOCOL DEVIATION

Protocol Deviation#: PADR220117002
Sponsor Name: Avitide
Contact: Warren Kett

Project No.: 21-03949-N2
Study Name: Single Dose IV Injection Systemic Toxicity in Rats
Test Article: SMP-00082

Lot/Batch: NL-93
CAS Code: Not Supplied by Sponsor

Content

Due to: Protocol Deviation

Original Requirement: 7.4.2 Moribundity/ Mortality:
The animals will also be observed once daily for moribundity/mortality, at a separate time from the clinical observations.

Description: The animals were not observed once daily for moribundity/mortality, at a separate time from the clinical observations on study Day 2.

Impact of Change: The animals were assessed during clinical observations on Day 2. There were no abnormal clinical observations noted. There is no impact of change on the study outcome due to the missed moribundity/mortality check on study Day 2.

Created by: TOXIKON\jkydd Date: 1/17/2022

Approvals

Study Director: TOXIKON\jkydd Date: 1/17/2022