Standard Operating Procedure

Intravenous self-administration (IVSA) paradigm
CSNA IVSA v1.0

Area: G3B	JAX-CSNA-BPC

Controls:	
Superseded Document	N/A, New
Reason for Revision Major or Minor changes	N/A N/A, New
Effective Date	September 21, 2017

Signatures:	
Author	I indicate that I have authored or updated this SOP according to applicable business requirements and our company procedure: Preparing and Updating Standard Operating Procedures. Name: Price E. Dickson & Tyler A. Roy Signature: _____ Date: ___
Approver	I indicate that I have reviewed this SOP, and find it meets all applicable business requirements and that it reflects the procedure described. I approve it for use. Name: _____ Signature: _____ Date: _____

1. PURPOSE

This SOP addresses the routine procedures used for conducting the Intravenous Cocaine Self-administration procedure in mice including methods for analysis of data, and quality monitoring procedures.

2. SCOPE

The SOP applies to laboratories within the JAX CSNA Behavioral Phenotyping Core

3. RESPONSIBILITIES

3.1. **Laboratory Staff**

3.1.1. Remain up to date in training with this SOP

3.1.2. Comply with this SOP

3.2. **Principal Investigator/Core Manager of JAX-CSNA**

3.2.1. Ensures that all personnel involved running this SOP are trained to comply with this SOP

4. GLOSSARY/DEFINITIONS

Item	Definition
Active lever	This is the lever that is programed to reward the mice with an intravenous infusion of cocaine paired with the house light as a stimulus.
Inactive lever	This is the lever that is programed not to reward the mice with a dosage of cocaine matched with the house light as a stimulus.
% Active Press	This is the percentage of active lever presses relative to cumulative leverpresses of the active and inactive levers.
Acquisition.	The acquisition phase is the first phase of testing. During this phase responses on the active lever under a fixed-ratio-1 (FR-1) schedule of reinforcement are reinforced with an infusion of 1.0 mg/kg cocaine. The criterion for achieving acquisition and completing this phase is ≥ 10 infusions for 5 consecutive test sessions.. and two consecutive test days meet stabilization criteria (see below).An active lever press resulted in a cocaine

	infusion and the illumination of both stimulus lights for five seconds. This was followed by a twenty-second time-out during which the house light was off and lever presses were recorded but had no consequences.Throughout the entire session, right (inactive) lever presses were recorded but had no consequences.
Stabilization of Response	Stabilization is defined as two consecutive sessions during which the number of infusions received a) does not vary by more than 20% between the 2 consecutive sessions
Generation of the Dose-Response Curve	This is the second phase of testing. During this phase of testing subjects are assessed for self-administration responsesacross an 8-point cocaine dose-response curve. Doses were presented in the following order: 0.56, 0.32, saline, 0.18, 0.10, 0.056, 0.032, 1.8 mg/kg/infusion. Subjects are tested on consecutive days on the same dose until stabilization criteria are met. Once the subject meets stabilization criterion at each dose they are moved to the next subsequent dose on the following session.
Extinction of Cocaine IVSA	Following stabilization at the final dose of cocaine, responding on the previously-active and -inactive levers was examined during extinction conditions for 7 daily two-hour sessions. During extinction sessions, the house light was continuously illuminated, stimulus lights were never illuminated, and lever presses had no consequences. Mice were connected to infusion tubing which was connected to a sterile-saline filled syringe, but the infusion pump was never activated during extinction sessions.
Reinstatement of Cocaine IVSA	Following extinction, responding on the active and inactive levers was examined during reinstatement conditions for 2 daily two-hour sessions. During reinstatement sessions, drug paired stimuli including infusion pump were presented as in the acquisition and DR curve stages but without infusion into the mouse. Specifically, mice were connected to infusion tubing which was connected to a sterile-saline filled syringe, but the syringe was not in the pump.

5. MATERIALS

5.1 Instrumentation

5.1.1.Operant Conditioning Chambers: (wide, modular, ENV-307W-CT; Med Associates Inc., , Saint Albins, Vermont.) fitted on the front wall with 2 retractable

levers on right and left sides and a food hopper in the center panel. Directly over each lever (~ 2-3 inches above) are red stimulus lights Modified with a Plexiglas floor, fabricated at the Jackson Laboratory, fitted to cover the floor railing.

5.1.2.Counterbalance: (Med Associates Inc., PHM-124MW, Saint Albins, Vermont.)

5.1.4.Tether: (Med Associates Inc., PHM-KVAH62T/MED, Saint Albins, Vermont.)

5.1.5. Swivel: (Med Associates Inc., PHM-115IP-25, Saint Albins, Vermont.)

5.1.6. PE Tubing (approximate length and gauge – vendor info)

5.1.6. Catheter: Instech's mouse VAB™ permits quick, aseptic connection and disconnection of a catheterized mouse and an infusion tether. These are implanted by surgical services during their JUGULAR VEIN CATHETERIZATION AND MAINTENANCE procedure (CMQ/LAH #:CMQ02-01Most Recent Approval Date: 5/26/16)

5.1.7. 120V Single Speed Syringe Pump: (Med Associates Inc., PHM-100, Saint Albins, Vermont.) This pump is located in the back left corner of the sound attenuating chamber next to the operant conditioning box.

5.1.8. Expanded PVC Sound Attenuating Cubicle (Med Associates Inc., ENV-022V, Saint Albins, Vermont.)

5.1.9. VAB62CAP Protective aluminum cap: (Instech's., PHM-VAB95CAP,.) Protects the port.

5.1.10. Scale: A scale for weighing animals with .1 gram resolution

5.1.11. Restrainer: (TV-150 STD & TV-150 SM, Braintree Scientific, Inc., Braintree, MA)

5.2. Consumables

5.2.1 Cocaine HCl: Supplied by National Institute on Drug Abuse Drug Supply Program (NDSP) Division of Therapeutics and Medical Consequences. Stored in powder form until it is formulated into 0.9% Saline (100 mg/mL clear solution) in various concentrations. (1.8, 1.0, 0.56, 0.32, 0.18, 0.10, 0.056, 0.032 mg/mL) and stored at -20°C until the day before use.

5.2.1.1. On the day before use, pre-formulated, frozen solutions are brought to room temperature in preparation for the following days use.

5.2.1.1.1. Pre-formulated frozen solutions should not be heated (e.g by bath sonication or under warm water) as this may result in degradation of the cocaine.

5.2.1.2. Once a solution is at room temperature, it is used within 10 days.

5.2.1.2.1. Once at room temperature, syringes should be labeled with an expiration date 10 days from the date it is brought to room temperature.

5.2.2. 70% ethanol (ETOH) in water solution: used to sanitize the chambers between subjects. Between groups of animals (~ 2x per month) chambers are cleaned with standad Virkon wipes and then cleaned with ETOH.

5.2.3. Paper towels

5.2.4. Wavicide 01 disinfectant solution: (Performance Health, Item # 081545508, Akron, OH.) is used to flush the PE tubing at the conclusion of each test day.

5.2.5. Heparin Sodium Inj. USP 10,000 unites/ 10 mL: (NDC Code 63739-931-28 — Heparin Sodium)

5.2.5.1. Dilute to 1/10th concentration in sterile container and administer 20 µL regardless of mouse weight. Heparin is maintained at room temperature.

5.2.6. Bayer Baytril® (enrofloxacin) Injectable Solution 2.27%: Baytril Injection Solution is a broad-spectrum antibiotic designed for the management of bacterial pathogens, with activity against both Gram-negative and Gram-positive bacteria, including those causing dermal, urinary, and respiratory tract infections. Stock solution 22.7mg/mL is cut in half with sterile saline to 11.35mg/mL.

5.2.7. Brevital (methohexital)l: Brevital is an ultrashort acting barbiturate and is used to confirm catheter patency once subjects have completed IVSA testing and prior to euthanasia [see Table 1 below for dosing].

5.2.8. 1CC syringe with 25G 1cc BD™ U-100 insulin syringe with slip tip; 25 G x 1 in. BD PrecisionGlide™ detachable needle, regular bevel, regular wall. These are used to administer Heparin, Brevital, and Baytril.

5.2.10. 60mL BD Syringes with Luer-Lok™ Tips: Feature a clear barrel with bold scale markings. Tapered plunger rod for ease of aspiration, positive plunger rod stop, and BD Luer-Lok™ thread for increased secure connection.

Table 1. Drugs for IVSA study

Drug	Dose	Volume to administer	when to administer	purpose
Heparin lock [dilute if necessary with saline to reach 100 units per milliliter]	100 units per mL of saline	20 µL regardless of mouse weight	Daily before entering chamber and after coming out of chamber. When multiple solutions are infused, heparin lock should always be infused last so that it locks the catheter.	confirmation that catheter is not blocked (before entering chamber) and to lock the catheter with the intention of preventing it from becoming blocked (after exiting chamber).
Baytril (enrofloxacin) [dilute to 1/2]	22.7 mg per kilogram	2 µL per gram of mouse test weight (e.g., 25 g mouse gets 50 µL)	Daily after coming out of the chamber before heparin lock.	Baytril is an antibiotic. It is used daily throughout the study to forestall bacterial infection.
Brevital (methohexital)	5 mg per kilogram	100 µL	Once at the end of the study.	Brevital is an ultrashort acting barbiturate and is used to confirm catheter patency. Only used once.

6. PROCEDURE

6.1. **Subjects**

6.1.1. Species. Mice

6.1.1.1. Subjects undergo jugular vein catheterization prior to testing (see Jugular Vein Catheterization and Maintenance Procedure)

6.1.1.2. Subjects are provided a minimum 10 day postoperative recovery period in their home cage. Approval to initiate testing in individual subjects postoperatively is determined by veterinarian

6.1.2. Sex. Males or females

6.1.3. Age. The test is validated for mice ≥ 12 weeks of age.

6.1.4. Housing. Subjects are individually housed for this test.

6.1.5. Transport to Procedure Room. Subjects are transported in their home cages from the housing room to the procedure room on a wheeled transport rack. The procedure room is located ~ 5 feet from the housing room on the same floor.

6.1.6. Body Weight. If required such as for dosing, body weights are recorded to the nearest 0.1 gram. Body weights for dosing are taken on the first day of testing, and then again once per week on Tuesday prior to testing.

6.1.7. Subject Identification. Mice are all individually housed and identified by their JCMS number, group number, and box number printed on their cage card. Mice are also ear notched at six weeks of age.

6.1.8. Acclimation. Prior to the start of testing, upon transport to the procedure room, subjects are weighed (once a week), and briefly handled to be assessed for any welfare concerns that may result in exclusion from testing (e.g., wounds or looking sickly).

6.2. **Environment**

6.2.1. Procedure Room. The dimensions of the procedure room are 21ft x 10 ft. Thirty-two chambers, each placed on separate shelves located next to each other along the entire left side of the room and half of the right side of the room. A 5-ft. laboratory workbench with two computer systems and monitors, a -20°C freezer, and a large rack to hold all mice during testing subjects are positioned on the right side of the room.

6.2.2. Temperature. The temperature range in the testing room is 70± 3 F.

6.2.3. Humidity. The humidity range in the procedure room is 50 ± 20%.

6.2.4. 6.1.4. Lighting. Room lighting in the testing room is overhead flouresence lights with a dimmer switch illuminated to the maximal setting to produce a light level in the testing room of ~ 500 lux. This is verified monthly.

6.2.5. Noise. The background noise levels in the procedure room are 55-70dB. No additional or ancillary noise (white noise) is provided. Audible timers are not used during this test.

6.2.6. Time of day. The test is conducted during the light phase of the circadian cycle; beginning at least 30 min after the lights on and concluding at least 30 min prior to lights off.

6.3. **Test Compound**

6.3.1. Test compounds are prepared monthly. Cocaine powder is prepared weighed and solubilized in 0.9% sterile saline solution. A stock solution is prepared (1.8. mg/kg/infusion dose) and all other doses are made from dilutions of the stock solution. Solutions are then separated by concentrations and are 0.2 micron-filtered into sterile 60 mL syringes. Syringes are capped with sterile blunt needle and stored in -20°C freezer until the day before it is used.

6.3.2. 6.3.1.1. One day prior to the test, solutions are thawed overnight at room temperature.

6.4. **Experiment Prep Work**

6.4.1. Prepare MedPC macro Excel file. Using the Excel file titled “VBA script to create MedPC macro” on both computers for both control units, to create the macro used by MedPC to run the chambers.

6.4.2. Confirm MedPC macro Excel file is accurate.

6.4.3. Mouse ID, chamber, dose, sex, strain, active lever assignment and weight.

6.4.4. Confirm that all variable values on the Excel file (e.g. mouse ID, dose, sex, strain, and active lever) match the values on the paper tracking sheet. This is a separate step from preparing the Excel file and must be performed each time a macro is created.. If an error is identified, edit and re-create the macro. Save the Excel file after creating the macro.

6.4.5. Load cocaine syringes. Flush out Wavicide from the PE tubing by connecting the cocaine syringe to the tubing .Once connected, firmly seat the syringe in the pump and turn the knob one full turn to ensure that cocaine has completely filled the tubing. Before connecting ensure that there are no air bubbles in the syringe.

6.4.6. Confirm correct cocaine dose is prepared foreach chamber. After all cocaine syringes have been loaded in the chambers, confirm that the dose written on the tracking sheet matches the dose that has been loaded into the syringe pump. This is a separate step from loading the syringes and must be performed.

6.4.7. Test operant chamber hardware. Run the testing program on MedPC to ensure that hardware is working. In each chamber, press the right lever followed by the left lever. Both levers should retract. Then break the infrared beam in the pellet receptacle. Following this, both stimulus lights, the house light, and the syringe pump should turn on briefly. Verify that all of this occurs for each box. Repair any hardware issues before testing mice. Burned out house lights are the most common issue. This can be

done while cleaning the chambers with ethanol as described in the next step.

6.4.8. Wipe down Plexiglas floors of chambers with alcohol. Do this immediately before testing the hardware in the chambers for group 1 (i.e. morning group) and group 2 (i.e. afternoon group). The reason for doing it at the same time for both groups is so that the smell of alcohol is held constant between these two groups.

6.5. **Macro Software**

6.5.1. Prepare MedPC macro Excel file. Using the Excel file titled “VBA script to create MedPC macro”, create the macro used by MedPC to run the chambers.

6.5.2. Confirm mouse IDs. Critically review the Excel file against the paper tracking sheet every time a macro is created to ensure that the correct mouse ID, dose, sex, strain, and active lever are used in the macro. To do this, systematically look at each chamber on the Excel file and confirm that all variable values match the values on the paper tracking sheet. This is a separate step from preparing the Excel file and must be performed each time a macro is created. It is possible that any of these variables could have been inadvertently changed (mouse ID, dose, sex, strain, active lever). Ensure all columns are checked and confirmed as accurate. If an error is identified, adjust the macro with the correct information and create a new macro. Save the Excel file after creating the macro.

6.5.3. Open MED-PC IV program from desktop computer in the procedure room and navigate to “Open Macro”.

6.5.4. Navigate to Desktop -> Macro -> IVSA_day. Confirm the date and time is correct and matches the updated VBA script. Open the file and, confirm all chambers are ready and accurate. Once confirmed, start the macro.

6.6.

6.6.1. Test mouse on acquisition dose (1.0) until he completes 5 sessions with >= 10 infusions. If mouse also meets stabilization criteria (see below) on sessions 4 and 5 move to next dose. Else, keep testing on acquisition dose until mouse stabilizes. Once mouse has stabilized on the acquisition dose move to next dose and keep testing until mouse stabilizes OR until he has been tested for 5 sessions on that dose. Continue to do this through all doses. The only qualification to this is that the mouse should be tested for only 2 sessions on the saline dose which is presented directly after the .32 dose. Once the mouse has stabilized

on the last cocaine dose, test on extinction for 7 sessions. Then test on reinstatement for 2 sessions. The mouse has completed the experiment at this point.

6.7. **Criteria for acquisition of IVSA (only for acquisition dose)**

6.7.1. 5 sessions with ≥ 10 infusions. These sessions do not have to be consecutive.

6.7.2. Stabilization on the acquisition dose as defined below.

6.8. **Criteria for stabilization of IVSA (all doses)**

6.8.1. Number of infusions doesn't vary by more than 20% for the last 2 consecutive sessions

6.9. **How to calculate stabilization criterion #1 above**

6.9.1. Take highest number of infusions over last 2 days and multiply it by .80.

6.9.2. Follow standard rounding rules (i.e., 20.4 is rounded to 20; 20.5 is rounded to 21).

6.9.3. If the number of infusions for the other day is ≥ to this number then mouse meets stabilization criterion #1 above.

6.10. **Exception to stabilization, moving on, and exclusion**

6.10.1. After acquisition on all doses of cocaine, if a mouse has not stabilized (criterea shown above) on a dose after five days the mouse is forced on to the next dose.

6.10.2. Saline dose is two days.

6.10.3. If a mouse comes detached or runs out of solution the data for that mouse for that day is excluded. These days do not count towards the five day rule. Mice can stabilize around an excluded day. During extinction and reinstatement day is not excluded since they receive not injection during those procedures just note under comments.

6.10.4. Mice are excluded from the study if they do not acquire within 28 days of starting. A mouse may be excluded earlier if it is impossible for them to meet the acquisition criteria within the 28 days.

6.10.5. Mice are also excluded if the port becomes damaged or clogged in anyway that hinders their ability to receive doses. (A mouse may continue testing if they are on extinction when they are no longer patient)

6.10.6. All excluded mice are euthanized.

6.11. **Testing**

6.11.1. Start IVSA Program in MedPC. Before loading mice in the chambers, start the IVSA program in MedPC. For each chamber, the program will wait for you to press the right lever twice before the two-hour testing session begins. This will allow you to load a mouse in a chamber and then immediately press the right lever twice to start the testing session for that mouse. The stimulus lights and house light will flash to confirm that the session has started. This strategy will ensure that the program starts for each mouse as soon as he is loaded in the chamber. It will also shorten the time between groups because the mouse in chamber 1 will be ~45 minutes into the two-hour program by the time the mouse in chamber 32 is loaded.

6.11.2. Load mice into restrainer by guiding their tail through the slit on the top of the restrainer to the back so the mouse is completely in and place the stopper over the opening so they can not get out. Flush each mouse with 20 µL of heparin lock solution (100 units per milliliter). All mice get 20 µL of heparin lock solution regardless of weight. The purpose of this is to verify that solution will flow through the catheter. If the catheter is completely blocked, and can not be cleared out with the heparin, the mouse should not be tested. Provided that the catheter is not blocked, bring the restrainer to the chamber, connect mouse to the tether, place mouse in the chamber, hit the right lever twice, and close the chamber door.

6.11.3. Adjust counterbalance arm. After loading the mouse and before closing the door to the sound attenuating cubicle, adjust the knob on the counterbalance arm to ensure that the mouse can easily move to the levers without resistance.

6.11.4. Double check MedPC software after all mice have been loaded. Confirm that the session has started in all 32 chambers by looking at the MedPC program on the computer screen.

6.11.5. When program is finished remove mice from chambers. As soon as the mouse in chamber one has completed the session, he can be removed from his chamber. Before removing a mouse, verify that he really has completed his session by looking at MedPC on the computer screen. After removing mouse from chamber, flush with Baytril (2 µL per gram of mouse weight). Then flush with heparin lock solution (20 µL regardless of weight). Then put the mouse back in his home chamber. Proceed to the mouse in chamber number two as soon as his session has finished. Do this for all mice until they are all out and back in their home cages.

6.12. **Afternoon group - same as morning group unless noted**

6.12.1. Load cocaine syringes in each chamber. It is not necessary to put Wavicide in the tubing between the first and second groups. Put cocaine syringes that will not be used for the second group on top of the chambers.

6.12.2. Double check that the correct cocaine dose is in each chamber.

6.12.3. Vacuum all feces and urine from all of the chambers. Make sure to vacuum main chamber, metal tray below, and floor beneath the tray.

6.12.4. Wipe down main chamber, tray and main chamber with alcohol to remove as much of lingering scents as possible.

6.12.5. Test hardware in the chambers.

6.12.6. Prepare MedPC macro Excel file.

6.12.7. Double check MedPC macro Excel file.

6.12.8. Start IVSA Program in MedPC.

6.12.9. Load mice in chambers.

6.12.10. Adjust counterbalance arm.

6.12.11. Double check MedPC software after all mice have been loaded.

6.12.12. Remove mice from chambers.

6.13. **After all mice have finished testing**

6.13.1. Remove tubing from cocaine syringes

6.13.2. Fill all tubing in the chambers with Wavicide to sterilize overnight.

6.13.3. Clean chambers in the same manner as they are cleaned after the morning group with vacuuming and alcohol.

6.13.4. Analyze data. Using MedPC to Excel, analyze all data. A detailed discussion of this is provided in the section below entitled “Analyzing IVSA Data”.

6.13.5. The cocaine syringes are in the freezer, remove syringes that will be necessary tomorrow from the freezer and put on the counter. Check for low syringes.

6.13.6. Close MedPC.

6.13.7. Close all instances of Excel. Make sure to save changes to the macro Creator Excel file.

6.14. **Data Analysis and QC**

6.14.1. IVSA data should be analyzed every evening using MedPC to Excel.

6.14.2. First click on the IVSA Data shortcut icon found on the desktop

6.14.3. Using MedPC to Excel, filter data into the “currently testing” tab in the Excel file “IVSA data”

6.14.4. Once open click on the next available cell in column A (Subject) and then open MED-PC to Excel by clicking on the Icon on the desktop.

6.14.5. In the top section labelled Profile hit the select button follow file path Desktop>Misc and select file IVSA- all vars.MRP

6.14.6. Now back in MED_PC click transfer in second section of profile follow file path Desktop>CU1 data and select file with the date from this day of testing

6.14.7. Program will enter the data into the excel file

6.14.8. Highlight infusion column and insert column shifting infusions to the right and add column labeled Control Unit. Then add which of the two control units were recorded on. This will be CU1.

6.14.9. Now click the button in the corner of the excel sheet which highlights all data then sort data

6.14.10. Data should be sorted by Group# >Control Unit> Box > Subject > StartDate

6.14.11. Then, review the data and identify mice that have reached criterion to advance to the next dose. (criteria in supplemental sheet found below)

6.14.12. Highlight the two days on which mice have stabilized on a cocaine dose in yellow, sections they reach five day limit in blue, and loss of patency with green and move to next dose. Then cross the dose off the tracking sheet and circle the dose for the next day so whoever starts the next day of testing can look at the sheet and know what mouse gets what doses.

6.14.13. For the stages in which stabilization is not required to advance (saline, extinction, reinstatement) highlight just the last two day in yellow.

6.14.14. Save the excel file, close it and reopen on second computer with the second control unit. Repeat same steps for analyzing data labeling this control unit CU1

6.14.15. Then remove syringes for next day of testing from the freezer.

6.15. **Study Completion Criteria**

6.16. Subjects have completed the study at the conclusion of the reinstatement stage, or when he has definitively lost catheter patency (i.e. completely blocked catheter, absolutely no reaction to methohexital), or if he dies. When any of these happen, do the following:

6.17. Delete the subject ID from the paper tracking sheet and from the Excel file that generates the MedPC macros

6.18. Copy and paste the subject's data from the "currently testing" tab in the IVSA data Excel file and paste it into the "finished" tab in the same file. This ensures that only mice that are currently being tested are in the "currently testing" tab. Otherwise that tab would continue to grow indefinitely and it would be difficult to work with when trying to determine which mice have met criteria.

6.19. Create a new Excel file with the subject's ID information. Paste the subject's information into that file including column names. Put that file into the folder "individual mouse files" in the dropbox folder "Excel".

7. Data Upload

7.1. Data uploads are verified and performed as described in the CSNA Data QC and Upload SOP.

8. Variables

8.1. Derived variables : These are variables computed using a custom python script using the variables listed in 8.2. These variables are uploaded to MPD (https://phenome.jax.org). Variables in MPD are stored by mouse population used in the study (in: Inbred, cc:Collaborative Cross, do: Diversity Outbred)

CSNA Variable	MPD Variable Name(s)	Description	Units	Upload to MPD	Required for analysis	Required for QC
AQ_SessionsTo Acquisition	acquisition_cc acquisition_do acquisition_in	Sesssions taken to meet acquisition criteria during the acquisition stage	counts	Yes	Yes	Yes
DR_Inf_Total_1 p0mgkg	infusions_in_1 p0 infusions_cc_ 1p0	Total number of infusions at 1.0 mg/kg during the	counts	Yes	Yes	Yes

	infusions_do_1p0	dose response stage				
DR_Inf_Total_0p032mgkg	infusions_in_0p32 infusions_cc_0p32 infusions_do_0p32	Total number of infusions at 0.032 mg/kg during the dose response stage	counts	Yes	Yes	Yes
DR_Inf_Total_0p056mgkg	infusions_in_0p56 infusions_cc_0p56 infusions_do_0p56	Total number of infusions at 0.056 mg/kg during the dose response stage	counts	Yes	Yes	Yes
DR_Inf_Total_0p1mgkg	infusions_in_0p1 infusions_cc_0p1 infusions_do_0p1	Total number of infusions at 0.1 mg/kg during the dose response stage	counts	Yes	Yes	Yes
DR_Inf_Total_0p18mgkg	infusions_in_0p18 infusions_cc_0p18 infusions_do_0p18	Total number of infusions at 0.18 mg/kg during the dose response stage	counts	Yes	Yes	Yes
DR_Inf_Total_0p32mgkg	infusions_in_0p32 infusions_cc_0p32 infusions_do_0p32	Total number of infusions at 0.32 mg/kg during the dose response stage	counts	Yes	Yes	Yes
DR_Inf_Total_0p56mgkg	infusions_in_0p56 infusions_cc_0p56 infusions_do_0p56	Total number of infusions at 0.56 mg/kg during the dose	counts	Yes	Yes	Yes

		response stage				
DR_Inf_Total_1p8mgkg	infusions_in_1p8 infusions_cc_1p8 infusions_do_1p8	Total number of infusions at 1.8 mg/kg during the dose response stage	counts	Yes	Yes	Yes
DR_Inf_Total_1p0mgkgX2	infusions_in_1p0_2nd infusions_cc_1p0_2nd infusions_do_1p0_ 2nd	Total number of infusions at 1.0 mg/kg, second exposure, during the dose response stage	counts	Yes	Yes	Yes
DR_ALP_TfASoTD_1p8mgkg	infusions_active_in_1p8 infusions_active_cc_1p8 infusions_active_do_1p8	Total number of acitve lever presses on 1.8 mg/kg across all sessions	counts	Yes	Yes	Yes
DR_ALP_TfASoTD_1p0mgkgx2	infusions_active_in_1p0_2nd infusions_active_cc_1p0_2nd infusions_active_do_1p0_ 2nd	Total number of acitve lever presses on 1.0 mg/kg across all sessions during the second exposure	counts	Yes	Yes	Yes
EX_ALP_Total_s01	extinction_active_in_s1 extinction_active_cc_s1 extinction_active_do_s1	Total number of active lever presses during session 1 of extinction	counts	Yes	Yes	Yes
EX_ALP_Total_s02	extinction_active_in_s2 extinction_active_cc_s2	Total number of active lever presses during	counts	Yes	Yes	Yes

	extinction_active_do_s2	session 2 of extinction				
EX_ALP_Total_s03	extinction_active_in_s3 extinction_active_cc_s3 extinction_active_do_s3	Total number of active lever presses during session 3 of extinction	counts	Yes	Yes	Yes
EX_ALP_Total_s04	extinction_active_in_s4 extinction_active_cc_s4 extinction_active_do_s4	Total number of active lever presses during session 4 of extinction	counts	Yes	Yes	Yes
EX_ALP_Total_s05	extinction_active_in_s5 extinction_active_cc_s5 extinction_active_do_s5	Total number of active lever presses during session 5 of extinction	counts	Yes	Yes	Yes
EX_ALP_Total_s06	extinction_active_in_s6 extinction_active_cc_s6 extinction_active_do_s6	Total number of active lever presses during session 6 of extinction	counts	Yes	Yes	Yes
EX_ALP_Total_s07	extinction_active_in_s7 extinction_active_cc_s7 extinction_active_do_s7	Total number of active lever presses during session 7 of extinction	counts	Yes	Yes	Yes
EX_ALP_Total_s08	extinction_active_in_s8 extinction_active_cc_s8 extinction_active_do_s8	Total number of active lever presses during session 8 of extinction	counts	Yes	Yes	Yes
EX_ALP_Total_s09	extinction_active_in_s9 extinction_active_cc_s9	Total number of active lever presses during	counts	Yes	Yes	Yes

	extinction_active_do_s9	session 9 of extinction				
DR_ILP_TfASoTD_1p8mgkg	infusions_inactive_in_1p8 infusions_inactive_cc_1p8 infusions_inactive_do_1p8	Total number of inacitve lever presses on 1.8 mg/kg across all sessions	counts	Yes	Yes	Yes
DR_ILP_TfASoTD_1p0mgkgx2	infusions_inactive_in_1p0_2nd infusions_inactive_cc_1p0_2nd infusions_inactive_do_1p0_2nd	Total number of inacitve lever presses on 1.0 mg/kg across all sessions during the second exposure	counts	Yes	Yes	Yes
EX_ILP_Total_s01	extinction_inactive_in_s1 extinction_inactive_cc_s1 extinction_inactive_do_s1	Total number of inactive lever presses during session 1 of extinction	counts	Yes	Yes	Yes
EX_ILP_Total_s02	extinction_inactive_in_s2 extinction_inactive_cc_s2 extinction_inactive_do_s2	Total number of inactive lever presses during session 2 of extinction	counts	Yes	Yes	Yes
EX_ILP_Total_s03	extinction_inactive_in_s3 extinction_inactive_cc_s3 extinction_inactive_do_s3	Total number of inactive lever presses during session 3 of extinction	counts	Yes	Yes	Yes
EX_ILP_Total_s04	extinction_inactive_in_s4 extinction_inactive_cc_s4 extinction_inactive_do_s4	Total number of inactive lever presses during session 4 of extinction	counts	Yes	Yes	Yes

EX_ILP_Total_s05	extinction_inactive_in_s5 extinction_inactive_cc_s5 extinction_inactive_do_s5	Total number of inactive lever presses during session 5 of extinction	counts	Yes	Yes	Yes
EX_ILP_Total_s06	extinction_inactive_in_s6 extinction_inactive_cc_s6 extinction_inactive_do_s6	Total number of inactive lever presses during session 6 of extinction	counts	Yes	Yes	Yes
EX_ILP_Total_s07	extinction_inactive_in_s7 extinction_inactive_cc_s7 extinction_inactive_do_s7	Total number of inactive lever presses during session 7 of extinction	counts	Yes	Yes	Yes
EX_ILP_Total_s08	extinction_inactive_in_s8 extinction_inactive_cc_s8 extinction_inactive_do_s8	Total number of inactive lever presses during session 8 of extinction	counts	Yes	Yes	Yes
EX_ILP_Total_s09	extinction_inactive_in_s9 extinction_inactive_cc_s9 extinction_inactive_do_s9	Total number of inactive lever presses during session 9 of extinction	counts	Yes	Yes	Yes
RI_ALP_Total_s01	reinstatement_active_in_s1 reinstatement_active_cc_s1 reinstatement_active_do_s1	Total number of active lever presses during session 1 of reinstatement	counts	Yes	Yes	Yes
RI_ALP_Total_s02	reinstatement_active_in_s2 reinstatement_active_cc_s2 reinstatement_active_do_s2	Total number of active lever presses during session 2 of reinstatement	counts	Yes	Yes	Yes

RI_ILP_Total_s01	reinstatement_inactive_in_s1 reinstatement_inactive_cc_s1 reinstatement_inactive_do_s1	Total number of inactive lever presses during session 1 of reinstatement	counts	Yes	Yes	Yes
RI_ILP_Total_s02	reinstatement_inactive_in_s2 reinstatement_inactive_cc_s2 reinstatement_inactive_do_s2	Total number of inactive lever presses during session 2 of reinstatement	counts	Yes	Yes	Yes

8.2. Raw m/c output : The following variables are identified per session for a maximum of 28 session during acquisiton, 10 session during extinction and 3 sessions of reinstatement.

Variables	Description	Units	Upload to MPD	Required for analysis	Required for QC
Acquisition at 1.0 mg/kg-ActiveLeverPresses_Total-Session 01	Total number of active lever presses that occurred on acquisition session 01	counts	No	No	Yes
Acquisition at 1.0 mg/kg-ActiveLeverPresses_Total-Session 02	Total number of active lever presses that occurred on acquisition session 02	counts	No	No	Yes

Acquisition at 1.0 mg/kg-ActiveLeverPresses_Total-Session 03	Total number of active lever presses that occurred on acquisition session 03	counts	No	No	Yes
Acquisition at 1.0 mg/kg-ActiveLeverPresses_Total-Session 04	Total number of active lever presses that occurred on acquisition session 04	counts	No	No	Yes
Acquisition at 1.0 mg/kg-ActiveLeverPresses_Total-Session 05	Total number of active lever presses that occurred on acquisition session 05	counts	No	No	Yes
Acquisition at 1.0 mg/kg-ActiveLeverPresses_Total-Session 06	Total number of active lever presses that occurred on acquisition session 06	counts	No	No	Yes
Acquisition at 1.0 mg/kg-ActiveLeverPresses_Total-Session 07	Total number of active lever presses that occurred on acquisition session 07	counts	No	No	Yes
Acquisition at 1.0 mg/kg-ActiveLeverPresses_Total-Session 08	Total number of active lever presses that occurred on acquisition session 08	counts	No	No	Yes
Acquisition at 1.0 mg/kg-ActiveLeverPresses_Total-Session 09	Total number of active lever presses that occurred on acquisition session 09	counts	No	No	Yes

Acquisition at 1.0 mg/kg-ActiveLeverPresses_Total-Session 10	Total number of active lever presses that occurred on acquisition session 10	counts	No	No	Yes
Acquisition at 1.0 mg/kg-ActiveLeverPresses_Total-Session 11	Total number of active lever presses that occurred on acquisition session 11	counts	No	No	Yes
Acquisition at 1.0 mg/kg-ActiveLeverPresses_Total-Session 12	Total number of active lever presses that occurred on acquisition session 12	counts	No	No	Yes
Acquisition at 1.0 mg/kg-ActiveLeverPresses_Total-Session 13	Total number of active lever presses that occurred on acquisition session 13	counts	No	No	Yes
Acquisition at 1.0 mg/kg-ActiveLeverPresses_Total-Session 14	Total number of active lever presses that occurred on acquisition session 14	counts	No	No	Yes
Acquisition at 1.0 mg/kg-ActiveLeverPresses_Total-Session 15	Total number of active lever presses that occurred on acquisition session 15	counts	No	No	Yes
Acquisition at 1.0 mg/kg-ActiveLeverPresses_Total-Session 16	Total number of active lever presses that occurred on acquisition session 16	counts	No	No	Yes

Acquisition at 1.0 mg/kg-ActiveLeverPresses_Total-Session 17	Total number of active lever presses that occurred on acquisition session 17	counts	No	No	Yes
Acquisition at 1.0 mg/kg-ActiveLeverPresses_Total-Session 18	Total number of active lever presses that occurred on acquisition session 18	counts	No	No	Yes
Acquisition at 1.0 mg/kg-ActiveLeverPresses_Total-Session 19	Total number of active lever presses that occurred on acquisition session 19	counts	No	No	Yes
Acquisition at 1.0 mg/kg-ActiveLeverPresses_Total-Session 20	Total number of active lever presses that occurred on acquisition session 20	counts	No	No	Yes
Acquisition at 1.0 mg/kg-ActiveLeverPresses_Total-Session 21	Total number of active lever presses that occurred on acquisition session 21	counts	No	No	Yes
Acquisition at 1.0 mg/kg-ActiveLeverPresses_Total-Session 22	Total number of active lever presses that occurred on acquisition session 22	counts	No	No	Yes
Acquisition at 1.0 mg/kg-ActiveLeverPresses_Total-Session 23	Total number of active lever presses that occurred on acquisition session 23	counts	No	No	Yes

Acquisition at 1.0 mg/kg-ActiveLeverPresses_Total-Session 24	Total number of active lever presses that occurred on acquisition session 24	counts	No	No	Yes
Acquisition at 1.0 mg/kg-ActiveLeverPresses_Total-Session 25	Total number of active lever presses that occurred on acquisition session 25	counts	No	No	Yes
Acquisition at 1.0 mg/kg-ActiveLeverPresses_Total-Session 26	Total number of active lever presses that occurred on acquisition session 26	counts	No	No	Yes
Acquisition at 1.0 mg/kg-ActiveLeverPresses_Total-Session 27	Total number of active lever presses that occurred on acquisition session 27	counts	No	No	Yes
Acquisition at 1.0 mg/kg-ActiveLeverPresses_Total-Session 28	Total number of active lever presses that occurred on acquisition session 28	counts	No	No	Yes
Acquisition at 1.0 mg/kg-InactiveLeverPresses_Total-Session 01	Total number of inactive lever presses that occurred on acquisition session 01	counts	No	No	Yes
Acquisition at 1.0 mg/kg-InactiveLeverPresses_Total-Session 02	Total number of inactive lever presses that occurred on acquisition session 02	counts	No	No	Yes

Acquisition at 1.0 mg/kg-InactiveLeverPresses_Total-Session 03	Total number of inactive lever presses that occurred on acquisition session 03	counts	No	No	Yes
Acquisition at 1.0 mg/kg-InactiveLeverPresses_Total-Session 04	Total number of inactive lever presses that occurred on acquisition session 04	counts	No	No	Yes
Acquisition at 1.0 mg/kg-InactiveLeverPresses_Total-Session 05	Total number of inactive lever presses that occurred on acquisition session 05	counts	No	No	Yes
Acquisition at 1.0 mg/kg-InactiveLeverPresses_Total-Session 06	Total number of inactive lever presses that occurred on acquisition session 06	counts	No	No	Yes
Acquisition at 1.0 mg/kg-InactiveLeverPresses_Total-Session 07	Total number of inactive lever presses that occurred on acquisition session 07	counts	No	No	Yes
Acquisition at 1.0 mg/kg-InactiveLeverPresses_Total-Session 08	Total number of inactive lever presses that occurred on acquisition session 08	counts	No	No	Yes
Acquisition at 1.0 mg/kg-InactiveLeverPresses_Total-Session 09	Total number of inactive lever presses that occurred on acquisition session 09	counts	No	No	Yes

Acquisition at 1.0 mg/kg-InactiveLeverPresses_Total-Session 10	Total number of inactive lever presses that occurred on acquisition session 10	counts	No	No	Yes
Acquisition at 1.0 mg/kg-InactiveLeverPresses_Total-Session 11	Total number of inactive lever presses that occurred on acquisition session 11	counts	No	No	Yes
Acquisition at 1.0 mg/kg-InactiveLeverPresses_Total-Session 12	Total number of inactive lever presses that occurred on acquisition session 12	counts	No	No	Yes
Acquisition at 1.0 mg/kg-InactiveLeverPresses_Total-Session 13	Total number of inactive lever presses that occurred on acquisition session 13	counts	No	No	Yes
Acquisition at 1.0 mg/kg-InactiveLeverPresses_Total-Session 14	Total number of inactive lever presses that occurred on acquisition session 14	counts	No	No	Yes
Acquisition at 1.0 mg/kg-InactiveLeverPresses_Total-Session 15	Total number of inactive lever presses that occurred on acquisition session 15	counts	No	No	Yes
Acquisition at 1.0 mg/kg-InactiveLeverPresses_Total-Session 16	Total number of inactive lever presses that occurred on acquisition session 16	counts	No	No	Yes

Acquisition at 1.0 mg/kg-InactiveLeverPresses_Total-Session 17	Total number of inactive lever presses that occurred on acquisition session 17	counts	No	No	Yes
Acquisition at 1.0 mg/kg-InactiveLeverPresses_Total-Session 18	Total number of inactive lever presses that occurred on acquisition session 18	counts	No	No	Yes
Acquisition at 1.0 mg/kg-InactiveLeverPresses_Total-Session 19	Total number of inactive lever presses that occurred on acquisition session 19	counts	No	No	Yes
Acquisition at 1.0 mg/kg-InactiveLeverPresses_Total-Session 20	Total number of inactive lever presses that occurred on acquisition session 20	counts	No	No	Yes
Acquisition at 1.0 mg/kg-InactiveLeverPresses_Total-Session 21	Total number of inactive lever presses that occurred on acquisition session 21	counts	No	No	Yes
Acquisition at 1.0 mg/kg-InactiveLeverPresses_Total-Session 22	Total number of inactive lever presses that occurred on acquisition session 22	counts	No	No	Yes
Acquisition at 1.0 mg/kg-InactiveLeverPresses_Total-Session 23	Total number of inactive lever presses that occurred on acquisition session 23	counts	No	No	Yes

Acquisition at 1.0 mg/kg-InactiveLeverPresses_Total-Session 24	Total number of inactive lever presses that occurred on acquisition session 24	counts	No	No	Yes
Acquisition at 1.0 mg/kg-InactiveLeverPresses_Total-Session 25	Total number of inactive lever presses that occurred on acquisition session 25	counts	No	No	Yes
Acquisition at 1.0 mg/kg-InactiveLeverPresses_Total-Session 26	Total number of inactive lever presses that occurred on acquisition session 26	counts	No	No	Yes
Acquisition at 1.0 mg/kg-InactiveLeverPresses_Total-Session 27	Total number of inactive lever presses that occurred on acquisition session 27	counts	No	No	Yes
Acquisition at 1.0 mg/kg-InactiveLeverPresses_Total-Session 28	Total number of inactive lever presses that occurred on acquisition session 28	counts	No	No	Yes
Acquisition at 1.0 mg/kg-Infusions_Total-Session 01	Total number of infusions that occurred on acquisition session 01	counts	No	No	Yes
Acquisition at 1.0 mg/kg-Infusions_Total-Session 02	Total number of infusions that occurred on acquisition session 02	counts	No	No	Yes

Acquisition at 1.0 mg/kg-Infusions_Total-Session 03	Total number of infusions that occurred on acquisition session 03	counts	No	No	Yes
Acquisition at 1.0 mg/kg-Infusions_Total-Session 04	Total number of infusions that occurred on acquisition session 04	counts	No	No	Yes
Acquisition at 1.0 mg/kg-Infusions_Total-Session 05	Total number of infusions that occurred on acquisition session 05	counts	No	No	Yes
Acquisition at 1.0 mg/kg-Infusions_Total-Session 06	Total number of infusions that occurred on acquisition session 06	counts	No	No	Yes
Acquisition at 1.0 mg/kg-Infusions_Total-Session 07	Total number of infusions that occurred on acquisition session 07	counts	No	No	Yes
Acquisition at 1.0 mg/kg-Infusions_Total-Session 08	Total number of infusions that occurred on acquisition session 08	counts	No	No	Yes
Acquisition at 1.0 mg/kg-Infusions_Total-Session 09	Total number of infusions that occurred on acquisition session 09	counts	No	No	Yes

Acquisition at 1.0 mg/kg-Infusions_Total-Session 10	Total number of infusions that occurred on acquisition session 10	counts	No	No	Yes
Acquisition at 1.0 mg/kg-Infusions_Total-Session 11	Total number of infusions that occurred on acquisition session 11	counts	No	No	Yes
Acquisition at 1.0 mg/kg-Infusions_Total-Session 12	Total number of infusions that occurred on acquisition session 12	counts	No	No	Yes
Acquisition at 1.0 mg/kg-Infusions_Total-Session 13	Total number of infusions that occurred on acquisition session 13	counts	No	No	Yes
Acquisition at 1.0 mg/kg-Infusions_Total-Session 14	Total number of infusions that occurred on acquisition session 14	counts	No	No	Yes
Acquisition at 1.0 mg/kg-Infusions_Total-Session 15	Total number of infusions that occurred on acquisition session 15	counts	No	No	Yes
Acquisition at 1.0 mg/kg-Infusions_Total-Session 16	Total number of infusions that occurred on acquisition session 16	counts	No	No	Yes

Acquisition at 1.0 mg/kg-Infusions_Total-Session 17	Total number of infusions that occurred on acquisition session 17	counts	No	No	Yes
Acquisition at 1.0 mg/kg-Infusions_Total-Session 18	Total number of infusions that occurred on acquisition session 18	counts	No	No	Yes
Acquisition at 1.0 mg/kg-Infusions_Total-Session 19	Total number of infusions that occurred on acquisition session 19	counts	No	No	Yes
Acquisition at 1.0 mg/kg-Infusions_Total-Session 20	Total number of infusions that occurred on acquisition session 20	counts	No	No	Yes
Acquisition at 1.0 mg/kg-Infusions_Total-Session 21	Total number of infusions that occurred on acquisition session 21	counts	No	No	Yes
Acquisition at 1.0 mg/kg-Infusions_Total-Session 22	Total number of infusions that occurred on acquisition session 22	counts	No	No	Yes
Acquisition at 1.0 mg/kg-Infusions_Total-Session 23	Total number of infusions that occurred on acquisition session 23	counts	No	No	Yes

Acquisition at 1.0 mg/kg-Infusions_Total-Session 24	Total number of infusions that occurred on acquisition session 24	counts	No	No	Yes
Acquisition at 1.0 mg/kg-Infusions_Total-Session 25	Total number of infusions that occurred on acquisition session 25	counts	No	No	Yes
Acquisition at 1.0 mg/kg-Infusions_Total-Session 26	Total number of infusions that occurred on acquisition session 26	counts	No	No	Yes
Acquisition at 1.0 mg/kg-Infusions_Total-Session 27	Total number of infusions that occurred on acquisition session 27	counts	No	No	Yes
Acquisition at 1.0 mg/kg-Infusions_Total-Session 28	Total number of infusions that occurred on acquisition session 28	counts	No	No	Yes
Dose response FR1-ActiveLeverPresses_Total-0.032 mg/kg	Mean active lever presses that occurred on the final two sessions of this dose: 0.032 mg/kg	counts	No	No	Yes
Dose response FR1-ActiveLeverPresses_Total-0.056 mg/kg	Mean active lever presses that occurred on the final two sessions of this dose: 0.056 mg/kg	counts	No	No	Yes

Dose response FR1-ActiveLeverPresses_Total-0.1 mg/kg	Mean active lever presses that occurred on the final two sessions of this dose: 0.1 mg/kg	counts	No	No	Yes
Dose response FR1-ActiveLeverPresses_Total-0.18 mg/kg	Mean active lever presses that occurred on the final two sessions of this dose: 0.18 mg/kg	counts	No	No	Yes
Dose response FR1-ActiveLeverPresses_Total-0.32 mg/kg	Mean active lever presses that occurred on the final two sessions of this dose: 0.32 mg/kg	counts	No	No	Yes
Dose response FR1-ActiveLeverPresses_Total-0.56 mg/kg	Mean active lever presses that occurred on the final two sessions of this dose: 0.56 mg/kg	counts	No	No	Yes
Dose response FR1-ActiveLeverPresses_Total-1.0 mg/kg	Mean active lever presses that occurred on the final two sessions of this dose: 1.0 mg/kg	counts	No	No	Yes
Dose response FR1-ActiveLeverPresses_Total-1.8 mg/kg	Mean active lever presses that occurred on the final two sessions of this dose: 1.8 mg/kg	counts	No	No	Yes
Dose response FR1-InactiveLeverPresses_Total-0.032 mg/kg	Mean inactive lever presses that occurred on the final two sessions of this dose: 0.032 mg/kg	counts	No	No	Yes

Dose response FR1-InactiveLeverPresses_Total-0.056 mg/kg	Mean inactive lever presses that occurred on the final two sessions of this dose: 0.056 mg/kg	counts	No	No	Yes
Dose response FR1-InactiveLeverPresses_Total-0.1 mg/kg	Mean inactive lever presses that occurred on the final two sessions of this dose: 0.1 mg/kg	counts	No	No	Yes
Dose response FR1-InactiveLeverPresses_Total-0.18 mg/kg	Mean inactive lever presses that occurred on the final two sessions of this dose: 0.18 mg/kg	counts	No	No	Yes
Dose response FR1-InactiveLeverPresses_Total-0.32 mg/kg	Mean inactive lever presses that occurred on the final two sessions of this dose: 0.32 mg/kg	counts	No	No	Yes
Dose response FR1-InactiveLeverPresses_Total-0.56 mg/kg	Mean inactive lever presses that occurred on the final two sessions of this dose: 0.56 mg/kg	counts	No	No	Yes
Dose response FR1-InactiveLeverPresses_Total-1.0 mg/kg	Mean inactive lever presses that occurred on the final two sessions of this dose: 1.0 mg/kg	counts	No	No	Yes
Dose response FR1-InactiveLeverPresses_Total-1.8 mg/kg	Mean inactive lever presses that occurred on the final two sessions of this dose: 1.8 mg/kg	counts	No	No	Yes

Dose response FR1-Infusions_Total-0.032 mg/kg	Mean infusions that occurred on the final two sessions of this dose: 0.032 mg/kg	counts	Yes	Yes	Yes
Dose response FR1-Infusions_Total-0.056 mg/kg	Mean infusions that occurred on the final two sessions of this dose: 0.056 mg/kg	counts	Yes	Yes	Yes
Dose response FR1-Infusions_Total-0.1 mg/kg	Mean infusions that occurred on the final two sessions of this dose: 0.1 mg/kg	counts	Yes	Yes	Yes
Dose response FR1-Infusions_Total-0.18 mg/kg	Mean infusions that occurred on the final two sessions of this dose: 0.18 mg/kg	counts	Yes	Yes	Yes
Dose response FR1-Infusions_Total-0.32 mg/kg	Mean infusions that occurred on the final two sessions of this dose: 0.32 mg/kg	counts	Yes	Yes	Yes
Dose response FR1-Infusions_Total-0.56 mg/kg	Mean infusions that occurred on the final two sessions of this dose: 0.56 mg/kg	counts	Yes	Yes	Yes
Dose response FR1-Infusions_Total-1.0 mg/kg	Mean infusions that occurred on the final two sessions of this dose: 1.0 mg/kg	counts	Yes	Yes	Yes
Dose response FR1-Infusions_Total-1.8 mg/kg	Mean infusions that occurred on the final two sessions of this dose: 1.8 mg/kg	counts	Yes	Yes	Yes

Extinction-ActiveLeverPresses_Total-Session 01	Total number of active lever presses that occurred on extinction session 01	counts	Yes	Yes	Yes
Extinction-ActiveLeverPresses_Total-Session 02	Total number of active lever presses that occurred on extinction session 02	counts	Yes	Yes	Yes
Extinction-ActiveLeverPresses_Total-Session 03	Total number of active lever presses that occurred on extinction session 03	counts	Yes	Yes	Yes
Extinction-ActiveLeverPresses_Total-Session 04	Total number of active lever presses that occurred on extinction session 04	counts	Yes	Yes	Yes
Extinction-ActiveLeverPresses_Total-Session 05	Total number of active lever presses that occurred on extinction session 05	counts	Yes	Yes	Yes
Extinction-ActiveLeverPresses_Total-Session 06	Total number of active lever presses that occurred on extinction session 06	counts	Yes	Yes	Yes
Extinction-ActiveLeverPresses_Total-Session 07	Total number of active lever presses that occurred on extinction session 07	counts	Yes	Yes	Yes

Extinction-InactiveLeverPresses_Total-Session 01	Total number of inactive lever presses that occurred on extinction session 01	counts	Yes	Yes	Yes
Extinction-InactiveLeverPresses_Total-Session 02	Total number of inactive lever presses that occurred on extinction session 02	counts	Yes	Yes	Yes
Extinction-InactiveLeverPresses_Total-Session 03	Total number of inactive lever presses that occurred on extinction session 03	counts	Yes	Yes	Yes
Extinction-InactiveLeverPresses_Total-Session 04	Total number of inactive lever presses that occurred on extinction session 04	counts	Yes	Yes	Yes
Extinction-InactiveLeverPresses_Total-Session 05	Total number of inactive lever presses that occurred on extinction session 05	counts	Yes	Yes	Yes
Extinction-InactiveLeverPresses_Total-Session 06	Total number of inactive lever presses that occurred on extinction session 06	counts	Yes	Yes	Yes
Extinction-InactiveLeverPresses_Total-Session 07	Total number of inactive lever presses that occurred on extinction session 07	counts	Yes	Yes	Yes

Reinstatement-ActiveLeverPresses_Total-Session 01	Total number of active lever presses that occurred on reinstatement session 01	counts	Yes	Yes	Yes
Reinstatement-ActiveLeverPresses_Total-Session 02	Total number of active lever presses that occurred on reinstatement session 02	counts	Yes	Yes	Yes
Reinstatement-InactiveLeverPresses_Total-Session 01	Total number of inactive lever presses that occurred on reinstatement session 01	counts	Yes	Yes	Yes
Reinstatement-InactiveLeverPresses_Total-Session 02	Total number of inactive lever presses that occurred on reinstatement session 02	counts	Yes	Yes	Yes
Reinstatement-InactiveLeverPresses_Total-Session 02	Total number of inactive lever presses that occurred on reinstatement session 02	counts	Yes	Yes	Yes