

DSMB Report

Project Title: STAAR Study
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Data as of: 03/28/2022

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Section 1. Recruitment and Participant Status (as of 03/28/2022)

Figure 1. Enrollment and Accrual of Study Participants

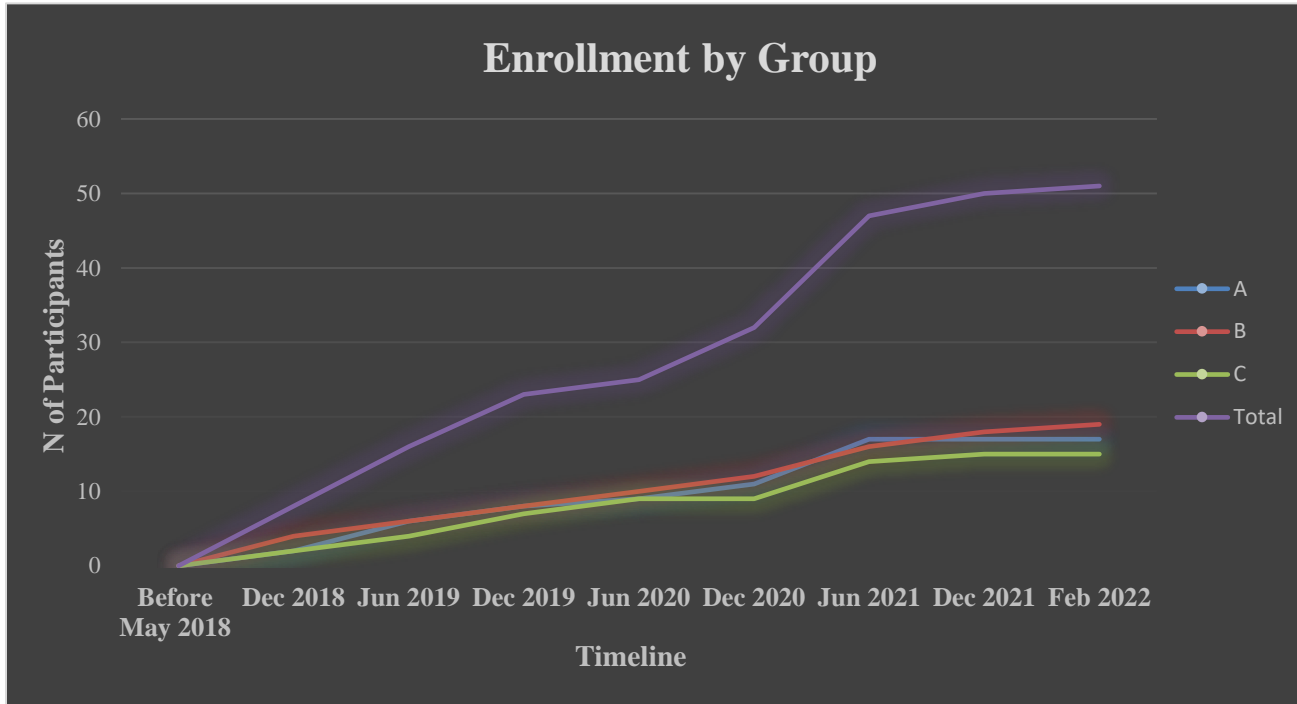
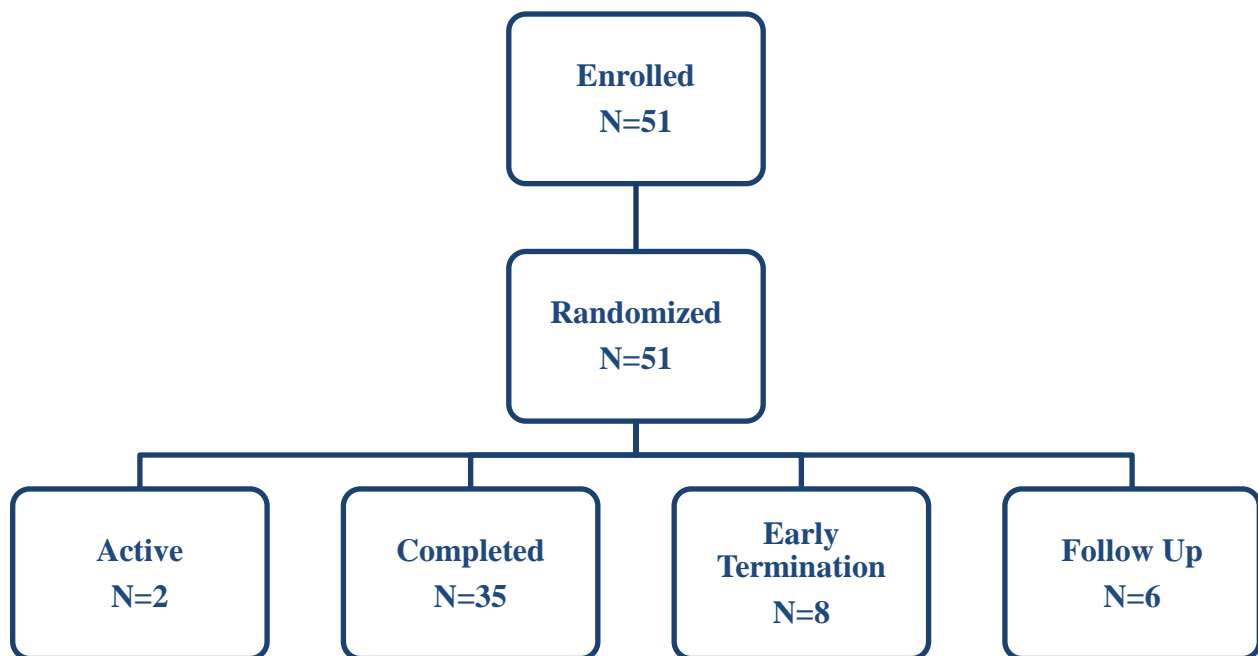


Figure 2. Overall Study Status



Section 2. Demographics (as of 03/28/2022)

Figure 3. Gender of Study Participants

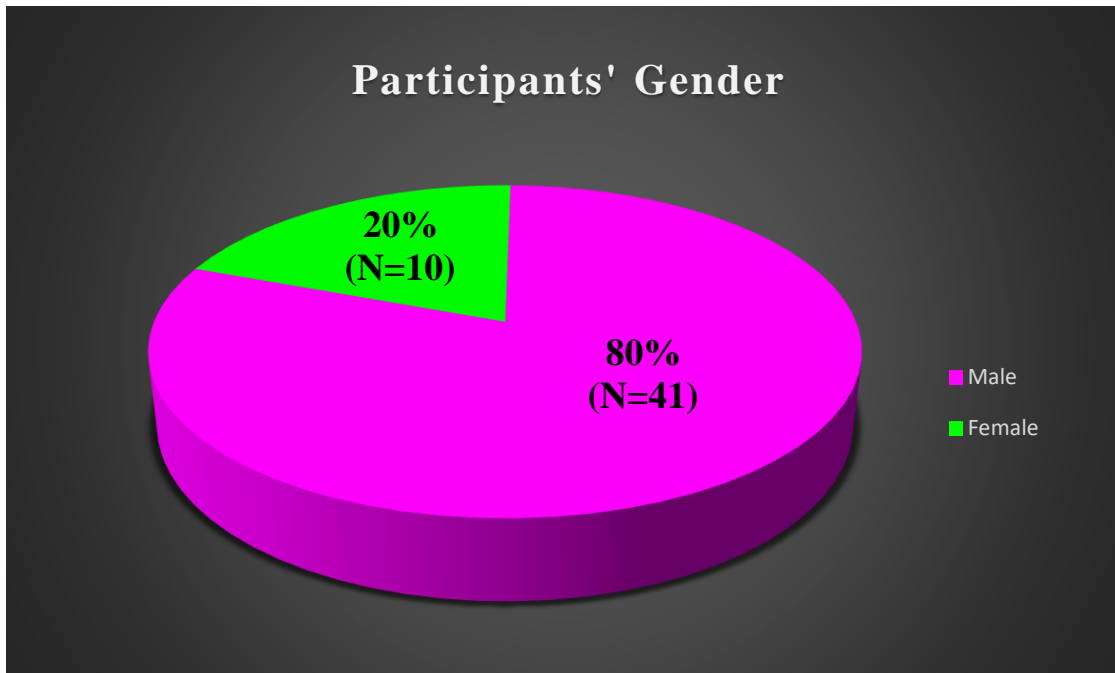


Figure 4. Ethnicity of Study Participants by Study Groups

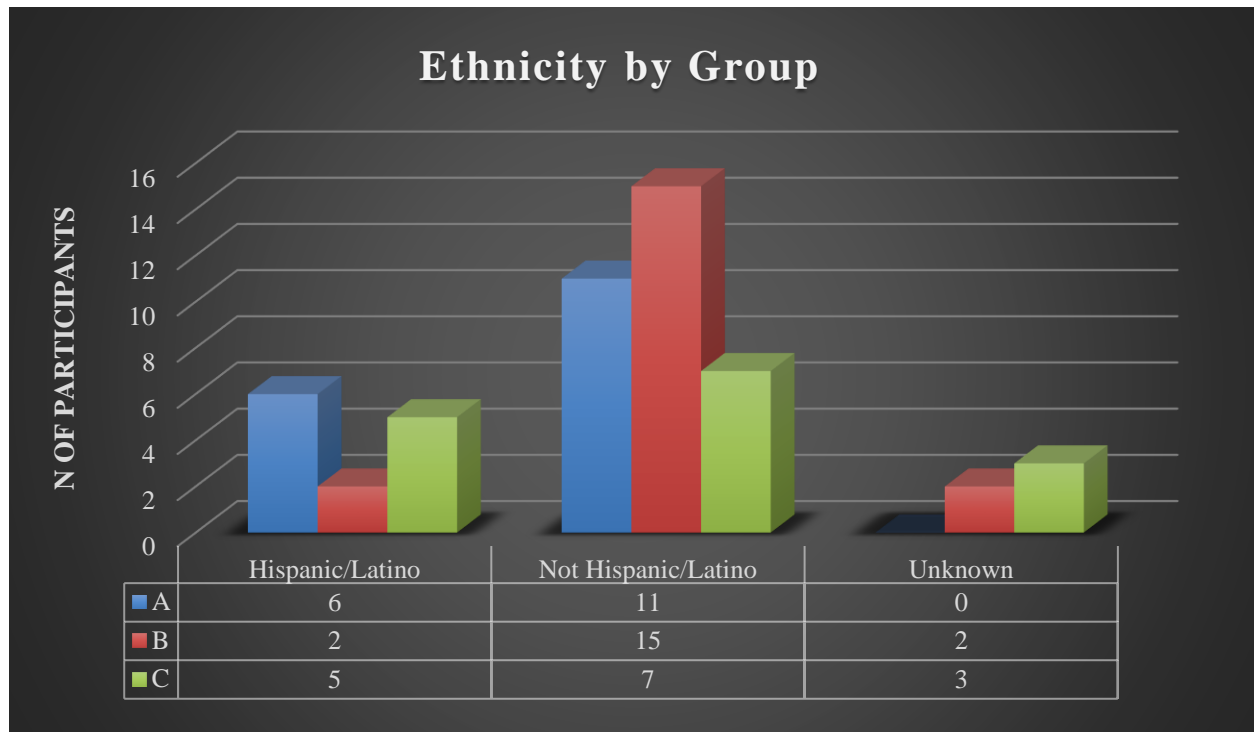
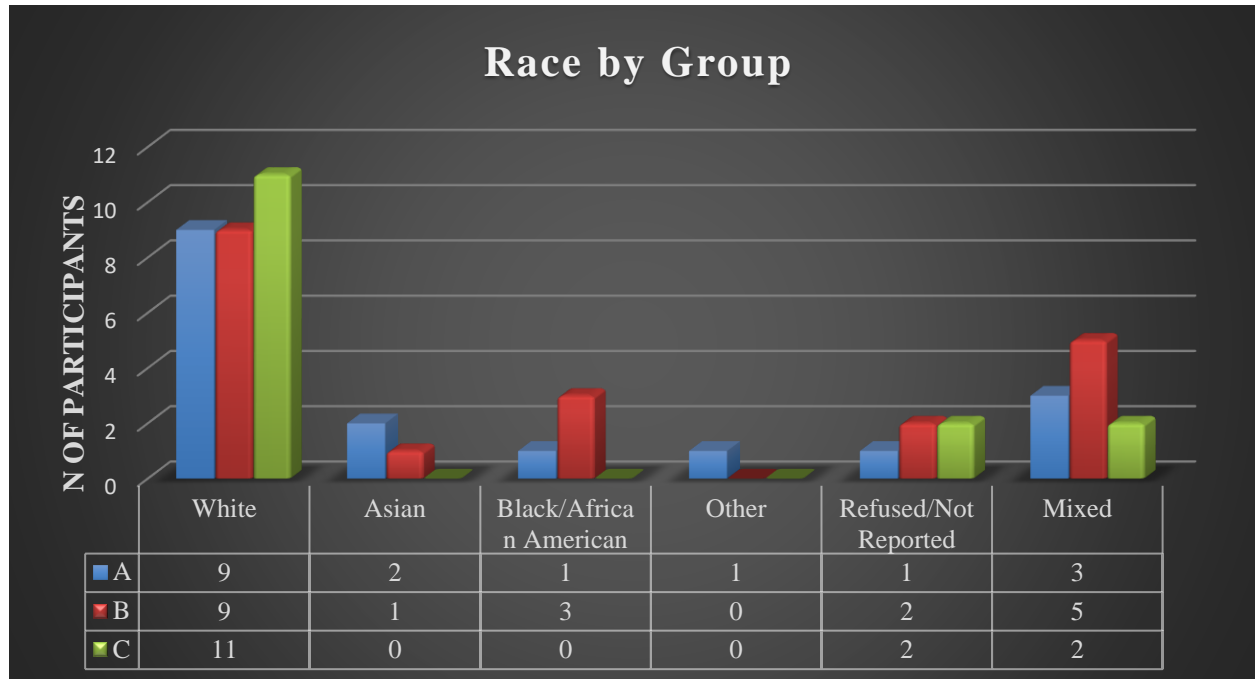


Figure 5. Race of Study Participants by Study Group



**"Other" includes American Indian, Hawaiian/Pacific Islander, etc*

Table 1. Enrollment Age Descriptive of Study Participants by Study Group

		Group A	Group B	Group C
Age	Mean	11.59	10.78	10.14
	Median	11.23	10.52	10.11
	SD	2.83	1.43	1.63
	Minimum	9.02	8.86	8.26
	Maximum	19.64	13.96	12.64

Table 2. Group Difference Test Result

	Gender	Ethnicity	Race	Age
Group Difference P-Value	0.25	0.09	0.62	0.40

* Group Difference was determined by Fisher's Exact test for categorical variables and ANOVA test for age.

Section 2. Safety Assessments for All Participants

The AE data are available for 51 participants as of 03/28/2022. The following statistics were based on the AE data obtained from those 51 participants randomized to treatment groups. Participants had 3.81 events on average with SD = 2.62.

Table 4. Incidence of Adverse Events by Standardized AE Category

Standardized AE Category	Total Participants*	Total %**	Total Events***
Aggression	1	1.96%	1
Allergies	2	3.92%	2
Anxiety	4	7.84%	6 [#]
Avoidant behaviors	1	1.96%	1
Bruxism	1	1.96%	2 [#]
Choking	1	1.96%	1
Constipation	3	5.88%	3
Cough	1	1.96%	2 [#]
COVID-19	2	3.92%	2
COVID-19 Vaccine side effect	3	5.88%	4 [#]
Decreased Academic Performance	1	1.96%	1
Diarrhea	4	7.84%	5 [#]
Disruptive behavior	1	1.96%	2 [#]
Dizziness	2	3.92%	2
Dysgeusia	1	1.96%	2 [#]
Dysphagia	1	1.96%	1
Ear Infection	2	3.92%	2
Elevated Transaminase	1	1.96%	1
Emotional Lability	2	3.92%	2
Enterobiasis	1	1.96%	1
Epistaxis	1	1.96%	1
Eye Blinking	1	1.96%	1
Fatigue	3	5.88%	3
Fever	3	5.88%	3
Fine Motor Impairment	1	1.96%	1
Gastrointestinal Issues	4	7.84%	5 [#]
Headache	5	9.8%	12 [#]
Heartburn	1	1.96%	1
Hematochezia	1	1.96%	1
Hypoglycemia	1	1.96%	1

Standardized AE Category	Total Participants*	Total %**	Total Events***
Hypokalemia	1	1.96%	1
Incontinence	1	1.96%	1
Influenza	1	1.96%	1
Insect Sting	2	3.92%	2
Irritability	1	1.96%	1
Itchiness	1	1.96%	1
Listlessness	1	1.96%	1
Lymphocytic Variant	1	1.96%	1
Menstrual Cramps	1	1.96%	1
Mouthing	1	1.96%	1
Muscle Spasm	1	1.96%	1
Musculoskeletal Injury	2	3.92%	2
Nausea	2	3.92%	2
Obsessive Compulsive Behavior	1	1.96%	2 [#]
Panic Attack	1	1.96%	1
Pharyngitis	2	3.92%	2
Rash	5	9.8%	5
Self-injurious behavior	1	1.96%	1
Skin Abrasion	3	5.88%	3
Skin Infection	1	1.96%	1
Skin Laceration	1	1.96%	1
Sleep disturbance	7	13.7%	8 [#]
Sprain	2	3.92%	3 [#]
Suicidal thinking	3	5.88%	3
TMJ Pain	1	1.96%	1
Teeth chattering	1	1.96%	1
Tics	2	3.92%	2
Upper respiratory infection	7	13.7%	10 [#]
Viral Infection	1	1.96%	1
Vomiting	4	7.84%	5 [#]
Wheezing	2	3.92%	3 [#]

* Number of participants experiencing an adverse event (participant is to be counted only once for each adverse event)

** % of total number of participants with AE data available to date (total N=51) in the study

*** Total number of events overall

Indicate recurrence of same adverse event

**Table 5. Incidence of Adverse Events by Standardized AE Category,
Stratified by Treatment Group**

	Group A (n=17)			Group B (n=19)			Group C (n=15)		
Standardized AE Category	Total Partici- pants*	Total %**	Total Events ***	Total Partici- pants*	Total %**	Total Events ***	Total Partici- pants*	Total %**	Total Events ***
Aggression	0	0	0	0	0	0	1	1.96%	1
Allergies	1	1.96%	1	0	0	0	1	1.96%	1
Anxiety	2	3.92%	3 [#]	0	0	0	2	3.92%	3 [#]
Avoidant Behavior	1	1.96%	1	0	0	0	0	0	0
Bruxism	1	1.96%	2 [#]	0	0	0	0	0	0
Choking	1	1.96%	1	0	0	0	0	0	0
Constipation	3	5.88%	3	0	0	0	0	0	0
Cough	1	1.96%	2 [#]	0	0	0	0	0	0
COVID-19 Infection	0	0	0	1	1.96%	1	1	1.96%	1
COVID-19 Vaccine Side Effect	1	1.96%	2 [#]	0	0	0	2	3.92%	2
Decreased academic performance	1	1.96%	1	0	0	0	0	0	0
Diarrhea	2	3.92%	3 [#]	0	0	0	2	3.92%	2
Disruptive Behavior	1	1.96%	2 [#]	0	0	0	0	0	0
Dizziness	1	1.96%	1	0	0	0	1	1.96%	1
Dysgeusia	0	0	0	0	0	0	1	1.96%	2 [#]
Dysphagia	0	0	0	0	0	0	1	1.96%	1
Ear infection	1	1.96%	1	0	0	0	1	1.96%	1
Elevated transaminase	1	1.96%	1	0	0	0	0	0	0
Emotional lability	1	1.96%	1	0	0	0	1	1.96%	1
Enterobiasis	0	0	0	0	0	0	1	1.96%	1
Epistaxis	1	1.96%	1	0	0	0	0	0	0
Eye Blinking	1	1.96%	1	0	0	0	0	0	0
Fatigue	3	5.88%	3	0	0	0	0	0	0
Fever	2	3.92%	2	0	0	0	1	1.96%	1

	Group A (n=17)			Group B (n=19)			Group C (n=15)		
Standardized AE Category	Total Participants*	Total %**	Total Events***	Total Participants*	Total %**	Total Events***	Total Participants*	Total %**	Total Events***
Fine motor impairment	0	0	0	0	0	0	1	1.96%	1
Gastrointestinal Issue	2	3.92%	2	1	1.96%	1	1	1.96%	2 [#]
Headache	3	5.88%	8 [#]	1	1.96%	2 [#]	1	1.96%	2 [#]
Heartburn	1	1.96%	1	0	0	0	0	0	0
Hematochezia	0	0	0	0	0	0	1	1.96%	1
Hypoglycemia	0	0	0	0	0	0	1	1.96%	1
Hypokalemia	0	0	0	0	0	0	1	1.96%	1
Incontinence	1	1.96%	1	0	0	0	0	0	0
Influenza	0	0	0	0	0	0	1	1.96%	1
Insect Sting	1	1.96%	1	0	0	0	1	1.96%	1
Irritability	1	1.96%	1	0	0	0	0	0	0
Itchiness	1	1.96%	1	0	0	0	0	0	0
Listlessness	1	1.96%	1	0	0	0	0	0	0
Lymphocytic Variant	1	1.96%	1	0	0	0	0	0	0
Menstrual Cramps	1	1.96%	1	0	0	0	0	0	0
Mouthing	1	1.96%	1	0	0	0	0	0	0
Muscle Spasm	0	0	0	0	0	0	1	1.96%	1
Musculoskeletal Injury	2	3.92%	2	0	0	0	0	0	0
Nausea	1	1.96%	1	1	1.96%	1	0	0	0
Obsessive Compulsive Behavior	1	1.96%	2 [#]	0	0	0	0	0	0
Panic Attack	0	0	0	0	0	0	1	1.96%	1
Pharyngitis	2	3.92%	2	0	0	0	0	0	0
Rash	4	7.84%	4	0	0	0	1	1.96%	1
Self-injurious behavior	0	0	0	1	1.96%	1	0	0	0
Skin abrasion	2	3.92%	2	0	0	0	1	1.96%	1
Skin infection	0	0	0	0	0	0	1	1.96%	1
Skin Laceration	0	0	0	1	1.96%	1	0	0	0
Sleep disturbance	4	7.84%	5 [#]	1	1.96%	1	2	3.92%	2

	Group A (n=17)			Group B (n=19)			Group C (n=15)		
Standardized AE Category	Total Participants*	Total %**	Total Events***	Total Participants*	Total %**	Total Events***	Total Participants*	Total %**	Total Events***
Sprain	0	0	0	0	0	0	2	3.92%	3 [#]
Suicidal Thinking	1	1.96%	1	1	1.96%	1	1	1.96%	1
TMJ Pain	0	0	0	0	0	0	1	1.96%	1
Teeth Chattering	1	1.96%	1	0	0	0	0	0	0
Tics	2	3.92%	2	0	0	0	0	0	0
Upper Respiratory Infection	1	1.96%	2 [#]	2	3.92%	3 [#]	4	7.84%	5 [#]
Viral Infection	1	1.96%	1	0	0	0	0	0	0
Vomiting	3	5.88%	4 [#]	0	0	0	1	1.96%	1
Wheezing	1	1.96%	2 [#]	0	0	0	1	1.96%	1

* Number of participants experiencing an adverse event (participant is to be counted only once for each adverse event)

** % of total number of participants with AE data available to date (total N=51) in the study

*** Total number of events overall

Indicate recurrence of same adverse event

Table 6. Severity of Adverse Events by Treatment Group

	Total Number of Participants * (%**) with				
Treatment Group	NO AE	Mild Event	Moderate Event	Serious Event	Group Difference p-value
Overall	14 (27.5%)	24 (47.1%)	12 (23.5%)	1 (1.96%)	7.45e-05
Group A	0	9	7	1	
Group B	12	4	3	0	
Group C	2	11	2	0	

* Number of **participants** experiencing a certain severity of an adverse event where each participant is counted only once at the highest level of severity for the event

** % of participants experiencing a certain severity of an adverse event

	Total Number of Adverse Events* (%**)			
Treatment Group	Mild	Moderate	Serious	Group Difference p-value
Overall	124 (87.9%)	16 (9.68%)	1 (0.8%)	0.117
Group A	70	11	1	
Group B	9	3	0	
Group C	45	2	0	

* Total number of **events** experiencing a certain severity of an adverse event

** % of events experiencing a certain severity of an adverse event

Appendix

Listing 1: Adverse Events *

Participant ID	Adverse Event	Severity	Frequency	Action Taken	Outcome**	Relationship to Study Medication***
003X	Diarrhea	1	1	1	1	1
003X	Diarrhea	1	1	1	1	1
005X	Anxiety	1	1	1	1	2
005X	Anxiety	1	1	1	1	2
005X	Sprain	1	3	1	1	1
005X	Sprain	1	3	1	1	1
007V	Dysgeusia	1	1	1	1	3
007V	Dysgeusia	1	1	1	1	2
009V	Mouthing	2	1	1	6	2
009V	Sleep disturbance	1	1	1	1	2
009V	Disruptive Behavior	1	1	1	1	2
009V	Fever	2	1	1	3	1
009V	Ear infection	2	1	1	3	1
009V	Disruptive Behavior	1	1	1	1	1
011X	Anxiety	1	1	1	1	1
011X	Tics	1	1	1	3	2
011X	Listlessness	1	1	1	1	1
011X	Anxiety	2	2	4	1	4
011X	Rash	1	3	1	3	2
006X	Upper respiratory infection	1	1	1	1	1
003X	Rash	1	1	1	3	2
010X	Suicidal thinking	2	1	1	1	2
010X	Anxiety	1	1	1	1	3
010X	Allergies	1	1	1	1	1
022W	Upper respiratory infection	1	2	1	3	1
022W	Nausea	1	3	1	1	1
022W	Upper respiratory infection	2	2	1	1	1
016W	Upper respiratory infection	1	1	1	1	1
016W	Upper respiratory infection	1	1	1	1	1
016W	Fine motor impairment	1	1	1	3	2
023W	Self-injurious behavior	1	3	1	1	1

Participant ID	Adverse Event	Severity	Frequency	Action Taken	Outcome**	Relationship to Study Medication***
019W	Cough	1	1	1	1	1
019W	Cough	1	1	1	1	1
019W	Sleep disturbance	1	1	1	4	3
020W	Constipation	3	2	1	3	3
020W	Vomiting	1	1	1	1	3
020W	Sleep disturbance	1	1	1	1	3
020W	Vomiting	1	1	1	1	1
020W	Diarrhea	1	1	1	1	1
017W	Fatigue	1	1	1	1	2
018W	Hematochezia	1	1	1	3	1
018W	Skin abrasion	1	3	1	3	1
018W	Upper respiratory infection	1	1	1	1	1
002X	Rash	1	1	1	1	1
014W	Aggression	1	1	1	1	2
014W	Vomiting	1	1	1	1	2
014W	Diarrhea	1	1	1	1	2
024W	Obsessive compulsive behavior	1	1	1	1	2
024W	Pharyngitis	1	1	1	1	1
024W	Obsessive compulsive behavior	1	1	1	6	2
015W	Hypoglycemia	1	1	1	1	2
015W	Hypokalemia	1	1	1	1	2
015W	Skin infection	1	1	1	1	1
010X	Sprain	1	3	1	1	1
015W	Influenza	1	1	1	1	1
015W	Upper respiratory infection	1	1	1	1	1
031Y	Fatigue	1	1	1	1	2
031Y	Wheezing	1	1	1	1	1
031Y	Elevated transaminase	1	1	3	6	4
031Y	Wheezing	1	1	1	1	1
031Y	Emotional lability	2	1	5	3	4
031Y	Irritability	2	1	5	3	4
031Y	Teeth chattering	2	1	5	3	4
012W	Dizziness	1	1	1	1	3
012W	Rash	1	1	1	1	1
012W	Fever	1	1	1	1	1
012W	Ear infection	1	1	1	1	1

Participant ID	Adverse Event	Severity	Frequency	Action Taken	Outcome**	Relationship to Study Medication***
012W	Diarrhea	1	1	1	6	1
033Y	Gastrointestinal issues	1	1	1	1	2
033Y	Decreased academic performance	1	2	1	ongoing	2
029Y	Choking	1	1	1	1	5
034Y	Emotional lability	1	1	1	1	2
034Y	Sleep disturbance	1	1	1	6	2
034Y	Wheezing	1	1	1	1	1
029Y	Headache	1	1	1	1	2
034Y	Headache	1	1	1	1	2
034Y	Headache	1	1	1	1	2
034Y	TMJ pain	1	3	1	1	2
034Y	Panic attack	1	3	1	1	2
034Y	COVID-19 infection	2	3	1	1	2
036Y	Muscle spasm	1	1	1	1	2
045Z	Sleep disturbance	1	1	1	6	2
045Z	Dysphagia	1	3	1	1	3
027Y	Musculoskeletal injury	1	1	1	1	1
027Y	Dizziness	1	3	1	1	2
027Y	Headache	1	1	1	1	1
038Z	Headache	1	1	1	1	1
038Z	Headache	1	1	1	1	1
038Z	COVID-19 vaccine side effect	1	1	1	1	1
038Z	COVID-19 vaccine side effect	1	3	1	1	1
038Z	Epistaxis	1	1	1	1	2
038Z	Nausea	1	3	1	1	3
038Z	Headache	1	1	1	1	2
038Z	Viral infection	1	3	1	1	2
038Z	Rash	1	3	1	1	1
038Z	Insect Stings	1	3	1	1	1
038Z	Headache	1	3	1	1	2
038Z	Headache	1	3	1	1	2
038Z	Headache	1	3	1	1	2
046Z	Enterobiasis	1	3	1	1	1
046Z	Gastrointestinal issues	1	1	1	1	2

Participant ID	Adverse Event	Severity	Frequency	Action Taken	Outcome**	Relationship to Study Medication***
046Z	COVID-19 vaccine side effect	1	3	1	1	2
046Z	Gastrointestinal issues	1	1	1	1	2
046Z	Insect Stings	1	3	1	3	2
042Z	Upper respiratory infection	1	3	1	1	2
042Z	COVID-19 vaccine side effect	1	3	1	1	1
039Z	Sleep disturbance	1	1	1	1	2
039Z	Bruxism	1	1	1	3	2
039Z	Bruxism	2	1	3	6	3
039Z	Sleep disturbance	1	1	1	6	2
039Z	Eye Blinking	1	1	1	1	2
039Z	Constipation	1	1	1	6	2
039Z	Lymphocytic Variant	1	3	1	6	2
048Z	Upper respiratory infection	1	3	1	1	2
048Z	Vomiting	1	3	1	1	2
048Z	Fever	1	1	1	1	1
048Z	Fatigue	1	3	1	1	2
048Z	Incontinence	1	1	1	1	2
048Z	Tics	1	1	1	1	2
048Z	Suicidal thinking	2	1	1	4	2
048Z	Upper respiratory infection	1	3	1	1	2
048Z	Itchiness	1	1	1	1	2
052Z	Musculoskeletal injury	1	3	1	1	1
052Z	Skin abrasion	1	1	1	6	2
052Z	Allergies	1	1	1	1	2
052Z	Pharyngitis	1	1	1	6	2
052Z	Avoidant behaviors	2	2	1	1	4
052Z	Vomiting	1	3	1	1	2
052Z	Constipation	1	2	1	6	3
044Z	Anxiety	2	1	1	4	3
044Z	Skin abrasion	1	1	1	1	2
044Z	Gastrointestinal issues	1	3	1	1	2
044Z	Heartburn	1	1	1	1	2
044Z	Menstrual cramps	1	1	1	1	2

Participant ID	Adverse Event	Severity	Frequency	Action Taken	Outcome**	Relationship to Study Medication***
028Y	Headache	1	3	1	1	2
028Y	Headache	1	3	1	1	2
028Y	Gastrointestinal issues	1	3	1	1	2
035Y	Skin laceration	2	3	1	1	1
035Y	Sleep disturbance	1	3	1	1	2
051Z	COVID-19	2	3	1	1	2
049Z	Suicidal thinking	1	1	1	1	2

* *This listing was sorted by Participant dummy ID.*

Severity	Frequency	Action taken with Study Drug	Outcome	Relationship to study drug
1 = mild 2 = moderate 3 = severe	1 = Intermittent 2 = Continuous 3 = Single	1 = None 2 = Study Drug Temporarily Discontinued 3 = Dose Decrease 4 = Study Drug Permanently Discontinued 5 = Concomitant Medication/ Therapy 6 = Hospitalization/ Hospitalization Prolonged	1 = Recovered 2 = Recovered with sequelae 3 = Recovering 4 = Not Recovered 5 = Fatal 6 = Unknown	1 = Not Related 2 = Unlikely 3 = Possibly related (<50%) 4 = Probably related (>50%) 5 = Definitely related

Listing 2: Demographics

ID	Blinded Group (A, B, or C)	Age at Enrollment (years)	Gender	Race	Ethnicity	Status of Enrollment
001V	B	10	F	Asian	Not Hispanic/Latino	Completed
002X	A	12	M	White	Not Hispanic/Latino	Completed
003X	A	9	M	White	Not Hispanic/Latino	Completed
004V	B	9	M	White and Black/African American	Not Hispanic/Latino	Early Termination
005X	C	8	M	White	Not Hispanic/Latino	Completed
006X	B	12	M	Black/African American	Not Hispanic/Latino	Completed
007V	C	10	M	White and Black/African American	Not Hispanic/Latino	Early Termination
008X	B	9	M	White	Not Hispanic/Latino	Completed
009V	A	9	M	White and American Indian	Hispanic/Latino	Completed
010X	C	12	M	White	Hispanic/Latino	Completed
011X	A	11	M	White and Asian	Hispanic/Latino	Early Termination
022W	B	9	M	White	Hispanic/Latino	Completed
016W	C	8	M	White	Not Hispanic/Latino	Completed
023W	B	11	M	Unknown/Not Reported	Unknown	Completed
019W	A	9	M	Black/African American	Not Hispanic/Latino	Completed
020W	A	9	M	White	Hispanic/Latino	Completed
017W	A	11	M	Other/Refused	Hispanic/Latino	Completed
018W	C	10	M	White	Not Hispanic/Latino	Completed
014W	C	8	M	White	Hispanic/Latino	Early Termination
024W	A	9	M	Other	Hispanic/Latino	Completed
013W	B	11	M	Black/African American	Not Hispanic/Latino	Completed

ID	Blinded Group (A, B, or C)	Age at Enrollment (years)	Gender	Race	Ethnicity	Status of Enrollment
021W	B	10	M	White	Not Hispanic/Latino	Early Termination
015W	C	9	F	White and Native Hawaiian or Pacific Islander	Hispanic/Latino	Completed
025W	B	13	M	White	Not Hispanic/Latino	Early Termination
012W	C	10	F	Unknown/Not Reported	Unknown	Completed
026Y	C	11	M	White	Not Hispanic/Latino	Early Termination
030Y	B	11	M	Black/African American	Not Hispanic/Latino	Completed
031Y	A	11	M	White	Not Hispanic/Latino	Completed
033Y	A	12	F	White and Black/African American	Not Hispanic/Latino	Active
029Y	A	9	F	White	Hispanic/Latino	Active
034Y	C	8	F	White	Unknown	Active
035Y	B	10	F	White	Not Hispanic/Latino	Active
036Y	C	12	M	White	Hispanic/Latino	Active
028Y	B	8	M	White	Not Hispanic/Latino	Active
027Y	A	11	M	Asian	Not Hispanic/Latino	Active
032Y	B	10	M	White	Not Hispanic/Latino	Active
045Z	C	12	M	Unknown/Not Reported	Unknown	Completed
038Z	A	13	M	White	Not Hispanic/Latino	Completed
041Z	B	9	M	White and American Indian	Not Hispanic/Latino	Completed
043Z	B	11	M	White and American Indian	Not Hispanic/Latino	Completed
046Z	C	8	F	White	Not Hispanic/Latino	Completed

ID	Blinded Group (A, B, or C)	Age at Enrollment (years)	Gender	Race	Ethnicity	Status of Enrollment
042Z	C	12	M	White	Hispanic/Latino	Active Phase 2
039Z	A	8	M	Asian	Not Hispanic/Latino	Completed
048Z	A	9	M	White	Not Hispanic/Latino	Completed
052Z	A	12	M	White	Not Hispanic/Latino	Early Termination
044Z	A	12	F	White	Not Hispanic/Latino	Follow-up
040Z	B	13	M	White	Hispanic/Latino	Follow-up
051Z	B	13	M	White	Not Hispanic/Latino	Follow-up
049Z	B	11	M	White and Asian	Not Hispanic/Latino	Follow-up
047Z	C	11	F	White	Not Hispanic/Latino	Follow-up
050Z	B	8	M	Unknown/Not Reported	Unknown	Active