

U.S. Food and Drug Administration
Generic Clearance: Request for Data to Support Social and Behavioral Research
OMB Control Number 0910-0847
Gen IC Request for Approval

Title of Gen IC: NMURx Express Survey to Evaluate Stimulant Abuse in the United States: Trajectories from Medical Use to Non-Medical Use

1. Statement of Need:

Total prescription stimulant dispensing in the United States (US) doubled from 2006 to 2016 (Ref. 1), and in 2018 an estimated 5.1 million Americans over the age of 12 misused a prescription stimulant (Ref. 2). The same year, 1 million people misused a prescription stimulant drug for the first time, and the estimated number of those with cocaine, methamphetamine, or prescription stimulant use disorder was higher than for heroin. Prescription stimulant non-medical use (NMU) has been documented in several sectors of society (Ref. 3), with high risk particularly noted among younger adults and adolescents (Refs. 4-7). In parallel with increased prescription stimulant availability and non-medical use, severe outcomes have also been increasing. Mortality involving psychostimulants has risen dramatically, with 15% of all drug overdose deaths in 2017 involving a stimulant (Ref. 8). Additionally, high risk behaviors, such as injection of prescription stimulants and increased risk of associated HIV, have been reported internationally (Refs. 9,10).

Crucial components of prescription stimulant misuse and abuse still remain poorly understood. In particular, the trajectories of prescription stimulant NMU are not yet well described, including potential interactions with illicit stimulant use and patterns of co-use with other drug classes such as opioids. Understanding these patterns of stimulant use will be crucial to developing future public health and regulatory interventions to prevent and treat stimulant use disorders. Such class-wide surveillance is not the responsibility of any single drug product sponsor, so Rocky Mountain Poison and Data Center (RMPDS) has therefore partnered with FDA under BAA #145 in order to work towards addressing this gap. The Researched Abuse, Diversion and Addiction-Related Surveillance (RADARS®) System will utilize the NMURx Express survey to understand the landscape of stimulant non-medical use in the United States. The goal of this study is to provide understanding on how and why specific active pharmaceutical and illicit ingredients are used by the population as well as trajectory of use over time.

The NMURx Express is a short survey which collects additional data from individuals who have non-medically used a prescription stimulant or used an illicit stimulant by asking in-depth questions that investigate nuanced behavior related to substance use.

2. Intended Use of the Information:

The objective of the NMURx Express online survey is to identify progression of behaviors for individuals and quantify the timing of initiation of non-medical use (NMU) of stimulant drugs. This survey was developed for individuals who have a history of reported prescription stimulant use or illicit stimulant use. These individuals will be questioned on specific behaviors regarding stimulant use, prescribing history, and attention deficit disorder or attention deficit/hyperactivity disorder (ADHD) diagnosis history.

A total of 16 behaviors and experiences will be asked about on the questionnaire. Respondents will indicate whether they have engaged in a behavior and at what age they first initiated it. These questions will form the basis of the multivariable analysis to assess trajectory of use. In addition, perceived risk of drug use activities will also be measured. The behaviors below and experiences related to stimulant use will be asked about for each drug. Using information on the age of initiation of these behaviors, a progression of behaviors will be constructed using multivariable modelling.

- Personal prescription from a healthcare provider
- ADHD diagnosis
- Non-medical use for weight loss
- Non-medical use to improve work or school performance
- Non-medical use to improve athletic performance
- Obtained a drug from a friend or family member
- Online purchases without a prescription
- Purchase from a dealer
- Using the stimulant to replace another drug
- Concomitant use of another drug(s) with a stimulant
- Use to feel good or get high
- Injection
- Needle sharing
- Smoking or vaping
- Snorting
- Tampering with a drug

3. **Description of Respondents:**

Respondents who complete the Survey of Non-Medical Use of Prescription Drugs survey and endorse a history or lifetime use or abuse of a stimulant will be invited to take the NMURx Express follow-up survey. Respondents are adult volunteers from the general United States population that have opted to participate in a commercial survey panel. Demographics from the panel are shown below; respondents will be a subset of the Panel.

Based on previous NMURx surveys, approximately 7,000 respondents are expected to report lifetime use of a stimulant in the main survey. Of these, 20% are expected to consent to follow-up, resulting in an expected sample size of 1,400 for the NMURx Express follow-up survey.

Table 1. Nationally Estimated Demographic Characteristics

**RADARS® System Survey of Non-Medical Use of Prescription Drugs Program
3rd Quarter 2018 through 1st Quarter 2019**

Characteristics	Overall % (95% CI)
Sex	
Male	48.67 (48.21, 49.13)
Female	51.33 (50.87, 51.79)
Age Categories (years)	
18-24	12.23 (11.85, 12.62)
25-34	17.8 (17.43, 18.17)
35-44	16.39 (16.05, 16.73)
45-54	16.77 (16.42, 17.12)
55-64	16.66 (16.36, 16.97)
65 or Older	20.15 (19.83, 20.46)
Race/Ethnicity^b	
Hispanic	9.02 (8.73, 9.30)
American Indian or Alaska Native	1.73 (1.61, 1.85)
Asian	5.45 (5.22, 5.68)
Black or African American	10.29 (9.99, 10.58)
Native Hawaiian or Other Pacific Islander	0.38 (0.32, 0.45)
White	81.14 (80.76, 81.52)
Prefer Not to Answer	3.81 (3.62, 4.00)
Household Income	
Less than \$25,000	18.14 (17.78, 18.50)
Between \$25,000 and \$49,999	26.57 (26.17, 26.98)
Between \$50,000 and \$74,999	22.33 (21.95, 22.72)
Between \$75,000 and \$99,999	14.76 (14.44, 15.09)
\$100,000 or More	18.19

4. How the Information is Collected:

Participant information is kept secure to the extent permitted by law. Information will be collected via an online survey to the general adult population through a commercial survey panel through a commercial survey administration company, which has enrolled a large panel of respondents in the United States. For each launch, the survey administration company sends an email invitation to adult panel members. These panel members are individuals who sign up to complete surveys in exchange for points, which can be redeemed for modest compensation. Each deployment of the survey is a new sample of respondents, as this is not a longitudinal study. The final sample reflects the geographical and gender distribution of the population. Respondents for the NMURx Express Survey will be recruited from a commercial survey panel, namely the Survey of Non-Medical Use of Prescription Drugs.

5. Confidentiality of Respondents:

Responses to the NMURx Express survey are provided confidentially to the survey panel, which then transfers a limited dataset to RMPDS. No PHI or other identifying information is shared with RMPDS nor stored in any internal datasets. The questionnaire does collect demographic information (age, sex, and income), the first three digits of the respondent's current zip code, and whether the respondent is a student, member of the armed forces, or a healthcare professional. This study has been issued a certificate of confidentiality by NIH.

6. Amount and Justification for Proposed Incentive:

Is an incentive (e.g., stipend, reimbursement of expenses, token of appreciation) provided to participants? Yes No

If yes, describe the incentive and provide a justification for the amount. If no, delete this instruction.]

Monetary incentive

- Compensation is approximately \$1 USD for completing the survey. This aligns with the compensation of other surveys the panelists are invited to complete with comparable completion time. Multiple panels are used to recruit respondents into the survey and compensation method is proprietary for each panel.

Non-monetary incentives

- Panelists may earn points by completing multiple surveys offered by the survey administration company, which can then be redeemed for a chance to enter sweepstakes, or some other reward.

7. Questions of a Sensitive Nature:

Some questions on this survey may be considered sensitive by the respondent from a social desirability perspective. This survey enquires about the previous use of prescription and illicit stimulant drugs. However, no protected health information or information that could be used

to identify the individual is collected. Data is de-identified prior to being transferred from the survey panel to RMPDS.

8. Description of Statistical Methods:

Univariate analyses of the data are necessary to contextualize the multivariable analysis that follows. Demographics of the sample will be provided (e.g., sex, age, ethnicity, race, income, Census region, student status, veteran status, DAST-10 profile). Percentages of endorsement of each behavior out of the entire cohort and percentages of each behavior out of those who endorse each drug will be reported as a univariate analysis. Mean perceived risk scores will be reported for the entire cohort and stratified by those who reported each of the behaviors and by demographics. Univariate progression of behaviors by age of initiation will be displayed graphically.

A series of latent transition analyses (LTA) models will be fit to determine the optimal number of latent categories (15). Models with 1 through 6 statuses will be fit, and the most parsimonious model with the smallest Bayesian Information Criterion (BIC) will be selected. The BIC will be used as a guide and not a strict selection criterion. When two models can be similarly interpreted, the most parsimonious model with fewer statuses is preferred. Once a model is selected, the prevalence of each status at each time point and transition probabilities will be reported. Prevalence of each behavior within the statuses will be described. Two assumptions will be tested using sensitivity analyses. First, it is assumed that 4-year age buckets represent periods when new behaviors are initiated. This range could be too large or too small. Therefore, the model will be tested with 2- and 10-year age buckets to see if the interpretation of the statuses or transitions between statuses changes substantially. Second, there could be birth cohort differences in the responses, the LTA will be stratified the age of the respondent into three categories: 18-30, 31-50, and 50+.

9. Burden Hour Computation: [Complete the table below.]

We estimate the time to complete the survey is 10 minutes based on an anticipated response rate of 20% which corresponds to 1400 respondents. The NMURx Express Survey will contain 12 items.

Type/Category of Respondent	No. of Respondents	Participation Time (minutes)	Burden (hours)
	1,400	10	233

10. Date(s) to be Conducted:

The survey is anticipated to launch in August 2021 (pending OMB approval), and will continue through October 2021. It will be conducted as an online platform and therefore will not have a physical location.

11. FDA Contacts:

Program Office Contact	FDA PRA Contact
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