The NIDA Standardized Research E-Cigarette (SREC)

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NIDA and NIH Interest in E-Cigarettes

The full impact of e-cigarettes on public health remains to be determined.

Questions include:

- What harms are associated with e-cigarette use?
- How do these harms compare with those from smoked tobacco (is there a reduction in harm)?
- What is addictive potential of e-cigarettes and how does this compare to other tobacco products?
- Do e-cigarettes represent a path towards tobacco harm reduction or cessation of nicotine use?
- What is the appeal of e-cigarettes to vulnerable populations and what factors influence the appeal?
- What harms are associated with environmental (second-hand) aerosol exposure?

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Current E-Cigarettes in Clinical Research

Currently available commercial e-cigarettes have limited access to information concerning:

- **How well does the device deliver nicotine?**
- **How reproducible is the nicotine delivery during cartridge and battery lifetime?**
- **What is the composition of the e-liquid?**
- **Will the characteristics of the device remain unchanged?**
- **How long will the device be commercially available?**

NOTE:

- Products introduced after August 2016 need FDA authorization
- FDA authorization will require a Product Master File
- Earlier products can only be sold until 2018/9 (unless authorized)

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NIDA Standardized Research E-cigarette

To address the needs of clinical researchers, NIDA launched a competitive SBIR contract to produce a standardized e-cigarette

Several companies were funded through the SBIR

NJOY LLC is the first to complete the process and produce a Standardized Research E-Cigarette **(SREC)**

- **SREC has a detailed Product Master File (PMF)**
- **SREC is expected to be available for an extended period (to serve as a standard between studies)**
- **All purchasers will get a Letter of Authorization to allow them to cross-reference the PMF in FDA filings**

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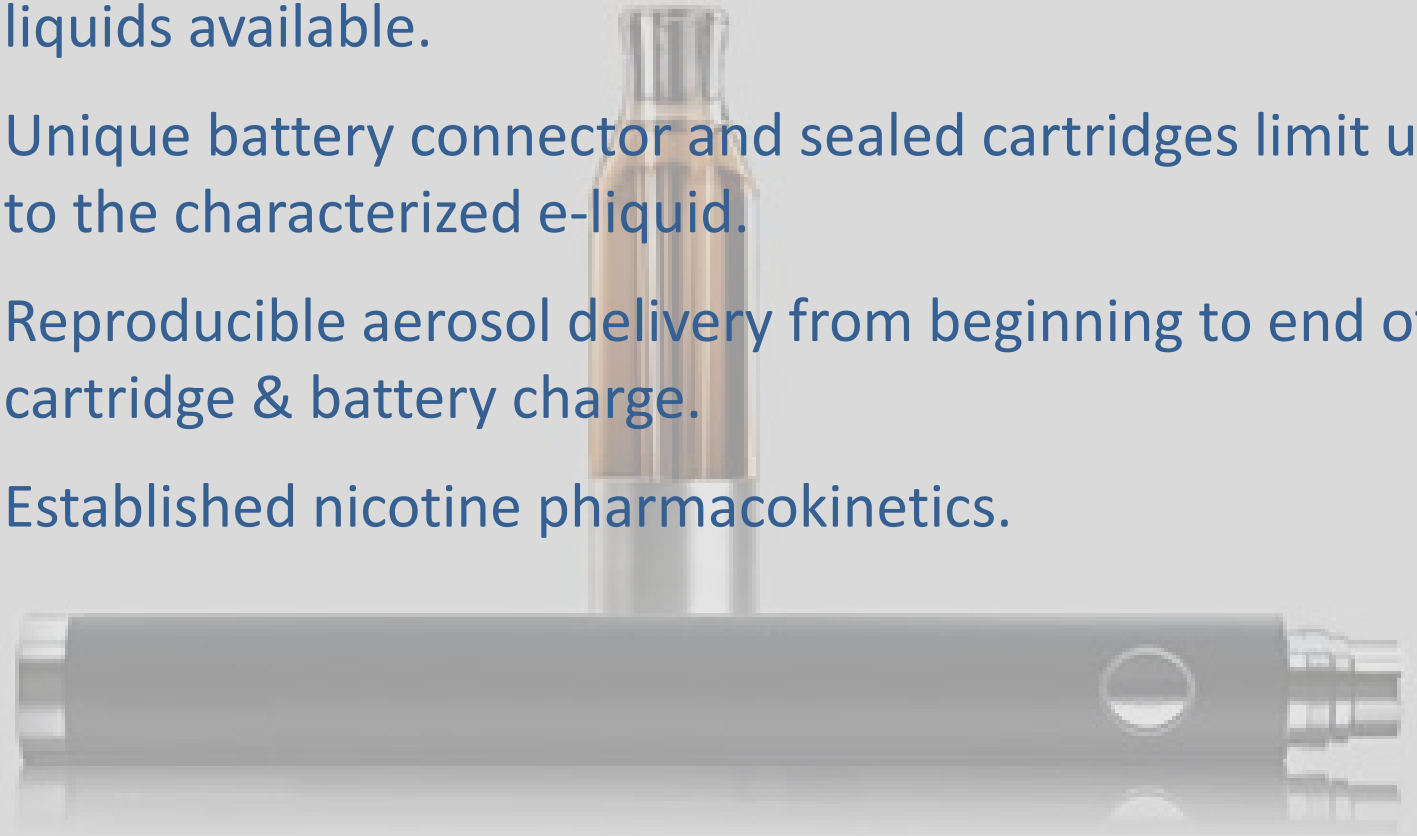
Key features of the SREC

- E-liquids made under GMP-like conditions.
- Fully characterized e-liquid and aerosol.
- Tobacco flavored nicotine-containing and placebo e-liquids available.
- Unique battery connector and sealed cartridges limit use to the characterized e-liquid.
- Reproducible aerosol delivery from beginning to end of cartridge & battery charge.
- Established nicotine pharmacokinetics.



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NIDA SREC

Device Characteristics

- Rechargeable (USB): 180mm (L) x 14 mm (D)
- Mass: 43.3g (with full tank)
- Breath actuated (0.5-0.8LPM), child-resistant
- Single charge outlasts an individual e-liquid cartridge

E-liquid Characteristics

- “Tobacco” flavored 3 mL sealed disposable tanks
- Nicotine (15 mg/ml) and placebo versions available
- Delivers 100 ug nicotine / puff, >350 puffs / cartridge
- Puff-to-puff reproducibility data available

NOTE:

The Product Master File is expected to satisfy FDA CTP requirements for harm reduction studies (ITP), but will **NOT** currently satisfy FDA CDER requirements for nicotine cessation studies (IND)

SREC technical characteristics

	SREC[1]	COMMERCIAL[2]
E-LIQUID		
Puffs (3 s) per Cartridge	> 350	Variable
Nicotine Concentration	15 mg/mL	7-21 mg/mL
AEROSOL CHARACTERISTICS (per 10 puffs)		
Nicotine	1 mg	0.3 – 3 mg
Formaldehyde	1 µg	0.6 - 5 µg
Acetaldehyde	0.9 µg	0.4 – 21 µg
Acrolein	0.2 µg	? – 1.4 µg

1. https://www.drugabuse.gov/funding/supplemental-information-nida-e-cig
2. 2016 El-Hellani et al, Nicotine and Carbonyl Emissions From Popular Electronic Cigarette Products: Correlation to Liquid Composition and Design Characteristics. Nic Tob Res

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SREC pharmacokinetic nicotine delivery

Subjects were users (n=14) of unmodified commercial e-cigarettes that contain between 10-20 mg/ml nicotine

Protocol

Subjects arrive at residential facility evening prior to study (to ensure abstinence).

Day 1: nicotine delivery by "own device" evaluated

1. Subjects complete a 10-inhalation session over 4.5 minutes, followed by 2h abstinence period with regular PK blood draws.
2. After 2h, a 2nd 10-inhalation session followed by spirometry assessment.
3. Over the next 6h, device is used *ad lib* with regular blood draws.
4. After t=8h, subjects return home with SREC to gain familiarity.

Day 2 Evening: subjects return for overnight abstinence

Day 3: SREC is evaluated using procedure above

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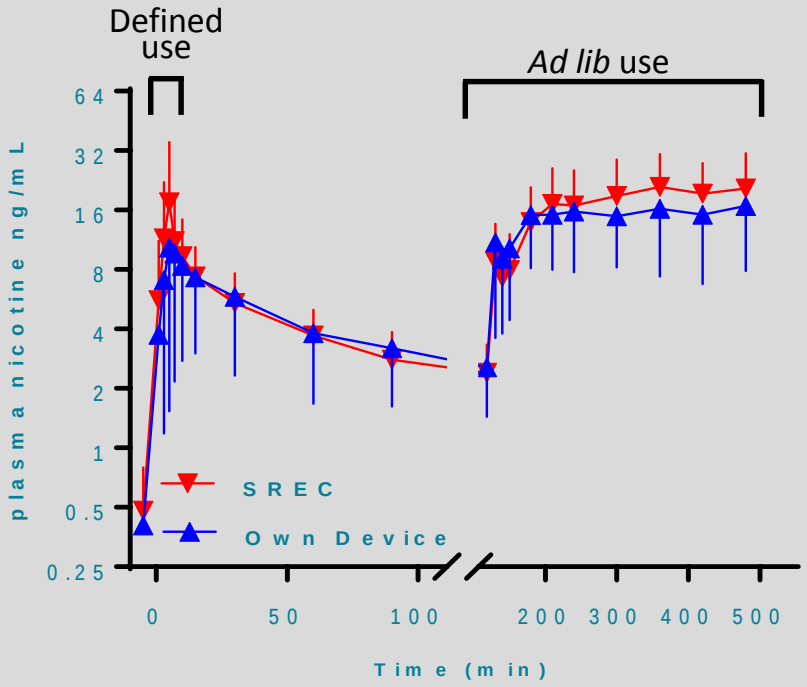
Nicotine Pharmacokinetic Profile
(mean ± SD)



"t" Test results

Cmax		
	Own Device	SREC
Mean (ng/ml)	11.08	17.68
Variance	72.71	306.69
Observations	14	14
P(T<=t) two-tail	0.21	

Tmax		
	Own Device	SREC
Mean (min)	9.07	5.71
Variance	42.69	0.99
Observations	14	14
P(T<=t) two-tail	0.06	

- Each individual's Cmax characteristics were generally similar between the SREC and their own device
- Full data sets with additional measures, including safety biomarkers, will be published ASAP

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SREC Availability

- SREC devices and refills will be purchased directly from NJOY LLC.
- Availability is expected in Q4 2017. **Contact information will be available upon product release.**
- Devices will be priced at $10/unit. Refill cartridges are also $10/unit.
- Access to SREC is assured for all NIH grantees. NJOY also welcomes other researchers to contact them concerning availability.

NIH Funding opportunities using SREC

- Researchers are welcome to include use of the SREC in any appropriate grant applications.

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