16.1.3 List of Institutional Review Boards and Sample Consent Forms

ADVARRA
advancing better research

IRB Membership Roster

OHRP/FDA Registration Number:
IRB#00000971
IORG #0000635

Full Accreditation

*Executive Chair ** Chairperson

	Member's Name	Profession	Status	Main Roster Member Role	Affiliated Y/N
1.	(b) (6)	Regulatory	Non-Scientist	Primary	Y
2.		Compliance Director	Non-Scientist	Primary	N
3.		Physician Internal Medicine	Physician Scientist	Primary	N
4.		Physician Internal Medicine	Physician Scientist	Primary	N
5.		Ethics and Research Consultant/Ethicist	Other Scientist	Primary	N
6.		Toxicologist/Regulatory Affairs Consultant	Other Scientist	Primary	N
7.		Pharmacology	Other Scientist	Primary	N
8.		Regulatory	Non-Scientist	Alt	Y
9.		Ethics	Non-Scientist	Alt.	Y
10.		University Professor, Religious Studies, Ethicist	Non-Scientist	Alt.	N
11.		Clinical Research Administration; Respiratory Therapy	Other Scientist	Alt.	Y
12.		Regulatory	Non-Scientist	Alt.	Y
13.		Clinical Pharmacist	Other Scientist	Alt.	N
14.		Professional Translator/French	Non-Scientist	Alt.	N
15.		Physician – Internal Medicine/Pulmonologist	Physician Scientist	Alt.	N
16.		Regulatory	Non-Scientist	Alt	Y
17.		Regulatory	Non-Scientist	Alt.	Y
18.		Adult Neuroscience	Other Scientist	Alt.	N
19.		Regulatory	Non-Scientist	Alt.	Y
20.		Community Health, Nursing	Other Scientist	Alt.	Y
21.		Public Health	Other Scientist	Alt.	N
22.		Pharmacology	Physician Scientist	Alt.	N
23.		Community Health, Nursing	Other Scientist	Alt.	Y
24.		County Government Administrator	Non-Scientist	Alt.	N
25.		Research Ethics	Non-scientist	Alt.	Y
26.		Oncology Research Coordinator	Other Scientist	Alt.	Y
27.		Research Consultant	Non-Scientist	Alt.	Y
28.		Pediatric Clinical Research Manager	Other Scientist	Alt.	N
29.		Social Work, Subject Advocate	Non-Scientist	Alt.	N
30.		Emergency Trauma Nursing/Public Health	Other Scientist	Alt.	N
31.		Physician - Oncology Pediatric	Physician Scientist	Alt.	N
32.		Physician – Pediatrics, Hematology Oncology	Physician Scientist	Alt.	N
33.		Clinical Research Nursing	Other Scientist	Alt.	Y

	Member's Name	Profession	Status	Main Roster Member Role	Affiliated Y/N
34.	(b) (6)	Phase I	Other Scientist	Alt.	N
35.		Oncology Nurse	Other Scientist	Alt.	N
36.		Physician - Medical Advisor	Physician Scientist	Alt.	N
37.		Ministry	Non-Scientist	Alt.	N
38.		Psychiatry, Legal	Other Scientist	Alt.	N
39.		Physician-Cardiologist	Physician Scientist	Alt.	N
40.		Physician–Alzheimer and Neurology	Physician Scientist	Alt.	N
41.		Physician-Family Practice	Physician Scientist	Alt.	N
42.		Ministry	Non-Scientist	Alt.	N
43.		Psychiatry and Behavioral Neuroscience	Other Scientist	Alt	N
44.		Oncology Nurse	Other Scientist	Alt.	N
45.		Physician - Immunology, Internal Medicine	Physician Scientist	Alt.	N
46.		Physician - Radiologist	Physician Scientist	Alt.	N
47.		Oncology Nurse	Other Scientist	Alt.	N
48.		Legal & Healthcare/Research Compliance	Non-Scientist	Alt.	N
49.		Translation	Non-scientist	Alt.	N
50.		Physician - Oncology, Lymphoma	Physician Scientist	Alt.	N
51.		Nurse, Device specialist	Other Scientist	Alt.	N
52.		Physician-Internal Medicine	Physician Scientist	Alt.	N
53.		Immunologist	Other Scientist	Alt.	N
54.		Physician - Oncology, Genitourinary Cancer	Physician Scientist	Alt.	N
55.		Legal, Ethicist	Non-scientist	Alt.	N
56.		Physician – Emergency Medicine	Physician Scientist	Alt.	N
57.		Lawyer	Non-scientist	Alt.	N
58.		Ethics	Non-Scientist	Alt.	N
59.		Physician – Oncology, Gastroenteritis and Phase I	Physician Scientist	Alt	N
60.		Physician- General Practice, Non-Cancer Pain Management	Physician Scientist;	Alt.	N
61.		Physician - Allergy, Immunology	Physician Scientist	Alt.	N
62.		Patient Advocacy	Non-Scientist	Alt.	N
63.		Guidance Counselor	Non-Scientist	Alt.	N
64.		Clinical Development & Compliance Consultant	Other Scientist	Alt.	N
65.		Physician - Obstetrics/Gynecology	Physician Scientist	Alt.	N
66.		Regulatory	Non-Scientist	Alt.	Y
67.		Pharmacist	Other Scientist	Alt.	N
68.		Physician-Pediatrics, Infectious Diseases	Physician Scientist	Alt.	N

	Member's Name	Profession	Status	Main Roster Member Role	Affiliated Y/N
69.	(b) (6)	Physician - Pediatric Emergency Medicine	Other Scientist	Alt.	N
70.		Physician - Ophthalmologist, Neuroscientist	Physician Scientist	Alt.	N
71.		Clinical Research Consultant	Other Scientist	Alt.	N
72.		Statistics	Other Scientist	Alt.	N
73.		Nursing Research Director/Consultant	Other Scientist	Alt	N
74.		Physician – Internal Med., Infectious Diseases	Physician Scientist	Alt.	N
75.		Biomedical Engineering	Other Scientist	Alt.	N
76.		Physician-Oncologist/Hematologist	Physician Scientist	Alt.	N
77.		Regulatory	Non-Scientist	Alt.	Y
78.		Stem Cell & Tissue Research	Other Scientist	Alt.	N
79.		Prisoner Advocate	Non-Scientist	Alt.	N
80.		Ministry	Non-Scientist	Alt.	N
81.		Physician – Medical Research	Physician Scientist	Alt.	N
82.		Physician –Anesthesiologist	Physician Scientist	Alt.	N
83.		Communications	Non-scientist	Alt.	N
84.		Community Member	Non-Scientist	Alt.	N
85.		Physician – OB/Gyn, Clinical Safety Director	Physician Scientist	Alt.	N
86.		Nursing- Clinical Trials Research	Other Scientist	Alt.	N
87.		Quality Assurance, Research Ethics	Other Scientist	Alt.	N
88.		Physician - Pediatric Pulmonology	Physician Scientist	Alt.	N
89.		Physician- Neurologist and Psychiatrist	Physician Scientist	Alt.	N
90.		Hospital and Research Pharmacist	Other Scientist	Alt.	N
91.		Social Psychology	Other Scientist	Alt.	N
92.		Physician- Family Medicine	Physician Scientist	Alt.	N
93.		Attorney, Prisoner Representative	Non-Scientist	Alt.	N
94.		Physician - Neonatal Intensive Care	Physician Scientist	Alt.	N
95.		Pharmacokinetics & Biopharmaceutics	Other Scientist	Alt.	N
96.		Human Subject Protection Consultant	Non-Scientist	Alt.	N
97.		Pharmacist	Other Scientist	Alt.	N
98.		Oncological Nursing	Other Scientist	Alt.	N
99.		Engineer	Non-scientist	Alt.	N
100.		Physician – Phase I, Cardiovascular, Dermatology	Physician Scientist	Alt.	N.

	Member's Name	Profession	Status	Main Roster Member Role	Affiliated Y/N
101.	(b) (6)	Physician - Surgical Oncology	Physician Scientist	Alt.	N
102.		Physician - Psychiatrist	Physician Scientist	Alt,	N
103.		Legal	Non-Scientist	Alt.	N
104.		Physician – Pediatrics, Infectious Disease	Physician Scientist	Alt.	N
105.		Physician - Pulmonary, Critical Care	Physician Scientist	Alt.	N
106.		Physician - Obstetrics/Gynecology	Physician Scientist	Alt.	N
107.		Educator	Non-Scientist	Alt.	N
108.		Physician – Research	Physician Scientist	Alt.	N
109.		Physician - Oncology, Melanoma	Physician Scientist	Alt.	N
110.		Educator	Non-Scientist	Alt.	N
111.		Pharmacology	Other Scientist	Alt.	N
112.		Oncology, Women's Cancer	Physician Scientist	Alt.	N
113.		Ethicist, Pharmacy	Other Scientist	Alt.	N
114.		Public Health	Other Scientist	Alt.	N
115.		Human Subject Protection: Regulatory Affairs	Non-Scientist	Alt.	Y
116.		Nursing Sciences	Other Scientist	Alt.	Y
117.		Attorney	Non-Scientist	Alt.	N
118.		Physician- Oncology – Medical	Physician Scientist	Alt	N

Advarra IRB is organized and operates to assure the protection of the rights and welfare of human subjects participating in human subjects research is further supported by the IRB's commitment to maintaining IRB written policies and procedures based on the US federal regulations (including, but not limited to 21 CFR 50 and 56, and 45 CFR 46), various guidelines as applicable (both domestic and international, including OHRP, FDA, ICH GCP specific to IRB review, and CIOMS), and the ethical principles (The Belmont Report, Nuremberg Code, Declaration of Helsinki) underlying the involvement of human subjects in research. Advarra IRB is Fully Accredited by the Association for the Accreditation of Human Research Protection Programs®, Inc. (AAHRPP).

Alternate Members (Alt.)
Any Non-Scientist alternate member can serve as a voting alternate for Primary Non-Scientist member. Any Physician-Scientist alternate member can serve as a voting alternate for a Primary Physician-Scientist member OR Other Scientist member. Any Other-Scientist alternate member can serve as a voting alternate for a Primary Other-Scientist member.

ROSTER UPDATES

Name	Effective Date	Membership Change
(b) (6)	5/01/2018	Changed from Unaffiliated to Affiliated
	10/19/2018	Added
	11/08/2018	Added
	11/082018	Added
	11/14/2018	Added
	11/20/2018	Added
	11/20/2018	Added
	12/04/2018	Added
	12/11/2018	Added
	12/12/2018	Added
	12/19/2018	Removed
	12/21/2018	Removed as Chairperson; remains on the Board
	01/08/2019	Removed
	01/14/2019	Removed
	01/21/2019	Added
	02/04/2019	Removed
	02/05/2019	Removed
	02/05/2019	Removed

IRB Membership Roster

OHRP/FDA Registration Number:
IRB#00000971
IORG #0000635

*Executive Chair ** Chairperson

	Member's Name	Profession	Status	Main Roster Member Role	Affiliated Y/N
1.	(b) (6)	Regulatory	Non-Scientist	Primary	Y
2.		Compliance Director	Non-Scientist	Primary	N
3.		Physician Internal Medicine	Physician Scientist	Primary	N
4.		Physician Internal Medicine	Physician Scientist	Primary	N
5.		Ethics and Research Consultant/Ethicist	Other Scientist	Primary	N
6.		Toxicologist/Regulatory Affairs Consultant	Other Scientist	Primary	N
7.		Pharmacology	Other Scientist	Primary	N
8.		Regulatory	Non-Scientist	Alt	Y
9.		Ethics	Non-Scientist	Alt.	Y
10.		University Professor, Religious Studies, Ethicist	Non-Scientist	Alt.	N
11.		Clinical Research Administration; Respiratory Therapy	Other Scientist	Alt.	Y
12.		Regulatory	Non-Scientist	Alt.	Y
13.		Clinical Pharmacist	Other Scientist	Alt.	N
14.		Professional Translator/French	Non-Scientist	Alt.	N
15.		Physician – Internal Medicine/Pulmonologist	Physician Scientist	Alt.	N
16.		Regulatory	Non-Scientist	Alt	Y
17.		Regulatory	Non-Scientist	Alt.	Y
18.		Adult Neuroscience	Other Scientist	Alt.	N
19.		Regulatory	Non-Scientist	Alt.	Y
20.		Community Health, Nursing	Other Scientist	Alt.	Y
21.		Public Health	Other Scientist	Alt.	N
22.		Pharmacology	Physician Scientist	Alt.	N
23.		Community Health, Nursing	Other Scientist	Alt.	Y
24.		County Government Administrator	Non-Scientist	Alt.	N
25.		Research Ethics	Non-scientist	Alt.	Y
26.		Oncology Research Coordinator	Other Scientist	Alt.	Y
27.		Research Consultant	Non-Scientist	Alt.	Y
28.		Pediatric Clinical Research Manager	Other Scientist	Alt.	N
29.		Social Work, Subject Advocate	Non-Scientist	Alt.	N
30.		Emergency Trauma Nursing/Public Health	Other Scientist	Alt.	N
31.		Physician - Oncology Pediatric	Physician Scientist	Alt.	N
32.		Physician – Pediatrics, Hematology Oncology	Physician Scientist	Alt.	N
33.		Clinical Research Nursing	Other Scientist	Alt.	Y

	Member's Name	Profession	Status	Main Roster Member Role	Affiliated Y/N
34.	(b) (6)	Phase I	Other Scientist	Alt.	N
35.		Oncology Nurse	Other Scientist	Alt.	N
36.		Physician - Medical Advisor	Physician Scientist	Alt.	N
37.		Ministry	Non-Scientist	Alt.	N
38.		Psychiatry, Legal	Other Scientist	Alt.	N
39.		Physician-Cardiologist	Physician Scientist	Alt.	N
40.		Physician–Alzheimer and Neurology	Physician Scientist	Alt.	N
41.		Physician-Family Practice	Physician Scientist	Alt.	N
42.		Ministry	Non-Scientist	Alt.	N
43.		Psychiatry and Behavioral Neuroscience	Other Scientist	Alt	N
44.		Oncology Nurse	Other Scientist	Alt.	N
45.		Physician - Immunology, Internal Medicine	Physician Scientist	Alt.	N
46.		Physician - Radiologist	Physician Scientist	Alt.	N
47.		Oncology Nurse	Other Scientist	Alt.	N
48.		Legal & Healthcare/Research Compliance	Non-Scientist	Alt.	N
49.		Translation	Non-scientist	Alt.	N
50.		Physician - Oncology, Lymphoma	Physician Scientist	Alt.	N
51.		Nurse, Device specialist	Other Scientist	Alt.	N
52.		Physician-Internal Medicine	Physician Scientist	Alt.	N
53.		Immunologist	Other Scientist	Alt.	N
54.		Physician - Oncology, Genitourinary Cancer	Physician Scientist	Alt.	N
55.		Legal, Ethicist	Non-scientist	Alt.	N
56.		Physician – Emergency Medicine	Physician Scientist	Alt.	N
57.		Lawyer	Non-scientist	Alt.	N
58.		Ethics	Non-Scientist	Alt.	N
59.		Physician – Oncology, Gastroenteritis and Phase I	Physician Scientist	Alt	N
60.		Physician- General Practice, Non-Cancer Pain Management	Physician Scientist;	Alt.	N
61.		Physician - Allergy, Immunology	Physician Scientist	Alt.	N
62.		Patient Advocacy	Non-Scientist	Alt.	N
63.		Guidance Counselor	Non-Scientist	Alt.	N
64.		Clinical Development & Compliance Consultant	Other Scientist	Alt.	N
65.		Physician - Obstetrics/Gynecology	Physician Scientist	Alt.	N
66.		Regulatory	Non-Scientist	Alt.	Y
67.		Pharmacist	Other Scientist	Alt.	N
68.		Physician-Pediatrics, Infectious Diseases	Physician Scientist	Alt.	N

	Member's Name	Profession	Status	Main Roster Member Role	Affiliated Y/N
69.	(b) (6)	Physician - Pediatric Emergency Medicine	Other Scientist	Alt.	N
70.		Physician - Ophthalmologist, Neuroscientist	Physician Scientist	Alt.	N
71.		Clinical Research Consultant	Other Scientist	Alt.	N
72.		Statistics	Other Scientist	Alt.	N
73.		Nursing Research Director/Consultant	Other Scientist	Alt	N
74.		Physician – Internal Med., Infectious Diseases	Physician Scientist	Alt.	N
75.		Biomedical Engineering	Other Scientist	Alt.	N
76.		Physician-Oncologist/Hematologist	Physician Scientist	Alt.	N
77.		Regulatory	Non-Scientist	Alt.	Y
78.		Stem Cell & Tissue Research	Other Scientist	Alt.	N
79.		Prisoner Advocate	Non-Scientist	Alt.	N
80.		Ministry	Non-Scientist	Alt.	N
81.		Physician – Medical Research	Physician Scientist	Alt.	N
82.		Physician –Anesthesiologist	Physician Scientist	Alt.	N
83.		Communications	Non-scientist	Alt.	N
84.		Community Member	Non-Scientist	Alt.	N
85.		Physician – OB/Gyn, Clinical Safety Director	Physician Scientist	Alt.	N
86.		Nursing- Clinical Trials Research	Other Scientist	Alt.	N
87.		Quality Assurance, Research Ethics	Other Scientist	Alt.	N
88.		Physician - Pediatric Pulmonology	Physician Scientist	Alt.	N
89.		Physician- Neurologist and Psychiatrist	Physician Scientist	Alt.	N
90.		Hospital and Research Pharmacist	Other Scientist	Alt.	N
91.		Social Psychology	Other Scientist	Alt.	N
92.		Physician- Family Medicine	Physician Scientist	Alt.	N
93.		Nursing	Other Scientist	Alt.	N
94.		Attorney, Prisoner Representative	Non-Scientist	Alt.	N
95.		Physician - Neonatal Intensive Care	Physician Scientist	Alt.	N
96.		Pharmacokinetics & Biopharmaceutics	Other Scientist	Alt.	N
97.		Human Subject Protection Consultant	Non-Scientist	Alt.	N
98.		Pharmacist	Other Scientist	Alt.	N
99.		Oncological Nursing	Other Scientist	Alt.	N
100.		Engineer	Non-scientist	Alt.	N
101.		Physician – Phase I, Cardiovascular, Dermatology	Physician Scientist	Alt.	N.

	Member's Name	Profession	Status	Main Roster Member Role	Affiliated Y/N
102.	(b) (6)	Physician - Surgical Oncology	Physician Scientist	Alt.	N
103.		Physician - Psychiatrist	Physician Scientist	Alt,	N
104.		Legal	Non-Scientist	Alt.	N
105.		Physician – Pediatrics, Infectious Disease	Physician Scientist	Alt.	N
106.		Physician - Pulmonary, Critical Care	Physician Scientist	Alt.	N
107.		Physician - Obstetrics/Gynecology	Physician Scientist	Alt.	N
108.		Educator	Non-Scientist	Alt.	N
109.		Physician – Research	Physician Scientist	Alt.	N
110.		Physician - Oncology, Melanoma	Physician Scientist	Alt.	N
111.		Educator	Non-Scientist	Alt.	N
112.		Pharmacology	Other Scientist	Alt.	N
113.		Scientific Affairs Consultant – Nutrition	Other Scientist	Alt.	N
114.		Oncology, Women's Cancer	Physician Scientist	Alt.	N
115.		Ethicist, Pharmacy	Other Scientist	Alt.	N
116.		Public Health	Other Scientist	Alt.	N
117.		Human Subject Protection: Regulatory Affairs	Non-Scientist	Alt.	Y
118.		Nursing Sciences	Other Scientist	Alt.	Y
119.		Attorney	Non-Scientist	Alt.	N
120.		Physician – Oncologist, Hematology/Oncology	Physician Scientist	Alt.	N
121.		Physician- Oncology – Medical	Physician Scientist	Alt	N

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Alternate Members (Alt.)
Any Non-Scientist alternate member can serve as a voting alternate for Primary Non-Scientist member. Any Physician-Scientist alternate member can serve as a voting alternate for a Primary Physician-Scientist member OR Other Scientist member. Any Other-Scientist alternate member can serve as a voting alternate for a Primary Other-Scientist member.

ROSTER UPDATES

Name	Effective Date	Membership Change
(b) (6)	5/01/2018	Changed from Unaffiliated to Affiliated
	10/19/2018	Added
	11/08/2018	Added
	11/082018	Added
	11/14/2018	Added
	11/20/2018	Added
	11/20/2018	Added
	12/04/2018	Added
	12/11/2018	Added
	12/12/2018	Added
	12/19/2018	Removed
	12/21/2018	Removed as Chairperson; remains on the Board
	01/08/2019	Removed
	01/14/2019	Removed
	01/21/2019	Added

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advancing better research

IRB Membership Roster

OHRP/FDA Registration Number:
IRB#00000971
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Full Accreditation

*Executive Chair ** Chairperson

	Member's Name	Profession	Status	Main Roster Member Role	Affiliated Y/N
1.	(b) (6)	Regulatory	Non-Scientist	Primary	Y
2.		Compliance Director	Non-Scientist	Primary	N
3.		Internal Medicine	Physician Scientist	Primary	N
4.		Internal Medicine	Physician Scientist	Primary	N
5.		Ethics and Research Consultant/Ethicist	Other Scientist	Primary	N
6.		Toxicologist/Regulatory Affairs Consultant	Other Scientist	Primary	N
7.		Pharmacology	Other Scientist	Primary	N
8.		Ethics	Non-Scientist	Alt.	Y
9.		University Professor, Religious Studies, Ethicist	Non-Scientist	Alt.	N
10.		Clinical Research Administration; Respiratory Therapy	Other Scientist	Alt.	Y
11.		Attorney	Non-Scientist	Alt.	N
12.		Regulatory	Non-Scientist	Alt.	Y
13.		Clinical Pharmacist	Other Scientist	Alt.	N
14.		Professional Translator/French	Non-Scientist	Alt.	N
15.		Physician – Internal Medicine/Pulmonologist	Physician Scientist	Alt.	N
16.		Regulatory	Non-Scientist	Alt	Y
17.		Regulatory	Non-Scientist	Alt.	Y
18.		Adult Neuroscience	Other Scientist	Alt.	N
19.		Regulatory	Non-Scientist	Alt.	Y
20.		Community Health, Nursing	Other Scientist	Alt.	Y
21.		Public Health	Other Scientist	Alt.	N
22.		Pharmacology	Physician Scientist	Alt.	N
23.		Community Health, Nursing	Other Scientist	Alt.	Y
24.		County Government Administrator	Non-Scientist	Alt.	N
25.		Research Ethics	Non-scientist	Alt.	Y
26.		Oncology Research Coordinator	Other Scientist	Alt.	Y
27.		Research Consultant	Non-Scientist	Alt.	N
28.		Pediatric Clinical Research Manager	Other Scientist	Alt.	N
29.		Social Work, Subject Advocate	Non-Scientist	Alt.	N
30.		Emergency Trauma Nursing/Public Health	Other Scientist	Alt.	N
31.		Oncology Pediatric	Physician Scientist	Alt.	N
32.		Physician – Pediatrics, Hematology Oncology	Physician Scientist	Alt.	N
33.		Clinical Research Nursing	Other Scientist	Alt.	Y

	Member's Name	Profession	Status	Main Roster Member Role	Affiliated Y/N
34.	(b) (6)	Phase I	Other Scientist	Alt.	N
35.		Oncology Nurse	Other Scientist	Alt.	N
36.		Medical Advisor	Physician Scientist	Alt.	N
37.		Ministry	Non-Scientist	Alt.	N
38.		Psychiatry, Legal	Other Scientist	Alt.	N
39.		Physician-Cardiologist	Physician Scientist	Alt.	N
40.		Physician-Family Practice	Physician Scientist	Alt.	N
41.		Ministry	Non-Scientist	Alt.	N
42.		Oncology Nurse	Other Scientist	Alt.	N
43.		Immunology, Internal Medicine	Physician Scientist	Alt.	N
44.		Physician - Radiologist	Physician Scientist	Alt.	N
45.		Oncology Nurse	Other Scientist	Alt.	N
46.		Legal & Healthcare/Research Compliance	Non-Scientist	Alt.	N
47.		Translation	Non-scientist	Alt.	N
48.		Oncology, Lymphoma	Physician Scientist	Alt.	N
49.		Nurse, Device specialist	Other Scientist	Alt.	N
50.		Physician-Internal Medicine	Physician Scientist	Alt.	N
51.		Immunologist	Other Scientist	Alt.	N
52.		Oncology, Genitourinary Cancer	Physician Scientist	Alt.	N
53.		Legal, Ethicist	Non-scientist	Alt.	N
54.		Physician – Emergency Medicine	Physician Scientist	Alt.	N
55.		Lawyer	Non-scientist	Alt.	N
56.		Ethics	Non-Scientist	Alt.	N
57.		General Practice, Non-Cancer Pain Management	Physician Scientist;	Alt.	N
58.		Allergy, Immunology	Physician Scientist	Alt.	N
59.		Patient Advocacy	Non-Scientist	Alt.	N
60.		Guidance Counselor	Non-Scientist	Alt.	N
61.		Clinical Development & Compliance Consultant	Other Scientist	Alt.	N
62.		Obstetrics/Gynecology	Physician Scientist	Alt.	N
63.		Regulatory	Non-Scientist	Alt.	Y
64.		Pharmacist	Other Scientist	Alt.	N
65.		Physician-Pediatrics, Infectious Diseases	Physician Scientist	Alt.	N
66.		Pediatric Emergency Medicine	Other Scientist	Alt.	N
67.		Ophthalmologist, Neuroscientist	Physician Scientist	Alt.	N
68.		Clinical Research Consultant	Other Scientist	Alt.	N

	Member's Name	Profession	Status	Main Roster Member Role	Affiliated Y/N
69.	(b) (6)	Statistics	Other Scientist	Alt.	N
70.		Nursing Research Director/Consultant	Other Scientist	Alt	N
71.		Physician – Internal Med., Infectious Diseases	Physician Scientist	Alt.	N
72.		Biomedical Engineering	Other Scientist	Alt.	N
73.		Physician-Oncologist/Hematologist	Physician Scientist	Alt.	N
74.		Regulatory	Non-Scientist	Alt.	Y
75.		Prisoner Advocate	Non-Scientist	Alt.	N
76.		Ministry	Non-Scientist	Alt.	N
77.		Physician – Medical Research	Physician Scientist	Alt.	N
78.		Physician –Anesthesiologist	Physician Scientist	Alt.	N
79.		Communications	Non-scientist	Alt.	N
80.		Community Member	Non-Scientist	Alt.	N
81.		Physician – OB/Gyn, Clinical Safety Director	Physician Scientist	Alt.	N
82.		Quality Assurance, Research Ethics	Other Scientist	Alt.	N
83.		Pediatric Pulmonology	Physician Scientist	Alt.	N
84.		Hospital and Research Pharmacist	Other Scientist	Alt.	N
85.		Social Psychology	Other Scientist	Alt.	N
86.		Family Medicine	Physician Scientist	Alt.	N
87.		Nursing	Other Scientist	Alt.	N
88.		Attorney, Prisoner Representative	Non-Scientist	Alt.	N
89.		Neonatal Intensive Care	Physician Scientist	Alt.	N
90.		Pharmacokinetics & Biopharmaceutics	Other Scientist	Alt.	N
91.		Human Subject Protection Consultant	Non-Scientist	Alt.	N
92.		Pharmacist	Other Scientist	Alt.	N
93.		Oncological Nursing	Other Scientist	Alt.	N
94.		Regulatory, Legal	Non-Scientist	Alt.	Y
95.		Engineer	Non-scientist	Alt.	N
96.		Surgical Oncology	Physician Scientist	Alt.	N
97.		Legal	Non-Scientist	Alt.	N
98.		Physician – Pediatrics, Infectious Disease	Physician Scientist	Alt.	N
99.		Pulmonary, Critical Care	Physician Scientist	Alt.	N
100.		Obstetrics/Gynecology	Physician Scientist	Alt.	N

	Member's Name	Profession	Status	Main Roster Member Role	Affiliated Y/N
101.	(b) (6)	Regulatory Affairs	Other Scientist	Alt.	N
102.		Educator	Non-Scientist	Alt.	N
103.		Physician – Research	Physician Scientist	Alt.	N
104.		Oncology, Melanoma	Physician Scientist	Alt.	N
105.		Educator	Non-Scientist	Alt.	N
106.		Pharmacology	Other Scientist	Alt.	N
107.		Scientific Affairs Consultant – Nutrition	Other Scientist	Alt.	N
108.		Oncology, Women's Cancer	Physician Scientist	Alt.	N
109.		Ethicist, Pharmacy	Other Scientist	Alt.	N
110.		Public Health	Other Scientist	Alt.	N
111.		Human Subject Protection: Regulatory Affairs	Non-Scientist	Alt.	Y
112.		Nursing Sciences	Other Scientist	Alt.	Y
113.		Physician – Oncologist, Hematology	Physician Scientist	Alt.	N
114.		Oncologist – Hematology/Oncology	Physician Scientist	Alt.	N

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Alternate Members (Alt.)
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ROSTER UPDATES

Name	Effective Date	Membership Change
(b) (6)	07/16/2018	Removed
	07/25/2018	Added
	07/26/2018	Removed
	08/22/2018	Removed
	08/27/2018	Change from Affiliated Chairperson to Unaffiliated member
	09/26/2018	Removed
	9/27/2018	Added
	10/03/2018	Added
	10/05/2018	Removed
	10/05/2018	Removed
	10/05/2018	Removed
	10/05/2018	Updated Profession
	10/19/2018	Updated Profession

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IRB Membership Roster

OHRP/FDA Registration Number:
IRB#00000971
IORG #0000635

*Executive Chair ** Chairperson

	Member's Name	Profession	Status	Main Roster Member Role	Affiliated Y/N
1.	(b) (6)	Regulatory	Non-Scientist	Primary	Y
2.		Compliance Director	Non-Scientist	Primary	N
3.		Internal Medicine	Physician Scientist	Primary	N
4.		Internal Medicine	Physician Scientist	Primary	N
5.		Ethics and Research Consultant/Ethicist	Other Scientist	Primary	N
6.		Toxicologist/Regulatory Affairs Consultant	Other Scientist	Primary	N
7.		Pharmacology	Other Scientist	Primary	Y
8.		Ethics	Non-Scientist	Alt.	Y
9.		University Professor, Religious Studies, Ethicist	Non-Scientist	Alt.	N
10.		Clinical Research Administration; Respiratory Therapy	Other Scientist	Alt.	Y
11.		Attorney	Non-Scientist	Alt.	N
12.		Regulatory	Non-Scientist	Alt.	Y
13.		Clinical Pharmacist	Other Scientist	Alt.	N
14.		Professional Translator/French	Non-Scientist	Alt.	N
15.		Physician – Internal Medicine/Pulmonologist	Physician Scientist	Alt.	N
16.		Regulatory	Non-Scientist	Alt.	Y
17.		Regulatory Affairs, IRB specialist	Non-Scientist	Alt.	Y
18.		Adult Neuroscience	Other Scientist	Alt.	N
19.		Regulatory	Non-Scientist	Alt.	Y
20.		Community Health, Nursing	Other Scientist	Alt.	Y
21.		Public Health	Other Scientist	Alt.	N
22.		Pharmacology	Physician Scientist	Alt.	N
23.		Pharmacy	Other Scientist	Alt.	N
24.		County Government Administrator	Non-Scientist	Alt.	N
25.		Research Ethics	Non-scientist	Alt.	Y
26.		Oncology Research Coordinator	Other Scientist	Alt.	Y
27.		Research Consultant	Non-Scientist	Alt.	N
28.		Pediatric Clinical Research Manager	Other Scientist	Alt.	N
29.		Social Work, Subject Advocate	Non-Scientist	Alt.	N
30.		Emergency Trauma Nursing/Public Health	Other Scientist	Alt.	N
31.		Oncology Pediatric	Physician Scientist	Alt.	N
32.		Physician – Pediatrics, Hematology Oncology	Physician Scientist	Alt.	N
33.		Phase I	Other Scientist	Alt.	N

	Member's Name	Profession	Status	Main Roster Member Role	Affiliated Y/N
34.	(b) (6)	Oncology Nurse	Other Scientist	Alt.	N
35.		Medical Advisor	Physician Scientist	Alt.	N
36.		Ministry	Non-Scientist	Alt.	N
37.		Psychiatry, Legal	Other Scientist	Alt.	N
38.		Physician-Cardiologist	Physician Scientist	Alt.	N
39.		Physician-Family Practice	Physician Scientist	Alt.	N
40.		Ministry	Non-Scientist	Alt.	N
41.		Patient Advocate for Cystic Fibrosis	Non-Scientist	Alt.	N
42.		Oncology Nurse	Other Scientist	Alt.	N
43.		Immunology, Internal Medicine	Physician Scientist	Alt.	N
44.		Physician - Radiologist	Physician Scientist	Alt.	N
45.		Investigator – Human Research Experience	Other Scientist	Alt.	N
46.		Legal & Healthcare/Research Compliance	Non-Scientist	Alt.	N
47.		Translation	Non-scientist	Alt.	N
48.		Oncology, Lymphoma	Physician Scientist	Alt.	N
49.		Physician – Surgery	Physician Scientist	Alt.	N
50.		Nurse, Device specialist	Other Scientist	Alt.	N
51.		Physician-Internal Medicine	Physician Scientist	Alt.	N
52.		Immunologist	Other Scientist	Alt.	N
53.		Oncology, Genitourinary Cancer	Physician Scientist	Alt.	N
54.		Legal, Ethicist	Non-scientist	Alt.	N
55.		Physician – Emergency Medicine	Physician Scientist	Alt.	N
56.		Lawyer	Non-scientist	Alt.	N
57.		Ethics	Non-Scientist	Alt.	N
58.		General Practice, Non-Cancer Pain Management	Physician Scientist;	Alt.	N
59.		Allergy, Immunology	Physician Scientist	Alt.	N
60.		Patient Advocacy	Non-Scientist	Alt.	N
61.		Guidance Counselor	Non-Scientist	Alt.	N
62.		Clinical Development & Compliance Consultant	Other Scientist	Alt.	N
63.		Obstetrics/Gynecology	Physician Scientist	Alt.	N
64.		Regulatory	Non-Scientist	Alt.	Y
65.		Pharmacist	Other Scientist	Alt.	N
66.		Physician-Pediatrics, Infectious Diseases	Physician Scientist	Alt.	N
67.		Pediatric Emergency Medicine	Other Scientist	Alt.	N
68.		Ophthalmologist, Neuroscientist	Physician Scientist	Alt.	N

	Member's Name	Profession	Status	Main Roster Member Role	Affiliated Y/N
69.	(b) (6)	Clinical Research Consultant	Other Scientist	Alt.	N
70.		Statistics	Other Scientist	Alt.	N
71.		Nursing Research Director/Consultant	Other Scientist	Alt	N
72.		Physician – Internal Med., Infectious Diseases	Physician Scientist	Alt.	N
73.		Biomedical Engineering	Other Scientist	Alt.	N
74.		Physician-Oncologist/Hematologist	Physician Scientist	Alt.	N
75.		Regulatory	Non-Scientist	Alt.	Y
76.		Regulatory Affairs, IRB specialist	Non-Scientist	Alt.	Y
77.		Prisoner Advocate	Non-Scientist	Alt.	N
78.		Ministry	Non-Scientist	Alt.	N
79.		Physician – Medical Research	Physician Scientist	Alt.	N
80.		Physician –Anesthesiologist	Physician Scientist	Alt.	N
81.		Communications	Non-scientist	Alt.	N
82.		Community Member	Non-Scientist	Alt.	N
83.		Physician – OB/Gyn, Clinical Safety Director	Physician Scientist	Alt.	N
84.		Quality Assurance, Research Ethics	Other Scientist	Alt.	N
85.		Pediatric Pulmonology	Physician Scientist	Alt.	N
86.		Hospital and Research Pharmacist	Other Scientist	Alt.	N
87.		Social Psychology	Other Scientist	Alt.	N
88.		Family Medicine	Physician Scientist	Alt.	N
89.		Nursing	Other Scientist	Alt.	N
90.		Attorney, Prisoner Representative	Non-Scientist	Alt.	N
91.		Neonatal Intensive Care	Physician Scientist	Alt.	N
92.		Pharmacokinetics & Biopharmaceutics	Other Scientist	Alt.	N
93.		Human Subject Protection Consultant	Non-Scientist	Alt.	N
94.		Pharmacist	Other Scientist	Alt.	N
95.		Oncological Nursing	Other Scientist	Alt.	N
96.		Regulatory, Legal	Non-Scientist	Alt.	Y
97.		Engineer	Non-scientist	Alt.	N
98.		Surgical Oncology	Physician Scientist	Alt.	N
99.		Legal	Non-Scientist	Alt.	N
100.		Physician – Pediatrics, Infectious Disease	Physician Scientist	Alt.	N

	Member's Name	Profession	Status	Main Roster Member Role	Affiliated Y/N
101.	(b) (6)	Pulmonary, Critical Care	Physician Scientist	Alt.	N
102.		Obstetrics/Gynecology	Physician Scientist	Alt.	N
103.		Regulatory Affairs	Other Scientist	Alt.	N
104.		Educator	Non-Scientist	Alt.	N
105.		Physician – Research	Physician Scientist	Alt.	N
106.		Oncology, Melanoma	Physician Scientist	Alt.	N
107.		Educator	Non-Scientist	Alt.	N
108.		Pharmacology	Other Scientist	Alt.	N
109.		Scientific Affairs Consultant – Nutrition	Other Scientist	Alt.	N
110.		Oncology, Women's Cancer	Physician Scientist	Alt.	N
111.		Ethicist, Pharmacy	Other Scientist	Alt.	N
112.		Public Health	Other Scientist	Alt.	N
113.		Pharmacist	Other Scientist	Alt.	Y
114.		Regulatory Affairs, IRB specialist	Non-Scientist	Alt.	Y
115.		Human Subject Protection: Regulatory Affairs	Non-Scientist	Alt.	Y
116.		Nursing Sciences	Other Scientist	Alt.	Y
117.		Physician – Oncologist	Physician Scientist	Alt.	N
118.		Oncologist – Hematology/Oncology	Physician Scientist	Alt.	N

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ROSTER UPDATES

Name	Effective Date	Membership Change
(b) (6)	04/30/2018	Appointed to Chairperson
	05/01/2018	Remove
	05/21/2018	Remove
	06/12/2018	Remove
	06/13/2018	Change from Alternate to Primary
	06/19/2018	Remove
	06/29/2018	Remove

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IRB Membership Roster

OHRP/FDA Registration Number:
IRB#00000971
IORG #0000635

*Executive Chair ** Chairperson

	Member's Name	Profession	Status	Main Roster Member Role	Affiliated Y/N
1.	(b) (6)	Regulatory	Non-Scientist	Primary	Y
2.		Compliance Director	Non-Scientist	Primary	N
3.		Internal Medicine	Physician Scientist	Primary	N
4.		Internal Medicine, Cardiovascular Disease	Physician Scientist	Primary	N
5.		Ethics and Research Consultant / Ethicist	Other Scientist	Primary	N
6.		Toxicologist/Regulatory Affairs Consultant	Other Scientist	Primary	N
7.		Pharmacology	Other Scientist	Primary	Y
8.		University Professor, Religious Studies, Ethicist	Non-Scientist	Alt.	N
9.		Clinical Research Administration; Respiratory Therapy	Other Scientist	Alt.	Y
10.		Attorney	Non-Scientist	Alt.	N
11.		Regulatory	Non-Scientist	Alt.	Y
12.		Clinical Pharmacist	Other Scientist	Alt.	N
13.		Professional Translator/French	Non-Scientist	Alt.	N
14.		Physician – Internal Medicine / Pulmonologist	Physician Scientist	Alt.	N
15.		Regulatory	Non-Scientist	Alt.	Y
16.		Regulatory Affairs, IRB specialist	Non-Scientist	Alt.	Y
17.		Adult Neuroscience	Other Scientist	Alt.	N
18.		Regulatory	Non-Scientist	Alt.	Y
19.		Community Health, Nursing	Other Scientist	Alt.	Y
20.		Public Health	Other Scientist	Alt.	N
21.		Pharmacology	Physician Scientist	Alt.	N
22.		Pharmacy	Other Scientist	Alt.	N
23.		County Government Administrator	Non-Scientist	Alt.	N
24.		Research Ethics	Non-scientist	Alt.	Y
25.		Oncology Research Coordinator	Other Scientist	Alt.	Y
26.		Research Consultant	Non-Scientist	Alt.	N
27.		Pediatric Clinical Research Manager	Other Scientist	Alt.	N
28.		Biostatistics	Other Scientist	Alt.	N
29.		Social Work, Subject Advocate	Non-Scientist	Alt.	N
30.		Emergency Trauma Nursing/Public Health	Other Scientist	Alt.	N
31.		Oncology Pediatric	Physician Scientist	Alt.	N

32.	(b) (6)		Physician – Pediatrics, Hematology Oncology	Physician Scientist	Alt.	N
33.			Phase I	Other Scientist	Alt.	N
34.			Oncology Nurse	Other Scientist	Alt.	N
35.			Medical Advisor	Physician Scientist	Alt.	N
36.			Ministry	Non-Scientist	Alt.	N
37.			Psychiatry, Legal	Other Scientist	Alt.	N
38.			Physician-Cardiologist	Physician Scientist	Alt.	N
39.			Physician-Family Practice	Physician Scientist	Alt.	N
40.			Ministry	Non-Scientist	Alt.	N
41.			Patient Advocate for Cystic Fibrosis	Non-Scientist	Alt.	N
42.			Oncology Nurse	Other Scientist	Alt.	N
43.			Immunology, Internal Medicine	Physician Scientist	Alt.	N
44.			Physician - Radiologist	Physician Scientist	Alt.	N
45.			Investigator - Human Research Experience	Other Scientist	Alt.	N
46.			Legal & Healthcare / Research Compliance	Non-Scientist	Alt.	N
47.			Translation	Non-scientist	Alt.	N
48.			Oncology, Lymphoma	Physician Scientist	Alt.	N
49.			Physician – Surgery	Physician Scientist	Alt.	N
50.			Nurse, Device specialist	Other Scientist	Alt.	N
51.			Physician-Internal Medicine	Physician Scientist	Alt.	N
52.			Immunologist	Other Scientist	Alt.	N
53.			Oncology, Genitourinary Cancer	Physician Scientist	Alt.	N
54.			Legal, Ethicist	Non-scientist	Alt.	N
55.			Physician – Emergency Medicine	Physician Scientist	Alt.	N
56.			Lawyer	Non-scientist	Alt.	N
57.			Ethics	Non-Scientist	Alt.	N
58.			General Practice, Non-Cancer Pain Management	Physician Scientist;	Alt.	N
59.			Allergy, Immunology	Physician Scientist	Alt.	N
60.			Patient Advocacy	Non-Scientist	Alt.	N
61.			Guidance Counselor	Non-Scientist	Alt.	N
62.			Clinical Development & Compliance Consultant	Other Scientist	Alt.	N
63.			Obstetrics / Gynecology	Physician Scientist	Alt.	N
64.			Regulatory	Non-Scientist	Alt.	Y
65.			Pharmacist	Other Scientist	Alt.	N
66.			Physician-Pediatrics, Infectious Diseases	Physician Scientist	Alt.	N
67.			Pediatric Emergency Medicine	Other Scientist	Alt.	N

68.	(b) (6)	Internet/Computer Based Research	Other Scientist	Alt.	N
69.		Ophthalmologist, Neuroscientist	Physician Scientist	Alt.	N
70.		Clinical Research Consultant	Other Scientist	Alt.	N
71.		Statistics	Other Scientist	Alt.	N
72.		Nursing Research Director/Consultant	Other Scientist	Alt	N
73.		Physician – Internal Med., Infectious Diseases	Physician Scientist	Alt.	N
74.		Biomedical Engineering	Other Scientist	Alt.	N
75.		Physician-Oncologist/Hematologist	Physician Scientist	Alt.	N
76.		Regulatory	Non-Scientist	Alt.	Y
77.		Regulatory Affairs, IRB specialist	Non-Scientist	Alt.	Y
78.		Prisoner Advocate	Non-Scientist	Alt.	N
79.		Ministry	Non-Scientist	Alt.	N
80.		Physician - Medical Research	Physician Scientist	Alt.	N
81.		Physician –Anesthesiologist	Physician Scientist	Alt.	N
82.		Communications	Non-scientist	Alt.	N
83.		Community Member	Non-Scientist	Alt.	N
84.		Ethics	Non-Scientist	Alt.	Y
85.		Physician – OB/Gyn, Clinical Safety Director	Physician Scientist	Alt.	N
86.		Quality Assurance, Research Ethics	Other Scientist	Alt.	N
87.		Pediatric Pulmonology	Physician Scientist	Alt.	N
88.		Hospital and Research Pharmacist	Other Scientist	Alt.	N
89.		Social Psychology	Other Scientist	Alt.	N
90.		Family Medicine	Physician Scientist	Alt.	N
91.		Nursing	Other Scientist	Alt.	N
92.		Attorney, Prisoner Representative	Non-Scientist	Alt.	N
93.		Neonatal Intensive Care	Physician Scientist	Alt.	N
94.		Pharmacokinetics & Biopharmaceutics	Other Scientist	Alt.	N
95.		Human Subject Protection Consultant	Non-Scientist	Alt.	N
96.		Pharmacist	Other Scientist	Alt.	N
97.		Oncological Nursing	Other Scientist	Alt.	N
98.		Regulatory, Legal	Non-Scientist	Alt.	Y
99.		Engineer	Non-scientist	Alt.	N
100.		Surgical Oncology	Physician Scientist	Alt.	N
101.		Legal	Non-Scientist	Alt.	N

102.	(b) (6)		Physician - Pediatrics, Infectious Disease	Physician Scientist	Alt.	N
103.			Psychologist	Other Scientist	Alt.	N
104.			Pulmonary, Critical Care	Physician Scientist	Alt.	N
105.			Obstetrics / Gynecology	Physician Scientist	Alt.	N
106.			Regulatory Affairs	Other Scientist	Alt.	N
107.			Educator	Non-Scientist	Alt.	N
108.			Physician – Research	Physician Scientist	Alt.	N
109.			Oncology, Melanoma	Physician Scientist	Alt.	N
110.			Educator	Non-Scientist	Alt.	N
111.			Pharmacology	Other Scientist	Alt.	N
112.			Managing Director, Teacher	Other Scientist	Alt.	N
113.			Scientific Affairs Consultant – Nutrition	Other Scientist	Alt.	N
114.			Oncology, Women's Cancer	Physician Scientist	Alt.	N
115.			Ethicist, Pharmacy	Other Scientist	Alt.	N
116.			Public Health	Other Scientist	Alt.	N
117.			Pharmacist	Other Scientist	Alt.	Y
118.			Regulatory Affairs, IRB specialist	Non-Scientist	Alt.	Y
119.			Human Subject Protection: Regulatory Affairs	Non-Scientist	Alt.	Y
120.			Nursing Sciences	Other Scientist	Alt.	Y
121.			Physician – Oncologist	Physician Scientist	Alt.	N
122.			Oncologist - Hematology/Oncology	Physician Scientist	Alt.	N
123.			Internal Medicine	Physician Scientist	Alt.	N

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CONSENT TO TAKE PART IN A CLINICAL RESEARCH STUDY AND AUTHORIZATION TO DISCLOSE HEALTH INFORMATION

Sponsor / Study Title:	**22nd Century Group, Inc. / "A Longitudinal Ambulatory Study to Assess Changes in Cigarette Consumption Behavior and Biomarkers of Exposure during a 6-Week Switch to Very Low Nicotine Cigarettes"**
Protocol Number:	**CA24914**
Principal Investigator: (Study Doctor)	**Philip Mathew, M.D.**
Telephone:	(b) (6) [redacted] **(402) 613-5822 (24-hour Nurses' Line AFTER 1st Study Check In)**
Address:	**Celerion** **621 Rose Street** **Lincoln, NE 68502**

It is important that you give a true and complete medical history. You must be honest about your past and present usage of medications. Giving information that is not true or incomplete could be very harmful to your health. If you give false information, you may be dismissed from the study.

You are being invited to take part in a research study sponsored by 22nd Century Group, Inc. You must read this Informed Consent Form before you decide if you want to take part in the study. This form will tell you about the study. The Study Doctor or study staff can explain words or information that you do not understand. Ask the study staff as many questions as needed for you to decide if you want to take part in the study. Your participation in this research is voluntary and we will include only those who wish to take part. If you decide to take part in this study, you must sign your name at the end of the form and date it. You cannot take part in this study until you sign and date this form.

PURPOSE OF THE STUDY

This is a research study and is not to be used to encourage product use, and is not to treat any medical disease. This study is planned:

- To measure your cigarette use or how many cigarettes smoked per day when you change from smoking your regular cigarettes to cigarettes with a very low nicotine level.

- To find out how much nicotine is in the blood after smoking the cigarettes with very low nicotine.
- To find out more about your smoking urges, any withdrawal symptoms you may feel, and any health risks, when you switch to cigarettes with a very low nicotine level.

This is an open label study which means you will know what kind of filtered king size study cigarettes you will be smoking. There will be a total of 140 participants in this study. Seventy will be smokers of non-mentholated and seventy will be smokers of mentholated king size cigarettes.

For one week prior to starting on the assigned study product you will be asked to smoke king size of your own usual brand of cigarettes as you would usually do each day. If your usual brand of cigarette is a 100s cigarette, you will be asked to switch your usual brand of cigarette to a king size cigarette two weeks prior to your participation in this study.

For the entire study you will be asked to report the number of cigarettes used each day using an electronic diary (e-diary). The diary entry should be completed at the end of each day. Training for the e-diary will be provided at the visit at the start of Week -1. You may install the e-diary app on your phone or tablet or a device can be provided to you for this daily reporting.

You will also be asked to collect and bring to the clinic all cigarette butts you smoke from the first clinic visit when you start recording your daily use to the end of the study at the end of week 6. Containers for butt collection will be provided by the clinic. These will be counted by the staff to confirm your daily reported use.

Each time you return to the clinic you will be given an alcohol and drug screen to test for drugs of abuse.

You will return to the research unit at the end of Week -1, at a time scheduled by the clinic. At this visit you will check-in to the clinic to stay for approximately 30 hours. During this visit you will have blood samples drawn and start a 24 hour urine collection. You will also answer questionnaires on your smoking behavior, any withdrawal symptoms, urges to smoke, and noticed health risks.

During this visit, you will be randomly (like the flip of a coin) be selected to either continue to smoke your own usual brand of cigarettes, or you may be randomly selected to switch to smoking very low nicotine study cigarettes within your choice of your usual cigarette flavor (menthol or non-menthol).

Of those selected to the very low nicotine study cigarettes you will be randomly (like the flip of a coin) selected to collect smoking behavior data called puff topography. This data is collected by a device that is worn via a shoulder strap and connects to the end of your cigarette while you smoke through a mouth piece.

Of those selected for puff topography, a smaller group will be randomly (like the flip of a coin) selected to participate in a special nicotine blood draw group. This group will stay in the clinic

an additional 24 hours following checkout of the other subjects. If in this group, you will be not be allowed to smoke for 12 hours prior to smoking a single very low nicotine cigarette over a 5 minute time period followed by a series of blood collections.

At the end of your stay you will be sent home to continue to smoke your usual brand cigarettes, which will not be provided as part of the study, or with enough very low nicotine cigarettes for two weeks. During this time you will make daily entries into the e-diary and collect your used cigarette butts to bring to the clinic.

You will return to the research unit at the end of Weeks 2 and 6, at a time scheduled by the clinic for an overnight stay lasting about 30 hours. You will repeat the same procedures that were performed at the first 30 hour clinical stay.

At the end of Week 4 you will return to the research unit for a short visit. You will be asked questions about your heath and cigarette behavior, urges, withdrawal, and health risks. Compliance will be evaluated via cigarette butt collection and e-diary entries. You will receive an additional supply of cigarettes if you are assigned to the very low nicotine group and to complete the questionnaires.

STUDY PRODUCT

The following study products will be used in the study:

- Your own brand of non-mentholated filtered king size cigarettes.
- Your own brand of mentholated filtered king size cigarettes.
- The study non-mentholated very low nicotine cigarettes filtered king size cigarettes.
- The study mentholated very low nicotine cigarettes filtered king size cigarettes.

Very Low Nicotine cigarettes contain 0.4 mg nicotine per gram of tobacco. Normal cigarettes contain about 10 mg nicotine per gram of tobacco The cigarettes provided are for Clinical Trial use only and should be kept out of the reach of children.

SUBJECT RESPONSIBILITIES

You must:

- Follow all clinic rules and instructions of the study staff.
- Follow the study restrictions using only study approved tobacco products.
- Report any unfavorable health or medical events, referred to as adverse events.
- Give true and complete answers to any questions you choose to answer.
- Report daily cigarette use via an electronic diary.
- Comply with the terms of the Informed Consent Form.

STUDY RESTRICTIONS

- You must be a healthy adult male or female adult smoker, 26 to 65 years of age who has been a smoker for at least 5 years at Screening.
- You smoke an average of 10 or more manufactured cigarettes per day.

- Your usual brand of cigarette is a filtered king size cigarette, or you are willing to switch your usual brand of cigarette to a king size cigarette. You may not use any nicotine-containing products other than factory manufactured cigarettes, such as roll-your-own cigarettes, e-vapor products, bidis (a type of cheap cigarette made of unprocessed tobacco wrapped in leaves), snuff, nicotine inhaler, pipe, cigar, chewing tobacco, nicotine patch, nicotine spray, nicotine lozenge, or nicotine gum, within 28 days prior to Screening.
- If female and able to have children, you must be practicing an acceptable method of birth control.
- You may not participate if you are a female subject who is pregnant, lactating, or intend to become pregnant from Screening through the End of Study.
- You may not use any prescription smoking cessation treatments, including, but not limited to, varenicline (Chantix®) or bupropion (Zyban®) within 3 months prior to Screening.
- You may not be a self-reported puffer/non-inhaler (a smoker who draws smoke from the cigarette into the mouth and throat but does not inhale).
- You may not be planning to quit smoking during the study period or delay a quit attempt in order to participate in the study.
- You may not have any significant abnormal findings on your physical examination, medical history, ECG (a test that measures and records the electrical activity of your heart), or clinical laboratory results, in the opinion of the Investigator.
- You may not have a positive test for human immunodeficiency virus (HIV), hepatitis B surface antigen (HBsAg), or hepatitis C virus (HCV).
- You may not have had an illness such as an upper respiratory infection or viral infection that required you to take prescription medication(s) within 14 days prior to first clinic visit.
- You may not have a fever (greater than or equal to100.5°F) at first clinic visit or screening.
- Your Body mass index (BMI) may not be greater than 40.0 kg/m^2 or less than 18.0 kg/m^2 at Screening.
- You may not have a history of drug or alcohol abuse or have used medical/recreational marijuana within 12 months of Screening.
- You cannot have diabetes mellitus that is not controlled by diet/exercise alone, in the opinion of the Investigator.
- Your heart rate while sitting may not be lower than 40 bpm (beats per minute) or higher than 99 bpm at Screening, unless deemed not clinically significant by the PI.
- While sitting your systolic blood pressure may not be lower than 90 mmHg (millimeters of mercury) or higher than 150 mmHg, diastolic blood pressure should not be lower than 40 mmHg or higher than 95 mmHg at Screening, unless deemed not clinically significant by the PI.
- You may not have a positive urine screen for drugs of abuse or alcohol at Screening or at the first clinic visit.
- You may not have used any inhalers to treat any medical condition within 3 months prior to Screening and throughout the study.

- You cannot have donated plasma within 7 days prior to Screening or at any time during the study.
- You cannot have donated blood or blood products (with the exception of plasma as noted above), had significant blood loss, or received whole blood or a blood product transfusion within 56 days prior to Screening.
- You may not have participation in a previous clinical study for an investigational drug, device, biologic, or tobacco product within 30 days prior to Screening.
- If you are a subject or a first-degree relative (parent, sibling, child) is a current or former employee of the tobacco industry or a named party or class representative in litigation with the tobacco industry you may not participate in this study.
- If you are a subject or a first-degree relative (parent, sibling, child) is a current employee of the clinic sites you may not participate in this study.
- You must report any changes or new medication you are taking during the study. Some medications known to interact with the nicotine results may disqualify you from participating.
- You must plan to stay in the area during the course of the study to attend the clinic visits as required.
- You must be willing to comply with the protocol including use of the test product and collection of samples required of your group.
- Beverages containing caffeine are not allowed with the exception of one caffeinated beverage with each meal.
- You must not consume any alcohol product 48 hours prior to and during each clinic visit.
- You will be instructed to refrain from strenuous physical activity except for your usual routine activity during the whole study participation.

NUMBER OF SUBJECTS AND LENGTH OF STUDY

This study will enroll about 140 subjects, at 2 research clinics. The entire study will last about 11 weeks, 4 weeks for screening, 6 weeks of product use and reporting, plus a 7-day safety follow up period.

If randomized to use the very low nicotine cigarettes, the test products will be provided to you during the study at no charge. If you are randomized to continue to smoke your own cigarettes you will need to purchase your own product.

POSSIBLE RISKS ASSOCIATED WITH THE STUDY PRODUCTS

There is always a chance that an unexpected or serious adverse event may happen. Smokers who use light cigarettes do not reduce their risk for developing smoking-related cancers and other diseases. You must report any adverse events to the study nurses any time after you have signed this informed consent form.

PROCEDURES AND POSSIBLE RISKS OR DISCOMFORTS

Procedures will be done during the study at assigned times. The procedures will be done to monitor your health, assess the safety of the study products, and to see how the nicotine from the study products is absorbed into your body.

BLOOD COLLECTIONS

A needle will be used to take blood samples from a vein in your arm. The number of samples and times will depend upon the group you are randomized to on Day -1.

All subjects will have 2 draws completed for Clinical Laboratory samples and 3 draws for compliance testing. About 65mL of blood (approximately 4 tablespoons) will be taken.

If randomized to the nicotine special blood draw group, an additional 42 samples will be drawn over three days for an approximate volume of 245mL or 17 tablespoons.

Additional samples may need to be taken. This amount is less than the amount you would give if you were donating blood.

You may have discomfort or pain when your blood is collected. You may feel faint or pass out. There is a risk of infection, bleeding, or bruising at the puncture site. You may develop a small scar at the puncture site where multiple blood samples are taken.

URINE COLLECTION

Urine samples will be collected to test for drugs of abuse and alcohol at Screening, start of week -1, end of weeks -1 2, 4, 6, and end of study. A urine sample will be collected for women to test for pregnancy at the start of week -1, end of weeks -1, 2, 4, and 6.

Twenty-four hour study urine collections will be complete on days -1, end of week 2 and 6 to test for nicotine and other substances related to tobacco/nicotine use.

NICOTINE WITHDRAWAL & CONFINEMENT

Symptoms of nicotine withdrawal include:

- irritability
- anger
- frustration
- anxiety/feeling restless
- depression/feeling sad
- sleep problems/nightmares
- sensitivity to pain
- tremors
- slow heart rate
- nausea
- constipation
- increased appetite
- weight gain

- coughing
- dizziness
- sore throat
- mouth ulcer
- difficulty concentrating
- impaired memory

There are also other dietary and activity restrictions while you are staying at the study site that may cause you some discomfort.

e-DIARY and QUESTIONNAIRES

You will have training on the eDiary that you will use on your smartphone/tablet. If you do not have a device for use one will be provided to you. Each day you will report the number of cigarettes you smoke for the day from the start of week -1 to the end of the study.

You will be completing 4 separate questionnaires about your cigarette dependence, smoking urges, nicotine withdrawal, and a perceived health risk scale. These will be done 4 times during the study, at the end of weeks -1, 2, 4, and 6.

SCREENING VISIT

The following procedures will be done during this visit to help the Study Doctor determine if you qualify for this study. This is called the screening visit.

- Read, sign and date the Informed Consent Form.
- You will provide your medical history, including all medications, vitamins, herbal products or supplements you are taking and have taken for the past 30 days.
- You will have a physical examination including checking inside your mouth.
- Height and weight will be measured and body mass index (BMI) will be calculated.
- An Electrocardiogram (ECG) will be performed (a test that measures and records the electrical activity of your heart).
- Your blood pressure, heart rate, respiratory rate and temperature will be taken.
- You will provide a urine sample. The sample will be used to test for general health, nicotine exposure, alcohol and drugs of abuse. You will not be allowed to continue if the tests for drugs of abuse are positive.
- You will have a carbon monoxide (CO) breath test.
- You will be asked about your tobacco product and nicotine product use and if you plan on quitting in the next 3 months.
- A photo will be taken of the front and back of your cigarette pack along with a ruler.
- Blood samples will be taken. These samples will be used to test for general health and, if female, a pregnancy test will be done. If you are a post-menopausal female, a serum FSH (follicle stimulating hormone) test to confirm postmenopausal status will be done.
- You will have your blood tested for the hepatitis viruses and for HIV. HIV is the virus that causes AIDS. If you have a positive HIV or hepatitis test, you cannot be in the study. If the HIV or hepatitis test are positive, you will be notified by the research site

and given information on how to follow up for further medical care. As required by law, positive test results must be reported by the research site to the State Department of Health. If you have any questions about what information is required to be reported, please ask the study staff. Although the test results are supposed to be private, this cannot be guaranteed. For example, it is possible for a court of law to get health or study records without your permission.

- You will be given information about quitting tobacco use.
- You may try the very low cigarette products that will be used in the study.

SCHEDULE OF EVENTS

Baseline Visit (Start of Week -1)

You will visit the clinic at the start of Week -1 at a time scheduled by the clinic. The following procedures will take place during this visit:

- Review of inclusion and exclusion criteria to verify nothing has changed since Screening.
- Confirm you are still using your usual brand of cigarettes.
- You will be asked about any adverse events and any changes in your medication.
- You will have a urine test for drug and alcohol screening and to see how much nicotine is in your system. If female this sample will also be tested for pregnancy.
- Your blood pressure, heart rate, respiratory rate, temperature, and weight will be taken
- You may have a physical examination if you have any new symptoms since your last visit.
- Your weight will be recorded.
- You will receive training on e-diary use.
- You will receive dispense canisters for used cigarette butt collection.
- Your smoking and nicotine product use restrictions will be reviewed.
- You will have a carbon monoxide (CO) breath test.

BETWEEN CLINIC VISITS

You will be required to record your daily cigarette use in the electronic diary and to collect all used cigarette butts in the provided container. You will receive a reminder contact to return to the research unit. At each visit adverse events and any changes in your medication will be reviewed.

CLINIC VISIT (End of Weeks -1, 2 and 6)

You will check in to the clinic at the end of Weeks, -1, 2 and 6 at times scheduled by the clinic. You will stay at the clinic until after the 24-hour urine collection and other study procedures. The following procedures will take place during this visit for all subjects:

- Review of inclusion and exclusion criteria have not changed since your last visit.
- Confirm you are still using your usual brand of cigarettes at the end of week -1.
- Confirm you are still using your usual brand of cigarettes if you were not provided very low nicotine cigarettes for use for weeks 2 and 6.
- You will be asked about any adverse events and any changes in your medication.

- You will have a urine test for drug and alcohol use. If female, your sample will also be tested for a positive pregnancy.
- You will have a blood sample taken to test for cotinine
- Your blood pressure, heart rate, respiratory rate, temperature, and weight will be taken.
- Your smoking and nicotine product use restrictions will be reviewed.
- Review that you have not changed your usual brand cigarette at Week -1.
- Verify the returned the canister with used cigarette butts for counting.
- You will start a 24-hour urine collection.
- You will have blood samples drawn for study testing.
- Daily recording of cigarettes per day in the e-diary will be reviewed. You will complete 4 questionnaires about your smoking behavior. You will complete a puffing topography assessment, this is a device for measuring the flow, time and amount of puffing when you smoke cigarettes if randomized to this group
- If you are on the Nicotine PK group you will stay an additional night where you will not have any nicotine containing products for 12 hours until you have a single very low nicotine cigarette and 14 timed PK blood draws based on the time you begin to smoke.

Prior to checkout on weeks -1 and 2:

- You will get a new container for collecting used cigarette butts to be returned at your next visit.
- You will get test product for the following period if selected to the very low nicotine group.

You will have your personal items thoroughly checked at the start of these clinic visits.

CLINIC VISIT (End of Week 4)

You will visit the clinic at the end of Week 4 at a time specified by the clinic. The following procedures will take place during this visit:

- Review of inclusion and exclusion criteria have not changed since your last visit.
- You are documenting and still using your usual brand of cigarettes if that is what you were assigned to.
- You will be asked about any adverse events and any changes in your medication.
- You will have a urine test for drug and alcohol use. If female, your sample will also be tested for a positive pregnancy. Your blood pressure, heart rate, respiratory rate, temperature, and weight will be taken.
- You have returned the canister with used cigarette butts for counting.
- You will complete the 4 questionnaires.
- You will receive new container for collecting used cigarette butts during next out of clinic period.
- Smoking and nicotine product use restrictions will be reviewed.
- You will receive study product for the following out of clinic period if selected to the very low nicotine group.

END OF STUDY (End of Week 6 Visit or on Early Discontinuation)

At the end of the study, the following procedures will be performed:

- You will be asked about any adverse events and any changes in your medication.
- Your blood pressure, heart rate, respiratory rate, temperature, and weight will be taken.
- You will have an ECG
- You will have routine lab work complete Clinical chemistry, hematology and urinalysis.
- You may have a physical examination if you have any new symptoms since your last visit.
- You will be given information about quitting tobacco use.

FOLLOW-UP CALL

The study team will contact you approximately 7 days after the study to review any adverse events and any changes in your medication and provide information about quitting tobacco use.

POSSIBLE RISKS TO AN UNBORN BABY OR CHILD WHO IS BREASTFEEDING

The effects of smoking on the unborn child are known to be hazardous. It is possible that the study products may cause harm to an unborn baby (fetus or embryo). You must not become pregnant during the study. If you are pregnant, lactating or planning to become pregnant at any time from Screening until study completion, you will not be allowed to take part in this study.

Females

If you are having sex with a male and able to become pregnant, you must agree to use an approved accepted method of birth control from Screening Visit until the end of the safety follow-up.

- Intrauterine device (IUD), intrauterine system,
- Barrier methods of contraception (condoms, occlusive caps) with spermicidal foam/gel/film/suppository,
- Hormonal contraception containing progesterone only,
- Essure® or similar nonsurgical sterilization
- Vasectomized partner(s),
- True abstinence (periodic abstinence and withdrawal are not effective methods)

Hormonal contraception made with estrogen is NOT allowed in this study because this may affect the nicotine reported in your blood.

A pregnancy may still occur even while using birth control. Not having sex with a partner of the opposite sex is the only way to be certain that a pregnancy will not occur.

You must tell the Study Doctor/study staff right away if you become pregnant during the study. The Study Doctor/study staff will request to follow the progress of the pregnancy to the outcome of the pregnancy (for example birth, loss, or termination).

UNKNOWN / UNFORESEEABLE RISKS

In addition to the risks listed above, there may be unknown risks, events that do not happen very often, and events we could not expect associated with the use of these products, including severe or life threatening allergic reactions or an unexpected reaction with another medication. Allergic reactions may include:

- skin rash
- itching
- swelling in the face or throat

If you experience an injury, bad effect, or any other unusual health experience during this study, you should immediately contact the Study Doctor or the study staff.

Your privacy is very important to us, and we will take precautions to protect your privacy, but cannot guarantee that your identity will never become known to other researchers or third parties. It is possible that there could be security breaches of the systems or files used to store your personal and health information and specimens collected from you during this study. There may also be other privacy risks that we have not foreseen.

SIGNIFICANT NEW SAFETY INFORMATION DURING THE STUDY

You will be told of any significant new safety information that the study site is made aware of by the Sponsor that might influence your willingness to continue your participation in this study.

POSSIBLE BENEFITS FROM THE STUDY

You will not receive any personal or health benefits from being in this study. The tests provided may help you learn about your general health. They may also help you discover an unknown medical condition.

TAKING PART IN THIS STUDY IS OF YOUR OWN FREE WILL

You are being asked to take part in this study because you are healthy. The only other option is not to take part in this study. You will never be forced to use cigarettes during the study. If you wish to completely stop using cigarettes while you are in the study, you will be allowed to leave the study.

If you decide to take part in the study, it should be by your own choice and your own free will. No one will force you to be in the study. If you enter the study, no one will force you to stay in the study. If you choose not to be in the study or if you leave the study early, there will be no penalty or loss of benefits to which you are otherwise entitled. **If you leave or are removed from the study for any reason your stipend will be prorated to the amount of the study that you complete.** You will not lose any rights that you are entitled to as a research subject.

COSTS OF PARTICIPATION

There is no cost to you for participating in this study.

COMPENSATION FOR TAKING PART IN THE STUDY

Treatments A and B:
Celerion will pay you by check. The amount you will be paid will depend on how much of the study you complete. You will earn $75 for each study phone call that you complete. You will earn $250 for the first study return visit that you complete. You will earn $500 if you complete the first confinement period (your stay in the clinic). You will earn $665 if you complete the second confinement period. You will earn $350 for the second study return visit that you complete. You will earn $800 if you complete the third confinement period. You will earn a completion bonus ($750) if you complete the entire study. You will be paid a total of $3,765 for completing the entire study.

You will receive a partial payment check at the times listed below:
- $1,640 shortly following completion of the second confinement period
- $425 shortly following completion of the second study return visit
- $875 shortly following completion of the third confinement period
- $825 shortly following completion of the final study phone call

Treatments C & D:
Celerion will pay you by check. The amount you will be paid will depend on how much of the study you complete. You will earn $75 for each study phone call that you complete. You will earn $250 for the first study return visit that you complete. You will earn $650 if you complete the first confinement period (your stay in the clinic). You will earn $840 if you complete the second confinement period. You will earn $350 for the second study return visit that you complete. You will earn $1,005 if you complete the third confinement period. You will earn a completion bonus ($885) if you complete the entire study. You will be paid a total of $4,430 for completing the entire study.

You will receive a partial payment check at the times listed below:
- $1,965 shortly following completion of the second confinement period
- $425 shortly following completion of the second study return visit
- $1,080 shortly following completion of the third confinement period
- $960 shortly following completion of the final study phone call

Treatments E & F:
Celerion will pay you by check. The amount you will be paid will depend on how much of the study you complete. You will earn $75 for each study phone call that you complete. You will earn $250 for the first study return visit that you complete. You will earn $550 if you complete the first confinement period (your stay in the clinic). You will earn $715 if you complete the second confinement period. You will earn $350 for the second study return visit that you complete. You will earn $900 if you complete the third confinement period. You will earn a completion bonus ($800) if you complete the entire study. You will be paid a total of $4,015 for completing the entire study.

You will receive a partial payment check at the times listed below:
- $1,740 shortly following completion of the second confinement period
- $425 shortly following completion of the second study return visit

- $975 shortly following completion of the third confinement period
- $875 shortly following completion of the final study phone call

All Treatments:
In addition to the above, if you complete the test product trial during the second screening visit you will receive $150 shortly following completion of the visit.

If you leave the study early, you will receive a pro-rated amount based on the study days you completed. If you complete an unscheduled study return visit you will be paid $150 for travel and time.

To ensure that the study randomizes the required number of subjects, extra subjects are recruited. These extra subjects are called alternates. If you are randomly chosen to be an alternate you will be told after you check in to the clinic. As an alternate you will be asked to complete study procedures up to the time of randomization during the first confinement period. In the event that an on study subject is unable to randomize, you may be chosen to take that subject's place on the study. If you are not needed, you will be released from the clinic after randomization. If you complete all the alternate requirements, you will receive an alternate stipend check for $950 (Treatments A & B) or $1,015 (Treatments C & D) or $975 (Treatments E & F) within approximately 1 week after being released from the clinic. If you are an alternate or a study subject who is released prior to the initial randomization you will receive a prorated portion of the alternate stipend based on the amount of the study that you complete.

If you choose to withdraw from the research study, you will receive compensation only for the portion of the study that you have completed as outlined above. For more information, please talk to your Study Doctor.

If it is determined by your Study Doctor that you should stop the study early, you will be compensated for the portion of the study you completed.

You understand the following:

- No deductions will be withheld from your stipend check for tax purposes. You are responsible for reporting any payment on your state and federal tax returns. At the end of each year, the study site will notify the IRS of all stipends you have received throughout the year.
- Being in this study does not make you an employee of the sponsor, the study site, or the FDA.
- You will not receive the full payment for the study if you leave before it is complete or are removed from the study for any reason. **This includes leaving the study due to an adverse event.**

<u>COMPENSATION FOR AN INJURY DIRECTLY RELATED TO YOUR PARTICIPATION IN THIS STUDY</u>
There is a chance that you could become ill or injured while being in this study. The study site will help you make arrangement if your illness or injury requires care outside of the study site (hospital, medical specialist). Unless other arrangements have been made by the study site, all

billing will be under your name. The cost of this care will be billed to you or your insurer in the ordinary manner. If you do not have insurance, the cost of the care will be billed to you directly.

The Study Doctor will decide if an injury or illness is directly related to the performance of the protocol (study plan) or use of the study products. If your injury or illness is directly related to the performance of the protocol or use of the study products, the Sponsor and/or the study site will reimburse you for your reasonable out-of-pocket medical costs (not covered by insurance) to treat an illness or injury that is directly caused by the study procedures or products.

To pay these medical expenses, the sponsor will need to know some information about you like your name, date of birth, and social security number or Medicare Health Insurance Claim Number. This is because the sponsor has to check to see if you receive Medicare and if you do, report the payment it makes to Medicare. The sponsor will not use this information for any other purpose.

You will need to sign a "release of information" form. This form will allow the study site to obtain your medical records related to the illness or injury. These records will help the study doctor determine the cause of the illness or injury. They may also help the sponsor learn more about the safety of the study products.

Any injury or illness that is not directly related to the performance of the protocol or use of the study products will be your responsibility to pay. This includes any injury or illness that would have occurred even if you had not participated in the study.

You do not give up any of your legal rights by signing and dating this consent form, accepting medical care, or accepting payment for medical expenses.

REASONS YOU CAN BE REMOVED FROM THE STUDY

You can be removed from the study at any time and for any reason without your consent. Some of the reasons you can be removed are listed below.

- You do not follow the instructions, rules, and restrictions given by the study staff.
- You do not follow the requirement for exclusive use of your assigned study product.
- You do not continue to meet the requirements for the study.
- Your Study Doctor decides it is best for your health.
- The Sponsor stops the study.
- If you become pregnant.

LEAVING THE STUDY BEFORE IT IS COMPLETED

If you choose to leave the study, you must notify your Study Doctor or study staff. It is very important that you agree to have the following procedure completed. The procedures listed below will be done for your safety and well-being. You must return all used or unused study products.

- Physical examination

- Vital Signs
- Weight
- An ECG - electrocardiogram (a test that measures and records the electrical activity of your heart) will be done.
- Record any adverse events you may have, or medications you have taken
- Your blood and urine will be collected for Clinical laboratory tests.
- Drug and Alcohol screen
- Information about smoking cessation will be provided.

All data that has been collected from you will be used for its original intention.

If you leave the study early or you are removed from the study, all samples collected from you before you leave will be used and analyzed as described in this Informed Consent Form. If you do not want your samples collected until the time of withdrawal and not analyzed yet to be analyzed, you must notify your Study Doctor in writing at the address on page 1 of this consent form.

CONFIDENTIALITY, DATA PROTECTION, AND PRIVACY

Information collected about you and your participation in this study, including all medical and health information as outlined below will be kept confidential according to privacy laws in this country. The information in both paper and electronic format that Celerion will collect about you will include study records that may contain your name and other personally identifiable information such as your date of birth (PII). PII is information that directly identifies you, and will also include special information such as your racial or ethnic origin, physical or mental health, sexual life, or genetic data and/or biometric data for the purpose of uniquely identifying you. These records (including any photographs) containing your PII will be kept for a minimum of either two years following the approval of the study drug, or two years after the sponsor discontinues its research on the study drug, and may be kept for as long as sponsor is developing or commercializing the study drug, which may be indefinitely. Your study results will be coded with numbers and/or initials wherever possible. Celerion will keep a list that links your name to your study results. This list will be kept confidential, however it may be provided to the sponsor and third parties listed below. Celerion may share your PII among Celerion affiliates who are located in other countries around the world. All Celerion affiliates will comply with the terms of this ICF and all Celerion policies and applicable laws and regulations at all times with respect to your PII.

The study results, including your PII, may be disclosed to, audited by, and/or monitored by the people listed below. This is to analyze the study data for the purposes of development and/or commercialization of the study drug, and also to make sure the study was done correctly. In order for this to take place, some third parties will have direct access to your PII, and may copy some of the original records that contains your PII. This includes the laboratory report linking your name to your HIV and/or hepatitis test results. Your original records maintained by Celerion and accessed by the people listed below may contain your PII. PII may be disclosed to the third parties listed below as necessary with respect to any investigation, complaint, or claim, including with respect to any investigation by a governmental authority. These third parties include:

- Regulatory authorities, such as the FDA, MHRA (Medicines and Healthcare products Regulatory Agency), EMA (European Medicines Agency) or Health Canada
- The Sponsor and third parties working with the sponsor
- Celerion and third parties working with Celerion
- The Institutional Review Board (IRB is a group of people who review research studies to protect the rights and welfare of research subjects.)

All of the parties listed above will maintain, use, disclose, transfer and access your PII confidentially and in accordance with applicable law or regulation.

Under certain circumstances, some tests results will be reported to health and regulatory authorities. This is done when required by law or regulation. If a medical emergency happens, your study results, including your PII, may be given to emergency medical staff not employed by Celerion or the Sponsor.

In addition to the purposes outlined above, Celerion or the sponsor may utilize your study results, including your PII, for publication purposes, such as presenting on the study results at a conference, publishing in a medical book or journal, writing a white paper about the study, or used for teaching purposes. In the event of any such publication, your PII will be anonymized prior to disclosure to third parties. Neither your name nor other identifiers will be used in any publication or teaching material. Further, Celerion may use your PII to make automated decisions, such as whether or not you are eligible to participate in any other study at Celerion.

You may withdraw your consent from Celerion's collection, use, processing, disclosure, and onward transfer of your PII at any time. If you withdraw your consent, Celerion will not collect any further PII about you, and you may be removed from the study. If you required that your PII be erased, the PII already gathered will still be kept in the study database where required under regulations applicable to clinical trial study files, however all other PII will be erased from our databases. Any PII that cannot be erased will be used as described in this Informed Consent Form. In accordance with applicable law, you may request (in writing) to see or have a copy of the study data collected about you. You have the right to request a correction to any PII about you that is not correct. You may not be able to see some data until after the study is over.

By signing and dating this form, you are allowing the collection, processing, use, disclosure, and onward transfer of your PII as described in this consent.

If you have any questions or concerns about Celerion's collection of your PII or the information outlined in this ICF, you may contact the Celerion Privacy Officer by electronic message at privacy@celerion.com; or by mail at 621 Rose Street, Lincoln, NE 68502. In addition, you have the right to lodge a complaint with any applicable governmental authority if you believe we have not complied with the requirements of applicable law with regard to your PII.

By signing this Informed Consent Form, you are allowing the use and disclosure of your personal data as described in this Informed Consent Form.

You will receive a signed and dated copy of this form.

WHOM TO CONTACT ABOUT THIS STUDY

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, please contact the Investigator at the telephone number listed on the first page of this consent document. If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research subjects. If you have any questions about your rights as a research subject, and/or concerns or complaints regarding this research study, contact**:**

- By mail:
  Study Subject Adviser
  Advarra IRB
  6940 Columbia Gateway Drive, Suite 110
  Columbia, MD 21046
- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: Pro00027736.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

See Next Page

YOUR CONSENT

Your signature below verifies that:

- You have read this written Informed Consent Form.
- A study staff member has explained this Informed Consent Form to you.
- You have had the chance to ask questions about the study.
- All of your questions have been answered to your satisfaction.
- You understand the information in this Informed Consent Form.
- You have been exhaustively informed by site staff about the purposes, type and character of the study and about the risk and benefits related to your participation in this study.
- You agree to follow the restrictions of the study.
- You agree that your blood samples will be collected in order to rule out infection with HIV, Hepatitis C virus and Hepatitis B.
- You agree voluntarily to take part in the study and give your consent for study procedures.
- You are aware that nothing contained in this Informed Consent Form waives any of your legal rights as a research subject, nor does it release the Study Doctor, the Sponsor, the study site, or its agents from any liability for negligence.
- You understand that the Sponsor, the Sponsor's designees, the monitor (s), the auditor (s) and the IRB will be granted direct access to your original medical records for verification of study procedures and / or data without violating your confidentiality.
- You are allowing the use and disclosure of your personal data as described in this Informed Consent Form
- You will receive a signed and dated copy of this consent form to keep.

Would you like the study site to inform your healthcare provider of your participation in this study? Check one: Yes ☐ No ☐

Name of healthcare provider: _____

Address of healthcare provider: _____

Subject Name (Print): _____

Subject Signature: _____ Date [dd-mmm-yyyy]: _____

FOR SITE STAFF

I have discussed this study with the above subject. This person had an opportunity to ask questions. The Subject signed and dated in my presence.

Study Staff Member explaining study and ICF (Print): _____

Signature: _____

Date [dd-mmm-yyyy] Time [hh:mm]

ACKNOWLEDGMENT

You have been given a signed and dated copy of this document. Subject Initials_____

CONSENT TO TAKE PART IN A CLINICAL RESEARCH STUDY AND AUTHORIZATION TO DISCLOSE HEALTH INFORMATION

Sponsor / Study Title:	**22nd Century Group, Inc. / "A Longitudinal Ambulatory Study to Assess Changes in Cigarette Consumption Behavior and Biomarkers of Exposure during a 6-Week Switch to Very Low Nicotine Cigarettes"**
Protocol Number:	**CA24914**
Principal Investigator: (Study Doctor)	**Melanie Fein, MD, CPI**
Telephone:	**(b) (6)** [redacted] **(336) 862-0634 (24-hour)**
Address:	**High Point Clinical Trials Center** **4160 Mendenhall Oaks Parkway** **Suite 105** **High Point, NC 27265**

It is important that you give a true and complete medical history. You must be honest about your past and present usage of medications. Giving information that is not true or incomplete could be very harmful to your health. If you give false information, you may be dismissed from the study.

You are being invited to take part in a research study sponsored by 22nd Century Group, Inc. You must read this Informed Consent Form before you decide if you want to take part in the study. This form will tell you about the study. The Study Doctor or study staff can explain words or information that you do not understand. Ask the study staff as many questions as needed for you to decide if you want to take part in the study. Your participation in this research is voluntary and we will include only those who wish to take part. If you decide to take part in this study, you must sign your name at the end of the form and date it. You cannot take part in this study until you sign and date this form.

PURPOSE OF THE STUDY

This is a research study and is not to be used to encourage product use, and is not to treat any medical disease. This study is planned:

- To measure your cigarette use or how many cigarettes smoked per day when you change from smoking your regular cigarettes to cigarettes with a very low nicotine level.
- To find out how much nicotine is in the blood after smoking the cigarettes with very low nicotine.

- To find out more about your smoking urges, any withdrawal symptoms you may feel, and any health risks, when you switch to cigarettes with a very low nicotine level.

This is an open label study which means you will know what kind of filtered king size study cigarettes you will be smoking. There will be a total of 140 participants in this study. Seventy will be smokers of non-mentholated and seventy will be smokers of mentholated King size cigarettes.

For one week prior to starting on the assigned study product you will be asked to smoke your own usual brand of cigarettes as you would usually do each day. During this time you should only smoke your usual brand of King size cigarettes.

For the entire study you will be asked to report the number of cigarettes used each day using an electronic diary (e-diary). The diary entry should be completed at the end of each day. Training for the e-diary will be provided at the visit at the start of Week -1. You may install the e-diary app on your phone or tablet or a device can be provided to you for this daily reporting.

You will also be asked to collect and bring to the clinic all cigarette butts you smoke from the first clinic visit when you start recording your daily use to the end of the study at the end of week 6. Containers for butt collection will be provided by the clinic. These will be counted by the staff to confirm your daily reported use.

Each time you return to the clinic you will be given an alcohol and drug screen to test for drugs of abuse.

You will return to the research unit at the end of Week -1, at a time scheduled by the clinic. At this visit you will check-in to the clinic to stay for approximately 30 hours. During this visit you will have blood samples drawn and start a 24 hour urine collection. You will also answer questionnaires on your smoking behavior, any withdrawal symptoms, urges to smoke, and noticed health risks.

During this visit, you will be randomly (like the flip of a coin) be selected to either continue to smoke your own usual brand of cigarettes, or you may be randomly selected to switch to smoking very low nicotine study cigarettes within your choice of your usual cigarette flavor (menthol or non-menthol). If you are randomized to the very low nicotine cigarette group, you will not be allowed to use any other tobacco or nicotine containing products (i.e. vape products) during the study, including your usual brand cigarettes.

At the end of your stay you will be sent home to continue to smoke your usual brand cigarettes, which will not be provided as part of the study, or with enough very low nicotine cigarettes for two weeks. During this time you will make daily entries into the e-diary and collect your used cigarette butts to bring back to the clinic.

You will return to the research unit at the end of Weeks 2 and 6, at a time scheduled by the clinic for an overnight stay lasting about 30 hours. You will repeat the same procedures that were performed at the first 30 hour clinical stay.

At the end of Week 4 you will return to the research unit for a short visit. You will be asked questions about your heath and cigarette behavior, urges, withdrawal, and health risks. Compliance will be evaluated via cigarette butt collection and e-diary entries. You will receive an additional supply of cigarettes if you are assigned to the very low nicotine group and to complete the questionnaires.

STUDY PRODUCT

The following study products will be used in the study:

- Your own brand of non-mentholated filtered king size cigarettes.
- Your own brand of mentholated filtered king size cigarettes.
- The study non-mentholated very low nicotine cigarettes filtered king size cigarettes.
- The study mentholated very low nicotine cigarettes filtered king size cigarettes.

Very Low Nicotine cigarettes contain 0.4 mg nicotine per gram of tobacco. Normal cigarettes contain about 10 mg nicotine per gram of tobacco. The cigarettes provided are for Clinical Trial use only and should be kept out of the reach of children and not shared with anyone else.

VERIFIED CLINICAL TRIALS DATABASE

Verified Clinical Trials (VCT) is a secure internet-based registry of subjects who are, or have recently been, in clinical research studies. VCT protects the safety of subjects by helping to ensure they are not in more than one study at a time. Your health could be harmed if you start a new study while another investigational product is still in your body. Also, the data obtained about how your body responds to an investigational product may be affected if you are using another or have another research drug in your system. For these reasons, VCT will be used for all subjects in this study. Your signature on this consent form grants your permission to give your data to VCT. If you decline, you may not be able to participate in this study.

How Will the Study Site Check My Participation in Other Clinical Research Studies?

VCT stores clinical visit dates for subjects who are in clinical research studies. You may be in this registry if you have already given permission to be in a research study registry. The VCT registry will be checked to make sure you are not in another clinical trial. It will also check that enough time has passed since your last study.

What Data Does the Study Site Need to Check My Participation in Other Clinical Research Studies?

The following data will be entered into the registry at the Screening visit: parts of your first and last name, with or without biometrics such as fingerprint template, date of birth, gender, and an ID number (for example, Driver's license number, passport number, cedula number or military ID number). A Unique Identification Code (UIC) will be created for you from some of this data. This means that a person looking at the UIC would not be able to tell what your name is or your private data.

The following dates will be collected: screening, product usage, your last blood draw, and when you stopped being in the study. Other people cannot access your personal data, or even your UIC. Only the study site and VCT personnel will be able to access the registry data. If you ever decide to delete your personal data from the registry, your (UIC) with your study

history will remain in the VCT system.

If VCT detects a potential conflict with another study during your time in this study, the study site will be informed. This site will not be informed about the other study sponsor (company) or other research sites. However, VCT will have access to your registry data from all the other sites that use VCT to make sure your data is correct and up to date. At your study exit, the study site or VCT will update your status in the registry. It will be used in the future when screening and enrolling in clinical trials only. VCT may store your data in the database for up to fifty (50) years, at which point it will be destroyed.

You may review your personal data in the database at any point in time by calling VCT at 516-998-7499 or by writing: VCT, 1305 Franklin Ave #150 Garden City, NY 11530. You may withdraw your personal data (name, date of birth, ID data) from the VCT registry at any time without penalty or loss of benefits.

SUBJECT RESPONSIBILITIES

You must:

- Follow all clinic rules and instructions of the study staff.
- Follow the study restrictions using only study approved tobacco products.
- Report any unfavorable health or medical events, referred to as adverse events.
- Give true and complete answers to any questions you choose to answer.
- Report daily cigarette use via an electronic diary.
- Return your used butts back to the clinic.
- Comply with the terms of the Informed Consent Form.

GENERAL CLINIC RULES AND STUDY RESTRICTIONS

Meals and snacks will be served at scheduled times during your stay in the study clinic. You can eat only the food and drink provided to you. You can eat only at the times food is provided. Some of the requirements and restrictions for this study are listed below.

You must agree to follow all the study restrictions and research center rules and regulations. These will be reviewed with you by the study staff. You will be given a copy of these rules. Failure to follow the study restrictions, rules and regulations may result in you being fined or your participation in the study coming to an end which will require you to leave the study site.

You will be required to wear an ID band for the entire duration of the study. Removal may result in a reduction in the amount of compensation you receive for participating in the study. You will be required to follow the research center rules and regulations and your amount of compensation may be reduced, if you do not do so. You will be given the rules and regulations to read and sign during the Screening Visit.

If you are discharged from the study because you have a positive drug screen result, you will not be compensated for any of your participation in the study.

If you damage or do not return research center property, the cost of the item or of the repair will be deducted from your study payment. Please bring cash or a credit card for your ride home

from all visits. If you do not bring enough cash or a credit card, and the research center needs to pay for your transport, this may be taken out of your study payment.

STUDY RESTRICTIONS

- You must be a healthy adult male or female adult smoker, 26 to 65 years of age who has been a smoker for at least 5 years at Screening.
- You smoke an average of 10 or more manufactured cigarettes per day.
- Your usual brand of cigarette is a filtered king size cigarette.
- You may not use any nicotine-containing products other than factory manufactured cigarettes, such as roll-your-own cigarettes, e-vapor products, bidis (a type of cheap cigarette made of unprocessed tobacco wrapped in leaves), snuff, nicotine inhaler, pipe, cigar, chewing tobacco, nicotine patch, nicotine spray, nicotine lozenge, or nicotine gum, within 28 days prior to Screening.
- If female and able to have children, you must be practicing an acceptable method of birth control.
- You may not participate if you are a female subject who is pregnant, lactating, or intend to become pregnant from Screening through the End of Study.
- You may not use any prescription smoking cessation treatments, including, but not limited to, varenicline (Chantix®) or buproprion (Zyban®) within 3 months prior to Screening.
- You may not be a self-reported puffer/non-inhaler (a smoker who draws smoke from the cigarette into the mouth and throat but does not inhale).
- You may not be planning to quit smoking during the study period or delay a quit attempt in order to participate in the study.
- You may not have any significant abnormal findings on your physical examination, medical history, ECG (a test that measures and records the electrical activity of your heart), or clinical laboratory results, in the opinion of the Investigator.
- You may not have a positive test for human immunodeficiency virus (HIV), hepatitis B surface antigen (HBsAg), or hepatitis C virus (HCV).
- You may not have had an illness such as an upper respiratory infection or viral infection that required you to take prescription medication(s) within 14 days prior to first clinic visit.
- You may not have a fever (greater than or equal to100.5°F) at first clinic visit or screening.
- Your Body mass index (BMI) may not be greater than 40.0 kg/m^2 or less than 18.0 kg/m^2 at Screening.
- You may not have a history of drug or alcohol abuse or have used medical/recreational marijuana within 12 months of Screening.
- You cannot have diabetes mellitus that is not controlled by diet/exercise alone, in the opinion of the Investigator.
- Your heart rate while sitting may not be lower than 40 bpm (beats per minute) or higher than 99 bpm at Screening, unless deemed not clinically significant by the PI.
- While sitting your systolic blood pressure may not be lower than 90 mmHg (millimeters of mercury) or higher than 150 mmHg, diastolic blood pressure should not be lower than 40 mmHg or higher than 95 mmHg at Screening, unless deemed not clinically significant by the PI.

- You may not have a positive urine screen for drugs of abuse or alcohol at Screening or at the first clinic visit.
- You may not have used any inhalers to treat any medical condition within 3 months prior to Screening and throughout the study.
- You cannot have donated plasma within 7 days prior to Screening or at any time during the study.
- You cannot have donated blood or blood products (with the exception of plasma as noted above), had significant blood loss, or received whole blood or a blood product transfusion within 56 days prior to Screening.
- You may not have participation in a previous clinical study for an investigational drug, device, biologic, or tobacco product within 30 days prior to Screening.
- If you are a subject or a first-degree relative (parent, sibling, child) is a current or former employee of the tobacco industry or a named party or class representative in litigation with the tobacco industry you may not participate in this study.
- If you are a subject or a first-degree relative (parent, sibling, child) is a current employee of the clinic sites you may not participate in this study.
- You must report any changes or new medication you are taking during the study. Some medications known to interact with the nicotine results may disqualify you from participating.
- You must plan to stay in the area during the course of the study to attend the clinic visits as required.
- You must be willing to comply with the protocol including use of the test product and collection of samples required of your group.
- Beverages containing caffeine are not allowed with the exception of one caffeinated beverage with each meal.
- You must not consume any alcohol product 48 hours prior to and during each clinic visit.
- You will be instructed to refrain from strenuous physical activity except for your usual routine activity during the whole study participation.

NUMBER OF SUBJECTS AND LENGTH OF STUDY

This study will enroll about 140 subjects, at 2 research clinics. The entire study will last about 11 weeks, 4 weeks for screening, 7 weeks of product use and reporting, plus a 7-day safety follow up period.

If randomized to use the very low nicotine cigarettes, the test products will be provided to you during the study at no charge. If you are randomized to continue to smoke your own cigarettes you will need to purchase your own product.

POSSIBLE RISKS ASSOCIATED WITH THE STUDY PRODUCTS

There is always a chance that an unexpected or serious adverse event may happen. Smokers who use light cigarettes do not reduce their risk for developing smoking-related cancers and other diseases. You must report any adverse events to the study team any time after you have signed this informed consent form.

POSSIBLE RISKS ASSOCIATED WITH THE STUDY PRODUCTS OR SMOKING IN GENERAL

The packaging for cigarettes currently commercially available in the United States carry one of the following rotating warning labels:

SURGEON GENERAL'S WARNING: Smoking Causes Lung Cancer, Heart Disease, Emphysema, and May Complicate Pregnancy.

SURGEON GENERAL'S WARNING: Quitting Smoking Now Greatly Reduces Serious Risks to Your Health.

SURGEON GENERAL'S WARNING: Smoking By Pregnant Women May Result in Fetal Injury, Premature Birth, and Low Birth Weight.

SURGEON GENERAL'S WARNING: Cigarette Smoke Contains Carbon Monoxide.

If you are concerned about the health effects of smoking, do not participate in this study.

PROCEDURES AND POSSIBLE RISKS OR DISCOMFORTS

Procedures will be done during the study at assigned times. The procedures will be done to monitor your health, assess the safety of the study products, and to see how the nicotine from the study products is absorbed into your body.

BLOOD COLLECTIONS

A needle will be used to take blood samples from a vein in your arm. The number of samples and times will depend upon the group you are randomized to on Day -1.

All subjects will have 2 draws completed for Clinical Laboratory samples and 3 draws for compliance testing. About 65mL of blood (approximately 4 tablespoons) will be taken.

Additional samples may need to be taken. This amount is less than the amount you would give if you were donating blood.

You may have discomfort or pain when your blood is collected. You may feel faint or pass out. There is a risk of infection, bleeding, or bruising at the puncture site. You may develop a small scar at the puncture site where multiple blood samples are taken.

URINE COLLECTION

Urine samples will be collected to test for drugs of abuse and alcohol at Screening, start of week -1, end of weeks -1 2, 4, 6, and end of study. A urine sample will be collected for women to test for pregnancy at the start of week -1, end of weeks -1, 2, 4, and 6.

Twenty-four hour study urine collections will be complete on days -1, end of week 2 and 6 to test for nicotine and other substances related to tobacco/nicotine use.

NICOTINE WITHDRAWAL & CONFINEMENT

Symptoms of nicotine withdrawal include:

- irritability
- anger
- frustration

- anxiety/feeling restless
- depression/feeling sad
- sleep problems/nightmares
- sensitivity to pain
- tremors
- slow heart rate
- nausea
- constipation
- increased appetite
- weight gain
- coughing
- dizziness
- sore throat
- mouth ulcer
- difficulty concentrating
- impaired memory

There are also other dietary and activity restrictions while you are staying at the study site that you may not be used to.

e-DIARY and QUESTIONNAIRES

You will have training on the eDiary that you will use on your smartphone/tablet. If you do not have a device for use one will be provided to you. This devise, if provided, will be returned to the site at the end of the study. Each day you will report the number of cigarettes you smoke for the day from the start of week -1 to the end of the study. If your eDiary completion compliance falls below 70%, you may be withdrawn from the study.

You will be completing 4 separate questionnaires about your cigarette dependence, smoking urges, nicotine withdrawal, and a perceived health risk scale. These will be done 4 times during the study, at the end of weeks -1, 2, 4, and 6.

SCREENING VISIT

The following procedures will be done during this visit to help the Study Doctor determine if you qualify for this study. This is called the screening visit.

- Read, sign and date the Informed Consent Form.
- You will provide your medical history, including all medications, vitamins, herbal products or supplements you are taking and have taken for the past 30 days.
- You will have a physical examination including checking inside your mouth.
- Height and weight will be measured and body mass index (BMI) will be calculated.
- An Electrocardiogram (ECG) will be performed (a test that measures and records the electrical activity of your heart).

- Your blood pressure, heart rate, respiratory rate and temperature will be taken.
- You will provide a urine sample. The sample will be used to test for general health, nicotine exposure, alcohol and drugs of abuse. You will not be allowed to continue if the tests for drugs of abuse are positive.
- You will have a carbon monoxide (CO) breath test.
- You will be asked about your tobacco product and nicotine product use and if you plan on quitting in the next 3 months.
- A photo will be taken of the front and back of your cigarette pack along with a ruler.
- Blood samples will be taken. These samples will be used to test for general health and, if female, a pregnancy test will be done. If you are a post-menopausal female, a serum FSH (follicle stimulating hormone) test to confirm postmenopausal status will be done.
- You will have your blood tested for the hepatitis viruses and for HIV. HIV is the virus that causes AIDS. If you have a positive HIV or hepatitis test, you cannot be in the study. If the HIV or hepatitis test are positive, you will be notified by the research site and given information on how to follow up for further medical care. As required by law, positive test results must be reported by the research site to the State Department of Health. If you have any questions about what information is required to be reported, please ask the study staff. Although the test results are supposed to be private, this cannot be guaranteed. For example, it is possible for a court of law to get health or study records without your permission.
- You will be given information about quitting tobacco use.
- You may try the very low cigarette products that will be used in the study.

SCHEDULE OF EVENTS

Baseline Visit (Start of Week -1)

You will visit the clinic at the start of Week -1 at a time scheduled by the clinic. The following procedures will take place during this visit:

- Review of inclusion and exclusion criteria to verify nothing has changed since Screening.
- Confirm you are still using your usual brand of cigarettes.
- You will be asked about any adverse events and any changes in your medication.
- You will have a urine test for drug and alcohol screening and to see how much nicotine is in your system. If female this sample will also be tested for pregnancy.
- Your blood pressure, heart rate, respiratory rate, temperature, and weight will be taken
- You may have a physical examination if you have any new symptoms since your last visit.
- Your weight will be recorded.
- You will receive training on e-diary use.
- You will receive canisters for used cigarette butt collection.
- Your smoking and nicotine product use restrictions will be reviewed.

BETWEEN CLINIC VISITS

You will be required to record your daily cigarette use in the electronic diary and to collect all used cigarette butts in the provided container. You will receive a reminder contact to return to

the research unit. At each visit adverse events and any changes in your medication will be reviewed.

CLINIC VISIT (End of Weeks -1, 2 and 6)

You will check in to the clinic at the end of Weeks, -1, 2 and 6 at times scheduled by the clinic. You will stay at the clinic until after the 24-hour urine collection and other study procedures. The following procedures will take place during this visit for all subjects:

- Review of inclusion and exclusion criteria have not changed since your last visit.
- Confirm you are still using your usual brand of cigarettes if you were not provided very low nicotine cigarettes for us.
- You will be asked about any adverse events and any changes in your medication.
- You will have a urine test for drug and alcohol use. If female, your sample will also be tested for a positive pregnancy.
- You will have a blood sample taken to test for cotinine
- Your blood pressure, heart rate, respiratory rate, temperature, and weight will be taken.
- Your smoking and nicotine product use restrictions will be reviewed.
- Review that you have not changed your usual brand cigarette at Week -1.
- Verify the returned the canister with used cigarette butts for counting.
- You will start a 24-hour urine collection.
- You will have blood samples drawn for study testing, including cotinine testing.
- Daily recording of cigarettes per day in the e-diary will be reviewed. You will complete 4 questionnaires about your smoking behavior.

Prior to checkout on weeks -1 and 2:

- You will get a new container for collecting used cigarette butts to be returned at your next visit.
- You will get test product for the following period if selected to the very low nicotine group.

You will have your personal items thoroughly checked at the start of these clinic visits.

CLINIC VISIT (End of Week 4)

You will visit the clinic at the end of Week 4 at a time specified by the clinic. The following procedures will take place during this visit:

- Review of inclusion and exclusion criteria have not changed since your last visit.
- You are documenting and still using your usual brand of cigarettes if that is what you were assigned to.
- You will be asked about any adverse events and any changes in your medication.
- You will have a urine test for drug and alcohol use If female, your sample will also be tested for a positive pregnancy. Your blood pressure, heart rate, respiratory rate, temperature, and weight will be taken.
- You have returned the canister with used cigarette butts for counting.
- You will complete the 4 questionnaires.

- You will receive new container for collecting used cigarette butts during next out of clinic period.
- Smoking and nicotine product use restrictions will be reviewed.
- You will receive study product for the following out of clinic period if selected to the very low nicotine group.

END OF STUDY (End of Week 6 Visit or on Early Discontinuation)

At the end of the study, the following procedures will be performed:

- You will be asked about any adverse events and any changes in your medication.
- Your blood pressure, heart rate, respiratory rate, temperature, and weight will be taken.
- You will have an ECG
- You will have routine lab work complete Clinical chemistry, hematology and urinalysis.
- You may have a physical examination if you have any new symptoms since your last visit.
- You will be given information about quitting tobacco use.

FOLLOW-UP CALL

The study team will contact you approximately 7 days after the study to review any adverse events and any changes in your medication and provide information about quitting tobacco use. You may be asked to return to the clinic to have a physical examination or further testing if you have any new symptoms since your last visit.

POSSIBLE RISKS TO AN UNBORN BABY OR CHILD WHO IS BREASTFEEDING

The effects of smoking on the unborn child are known to be hazardous. It is possible that the study products may cause harm to an unborn baby (fetus or embryo). You must not become pregnant during the study. If you are pregnant, lactating or planning to become pregnant at any time from Screening until study completion, you will not be allowed to take part in this study.

Females

If you are having sex with a male and able to become pregnant, you must agree to use an approved accepted method of birth control from Screening Visit until the end of the safety follow-up.

- Intrauterine device (IUD), intrauterine system,
- Barrier methods of contraception (condoms, occlusive caps) with spermicidal foam/gel/film/suppository,
- Hormonal contraception containing progesterone only,
- Essure® or similar nonsurgical sterilization
- Vasectomized partner(s),
- True abstinence (periodic abstinence and withdrawal are not effective methods)

Hormonal contraception made with estrogen is NOT allowed in this study because this may affect the nicotine reported in your blood.

A pregnancy may still occur even while using birth control. Not having sex with a partner of the opposite sex is the only way to be certain that a pregnancy will not occur.

You must tell the Study Doctor/study staff right away if you become pregnant during the study. The Study Doctor/study staff will request to follow the progress of the pregnancy to the outcome of the pregnancy (for example birth, loss, or termination).

UNKNOWN / UNFORESEEABLE RISKS

In addition to the risks listed above, there may be unknown risks, events that do not happen very often, and events we could not expect associated with the use of these products, including severe or life threatening allergic reactions or an unexpected reaction with another medication. Allergic reactions may include:

- skin rash
- itching
- swelling in the face or throat

If you experience an injury, bad effect, or any other unusual health experience during this study, you should immediately contact the Study Doctor or the study staff.

Subjects who develop any visible skin reaction may have the area photographed to document the extent of the reaction. These photographs will only be labeled with your subject ID number and not any personal information.

Your privacy is very important to us, and we will take precautions to protect your privacy, but cannot guarantee that your identity will never become known to other researchers or third parties. It is possible that there could be security breaches of the systems or files used to store your personal and health information and specimens collected from you during this study. There may also be other privacy risks that we have not foreseen.

SIGNIFICANT NEW SAFETY INFORMATION DURING THE STUDY

You will be told of any significant new safety information that the study site is made aware of by the Sponsor that might influence your willingness to continue your participation in this study.

POSSIBLE BENEFITS FROM THE STUDY

You will not receive any personal or health benefits from being in this study. The tests provided may help you learn about your general health. They may also help you discover an unknown medical condition.

TAKING PART IN THIS STUDY IS OF YOUR OWN FREE WILL

You are being asked to take part in this study because you are healthy. The only other option is not to take part in this study. You will never be forced to use cigarettes during the study. If you wish to completely stop using cigarettes while you are in the study, you will be allowed to leave the study.

If you decide to take part in the study, it should be by your own choice and your own free will. No one will force you to be in the study. If you enter the study, no one will force you to stay in the study. If you choose not to be in the study or if you leave the study early, there will be no penalty or loss of benefits to which you are otherwise entitled. **If you leave or are removed from the study for any reason your stipend will be prorated to the amount of the study that you complete.** You will not lose any rights that you are entitled to as a research subject.

COSTS OF PARTICIPATION

There is no cost to you for participating in this study.

COMPENSATION FOR TAKING PART IN THE STUDY

You will be compensated for taking part in this research study as outlined below. This is to compensate you for your time and inconvenience. If you do not finish the study, you will be compensated for the part you do complete.

Visit	**All Participants**
Screening	You will not be compensated for this visit
Visit at the Start of Week -1 (Outpatient)	$ 75.00
Week -1 Overnight Stay – Admission Day	$ 200.00
Week -1 Overnight Stay – Discharge Day	$ 75.00
Week 2 Overnight Stay – Admission Day	$ 200.00
Week 2 Overnight Stay – Discharge Day	$ 75.00
Week 4 Visit	$ 75.00
Week 6 Overnight Stay – Admission Day	$ 200.00
Week 6 Overnight Stay – Discharge Day	$ 75.00
End of Study	$ 75.00
Follow-up Call	$ 25.00
Compliance Bonus	$ 325.00
Use of Own Electronic Device	$ 50.00
Study Total	$ 1450.00

If you choose to withdraw from the research study, you will receive compensation only for the portion of the study that you have completed as outlined above. If it is necessary for you to return to the research unit for additional safety follow up visits, you will be compensated for travel expenses at $25.00 for each completed visit. For more information, please talk to your Study Doctor.

You will receive your compensation within 7 days of the completion of each study visit.

If it is determined by your Study Doctor that you should stop the study early, you will be compensated for the portion of the study you completed.

You understand the following:

- No deductions will be withheld from your stipend check for tax purposes. You are responsible for reporting any payment on your state and federal tax returns. At the end

of each year, the study site will notify the IRS of all stipends you have received throughout the year.
- Being in this study does not make you an employee of the sponsor, the study site, or the FDA.

COMPENSATION FOR AN INJURY DIRECTLY RELATED TO YOUR PARTICIPATION IN THIS STUDY

There is a chance that you could become ill or injured while being in this study. The study site will help you make arrangement if your illness or injury requires care outside of the study site (hospital, medical specialist). Unless other arrangements have been made by the study site, all billing will be under your name. The cost of this care will be billed to you or your insurer in the ordinary manner. If you do not have insurance, the cost of the care will be billed to you directly.

The Study Doctor will decide if an injury or illness is directly related to the performance of the protocol (study plan) or use of the study products. If your injury or illness is directly related to the performance of the protocol or use of the study products, the Sponsor and/or the study site will reimburse you for your reasonable out-of-pocket medical costs (not covered by insurance) to treat an illness or injury that is directly caused by the study procedures or products.

To pay these medical expenses, the sponsor will need to know some information about you like your name, date of birth, and social security number or Medicare Health Insurance Claim Number. This is because the sponsor has to check to see if you receive Medicare and if you do, report the payment it makes to Medicare. The sponsor will not use this information for any other purpose.

You will need to sign a "release of information" form. This form will allow the study site to obtain your medical records related to the illness or injury. These records will help the study doctor determine the cause of the illness or injury. They may also help the sponsor learn more about the safety of the study products.

Any injury or illness that is not directly related to the performance of the protocol or use of the study products will be your responsibility to pay. This includes any injury or illness that would have occurred even if you had not participated in the study.

You do not give up any of your legal rights by signing and dating this consent form, accepting medical care, or accepting payment for medical expenses.

REASONS YOU CAN BE REMOVED FROM THE STUDY

You can be removed from the study at any time and for any reason without your consent. Some of the reasons you can be removed are listed below.

- You do not follow the instructions, rules, and restrictions given by the study staff.
- You do not follow the requirement for exclusive use of your assigned study product.
- You do not continue to meet the requirements for the study.
- Your Study Doctor decides it is best for your health.

- The Sponsor stops the study.
- If you become pregnant.

LEAVING THE STUDY BEFORE IT IS COMPLETED

If you choose to leave the study, you must notify your Study Doctor or study staff. It is very important that you agree to have the following procedure completed. The procedures listed below will be done for your safety and well-being. You must return all used or unused study products.

- Physical examination
- Vital Signs
- Weight
- An ECG - electrocardiogram (a test that measures and records the electrical activity of your heart) will be done.
- Record any adverse events you may have, or medications you have taken
- Your blood and urine will be collected for Clinical laboratory tests.
- Drug and Alcohol screen
- Information about smoking cessation will be provided.

All data that has been collected from you will be used for its original intention.

If you leave the study early or you are removed from the study, all samples collected from you before you leave will be used and analyzed as described in this Informed Consent Form. If you do not want your samples collected until the time of withdrawal and not analyzed yet to be analyzed, you must notify your Study Doctor in writing at the address on page 1 of this consent form.

CONFIDENTIALITY, DATA PROTECTION, AND PRIVACY

Information collected about you and your participation in this study, including all medical and health information as outlined below will be kept confidential according to privacy laws in this country. The information in both paper and electronic format that HPCTC will collect about you will include study records that may contain your name and other personally identifiable information such as your date of birth (PII). PII is information that directly identifies you, and will also include special information such as your racial or ethnic origin, physical or mental health, sexual life, or genetic data and/or biometric data for the purpose of uniquely identifying you. These records (including any photographs) containing your PII will be kept for a minimum of either two years following the approval of the study drug, or two years after the sponsor discontinues its research on the study drug, and may be kept for as long as sponsor is developing or commercializing the study drug, which may be indefinitely. Your study results will be coded with numbers and/or initials wherever possible. HPCTC will keep a list that links your name to your study results. This list will be kept confidential, however it may be provided to the sponsor and third parties listed below. HPCTC may share your PII among HPCTC affiliates who are located in other countries around the world. All HPCTC affiliates will comply with the terms of this ICF and all HPCTC policies and applicable laws and regulations at all times with respect to your PII.

The study results, including your PII, may be disclosed to, audited by, and/or monitored by the people listed below. This is to analyze the study data for the purposes of development and/or commercialization of the study drug, and also to make sure the study was done correctly. In order for this to take place, some third parties will have direct access to your PII, and may copy some of the original records that contains your PII. This includes the laboratory report linking your name to your HIV and/or hepatitis test results. Your original records maintained by HPCTC and accessed by the people listed below may contain your PII. PII may be disclosed to the third parties listed below as necessary with respect to any investigation, complaint, or claim, including with respect to any investigation by a governmental authority. These third parties include:

- Regulatory authorities, such as the FDA, MHRA (Medicines and Healthcare products Regulatory Agency), EMA (European Medicines Agency) or Health Canada
- The Sponsor and third parties working with the sponsor
- HPCTC and third parties working with HPCTC
- The Institutional Review Board (IRB is a group of people who review research studies to protect the rights and welfare of research subjects.)

All of the parties listed above will maintain, use, disclose, transfer and access your PII confidentially and in accordance with applicable law or regulation.

Under certain circumstances, some tests results will be reported to health and regulatory authorities. This is done when required by law or regulation. If a medical emergency happens, your study results, including your PII, may be given to emergency medical staff not employed by HPCTC or the Sponsor.

In addition to the purposes outlined above, HPCTC or the sponsor may utilize your study results, including your PII, for publication purposes, such as presenting on the study results at a conference, publishing in a medical book or journal, writing a white paper about the study, or used for teaching purposes. In the event of any such publication, your PII will be anonymized prior to disclosure to third parties. Neither your name nor other identifiers will be used in any publication or teaching material. Further, HPCTC may use your PII to make automated decisions, such as whether or not you are eligible to participate in any other study at HPCTC.

You may withdraw your consent from HPCTC's collection, use, processing, disclosure, and onward transfer of your PII at any time. If you withdraw your consent, HPCTC will not collect any further PII about you, and you may be removed from the study. If you required that your PII be erased, the PII already gathered will still be kept in the study database where required under regulations applicable to clinical trial study files, however all other PII will be erased from our databases. Any PII that cannot be erased will be used as described in this Informed Consent Form. In accordance with applicable law, you may request (in writing) to see or have a copy of the study data collected about you. You have the right to request a correction to any PII about you that is not correct. You may not be able to see some data until after the study is over.

By signing and dating this form, you are allowing the collection, processing, use, disclosure, and onward transfer of your PII as described in this consent.

If you have any questions or concerns about HPCTC collection of your PII or the information outlined in this ICF, you may contact the study doctor at 336-862-0634. In addition, you have the right to lodge a complaint with any applicable governmental authority if you believe we have not complied with the requirements of applicable law with regard to your PII.

By signing this Informed Consent Form, you are allowing the use and disclosure of your personal data as described in this Informed Consent Form.

You will receive a signed and dated copy of this form.

WHOM TO CONTACT ABOUT THIS STUDY

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, please contact the Investigator at the telephone number listed on the first page of this consent document. If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research subjects. If you have any questions about your rights as a research subject, and/or concerns or complaints regarding this research study, contact**:**

- By mail:
  Study Subject Adviser
  Advarra IRB
  6940 Columbia Gateway Drive, Suite 110
  Columbia, MD 21046
- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: Pro00027736.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

YOUR CONSENT

Your signature below verifies that:

- You have read this written Informed Consent Form.
- A study staff member has explained this Informed Consent Form to you.
- You have had the chance to ask questions about the study.
- All of your questions have been answered to your satisfaction.
- You understand the information in this Informed Consent Form.
- You have been exhaustively informed by site staff about the purposes, type and character of the study and about the risk and benefits related to your participation in this study.
- You agree to follow the restrictions of the study.
- You agree that your blood samples will be collected in order to rule out infection with HIV, Hepatitis C virus and Hepatitis B.
- You agree voluntarily to take part in the study and give your consent for study procedures.
- You are aware that nothing contained in this Informed Consent Form waives any of your legal rights as a research subject, nor does it release the Study Doctor, the Sponsor, the study site, or its agents from any liability for negligence.
- You understand that the Sponsor, the Sponsor's designees, the monitor (s), the auditor (s) and the IRB will be granted direct access to your original medical records for verification of study procedures and / or data without violating your confidentiality.
- You are allowing the use and disclosure of your personal data as described in this Informed Consent Form
- You agree to participate in the VCT database as described in this document.
- You will receive a signed and dated copy of this consent form to keep.

Would you like the study site to inform your healthcare provider of your participation in this study? Check one: Yes ☐ No ☐

Name of healthcare provider: _____

Address of healthcare provider: _____

Subject Initials: _____ Date: _____

Subject Name (Print): _____ Time [hh:mm]: _____

Subject Signature: _____ Date [dd-mmm-yyyy]: _____

FOR SITE STAFF

I have discussed this study with the above subject. This person had an opportunity to ask questions. The Subject signed and dated in my presence.

Study Staff Member explaining study and ICF (Print): _____

Signature: _____

Date [dd-mmm-yyyy] Time [hh:mm]

ACKNOWLEDGMENT

You have been given a signed and dated copy of this document. Subject Initials_____