

16.1.7 Randomization Scheme and Codes

19JUL2018 12:00

CA24914 - 22nd Century Group, Inc. Protocol: VLN Cigarette Consumption Study, Amended Protocol Date 18JUN2018. Product: VLN Cigarettes
An Open-Label, 2-Site, Randomized Study to Assess Cigarette Consumption and Biomarkers
Randomization Schedule

Site	Flavor	Subject Number	Product	Topography Assessment	PK Assessment	Gender	Age
1	Menthol	1	VLN	Y	Y	M	≤40
	Menthol	2	VLN	Y	Y	M	≥40
	Menthol	3	UB	N	N	M	≤40
	Menthol	4	VLN	Y	Y	F	≥40
	Menthol	5	UB	N	N	F	≥40
	Menthol	6	VLN	Y	Y	F	≥40
	Menthol	7	VLN	Y	Y	F	≤40
	Menthol	8	VLN	Y	Y	F	≤40
	Menthol	9	UB	N	N	F	≤40
	Menthol	10	VLN	Y	Y	F	≥40 (b) (6) 18JUN2018
	Menthol	11	VLN	Y	Y	M	≤40
	Menthol	12	VLN	Y	Y	M	≥40
	Menthol	13	UB	N	N	F	≤40
	Menthol	14	VLN	Y	Y	F	≤40

Product Descriptions:

UB: Usual brand filtered king size cigarettes sourced by the subjects

VLN: Very low nicotine cigarettes sourced by 22nd Century Group, Inc.

Each study group (for the purpose of the randomization defined as this group of 35 subjects) will include no fewer than 10 subjects of either gender and no fewer than 10 subjects from each age group (≤ 40 years old and > 40 years old).

The first 12 subjects randomized to VLN will participate in both topography and pharmacokinetics assessments.

The next 6 subjects randomized to VLN will participate in a topography assessment only

Creator Date:

Approver Date:

Pharmacist Date:

(b) (6)

19-Jul-2018

19JUL2018

19JUL2018

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Randomization Schedule

Site	Flavor	Subject Number	Product	Topography Assessment	PK Assessment	Gender	Age
1	Menthol	15	UB	N	N	M	≤40
	Menthol	16	UB	N	N	M	>40
	Menthol	17	VLN	Y	Y	M	≤40
	Menthol	18	VLN	Y	Y	M	>40
	Menthol	19	VLN	Y	N	M	>40
	Menthol	20	VLN	Y	N	M	≤40
	Menthol	21	VLN	Y	N	M	>40
	Menthol	22	VLN	Y	N	M	≤40
	Menthol	23	VLN	Y	N	F	>40
	Menthol	24	VLN	Y	N	M	≤40
	Menthol	25	VLN	N	N	F	>40
	Menthol	0226	UB	N	N		
	Menthol	0227	VLN	N	N		
	Menthol	0228	UB	N	N		

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The next 6 subjects randomized to VLN will participate in a topography assessment only

Creator, Date:

(b) (6)

19 JUL 2018

Approver, Date:

(b) (6)

19 JUL 2018

Pharmacist, Date:

(b) (6)

19 JUL 2018

0 subjects randomized at high point (HPCTC). see copy signed 04 FEB 2019. (b) (6) 04 FEB 2019

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Randomization Schedule

Site	Flavor	Subject Number	Product	Topography Assessment	PK Assessment
1	Menthol	① 229	VLN	N/A	N
	Menthol	① 230	UB	N	N
	Menthol	① 231	VLN	N	N
	Menthol	① 232	VLN	N	N
	Menthol	① 233	VLN	N	N
	Menthol	① 234	UB	N	N
	Menthol	① 235	VLN	N	N

① lined in error. (b) (6) 10SEP2018

② subjects randomized at high point (HPTC). See copy signed 04FEB2019. (b) (6) 04FEB2019

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Coordinator, Date: (b) (6)

19-JUL-2018

Approver, Date: (b) (6)

19JUL2018

Pharmacist, Date: (b) (6)

19JUL2018

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Site	Flavor	Subject Number	Product	Topography Assessment	PK Assessment	Gender	Age
1	Menthol	1	VLN	Y	Y	M	<40
	Menthol	2	VLN	Y	Y	M	>40
	Menthol	3	UB	N	N	M	<40
	Menthol	4	VLN	Y	Y	F	>40
	Menthol	5	UB	N	N	F	>40
	Menthol	6	VLN	Y	Y	F	>40
	Menthol	7	VLN	Y	Y	F	<40
	Menthol	8	VLN	Y	Y	F	<40
	Menthol	9	UB	N	N	F	<40
	Menthol	10	VLN	Y	Y	F	>50
	Menthol	11	VLN	Y	Y	M	<40
	Menthol	12	VLN	Y	Y	M	>40
	Menthol	13	UB	N	N	F	<40
	Menthol	14	VLN	Y	Y	F	<40

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Creator, Date:

Reviewer, Date:

Pharmacist, Date:

(b) (6)

19-Jul-2018

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Randomization Schedule

Site	Flavor	Subject Number	Product	Topography Assessment	PK Assessment	Gender	Age	Screening #	Initials
1	Menthol	15	UB	N	N	M	40		
	Menthol	16	UB	N	N	M	740		
	Menthol	17	VLN	Y	Y	M	40		
	Menthol	18	VLN	Y	Y	M	740		
	Menthol	19	VLN	Y	N	M	740		
	Menthol	20	VLN	Y	N	M	40		
	Menthol	21	VLN	Y	N	M	740		
	Menthol	22	VLN	Y	N	M	40		
	Menthol	23	VLN	Y	N	F	740		
	Menthol	24	VLN	Y	N	M	40		
	Menthol	25	VLN	N	N	F	740		
	Menthol	26	UB	N	N	M	≤ 40	002-212	(b) (6)
	Menthol	27	VLN	N	N	M	≤ 40	002-213	
	Menthol	28	UB	N	N	F	≤ 40	002-175	

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The next 6 subjects randomized to VLN will participate in a topography assessment only

Creator, Date:

Approver, Date:

Pharmacist, Date:

(b) (6)

19-Jul-2018

19 JUL 2018

19 JUL 2018

09 Feb 2019

① Subjects were randomized according to previous guidance to HCTC from Leluth in the order 1) male ≤ 40, 2) male > 40, 3) Female ≤ 40, 4) Female > 40. (b) (6) 28 Oct 2018

19JUL2018 12:00

CA24914 - 22nd Century Group, Inc. Protocol: VLN Cigarette Consumption Study, Amended Protocol Date 18JUN2018. Product: VLN Cigarettes
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Randomization Schedule

Site	Flavor	Subject Number	Product	Topography Assessment	PK Assessment	Gender	Age	Screening #	Initials
1	Menthol	③ 2 29	VLN	N ⁰	N	F	≤ 40	002-211	(b) (6)
	Menthol	② 2 30	UB	N	N	F	> 40	002-215	
	Menthol	③ 2 31	VLN	N	N	F	≤ 40	002-235	
	Menthol	④ 2 32	VLN	N	N	M	≤ 40	002-247	
	Menthol	④ 2 33	VLN	N	N	M	≤ 40	002-272	
	Menthol	④ 2 34	UB	N	N	M	> 40	002-259	
	Menthol	④ 2 35	VLN	N	N	M	> 40	002-269	

① Linea in error (b) (6) 05 SEP 2018

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The next 6 subjects randomized to VLN will participate in a topography assessment only

Creator, Date:

Approver, Date:

Pharmacist, Date:

(b) (6)

19-JUL-2018

19JUL2018

19JUL2018

07 DEC 2018

- ② Subjects were randomized according to previous guidance to HPCTC from criterion in the order: 1) male ≤ 40, 2) male > 40, 3) Female ≤ 40, 4) Female > 40. (b) (6) 26 OCT 2018. ③ Subject randomized at HPCTC on 03 MAR 2018. (b) (6) 03 MAR 2018 (b) (6) 03 MAR 2018 ④ Randomized 07 Dec 2018 (b) (6) 07 Dec 2018

09JUL2018 13:06

CA24914 - 22nd Century Group, Inc. Protocol: VLN Cigarette Consumption Study, Amended Protocol Date 18JUN2018. Product: VLN Cigarettes
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Randomization Schedule

FOR EACH ENROLLMENT GROUP ASSIGN MALE SUBJECTS GOING DOWN THE LIST STARTING WITH SUBJECT NUMBER 1 WITH ALL <= 40 YEAR OLD SUBJECTS FIRST, FOLLOWED BY ALL > 40 YEAR OLD SUBJECTS. ASSIGN FEMALE SUBJECTS GOING UP THE LIST STARTING WITH NUMBER 35 WITH THE <= 40 YEAR SUBJECTS AT THE BOTTOM OF THE LIST

Site	Flavor	Subject Number	Gender & Age Group	Product
2	Menthol	1	Male <40	UB 002-010
	Menthol	2	Male <40	VLN 002-014
	Menthol	3	Male <40	VLN 002-017
	Menthol	4	Male <40	VLN 002-021
	Menthol	5	Male <40	VLN 002-023
	Menthol	6	Male >40	VLN 002-008
	Menthol	7	Male >40	UB 002-002
	Menthol	8	Male >40	UB 002-029
	Menthol	9	Male <40	VLN 002-075
	Menthol	10	Male >40	UB 002-050
	Menthol	11	Male >40	VLN 002-052
	Menthol	12	Male >40	VLN 002-057
	Menthol	13	Male >40	VLN 002-064
	Menthol	14	Male >40	VLN 002-076

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17JUL2018

17JUL2018

7/12/18

Cohort 1

(b) (6)

24JUL2018

24JUL2018

Cohort 2

(b) (6)

08AUG2018

08AUG2018

Cohort 3

(b) (6)

01SEP2018

(b) (6)

01SEP2018

Cohort 4

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Creator, Date:

(b) (6)

09-JUL-2018

Approver, Date:

(b) (6)

09JUL2018

Pharmacist, Date:

(b) (6)

04Feb2019

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Site	Flavor	Subject Number	Gender & Age Group	Product	
2	Menthol	15	Male <40	UB 002-125	(b) (6)
	Menthol	16	Male <40	VLN 002-126	(b) (6) 07 Sep 2018
	Menthol	17	Male >40	VLN 002-119	(b) (6) 06 Sep 2018 Cohort 5
	Menthol	18	Male <40	VLN 002-184	(b) (6) Cohort 7
	Menthol	19	Female >40	VLN 002-115	(b) (6) Cohort 5
	Menthol	20	Female >40	VLN 002-113	(b) (6) Cohort 5
	Menthol	21	Female >40	UB 002-110	(b) (6) Cohort 4
	Menthol	22	Female >40	UB 002-100	(b) (6) Cohort 4
	Menthol	23	Female >40	VLN 002-092	(b) (6)
	Menthol	24	Female <40	VLN 002-088	(b) (6) Cohort 3
	Menthol	25	Female >40	UB 002-059	(b) (6) Cohort 3
	Menthol	26	Female <40	VLN 002-066	(b) (6) Cohort 3
	Menthol	27	Female <40	VLN 002-060	(b) (6) Cohort 3
	Menthol	28	Female <40	VLN 002-058	(b) (6) Cohort 3

Product Descriptions:

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Each study group (for the purpose of the randomization defined as this group of 35 subjects) will include no fewer than 10 subjects of either gender and no fewer than 10 subjects from each age group (<= 40 years old and > 40 years old).

- ① Gender/Age Group for Subject 002-059 should read "Female >40". (b) (6) 07 Sep 2018

Creator, Date:

(b) (6)

09-JUL-2018

Approver, Date:

(b) (6)

09 JUL 2018

Pharmacist, Date:

(b) (6)

04 Feb 2019

09JUL2018 13:06

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Site	Flavor	Subject Number	Gender & Age Group	Product		
2	Menthol	29	Female < 40 VLN	002-039	(b) (6)	(b) (6) 24 JUL 2018 Cohort 2
	Menthol	30	Female > 40 VLN	002-020	(b) (6)	(b) (6) 24 JUL 2018 Cohort 1
	Menthol	31	Female > 40 VLN	002-016	(b) (6)	(b) (6) 17 JUL 2018 Cohort 1
	Menthol	32	Female > 40 UB	002-015	(b) (6)	(b) (6) 17 JUL 2018 Cohort 1
	Menthol	33	Female > 40 VLN	002-003	(b) (6)	
	Menthol	34	Female < 40 UB	002-018	(b) (6)	
	Menthol	35	Female < 40 VLN	002-011	(b) (6)	

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(b) (6)

09 JUL 2018

Reviewer, Date:

(b) (6)

09 JUL 2018

Pharmacist, Date:

(b) (6)

09 FEB 2019

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CA24914 - 22nd Century Group, Inc. Protocol: VLN Cigarette Consumption Study, Amended Protocol Date 18JUN2018. Product: VLN Cigarettes
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Randomization Schedule

Site	Flavor	Subject Number	Product	Topography Assessment	PK Assessment	Gender	Age
1	Non-Menthol	36	VLN	Y	Y	F	>40
	Non-Menthol	37	VLN	Y	Y	M	≤40
	Non-Menthol	38	VLN	Y	Y	M	≤40
	Non-Menthol	39	UB	N	N	M	≤40
	Non-Menthol	40	VLN	Y	Y	M	≤40
	Non-Menthol	41	UB	N	N	F	>40
	Non-Menthol	42	VLN	Y	Y	F	≤40
	Non-Menthol	43	VLN	Y	Y	F	750.40 (b) (6) 8-EP2018
	Non-Menthol	44	VLN	Y	Y	F	≤40
	Non-Menthol	45	UB	N	N	M	>40
	Non-Menthol	46	VLN	Y	Y	M	>40
	Non-Menthol	47	VLN	Y	Y	M	≤40
	Non-Menthol	48	VLN	Y	Y	M	>40
	Non-Menthol	49	UB	N	N	M	>40

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The next 6 subjects randomized to VLN will participate in a topography assessment only

Creator, Date:

(b) (6)

19-Jul-2018

Approver, Date:

(b) (6)

19JUL2018

Pharmacist, Date:

(b) (6)

19JUL2018

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Site	Flavor	Subject Number	Product	Topography Assessment	PK Assessment	Gender	Age
1	Non-Menthol	50	VLN	Y	Y	F	≤40
	Non-Menthol	51	VLN	Y	Y	M	>40
	Non-Menthol	52	VLN	Y	N	F	≤40
	Non-Menthol	53	VLN	Y	N	M	>40
	Non-Menthol	54	UB	N	N	M	>40
	Non-Menthol	55	UB	N	N	M	≤40
	Non-Menthol	56	VLN	Y	N	M	>40
	Non-Menthol	57	UB	N	N	M	≤40
	Non-Menthol	58	VLN	Y	N	F	>40
	Non-Menthol	59	VLN	Y	N	M	>40
	Non-Menthol	60	VLN	Y	N	M	>40
	Non-Menthol	61	UB	N	N	F	≤40
	Non-Menthol	62	VLN	N	N	M	≤40
	Non-Menthol	63	VLN	N	N	F	>40

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19-Jul-2018

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19 JUL 2018

Pharmacist Date:

(b) (6)

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Site	Flavor	Subject Number	Product	Topography Assessment	PK Assessment	Gender	Age
1	Non-Menthol	64	VLN	N	N	M	>40
	Non-Menthol	65	UB	N	N	F	≤40
	Non-Menthol	66	UB	N	N	F	>40
	Non-Menthol	67	VLN	N	N	F	>40
	Non-Menthol	68	VLN	N	N	M	>40
	Non-Menthol	69	VLN	N	N	M	>40
	Non-Menthol	70	VLN	N	N	F	>40

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Creator, Date:

(b) (6)

19-JUL-2018

Approver, Date:

(b) (6)

19 JUL 2018

Pharmacist, Date:

(b) (6)

19 JUL 2018

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(b) (6) 275.09208

09JUL2018 13:07

CA24914 - 22nd Century Group, Inc. Protocol: VLN Cigarette Consumption Study, Amended Protocol Date 18JUN2018. Product: VLN Cigarettes
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Site	Flavor	Subject Number	Gender & Age Group	Product
2	Non-Menthol	36	male <40	UB 002-024
	Non-Menthol	37	male <40	VLN 002-028
	Non-Menthol	38	male >40	VLN 002-009
	Non-Menthol	39	male >40	UB 002-025
	Non-Menthol	40	male <40	VLN 002-067
	Non-Menthol	41	male <40	VLN 002-086
	Non-Menthol	42	male >40	VLN 002-099
	Non-Menthol	43	male >40	UB 002-122
	Non-Menthol	44	male >40	VLN 002-136
	Non-Menthol	45	male >40	VLN 002-143
	Non-Menthol	① 46	male <40	VLN 001-115
	Non-Menthol	① 47	male >40	UB 001-106
	Non-Menthol	① 48	male >40	VLN 001-098
	Non-Menthol	① 49	male >40	VLN 001-160

(b) (6) 09 Jul 2018
17 Jul 2018 Cohort 1
01 Sep 2018 Cohort 3
01 Sep 2018 Cohort 4
01 Sep 2018 Cohort 5
24 Sep 2018 Cohort 6

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(b) (6)

09 JUL 2018

(b) (6)

09 JUL 2018

Approver, Date:

Pharmacist, Date: ②

① Subjects 146-149 randomized at Celerion (site 1). (b) (6) 03 OCT 2018

② see signed copy dated 04 FEB 2019. (b) (6) 04 FEB 2019

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(b) (6) 09 JUL 2018

09JUL2018 13:07

CA24914 - 22nd Century Group, Inc. Protocol: VIN Cigarette Consumption Study, Amended Protocol Date 18JUN2018. Product: VIN Cigarettes
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Site	Flavor	Subject Number	Gender & Age Group	Product
2	Non-Menthol	0150	Male >40	VIN 001-103
	Non-Menthol	0151	Male >40	VIN 001-101
	Non-Menthol	0152	Male >40	UB 001-108
	Non-Menthol	53		VIN
	Non-Menthol	0154	Male >40	VIN 001-107
	Non-Menthol	0155	Male >40	UB 001-109
	Non-Menthol	56		VIN
	Non-Menthol	57		VIN
	Non-Menthol	58		UB
	Non-Menthol	59		VIN
	Non-Menthol	60		UB
	Non-Menthol	61		VIN
	Non-Menthol	0162	Female >40	VIN 001-112
	Non-Menthol	0163	Female >40	VIN 001-099

Product Descriptions:

UB: Usual brand filtered king size cigarettes sourced by the subjects

VIN: Very low nicotine cigarettes sourced by 22nd Century Group, Inc.

Each study group (for the purpose of the randomization defined as this group of 35 subjects) will include no fewer than 10 subjects of either gender and no fewer than 10 subjects from each age group (≤ 40 years old and > 40 years old).

Creator, Date:

(b) (6)
09 JUL 2018

Reviewer, Date:

(b) (6)
09 JUL 2018

Pharmacist, Date: ②

② sec signed copy dated 04 FEB 2019. (b) (6) 04 FEB 2019

① subjects 150-152, 154, 155, 162, and 163 randomized at extension (site 1). (b) (6) 03 OCT 2018

COPY

(b) (6) 27 Sep 2018

09JUL2018 13:07

CA24914 - 22nd Century Group, Inc. Protocol: VLN Cigarette Consumption Study, Amended Protocol Date 18JUN2018. Product: VLN Cigarettes
An Open-Label, 2-Site, Randomized Study to Assess Cigarette Consumption and Biomarkers

Randomization Schedule

FOR EACH ENROLLMENT GROUP ASSIGN MALE SUBJECTS GOING DOWN THE LIST STARTING WITH SUBJECT NUMBER 35 WITH ALL <= 40 YEAR OLD SUBJECTS FIRST, FOLLOWED BY ALL > 40 YEAR OLD SUBJECTS. ASSIGN FEMALE SUBJECTS GOING UP THE LIST STARTING WITH NUMBER 70 WITH THE <= 40 YEAR SUBJECTS AT THE BOTTOM OF THE LIST

Site	Flavor	Subject Number	Gender & Age Group	Product
2	Non-Menthol	0164	Female >40	VLN 001-105
	Non-Menthol	0165	Female <=40	UB 001-114
	Non-Menthol	66	Female >40	UB 002-140
	Non-Menthol	67	Female <=40	VLN 002-142
	Non-Menthol	68	Female >40	VLN 002-120
	Non-Menthol	69	Female >40	VLN 002-108
	Non-Menthol	70	Female >40	VLN 002-007

(b) (6) 24 Sep 2018 (b) (6) 24 Sep 2018 Cohort 6
(b) (6) 24 Sep 2018 (b) (6) 24 Sep 2018 (b) (6) 24 Sep 2018 Cohort 5
(b) (6) 17 Jul 2018 Cohort 4
(b) (6) 17 Jul 2018 Cohort 1

Product Descriptions:

UB: Usual brand filtered king size cigarettes sourced by the subjects

VLN: Very low nicotine cigarettes sourced by 22nd Century Group, Inc.

Each study group (for the purpose of the randomization defined as this group of 35 subjects) will include no fewer than 10 subjects of either gender and no fewer than 10 subjects from each age group (<= 40 years old and > 40 years old).

Creator, Date:

(b) (6)

09 JUL 2018

As Owner, Date:

(b) (6)

09 JUL 2018

Pharmacist, Date: (2)

① subjects 104 and 105 randomized at celerion (site 1). (b) (6) 03 OCT 2018

② see signed copy dated 04 FEB 2019 (b) (6) 04 FEB 2019

09JUL2018 13:07

CA24914 - 22nd Century Group, Inc. Protocol: VLN Cigarette Consumption Study, Amended Protocol Date 18JUN2018. Product: VLN Cigarettes
An Open-Label, 2-Site, Randomized Study to Assess Cigarette Consumption and Biomarkers
Randomization Schedule

FOR EACH ENROLLMENT GROUP ASSIGN MALE SUBJECTS GOING DOWN THE LIST STARTING WITH SUBJECT NUMBER 35 WITH ALL <= 40 YEAR OLD SUBJECTS FIRST, FOLLOWED BY ALL > 40 YEAR OLD SUBJECTS. ASSIGN FEMALE SUBJECTS GOING UP THE LIST STARTING WITH NUMBER 70 WITH THE <= 40 YEAR SUBJECTS AT THE BOTTOM OF THE LIST

Replacements	Gender & Age	Site	Flavor	Subject Number	Gender & Age Group	Product	
002-251	(b) (6) male <= 40	2	Non-Menthol	36	male <= 40	UB 002-024	(b) (6)
			Non-Menthol	37	male <= 40	VLN 002-025	
			Non-Menthol	38	male > 40	VLN 002-009	
			Non-Menthol	39	male > 40	UB 002-029	
			Non-Menthol	40	male > 40	VLN 002-067	
			Non-Menthol	41	male <= 40	VLN 002-086	
			Non-Menthol	42	male > 40	VLN 002-099	
			Non-Menthol	43	male > 40	UB 002-122	
			Non-Menthol	44	male > 40	VLN 002-136	
			Non-Menthol	45	male > 40	VLN 002-143	
			Non-Menthol	146	male <= 40	VLN 001-115	
			Non-Menthol	147	male > 40	UB 001-106	
			Non-Menthol	148	male > 40	VLN 001-098	
			Non-Menthol	149	male > 40	VLN 001-100	

Product Descriptions:

UB: Usual brand filtered king size cigarettes sourced by the subjects

VLN: Very low nicotine cigarettes sourced by 22nd Century Group, Inc.

Each study group (for the purpose of the randomization defined as this group of 35 subjects) will include no fewer than 10 subjects of either gender and no fewer than 10 subjects from each age group (<= 40 years old and > 40 years old).

(b) (6)

09 JUL 2018

(b) (6)

09 JUL 2018

(b) (6)

04 FEB 2019

(1) Transcribed from randomization schedule on 03 Oct 2018 at Celrium (Site 1). (b) (6) 10 Oct 2018 (2) Randomized 07 Dec 2018 (b) (6) 07 Dec 2018

C9JUL2018 13:07

CA24914 - 22nd Century Group, Inc. Protocol: VLN Cigarette Consumption Study, Amended Protocol Date 18JUN2018. Product: VLN Cigarettes
An Open-Label, 2-Site, Randomized Study to Assess Cigarette Consumption and Biomarkers

Randomization Schedule

FOR EACH ENROLLMENT GROUP ASSIGN MALE SUBJECTS GOING DOWN THE LIST STARTING WITH SUBJECT NUMBER 35 WITH ALL <= 40 YEAR OLD SUBJECTS FIRST, FOLLOWED BY ALL > 40 YEAR OLD SUBJECTS. ASSIGN FEMALE SUBJECTS GOING UP THE LIST STARTING WITH NUMBER 70 WITH THE <= 40 YEAR SUBJECTS AT THE BOTTOM OF THE LIST

(b) (6) 07Dec2018

Replacement ^② Gender & Age

Site	Flavor	Subject Number	Gender & Age Group	Product
2	Non-Menthol	① 50	Male > 40	VLN 001-103
	Non-Menthol	① 51	Male > 40	VLN 001-101
	Non-Menthol	① 52	Male > 40	UB 001-108
	Non-Menthol	② 53	Male < 40	VLN 002-154 (b) (6)
	Non-Menthol	① 54	Male > 40	VLN 001-107
	Non-Menthol	① 55	Male > 40	UB 001-109 (b) (6)
	Non-Menthol	56	Male < 40	VLN 002-220 (b) (6) 20Oct2018 (b) (6) 20Oct2018 Cohort 7
	Non-Menthol	57	Male < 40	VLN 002-244 (b) (6) 03Nov2018 (b) (6) 03Nov2018 Cohort 8
	Non-Menthol	58	Female > 40	UB 002-170 (b) (6) 22Oct2018 (b) (6) 00Oct2018 Cohort 7
	Non-Menthol	59	Female > 40	VLN 002-164
002-257 (b) (6)	Non-Menthol	③ 360	Female > 40	UB 002-158
	Non-Menthol	61	Female < 40	VLN 002-168
	Non-Menthol	① 62	Female > 40	VLN 001-112
	Non-Menthol	① 63	Female > 40	VLN 001-099

Product Descriptions:

UB: Usual brand filtered king size cigarettes sourced by the subjects

VLN: Very low nicotine cigarettes sourced by 22nd Century Group, Inc.

Each study group (for the purpose of the randomization defined as this group of 35 subjects) will include no fewer than 10 subjects of either gender and no fewer than 10 subjects from each age group (<= 40 years old and > 40 years old).

(b) (6)

09 JUL 2018

(b) (6)

09 JUL 2018

Pharmacist, Date:

(b) (6)

04 Feb 2019

② Subject 53 is part of HITC's Cohort 7. (b) (6) 20Oct2018

① Transcribed from randomization schedule on 03Oct2018 at Celtrion (site 1). (b) (6) 20Oct2018 ③ Randomized 07Dec2018 (b) (6) 07Dec2018

09JUL2018 13:07

CA24914 - 22nd Century Group, Inc. Protocol: VLN Cigarette Consumption Study, Amended Protocol Date 18JUN2018. Product: VLN Cigarettes
An Open-Label, 2-Site, Randomized Study to Assess Cigarette Consumption and Biomarkers
Randomization Schedule

FOR EACH ENROLLMENT GROUP ASSIGN MALE SUBJECTS GOING DOWN THE LIST STARTING WITH SUBJECT NUMBER 35 WITH ALL <= 40 YEAR OLD SUBJECTS FIRST, FOLLOWED BY ALL > 40 YEAR OLD SUBJECTS. ASSIGN FEMALE SUBJECTS GOING UP THE LIST STARTING WITH NUMBER 70 WITH THE <= 40 YEAR SUBJECTS AT THE BOTTOM OF THE LIST

Site	Flavor	Subject Number	Gender & Age Group	Product	
2	Non-Menthol	164	Female >40	VLN 001-105	
	Non-Menthol	165	Female <=40	UB 001-114	
	Non-Menthol	66	Female >40	UB 002-140	(b) (6) 24 Sep 2018 Cohort 6
	Non-Menthol	67	Female <=40	VLN 002-142	(b) (6) 24 Sep 2018 Cohort 5
	Non-Menthol	68	Female >40	VLN 002-120	(b) (6) 17 Jul 2018 Cohort 4
	Non-Menthol	69	Female >40	VLN 002-108	(b) (6) 17 Sep 2018 Cohort 1
	Non-Menthol	70	Female >40	VLN 002-007	(b) (6) 17 Jul 2018

Product Descriptions:

UB: Usual brand filtered king size cigarettes sourced by the subjects

VLN: Very low nicotine cigarettes sourced by 22nd Century Group, Inc.

Each study group (for the purpose of the randomization defined as this group of 35 subjects) will include no fewer than 10 subjects of either gender and no fewer than 10 subjects from each age group (<= 40 years old and > 40 years old).

Creator, Date:
(b) (6)
09-JUL-2018

Reviewer, Date:
(b) (6)
09 JUL 2018

Pharmacist, Date:
(b) (6)
04 Feb 2019

(f) Transcribed from randomization schedule on 03 Oct 2018 at Colindale (Site 1). (b) (6) 20 Oct 2018