



## PMI RESEARCH & DEVELOPMENT

### **Study ZRHR-REXC-03-EU** **Clinical Study Report Appendix 16.1.2** **Sample Case Report Form, Subject Questionnaire and** **Subject Smoking Diary**

**Study Title:** A randomized, controlled, open-label, 3-arm parallel group, single-center study to demonstrate reductions in exposure to selected smoke constituents in smoking, healthy subjects switching to the Tobacco Heating System 2.2 (THS 2.2) or smoking abstinence, compared to continuing to use conventional cigarettes, for 5 days in confinement

**Study Number:** ZRHR-REXC-03-EU

**Product Name:** Tobacco Heating System 2.2 (THS 2.2)

**Study Initiated (first subject enrolled):** 29 June 2013

**Study Completed (last subject last visit):** 26 September 2013

**Principal Investigator and Affiliation:** Katarzyna Jarus-Dziedzic, MD, PhD  
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Andrea Donelli, Clinical Scientist  
Guillaume de La Bourdonnaye, MEng, MSc, Biostatistician  
Kausar Aamir, MD, PhD, Medical Safety Officer

**Version:** 2.0

**Date:** 08 March 2016

This study was conducted in accordance with Good Clinical Practice.

#### **Confidentiality Statement**

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This document is confidential. Disclosure of any of its contents to third parties is not permitted except by the prior written consent of Philip Morris Products S.A.

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**Table of Contents**

16.1.2.1 SAMPLE CASE REPORT FORM.....	3
16.1.2.2 SUBJECT QUESTIONNAIRE ENGLISH .....	521
16.1.2.2.1 Cough Assessment .....	521
16.1.2.2.2 Fagerström Nicotine Dependence Test.....	523
16.1.2.2.3 Human Smoking Topography Questionnaire .....	526
16.1.2.2.4 Modified Cigarette Evaluation Questionnaire .....	529
16.1.2.2.5 Minnesota Nicotine Dependence/Withdrawal Scale .....	533
16.1.2.2.6 Questionnaire on Smoking Urges .....	536
16.1.2.3 SUBJECT QUESTIONNAIRE LOCAL LANGUAGE.....	540
16.1.2.3.1 Cough Assessment .....	540
16.1.2.3.2 Fagerström Nicotine Dependence Test.....	544
16.1.2.3.3 Human Smoking Topography Questionnaire .....	548
16.1.2.3.4 Modified Cigarette Evaluation Questionnaire .....	552
16.1.2.3.5 Minnesota Nicotine Dependence/Withdrawal Scale .....	557
16.1.2.3.6 Questionnaire on Smoking Urges .....	561
16.1.2.4 SUBJECT SMOKING DIARY ENGLISH .....	566
16.1.2.5 SUBJECT SMOKING DIARY LOCAL LANGUAGE.....	567





### **16.1.2.1 SAMPLE CASE REPORT FORM**



Subject Case Report Forms

Final version 5.0 (Main CRF) - Case Book

Generated On: 28 Oct 2013 17:39:05

All time stamps listed in this document are displayed in GMT



**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: Subject**  
**Generated On: 28 Oct 2013 17:39:05**

Screening number

Site number





**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: Subject Status**  
**Generated On: 28 Oct 2013 17:39:05**

Date of 'Screen Failed' Event

Fixed Unit:  
DD/MMM/YYYY

Date of 'Discontinued From  
Enrollment' Event

Fixed Unit:  
DD/MMM/YYYY

Randomization Date

Fixed Unit:  
DD/MMM/YYYY

Randomization Time

Fixed Unit:  
hour:min 24-hour clock



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Screen Failure  
Generated On: 28 Oct 2013 17:39:05

Reason for Screen Failure

Entry criteria not met ☐  
Withdrawal by subject ☐  
Adverse Event ☐  
Other ☐

If Other, Specify: \_\_\_\_\_

Is there a pregnancy event?

No ☐  
Yes ☐  
NA ☐



**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: Date of Visit**  
**Generated On: 28 Oct 2013 17:39:05**

Date of Visit

Fixed Unit:  
DD/MMM/YYYY





**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: Date of Discharge**  
**Generated On: 28 Oct 2013 17:39:05**

Date of Visit

Fixed Unit:  
DD/MMM/YYYY

Discharge Time

Fixed Unit:  
hour:min 24-hour clock



**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: Additional Informed Consent**  
**Generated On: 28 Oct 2013 17:39:05**

Has the subject given written informed consent for  
Bio-banking for Biomarkers of Exposure and Risk  
Markers?

No ☐  
Yes ☐

Consent Date

Fixed Unit:  
DD/MMM/YYYY

Has the subject given written informed consent for  
Bio-banking for Transcriptomics (Pharmacogenomics)?

No ☐  
Yes ☐

Consent Date

Fixed Unit:  
DD/MMM/YYYY



**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: Inclusion Criteria**  
**Generated On: 28 Oct 2013 17:39:05**

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\*If any has been answered No, subject must not be included in the study.

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Inclusion Criterion Number	1
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Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Inclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

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Inclusion Criterion

Subject has signed the ICF and is able to understand the information provided in the Subject Information Sheet and ICF. ☒

Subject is aged from 21 to 65 years (inclusive). ☐

Subject is of Caucasian origin. ☐

Smoking, healthy subject as judged by the Investigator based on all available assessments in the Screening period/day of Admission ☐

Subject is a current smoker (based on self-reporting), who for the last 4 weeks has smoked at least 10 commercially available non-menthol CCs per day (no brand restrictions) with a maximum yield of 1 mg nicotine ISO per cigarette, as labeled on the cigarette package. Furthermore, the subject has smoked for at least the last 3 consecutive years. The smoking status will be verified with a urinary cotinine test (cotinine 200 ng/ml). ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Inclusion Criteria

Generated On: 28 Oct 2013 17:39:05

---

The subject is a current  
smoker who does not plan  
to quit smoking in the next  
3 months. ☐

The subject is ready to  
accept 5 days of SA. ☐

The subject is ready to  
accept using the THS 2.2  
product. ☐

---

Result No ☐  
Yes ☐

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Inclusion Criterion Number 2

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Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Inclusion Criteria

Generated On: 28 Oct 2013 17:39:05

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Inclusion Criterion

Subject has signed the ICF ☐  
and is able to understand  
the information provided in  
the Subject Information  
Sheet and ICF.  
Subject is aged from 21 to ☒  
65 years (inclusive).  
Subject is of Caucasian ☐  
origin.  
Smoking, healthy subject ☐  
as judged by the  
Investigator based on all  
available assessments in  
the Screening period/day  
of Admission  
Subject is a current smoker ☐  
(based on  
self-reporting), who for the  
last 4  
weeks has smoked at least  
10  
commercially available  
non-menthol  
CCs per day (no brand  
restrictions)  
with a maximum yield of 1  
mg  
nicotine ISO per cigarette,  
as labeled  
on the cigarette package.  
Furthermore, the subject  
has smoked  
for at least the last 3  
consecutive  
years. The smoking status  
will be  
verified with a urinary  
cotinine test  
(cotinine 200 ng/ml).





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Inclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

The subject is a current  
smoker who does not plan  
to quit smoking in the next  
3 months. ☐  
The subject is ready to  
accept 5 days of SA. ☐  
The subject is ready to  
accept using the THS 2.2  
product. ☐

Result No ☐  
Yes ☐

Inclusion Criterion Number 3



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Inclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

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Inclusion Criterion

Subject has signed the ICF ☐  
and is able to understand  
the information provided in  
the Subject Information  
Sheet and ICF.  
Subject is aged from 21 to ☐  
65 years (inclusive).  
Subject is of Caucasian ☒  
origin.  
Smoking, healthy subject ☐  
as judged by the  
Investigator based on all  
available assessments in  
the Screening period/day  
of Admission  
Subject is a current smoker ☐  
(based on  
self-reporting), who for the  
last 4  
weeks has smoked at least  
10  
commercially available  
non-menthol  
CCs per day (no brand  
restrictions)  
with a maximum yield of 1  
mg  
nicotine ISO per cigarette,  
as labeled  
on the cigarette package.  
Furthermore, the subject  
has smoked  
for at least the last 3  
consecutive  
years. The smoking status  
will be  
verified with a urinary  
cotinine test  
(cotinine 200 ng/ml).



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Inclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

The subject is a current  
smoker who does not plan  
to quit smoking in the next  
3 months. ☐  
The subject is ready to  
accept 5 days of SA. ☐  
The subject is ready to  
accept using the THS 2.2  
product. ☐

Result No ☐  
Yes ☐

Inclusion Criterion Number 4



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Inclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

---

Inclusion Criterion

Subject has signed the ICF and is able to understand the information provided in the Subject Information Sheet and ICF. ☐  
Subject is aged from 21 to 65 years (inclusive). ☐  
Subject is of Caucasian origin. ☐  
Smoking, healthy subject as judged by the Investigator based on all available assessments in the Screening period/day of Admission ☒  
Subject is a current smoker (based on self-reporting), who for the last 4 weeks has smoked at least 10 commercially available non-menthol CCs per day (no brand restrictions) with a maximum yield of 1 mg nicotine ISO per cigarette, as labeled on the cigarette package. Furthermore, the subject has smoked for at least the last 3 consecutive years. The smoking status will be verified with a urinary cotinine test (cotinine 200 ng/ml). ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Inclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

The subject is a current  
smoker who does not plan  
to quit smoking in the next  
3 months. ☐  
The subject is ready to  
accept 5 days of SA. ☐  
The subject is ready to  
accept using the THS 2.2  
product. ☐

Result No ☐  
Yes ☐

Inclusion Criterion Number 5



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Inclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

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Inclusion Criterion

Subject has signed the ICF ☐  
and is able to understand  
the information provided in  
the Subject Information  
Sheet and ICF.  
Subject is aged from 21 to ☐  
65 years (inclusive).  
Subject is of Caucasian ☐  
origin.  
Smoking, healthy subject ☐  
as judged by the  
Investigator based on all  
available assessments in  
the Screening period/day  
of Admission  
Subject is a current smoker ☒  
(based on  
self-reporting), who for the  
last 4  
weeks has smoked at least  
10  
commercially available  
non-menthol  
CCs per day (no brand  
restrictions)  
with a maximum yield of 1  
mg  
nicotine ISO per cigarette,  
as labeled  
on the cigarette package.  
Furthermore, the subject  
has smoked  
for at least the last 3  
consecutive  
years. The smoking status  
will be  
verified with a urinary  
cotinine test  
(cotinine 200 ng/ml).



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Inclusion Criteria  
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The subject is a current  
smoker who does not plan  
to quit smoking in the next  
3 months. ☐  
The subject is ready to  
accept 5 days of SA. ☐  
The subject is ready to  
accept using the THS 2.2  
product. ☐

Result No ☐  
Yes ☐

Inclusion Criterion Number 6





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Inclusion Criteria  
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Inclusion Criterion

Subject has signed the ICF ☐  
and is able to understand  
the information provided in  
the Subject Information  
Sheet and ICF.  
Subject is aged from 21 to ☐  
65 years (inclusive).  
Subject is of Caucasian ☐  
origin.  
Smoking, healthy subject ☐  
as judged by the  
Investigator based on all  
available assessments in  
the Screening period/day  
of Admission  
Subject is a current smoker ☐  
(based on  
self-reporting), who for the  
last 4  
weeks has smoked at least  
10  
commercially available  
non-menthol  
CCs per day (no brand  
restrictions)  
with a maximum yield of 1  
mg  
nicotine ISO per cigarette,  
as labeled  
on the cigarette package.  
Furthermore, the subject  
has smoked  
for at least the last 3  
consecutive  
years. The smoking status  
will be  
verified with a urinary  
cotinine test  
(cotinine 200 ng/ml).





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Inclusion Criteria  
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The subject is a current  
smoker who does not plan  
to quit smoking in the next  
3 months. ☒  
The subject is ready to  
accept 5 days of SA. ☐  
The subject is ready to  
accept using the THS 2.2  
product. ☐

Result No ☐  
Yes ☐

Inclusion Criterion Number 7



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Inclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

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Inclusion Criterion

Subject has signed the ICF ☐  
and is able to understand  
the information provided in  
the Subject Information  
Sheet and ICF.  
Subject is aged from 21 to ☐  
65 years (inclusive).  
Subject is of Caucasian ☐  
origin.  
Smoking, healthy subject ☐  
as judged by the  
Investigator based on all  
available assessments in  
the Screening period/day  
of Admission  
Subject is a current smoker ☐  
(based on  
self-reporting), who for the  
last 4  
weeks has smoked at least  
10  
commercially available  
non-menthol  
CCs per day (no brand  
restrictions)  
with a maximum yield of 1  
mg  
nicotine ISO per cigarette,  
as labeled  
on the cigarette package.  
Furthermore, the subject  
has smoked  
for at least the last 3  
consecutive  
years. The smoking status  
will be  
verified with a urinary  
cotinine test  
(cotinine 200 ng/ml).



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Inclusion Criteria  
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The subject is a current  
smoker who does not plan  
to quit smoking in the next  
3 months. ☐  
The subject is ready to  
accept 5 days of SA. ☒  
The subject is ready to  
accept using the THS 2.2  
product. ☐

Result No ☐  
Yes ☐



**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: Inclusion Criteria-Screen Failure**  
**Generated On: 28 Oct 2013 17:39:05**

\_\_\_\_\_  
\*If any has been answered No, subject must not be included in the study.

\_\_\_\_\_  
H\_NOW (Derived): \_\_\_\_\_  
\_\_\_\_\_

\_\_\_\_\_  
Inclusion Criterion Number 1  
\_\_\_\_\_



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Inclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

---

Inclusion Criterion

Subject has signed the ICF and is able to understand the information provided in the Subject Information Sheet and ICF. ☒

Subject is aged from 21 to 65 years (inclusive). ☐

Subject is of Caucasian origin. ☐

Smoking, healthy subject as judged by the Investigator based on all available assessments in the Screening period/day of Admission ☐

Subject is a current smoker (based on self-reporting), who for the last 4 weeks has smoked at least 10 commercially available non-menthol CCs per day (no brand restrictions) with a maximum yield of 1 mg nicotine ISO per cigarette, as labeled on the cigarette package. Furthermore, the subject has smoked for at least the last 3 consecutive years. The smoking status will be verified with a urinary cotinine test (cotinine 200 ng/ml). ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Inclusion Criteria-Screen Failure  
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The subject is a current  
smoker who does not plan  
to quit smoking in the next  
3 months. ☐  
The subject is ready to  
accept 5 days of SA. ☐  
The subject is ready to  
accept using the THS 2.2  
product. ☐

Result ☐ No  
☐ Yes  
☐ Not Done

Inclusion Criterion Number 2



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Inclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

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Inclusion Criterion

Subject has signed the ICF and is able to understand the information provided in the Subject Information Sheet and ICF. ☐

Subject is aged from 21 to 65 years (inclusive). ☒

Subject is of Caucasian origin. ☐

Smoking, healthy subject as judged by the Investigator based on all available assessments in the Screening period/day of Admission ☐

Subject is a current smoker (based on self-reporting), who for the last 4 weeks has smoked at least 10 commercially available non-menthol CCs per day (no brand restrictions) with a maximum yield of 1 mg nicotine ISO per cigarette, as labeled on the cigarette package. Furthermore, the subject has smoked for at least the last 3 consecutive years. The smoking status will be verified with a urinary cotinine test (cotinine 200 ng/ml). ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Inclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

The subject is a current  
smoker who does not plan  
to quit smoking in the next  
3 months. ☐  
The subject is ready to  
accept 5 days of SA. ☐  
The subject is ready to  
accept using the THS 2.2  
product. ☐

Result ☐ No  
☐ Yes  
☐ Not Done

Inclusion Criterion Number 3





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Inclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

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Inclusion Criterion

Subject has signed the ICF and is able to understand the information provided in the Subject Information Sheet and ICF. ☐

Subject is aged from 21 to 65 years (inclusive). ☐

Subject is of Caucasian origin. ☒

Smoking, healthy subject as judged by the Investigator based on all available assessments in the Screening period/day of Admission ☐

Subject is a current smoker (based on self-reporting), who for the last 4 weeks has smoked at least 10 commercially available non-menthol CCs per day (no brand restrictions) with a maximum yield of 1 mg nicotine ISO per cigarette, as labeled on the cigarette package. Furthermore, the subject has smoked for at least the last 3 consecutive years. The smoking status will be verified with a urinary cotinine test (cotinine 200 ng/ml). ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Inclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

The subject is a current  
smoker who does not plan  
to quit smoking in the next  
3 months. ☐  
The subject is ready to  
accept 5 days of SA. ☐  
The subject is ready to  
accept using the THS 2.2  
product. ☐

Result ☐ No  
☐ Yes  
☐ Not Done

Inclusion Criterion Number 4



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Inclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

---

Inclusion Criterion

Subject has signed the ICF and is able to understand the information provided in the Subject Information Sheet and ICF. ☐

Subject is aged from 21 to 65 years (inclusive). ☐

Subject is of Caucasian origin. ☐

Smoking, healthy subject as judged by the Investigator based on all available assessments in the Screening period/day of Admission ☒

Subject is a current smoker (based on self-reporting), who for the last 4 weeks has smoked at least 10 commercially available non-menthol CCs per day (no brand restrictions) with a maximum yield of 1 mg nicotine ISO per cigarette, as labeled on the cigarette package. Furthermore, the subject has smoked for at least the last 3 consecutive years. The smoking status will be verified with a urinary cotinine test (cotinine 200 ng/ml). ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Inclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

The subject is a current  
smoker who does not plan  
to quit smoking in the next  
3 months. ☐  
The subject is ready to  
accept 5 days of SA. ☐  
The subject is ready to  
accept using the THS 2.2  
product. ☐

Result ☐ No  
☐ Yes  
☐ Not Done

Inclusion Criterion Number 5



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Inclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

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Inclusion Criterion

Subject has signed the ICF ☐  
and is able to understand  
the information provided in  
the Subject Information  
Sheet and ICF.  
Subject is aged from 21 to ☐  
65 years (inclusive).  
Subject is of Caucasian ☐  
origin.  
Smoking, healthy subject ☐  
as judged by the  
Investigator based on all  
available assessments in  
the Screening period/day  
of Admission  
Subject is a current smoker ☒  
(based on  
self-reporting), who for the  
last 4  
weeks has smoked at least  
10  
commercially available  
non-menthol  
CCs per day (no brand  
restrictions)  
with a maximum yield of 1  
mg  
nicotine ISO per cigarette,  
as labeled  
on the cigarette package.  
Furthermore, the subject  
has smoked  
for at least the last 3  
consecutive  
years. The smoking status  
will be  
verified with a urinary  
cotinine test  
(cotinine 200 ng/ml).



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Inclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

The subject is a current  
smoker who does not plan  
to quit smoking in the next  
3 months. ☐  
The subject is ready to  
accept 5 days of SA. ☐  
The subject is ready to  
accept using the THS 2.2  
product. ☐

Result ☐ No  
☐ Yes  
☐ Not Done

Inclusion Criterion Number 6



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Inclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

---

Inclusion Criterion

Subject has signed the ICF ☐  
and is able to understand  
the information provided in  
the Subject Information  
Sheet and ICF.  
Subject is aged from 21 to ☐  
65 years (inclusive).  
Subject is of Caucasian ☐  
origin.  
Smoking, healthy subject ☐  
as judged by the  
Investigator based on all  
available assessments in  
the Screening period/day  
of Admission  
Subject is a current smoker ☐  
(based on  
self-reporting), who for the  
last 4  
weeks has smoked at least  
10  
commercially available  
non-menthol  
CCs per day (no brand  
restrictions)  
with a maximum yield of 1  
mg  
nicotine ISO per cigarette,  
as labeled  
on the cigarette package.  
Furthermore, the subject  
has smoked  
for at least the last 3  
consecutive  
years. The smoking status  
will be  
verified with a urinary  
cotinine test  
(cotinine 200 ng/ml).





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Inclusion Criteria-Screen Failure  
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The subject is a current  
smoker who does not plan  
to quit smoking in the next  
3 months. ☒  
The subject is ready to  
accept 5 days of SA. ☐  
The subject is ready to  
accept using the THS 2.2  
product. ☐

Result No ☐  
Yes ☐  
Not Done ☐

Inclusion Criterion Number 7





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Inclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

---

Inclusion Criterion

Subject has signed the ICF ☐  
and is able to understand  
the information provided in  
the Subject Information  
Sheet and ICF.  
Subject is aged from 21 to ☐  
65 years (inclusive).  
Subject is of Caucasian ☐  
origin.  
Smoking, healthy subject ☐  
as judged by the  
Investigator based on all  
available assessments in  
the Screening period/day  
of Admission  
Subject is a current smoker ☐  
(based on  
self-reporting), who for the  
last 4  
weeks has smoked at least  
10  
commercially available  
non-menthol  
CCs per day (no brand  
restrictions)  
with a maximum yield of 1  
mg  
nicotine ISO per cigarette,  
as labeled  
on the cigarette package.  
Furthermore, the subject  
has smoked  
for at least the last 3  
consecutive  
years. The smoking status  
will be  
verified with a urinary  
cotinine test  
(cotinine 200 ng/ml).



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Inclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

The subject is a current  
smoker who does not plan  
to quit smoking in the next  
3 months. ☐  
The subject is ready to  
accept 5 days of SA. ☒  
The subject is ready to  
accept using the THS 2.2  
product. ☐

Result No ☐  
Yes ☐  
Not Done ☐

Inclusion Criterion Number 8



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Inclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

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Inclusion Criterion

Subject has signed the ICF ☐  
and is able to understand  
the information provided in  
the Subject Information  
Sheet and ICF.  
Subject is aged from 21 to ☐  
65 years (inclusive).  
Subject is of Caucasian ☐  
origin.  
Smoking, healthy subject ☐  
as judged by the  
Investigator based on all  
available assessments in  
the Screening period/day  
of Admission  
Subject is a current smoker ☐  
(based on  
self-reporting), who for the  
last 4  
weeks has smoked at least  
10  
commercially available  
non-menthol  
CCs per day (no brand  
restrictions)  
with a maximum yield of 1  
mg  
nicotine ISO per cigarette,  
as labeled  
on the cigarette package.  
Furthermore, the subject  
has smoked  
for at least the last 3  
consecutive  
years. The smoking status  
will be  
verified with a urinary  
cotinine test  
(cotinine 200 ng/ml).



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Inclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

The subject is a current  
smoker who does not plan  
to quit smoking in the next  
3 months. ☐  
The subject is ready to  
accept 5 days of SA. ☐  
The subject is ready to  
accept using the THS 2.2  
product. ☒

Result

No ☐  
Yes ☐  
Not Done ☐



**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: Inclusion Criteria-Admission**  
**Generated On: 28 Oct 2013 17:39:05**

\_\_\_\_\_  
\*If any has been answered No, subject must not be included in the study.  
\_\_\_\_\_  
\_\_\_\_\_

\_\_\_\_\_  
Inclusion Criterion Number 4  
\_\_\_\_\_



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Inclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

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Inclusion Criterion

Subject has signed the ICF and is able to understand the information provided in the Subject Information Sheet and ICF. ☐  
Subject is aged from 21 to 65 years (inclusive). ☐  
Subject is of Caucasian origin. ☐  
Smoking, healthy subject as judged by the Investigator based on all available assessments in the Screening period/day of Admission ☒  
Subject is a current smoker (based on self-reporting), who for the last 4 weeks has smoked at least 10 commercially available non-menthol CCs per day (no brand restrictions) with a maximum yield of 1 mg nicotine ISO per cigarette, as labeled on the cigarette package. Furthermore, the subject has smoked for at least the last 3 consecutive years. The smoking status will be verified with a urinary cotinine test (cotinine 200 ng/ml). ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Inclusion Criteria-Admission

Generated On: 28 Oct 2013 17:39:05

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The subject is a current  
smoker who does not plan  
to quit smoking in the next  
3 months. ☐

The subject is ready to  
accept 5 days of SA. ☐

The subject is ready to  
accept using the THS 2.2  
product. ☐

---

Result No ☐  
Yes ☐

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Inclusion Criterion Number 5

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Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Inclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

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Inclusion Criterion

Subject has signed the ICF and is able to understand the information provided in the Subject Information Sheet and ICF. ☐  
Subject is aged from 21 to 65 years (inclusive). ☐  
Subject is of Caucasian origin. ☐  
Smoking, healthy subject as judged by the Investigator based on all available assessments in the Screening period/day of Admission ☐  
Subject is a current smoker (based on self-reporting), who for the last 4 weeks has smoked at least 10 commercially available non-menthol CCs per day (no brand restrictions) with a maximum yield of 1 mg nicotine ISO per cigarette, as labeled on the cigarette package. Furthermore, the subject has smoked for at least the last 3 consecutive years. The smoking status will be verified with a urinary cotinine test (cotinine 200 ng/ml). ☒





Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Inclusion Criteria-Admission

Generated On: 28 Oct 2013 17:39:05

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The subject is a current  
smoker who does not plan  
to quit smoking in the next  
3 months. ☐

The subject is ready to  
accept 5 days of SA. ☐

The subject is ready to  
accept using the THS 2.2  
product. ☐

---

Result No ☐  
Yes ☐

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Inclusion Criterion Number 7

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Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Inclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

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Inclusion Criterion

Subject has signed the ICF ☐  
and is able to understand  
the information provided in  
the Subject Information  
Sheet and ICF.  
Subject is aged from 21 to ☐  
65 years (inclusive).  
Subject is of Caucasian ☐  
origin.  
Smoking, healthy subject ☐  
as judged by the  
Investigator based on all  
available assessments in  
the Screening period/day  
of Admission  
Subject is a current smoker ☐  
(based on  
self-reporting), who for the  
last 4  
weeks has smoked at least  
10  
commercially available  
non-menthol  
CCs per day (no brand  
restrictions)  
with a maximum yield of 1  
mg  
nicotine ISO per cigarette,  
as labeled  
on the cigarette package.  
Furthermore, the subject  
has smoked  
for at least the last 3  
consecutive  
years. The smoking status  
will be  
verified with a urinary  
cotinine test  
(cotinine 200 ng/ml).



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Inclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

The subject is a current  
smoker who does not plan  
to quit smoking in the next  
3 months. ☐  
The subject is ready to  
accept 5 days of SA. ☒  
The subject is ready to  
accept using the THS 2.2  
product. ☐

Result No ☐  
Yes ☐

Inclusion Criterion Number 8



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Inclusion Criteria-Admission

Generated On: 28 Oct 2013 17:39:05

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Inclusion Criterion

Subject has signed the ICF ☐  
and is able to understand  
the information provided in  
the Subject Information  
Sheet and ICF.  
Subject is aged from 21 to ☐  
65 years (inclusive).  
Subject is of Caucasian ☐  
origin.  
Smoking, healthy subject ☐  
as judged by the  
Investigator based on all  
available assessments in  
the Screening period/day  
of Admission  
Subject is a current smoker ☐  
(based on  
self-reporting), who for the  
last 4  
weeks has smoked at least  
10  
commercially available  
non-menthol  
CCs per day (no brand  
restrictions)  
with a maximum yield of 1  
mg  
nicotine ISO per cigarette,  
as labeled  
on the cigarette package.  
Furthermore, the subject  
has smoked  
for at least the last 3  
consecutive  
years. The smoking status  
will be  
verified with a urinary  
cotinine test  
(cotinine 200 ng/ml).



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Inclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

The subject is a current  
smoker who does not plan  
to quit smoking in the next  
3 months. ☐  
The subject is ready to  
accept 5 days of SA. ☐  
The subject is ready to  
accept using the THS 2.2  
product. ☒

Result No ☐  
Yes ☐



**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: Exclusion Criteria**  
**Generated On: 28 Oct 2013 17:39:05**

\_\_\_\_\_  
\*If any has been answered Yes, subject must not be included in the study.  
\_\_\_\_\_  
\_\_\_\_\_

\_\_\_\_\_  
Exclusion Criterion Number 1  
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Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

- As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☒
- A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐
- The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐
- The subject has a body mass index (BMI)  $<18.5$  or  $\geq 32$  kg/m<sup>2</sup>. ☐
- As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐
- The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

- The subject has received medication (prescription or over-the-counter) within 14 days or within 5 half lives of the drug (whichever is longer) prior to the Admission Day (Day -2), which has an impact on CYP1A2 or CYP2A6 activity. ☐
- If a subject has received any medication (prescribed or over-the-counter) within 14 days prior to Screening or prior to the Admission Day (Day -2), it will be decided at the discretion of the Investigator or designee if these can potentially interfere with the study objectives or subject's safety. ☐
- Concomitant use of nonsteroidal anti-inflammatory drugs (NSAIDs) or acetylsalicylic acid. ☐
- The subject has a positive alcohol test and/or the subject has a history of alcohol abuse that could interfere with subject's participation in the study. ☐
- The subject has a positive urine drug test. ☐
- Positive serology test for human immunodeficiency virus (HIV) 1/2, Hepatitis B or Hepatitis C. ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Exclusion Criteria

Generated On: 28 Oct 2013 17:39:05

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- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

Result

No ☐  
Yes ☐  
NA ☐

Exclusion Criterion Number

2



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐

A subject who is legally incompetent, physically or mentally incapable of giving consent. ☒

The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐

The subject has a body mass index (BMI) <18.5 or  $\geq 32$  kg/m<sup>2</sup>. ☐

As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐

The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

- The subject has received medication (prescription or over-the-counter) within 14 days or within 5 half lives of the drug (whichever is longer) prior to the Admission Day (Day -2), which has an impact on CYP1A2 or CYP2A6 activity. ☐
- If a subject has received any medication (prescribed or over-the-counter) within 14 days prior to Screening or prior to the Admission Day (Day -2), it will be decided at the discretion of the Investigator or designee if these can potentially interfere with the study objectives or subject's safety. ☐
- Concomitant use of nonsteroidal anti-inflammatory drugs (NSAIDs) or acetylsalicylic acid. ☐
- The subject has a positive alcohol test and/or the subject has a history of alcohol abuse that could interfere with subject's participation in the study. ☐
- The subject has a positive urine drug test. ☐
- Positive serology test for human immunodeficiency virus (HIV) 1/2, Hepatitis B or Hepatitis C. ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

- 
- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

Result

No ☐  
Yes ☐  
NA ☐

Exclusion Criterion Number

3





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

- As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐
- A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐
- The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☒
- The subject has a body mass index (BMI)  $<18.5$  or  $\geq 32$  kg/m<sup>2</sup>. ☐
- As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐
- The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Exclusion Criteria

Generated On: 28 Oct 2013 17:39:05

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The subject has received ☐  
medication (prescription or  
over-the-counter) within  
14 days or within 5 half  
lives of the drug  
(whichever is longer) prior  
to the Admission Day (Day  
-2), which has an impact  
on CYP1A2 or CYP2A6  
activity.

If a subject has received ☐  
any medication (prescribed  
or over-the-counter) within  
14 days prior to Screening  
or prior to the Admission  
Day (Day -2), it will be  
decided at the discretion of  
the Investigator or  
designee if these can  
potentially interfere with  
the study objectives or  
subject's safety.

Concomitant use of ☐  
nonsteroidal  
anti-inflammatory drugs  
(NSAIDs) or acetylsalicylic  
acid.

The subject has a positive ☐  
alcohol test and/or the  
subject has a history of  
alcohol abuse that could  
interfere with subject's  
participation in the study.

The subject has a positive ☐  
urine drug test.

Positive serology test for ☐  
human immunodeficiency  
virus (HIV) 1/2, Hepatitis B  
or Hepatitis C.



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

- 
- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

Result

No ☐  
Yes ☐  
NA ☐

Exclusion Criterion Number

4



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

- As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐
- A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐
- The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐
- The subject has a body mass index (BMI) <18.5 or  $\geq 32$  kg/m<sup>2</sup>. ☒
- As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐
- The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Exclusion Criteria

Generated On: 28 Oct 2013 17:39:05

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The subject has received ☐  
medication (prescription or  
over-the-counter) within  
14 days or within 5 half  
lives of the drug  
(whichever is longer) prior  
to the Admission Day (Day  
-2), which has an impact  
on CYP1A2 or CYP2A6  
activity.

If a subject has received ☐  
any medication (prescribed  
or over-the-counter) within  
14 days prior to Screening  
or prior to the Admission  
Day (Day -2), it will be  
decided at the discretion of  
the Investigator or  
designee if these can  
potentially interfere with  
the study objectives or  
subject's safety.

Concomitant use of ☐  
nonsteroidal  
anti-inflammatory drugs  
(NSAIDs) or acetylsalicylic  
acid.

The subject has a positive ☐  
alcohol test and/or the  
subject has a history of  
alcohol abuse that could  
interfere with subject's  
participation in the study.

The subject has a positive ☐  
urine drug test.

Positive serology test for ☐  
human immunodeficiency  
virus (HIV) 1/2, Hepatitis B  
or Hepatitis C.





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

- 
- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

Result

No ☐  
Yes ☐  
NA ☐

Exclusion Criterion Number

5



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐

A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐

The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐

The subject has a body mass index (BMI)  $<18.5$  or  $\geq 32$  kg/m<sup>2</sup>. ☐

As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☒

The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Exclusion Criteria

Generated On: 28 Oct 2013 17:39:05

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The subject has received ☐  
medication (prescription or  
over-the-counter) within  
14 days or within 5 half  
lives of the drug  
(whichever is longer) prior  
to the Admission Day (Day  
-2), which has an impact  
on CYP1A2 or CYP2A6  
activity.

If a subject has received ☐  
any medication (prescribed  
or over-the-counter) within  
14 days prior to Screening  
or prior to the Admission  
Day (Day -2), it will be  
decided at the discretion of  
the Investigator or  
designee if these can  
potentially interfere with  
the study objectives or  
subject's safety.

Concomitant use of ☐  
nonsteroidal  
anti-inflammatory drugs  
(NSAIDs) or acetylsalicylic  
acid.

The subject has a positive ☐  
alcohol test and/or the  
subject has a history of  
alcohol abuse that could  
interfere with subject's  
participation in the study.

The subject has a positive ☐  
urine drug test.

Positive serology test for ☐  
human immunodeficiency  
virus (HIV) 1/2, Hepatitis B  
or Hepatitis C.



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Exclusion Criteria

Generated On: 28 Oct 2013 17:39:05

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- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

Result

No ☐  
Yes ☐  
NA ☐

Exclusion Criterion Number

6



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐

A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐

The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐

The subject has a body mass index (BMI)  $<18.5$  or  $\geq 32$  kg/m<sup>2</sup>. ☐

As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐

The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☒





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

- The subject has received medication (prescription or over-the-counter) within 14 days or within 5 half lives of the drug (whichever is longer) prior to the Admission Day (Day -2), which has an impact on CYP1A2 or CYP2A6 activity. ☐
- If a subject has received any medication (prescribed or over-the-counter) within 14 days prior to Screening or prior to the Admission Day (Day -2), it will be decided at the discretion of the Investigator or designee if these can potentially interfere with the study objectives or subject's safety. ☐
- Concomitant use of nonsteroidal anti-inflammatory drugs (NSAIDs) or acetylsalicylic acid. ☐
- The subject has a positive alcohol test and/or the subject has a history of alcohol abuse that could interfere with subject's participation in the study. ☐
- The subject has a positive urine drug test. ☐
- Positive serology test for human immunodeficiency virus (HIV) 1/2, Hepatitis B or Hepatitis C. ☐





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

- 
- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

Result

No ☐  
Yes ☐  
NA ☐

Exclusion Criterion Number

8



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

- As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐
- A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐
- The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐
- The subject has a body mass index (BMI) <18.5 or  $\geq 32$  kg/m<sup>2</sup>. ☐
- As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐
- The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Exclusion Criteria

Generated On: 28 Oct 2013 17:39:05

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The subject has received ☐  
medication (prescription or  
over-the-counter) within  
14 days or within 5 half  
lives of the drug  
(whichever is longer) prior  
to the Admission Day (Day  
-2), which has an impact  
on CYP1A2 or CYP2A6  
activity.

If a subject has received ☒  
any medication (prescribed  
or over-the-counter) within  
14 days prior to Screening  
or prior to the Admission  
Day (Day -2), it will be  
decided at the discretion of  
the Investigator or  
designee if these can  
potentially interfere with  
the study objectives or  
subject's safety.

Concomitant use of ☐  
nonsteroidal  
anti-inflammatory drugs  
(NSAIDs) or acetylsalicylic  
acid.

The subject has a positive ☐  
alcohol test and/or the  
subject has a history of  
alcohol abuse that could  
interfere with subject's  
participation in the study.

The subject has a positive ☐  
urine drug test.

Positive serology test for ☐  
human immunodeficiency  
virus (HIV) 1/2, Hepatitis B  
or Hepatitis C.



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Exclusion Criteria

Generated On: 28 Oct 2013 17:39:05

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- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-



**Final version 5.0 (Main CRF): Case Book**

**Project Name: ZRHR-REXC-03-EU**

**Form: Exclusion Criteria**

**Generated On: 28 Oct 2013 17:39:05**

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Result

No ☐

Yes ☐

NA ☐

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Exclusion Criterion Number

9

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Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

- As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐
- A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐
- The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐
- The subject has a body mass index (BMI) <18.5 or  $\geq 32$  kg/m<sup>2</sup>. ☐
- As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐
- The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

The subject has received ☐  
medication (prescription or  
over-the-counter) within  
14 days or within 5 half  
lives of the drug  
(whichever is longer) prior  
to the Admission Day (Day  
-2), which has an impact  
on CYP1A2 or CYP2A6  
activity.

If a subject has received ☐  
any medication (prescribed  
or over-the-counter) within  
14 days prior to Screening  
or prior to the Admission  
Day (Day -2), it will be  
decided at the discretion of  
the Investigator or  
designee if these can  
potentially interfere with  
the study objectives or  
subject's safety.

Concomitant use of ☒  
nonsteroidal  
anti-inflammatory drugs  
(NSAIDs) or acetylsalicylic  
acid.

The subject has a positive ☐  
alcohol test and/or the  
subject has a history of  
alcohol abuse that could  
interfere with subject's  
participation in the study.

The subject has a positive ☐  
urine drug test.

Positive serology test for ☐  
human immunodeficiency  
virus (HIV) 1/2, Hepatitis B  
or Hepatitis C.



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Exclusion Criteria

Generated On: 28 Oct 2013 17:39:05

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- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

Result

No ☐  
Yes ☐  
NA ☐

Exclusion Criterion Number

10



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

- As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐
- A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐
- The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐
- The subject has a body mass index (BMI) <18.5 or  $\geq 32$  kg/m<sup>2</sup>. ☐
- As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐
- The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Exclusion Criteria

Generated On: 28 Oct 2013 17:39:05

The subject has received ☐  
medication (prescription or  
over-the-counter) within  
14 days or within 5 half  
lives of the drug  
(whichever is longer) prior  
to the Admission Day (Day  
-2), which has an impact  
on CYP1A2 or CYP2A6  
activity.

If a subject has received ☐  
any medication (prescribed  
or over-the-counter) within  
14 days prior to Screening  
or prior to the Admission  
Day (Day -2), it will be  
decided at the discretion of  
the Investigator or  
designee if these can  
potentially interfere with  
the study objectives or  
subject's safety.

Concomitant use of ☐  
nonsteroidal  
anti-inflammatory drugs  
(NSAIDs) or acetylsalicylic  
acid.

The subject has a positive ☒  
alcohol test and/or the  
subject has a history of  
alcohol abuse that could  
interfere with subject's  
participation in the study.

The subject has a positive ☐  
urine drug test.

Positive serology test for ☐  
human immunodeficiency  
virus (HIV) 1/2, Hepatitis B  
or Hepatitis C.



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Exclusion Criteria

Generated On: 28 Oct 2013 17:39:05

---

- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

Result

No ☐  
Yes ☐  
NA ☐

Exclusion Criterion Number

11





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

- As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐
- A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐
- The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐
- The subject has a body mass index (BMI) <18.5 or  $\geq 32$  kg/m<sup>2</sup>. ☐
- As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐
- The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

- The subject has received medication (prescription or over-the-counter) within 14 days or within 5 half lives of the drug (whichever is longer) prior to the Admission Day (Day -2), which has an impact on CYP1A2 or CYP2A6 activity. ☐
- If a subject has received any medication (prescribed or over-the-counter) within 14 days prior to Screening or prior to the Admission Day (Day -2), it will be decided at the discretion of the Investigator or designee if these can potentially interfere with the study objectives or subject's safety. ☐
- Concomitant use of nonsteroidal anti-inflammatory drugs (NSAIDs) or acetylsalicylic acid. ☐
- The subject has a positive alcohol test and/or the subject has a history of alcohol abuse that could interfere with subject's participation in the study. ☐
- The subject has a positive urine drug test. ☒
- Positive serology test for human immunodeficiency virus (HIV) 1/2, Hepatitis B or Hepatitis C. ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

- 
- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

Result

No ☐  
Yes ☐  
NA ☐

Exclusion Criterion Number

12



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

- As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐
- A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐
- The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐
- The subject has a body mass index (BMI) <18.5 or  $\geq 32$  kg/m<sup>2</sup>. ☐
- As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐
- The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

- The subject has received medication (prescription or over-the-counter) within 14 days or within 5 half lives of the drug (whichever is longer) prior to the Admission Day (Day -2), which has an impact on CYP1A2 or CYP2A6 activity. ☐
- If a subject has received any medication (prescribed or over-the-counter) within 14 days prior to Screening or prior to the Admission Day (Day -2), it will be decided at the discretion of the Investigator or designee if these can potentially interfere with the study objectives or subject's safety. ☐
- Concomitant use of nonsteroidal anti-inflammatory drugs (NSAIDs) or acetylsalicylic acid. ☐
- The subject has a positive alcohol test and/or the subject has a history of alcohol abuse that could interfere with subject's participation in the study. ☐
- The subject has a positive urine drug test. ☐
- Positive serology test for human immunodeficiency virus (HIV) 1/2, Hepatitis B or Hepatitis C. ☒





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

- 
- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

---

Result

No ☐  
Yes ☐  
NA ☐

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Exclusion Criterion Number

13

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Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

- As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐
- A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐
- The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐
- The subject has a body mass index (BMI) <18.5 or  $\geq 32$  kg/m<sup>2</sup>. ☐
- As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐
- The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Exclusion Criteria

Generated On: 28 Oct 2013 17:39:05

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The subject has received ☐  
medication (prescription or  
over-the-counter) within  
14 days or within 5 half  
lives of the drug  
(whichever is longer) prior  
to the Admission Day (Day  
-2), which has an impact  
on CYP1A2 or CYP2A6  
activity.

If a subject has received ☐  
any medication (prescribed  
or over-the-counter) within  
14 days prior to Screening  
or prior to the Admission  
Day (Day -2), it will be  
decided at the discretion of  
the Investigator or  
designee if these can  
potentially interfere with  
the study objectives or  
subject's safety.

Concomitant use of ☐  
nonsteroidal  
anti-inflammatory drugs  
(NSAIDs) or acetylsalicylic  
acid.

The subject has a positive ☐  
alcohol test and/or the  
subject has a history of  
alcohol abuse that could  
interfere with subject's  
participation in the study.

The subject has a positive ☐  
urine drug test.

Positive serology test for ☐  
human immunodeficiency  
virus (HIV) 1/2, Hepatitis B  
or Hepatitis C.



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

- 
- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☒
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

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Result

No ☐  
Yes ☐  
NA ☐

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Exclusion Criterion Number14

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Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

- As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐
- A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐
- The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐
- The subject has a body mass index (BMI)  $<18.5$  or  $\geq 32$  kg/m<sup>2</sup>. ☐
- As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐
- The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐





Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Exclusion Criteria

Generated On: 28 Oct 2013 17:39:05

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The subject has received ☐  
medication (prescription or  
over-the-counter) within  
14 days or within 5 half  
lives of the drug  
(whichever is longer) prior  
to the Admission Day (Day  
-2), which has an impact  
on CYP1A2 or CYP2A6  
activity.

If a subject has received ☐  
any medication (prescribed  
or over-the-counter) within  
14 days prior to Screening  
or prior to the Admission  
Day (Day -2), it will be  
decided at the discretion of  
the Investigator or  
designee if these can  
potentially interfere with  
the study objectives or  
subject's safety.

Concomitant use of ☐  
nonsteroidal  
anti-inflammatory drugs  
(NSAIDs) or acetylsalicylic  
acid.

The subject has a positive ☐  
alcohol test and/or the  
subject has a history of  
alcohol abuse that could  
interfere with subject's  
participation in the study.

The subject has a positive ☐  
urine drug test.

Positive serology test for ☐  
human immunodeficiency  
virus (HIV) 1/2, Hepatitis B  
or Hepatitis C.





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

- 
- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☒
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-



**Final version 5.0 (Main CRF): Case Book**

**Project Name: ZRHR-REXC-03-EU**

**Form: Exclusion Criteria**

**Generated On: 28 Oct 2013 17:39:05**

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Result

No ☐

Yes ☐

NA ☐

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Exclusion Criterion Number

15

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Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Exclusion Criteria

Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐

A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐

The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐

The subject has a body mass index (BMI) <18.5 or  $\geq 32$  kg/m<sup>2</sup>. ☐

As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐

The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Exclusion Criteria

Generated On: 28 Oct 2013 17:39:05

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The subject has received ☐  
medication (prescription or  
over-the-counter) within  
14 days or within 5 half  
lives of the drug  
(whichever is longer) prior  
to the Admission Day (Day  
-2), which has an impact  
on CYP1A2 or CYP2A6  
activity.

If a subject has received ☐  
any medication (prescribed  
or over-the-counter) within  
14 days prior to Screening  
or prior to the Admission  
Day (Day -2), it will be  
decided at the discretion of  
the Investigator or  
designee if these can  
potentially interfere with  
the study objectives or  
subject's safety.

Concomitant use of ☐  
nonsteroidal  
anti-inflammatory drugs  
(NSAIDs) or acetylsalicylic  
acid.

The subject has a positive ☐  
alcohol test and/or the  
subject has a history of  
alcohol abuse that could  
interfere with subject's  
participation in the study.

The subject has a positive ☐  
urine drug test.

Positive serology test for ☐  
human immunodeficiency  
virus (HIV) 1/2, Hepatitis B  
or Hepatitis C.



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

- 
- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☒
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

Result

No ☐  
Yes ☐  
NA ☐

Exclusion Criterion Number

16





Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Exclusion Criteria

Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐

A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐

The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐

The subject has a body mass index (BMI) <18.5 or  $\geq 32$  kg/m<sup>2</sup>. ☐

As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐

The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐





Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Exclusion Criteria

Generated On: 28 Oct 2013 17:39:05

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The subject has received ☐  
medication (prescription or  
over-the-counter) within  
14 days or within 5 half  
lives of the drug  
(whichever is longer) prior  
to the Admission Day (Day  
-2), which has an impact  
on CYP1A2 or CYP2A6  
activity.

If a subject has received ☐  
any medication (prescribed  
or over-the-counter) within  
14 days prior to Screening  
or prior to the Admission  
Day (Day -2), it will be  
decided at the discretion of  
the Investigator or  
designee if these can  
potentially interfere with  
the study objectives or  
subject's safety.

Concomitant use of ☐  
nonsteroidal  
anti-inflammatory drugs  
(NSAIDs) or acetylsalicylic  
acid.

The subject has a positive ☐  
alcohol test and/or the  
subject has a history of  
alcohol abuse that could  
interfere with subject's  
participation in the study.

The subject has a positive ☐  
urine drug test.

Positive serology test for ☐  
human immunodeficiency  
virus (HIV) 1/2, Hepatitis B  
or Hepatitis C.



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

- 
- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☒
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

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Result

No ☐  
Yes ☐  
NA ☐

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Exclusion Criterion Number

17

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Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Exclusion Criteria

Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐

A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐

The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐

The subject has a body mass index (BMI) <18.5 or  $\geq 32$  kg/m<sup>2</sup>. ☐

As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐

The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

- The subject has received medication (prescription or over-the-counter) within 14 days or within 5 half lives of the drug (whichever is longer) prior to the Admission Day (Day -2), which has an impact on CYP1A2 or CYP2A6 activity. ☐
- If a subject has received any medication (prescribed or over-the-counter) within 14 days prior to Screening or prior to the Admission Day (Day -2), it will be decided at the discretion of the Investigator or designee if these can potentially interfere with the study objectives or subject's safety. ☐
- Concomitant use of nonsteroidal anti-inflammatory drugs (NSAIDs) or acetylsalicylic acid. ☐
- The subject has a positive alcohol test and/or the subject has a history of alcohol abuse that could interfere with subject's participation in the study. ☐
- The subject has a positive urine drug test. ☐
- Positive serology test for human immunodeficiency virus (HIV) 1/2, Hepatitis B or Hepatitis C. ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

- 
- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☒
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-





**Final version 5.0 (Main CRF): Case Book**

**Project Name: ZRHR-REXC-03-EU**

**Form: Exclusion Criteria**

**Generated On: 28 Oct 2013 17:39:05**

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Result

No ☐

Yes ☐

NA ☐

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Exclusion Criterion Number

18

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Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

- As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐
- A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐
- The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐
- The subject has a body mass index (BMI)  $<18.5$  or  $\geq 32$  kg/m<sup>2</sup>. ☐
- As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐
- The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Exclusion Criteria

Generated On: 28 Oct 2013 17:39:05

---

The subject has received ☐  
medication (prescription or  
over-the-counter) within  
14 days or within 5 half  
lives of the drug  
(whichever is longer) prior  
to the Admission Day (Day  
-2), which has an impact  
on CYP1A2 or CYP2A6  
activity.

If a subject has received ☐  
any medication (prescribed  
or over-the-counter) within  
14 days prior to Screening  
or prior to the Admission  
Day (Day -2), it will be  
decided at the discretion of  
the Investigator or  
designee if these can  
potentially interfere with  
the study objectives or  
subject's safety.

Concomitant use of ☐  
nonsteroidal  
anti-inflammatory drugs  
(NSAIDs) or acetylsalicylic  
acid.

The subject has a positive ☐  
alcohol test and/or the  
subject has a history of  
alcohol abuse that could  
interfere with subject's  
participation in the study.

The subject has a positive ☐  
urine drug test.

Positive serology test for ☐  
human immunodeficiency  
virus (HIV) 1/2, Hepatitis B  
or Hepatitis C.



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Exclusion Criteria

Generated On: 28 Oct 2013 17:39:05

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- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☒
- Subject does not agree to use an acceptable method of effective contraception ☐
-



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

Result

No ☐  
Yes ☐  
NA ☐

Exclusion Criterion Number

19



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐

A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐

The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐

The subject has a body mass index (BMI)  $<18.5$  or  $\geq 32$  kg/m<sup>2</sup>. ☐

As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐

The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Exclusion Criteria

Generated On: 28 Oct 2013 17:39:05

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The subject has received ☐  
medication (prescription or  
over-the-counter) within  
14 days or within 5 half  
lives of the drug  
(whichever is longer) prior  
to the Admission Day (Day  
-2), which has an impact  
on CYP1A2 or CYP2A6  
activity.

If a subject has received ☐  
any medication (prescribed  
or over-the-counter) within  
14 days prior to Screening  
or prior to the Admission  
Day (Day -2), it will be  
decided at the discretion of  
the Investigator or  
designee if these can  
potentially interfere with  
the study objectives or  
subject's safety.

Concomitant use of ☐  
nonsteroidal  
anti-inflammatory drugs  
(NSAIDs) or acetylsalicylic  
acid.

The subject has a positive ☐  
alcohol test and/or the  
subject has a history of  
alcohol abuse that could  
interfere with subject's  
participation in the study.

The subject has a positive ☐  
urine drug test.

Positive serology test for ☐  
human immunodeficiency  
virus (HIV) 1/2, Hepatitis B  
or Hepatitis C.





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

- 
- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☒
-





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria  
Generated On: 28 Oct 2013 17:39:05

Result

No ☐  
Yes ☐  
NA ☐



**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: Exclusion Criteria-Screen Failure**  
**Generated On: 28 Oct 2013 17:39:05**

\_\_\_\_\_  
\*If any has been answered Yes, subject must not be included in the study.

\_\_\_\_\_  
H\_NOW (Derived): \_\_\_\_\_  
\_\_\_\_\_

\_\_\_\_\_  
Exclusion Criterion Number 1  
\_\_\_\_\_



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

- As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☒
- A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐
- The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐
- The subject has a body mass index (BMI)  $<18.5$  or  $\geq 32$  kg/m<sup>2</sup>. ☐
- As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐
- The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

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The subject has received ☐  
medication (prescription or  
over-the-counter) within  
14 days or within 5 half  
lives of the drug  
(whichever is longer) prior  
to the Admission Day (Day  
-2), which has an impact  
on CYP1A2 or CYP2A6  
activity.

If a subject has received ☐  
any medication (prescribed  
or over-the-counter) within  
14 days prior to Screening  
or prior to the Admission  
Day (Day -2), it will be  
decided at the discretion of  
the Investigator or  
designee if these can  
potentially interfere with  
the study objectives or  
subject's safety.

Concomitant use of ☐  
nonsteroidal  
anti-inflammatory drugs  
(NSAIDs) or acetylsalicylic  
acid.

The subject has a positive ☐  
alcohol test and/or the  
subject has a history of  
alcohol abuse that could  
interfere with subject's  
participation in the study.

The subject has a positive ☐  
urine drug test.

Positive serology test for ☐  
human immunodeficiency  
virus (HIV) 1/2, Hepatitis B  
or Hepatitis C.



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

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- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-



**Final version 5.0 (Main CRF): Case Book**

**Project Name: ZRHR-REXC-03-EU**

**Form: Exclusion Criteria-Screen Failure**

**Generated On: 28 Oct 2013 17:39:05**

---

Result

No ☐

Yes ☐

Not Done ☐

NA ☐

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Exclusion Criterion Number

2

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Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐

A subject who is legally incompetent, physically or mentally incapable of giving consent. ☒

The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐

The subject has a body mass index (BMI)  $<18.5$  or  $\geq 32$  kg/m<sup>2</sup>. ☐

As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐

The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

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The subject has received ☐  
medication (prescription or  
over-the-counter) within  
14 days or within 5 half  
lives of the drug  
(whichever is longer) prior  
to the Admission Day (Day  
-2), which has an impact  
on CYP1A2 or CYP2A6  
activity.

If a subject has received ☐  
any medication (prescribed  
or over-the-counter) within  
14 days prior to Screening  
or prior to the Admission  
Day (Day -2), it will be  
decided at the discretion of  
the Investigator or  
designee if these can  
potentially interfere with  
the study objectives or  
subject's safety.

Concomitant use of ☐  
nonsteroidal  
anti-inflammatory drugs  
(NSAIDs) or acetylsalicylic  
acid.

The subject has a positive ☐  
alcohol test and/or the  
subject has a history of  
alcohol abuse that could  
interfere with subject's  
participation in the study.

The subject has a positive ☐  
urine drug test.

Positive serology test for ☐  
human immunodeficiency  
virus (HIV) 1/2, Hepatitis B  
or Hepatitis C.



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

- 
- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

Result

No ☐  
Yes ☐  
Not Done ☐  
NA ☐

Exclusion Criterion Number

3



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

- As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐
- A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐
- The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☒
- The subject has a body mass index (BMI)  $<18.5$  or  $\geq 32$  kg/m<sup>2</sup>. ☐
- As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐
- The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

The subject has received ☐  
medication (prescription or  
over-the-counter) within  
14 days or within 5 half  
lives of the drug  
(whichever is longer) prior  
to the Admission Day (Day  
-2), which has an impact  
on CYP1A2 or CYP2A6  
activity.

If a subject has received ☐  
any medication (prescribed  
or over-the-counter) within  
14 days prior to Screening  
or prior to the Admission  
Day (Day -2), it will be  
decided at the discretion of  
the Investigator or  
designee if these can  
potentially interfere with  
the study objectives or  
subject's safety.

Concomitant use of ☐  
nonsteroidal  
anti-inflammatory drugs  
(NSAIDs) or acetylsalicylic  
acid.

The subject has a positive ☐  
alcohol test and/or the  
subject has a history of  
alcohol abuse that could  
interfere with subject's  
participation in the study.

The subject has a positive ☐  
urine drug test.

Positive serology test for ☐  
human immunodeficiency  
virus (HIV) 1/2, Hepatitis B  
or Hepatitis C.



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

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- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-





**Final version 5.0 (Main CRF): Case Book**

**Project Name: ZRHR-REXC-03-EU**

**Form: Exclusion Criteria-Screen Failure**

**Generated On: 28 Oct 2013 17:39:05**

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Result

No ☐

Yes ☐

Not Done ☐

NA ☐

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Exclusion Criterion Number

4

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Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐

A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐

The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐

The subject has a body mass index (BMI)  $<18.5$  or  $\geq 32$  kg/m<sup>2</sup>. ☒

As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐

The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

- The subject has received medication (prescription or over-the-counter) within 14 days or within 5 half lives of the drug (whichever is longer) prior to the Admission Day (Day -2), which has an impact on CYP1A2 or CYP2A6 activity. ☐
- If a subject has received any medication (prescribed or over-the-counter) within 14 days prior to Screening or prior to the Admission Day (Day -2), it will be decided at the discretion of the Investigator or designee if these can potentially interfere with the study objectives or subject's safety. ☐
- Concomitant use of nonsteroidal anti-inflammatory drugs (NSAIDs) or acetylsalicylic acid. ☐
- The subject has a positive alcohol test and/or the subject has a history of alcohol abuse that could interfere with subject's participation in the study. ☐
- The subject has a positive urine drug test. ☐
- Positive serology test for human immunodeficiency virus (HIV) 1/2, Hepatitis B or Hepatitis C. ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

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- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

Result

No ☐  
Yes ☐  
Not Done ☐  
NA ☐

Exclusion Criterion Number

5



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐

A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐

The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐

The subject has a body mass index (BMI)  $<18.5$  or  $\geq 32$  kg/m<sup>2</sup>. ☐

As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☒

The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

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The subject has received ☐  
medication (prescription or  
over-the-counter) within  
14 days or within 5 half  
lives of the drug  
(whichever is longer) prior  
to the Admission Day (Day  
-2), which has an impact  
on CYP1A2 or CYP2A6  
activity.

If a subject has received ☐  
any medication (prescribed  
or over-the-counter) within  
14 days prior to Screening  
or prior to the Admission  
Day (Day -2), it will be  
decided at the discretion of  
the Investigator or  
designee if these can  
potentially interfere with  
the study objectives or  
subject's safety.

Concomitant use of ☐  
nonsteroidal  
anti-inflammatory drugs  
(NSAIDs) or acetylsalicylic  
acid.

The subject has a positive ☐  
alcohol test and/or the  
subject has a history of  
alcohol abuse that could  
interfere with subject's  
participation in the study.

The subject has a positive ☐  
urine drug test.

Positive serology test for ☐  
human immunodeficiency  
virus (HIV) 1/2, Hepatitis B  
or Hepatitis C.





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

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- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-





**Final version 5.0 (Main CRF): Case Book**

**Project Name: ZRHR-REXC-03-EU**

**Form: Exclusion Criteria-Screen Failure**

**Generated On: 28 Oct 2013 17:39:05**

---

Result

No ☐

Yes ☐

Not Done ☐

NA ☐

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Exclusion Criterion Number

6

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Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐

A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐

The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐

The subject has a body mass index (BMI)  $<18.5$  or  $\geq 32$  kg/m<sup>2</sup>. ☐

As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐

The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☒



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

- The subject has received medication (prescription or over-the-counter) within 14 days or within 5 half lives of the drug (whichever is longer) prior to the Admission Day (Day -2), which has an impact on CYP1A2 or CYP2A6 activity. ☐
- If a subject has received any medication (prescribed or over-the-counter) within 14 days prior to Screening or prior to the Admission Day (Day -2), it will be decided at the discretion of the Investigator or designee if these can potentially interfere with the study objectives or subject's safety. ☐
- Concomitant use of nonsteroidal anti-inflammatory drugs (NSAIDs) or acetylsalicylic acid. ☐
- The subject has a positive alcohol test and/or the subject has a history of alcohol abuse that could interfere with subject's participation in the study. ☐
- The subject has a positive urine drug test. ☐
- Positive serology test for human immunodeficiency virus (HIV) 1/2, Hepatitis B or Hepatitis C. ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

---

- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

Result

No ☐  
Yes ☐  
Not Done ☐  
NA ☐

Exclusion Criterion Number

7



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

- As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐
- A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐
- The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐
- The subject has a body mass index (BMI)  $<18.5$  or  $\geq 32$  kg/m<sup>2</sup>. ☐
- As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐
- The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

---

- The subject has received medication (prescription or over-the-counter) within 14 days or within 5 half lives of the drug (whichever is longer) prior to the Admission Day (Day -2), which has an impact on CYP1A2 or CYP2A6 activity. ☒
- If a subject has received any medication (prescribed or over-the-counter) within 14 days prior to Screening or prior to the Admission Day (Day -2), it will be decided at the discretion of the Investigator or designee if these can potentially interfere with the study objectives or subject's safety. ☐
- Concomitant use of nonsteroidal anti-inflammatory drugs (NSAIDs) or acetylsalicylic acid. ☐
- The subject has a positive alcohol test and/or the subject has a history of alcohol abuse that could interfere with subject's participation in the study. ☐
- The subject has a positive urine drug test. ☐
- Positive serology test for human immunodeficiency virus (HIV) 1/2, Hepatitis B or Hepatitis C. ☐





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

- 
- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-



**Final version 5.0 (Main CRF): Case Book**

**Project Name: ZRHR-REXC-03-EU**

**Form: Exclusion Criteria-Screen Failure**

**Generated On: 28 Oct 2013 17:39:05**

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Result

No ☐

Yes ☐

Not Done ☐

NA ☐

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Exclusion Criterion Number

8

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Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐

A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐

The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐

The subject has a body mass index (BMI)  $<18.5$  or  $\geq 32$  kg/m<sup>2</sup>. ☐

As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐

The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

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The subject has received ☐  
medication (prescription or  
over-the-counter) within  
14 days or within 5 half  
lives of the drug  
(whichever is longer) prior  
to the Admission Day (Day  
-2), which has an impact  
on CYP1A2 or CYP2A6  
activity.

If a subject has received ☒  
any medication (prescribed  
or over-the-counter) within  
14 days prior to Screening  
or prior to the Admission  
Day (Day -2), it will be  
decided at the discretion of  
the Investigator or  
designee if these can  
potentially interfere with  
the study objectives or  
subject's safety.

Concomitant use of ☐  
nonsteroidal  
anti-inflammatory drugs  
(NSAIDs) or acetylsalicylic  
acid.

The subject has a positive ☐  
alcohol test and/or the  
subject has a history of  
alcohol abuse that could  
interfere with subject's  
participation in the study.

The subject has a positive ☐  
urine drug test.

Positive serology test for ☐  
human immunodeficiency  
virus (HIV) 1/2, Hepatitis B  
or Hepatitis C.



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

- 
- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

Result

No ☐  
Yes ☐  
Not Done ☐  
NA ☐

Exclusion Criterion Number

9





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

- As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐
- A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐
- The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐
- The subject has a body mass index (BMI)  $<18.5$  or  $\geq 32$  kg/m<sup>2</sup>. ☐
- As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐
- The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

---

The subject has received ☐  
medication (prescription or  
over-the-counter) within  
14 days or within 5 half  
lives of the drug  
(whichever is longer) prior  
to the Admission Day (Day  
-2), which has an impact  
on CYP1A2 or CYP2A6  
activity.

If a subject has received ☐  
any medication (prescribed  
or over-the-counter) within  
14 days prior to Screening  
or prior to the Admission  
Day (Day -2), it will be  
decided at the discretion of  
the Investigator or  
designee if these can  
potentially interfere with  
the study objectives or  
subject's safety.

Concomitant use of ☒  
nonsteroidal  
anti-inflammatory drugs  
(NSAIDs) or acetylsalicylic  
acid.

The subject has a positive ☐  
alcohol test and/or the  
subject has a history of  
alcohol abuse that could  
interfere with subject's  
participation in the study.

The subject has a positive ☐  
urine drug test.

Positive serology test for ☐  
human immunodeficiency  
virus (HIV) 1/2, Hepatitis B  
or Hepatitis C.



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

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- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

Result

No ☐  
Yes ☐  
Not Done ☐  
NA ☐

Exclusion Criterion Number

10



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

- As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐
- A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐
- The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐
- The subject has a body mass index (BMI)  $<18.5$  or  $\geq 32$  kg/m<sup>2</sup>. ☐
- As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐
- The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

The subject has received ☐  
medication (prescription or  
over-the-counter) within  
14 days or within 5 half  
lives of the drug  
(whichever is longer) prior  
to the Admission Day (Day  
-2), which has an impact  
on CYP1A2 or CYP2A6  
activity.

If a subject has received ☐  
any medication (prescribed  
or over-the-counter) within  
14 days prior to Screening  
or prior to the Admission  
Day (Day -2), it will be  
decided at the discretion of  
the Investigator or  
designee if these can  
potentially interfere with  
the study objectives or  
subject's safety.

Concomitant use of ☐  
nonsteroidal  
anti-inflammatory drugs  
(NSAIDs) or acetylsalicylic  
acid.

The subject has a positive ☒  
alcohol test and/or the  
subject has a history of  
alcohol abuse that could  
interfere with subject's  
participation in the study.

The subject has a positive ☐  
urine drug test.

Positive serology test for ☐  
human immunodeficiency  
virus (HIV) 1/2, Hepatitis B  
or Hepatitis C.



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

- 
- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

Result

No ☐  
Yes ☐  
Not Done ☐  
NA ☐

Exclusion Criterion Number

11



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

- As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐
- A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐
- The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐
- The subject has a body mass index (BMI)  $<18.5$  or  $\geq 32$  kg/m<sup>2</sup>. ☐
- As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐
- The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

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The subject has received ☐  
medication (prescription or  
over-the-counter) within  
14 days or within 5 half  
lives of the drug  
(whichever is longer) prior  
to the Admission Day (Day  
-2), which has an impact  
on CYP1A2 or CYP2A6  
activity.

If a subject has received ☐  
any medication (prescribed  
or over-the-counter) within  
14 days prior to Screening  
or prior to the Admission  
Day (Day -2), it will be  
decided at the discretion of  
the Investigator or  
designee if these can  
potentially interfere with  
the study objectives or  
subject's safety.

Concomitant use of ☐  
nonsteroidal  
anti-inflammatory drugs  
(NSAIDs) or acetylsalicylic  
acid.

The subject has a positive ☐  
alcohol test and/or the  
subject has a history of  
alcohol abuse that could  
interfere with subject's  
participation in the study.

The subject has a positive ☒  
urine drug test.

Positive serology test for ☐  
human immunodeficiency  
virus (HIV) 1/2, Hepatitis B  
or Hepatitis C.



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

- 
- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-



**Final version 5.0 (Main CRF): Case Book**

**Project Name: ZRHR-REXC-03-EU**

**Form: Exclusion Criteria-Screen Failure**

**Generated On: 28 Oct 2013 17:39:05**

---

Result

No ☐

Yes ☐

Not Done ☐

NA ☐

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Exclusion Criterion Number

12

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Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

- As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐
- A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐
- The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐
- The subject has a body mass index (BMI)  $<18.5$  or  $\geq 32$  kg/m<sup>2</sup>. ☐
- As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐
- The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

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The subject has received ☐  
medication (prescription or  
over-the-counter) within  
14 days or within 5 half  
lives of the drug  
(whichever is longer) prior  
to the Admission Day (Day  
-2), which has an impact  
on CYP1A2 or CYP2A6  
activity.

If a subject has received ☐  
any medication (prescribed  
or over-the-counter) within  
14 days prior to Screening  
or prior to the Admission  
Day (Day -2), it will be  
decided at the discretion of  
the Investigator or  
designee if these can  
potentially interfere with  
the study objectives or  
subject's safety.

Concomitant use of ☐  
nonsteroidal  
anti-inflammatory drugs  
(NSAIDs) or acetylsalicylic  
acid.

The subject has a positive ☐  
alcohol test and/or the  
subject has a history of  
alcohol abuse that could  
interfere with subject's  
participation in the study.

The subject has a positive ☐  
urine drug test.

Positive serology test for ☒  
human immunodeficiency  
virus (HIV) 1/2, Hepatitis B  
or Hepatitis C.



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

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- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

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Result

No ☐  
Yes ☐  
Not Done ☐  
NA ☐

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Exclusion Criterion Number

13

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Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐

A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐

The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐

The subject has a body mass index (BMI)  $<18.5$  or  $\geq 32$  kg/m<sup>2</sup>. ☐

As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐

The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

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The subject has received ☐  
medication (prescription or  
over-the-counter) within  
14 days or within 5 half  
lives of the drug  
(whichever is longer) prior  
to the Admission Day (Day  
-2), which has an impact  
on CYP1A2 or CYP2A6  
activity.

If a subject has received ☐  
any medication (prescribed  
or over-the-counter) within  
14 days prior to Screening  
or prior to the Admission  
Day (Day -2), it will be  
decided at the discretion of  
the Investigator or  
designee if these can  
potentially interfere with  
the study objectives or  
subject's safety.

Concomitant use of ☐  
nonsteroidal  
anti-inflammatory drugs  
(NSAIDs) or acetylsalicylic  
acid.

The subject has a positive ☐  
alcohol test and/or the  
subject has a history of  
alcohol abuse that could  
interfere with subject's  
participation in the study.

The subject has a positive ☐  
urine drug test.

Positive serology test for ☐  
human immunodeficiency  
virus (HIV) 1/2, Hepatitis B  
or Hepatitis C.



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

- 
- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☒
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

Result

No ☐  
Yes ☐  
Not Done ☐  
NA ☐

Exclusion Criterion Number

14



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

- As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐
- A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐
- The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐
- The subject has a body mass index (BMI)  $<18.5$  or  $\geq 32$  kg/m<sup>2</sup>. ☐
- As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐
- The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

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The subject has received ☐  
medication (prescription or  
over-the-counter) within  
14 days or within 5 half  
lives of the drug  
(whichever is longer) prior  
to the Admission Day (Day  
-2), which has an impact  
on CYP1A2 or CYP2A6  
activity.

If a subject has received ☐  
any medication (prescribed  
or over-the-counter) within  
14 days prior to Screening  
or prior to the Admission  
Day (Day -2), it will be  
decided at the discretion of  
the Investigator or  
designee if these can  
potentially interfere with  
the study objectives or  
subject's safety.

Concomitant use of ☐  
nonsteroidal  
anti-inflammatory drugs  
(NSAIDs) or acetylsalicylic  
acid.

The subject has a positive ☐  
alcohol test and/or the  
subject has a history of  
alcohol abuse that could  
interfere with subject's  
participation in the study.

The subject has a positive ☐  
urine drug test.

Positive serology test for ☐  
human immunodeficiency  
virus (HIV) 1/2, Hepatitis B  
or Hepatitis C.



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

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- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☒
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

Result

No ☐  
Yes ☐  
Not Done ☐  
NA ☐

Exclusion Criterion Number

15



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

- As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐
- A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐
- The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐
- The subject has a body mass index (BMI)  $<18.5$  or  $\geq 32$  kg/m<sup>2</sup>. ☐
- As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐
- The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

- The subject has received medication (prescription or over-the-counter) within 14 days or within 5 half lives of the drug (whichever is longer) prior to the Admission Day (Day -2), which has an impact on CYP1A2 or CYP2A6 activity. ☐
- If a subject has received any medication (prescribed or over-the-counter) within 14 days prior to Screening or prior to the Admission Day (Day -2), it will be decided at the discretion of the Investigator or designee if these can potentially interfere with the study objectives or subject's safety. ☐
- Concomitant use of nonsteroidal anti-inflammatory drugs (NSAIDs) or acetylsalicylic acid. ☐
- The subject has a positive alcohol test and/or the subject has a history of alcohol abuse that could interfere with subject's participation in the study. ☐
- The subject has a positive urine drug test. ☐
- Positive serology test for human immunodeficiency virus (HIV) 1/2, Hepatitis B or Hepatitis C. ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

- 
- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☒
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

Result

No ☐  
Yes ☐  
Not Done ☐  
NA ☐

Exclusion Criterion Number

16



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

- As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐
- A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐
- The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐
- The subject has a body mass index (BMI)  $<18.5$  or  $\geq 32$  kg/m<sup>2</sup>. ☐
- As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐
- The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

- The subject has received medication (prescription or over-the-counter) within 14 days or within 5 half lives of the drug (whichever is longer) prior to the Admission Day (Day -2), which has an impact on CYP1A2 or CYP2A6 activity. ☐
- If a subject has received any medication (prescribed or over-the-counter) within 14 days prior to Screening or prior to the Admission Day (Day -2), it will be decided at the discretion of the Investigator or designee if these can potentially interfere with the study objectives or subject's safety. ☐
- Concomitant use of nonsteroidal anti-inflammatory drugs (NSAIDs) or acetylsalicylic acid. ☐
- The subject has a positive alcohol test and/or the subject has a history of alcohol abuse that could interfere with subject's participation in the study. ☐
- The subject has a positive urine drug test. ☐
- Positive serology test for human immunodeficiency virus (HIV) 1/2, Hepatitis B or Hepatitis C. ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

- 
- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☒
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

Result

No ☐  
Yes ☐  
Not Done ☐  
NA ☐

Exclusion Criterion Number

17



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

- As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐
- A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐
- The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐
- The subject has a body mass index (BMI)  $<18.5$  or  $\geq 32$  kg/m<sup>2</sup>. ☐
- As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐
- The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

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The subject has received ☐  
medication (prescription or  
over-the-counter) within  
14 days or within 5 half  
lives of the drug  
(whichever is longer) prior  
to the Admission Day (Day  
-2), which has an impact  
on CYP1A2 or CYP2A6  
activity.

If a subject has received ☐  
any medication (prescribed  
or over-the-counter) within  
14 days prior to Screening  
or prior to the Admission  
Day (Day -2), it will be  
decided at the discretion of  
the Investigator or  
designee if these can  
potentially interfere with  
the study objectives or  
subject's safety.

Concomitant use of ☐  
nonsteroidal  
anti-inflammatory drugs  
(NSAIDs) or acetylsalicylic  
acid.

The subject has a positive ☐  
alcohol test and/or the  
subject has a history of  
alcohol abuse that could  
interfere with subject's  
participation in the study.

The subject has a positive ☐  
urine drug test.

Positive serology test for ☐  
human immunodeficiency  
virus (HIV) 1/2, Hepatitis B  
or Hepatitis C.



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

- 
- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☒
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-



**Final version 5.0 (Main CRF): Case Book**

**Project Name: ZRHR-REXC-03-EU**

**Form: Exclusion Criteria-Screen Failure**

**Generated On: 28 Oct 2013 17:39:05**

---

Result

No ☐

Yes ☐

Not Done ☐

NA ☐

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Exclusion Criterion Number

18

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Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

- As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐
- A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐
- The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐
- The subject has a body mass index (BMI)  $<18.5$  or  $\geq 32$  kg/m<sup>2</sup>. ☐
- As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐
- The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

The subject has received ☐  
medication (prescription or  
over-the-counter) within  
14 days or within 5 half  
lives of the drug  
(whichever is longer) prior  
to the Admission Day (Day  
-2), which has an impact  
on CYP1A2 or CYP2A6  
activity.

If a subject has received ☐  
any medication (prescribed  
or over-the-counter) within  
14 days prior to Screening  
or prior to the Admission  
Day (Day -2), it will be  
decided at the discretion of  
the Investigator or  
designee if these can  
potentially interfere with  
the study objectives or  
subject's safety.

Concomitant use of ☐  
nonsteroidal  
anti-inflammatory drugs  
(NSAIDs) or acetylsalicylic  
acid.

The subject has a positive ☐  
alcohol test and/or the  
subject has a history of  
alcohol abuse that could  
interfere with subject's  
participation in the study.

The subject has a positive ☐  
urine drug test.

Positive serology test for ☐  
human immunodeficiency  
virus (HIV) 1/2, Hepatitis B  
or Hepatitis C.



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

- 
- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☒
- Subject does not agree to use an acceptable method of effective contraception ☐
-



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

Result

No ☐  
Yes ☐  
Not Done ☐  
NA ☐

Exclusion Criterion Number

19



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

- As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐
- A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐
- The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐
- The subject has a body mass index (BMI)  $<18.5$  or  $\geq 32$  kg/m<sup>2</sup>. ☐
- As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐
- The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

- The subject has received ☐  
medication (prescription or  
over-the-counter) within  
14 days or within 5 half  
lives of the drug  
(whichever is longer) prior  
to the Admission Day (Day  
-2), which has an impact  
on CYP1A2 or CYP2A6  
activity.
- If a subject has received ☐  
any medication (prescribed  
or over-the-counter) within  
14 days prior to Screening  
or prior to the Admission  
Day (Day -2), it will be  
decided at the discretion of  
the Investigator or  
designee if these can  
potentially interfere with  
the study objectives or  
subject's safety.
- Concomitant use of ☐  
nonsteroidal  
anti-inflammatory drugs  
(NSAIDs) or acetylsalicylic  
acid.
- The subject has a positive ☐  
alcohol test and/or the  
subject has a history of  
alcohol abuse that could  
interfere with subject's  
participation in the study.
- The subject has a positive ☐  
urine drug test.
- Positive serology test for ☐  
human immunodeficiency  
virus (HIV) 1/2, Hepatitis B  
or Hepatitis C.



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

- 
- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☒
-





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Screen Failure  
Generated On: 28 Oct 2013 17:39:05

Result

No ☐  
Yes ☐  
Not Done ☐  
NA ☐



**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: Exclusion Criteria-Admission**  
**Generated On: 28 Oct 2013 17:39:05**

\_\_\_\_\_  
\*If any has been answered Yes, subject must not be included in the study.  
\_\_\_\_\_  
\_\_\_\_\_

\_\_\_\_\_  
Exclusion Criterion Number 1  
\_\_\_\_\_



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

- As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☒
- A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐
- The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐
- The subject has a body mass index (BMI)  $<18.5$  or  $\geq 32$  kg/m<sup>2</sup>. ☐
- As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐
- The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

The subject has received ☐  
medication (prescription or  
over-the-counter) within  
14 days or within 5 half  
lives of the drug  
(whichever is longer) prior  
to the Admission Day (Day  
-2), which has an impact  
on CYP1A2 or CYP2A6  
activity.

If a subject has received ☐  
any medication (prescribed  
or over-the-counter) within  
14 days prior to Screening  
or prior to the Admission  
Day (Day -2), it will be  
decided at the discretion of  
the Investigator or  
designee if these can  
potentially interfere with  
the study objectives or  
subject's safety.

Concomitant use of ☐  
nonsteroidal  
anti-inflammatory drugs  
(NSAIDs) or acetylsalicylic  
acid.

The subject has a positive ☐  
alcohol test and/or the  
subject has a history of  
alcohol abuse that could  
interfere with subject's  
participation in the study.

The subject has a positive ☐  
urine drug test.

Positive serology test for ☐  
human immunodeficiency  
virus (HIV) 1/2, Hepatitis B  
or Hepatitis C.



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

- 
- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

Result

No ☐  
Yes ☐  
NA ☐

Exclusion Criterion Number

3





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

- As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐
- A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐
- The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☒
- The subject has a body mass index (BMI) <18.5 or  $\geq 32$  kg/m<sup>2</sup>. ☐
- As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐
- The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

- The subject has received medication (prescription or over-the-counter) within 14 days or within 5 half lives of the drug (whichever is longer) prior to the Admission Day (Day -2), which has an impact on CYP1A2 or CYP2A6 activity. ☐
- If a subject has received any medication (prescribed or over-the-counter) within 14 days prior to Screening or prior to the Admission Day (Day -2), it will be decided at the discretion of the Investigator or designee if these can potentially interfere with the study objectives or subject's safety. ☐
- Concomitant use of nonsteroidal anti-inflammatory drugs (NSAIDs) or acetylsalicylic acid. ☐
- The subject has a positive alcohol test and/or the subject has a history of alcohol abuse that could interfere with subject's participation in the study. ☐
- The subject has a positive urine drug test. ☐
- Positive serology test for human immunodeficiency virus (HIV) 1/2, Hepatitis B or Hepatitis C. ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

- 
- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

Result

No ☐  
Yes ☐  
NA ☐

Exclusion Criterion Number

4



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐

A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐

The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐

The subject has a body mass index (BMI)  $<18.5$  or  $\geq 32$  kg/m<sup>2</sup>. ☒

As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐

The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Exclusion Criteria-Admission

Generated On: 28 Oct 2013 17:39:05

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The subject has received ☐  
medication (prescription or  
over-the-counter) within  
14 days or within 5 half  
lives of the drug  
(whichever is longer) prior  
to the Admission Day (Day  
-2), which has an impact  
on CYP1A2 or CYP2A6  
activity.

If a subject has received ☐  
any medication (prescribed  
or over-the-counter) within  
14 days prior to Screening  
or prior to the Admission  
Day (Day -2), it will be  
decided at the discretion of  
the Investigator or  
designee if these can  
potentially interfere with  
the study objectives or  
subject's safety.

Concomitant use of ☐  
nonsteroidal  
anti-inflammatory drugs  
(NSAIDs) or acetylsalicylic  
acid.

The subject has a positive ☐  
alcohol test and/or the  
subject has a history of  
alcohol abuse that could  
interfere with subject's  
participation in the study.

The subject has a positive ☐  
urine drug test.

Positive serology test for ☐  
human immunodeficiency  
virus (HIV) 1/2, Hepatitis B  
or Hepatitis C.





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

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- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-



**Final version 5.0 (Main CRF): Case Book**

**Project Name: ZRHR-REXC-03-EU**

**Form: Exclusion Criteria-Admission**

**Generated On: 28 Oct 2013 17:39:05**

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Result

No ☐

Yes ☐

NA ☐

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Exclusion Criterion Number

5

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Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

- As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐
- A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐
- The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐
- The subject has a body mass index (BMI)  $<18.5$  or  $\geq 32$  kg/m<sup>2</sup>. ☐
- As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☒
- The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Exclusion Criteria-Admission

Generated On: 28 Oct 2013 17:39:05

---

The subject has received ☐  
medication (prescription or  
over-the-counter) within  
14 days or within 5 half  
lives of the drug  
(whichever is longer) prior  
to the Admission Day (Day  
-2), which has an impact  
on CYP1A2 or CYP2A6  
activity.

If a subject has received ☐  
any medication (prescribed  
or over-the-counter) within  
14 days prior to Screening  
or prior to the Admission  
Day (Day -2), it will be  
decided at the discretion of  
the Investigator or  
designee if these can  
potentially interfere with  
the study objectives or  
subject's safety.

Concomitant use of ☐  
nonsteroidal  
anti-inflammatory drugs  
(NSAIDs) or acetylsalicylic  
acid.

The subject has a positive ☐  
alcohol test and/or the  
subject has a history of  
alcohol abuse that could  
interfere with subject's  
participation in the study.

The subject has a positive ☐  
urine drug test.

Positive serology test for ☐  
human immunodeficiency  
virus (HIV) 1/2, Hepatitis B  
or Hepatitis C.



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

---

- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

Result

No ☐  
Yes ☐  
NA ☐

Exclusion Criterion Number

6





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐

A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐

The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐

The subject has a body mass index (BMI) <18.5 or  $\geq 32$  kg/m<sup>2</sup>. ☐

As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐

The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☒



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

- The subject has received medication (prescription or over-the-counter) within 14 days or within 5 half lives of the drug (whichever is longer) prior to the Admission Day (Day -2), which has an impact on CYP1A2 or CYP2A6 activity. ☐
- If a subject has received any medication (prescribed or over-the-counter) within 14 days prior to Screening or prior to the Admission Day (Day -2), it will be decided at the discretion of the Investigator or designee if these can potentially interfere with the study objectives or subject's safety. ☐
- Concomitant use of nonsteroidal anti-inflammatory drugs (NSAIDs) or acetylsalicylic acid. ☐
- The subject has a positive alcohol test and/or the subject has a history of alcohol abuse that could interfere with subject's participation in the study. ☐
- The subject has a positive urine drug test. ☐
- Positive serology test for human immunodeficiency virus (HIV) 1/2, Hepatitis B or Hepatitis C. ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

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- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

Result

No ☐  
Yes ☐  
NA ☐

Exclusion Criterion Number

7



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐

A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐

The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐

The subject has a body mass index (BMI) <18.5 or  $\geq 32$  kg/m<sup>2</sup>. ☐

As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐

The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

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- If a subject has received any medication (prescribed or over-the-counter) within 14 days prior to Screening or prior to the Admission Day (Day -2), it will be decided at the discretion of the Investigator or designee if these can potentially interfere with the study objectives or subject's safety. ☐
- Concomitant use of nonsteroidal anti-inflammatory drugs (NSAIDs) or acetylsalicylic acid. ☐
- The subject has a positive alcohol test and/or the subject has a history of alcohol abuse that could interfere with subject's participation in the study. ☐
- The subject has a positive urine drug test. ☐
- Positive serology test for human immunodeficiency virus (HIV) 1/2, Hepatitis B or Hepatitis C. ☐





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

- 
- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

Result

No ☐  
Yes ☐  
NA ☐

Exclusion Criterion Number

8



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

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- The subject has a body mass index (BMI)  $<18.5$  or  $\geq 32$  kg/m<sup>2</sup>. ☐
- As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐
- The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Exclusion Criteria-Admission

Generated On: 28 Oct 2013 17:39:05

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medication (prescription or  
over-the-counter) within  
14 days or within 5 half  
lives of the drug  
(whichever is longer) prior  
to the Admission Day (Day  
-2), which has an impact  
on CYP1A2 or CYP2A6  
activity.

If a subject has received ☒  
any medication (prescribed  
or over-the-counter) within  
14 days prior to Screening  
or prior to the Admission  
Day (Day -2), it will be  
decided at the discretion of  
the Investigator or  
designee if these can  
potentially interfere with  
the study objectives or  
subject's safety.

Concomitant use of ☐  
nonsteroidal  
anti-inflammatory drugs  
(NSAIDs) or acetylsalicylic  
acid.

The subject has a positive ☐  
alcohol test and/or the  
subject has a history of  
alcohol abuse that could  
interfere with subject's  
participation in the study.

The subject has a positive ☐  
urine drug test.

Positive serology test for ☐  
human immunodeficiency  
virus (HIV) 1/2, Hepatitis B  
or Hepatitis C.



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

- 
- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
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- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

Result

No ☐  
Yes ☐  
NA ☐

Exclusion Criterion Number

9





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

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- As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐
- The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

The subject has received ☐  
medication (prescription or  
over-the-counter) within  
14 days or within 5 half  
lives of the drug  
(whichever is longer) prior  
to the Admission Day (Day  
-2), which has an impact  
on CYP1A2 or CYP2A6  
activity.

If a subject has received ☐  
any medication (prescribed  
or over-the-counter) within  
14 days prior to Screening  
or prior to the Admission  
Day (Day -2), it will be  
decided at the discretion of  
the Investigator or  
designee if these can  
potentially interfere with  
the study objectives or  
subject's safety.

Concomitant use of ☒  
nonsteroidal  
anti-inflammatory drugs  
(NSAIDs) or acetylsalicylic  
acid.

The subject has a positive ☐  
alcohol test and/or the  
subject has a history of  
alcohol abuse that could  
interfere with subject's  
participation in the study.

The subject has a positive ☐  
urine drug test.

Positive serology test for ☐  
human immunodeficiency  
virus (HIV) 1/2, Hepatitis B  
or Hepatitis C.



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

- 
- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

Result

No ☐  
Yes ☐  
NA ☐

Exclusion Criterion Number

10



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐

A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐

The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐

The subject has a body mass index (BMI)  $<18.5$  or  $\geq 32$  kg/m<sup>2</sup>. ☐

As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐

The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

The subject has received ☐  
medication (prescription or  
over-the-counter) within  
14 days or within 5 half  
lives of the drug  
(whichever is longer) prior  
to the Admission Day (Day  
-2), which has an impact  
on CYP1A2 or CYP2A6  
activity.

If a subject has received ☐  
any medication (prescribed  
or over-the-counter) within  
14 days prior to Screening  
or prior to the Admission  
Day (Day -2), it will be  
decided at the discretion of  
the Investigator or  
designee if these can  
potentially interfere with  
the study objectives or  
subject's safety.

Concomitant use of ☐  
nonsteroidal  
anti-inflammatory drugs  
(NSAIDs) or acetylsalicylic  
acid.

The subject has a positive ☒  
alcohol test and/or the  
subject has a history of  
alcohol abuse that could  
interfere with subject's  
participation in the study.

The subject has a positive ☐  
urine drug test.

Positive serology test for ☐  
human immunodeficiency  
virus (HIV) 1/2, Hepatitis B  
or Hepatitis C.





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

- 
- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

---

Result

No ☐  
Yes ☐  
NA ☐

---

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Exclusion Criterion Number

11

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Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

---

Exclusion Criterion

- As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐
- A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐
- The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐
- The subject has a body mass index (BMI)  $<18.5$  or  $\geq 32$  kg/m<sup>2</sup>. ☐
- As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐
- The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

The subject has received ☐  
medication (prescription or  
over-the-counter) within  
14 days or within 5 half  
lives of the drug  
(whichever is longer) prior  
to the Admission Day (Day  
-2), which has an impact  
on CYP1A2 or CYP2A6  
activity.

If a subject has received ☐  
any medication (prescribed  
or over-the-counter) within  
14 days prior to Screening  
or prior to the Admission  
Day (Day -2), it will be  
decided at the discretion of  
the Investigator or  
designee if these can  
potentially interfere with  
the study objectives or  
subject's safety.

Concomitant use of ☐  
nonsteroidal  
anti-inflammatory drugs  
(NSAIDs) or acetylsalicylic  
acid.

The subject has a positive ☐  
alcohol test and/or the  
subject has a history of  
alcohol abuse that could  
interfere with subject's  
participation in the study.

The subject has a positive ☒  
urine drug test.

Positive serology test for ☐  
human immunodeficiency  
virus (HIV) 1/2, Hepatitis B  
or Hepatitis C.



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

- 
- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-



**Final version 5.0 (Main CRF): Case Book**

**Project Name: ZRHR-REXC-03-EU**

**Form: Exclusion Criteria-Admission**

**Generated On: 28 Oct 2013 17:39:05**

---

Result

No ☐

Yes ☐

NA ☐

---

---

Exclusion Criterion Number

13

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Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

- As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐
- A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐
- The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐
- The subject has a body mass index (BMI)  $<18.5$  or  $\geq 32$  kg/m<sup>2</sup>. ☐
- As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐
- The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

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The subject has received ☐  
medication (prescription or  
over-the-counter) within  
14 days or within 5 half  
lives of the drug  
(whichever is longer) prior  
to the Admission Day (Day  
-2), which has an impact  
on CYP1A2 or CYP2A6  
activity.

If a subject has received ☐  
any medication (prescribed  
or over-the-counter) within  
14 days prior to Screening  
or prior to the Admission  
Day (Day -2), it will be  
decided at the discretion of  
the Investigator or  
designee if these can  
potentially interfere with  
the study objectives or  
subject's safety.

Concomitant use of ☐  
nonsteroidal  
anti-inflammatory drugs  
(NSAIDs) or acetylsalicylic  
acid.

The subject has a positive ☐  
alcohol test and/or the  
subject has a history of  
alcohol abuse that could  
interfere with subject's  
participation in the study.

The subject has a positive ☐  
urine drug test.

Positive serology test for ☐  
human immunodeficiency  
virus (HIV) 1/2, Hepatitis B  
or Hepatitis C.



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

---

- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☒
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☐
-



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

Result

No ☐  
Yes ☐  
NA ☐

Exclusion Criterion Number

18



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

- As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐
- A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐
- The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐
- The subject has a body mass index (BMI)  $<18.5$  or  $\geq 32$  kg/m<sup>2</sup>. ☐
- As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐
- The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Exclusion Criteria-Admission

Generated On: 28 Oct 2013 17:39:05

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The subject has received ☐  
medication (prescription or  
over-the-counter) within  
14 days or within 5 half  
lives of the drug  
(whichever is longer) prior  
to the Admission Day (Day  
-2), which has an impact  
on CYP1A2 or CYP2A6  
activity.

If a subject has received ☐  
any medication (prescribed  
or over-the-counter) within  
14 days prior to Screening  
or prior to the Admission  
Day (Day -2), it will be  
decided at the discretion of  
the Investigator or  
designee if these can  
potentially interfere with  
the study objectives or  
subject's safety.

Concomitant use of ☐  
nonsteroidal  
anti-inflammatory drugs  
(NSAIDs) or acetylsalicylic  
acid.

The subject has a positive ☐  
alcohol test and/or the  
subject has a history of  
alcohol abuse that could  
interfere with subject's  
participation in the study.

The subject has a positive ☐  
urine drug test.

Positive serology test for ☐  
human immunodeficiency  
virus (HIV) 1/2, Hepatitis B  
or Hepatitis C.





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

- 
- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☒
- Subject does not agree to use an acceptable method of effective contraception ☐
-



**Final version 5.0 (Main CRF): Case Book**

**Project Name: ZRHR-REXC-03-EU**

**Form: Exclusion Criteria-Admission**

**Generated On: 28 Oct 2013 17:39:05**

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Result

No ☐

Yes ☐

NA ☐

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Exclusion Criterion Number

19

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Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

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Exclusion Criterion

- As per Investigator judgment, the subject cannot participate in the study for any reason (e.g., medical, psychiatric and/or social reason). ☐
- A subject who is legally incompetent, physically or mentally incapable of giving consent. ☐
- The subject has medical condition requiring smoking cessation, or clinically relevant diseases in the judgment of the Investigator. ☐
- The subject has a body mass index (BMI)  $<18.5$  or  $\geq 32$  kg/m<sup>2</sup>. ☐
- As per Investigator or designee judgment, the subject has medical conditions which require or will require in the course of the study, a medical intervention (e.g., start of treatment, surgery, hospitalization) which may interfere with the study participation and/or study results. ☐
- The subject has used nicotine containing products other than commercially available CC as well as electronic cigarettes and similar devices, within 4 weeks prior to assessment. ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

- The subject has received medication (prescription or over-the-counter) within 14 days or within 5 half lives of the drug (whichever is longer) prior to the Admission Day (Day -2), which has an impact on CYP1A2 or CYP2A6 activity. ☐
- If a subject has received any medication (prescribed or over-the-counter) within 14 days prior to Screening or prior to the Admission Day (Day -2), it will be decided at the discretion of the Investigator or designee if these can potentially interfere with the study objectives or subject's safety. ☐
- Concomitant use of nonsteroidal anti-inflammatory drugs (NSAIDs) or acetylsalicylic acid. ☐
- The subject has a positive alcohol test and/or the subject has a history of alcohol abuse that could interfere with subject's participation in the study. ☐
- The subject has a positive urine drug test. ☐
- Positive serology test for human immunodeficiency virus (HIV) 1/2, Hepatitis B or Hepatitis C. ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

---

- Donation or receipt of whole blood or blood products within 3 months prior to Admission. ☐
- The subject is a current or former employee of the tobacco industry or of their first-degree relatives (parent, sibling, child). ☐
- The subject is an employee of the investigational site or any other parties involved in the study or of their first-degree relatives (parent, sibling, or child). ☐
- The subject has participated in a clinical study within 3 months prior to the Screening Visit. ☐
- The subject has previously participated in the same study at a different time (i.e. each subject can be included in the study population only once). ☐
- Subject is pregnant (does not have negative pregnancy tests at Screening and at Admission) or is breast feeding. ☐
- Subject does not agree to use an acceptable method of effective contraception ☒
-



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Exclusion Criteria-Admission  
Generated On: 28 Oct 2013 17:39:05

Result

No ☐  
Yes ☐  
NA ☐





**Final version 5.0 (Main CRF): Case Book**

**Project Name: ZRHR-REXC-03-EU**

**Form: Randomization**

**Generated On: 28 Oct 2013 17:39:05**

Randomization number (4 digits) \_\_\_\_\_

Allocation Arm

THS 2.2 ☐

CC ☐

SA ☐

Cigarette Consumption

10 – 19 conventional  
cigarettes  
per day ☐

Greater than 19  
conventional  
cigarettes per day ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Demographics  
Generated On: 28 Oct 2013 17:39:05

Date of Birth

Fixed Unit:  
DD/MMM/YYYY

Sex

Male ☐  
Female ☐

Race

White ☒  
Black or African American ☐  
American Indian or Alaska  
Native ☐  
Asian ☐  
Native Hawaiian or Other  
Pacific Islander ☐  
Other ☐

Other, specify

Ethnicity

Caucasian ☐  
Not Caucasian ☐Date the Subject signed the Main  
Informed ConsentFixed Unit:  
DD/MMM/YYYY

Time the Subject signed the Main Informed Consent

Fixed Unit:  
hour:min 24-hour clock



**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: Demographics**  
**Generated On: 28 Oct 2013 17:39:05**

Age(Derived)



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Medical History/Concomitant Disease  
Generated On: 28 Oct 2013 17:39:05

Date of collection

Fixed Unit:  
DD/MMM/YYYY

Has the subject experienced any past and/ or  
concomitant diseases?

No ☐  
Yes ☐

Category for Medical History

Medical History

Number

Diagnosis Description

Onset Date  
DD/MMM/YYYY

Stop Date  
DD/MMM/YYYY

Ongoing?

H\_NOW (Derived):



**Final version 5.0 (Main CRF): Case Book**

**Project Name: ZRHR-REXC-03-EU**

**Form: Vital Signs Screening**

**Generated On: 28 Oct 2013 17:39:05**

Were Vitals Signs assessed?

No ☐  
Yes ☐

If No, please specify the reason: \_\_\_\_\_

Has the subject smoked within 15 minutes prior to  
assessment

No ☐  
Yes ☐

Date of assessment

Fixed Unit:  
DD/MM/YYYY

Time of assessment

Fixed Unit:  
hour:min 24-hour clock

Pulse rate

Fixed Unit:  
beats per minute

Respiratory rate

Fixed Unit:  
breaths per minute

Blood Pressure (systolic)

Fixed Unit:  
mmHg



**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: Vital Signs Screening**  
**Generated On: 28 Oct 2013 17:39:05**

Blood Pressure (diastolic)

Fixed Unit:  
mmHg

Vital Signs Position of Subject

Sitting ☐  
Standing ☐  
Supine ☒





Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Vital Signs

Generated On: 28 Oct 2013 17:39:05

Were Vitals Signs assessed?

No ☐

Yes ☐

If No, please specify the reason:

Has the subject smoked within 15 minutes prior to assessment

No ☐

Yes ☐

Time of assessment

Fixed Unit:  
hour:min 24-hour clock

Pulse rate

Fixed Unit:  
beats per minute

Respiratory rate

Fixed Unit:  
breaths per minute

Blood Pressure (systolic)

Fixed Unit:  
mmHg

Blood Pressure (diastolic)

Fixed Unit:  
mmHg



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Vital Signs  
Generated On: 28 Oct 2013 17:39:05

Vital Signs Position of Subject

Sitting ☐  
Standing ☐  
Supine ☒



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination screening

Generated On: 28 Oct 2013 17:39:05

Was the physical examination performed?

No ☐

Yes ☐

If No, please specify the reason:

Date of assessment

Fixed Unit:  
DD/MMM/YYYY

System

General Appearance ☒

HEENT ☐

(head, eyes, ears, nose,  
throat)

Thyroid Gland ☐

Heart ☐

Chest ☐

Lungs ☐

Gastrointestinal ☐

Cardiovascular System ☐

Neurologic ☐

Skin ☐

Back ☐

Musculoskeletal ☐

Abdomen ☐

Dentition ☐

Other ☐

Other, Specify



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination screening

Generated On: 28 Oct 2013 17:39:05

Outcome

Normal ☐

Abnormal ☐

Abnormal, please specify

Clinically significant

No ☐

Yes ☐

Not Done

Not Done; please specify the reason:

System

General Appearance ☐

HEENT ☒  
(head, eyes, ears, nose,  
throat)

Thyroid Gland ☐

Heart ☐

Chest ☐

Lungs ☐

Gastrointestinal ☐

Cardiovascular System ☐

Neurologic ☐

Skin ☐

Back ☐

Musculoskeletal ☐

Abdomen ☐

Dentition ☐

Other ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Physical Examination screening  
Generated On: 28 Oct 2013 17:39:05

Other, Specify \_\_\_\_\_

Outcome

Normal ☐

Abnormal ☐

Abnormal, please specify \_\_\_\_\_

Clinically significant

No ☐

Yes ☐

Not Done \_\_\_\_\_

Not Done; please specify the reason: \_\_\_\_\_



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination screening

Generated On: 28 Oct 2013 17:39:05

System

General Appearance ☐

HEENT ☐

(head, eyes, ears, nose,  
throat)

Thyroid Gland ☒

Heart ☐

Chest ☐

Lungs ☐

Gastrointestinal ☐

Cardiovascular System ☐

Neurologic ☐

Skin ☐

Back ☐

Musculoskeletal ☐

Abdomen ☐

Dentition ☐

Other ☐

Other, Specify

Outcome

Normal ☐

Abnormal ☐

Abnormal, please specify

Clinically significant

No ☐

Yes ☐

Not Done





Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination screening

Generated On: 28 Oct 2013 17:39:05

Not Done; please specify the reason:

System

General Appearance ☐

HEENT ☐

(head, eyes, ears, nose,  
throat)

Thyroid Gland ☐

Heart ☒

Chest ☐

Lungs ☐

Gastrointestinal ☐

Cardiovascular System ☐

Neurologic ☐

Skin ☐

Back ☐

Musculoskeletal ☐

Abdomen ☐

Dentition ☐

Other ☐

Other, Specify

Outcome

Normal ☐

Abnormal ☐

Abnormal, please specify

Clinically significant

No ☐

Yes ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination screening

Generated On: 28 Oct 2013 17:39:05

Not Done

Not Done; please specify the reason:

System

General Appearance ☐

HEENT ☐

(head, eyes, ears, nose,  
throat)

Thyroid Gland ☐

Heart ☐

Chest ☒

Lungs ☐

Gastrointestinal ☐

Cardiovascular System ☐

Neurologic ☐

Skin ☐

Back ☐

Musculoskeletal ☐

Abdomen ☐

Dentition ☐

Other ☐

Other, Specify

Outcome

Normal ☐

Abnormal ☐

Abnormal, please specify



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination screening

Generated On: 28 Oct 2013 17:39:05

Clinically significant No ☐  
Yes ☐

Not Done \_\_\_\_\_

Not Done; please specify the reason: \_\_\_\_\_

System	General Appearance <input type="checkbox"/>
	HEENT <input type="checkbox"/>
	(head, eyes, ears, nose, throat)
	Thyroid Gland <input type="checkbox"/>
	Heart <input type="checkbox"/>
	Chest <input type="checkbox"/>
	Lungs <input checked="" type="checkbox"/>
	Gastrointestinal <input type="checkbox"/>
	Cardiovascular System <input type="checkbox"/>
	Neurologic <input type="checkbox"/>
	Skin <input type="checkbox"/>
	Back <input type="checkbox"/>
	Musculoskeletal <input type="checkbox"/>
	Abdomen <input type="checkbox"/>
	Dentition <input type="checkbox"/>
	Other <input type="checkbox"/>

Other, Specify \_\_\_\_\_

Outcome Normal ☐  
Abnormal ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination screening

Generated On: 28 Oct 2013 17:39:05

Abnormal, please specify \_\_\_\_\_

Clinically significant

No ☐

Yes ☐

Not Done \_\_\_\_\_

Not Done; please specify the reason: \_\_\_\_\_

System

General Appearance ☐

HEENT ☐

(head, eyes, ears, nose,  
throat)

Thyroid Gland ☐

Heart ☐

Chest ☐

Lungs ☐

Gastrointestinal ☒

Cardiovascular System ☐

Neurologic ☐

Skin ☐

Back ☐

Musculoskeletal ☐

Abdomen ☐

Dentition ☐

Other ☐

Other, Specify \_\_\_\_\_



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination screening

Generated On: 28 Oct 2013 17:39:05

Outcome Normal ☐  
Abnormal ☐

Abnormal, please specify \_\_\_\_\_

Clinically significant No ☐  
Yes ☐

Not Done \_\_\_\_\_

Not Done; please specify the reason: \_\_\_\_\_

System General Appearance ☐  
HEENT ☐  
(head, eyes, ears, nose,  
throat)  
Thyroid Gland ☐  
Heart ☐  
Chest ☐  
Lungs ☐  
Gastrointestinal ☐  
Cardiovascular System ☒  
Neurologic ☐  
Skin ☐  
Back ☐  
Musculoskeletal ☐  
Abdomen ☐  
Dentition ☐  
Other ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Physical Examination screening  
Generated On: 28 Oct 2013 17:39:05

Other, Specify \_\_\_\_\_

Outcome

Normal ☐

Abnormal ☐

Abnormal, please specify \_\_\_\_\_

Clinically significant

No ☐

Yes ☐

Not Done \_\_\_\_\_

Not Done; please specify the reason: \_\_\_\_\_





Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination screening

Generated On: 28 Oct 2013 17:39:05

System

General Appearance ☐

HEENT ☐

(head, eyes, ears, nose,  
throat)

Thyroid Gland ☐

Heart ☐

Chest ☐

Lungs ☐

Gastrointestinal ☐

Cardiovascular System ☐

Neurologic ☒

Skin ☐

Back ☐

Musculoskeletal ☐

Abdomen ☐

Dentition ☐

Other ☐

Other, Specify

Outcome

Normal ☐

Abnormal ☐

Abnormal, please specify

Clinically significant

No ☐

Yes ☐

Not Done



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination screening

Generated On: 28 Oct 2013 17:39:05

Not Done; please specify the reason:

System

General Appearance ☐

HEENT ☐

(head, eyes, ears, nose,  
throat)

Thyroid Gland ☐

Heart ☐

Chest ☐

Lungs ☐

Gastrointestinal ☐

Cardiovascular System ☐

Neurologic ☐

Skin ☒

Back ☐

Musculoskeletal ☐

Abdomen ☐

Dentition ☐

Other ☐

Other, Specify

Outcome

Normal ☐

Abnormal ☐

Abnormal, please specify

Clinically significant

No ☐

Yes ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination screening

Generated On: 28 Oct 2013 17:39:05

Not Done

Not Done; please specify the reason:

System

General Appearance ☐

HEENT ☐

(head, eyes, ears, nose,  
throat)

Thyroid Gland ☐

Heart ☐

Chest ☐

Lungs ☐

Gastrointestinal ☐

Cardiovascular System ☐

Neurologic ☐

Skin ☐

Back ☒

Musculoskeletal ☐

Abdomen ☐

Dentition ☐

Other ☐

Other, Specify

Outcome

Normal ☐

Abnormal ☐

Abnormal, please specify



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination screening

Generated On: 28 Oct 2013 17:39:05

Clinically significant No ☐  
Yes ☐

Not Done \_\_\_\_\_

Not Done; please specify the reason: \_\_\_\_\_

System	General Appearance <input type="checkbox"/>
	HEENT <input type="checkbox"/>
	(head, eyes, ears, nose, throat)
	Thyroid Gland <input type="checkbox"/>
	Heart <input type="checkbox"/>
	Chest <input type="checkbox"/>
	Lungs <input type="checkbox"/>
	Gastrointestinal <input type="checkbox"/>
	Cardiovascular System <input type="checkbox"/>
	Neurologic <input type="checkbox"/>
	Skin <input type="checkbox"/>
	Back <input type="checkbox"/>
	Musculoskeletal <input checked="" type="checkbox"/>
	Abdomen <input type="checkbox"/>
	Dentition <input type="checkbox"/>
	Other <input type="checkbox"/>

Other, Specify \_\_\_\_\_

Outcome Normal ☐  
Abnormal ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination screening

Generated On: 28 Oct 2013 17:39:05

Abnormal, please specify \_\_\_\_\_

Clinically significant

No ☐

Yes ☐

Not Done \_\_\_\_\_

Not Done; please specify the reason: \_\_\_\_\_

System

General Appearance ☐

HEENT ☐

(head, eyes, ears, nose,  
throat)

Thyroid Gland ☐

Heart ☐

Chest ☐

Lungs ☐

Gastrointestinal ☐

Cardiovascular System ☐

Neurologic ☐

Skin ☐

Back ☐

Musculoskeletal ☐

Abdomen ☒

Dentition ☐

Other ☐

Other, Specify \_\_\_\_\_



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination screening

Generated On: 28 Oct 2013 17:39:05

Outcome Normal ☐  
Abnormal ☐

Abnormal, please specify \_\_\_\_\_

Clinically significant No ☐  
Yes ☐

Not Done \_\_\_\_\_

Not Done; please specify the reason: \_\_\_\_\_

System General Appearance ☐  
HEENT ☐  
(head, eyes, ears, nose,  
throat)  
Thyroid Gland ☐  
Heart ☐  
Chest ☐  
Lungs ☐  
Gastrointestinal ☐  
Cardiovascular System ☐  
Neurologic ☐  
Skin ☐  
Back ☐  
Musculoskeletal ☐  
Abdomen ☐  
Dentition ☒  
Other ☐





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Physical Examination screening  
Generated On: 28 Oct 2013 17:39:05

Other, Specify \_\_\_\_\_

Outcome

Normal ☐

Abnormal ☐

Abnormal, please specify \_\_\_\_\_

Clinically significant

No ☐

Yes ☐

Not Done \_\_\_\_\_

Not Done; please specify the reason: \_\_\_\_\_



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination screening

Generated On: 28 Oct 2013 17:39:05

System

General Appearance ☐

HEENT ☐

(head, eyes, ears, nose,  
throat)

Thyroid Gland ☐

Heart ☐

Chest ☐

Lungs ☐

Gastrointestinal ☐

Cardiovascular System ☐

Neurologic ☐

Skin ☐

Back ☐

Musculoskeletal ☐

Abdomen ☐

Dentition ☐

Other ☒

Other, Specify

Outcome

Normal ☐

Abnormal ☐

Abnormal, please specify

Clinically significant

No ☐

Yes ☐

Not Done



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination screening

Generated On: 28 Oct 2013 17:39:05

Not Done; please specify the reason:

System

General Appearance ☐

HEENT ☐

(head, eyes, ears, nose,  
throat)

Thyroid Gland ☐

Heart ☐

Chest ☐

Lungs ☐

Gastrointestinal ☐

Cardiovascular System ☐

Neurologic ☐

Skin ☐

Back ☐

Musculoskeletal ☐

Abdomen ☐

Dentition ☐

Other ☒

Other, Specify

Outcome

Normal ☐

Abnormal ☐

Abnormal, please specify

Clinically significant

No ☐

Yes ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination screening

Generated On: 28 Oct 2013 17:39:05

Not Done

Not Done; please specify the reason:

System

General Appearance ☐

HEENT ☐

(head, eyes, ears, nose,  
throat)

Thyroid Gland ☐

Heart ☐

Chest ☐

Lungs ☐

Gastrointestinal ☐

Cardiovascular System ☐

Neurologic ☐

Skin ☐

Back ☐

Musculoskeletal ☐

Abdomen ☐

Dentition ☐

Other ☒

Other, Specify

Outcome

Normal ☐

Abnormal ☐

Abnormal, please specify



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination screening

Generated On: 28 Oct 2013 17:39:05

Clinically significant No ☐  
Yes ☐

Not Done \_\_\_\_\_

Not Done; please specify the reason: \_\_\_\_\_

System General Appearance ☐  
HEENT ☐  
(head, eyes, ears, nose, throat)  
Thyroid Gland ☐  
Heart ☐  
Chest ☐  
Lungs ☐  
Gastrointestinal ☐  
Cardiovascular System ☐  
Neurologic ☐  
Skin ☐  
Back ☐  
Musculoskeletal ☐  
Abdomen ☐  
Dentition ☐  
Other ☒

Other, Specify \_\_\_\_\_

Outcome Normal ☐  
Abnormal ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination screening

Generated On: 28 Oct 2013 17:39:05

Abnormal, please specify \_\_\_\_\_

Clinically significant

No ☐

Yes ☐

Not Done \_\_\_\_\_

Not Done; please specify the reason: \_\_\_\_\_

System

General Appearance ☐

HEENT ☐

(head, eyes, ears, nose,  
throat)

Thyroid Gland ☐

Heart ☐

Chest ☐

Lungs ☐

Gastrointestinal ☐

Cardiovascular System ☐

Neurologic ☐

Skin ☐

Back ☐

Musculoskeletal ☐

Abdomen ☐

Dentition ☐

Other ☒

Other, Specify \_\_\_\_\_





Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination screening

Generated On: 28 Oct 2013 17:39:05

Outcome

Normal ☐

Abnormal ☐

Abnormal, please specify

Clinically significant

No ☐

Yes ☐

Not Done

Not Done; please specify the reason:



**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: Advice on the risk of smoking and debriefing**  
**Generated On: 28 Oct 2013 17:39:05**

Has the subject received advices on the risks of smoking?

No ☐  
Yes ☐

Has a debriefing been performed about THS 2.2?

No ☐  
Yes ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination

Generated On: 28 Oct 2013 17:39:05

Was the physical examination performed?

No ☐

Yes ☐

If No, please specify the reason:

System

General Appearance ☒

HEENT ☐

(head, eyes, ears, nose,  
throat)

Thyroid Gland ☐

Heart ☐

Chest ☐

Lungs ☐

Gastrointestinal ☐

Cardiovascular System ☐

Neurologic ☐

Skin ☐

Back ☐

Musculoskeletal ☐

Abdomen ☐

Dentition ☐

Other ☐

Other, Specify

Outcome

Normal ☐

Abnormal ☐

Abnormal, please specify



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination

Generated On: 28 Oct 2013 17:39:05

Clinically significant No ☐  
Yes ☐

Not Done \_\_\_\_\_

Not Done; please specify the reason: \_\_\_\_\_

System General Appearance ☐  
HEENT ☒  
(head, eyes, ears, nose, throat)  
Thyroid Gland ☐  
Heart ☐  
Chest ☐  
Lungs ☐  
Gastrointestinal ☐  
Cardiovascular System ☐  
Neurologic ☐  
Skin ☐  
Back ☐  
Musculoskeletal ☐  
Abdomen ☐  
Dentition ☐  
Other ☐

Other, Specify \_\_\_\_\_

Outcome Normal ☐  
Abnormal ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination

Generated On: 28 Oct 2013 17:39:05

Abnormal, please specify \_\_\_\_\_

Clinically significant

No ☐

Yes ☐

Not Done \_\_\_\_\_

Not Done; please specify the reason: \_\_\_\_\_

System

General Appearance ☐

HEENT ☐  
(head, eyes, ears, nose,  
throat)

Thyroid Gland ☒

Heart ☐

Chest ☐

Lungs ☐

Gastrointestinal ☐

Cardiovascular System ☐

Neurologic ☐

Skin ☐

Back ☐

Musculoskeletal ☐

Abdomen ☐

Dentition ☐

Other ☐

Other, Specify \_\_\_\_\_



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination

Generated On: 28 Oct 2013 17:39:05

Outcome Normal ☐  
Abnormal ☐

Abnormal, please specify \_\_\_\_\_

Clinically significant No ☐  
Yes ☐

Not Done \_\_\_\_\_

Not Done; please specify the reason: \_\_\_\_\_

System General Appearance ☐  
HEENT ☐  
(head, eyes, ears, nose,  
throat)  
Thyroid Gland ☐  
Heart ☒  
Chest ☐  
Lungs ☐  
Gastrointestinal ☐  
Cardiovascular System ☐  
Neurologic ☐  
Skin ☐  
Back ☐  
Musculoskeletal ☐  
Abdomen ☐  
Dentition ☐  
Other ☐



**Final version 5.0 (Main CRF): Case Book**

**Project Name: ZRHR-REXC-03-EU**

**Form: Physical Examination**

**Generated On: 28 Oct 2013 17:39:05**

Other, Specify \_\_\_\_\_

Outcome

Normal ☐

Abnormal ☐

Abnormal, please specify \_\_\_\_\_

Clinically significant

No ☐

Yes ☐

Not Done \_\_\_\_\_

Not Done; please specify the reason: \_\_\_\_\_





Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination

Generated On: 28 Oct 2013 17:39:05

System	General Appearance <input type="checkbox"/>
	HEENT <input type="checkbox"/>
	(head, eyes, ears, nose, throat)
	Thyroid Gland <input type="checkbox"/>
	Heart <input type="checkbox"/>
	Chest <input checked="" type="checkbox"/>
	Lungs <input type="checkbox"/>
	Gastrointestinal <input type="checkbox"/>
	Cardiovascular System <input type="checkbox"/>
	Neurologic <input type="checkbox"/>
	Skin <input type="checkbox"/>
	Back <input type="checkbox"/>
	Musculoskeletal <input type="checkbox"/>
	Abdomen <input type="checkbox"/>
	Dentition <input type="checkbox"/>
	Other <input type="checkbox"/>

Other, Specify \_\_\_\_\_

Outcome Normal ☐  
Abnormal ☐

Abnormal, please specify \_\_\_\_\_

Clinically significant No ☐  
Yes ☐

Not Done \_\_\_\_\_



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination

Generated On: 28 Oct 2013 17:39:05

Not Done; please specify the reason:

System

General Appearance ☐

HEENT ☐

(head, eyes, ears, nose,  
throat)

Thyroid Gland ☐

Heart ☐

Chest ☐

Lungs ☒

Gastrointestinal ☐

Cardiovascular System ☐

Neurologic ☐

Skin ☐

Back ☐

Musculoskeletal ☐

Abdomen ☐

Dentition ☐

Other ☐

Other, Specify

Outcome

Normal ☐

Abnormal ☐

Abnormal, please specify

Clinically significant

No ☐

Yes ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination

Generated On: 28 Oct 2013 17:39:05

Not Done

Not Done; please specify the reason:

System

General Appearance ☐

HEENT ☐

(head, eyes, ears, nose,  
throat)

Thyroid Gland ☐

Heart ☐

Chest ☐

Lungs ☐

Gastrointestinal ☒

Cardiovascular System ☐

Neurologic ☐

Skin ☐

Back ☐

Musculoskeletal ☐

Abdomen ☐

Dentition ☐

Other ☐

Other, Specify

Outcome

Normal ☐

Abnormal ☐

Abnormal, please specify



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination

Generated On: 28 Oct 2013 17:39:05

Clinically significant No ☐  
Yes ☐

Not Done \_\_\_\_\_

Not Done; please specify the reason: \_\_\_\_\_

System	General Appearance <input type="checkbox"/>
	HEENT <input type="checkbox"/>
	(head, eyes, ears, nose, throat)
	Thyroid Gland <input type="checkbox"/>
	Heart <input type="checkbox"/>
	Chest <input type="checkbox"/>
	Lungs <input type="checkbox"/>
	Gastrointestinal <input type="checkbox"/>
	Cardiovascular System <input checked="" type="checkbox"/>
	Neurologic <input type="checkbox"/>
	Skin <input type="checkbox"/>
	Back <input type="checkbox"/>
	Musculoskeletal <input type="checkbox"/>
	Abdomen <input type="checkbox"/>
	Dentition <input type="checkbox"/>
	Other <input type="checkbox"/>

Other, Specify \_\_\_\_\_

Outcome Normal ☐  
Abnormal ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination

Generated On: 28 Oct 2013 17:39:05

Abnormal, please specify \_\_\_\_\_

Clinically significant

No ☐

Yes ☐

Not Done \_\_\_\_\_

Not Done; please specify the reason: \_\_\_\_\_

System

General Appearance ☐

HEENT ☐

(head, eyes, ears, nose,  
throat)

Thyroid Gland ☐

Heart ☐

Chest ☐

Lungs ☐

Gastrointestinal ☐

Cardiovascular System ☐

Neurologic ☒

Skin ☐

Back ☐

Musculoskeletal ☐

Abdomen ☐

Dentition ☐

Other ☐

Other, Specify \_\_\_\_\_



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination

Generated On: 28 Oct 2013 17:39:05

Outcome Normal ☐  
Abnormal ☐

Abnormal, please specify \_\_\_\_\_

Clinically significant No ☐  
Yes ☐

Not Done \_\_\_\_\_

Not Done; please specify the reason: \_\_\_\_\_

System General Appearance ☐  
HEENT ☐  
(head, eyes, ears, nose,  
throat)  
Thyroid Gland ☐  
Heart ☐  
Chest ☐  
Lungs ☐  
Gastrointestinal ☐  
Cardiovascular System ☐  
Neurologic ☐  
Skin ☒  
Back ☐  
Musculoskeletal ☐  
Abdomen ☐  
Dentition ☐  
Other ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Physical Examination  
Generated On: 28 Oct 2013 17:39:05

Other, Specify \_\_\_\_\_

Outcome

Normal ☐

Abnormal ☐

Abnormal, please specify \_\_\_\_\_

Clinically significant

No ☐

Yes ☐

Not Done \_\_\_\_\_

Not Done; please specify the reason: \_\_\_\_\_





Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination

Generated On: 28 Oct 2013 17:39:05

System

General Appearance ☐

HEENT ☐

(head, eyes, ears, nose,  
throat)

Thyroid Gland ☐

Heart ☐

Chest ☐

Lungs ☐

Gastrointestinal ☐

Cardiovascular System ☐

Neurologic ☐

Skin ☐

Back ☒

Musculoskeletal ☐

Abdomen ☐

Dentition ☐

Other ☐

Other, Specify

Outcome

Normal ☐

Abnormal ☐

Abnormal, please specify

Clinically significant

No ☐

Yes ☐

Not Done



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination

Generated On: 28 Oct 2013 17:39:05

Not Done; please specify the reason: \_\_\_\_\_

System

General Appearance ☐

HEENT ☐

(head, eyes, ears, nose,  
throat)

Thyroid Gland ☐

Heart ☐

Chest ☐

Lungs ☐

Gastrointestinal ☐

Cardiovascular System ☐

Neurologic ☐

Skin ☐

Back ☐

Musculoskeletal ☒

Abdomen ☐

Dentition ☐

Other ☐

Other, Specify \_\_\_\_\_

Outcome

Normal ☐

Abnormal ☐

Abnormal, please specify \_\_\_\_\_

Clinically significant

No ☐

Yes ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination

Generated On: 28 Oct 2013 17:39:05

Not Done

Not Done; please specify the reason:

System

General Appearance ☐

HEENT ☐

(head, eyes, ears, nose,  
throat)

Thyroid Gland ☐

Heart ☐

Chest ☐

Lungs ☐

Gastrointestinal ☐

Cardiovascular System ☐

Neurologic ☐

Skin ☐

Back ☐

Musculoskeletal ☐

Abdomen ☒

Dentition ☐

Other ☐

Other, Specify

Outcome

Normal ☐

Abnormal ☐

Abnormal, please specify



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination

Generated On: 28 Oct 2013 17:39:05

Clinically significant No ☐  
Yes ☐

Not Done \_\_\_\_\_

Not Done; please specify the reason: \_\_\_\_\_

System	General Appearance <input type="checkbox"/>
	HEENT <input type="checkbox"/>
	(head, eyes, ears, nose, throat)
	Thyroid Gland <input type="checkbox"/>
	Heart <input type="checkbox"/>
	Chest <input type="checkbox"/>
	Lungs <input type="checkbox"/>
	Gastrointestinal <input type="checkbox"/>
	Cardiovascular System <input type="checkbox"/>
	Neurologic <input type="checkbox"/>
	Skin <input type="checkbox"/>
	Back <input type="checkbox"/>
	Musculoskeletal <input type="checkbox"/>
	Abdomen <input type="checkbox"/>
	Dentition <input checked="" type="checkbox"/>
	Other <input type="checkbox"/>

Other, Specify \_\_\_\_\_

Outcome Normal ☐  
Abnormal ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination

Generated On: 28 Oct 2013 17:39:05

Abnormal, please specify \_\_\_\_\_

Clinically significant

No ☐

Yes ☐

Not Done \_\_\_\_\_

Not Done; please specify the reason: \_\_\_\_\_

System

General Appearance ☐

HEENT ☐

(head, eyes, ears, nose,  
throat)

Thyroid Gland ☐

Heart ☐

Chest ☐

Lungs ☐

Gastrointestinal ☐

Cardiovascular System ☐

Neurologic ☐

Skin ☐

Back ☐

Musculoskeletal ☐

Abdomen ☐

Dentition ☐

Other ☒

Other, Specify \_\_\_\_\_



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination

Generated On: 28 Oct 2013 17:39:05

Outcome Normal ☐  
Abnormal ☐

Abnormal, please specify \_\_\_\_\_

Clinically significant No ☐  
Yes ☐

Not Done \_\_\_\_\_

Not Done; please specify the reason: \_\_\_\_\_

System General Appearance ☐  
HEENT ☐  
(head, eyes, ears, nose,  
throat)  
Thyroid Gland ☐  
Heart ☐  
Chest ☐  
Lungs ☐  
Gastrointestinal ☐  
Cardiovascular System ☐  
Neurologic ☐  
Skin ☐  
Back ☐  
Musculoskeletal ☐  
Abdomen ☐  
Dentition ☐  
Other ☒



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Physical Examination  
Generated On: 28 Oct 2013 17:39:05

Other, Specify \_\_\_\_\_

Outcome

Normal ☐

Abnormal ☐

Abnormal, please specify \_\_\_\_\_

Clinically significant

No ☐

Yes ☐

Not Done \_\_\_\_\_

Not Done; please specify the reason: \_\_\_\_\_





Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination

Generated On: 28 Oct 2013 17:39:05

System

General Appearance ☐

HEENT ☐

(head, eyes, ears, nose,  
throat)

Thyroid Gland ☐

Heart ☐

Chest ☐

Lungs ☐

Gastrointestinal ☐

Cardiovascular System ☐

Neurologic ☐

Skin ☐

Back ☐

Musculoskeletal ☐

Abdomen ☐

Dentition ☐

Other ☒

Other, Specify

Outcome

Normal ☐

Abnormal ☐

Abnormal, please specify

Clinically significant

No ☐

Yes ☐

Not Done



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination

Generated On: 28 Oct 2013 17:39:05

Not Done; please specify the reason:

System

General Appearance ☐

HEENT ☐

(head, eyes, ears, nose,  
throat)

Thyroid Gland ☐

Heart ☐

Chest ☐

Lungs ☐

Gastrointestinal ☐

Cardiovascular System ☐

Neurologic ☐

Skin ☐

Back ☐

Musculoskeletal ☐

Abdomen ☐

Dentition ☐

Other ☒

Other, Specify

Outcome

Normal ☐

Abnormal ☐

Abnormal, please specify

Clinically significant

No ☐

Yes ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination

Generated On: 28 Oct 2013 17:39:05

Not Done

Not Done; please specify the reason:

System

General Appearance ☐

HEENT ☐

(head, eyes, ears, nose,  
throat)

Thyroid Gland ☐

Heart ☐

Chest ☐

Lungs ☐

Gastrointestinal ☐

Cardiovascular System ☐

Neurologic ☐

Skin ☐

Back ☐

Musculoskeletal ☐

Abdomen ☐

Dentition ☐

Other ☒

Other, Specify

Outcome

Normal ☐

Abnormal ☐

Abnormal, please specify



**Final version 5.0 (Main CRF): Case Book**

**Project Name: ZRHR-REXC-03-EU**

**Form: Physical Examination**

**Generated On: 28 Oct 2013 17:39:05**

Clinically significant

No ☐

Yes ☐

Not Done

Not Done; please specify the reason:



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Product administration-CC  
Generated On: 28 Oct 2013 17:39:05

H\_NOW (Derived):

Date of product use  
DD/MMM/YYYY

Visit

Day -2 ☐  
Day -1 ☐  
Day 0 ☐  
Day 1 ☐  
Day 2 ☐  
Day 3 ☐  
Day 4 ☐  
Day 5 ☐  
Day 6 ☐

Type of Product Use

Conventional Cigarettes ☒  
Tobacco Heating System ☐

If type of Product Use different from the randomization  
please explain

Time of distribution

Time of butt return

CC with SODIM?

CC not compatible?



**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: Product administration-CC**  
**Generated On: 28 Oct 2013 17:39:05**

SODIM device number	
SODIM sample holder number	
SODIM file number	
Comment	



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Identification of Current Cigarette Brand  
Generated On: 28 Oct 2013 17:39:05

Date Fixed Unit:  
DD/MMM/YYYY

Brand name

ISO Tar Yield

Fixed Unit:  
MG

ISO Tar Yield unit

Milligram ☒

ISO Nicotine Yield

Fixed Unit:  
MG

ISO Nicotine Yield unit

Milligram ☒

ISO CO Yield

Fixed Unit:  
MG

ISO CO Yield unit

Milligram ☒





**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: THS 2.2 product test**  
**Generated On: 28 Oct 2013 17:39:05**

Was the THS 2.2 product trial performed?

No ☐  
Yes ☐

If the THS 2.2 product trial was not performed, please  
explain

How many THS 2.2 tobacco sticks did the subject use on  
this day?

Is the subject willing and able to use the product during  
the study?

No ☐  
Yes ☐



**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: THS 2.2 product demonstration**  
**Generated On: 28 Oct 2013 17:39:05**

Has the subject seen a THS 2.2 product demonstration?

No ☐  
Yes ☐

If the subject did not see the demonstration please  
explain



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Product administration-THS

Generated On: 28 Oct 2013 17:39:05

H\_NOW (Derived):

Date of product use  
DD/MMM/YYYY

Visit

Screen Failure ☐

Day -2 ☐

Day 0 ☐

Day 1 ☐

Day 2 ☐

Day 3 ☐

Day 4 ☐

Day 5 ☐

Day 6 ☐

Type of Product Use

Conventional Cigarettes ☐

Tobacco Heating System ☒

If type of Product Use different from the randomization  
please explain

Time of distribution

Time of product return

SODIM device number

SODIM sample holder number



**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: Product administration-THS**  
**Generated On: 28 Oct 2013 17:39:05**

Filter kit number	<input type="text"/>
Filter vial number	<input type="text"/>
Tobacco plug kit number	<input type="text"/>
Tobacco plug vial number	<input type="text"/>
SODIM file number	<input type="text"/>
Comment	<input type="text"/>
Batch Number	<input type="text"/>



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Smoking History  
Generated On: 28 Oct 2013 17:39:05

Date of Assessment

Fixed Unit:  
DD/MMM/YYYY

1. Does the subject plan to quit smoking during the next 3 months?

No ☐  
Yes ☐

2. Did the subject smoke for at least 3 consecutive years?

No ☐  
Yes ☐

3. How many cigarettes per day has the subject smoked on average during the last 4 weeks?

<10 ☐  
10 to 19 ☐  
>19 ☐

4. Did the subject smoke menthol cigarettes in the last 4 weeks?

No ☐  
Yes ☐

5. The subject has used nicotine-containing products other than commercially available CC (either tobacco-based products or nicotine-replacement therapy [NRT]), electronic cigarettes and similar devices, within 4 weeks prior to assessment.

No ☐  
Yes ☐

**Final version 5.0 (Main CRF): Case Book****Project Name: ZRHR-REXC-03-EU****Form: Topography files status for CC****Generated On: 28 Oct 2013 17:39:05**

SODIM file number \_\_\_\_\_

File Status

Accepted ☐Rejected ☐Error ☐

Rejection / Error reason \_\_\_\_\_

Date of analysis  
DD/MMM/YYYY \_\_\_\_\_

Operator

Valerie Poux ☐Thierry Bachmann ☐Anthony Bruchet ☐

Comment \_\_\_\_\_

H\_NOW (Derived): \_\_\_\_\_



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: FTND Questionnaire

Generated On: 28 Oct 2013 17:39:05

Type FTND

Date of Birth  
YYYY MMM DD

Fixed Unit:  
YYYY MMM DD

Date of assessment=  
YYYY MMM DD

Fixed Unit:  
YYYY MMM DD

Time of assessment=  
hour:min 24-hour clock

Fixed Unit:  
hour:min 24-hour clock

Assessment Status

Completed ☐

Abandoned ☐

1. How soon after you wake up do you smoke your first cigarette?

After 60 minutes ☐

31-60 minutes ☐

6-30 minutes ☐

Within 5 minutes ☐

Abandoned ☐

2. Do you find it difficult to refrain from smoking in places where it is forbidden?

No ☐

Yes ☐

Abandoned ☐





Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: FTND Questionnaire

Generated On: 28 Oct 2013 17:39:05

---

3. Which cigarette would you hate most to give up?      The first in the morning ☐  
Any other ☐  
Abandoned ☐

---

4. How many cigarettes per day do you smoke?      10 or less ☐  
11-20 ☐  
21-30 ☐  
31 or more ☐  
Abandoned ☐

---

5. Do you smoke more frequently during the first hours  
after awakening than during the  
rest of the day?      No ☐  
Yes ☐  
Abandoned ☐

---

6. Do you smoke even if you are so ill that you are in  
bed most of the day?      No ☐  
Yes ☐  
Abandoned ☐

---



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Topography files status for THS  
Generated On: 28 Oct 2013 17:39:05

SODIM file number

File Status

Accepted ☐

Rejected ☐

Error ☐

Rejection / Error reason

Date of analysis  
DD/MMM/YYYY

Operator

Valerie Poux ☐

Thierry Bachmann ☐

Anthony Bruchet ☐

Comment

H\_NOW (Derived):



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Visual Inspection of the Tobacco Plugs Results for THS

Generated On: 28 Oct 2013 17:39:05

Tobacco plug kit number

Tobacco plug vial number

Level

0 ☐

1 ☐

2 ☐

NA ☐

Observation

Ashes not anymore visible  
when shooting picture ☐

No tobacco in plug ☐

Not enough tobacco in the  
plug to perform the  
analysis ☐

Tobacco plug destroyed,  
analysis impossible ☐

No tobacco plug in the vial ☐

Other error ☐

Picture File Name

Date of analysis  
DD/MMM/YYYY

H\_NOW (Derived):



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Weight and Height  
Generated On: 28 Oct 2013 17:39:05

Measurement(s) assessed?

No ☐  
Yes ☐

If No, please specify the reason:

Date of assessment

Fixed Unit:  
DD/MMM/YYYY

Weight

Fixed Unit:  
kg

Height

Fixed Unit:  
cm

BMI (Derived)

Fixed Unit:  
kg/m<sup>2</sup>



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Weight  
Generated On: 28 Oct 2013 17:39:05

Measurement(s) assessed?

No ☐  
Yes ☐

If No, please specify the reason:

Time of assessment

Fixed Unit:  
hour:min 24-hour clock

Weight

Fixed Unit:  
kg



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: ECG (12-Lead Standard) screening  
Generated On: 28 Oct 2013 17:39:05

Method of ECG Test 12 Lead Placement Cabrera ☐

Was the ECG performed? No ☐  
Yes ☐

If No, please specify the reason: \_\_\_\_\_

Date of assessment: \_\_\_\_\_ Fixed Unit:  
DD/MM/YYYY

Position Sitting ☐  
Standing ☐  
Supine ☒

Heart Rate \_\_\_\_\_ Fixed Unit:  
beats per minute

Heart Rate unit \_\_\_\_\_ beats per minute

QRS Interval \_\_\_\_\_ Fixed Unit:  
msec

QRS Interval unit \_\_\_\_\_ msec

QT Interval \_\_\_\_\_ Fixed Unit:  
msec

Final version 5.0 (Main CRF) \_\_\_\_\_ 321 of 516  
(288)



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: ECG (12-Lead Standard) screening  
Generated On: 28 Oct 2013 17:39:05

QT Interval unit msec

QTcB Interval Fixed Unit:  
msec

QTcB Interval unit msec

PR Interval Fixed Unit:  
msec

PR Interval unit msec

Interpretation Normal ☐  
Abnormal ☐

If Abnormal, Clinical Significance Not clinically significant ☐  
Clinically significant ☐

If Not Clinically significant or clinically Significant, Please  
specify the finding(s)





Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: ECG (12-Lead Standard)

Generated On: 28 Oct 2013 17:39:05

Method of ECG Test 12 Lead Placement Cabrera ☐

Was the ECG performed? No ☐  
Yes ☐

If No, please specify the reason: \_\_\_\_\_

Position Sitting ☐  
Standing ☐  
Supine ☒

Heart Rate Fixed Unit:  
beats per minute

Heart Rate unit beats per minute

QRS Interval Fixed Unit:  
msec

QRS Interval unit msec

QT Interval Fixed Unit:  
msec

QT Interval unit



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: ECG (12-Lead Standard)  
Generated On: 28 Oct 2013 17:39:05

	msec
QTcB Interval	Fixed Unit: msec
QTcB Interval unit	msec
PR Interval	Fixed Unit: msec
PR Interval unit	msec
Interpretation	Normal <input type="checkbox"/> Abnormal <input type="checkbox"/>
If Abnormal, Clinical Significance	Not clinically significant <input type="checkbox"/> Clinically significant <input type="checkbox"/>
If Not Clinically significant or clinically Significant, Please specify the finding(s)	



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Spirometry

Generated On: 28 Oct 2013 17:39:05

Was the spirometry performed?

No ☐

Yes ☐

If No, please specify the reason:

Category

With short-acting  
bronchodilator ☐

Without short-acting  
bronchodilator ☒

Date of assessment  
DD/MMM/YYYY

Time of assessment

Name of bronchodilator

Dose

Fixed Unit:  
MG

Predicted FVC value

Fixed Unit:  
L

Best measured FVC value

Fixed Unit:  
L



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Spirometry

Generated On: 28 Oct 2013 17:39:05

Percent of predicted FVC value

Fixed Unit:  
%

Best measured FEV1 value

Fixed Unit:  
L

Predicted FEV1 value

Fixed Unit:  
L

Percent of predicted FEV1 value

Fixed Unit:  
%

Calculated ratio between FEV1/FVC

Interpretation

Normal ☐  
Abnormal ☐

If Abnormal, Clinical Significance

Not clinically significant ☐  
Clinically significant ☐

If Not Clinically Significant or Clinically Significant, Please  
specify the finding(s)



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Spirometry

Generated On: 28 Oct 2013 17:39:05

Was the spirometry performed?

No ☐

Yes ☐

If No, please specify the reason:

Category

With short-acting  
bronchodilator ☒

Without short-acting  
bronchodilator ☐

Date of assessment  
DD/MMM/YYYY

Time of assessment

Name of bronchodilator

Dose

Fixed Unit:  
MG

Predicted FVC value

Fixed Unit:  
L

Best measured FVC value

Fixed Unit:  
L



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Spirometry  
Generated On: 28 Oct 2013 17:39:05

Percent of predicted FVC value Fixed Unit:  
%

Best measured FEV1 value Fixed Unit:  
L

Predicted FEV1 value Fixed Unit:  
L

Percent of predicted FEV1 value Fixed Unit:  
%

Calculated ratio between FEV1/FVC

Interpretation Normal ☐  
Abnormal ☐

If Abnormal, Clinical Significance Not clinically significant ☐  
Clinically significant ☐

If Not Clinically Significant or Clinically Significant, Please  
specify the finding(s)



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Spirometry without a short-acting bronchodilator  
Generated On: 28 Oct 2013 17:39:05

Was the spirometry performed? No ☐  
Yes ☐

If No, please specify the reason: \_\_\_\_\_

Category With short-acting bronchodilator ☐  
Without short-acting bronchodilator ☒

Time of assessment Fixed Unit:  
hour:min 24-hour clock

Predicted FVC value Fixed Unit:  
L

Best measured FVC value Fixed Unit:  
L

Percent of predicted FVC value Fixed Unit:  
%

Best measured FEV1 value Fixed Unit:  
L





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Spirometry without a short-acting bronchodilator  
Generated On: 28 Oct 2013 17:39:05

Predicted FEV1 value Fixed Unit:  
L

Percent of predicted FEV1 value Fixed Unit:  
%

Interpretation Normal ☐  
Abnormal ☐

If Abnormal, Clinical Significance Not clinically significant ☐  
Clinically significant ☐

If Not Clinically Significant or Clinically Significant, Please  
specify the finding(s)



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Chest X-Ray

Generated On: 28 Oct 2013 17:39:05

Category for Examination Chest X-Ray ☐

Was a chest X-Ray with anterior-posterior and left lateral views performed? No ☐  
Yes ☐

If No, please specify the reason: \_\_\_\_\_

Date of assessment Fixed Unit:  
DD/MM/YYYY

System General Appearance ☐  
HEENT ☐  
(head, eyes, ears, nose,  
throat)  
Thyroid Gland ☐  
Heart ☐  
Chest ☒  
Lungs ☐  
Gastrointestinal ☐  
Cardiovascular System ☐  
Neurologic ☐  
Skin ☐  
Back ☐  
Musculoskeletal ☐  
Abdomen ☐  
Dentition ☐  
Other ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Chest X-Ray  
Generated On: 28 Oct 2013 17:39:05

Interpretation

Normal ☐  
Abnormal ☐

Clinically significant

No ☐  
Yes ☐

Abnormal, please specify:



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Haematology  
Generated On: 28 Oct 2013 17:39:05

Were samples collected?

No ☐  
Yes ☐

If No, please specify the reason:

Was the subject fasting for at least 8 hours at time of  
sample collection?

No ☐  
Yes ☐



**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: Urine analysis**  
**Generated On: 28 Oct 2013 17:39:05**

Were samples collected?

No ☐  
Yes ☐

If No, please specify the reason:



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Clinical Chemistry  
Generated On: 28 Oct 2013 17:39:05

Were samples collected?

No ☐  
Yes ☐

If No, please specify the reason: \_\_\_\_\_

Was the subject fasting for at least 8 hours at time of  
sample collection?

No ☐  
Yes ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Serology for HIV and Hepatitis B and C  
Generated On: 28 Oct 2013 17:39:05

Experiment Type SEROLOGY

Not Done

If Not Done, please specify the reason:





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Urine Drug Screen screening  
Generated On: 28 Oct 2013 17:39:05

Category

- Clinical Chemistry ☐  
Drug Screen ☐  
Haematology ☐  
Serology ☐  
Pregnancy Testing ☐  
Urinalysis ☒  
Cotinine Screening ☐  
Alcohol Breath Test ☐

Not Done? \_\_\_\_\_

If Not Done, please specify the reason: \_\_\_\_\_

Date of sample collection

Fixed Unit:  
DD/MMM/YYYY

Time of sample collection

Fixed Unit:  
hour:min 24-hour clock

Drug type

- Amphetamines ☒  
Barbiturates ☐  
Benzodiazepines ☐  
Cannabinoids ☐  
Cocaine ☐  
Opiates ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Urine Drug Screen screening

Generated On: 28 Oct 2013 17:39:05

Result Negative ☐  
Positive ☐

Drug type Amphetamines ☐  
Barbiturates ☒  
Benzodiazepines ☐  
Cannabinoids ☐  
Cocaine ☐  
Opiates ☐

Result Negative ☐  
Positive ☐

Drug type Amphetamines ☐  
Barbiturates ☐  
Benzodiazepines ☒  
Cannabinoids ☐  
Cocaine ☐  
Opiates ☐

Result Negative ☐  
Positive ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Urine Drug Screen screening  
Generated On: 28 Oct 2013 17:39:05

Drug type

Amphetamines ☐  
Barbiturates ☐  
Benzodiazepines ☐  
Cannabinoids ☒  
Cocaine ☐  
Opiates ☐

Result

Negative ☐  
Positive ☐

Drug type

Amphetamines ☐  
Barbiturates ☐  
Benzodiazepines ☐  
Cannabinoids ☐  
Cocaine ☒  
Opiates ☐

Result

Negative ☐  
Positive ☐

Drug type

Amphetamines ☐  
Barbiturates ☐  
Benzodiazepines ☐  
Cannabinoids ☐  
Cocaine ☐  
Opiates ☒



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Urine Drug Screen screening  
Generated On: 28 Oct 2013 17:39:05

Result

Negative ☐  
Positive ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Urine Drug Screen

Generated On: 28 Oct 2013 17:39:05

Category

- Clinical Chemistry ☐  
Drug Screen ☐  
Haematology ☐  
Serology ☐  
Pregnancy Testing ☐  
Urinalysis ☒  
Cotinine Screening ☐  
Alcohol Breath Test ☐

Not Done? \_\_\_\_\_

If Not Done, please specify the reason: \_\_\_\_\_

Time of sample collection

Fixed Unit:  
hour:min 24-hour clock

Drug type

- Amphetamines ☒  
Barbiturates ☐  
Benzodiazepines ☐  
Cannabinoids ☐  
Cocaine ☐  
Opiates ☐

Result

- Negative ☐  
Positive ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Urine Drug Screen

Generated On: 28 Oct 2013 17:39:05

---

Drug type

Amphetamines ☐  
Barbiturates ☒  
Benzodiazepines ☐  
Cannabinoids ☐  
Cocaine ☐  
Opiates ☐

---

Result

Negative ☐  
Positive ☐

---

Drug type

Amphetamines ☐  
Barbiturates ☐  
Benzodiazepines ☒  
Cannabinoids ☐  
Cocaine ☐  
Opiates ☐

---

Result

Negative ☐  
Positive ☐

---

Drug type

Amphetamines ☐  
Barbiturates ☐  
Benzodiazepines ☐  
Cannabinoids ☒  
Cocaine ☐  
Opiates ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Urine Drug Screen

Generated On: 28 Oct 2013 17:39:05

---

Result	Negative <input type="checkbox"/>
	Positive <input type="checkbox"/>

---

---

Drug type	Amphetamines <input type="checkbox"/>
	Barbiturates <input type="checkbox"/>
	Benzodiazepines <input type="checkbox"/>
	Cannabinoids <input type="checkbox"/>
	Cocaine <input checked="" type="checkbox"/>
	Opiates <input type="checkbox"/>

---

---

Result	Negative <input type="checkbox"/>
	Positive <input type="checkbox"/>

---

---

Drug type	Amphetamines <input type="checkbox"/>
	Barbiturates <input type="checkbox"/>
	Benzodiazepines <input type="checkbox"/>
	Cannabinoids <input type="checkbox"/>
	Cocaine <input type="checkbox"/>
	Opiates <input checked="" type="checkbox"/>

---

---

Result	Negative <input type="checkbox"/>
	Positive <input type="checkbox"/>

---





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Alcohol Breath Test screening  
Generated On: 28 Oct 2013 17:39:05

Category

Clinical Chemistry ☐  
Drug Screen ☐  
Haematology ☐  
Serology ☐  
Pregnancy Testing ☐  
Urinalysis ☒  
Cotinine Screening ☐  
Alcohol Breath Test ☐

Was the alcohol breath test performed?

No ☐  
Yes ☐

If No, please specify the reason:

Date of assessment

Fixed Unit:  
DD/MMM/YYYY

Time of assessment

Fixed Unit:  
hour:min 24-hour clock

Result

Negative ☐  
Positive ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Alcohol Breath Test

Generated On: 28 Oct 2013 17:39:05

Category

Clinical Chemistry ☐  
Drug Screen ☐  
Haematology ☐  
Serology ☐  
Pregnancy Testing ☐  
Urinalysis ☒  
Cotinine Screening ☐  
Alcohol Breath Test ☐

Was the alcohol breath test performed?

No ☐  
Yes ☐

If No, please specify the reason: \_\_\_\_\_

Time of assessment

Fixed Unit:  
hour:min 24-hour clock

Result

Negative ☐  
Positive ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Urine Pregnancy Test screening

Generated On: 28 Oct 2013 17:39:05

Category

- Clinical Chemistry ☐  
Drug Screen ☐  
Haematology ☐  
Serology ☐  
Pregnancy Testing ☐  
Urinalysis ☒  
Cotinine Screening ☐  
Alcohol Breath Test ☐

Not Done

If Not Done, specify reason

Date of Test

Fixed Unit:  
DD/MMM/YYYY

Time of Test

Fixed Unit:  
hour:min 24-hour clock

Specify result

- Negative ☐  
Positive ☐  
Unclear ☐

If unclear, please confirm with FSH test



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Urine Pregnancy Test screening  
Generated On: 28 Oct 2013 17:39:05

Specify result of FSH test

< 20 IU/L ☐  
>= 20 IU/L ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Urine Pregnancy Test

Generated On: 28 Oct 2013 17:39:05

Category

- Clinical Chemistry ☐  
Drug Screen ☐  
Haematology ☐  
Serology ☐  
Pregnancy Testing ☐  
Urinalysis ☒  
Cotinine Screening ☐  
Alcohol Breath Test ☐

Not Done

If Not Done, specify reason

Time of Test

Fixed Unit:  
hour:min 24-hour clock

Specify result

- Negative ☐  
Positive ☐  
Unclear ☐

If unclear, please confirm with FSH test

Specify result of FSH test

- < 20 IU/L ☐  
>= 20 IU/L ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Urine Cotinine Test screening  
Generated On: 28 Oct 2013 17:39:05

Category

Clinical Chemistry ☐  
Drug Screen ☐  
Haematology ☐  
Serology ☐  
Pregnancy Testing ☐  
Urinalysis ☐  
Cotinine Screening ☒  
Alcohol Breath Test ☐

Not Done

If Not Done, please specify the reason:

Date of Sample Collection

Fixed Unit:  
DD/MMM/YYYY

Time of Sample Collection

Fixed Unit:  
hour:min 24-hour clock

Result

Negative <200 ng/ml ☐  
Positive >=200 ng/ml ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Urine Cotinine Test  
Generated On: 28 Oct 2013 17:39:05

Category

Clinical Chemistry ☐  
Drug Screen ☐  
Haematology ☐  
Serology ☐  
Pregnancy Testing ☐  
Urinalysis ☐  
Cotinine Screening ☒  
Alcohol Breath Test ☐

Not Done

If Not Done, please specify the reason:

Time of Sample Collection

Fixed Unit:  
hour:min 24-hour clock

Result

Negative <200 ng/ml ☐  
Positive >=200 ng/ml ☐





**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: Plasma Nicotine Sample**  
**Generated On: 28 Oct 2013 17:39:05**

Not Done

If Not Done, please specify the reason:

Date  
DD/MMM/YYYY

Time  
hour:min 24-hour clock



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Plasma Nicotine Sample(D5)  
Generated On: 28 Oct 2013 17:39:05

H\_NOW (Derived):

Not Done

If Not Done, please specify the reason:

Date  
DD/MMM/YYYY

Time  
hour:min 24-hour clock

Timepoint

T0 -15 min ☒

T1 ☐

T2 ☐

T3 ☐

T4 ☐

T5 ☐

T6 ☐

T7 ☐

T8 ☐

T0 + 20H ☐

T0 + 24H ☐

Not Done

If Not Done, please specify the reason:



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Plasma Nicotine Sample(D5)

Generated On: 28 Oct 2013 17:39:05

Date

DD/MMM/YYYY

Time

hour:min 24-hour clock

Timepoint

T0 -15 min ☐

T1 ☒

T2 ☐

T3 ☐

T4 ☐

T5 ☐

T6 ☐

T7 ☐

T8 ☐

T0 + 20H ☐

T0 + 24H ☐

Not Done

If Not Done, please specify the reason:

Date

DD/MMM/YYYY

Time

hour:min 24-hour clock



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Plasma Nicotine Sample(D5)

Generated On: 28 Oct 2013 17:39:05

Timepoint	T0 -15 min <input type="checkbox"/>
	T1 <input type="checkbox"/>
	T2 <input checked="" type="checkbox"/>
	T3 <input type="checkbox"/>
	T4 <input type="checkbox"/>
	T5 <input type="checkbox"/>
	T6 <input type="checkbox"/>
	T7 <input type="checkbox"/>
	T8 <input type="checkbox"/>
	T0 + 20H <input type="checkbox"/>
	T0 + 24H <input type="checkbox"/>

Not Done \_\_\_\_\_

If Not Done, please specify the reason: \_\_\_\_\_

Date  
DD/MMM/YYYY \_\_\_\_\_

Time  
hour:min 24-hour clock \_\_\_\_\_



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Plasma Nicotine Sample(D5)  
Generated On: 28 Oct 2013 17:39:05

Timepoint	T0 -15 min <input type="checkbox"/>
	T1 <input type="checkbox"/>
	T2 <input type="checkbox"/>
	T3 <input checked="" type="checkbox"/>
	T4 <input type="checkbox"/>
	T5 <input type="checkbox"/>
	T6 <input type="checkbox"/>
	T7 <input type="checkbox"/>
	T8 <input type="checkbox"/>
	T0 + 20H <input type="checkbox"/>
	T0 + 24H <input type="checkbox"/>

Not Done \_\_\_\_\_

If Not Done, please specify the reason: \_\_\_\_\_

Date  
DD/MMM/YYYY \_\_\_\_\_

Time  
hour:min 24-hour clock \_\_\_\_\_



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Plasma Nicotine Sample(D5)  
Generated On: 28 Oct 2013 17:39:05

Timepoint	T0 -15 min <input type="checkbox"/>
	T1 <input type="checkbox"/>
	T2 <input type="checkbox"/>
	T3 <input type="checkbox"/>
	T4 <input checked="" type="checkbox"/>
	T5 <input type="checkbox"/>
	T6 <input type="checkbox"/>
	T7 <input type="checkbox"/>
	T8 <input type="checkbox"/>
	T0 + 20H <input type="checkbox"/>
	T0 + 24H <input type="checkbox"/>

Not Done \_\_\_\_\_

If Not Done, please specify the reason: \_\_\_\_\_

Date  
DD/MMM/YYYY \_\_\_\_\_

Time  
hour:min 24-hour clock \_\_\_\_\_



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Plasma Nicotine Sample(D5)  
Generated On: 28 Oct 2013 17:39:05

Timepoint	T0 -15 min <input type="checkbox"/>
	T1 <input type="checkbox"/>
	T2 <input type="checkbox"/>
	T3 <input type="checkbox"/>
	T4 <input type="checkbox"/>
	T5 <input checked="" type="checkbox"/>
	T6 <input type="checkbox"/>
	T7 <input type="checkbox"/>
	T8 <input type="checkbox"/>
	T0 + 20H <input type="checkbox"/>
	T0 + 24H <input type="checkbox"/>

Not Done \_\_\_\_\_

If Not Done, please specify the reason: \_\_\_\_\_

Date  
DD/MMM/YYYY \_\_\_\_\_

Time  
hour:min 24-hour clock \_\_\_\_\_





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Plasma Nicotine Sample(D5)  
Generated On: 28 Oct 2013 17:39:05

Timepoint	T0 -15 min <input type="checkbox"/>
	T1 <input type="checkbox"/>
	T2 <input type="checkbox"/>
	T3 <input type="checkbox"/>
	T4 <input type="checkbox"/>
	T5 <input type="checkbox"/>
	T6 <input checked="" type="checkbox"/>
	T7 <input type="checkbox"/>
	T8 <input type="checkbox"/>
	T0 + 20H <input type="checkbox"/>
	T0 + 24H <input type="checkbox"/>

Not Done \_\_\_\_\_

If Not Done, please specify the reason: \_\_\_\_\_

Date  
DD/MMM/YYYY \_\_\_\_\_

Time  
hour:min 24-hour clock \_\_\_\_\_



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Plasma Nicotine Sample(D5)

Generated On: 28 Oct 2013 17:39:05

Timepoint	T0 -15 min <input type="checkbox"/>
	T1 <input type="checkbox"/>
	T2 <input type="checkbox"/>
	T3 <input type="checkbox"/>
	T4 <input type="checkbox"/>
	T5 <input type="checkbox"/>
	T6 <input type="checkbox"/>
	T7 <input checked="" type="checkbox"/>
	T8 <input type="checkbox"/>
	T0 + 20H <input type="checkbox"/>
	T0 + 24H <input type="checkbox"/>

Not Done \_\_\_\_\_

If Not Done, please specify the reason: \_\_\_\_\_

Date  
DD/MMM/YYYY \_\_\_\_\_

Time  
hour:min 24-hour clock \_\_\_\_\_



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Plasma Nicotine Sample(D5)

Generated On: 28 Oct 2013 17:39:05

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Timepoint

T0 -15 min ☐

T1 ☐

T2 ☐

T3 ☐

T4 ☐

T5 ☐

T6 ☐

T7 ☐

T8 ☒

T0 + 20H ☐

T0 + 24H ☐

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Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Plasma Nicotine Sample(D6)

Generated On: 28 Oct 2013 17:39:05

H\_NOW (Derived):

Not Done

If Not Done, please specify the reason:

Date

DD/MMM/YYYY

Time

hour:min 24-hour clock

Timepoint

T0 -15 min ☐

T1 ☐

T2 ☐

T3 ☐

T4 ☐

T5 ☐

T6 ☐

T7 ☐

T8 ☐

T0 + 20H ☒

T0 + 24H ☐

Not Done

If Not Done, please specify the reason:



**Final version 5.0 (Main CRF): Case Book**

**Project Name: ZRHR-REXC-03-EU**

**Form: Plasma Nicotine Sample(D6)**

**Generated On: 28 Oct 2013 17:39:05**

Date  
DD/MMM/YYYY

Time  
hour:min 24-hour clock

Timepoint

T0 -15 min	<input type="checkbox"/>
T1	<input type="checkbox"/>
T2	<input type="checkbox"/>
T3	<input type="checkbox"/>
T4	<input type="checkbox"/>
T5	<input type="checkbox"/>
T6	<input type="checkbox"/>
T7	<input type="checkbox"/>
T8	<input type="checkbox"/>
T0 + 20H	<input type="checkbox"/>
T0 + 24H	<input checked="" type="checkbox"/>

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**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: Plasma Cotinine Sample**  
**Generated On: 28 Oct 2013 17:39:05**

Not Done

If Not Done, please specify the reason:

Date  
DD/MMM/YYYY

Time  
hour:min 24-hour clock



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Plasma Cotinine Sample(D5)  
Generated On: 28 Oct 2013 17:39:05

H\_NOW (Derived): \_\_\_\_\_

Not Done \_\_\_\_\_

If Not Done, please specify the reason: \_\_\_\_\_

Date  
DD/MMM/YYYY \_\_\_\_\_

Time  
hour:min 24-hour clock \_\_\_\_\_

Timepoint

T0 -15 min ☒

T1 ☐

T2 ☐

T3 ☐

T4 ☐

T5 ☐

T6 ☐

T7 ☐

T8 ☐

T0 + 20H ☐

T0 + 24H ☐

Not Done \_\_\_\_\_

If Not Done, please specify the reason: \_\_\_\_\_





Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Plasma Cotinine Sample(D5)

Generated On: 28 Oct 2013 17:39:05

Date

DD/MMM/YYYY

Time

hour:min 24-hour clock

Timepoint

T0 -15 min ☐

T1 ☒

T2 ☐

T3 ☐

T4 ☐

T5 ☐

T6 ☐

T7 ☐

T8 ☐

T0 + 20H ☐

T0 + 24H ☐

Not Done

If Not Done, please specify the reason:

Date

DD/MMM/YYYY

Time

hour:min 24-hour clock



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Plasma Cotinine Sample(D5)

Generated On: 28 Oct 2013 17:39:05

Timepoint	T0 -15 min <input type="checkbox"/>
	T1 <input type="checkbox"/>
	T2 <input checked="" type="checkbox"/>
	T3 <input type="checkbox"/>
	T4 <input type="checkbox"/>
	T5 <input type="checkbox"/>
	T6 <input type="checkbox"/>
	T7 <input type="checkbox"/>
	T8 <input type="checkbox"/>
	T0 + 20H <input type="checkbox"/>
	T0 + 24H <input type="checkbox"/>

Not Done \_\_\_\_\_

If Not Done, please specify the reason: \_\_\_\_\_

Date  
DD/MMM/YYYY \_\_\_\_\_

Time  
hour:min 24-hour clock \_\_\_\_\_



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Plasma Cotinine Sample(D5)

Generated On: 28 Oct 2013 17:39:05

Timepoint

T0 -15 min ☐

T1 ☐

T2 ☐

T3 ☒

T4 ☐

T5 ☐

T6 ☐

T7 ☐

T8 ☐

T0 + 20H ☐

T0 + 24H ☐

Not Done

If Not Done, please specify the reason:

Date

DD/MMM/YYYY

Time

hour:min 24-hour clock



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Plasma Cotinine Sample(D5)  
Generated On: 28 Oct 2013 17:39:05

Timepoint	T0 -15 min <input type="checkbox"/>
	T1 <input type="checkbox"/>
	T2 <input type="checkbox"/>
	T3 <input type="checkbox"/>
	T4 <input checked="" type="checkbox"/>
	T5 <input type="checkbox"/>
	T6 <input type="checkbox"/>
	T7 <input type="checkbox"/>
	T8 <input type="checkbox"/>
	T0 + 20H <input type="checkbox"/>
	T0 + 24H <input type="checkbox"/>

Not Done \_\_\_\_\_

If Not Done, please specify the reason: \_\_\_\_\_

Date  
DD/MMM/YYYY \_\_\_\_\_

Time  
hour:min 24-hour clock \_\_\_\_\_



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Plasma Cotinine Sample(D5)

Generated On: 28 Oct 2013 17:39:05

Timepoint	T0 -15 min <input type="checkbox"/>
	T1 <input type="checkbox"/>
	T2 <input type="checkbox"/>
	T3 <input type="checkbox"/>
	T4 <input type="checkbox"/>
	T5 <input checked="" type="checkbox"/>
	T6 <input type="checkbox"/>
	T7 <input type="checkbox"/>
	T8 <input type="checkbox"/>
	T0 + 20H <input type="checkbox"/>
	T0 + 24H <input type="checkbox"/>

---

Not Done ☐

---

If Not Done, please specify the reason:

---

Date  
DD/MMM/YYYY

---

Time  
hour:min 24-hour clock

---



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Plasma Cotinine Sample(D5)

Generated On: 28 Oct 2013 17:39:05

Timepoint	T0 -15 min <input type="checkbox"/>
	T1 <input type="checkbox"/>
	T2 <input type="checkbox"/>
	T3 <input type="checkbox"/>
	T4 <input type="checkbox"/>
	T5 <input type="checkbox"/>
	T6 <input checked="" type="checkbox"/>
	T7 <input type="checkbox"/>
	T8 <input type="checkbox"/>
	T0 + 20H <input type="checkbox"/>
	T0 + 24H <input type="checkbox"/>

Not Done \_\_\_\_\_

If Not Done, please specify the reason: \_\_\_\_\_

Date  
DD/MMM/YYYY \_\_\_\_\_

Time  
hour:min 24-hour clock \_\_\_\_\_



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Plasma Cotinine Sample(D5)

Generated On: 28 Oct 2013 17:39:05

Timepoint

T0 -15 min ☐

T1 ☐

T2 ☐

T3 ☐

T4 ☐

T5 ☐

T6 ☐

T7 ☒

T8 ☐

T0 + 20H ☐

T0 + 24H ☐

Not Done

If Not Done, please specify the reason:

Date

DD/MMM/YYYY

Time

hour:min 24-hour clock





Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Plasma Cotinine Sample(D5)

Generated On: 28 Oct 2013 17:39:05

---

Timepoint

T0 -15 min ☐

T1 ☐

T2 ☐

T3 ☐

T4 ☐

T5 ☐

T6 ☐

T7 ☐

T8 ☒

T0 + 20H ☐

T0 + 24H ☐

---



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Plasma Cotinine Sample(D6)

Generated On: 28 Oct 2013 17:39:05

H\_NOW (Derived):

Not Done

If Not Done, please specify the reason:

Date

DD/MMM/YYYY

Time

hour:min 24-hour clock

Timepoint

T0 -15 min ☐

T1 ☐

T2 ☐

T3 ☐

T4 ☐

T5 ☐

T6 ☐

T7 ☐

T8 ☐

T0 + 20H ☒

T0 + 24H ☐

Not Done

If Not Done, please specify the reason:



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Plasma Cotinine Sample(D6)  
Generated On: 28 Oct 2013 17:39:05

Date  
DD/MMM/YYYY

Time  
hour:min 24-hour clock

Timepoint

T0 -15 min ☐  
T1 ☐  
T2 ☐  
T3 ☐  
T4 ☐  
T5 ☐  
T6 ☐  
T7 ☐  
T8 ☐  
T0 + 20H ☐  
T0 + 24H ☒



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: COHb Blood Sample

Generated On: 28 Oct 2013 17:39:05

Not Done

If Not Done, please specify the reason:

Scheduled Time

Within 15 min prior to smoking ☐  
12:00 - 14:00 ☐  
16:00 - 18:00 ☐  
20:00 - 22:00 ☐  
08:00 - 10:00 ☒

Not Done

If Not Done, please specify the reason:

Scheduled Time

Within 15 min prior to smoking ☐  
12:00 - 14:00 ☒  
16:00 - 18:00 ☐  
20:00 - 22:00 ☐  
08:00 - 10:00 ☐

Not Done

If Not Done, please specify the reason:



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: COHb Blood Sample

Generated On: 28 Oct 2013 17:39:05

---

Scheduled Time	Within 15 min prior to smoking	<input type="checkbox"/>
	12:00 - 14:00	<input type="checkbox"/>
	16:00 - 18:00	<input checked="" type="checkbox"/>
	20:00 - 22:00	<input type="checkbox"/>
	08:00 - 10:00	<input type="checkbox"/>

---

---

Not Done	
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---

---

If Not Done, please specify the reason:	
---	--

---

---

Scheduled Time	Within 15 min prior to smoking	<input type="checkbox"/>
	12:00 - 14:00	<input type="checkbox"/>
	16:00 - 18:00	<input type="checkbox"/>
	20:00 - 22:00	<input checked="" type="checkbox"/>
	08:00 - 10:00	<input type="checkbox"/>

---



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: COHb Blood Sample<CC/THS Arm/>  
Generated On: 28 Oct 2013 17:39:05

Not Done

If Not Done, please specify the reason:

Scheduled Time

Within 15 min prior to smoking ☒  
12:00 - 14:00 ☐  
16:00 - 18:00 ☐  
20:00 - 22:00 ☐  
08:00 - 10:00 ☐

Not Done

If Not Done, please specify the reason:

Scheduled Time

Within 15 min prior to smoking ☐  
12:00 - 14:00 ☒  
16:00 - 18:00 ☐  
20:00 - 22:00 ☐  
08:00 - 10:00 ☐

Not Done

If Not Done, please specify the reason:



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: COHb Blood Sample<CC/THS Arm/>  
Generated On: 28 Oct 2013 17:39:05

---

Scheduled Time	Within 15 min prior to smoking <input type="checkbox"/>
	12:00 - 14:00 <input type="checkbox"/>
	16:00 - 18:00 <input checked="" type="checkbox"/>
	20:00 - 22:00 <input type="checkbox"/>
	08:00 - 10:00 <input type="checkbox"/>

---

---

Not Done	<input type="checkbox"/>
----------	--------------------------

---

---

If Not Done, please specify the reason:	<input type="checkbox"/>
---	--------------------------

---

---

Scheduled Time	Within 15 min prior to smoking <input type="checkbox"/>
	12:00 - 14:00 <input type="checkbox"/>
	16:00 - 18:00 <input type="checkbox"/>
	20:00 - 22:00 <input checked="" type="checkbox"/>
	08:00 - 10:00 <input type="checkbox"/>

---





**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: COHb Blood Sample**  
**Generated On: 28 Oct 2013 17:39:05**

Not Done

If Not Done, please specify the reason:



**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: CO Breath Test**  
**Generated On: 28 Oct 2013 17:39:05**

Assessment not done

If Not Done, please specify the reason:

Actual Time of Assessment

Fixed Unit:  
hour:min 24-hour clock

Result

Fixed Unit:  
ppm



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: CO Breath Test

Generated On: 28 Oct 2013 17:39:05

Assessment not done

If Not Done, please specify the reason:

Scheduled Time

Within 15 min prior to smoking ☒

12:00 - 14:00 ☐

16:00 - 18:00 ☐

20:00 - 22:00 ☐

08:00 - 10:00 ☐

Actual Time of Assessment  
hour:min 24-hour clock

Result(ppm)

Assessment not done

If Not Done, please specify the reason:

Scheduled Time

Within 15 min prior to smoking ☐

12:00 - 14:00 ☒

16:00 - 18:00 ☐

20:00 - 22:00 ☐

08:00 - 10:00 ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: CO Breath Test

Generated On: 28 Oct 2013 17:39:05

Actual Time of Assessment  
hour:min 24-hour clock

Result(ppm)

Assessment not done

If Not Done, please specify the reason:

Scheduled Time

Within 15 min prior to  
smoking

12:00 - 14:00

16:00 - 18:00

20:00 - 22:00

08:00 - 10:00

Actual Time of Assessment  
hour:min 24-hour clock

Result(ppm)

Assessment not done

If Not Done, please specify the reason:



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: CO Breath Test

Generated On: 28 Oct 2013 17:39:05

---

Scheduled Time	Within 15 min prior to smoking <input type="checkbox"/>
	12:00 - 14:00 <input type="checkbox"/>
	16:00 - 18:00 <input type="checkbox"/>
	20:00 - 22:00 <input checked="" type="checkbox"/>
	08:00 - 10:00 <input type="checkbox"/>

---

Actual Time of Assessment  
hour:min 24-hour clock \_\_\_\_\_

---

Result(ppm) \_\_\_\_\_

---



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: CO Breath Test <SA arm/>

Generated On: 28 Oct 2013 17:39:05

Assessment not done

If Not Done, please specify the reason:

Scheduled Time

Within 15 min prior to smoking ☐  
12:00 - 14:00 ☐  
16:00 - 18:00 ☐  
20:00 - 22:00 ☐  
08:00 - 10:00 ☒

Actual Time of Assessment  
hour:min 24-hour clock

Result(ppm)

Assessment not done

If Not Done, please specify the reason:

Scheduled Time

Within 15 min prior to smoking ☐  
12:00 - 14:00 ☒  
16:00 - 18:00 ☐  
20:00 - 22:00 ☐  
08:00 - 10:00 ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: CO Breath Test <SA arm/>

Generated On: 28 Oct 2013 17:39:05

Actual Time of Assessment  
hour:min 24-hour clock

Result(ppm)

Assessment not done

If Not Done, please specify the reason:

Scheduled Time

Within 15 min prior to  
smoking

12:00 - 14:00

16:00 - 18:00

20:00 - 22:00

08:00 - 10:00

Actual Time of Assessment  
hour:min 24-hour clock

Result(ppm)

Assessment not done

If Not Done, please specify the reason:





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: CO Breath Test <SA arm/>  
Generated On: 28 Oct 2013 17:39:05

Scheduled Time

Within 15 min prior to smoking ☐  
12:00 - 14:00 ☐  
16:00 - 18:00 ☐  
20:00 - 22:00 ☒  
08:00 - 10:00 ☐

Actual Time of Assessment  
hour:min 24-hour clock

\_\_\_\_\_

Result(ppm)

\_\_\_\_\_



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: CYP2A6 activity Sample  
Generated On: 28 Oct 2013 17:39:05

Not Done

If Not Done, please specify the reason:

H\_NOW (Derived):

Date of sample collection  
DD/MMM/YYYY

Time of sample collection  
hour:min 24-hour clock

Parameter

trans-3'-hydroxycotinine ☒  
cotinine ☐

Date of sample collection  
DD/MMM/YYYY

Time of sample collection  
hour:min 24-hour clock

Parameter

trans-3'-hydroxycotinine ☐  
cotinine ☒



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: CYP1A2 activity Sample

Generated On: 28 Oct 2013 17:39:05

Time of coffee intake

Fixed Unit:  
hour:min 24-hour clock

Sample collection Not Done

If Not Done, please specify the reason:

Date of sample collection  
DD/MMM/YYYY

Time of sample collection  
hour:min 24-hour clock

Parameter

Caffeine ☒  
Paraxanthine ☐

Date of sample collection  
DD/MMM/YYYY

Time of sample collection  
hour:min 24-hour clock

Parameter

Caffeine ☐  
Paraxanthine ☒



**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: Adverse Events Y/N**  
**Generated On: 28 Oct 2013 17:39:05**

Was there any Adverse Event for this subject?

No ☐  
Yes ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Adverse Events

Generated On: 28 Oct 2013 17:39:05

AE Identifier

Adverse Event

Start Date  
DD/MMM/YYYY

End Date  
DD/MMM/YYYY

Ongoing at final contact

No ☐  
Yes ☐

Severity

Mild Adverse Event ☐  
Moderate Adverse Event ☐  
Severe Adverse Event ☐

Serious AE

No ☐  
Yes ☐

Seriousness Criteria

Fatal ☐  
Is life-threatening ☐  
Requires hospitalization ☐  
Results in disability/incapacity ☐  
Congenital anomaly/birth defect ☐

Treatment given

No ☐  
Yes ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Adverse Events

Generated On: 28 Oct 2013 17:39:05

Relationship to study procedures Related ☐  
Not Related ☐

Relationship to CC/THS Related ☐  
Not Related ☐

AE expectedness No ☐  
Yes ☐

Action taken with study product Product use Interrupted ☐  
Product use Stopped ☐  
Product use Reduced ☐  
Not Applicable ☐  
None ☐

Other action taken \_\_\_\_\_

Outcome Death Related to Adverse Event ☐  
Not Recovered or Not Resolved ☐  
Recovered or Resolved ☐  
Recovered or Resolved with Sequelae ☐  
Recovering or Resolving ☐  
Unknown ☐

H\_NOW (Derived): \_\_\_\_\_



**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: Previous and Concomitant Medication Y/N**  
**Generated On: 28 Oct 2013 17:39:05**

Has the subject taken previous or concomitant  
medication?

No ☐  
Yes ☐





**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: Previous and Concomitant Medication**  
**Generated On: 28 Oct 2013 17:39:05**

Brand Name

Start Date  
DD/MMM/YYYY

Stop Date  
DD/MMM/YYYY

Ongoing at final contact

Total Daily dose - Dose



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Previous and Concomitant Medication  
Generated On: 28 Oct 2013 17:39:05

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Total Daily dose - Unit

- Ampule Dosing Unit ☐
  - Bolus Dosing Unit ☐
  - Capsule Dosing Unit ☐
  - Gram ☐
  - Inhalation Dosing Unit ☐
  - International Unit ☐
  - Milligram ☐
  - Milliliter ☐
  - Nebule Dosing Unit ☐
  - Patch Dosing Unit ☐
  - Puff Dosing Unit ☐
  - Suppository Dosing Unit ☐
  - Tablet Dosing Unit ☐
  - Tablespoon Dosing Unit ☐
  - Teaspoon Dosing Unit ☐
  - Microgram per Day ☐
  - Not Applicable ☐
  - Other Dosing Unit ☐
  - Application ☐
-



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Previous and Concomitant Medication  
Generated On: 28 Oct 2013 17:39:05

Route

- Auricular Route of Administration ☐
- Buccal Route of Administration ☐
- Conjunctival Route of Administration ☐
- Cutaneous Route of Administration ☐
- Dental Route of Administration ☐
- Electro-osmosis Route of Administration ☐
- Endocervical Route of Administration ☐
- Endosinusal Route of Administration ☐
- Endotracheal Route of Administration ☐
- Enteral Route of Administration ☐
- Epidural Route of Administration ☐
- Extraamniotic Route of Administration ☐
- Extracorporeal Circulation Route of Administration ☐
- Administration Via Hemodialysis ☐
- Infiltration Route of Administration ☐
- Interstitial Route of Administration ☐
- Intraabdominal Route of Administration ☐
- Intraamniotic Route of Administration ☐
- Intraarterial Route of Administration ☐
- Intraarticular Route of Administration ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Previous and Concomitant Medication  
Generated On: 28 Oct 2013 17:39:05

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- Intrabiliary Route of Administration ☐
- Intrabronchial Route of Administration ☐
- Intrabursal Route of Administration ☐
- Intracardiac Route of Administration ☐
- Intracartilaginous Route of Administration ☐
- Intracaudal Route of Administration ☐
- Intracavernous Route of Administration ☐
- Intracavitary Route of Administration ☐
- Intracerebral Route of Administration ☐
- Intracisternal Route of Administration ☐
- Intracorneal Route of Administration ☐
- Intracoronary Dental Route of Administration ☐
- Intracoronary Route of Administration ☐
- Intracorporus Cavernosum Route of Administration ☐
- Intradermal Route of Administration ☐
- Intradiscal Route of Administration ☐
- Intraductal Route of Administration ☐
- Intraduodenal Route of Administration ☐
- Intradural Route of Administration ☐
- Intraepidermal Route of Administration ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Previous and Concomitant Medication  
Generated On: 28 Oct 2013 17:39:05

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- Intraesophageal Route of Administration ☐
- Intragastric Route of Administration ☐
- Intralingival Route of Administration ☐
- Intraileal Route of Administration ☐
- Intralesional Route of Administration ☐
- Intraluminal Route of Administration ☐
- Intralymphatic Route of Administration ☐
- Intramedullary Route of Administration ☐
- Intrameningeal Route of Administration ☐
- Intramuscular Route of Administration ☐
- Intraocular Route of Administration ☐
- Intraovarian Route of Administration ☐
- Intrapericardial Route of Administration ☐
- Intraperitoneal Route of Administration ☐
- Intrapleural Route of Administration ☐
- Intraprostatic Route of Administration ☐
- Intrapulmonary Route of Administration ☐
- Intrasinal Route of Administration ☐
- Intraspinal Route of Administration ☐
- Intrasynovial Route of Administration ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Previous and Concomitant Medication  
Generated On: 28 Oct 2013 17:39:05

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- Intratendinous Route of Administration ☐
- Intratesticular Route of Administration ☐
- Intrathecal Route of Administration ☐
- Endothoracic Route of Administration ☐
- Intratubular Route of Administration ☐
- Intratumoral Route of Administration ☐
- Intratympanic Route of Administration ☐
- Intrauterine Route of Administration ☐
- Intravascular Route of Administration ☐
- Intravenous Route of Administration ☐
- Intravenous Bolus ☐
- Intravenous Drip ☐
- Intraventricular Route of Administration ☐
- Intravesical Route of Administration ☐
- Intravitreal Route of Administration ☐
- Iontophoresis Route of Administration ☐
- Irrigation-Route of Administration ☐
- Laryngeal Route of Administration ☐
- Nasal Route of Administration ☐
- Nasogastric Route of Administration ☐
- Route of Administration Not Applicable ☐





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Previous and Concomitant Medication  
Generated On: 28 Oct 2013 17:39:05

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- Occlusive Dressing ☐
- Technique ☐
- Ophthalmic Route of ☐
- Administration ☐
- Oral Route of ☐
- Administration ☐
- Oropharyngeal Route of ☐
- Administration ☐
- Other Route of ☐
- Administration ☐
- Parenteral Route of ☐
- Administration ☐
- Percutaneous Route of ☐
- Administration ☐
- Periarticular Route of ☐
- Administration ☐
- Peridural Route of ☐
- Administration ☐
- Perineural Route of ☐
- Administration ☐
- Periodontal Route of ☐
- Administration ☐
- Rectal Route of ☐
- Administration ☐
- Inhalation Route of ☐
- Administration ☐
- Retrobulbar Route of ☐
- Administration ☐
- Soft Tissue Route Of ☐
- Administration ☐
- Subarachnoid Route of ☐
- Administration ☐
- Subconjunctival Route of ☐
- Administration ☐
- Subcutaneous Route of ☐
- Administration ☐
- Sublingual Route of ☐
- Administration ☐
- Submucosal Route of ☐
- Administration ☐





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Previous and Concomitant Medication  
Generated On: 28 Oct 2013 17:39:05

- Topical Route of Administration ☐
- Transdermal Route of Administration ☐
- Mucosal Route of Administration ☐
- Transplacental Route of Administration ☐
- Transtracheal Route of Administration ☐
- Transtympanic Route of Administration ☐
- Unassigned Route of Administration ☐
- Unknown Route of Administration ☐
- Ureteral Route of Administration ☐
- Intraurethral Route of Administration ☐
- Vaginal Route of Administration ☐

Indication

Concomitant Disease Number

AE Number

Other



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: End of study  
Generated On: 28 Oct 2013 17:39:05

End of study date

Fixed Unit:  
DD/MMM/YYYY

Has the subject completed the study ?

No ☐  
Yes ☐

If No, please specify the reason:

Adverse Events ☐  
Protocol Violation ☐  
Withdrawal by Subject ☐  
Lost To Follow-up ☐  
Other ☐

Details:



**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: 24 hour urine collections**  
**Generated On: 28 Oct 2013 17:39:05**

Start Time Fixed Unit:  
hour:min 24-hour clock

End Date Fixed Unit:  
DD/MMM/YYYY

End Time Fixed Unit:  
hour:min 24-hour clock

Volume



**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: Sample Urine Collection**  
**Generated On: 28 Oct 2013 17:39:05**

Were samples collected?

No ☐  
Yes ☐

If No, please specify the reason:

How many primary tubes were collected?

How many back up tubes were collected?

Date of Sample Collection  
DD/MMM/YYYY

Time of Sample Collection



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Questionnaire on smoking urges (QSU)  
Generated On: 28 Oct 2013 17:39:05

Type QSU

Date of Birth Fixed Unit:  
YYYY MMM DD YYYY MMM DD

Date of assessment Fixed Unit:  
YYYY MMM DD YYYY MMM DD

Time of assessment Fixed Unit:  
hour:min 24-hour clock hour:min 24-hour clock

Assessment Status Completed ☐  
Abandoned ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Questionnaire on smoking urges (QSU)  
Generated On: 28 Oct 2013 17:39:05

- 
1. I have a desire for a cigarette right now
- Strongly disagree ☐
- Disagree ☐
- Somewhat disagree ☐
- Do not agree or disagree ☐
- Somewhat agree ☐
- Agree ☐
- Strongly agree ☐
- Abandoned ☐
- 
2. Nothing would be better than smoking a cigarette right now
- Strongly disagree ☐
- Disagree ☐
- Somewhat disagree ☐
- Do not agree or disagree ☐
- Somewhat agree ☐
- Agree ☐
- Strongly agree ☐
- Abandoned ☐
- 
3. If it were possible I would probably smoke now
- Strongly disagree ☐
- Disagree ☐
- Somewhat disagree ☐
- Do not agree or disagree ☐
- Somewhat agree ☐
- Agree ☐
- Strongly agree ☐
- Abandoned ☐
-



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Questionnaire on smoking urges (QSU)  
Generated On: 28 Oct 2013 17:39:05

---

4. I could control things better right now if I could smoke

Strongly disagree ☐  
Disagree ☐  
Somewhat disagree ☐  
Do not agree or disagree ☐  
Somewhat agree ☐  
Agree ☐  
Strongly agree ☐  
Abandoned ☐

---

5. All I want right now is a cigarette

Strongly disagree ☐  
Disagree ☐  
Somewhat disagree ☐  
Do not agree or disagree ☐  
Somewhat agree ☐  
Agree ☐  
Strongly agree ☐  
Abandoned ☐

---

6. I have an urge for a cigarette

Strongly disagree ☐  
Disagree ☐  
Somewhat disagree ☐  
Do not agree or disagree ☐  
Somewhat agree ☐  
Agree ☐  
Strongly agree ☐  
Abandoned ☐

---





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Questionnaire on smoking urges (QSU)  
Generated On: 28 Oct 2013 17:39:05

---

7. A cigarette would taste good now

Strongly disagree ☐  
Disagree ☐  
Somewhat disagree ☐  
Do not agree or disagree ☐  
Somewhat agree ☐  
Agree ☐  
Strongly agree ☐  
Abandoned ☐

---

8. I would do almost anything for a cigarette now

Strongly disagree ☐  
Disagree ☐  
Somewhat disagree ☐  
Do not agree or disagree ☐  
Somewhat agree ☐  
Agree ☐  
Strongly agree ☐  
Abandoned ☐

---

9. Smoking would make me less depressed

Strongly disagree ☐  
Disagree ☐  
Somewhat disagree ☐  
Do not agree or disagree ☐  
Somewhat agree ☐  
Agree ☐  
Strongly agree ☐  
Abandoned ☐

---



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Questionnaire on smoking urges (QSU)  
Generated On: 28 Oct 2013 17:39:05

- 
10. I am going to smoke as soon as possible
- Strongly disagree ☐
- Disagree ☐
- Somewhat disagree ☐
- Do not agree or disagree ☐
- Somewhat agree ☐
- Agree ☐
- Strongly agree ☐
- Abandoned ☐
-



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Questionnaire on smoking urges (QSU) (Paper)  
Generated On: 28 Oct 2013 17:39:05

Type Questionnaire on smoking  
urges

Date of assessment

DD/MMM/YYYY

Time of assessment

hour:min 24-hour clock

1. I have a desire for a cigarette right now

Strongly disagree ☐

Disagree ☐

Somewhat disagree ☐

Do not agree or disagree ☐

Somewhat agree ☐

Agree ☐

Strongly agree ☐

Abandoned ☐

2. Nothing would be better than smoking a cigarette  
right now

Strongly disagree ☐

Disagree ☐

Somewhat disagree ☐

Do not agree or disagree ☐

Somewhat agree ☐

Agree ☐

Strongly agree ☐

Abandoned ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Questionnaire on smoking urges (QSU) (Paper)  
Generated On: 28 Oct 2013 17:39:05

---

3. If it were possible I would probably smoke now

Strongly disagree ☐  
Disagree ☐  
Somewhat disagree ☐  
Do not agree or disagree ☐  
Somewhat agree ☐  
Agree ☐  
Strongly agree ☐  
Abandoned ☐

---

4. I could control things better right now if I could smoke

Strongly disagree ☐  
Disagree ☐  
Somewhat disagree ☐  
Do not agree or disagree ☐  
Somewhat agree ☐  
Agree ☐  
Strongly agree ☐  
Abandoned ☐

---

5. All I want right now is a cigarette

Strongly disagree ☐  
Disagree ☐  
Somewhat disagree ☐  
Do not agree or disagree ☐  
Somewhat agree ☐  
Agree ☐  
Strongly agree ☐  
Abandoned ☐

---



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Questionnaire on smoking urges (QSU) (Paper)  
Generated On: 28 Oct 2013 17:39:05

---

6. I have an urge for a cigarette

Strongly disagree ☐  
Disagree ☐  
Somewhat disagree ☐  
Do not agree or disagree ☐  
Somewhat agree ☐  
Agree ☐  
Strongly agree ☐  
Abandoned ☐

---

7. A cigarette would taste good now

Strongly disagree ☐  
Disagree ☐  
Somewhat disagree ☐  
Do not agree or disagree ☐  
Somewhat agree ☐  
Agree ☐  
Strongly agree ☐  
Abandoned ☐

---

8. I would do almost anything for a cigarette now

Strongly disagree ☐  
Disagree ☐  
Somewhat disagree ☐  
Do not agree or disagree ☐  
Somewhat agree ☐  
Agree ☐  
Strongly agree ☐  
Abandoned ☐

---



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Questionnaire on smoking urges (QSU) (Paper)  
Generated On: 28 Oct 2013 17:39:05

---

9. Smoking would make me less depressed

Strongly disagree ☐  
Disagree ☐  
Somewhat disagree ☐  
Do not agree or disagree ☐  
Somewhat agree ☐  
Agree ☐  
Strongly agree ☐  
Abandoned ☐

---

10. I am going to smoke as soon as possible

Strongly disagree ☐  
Disagree ☐  
Somewhat disagree ☐  
Do not agree or disagree ☐  
Somewhat agree ☐  
Agree ☐  
Strongly agree ☐  
Abandoned ☐

---



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Minnesota Nicotine Dependence/Withdrawal Scale (MNWS)  
Generated On: 28 Oct 2013 17:39:05

Type MNWS

Type Behaviour Rating Scale  
Self-Report

Date of Birth Fixed Unit:  
YYYY MMM DD YYYY MMM DD

Date of assessment Fixed Unit:  
YYYY MMM DD YYYY MMM DD

Time of assessment Fixed Unit:  
hour:min 24-hour clock hour:min 24-hour clock

Assessment Status Completed ☐  
Abandoned ☐

Please indicate for each of the items below, how you have been feeling over the past 24 hours





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Minnesota Nicotine Dependence/Withdrawal Scale (MNWS)  
Generated On: 28 Oct 2013 17:39:05

---

How have you been feeling over the past 24 hours?

1. Angry, irritable, frustrated

None ☐  
Slight ☐  
Mild ☐  
Moderate ☐  
Severe ☐  
Abandoned ☐

---

How have you been feeling over the past 24 hours?

2. Anxious, nervous

None ☐  
Slight ☐  
Mild ☐  
Moderate ☐  
Severe ☐  
Abandoned ☐

---

How have you been feeling over the past 24 hours?

3. Depressed Mood, sad

None ☐  
Slight ☐  
Mild ☐  
Moderate ☐  
Severe ☐  
Abandoned ☐

---

How have you been feeling over the past 24 hours?

4. Desire or craving to smoke

None ☐  
Slight ☐  
Mild ☐  
Moderate ☐  
Severe ☐  
Abandoned ☐

---



**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: Minnesota Nicotine Dependence/Withdrawal Scale (MNWS)**  
**Generated On: 28 Oct 2013 17:39:05**

---

How have you been feeling over the past 24 hours? None ☐  
Slight ☐  
5. Difficulty concentrating Mild ☐  
Moderate ☐  
Severe ☐  
Abandoned ☐

---

How have you been feeling over the past 24 hours? None ☐  
Slight ☐  
6. Increased appetite, hungry, weight gain Mild ☐  
Moderate ☐  
Severe ☐  
Abandoned ☐

---

How have you been feeling over the past 24 hours? None ☐  
Slight ☐  
7. Insomnia, sleep problems, awakening at night Mild ☐  
Moderate ☐  
Severe ☐  
Abandoned ☐

---

How have you been feeling over the past 24 hours? None ☐  
Slight ☐  
8. Restless Mild ☐  
Moderate ☐  
Severe ☐  
Abandoned ☐

---



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Minnesota Nicotine Dependence/Withdrawal Scale (MNWS)  
Generated On: 28 Oct 2013 17:39:05

---

How have you been feeling over the past 24 hours? None ☐  
Slight ☐  
9. Impatient Mild ☐  
Moderate ☐  
Severe ☐  
Abandoned ☐

---

How have you been feeling over the past 24 hours? None ☐  
Slight ☐  
10. Constipation Mild ☐  
Moderate ☐  
Severe ☐  
Abandoned ☐

---

How have you been feeling over the past 24 hours? None ☐  
Slight ☐  
11. Dizziness Mild ☐  
Moderate ☐  
Severe ☐  
Abandoned ☐

---

How have you been feeling over the past 24 hours? None ☐  
Slight ☐  
12. Coughing Mild ☐  
Moderate ☐  
Severe ☐  
Abandoned ☐

---



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Minnesota Nicotine Dependence/Withdrawal Scale (MNWS)  
Generated On: 28 Oct 2013 17:39:05

---

How have you been feeling over the past 24 hours? None ☐  
Slight ☐  
13. Dreaming or nightmares Mild ☐  
Moderate ☐  
Severe ☐  
Abandoned ☐

---

How have you been feeling over the past 24 hours? None ☐  
Slight ☐  
14. Nausea Mild ☐  
Moderate ☐  
Severe ☐  
Abandoned ☐

---

How have you been feeling over the past 24 hours? None ☐  
Slight ☐  
15. Sore Throat Mild ☐  
Moderate ☐  
Severe ☐  
Abandoned ☐

---



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Modifier Cigarette Evaluation Questionnaire (mCEQ)  
Generated On: 28 Oct 2013 17:39:05

Type MCEQ

Date of Birth Fixed Unit:  
YYYY MMM DD YYYY MMM DD

Date of assessment Fixed Unit:  
YYYY MMM DD YYYY MMM DD

Time of assessment Fixed Unit:  
hour:min 24-hour clock hour:min 24-hour clock

Assessment Status Completed ☐  
Abandoned ☐

1. Was smoking satisfying? Not at all ☐  
Very little ☐  
Little ☐  
Moderately ☐  
A lot ☐  
Quite a lot ☐  
Extremely ☐  
Abandoned ☐



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Project Name: ZRHR-REXC-03-EU

Form: Modifier Cigarette Evaluation Questionnaire (mCEQ)

Generated On: 28 Oct 2013 17:39:05

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2. Did cigarettes taste good?

Not at all ☐

Very little ☐

Little ☐

Moderately ☐

A lot ☐

Quite a lot ☐

Extremely ☐

Abandoned ☐

---

3. Did you enjoy the sensation in your throat and chest?

Not at all ☐

Very little ☐

Little ☐

Moderately ☐

A lot ☐

Quite a lot ☐

Extremely ☐

Abandoned ☐

---

4. Did smoking calm you down?

Not at all ☐

Very little ☐

Little ☐

Moderately ☐

A lot ☐

Quite a lot ☐

Extremely ☐

Abandoned ☐

---



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Modifier Cigarette Evaluation Questionnaire (mCEQ)  
Generated On: 28 Oct 2013 17:39:05

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5. Did smoking make you feel more awake?

Not at all ☐  
Very little ☐  
Little ☐  
Moderately ☐  
A lot ☐  
Quite a lot ☐  
Extremely ☐  
Abandoned ☐

---

6. Did smoking make you feel less irritable?

Not at all ☐  
Very little ☐  
Little ☐  
Moderately ☐  
A lot ☐  
Quite a lot ☐  
Extremely ☐  
Abandoned ☐

---

7. Did smoking help you concentrate?

Not at all ☐  
Very little ☐  
Little ☐  
Moderately ☐  
A lot ☐  
Quite a lot ☐  
Extremely ☐  
Abandoned ☐

---





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Modifier Cigarette Evaluation Questionnaire (mCEQ)  
Generated On: 28 Oct 2013 17:39:05

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8. Did smoking reduce your hunger for food?

Not at all ☐  
Very little ☐  
Little ☐  
Moderately ☐  
A lot ☐  
Quite a lot ☐  
Extremely ☐  
Abandoned ☐

---

9. Did smoking make you dizzy?

Not at all ☐  
Very little ☐  
Little ☐  
Moderately ☐  
A lot ☐  
Quite a lot ☐  
Extremely ☐  
Abandoned ☐

---

10. Did smoking make you nauseous?

Not at all ☐  
Very little ☐  
Little ☐  
Moderately ☐  
A lot ☐  
Quite a lot ☐  
Extremely ☐  
Abandoned ☐

---



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Modifier Cigarette Evaluation Questionnaire (mCEQ)  
Generated On: 28 Oct 2013 17:39:05

11. Did smoking immediately relieve your craving for a cigarette?

Not at all ☐  
Very little ☐  
Little ☐  
Moderately ☐  
A lot ☐  
Quite a lot ☐  
Extremely ☐  
Abandoned ☐

12. Did you enjoy smoking?

Not at all ☐  
Very little ☐  
Little ☐  
Moderately ☐  
A lot ☐  
Quite a lot ☐  
Extremely ☐  
Abandoned ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Modifier Cigarette Evaluation Questionnaire (mCEQ) (Paper)  
Generated On: 28 Oct 2013 17:39:05

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Type	Modifier Cigarette Evaluation Questionnaire
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---

Date of assessment	Fixed Unit:
DD/MMM/YYYY	DD/MMM/YYYY

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Time of assessment	Fixed Unit:
	hour:min 24-hour clock

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Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Modifier Cigarette Evaluation Questionnaire (mCEQ) (Paper)

Generated On: 28 Oct 2013 17:39:05

If you have smoked since you last completed this questionnaire, please mark what best represents how smoking made you feel

Was smoking satisfying? ☒

Did cigarettes taste good? ☐

Did you enjoy the sensation in your throat and chest? ☐

Did smoking calm you down? ☐

Did smoking make you feel more awake? ☐

Did smoking make you feel less irritable? ☐

Did smoking help you concentrate? ☐

Did smoking reduce your hunger for food? ☐

Did smoking make you dizzy? ☐

Did smoking make you nauseous? ☐

Did smoking immediately relieve your craving for a cigarette? ☐

Did you enjoy smoking? ☐

Response

Not at all ☐

Very little ☐

Little ☐

Moderately ☐

A lot ☐

Quite a lot ☐

Extremely ☐

Abandoned ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Modifier Cigarette Evaluation Questionnaire (mCEQ) (Paper)

Generated On: 28 Oct 2013 17:39:05

If you have smoked since you last completed this questionnaire, please mark what best represents how smoking made you feel

- Was smoking satisfying? ☐
- Did cigarettes taste good? ☒
- Did you enjoy the sensation in your throat and chest? ☐
- Did smoking calm you down? ☐
- Did smoking make you feel more awake? ☐
- Did smoking make you feel less irritable? ☐
- Did smoking help you concentrate? ☐
- Did smoking reduce your hunger for food? ☐
- Did smoking make you dizzy? ☐
- Did smoking make you nauseous? ☐
- Did smoking immediately relieve your craving for a cigarette? ☐
- Did you enjoy smoking? ☐

Response

- Not at all ☐
- Very little ☐
- Little ☐
- Moderately ☐
- A lot ☐
- Quite a lot ☐
- Extremely ☐
- Abandoned ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Modifier Cigarette Evaluation Questionnaire (mCEQ) (Paper)

Generated On: 28 Oct 2013 17:39:05

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- Did cigarettes taste good? ☐
- Did you enjoy the sensation in your throat and chest? ☒
- Did smoking calm you down? ☐
- Did smoking make you feel more awake? ☐
- Did smoking make you feel less irritable? ☐
- Did smoking help you concentrate? ☐
- Did smoking reduce your hunger for food? ☐
- Did smoking make you dizzy? ☐
- Did smoking make you nauseous? ☐
- Did smoking immediately relieve your craving for a cigarette? ☐
- Did you enjoy smoking? ☐

Response

- Not at all ☐
- Very little ☐
- Little ☐
- Moderately ☐
- A lot ☐
- Quite a lot ☐
- Extremely ☐
- Abandoned ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

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Generated On: 28 Oct 2013 17:39:05

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- Did cigarettes taste good? ☐
- Did you enjoy the sensation in your throat and chest? ☐
- Did smoking calm you down? ☒
- Did smoking make you feel more awake? ☐
- Did smoking make you feel less irritable? ☐
- Did smoking help you concentrate? ☐
- Did smoking reduce your hunger for food? ☐
- Did smoking make you dizzy? ☐
- Did smoking make you nauseous? ☐
- Did smoking immediately relieve your craving for a cigarette? ☐
- Did you enjoy smoking? ☐

Response

- Not at all ☐
- Very little ☐
- Little ☐
- Moderately ☐
- A lot ☐
- Quite a lot ☐
- Extremely ☐
- Abandoned ☐





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- Did cigarettes taste good? ☐
- Did you enjoy the sensation in your throat and chest? ☐
- Did smoking calm you down? ☐
- Did smoking make you feel more awake? ☒
- Did smoking make you feel less irritable? ☐
- Did smoking help you concentrate? ☐
- Did smoking reduce your hunger for food? ☐
- Did smoking make you dizzy? ☐
- Did smoking make you nauseous? ☐
- Did smoking immediately relieve your craving for a cigarette? ☐
- Did you enjoy smoking? ☐

Response

- Not at all ☐
- Very little ☐
- Little ☐
- Moderately ☐
- A lot ☐
- Quite a lot ☐
- Extremely ☐
- Abandoned ☐



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- Did you enjoy the sensation in your throat and chest? ☐
- Did smoking calm you down? ☐
- Did smoking make you feel more awake? ☐
- Did smoking make you feel less irritable? ☒
- Did smoking help you concentrate? ☐
- Did smoking reduce your hunger for food? ☐
- Did smoking make you dizzy? ☐
- Did smoking make you nauseous? ☐
- Did smoking immediately relieve your craving for a cigarette? ☐
- Did you enjoy smoking? ☐

Response

- Not at all ☐
- Very little ☐
- Little ☐
- Moderately ☐
- A lot ☐
- Quite a lot ☐
- Extremely ☐
- Abandoned ☐



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- Did smoking calm you down? ☐
- Did smoking make you feel more awake? ☐
- Did smoking make you feel less irritable? ☐
- Did smoking help you concentrate? ☒
- Did smoking reduce your hunger for food? ☐
- Did smoking make you dizzy? ☐
- Did smoking make you nauseous? ☐
- Did smoking immediately relieve your craving for a cigarette? ☐
- Did you enjoy smoking? ☐

Response

- Not at all ☐
- Very little ☐
- Little ☐
- Moderately ☐
- A lot ☐
- Quite a lot ☐
- Extremely ☐
- Abandoned ☐



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- Did you enjoy the sensation in your throat and chest? ☐
- Did smoking calm you down? ☐
- Did smoking make you feel more awake? ☐
- Did smoking make you feel less irritable? ☐
- Did smoking help you concentrate? ☐
- Did smoking reduce your hunger for food? ☒
- Did smoking make you dizzy? ☐
- Did smoking make you nauseous? ☐
- Did smoking immediately relieve your craving for a cigarette? ☐
- Did you enjoy smoking? ☐

Response

- Not at all ☐
- Very little ☐
- Little ☐
- Moderately ☐
- A lot ☐
- Quite a lot ☐
- Extremely ☐
- Abandoned ☐



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- Did you enjoy the sensation in your throat and chest? ☐
- Did smoking calm you down? ☐
- Did smoking make you feel more awake? ☐
- Did smoking make you feel less irritable? ☐
- Did smoking help you concentrate? ☐
- Did smoking reduce your hunger for food? ☐
- Did smoking make you dizzy? ☒
- Did smoking make you nauseous? ☐
- Did smoking immediately relieve your craving for a cigarette? ☐
- Did you enjoy smoking? ☐

Response

- Not at all ☐
- Very little ☐
- Little ☐
- Moderately ☐
- A lot ☐
- Quite a lot ☐
- Extremely ☐
- Abandoned ☐



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Generated On: 28 Oct 2013 17:39:05

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- Did cigarettes taste good? ☐
- Did you enjoy the sensation in your throat and chest? ☐
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- Did smoking make you feel more awake? ☐
- Did smoking make you feel less irritable? ☐
- Did smoking help you concentrate? ☐
- Did smoking reduce your hunger for food? ☐
- Did smoking make you dizzy? ☐
- Did smoking make you nauseous? ☒
- Did smoking immediately relieve your craving for a cigarette? ☐
- Did you enjoy smoking? ☐

Response

- Not at all ☐
- Very little ☐
- Little ☐
- Moderately ☐
- A lot ☐
- Quite a lot ☐
- Extremely ☐
- Abandoned ☐





Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Modifier Cigarette Evaluation Questionnaire (mCEQ) (Paper)

Generated On: 28 Oct 2013 17:39:05

If you have smoked since you last completed this questionnaire, please mark what best represents how smoking made you feel

- Was smoking satisfying? ☐
- Did cigarettes taste good? ☐
- Did you enjoy the sensation in your throat and chest? ☐
- Did smoking calm you down? ☐
- Did smoking make you feel more awake? ☐
- Did smoking make you feel less irritable? ☐
- Did smoking help you concentrate? ☐
- Did smoking reduce your hunger for food? ☐
- Did smoking make you dizzy? ☐
- Did smoking make you nauseous? ☐
- Did smoking immediately relieve your craving for a cigarette? ☒
- Did you enjoy smoking? ☐

Response

- Not at all ☐
- Very little ☐
- Little ☐
- Moderately ☐
- A lot ☐
- Quite a lot ☐
- Extremely ☐
- Abandoned ☐



**Final version 5.0 (Main CRF): Case Book****Project Name: ZRHR-REXC-03-EU****Form: Modifier Cigarette Evaluation Questionnaire (mCEQ) (Paper)****Generated On: 28 Oct 2013 17:39:05**

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If you have smoked since you last completed this questionnaire,  
please mark what best represents how smoking made you feel

- Was smoking satisfying? ☐
- Did cigarettes taste good? ☐
- Did you enjoy the sensation in your throat and chest? ☐
- Did smoking calm you down? ☐
- Did smoking make you feel more awake? ☐
- Did smoking make you feel less irritable? ☐
- Did smoking help you concentrate? ☐
- Did smoking reduce your hunger for food? ☐
- Did smoking make you dizzy? ☐
- Did smoking make you nauseous? ☐
- Did smoking immediately relieve your craving for a cigarette? ☐
- Did you enjoy smoking? ☒

---

Response

- Not at all ☐
- Very little ☐
- Little ☐
- Moderately ☐
- A lot ☐
- Quite a lot ☐
- Extremely ☐
- Abandoned ☐
-



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Cough Assessment

Generated On: 28 Oct 2013 17:39:05

Type VAS for Cough

Date of Birth Fixed Unit:  
YYYY MMM DD YYYY MMM DD

Date of assessment Fixed Unit:  
YYYY MMM DD YYYY MMM DD

Time of assessment Fixed Unit:  
hour:min 24-hour clock hour:min 24-hour clock

Assessment Status Completed ☐  
Abandoned ☐

Have you experienced a regular need to cough e.g.  
coughing several times in the last 24 hrs? Yes ☐  
No ☐  
Abandoned ☐

If YES, please answer the following questions:

First Question: Cough Impact Scale  
How much is your cough bothering you?



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Cough Assessment

Generated On: 28 Oct 2013 17:39:05

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Second Question: Cough Intensity Scale:  
How intense is your cough?

Very mild ☐  
Mild ☐  
Moderate ☐  
Severe ☐  
Very severe ☐  
Abandoned ☐  
Not Applicable ☐

---

Third Question: Cough Frequency Scale:  
How frequently do you normally have to cough each day?

Rarely ☐  
Sometimes ☐  
Fairly often ☐  
Often ☐  
Almost always ☐  
Abandoned ☐  
Not Applicable ☐

---

Fourth Question: Sputum Production  
To what extent do you produce sputum when coughing?

No sputum ☐  
A moderate amount of sputum ☐  
A large amount of sputum ☐  
A very large amount of sputum ☐  
Abandoned ☐  
Not Applicable ☐

---



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**Project Name: ZRHR-REXC-03-EU**

**Form: Cough Assessment (Paper)**

**Generated On: 28 Oct 2013 17:39:05**

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Type Cough Assessment

---

Date of assessment  
DD/MMM/YYYY

Fixed Unit:  
DD/MMM/YYYY

---

Time of assessment

Fixed Unit:  
hour:min 24-hour clock

---

Have you experienced a regular need to cough e.g.  
coughing several times in the last 24 hrs?

No ☐  
Yes ☐

---

If YES, please answer the following questions:

---

First Question: Cough Impact Scale  
How much is your cough bothering you?

---

Second Question: Cough Intensity Scale:  
How intense is your cough?

Very mild ☐  
Mild ☐  
Moderate ☐  
Severe ☐  
Very severe ☐  
Abandoned ☐  
Not Applicable ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Cough Assessment (Paper)

Generated On: 28 Oct 2013 17:39:05

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Third Question: Cough Frequency Scale:  
How frequently do you normally have to cough each day?

- Rarely ☐  
Sometimes ☐  
Fairly often ☐  
Often ☐  
Almost always ☐  
Abandoned ☐  
Not Applicable ☐

---

Fourth Question: Sputum Production  
To what extent do you produce sputum when coughing?

- No sputum ☐  
A moderate amount of sputum ☐  
A large amount of sputum ☐  
A very large amount of sputum ☐  
Abandoned ☐  
Not Applicable ☐

---

Are there any other important observations that you would like to share with us about you coughing? (open question)

---



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Human Smoking Topography Questionnaire  
Generated On: 28 Oct 2013 17:39:05

Type Human Smoking Topography  
Questionnaire

Date of assessment Fixed Unit:  
DD/MMM/YYYY

Time of assessment Fixed Unit:  
hour:min 24-hour clock

How do you agree with the following sentences/affirmations :

1. The smoking of the conventional cigarettes/products is different with the device. Strongly agree ☐  
Agree ☐  
Neither agree nor disagree ☐  
Disagree ☐  
Strongly disagree ☐

If you agree or strongly agree, please describe :

2. You enjoy smoking with the device as much as without it. Strongly agree ☐  
Agree ☐  
Neither agree nor disagree ☐  
Disagree ☐  
Strongly disagree ☐

If you disagree or strongly disagree, please describe :





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Project Name: ZRHR-REXC-03-EU  
Form: Human Smoking Topography Questionnaire  
Generated On: 28 Oct 2013 17:39:05

3. The taste of the conventional cigarettes/products is  
different with the device. Strongly agree ☐  
Agree ☐  
Neither agree nor disagree ☐  
Disagree ☐  
Strongly disagree ☐

If you agree or strongly agree, please describe : \_\_\_\_\_

4. The device is easy to use. Strongly agree ☐  
Agree ☐  
Neither agree nor disagree ☐  
Disagree ☐  
Strongly disagree ☐

If you disagree or strongly disagree, please describe : \_\_\_\_\_

5. Your smoking is disturbed by the device. Strongly agree ☐  
Agree ☐  
Neither agree nor disagree ☐  
Disagree ☐  
Strongly disagree ☐

If you agree or strongly agree, please describe : \_\_\_\_\_





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Device report - THS 2.2 Cigarette Holder  
Generated On: 28 Oct 2013 17:39:05

Were there any events with the device?

No ☐  
Yes ☐

Event Log Number

Date of Device Event  
DD/MMM/YYYY

Time of  
Device Event  
hour:min 24-hour clock

Event Relates to Device Type:

THS 2.2 Cigarette Holder

Unique Device Identifier Serial Number

Event Description

CH stops heating before ☐  
end of smoking experience  
CH does not charge when ☐  
inserted into the Mobil unit  
CH heater broken (LED ☐  
blinking red)  
Smoking experience does ☐  
not start when pressing the  
button  
Electronic malfunction ☐  
during  
the smoking experience  
Other ☐

Other Describe



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Device report - THS 2.2 Cigarette Holder  
Generated On: 28 Oct 2013 17:39:05

---

Severity of Event

Minor (can be resolved easily) ☐  
Major (cannot be resolved. Device needs to be exchanged) ☐

---

Adverse Event  
Relationship

Is related to AE ☐  
Is not related to AE ☐

---

If Related to AE, AE Number

---

Solution Proposed:

Device Replaced ☐  
Device Recharged ☐  
Device Withdrawn ☐

---

If the device was replaced, New Device Serial Number:

---

Date of Device Event Closure  
DD/MMM/YYYY

---

Time of Device Event Closure  
hour:min 24-hour clock



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Device report - THS 2.2 Charging Unit  
Generated On: 28 Oct 2013 17:39:05

Were there any events with the device?

No ☐  
Yes ☐

Event Log Number

Date of Device Event  
DD/MMM/YYYY

Time of  
Device Event  
hour:min 24-hour clock

Event Relates to  
Device Type:

THS 2.2 Charging Unit

Unique Device Identifier Serial Number

Event Description

Battery Malfunction ☐  
Device Discharged ☐  
Other ☐

Other Describe

Severity of Event

Minor (can be resolved easily) ☐  
Major (cannot be resolved. Device needs to be exchanged) ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Device report - THS 2.2 Charging Unit  
Generated On: 28 Oct 2013 17:39:05

Adverse Event  
Relationship

Is related to AE ☐  
Is not related to AE ☐

Solution Proposed:

Device Replaced ☐  
Device Recharged ☐  
Device Withdrawn ☐

If the device was replaced, New Device Serial Number: \_\_\_\_\_

Date of Device Event Closure  
DD/MMM/YYYY

Time of Device Event Closure  
hour:min 24-hour clock



**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: Device Inventory - THS 2.2 Cigarette Holder**  
**Generated On: 28 Oct 2013 17:39:05**

Device Inventory  
Log Number

Date of Device Distribution  
DD/MMM/YYYY

Time of  
Device Distribution  
hour:min 24-hour clock

Device Type THS 2.2 Cigarette Holder

Device Serial Number

Date of Device Collection  
DD/MMM/YYYY

Time of  
Device Collection  
hour:min 24-hour clock



**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: Device Inventory - THS 2.2 Charging Unit**  
**Generated On: 28 Oct 2013 17:39:05**

Device Inventory  
Log Number

Date of Device Distribution  
DD/MMM/YYYY

Time of  
Device Distribution  
hour:min 24-hour clock

Device Type THS 2.2 Charging Unit

Device Serial Number

Date of Device Collection  
DD/MMM/YYYY

Time of  
Device Collection  
hour:min 24-hour clock



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Bio-banking (Transcriptomics)  
Generated On: 28 Oct 2013 17:39:05

Was a Bio-banking sample for transcriptomics taken?

No ☐  
Yes ☐

Time of Sample Collection

Fixed Unit:  
hour:min 24-hour clock

Was the subject fasting for at least 8 hours at time of  
sample collection?

No ☐  
Yes ☐





**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: Minnesota Nicotine Dependence/Withdrawal Scale (MNWS) (Paper)**  
**Generated On: 28 Oct 2013 17:39:05**

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Type	MNWS
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Type	Behaviour Rating Scale Self-Report
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Date of assessment DD/MMM/YYYY	Fixed Unit: DD/MMM/YYYY
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Time of assessment	Fixed Unit: hour:min 24-hour clock
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Please indicate for each of the items below, how you have been feeling over the past 24 hours

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Form: Minnesota Nicotine Dependence/Withdrawal Scale (MNWS) (Paper)

Generated On: 28 Oct 2013 17:39:05

- 
1. Angry, irritable, frustrated ☒
2. Anxious, tense ☐
3. Depressed Mood, sad ☐
4. Desire or craving to smoke ☐
5. Difficulty concentrating ☐
6. Increased appetite, hungry, weight gain ☐
7. Insomnia, sleep problems, awakening at night ☐
8. Restless ☐
9. Impatient ☐
10. Constipation ☐
11. Dizziness ☐
12. Coughing ☐
13. Dreaming or nightmares ☐
14. Nausea ☐
15. Sore throat ☐

---

Result ☐ None

☐ Slight

☐ Mild

☐ Moderate

☐ Severe

☐ Abandoned

---

---



Final version 5.0 (Main CRF): Case Book  
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  10. Constipation ☐
  11. Dizziness ☐
  12. Coughing ☐
  13. Dreaming or nightmares ☐
  14. Nausea ☐
  15. Sore throat ☐

---

Result

None ☐

Slight ☐

Mild ☐

Moderate ☐

Severe ☐

Abandoned ☐

---

---



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

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14. Nausea ☐
15. Sore throat ☐

---

Result ☐ None

☐ Slight

☐ Mild

☐ Moderate

☐ Severe

☐ Abandoned

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  12. Coughing ☐
  13. Dreaming or nightmares ☐
  14. Nausea ☐
  15. Sore throat ☐

---

Result

None ☐

Slight ☐

Mild ☐

Moderate ☐

Severe ☐

Abandoned ☐

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13. Dreaming or nightmares ☐  
14. Nausea ☐  
15. Sore throat ☐
- 

Result ☐ None  
☐ Slight  
☐ Mild  
☐ Moderate  
☐ Severe  
☐ Abandoned

---

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14. Nausea ☐
15. Sore throat ☐
- 

Result ☐ None

☐ Slight

☐ Mild

☐ Moderate

☐ Severe

☐ Abandoned

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  14. Nausea ☐
  15. Sore throat ☐
- 

Result ☐ None ☐ Slight ☐ Mild ☐ Moderate ☐ Severe ☐ Abandoned

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Result ☐ None ☐ Slight ☐ Mild ☐ Moderate ☐ Severe ☐ Abandoned

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Result ☐ None ☐ Slight ☐ Mild ☐ Moderate ☐ Severe ☐ Abandoned

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  14. Nausea ☐
  15. Sore throat ☐

---

Result

None ☐

Slight ☐

Mild ☐

Moderate ☐

Severe ☐

Abandoned ☐

---

---



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  13. Dreaming or nightmares ☐
  14. Nausea ☐
  15. Sore throat ☐

---

Result

None ☐

Slight ☐

Mild ☐

Moderate ☐

Severe ☐

Abandoned ☐

---

---



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  13. Dreaming or nightmares ☐
  14. Nausea ☐
  15. Sore throat ☐
- 

Result ☐ None ☐ Slight ☐ Mild ☐ Moderate ☐ Severe ☐ Abandoned

---

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  13. Dreaming or nightmares ☒
  14. Nausea ☐
  15. Sore throat ☐
- 

Result ☐ None ☐ Slight ☐ Mild ☐ Moderate ☐ Severe ☐ Abandoned

---

---





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  11. Dizziness ☐
  12. Coughing ☐
  13. Dreaming or nightmares ☐
  14. Nausea ☒
  15. Sore throat ☐
- 

Result

None ☐

Slight ☐

Mild ☐

Moderate ☐

Severe ☐

Abandoned ☐

---

---



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  10. Constipation ☐
  11. Dizziness ☐
  12. Coughing ☐
  13. Dreaming or nightmares ☐
  14. Nausea ☐
  15. Sore throat ☒

---

Result

None ☐

Slight ☐

Mild ☐

Moderate ☐

Severe ☐

Abandoned ☐

---



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Deviation  
Generated On: 28 Oct 2013 17:39:05

Cohort \_\_\_\_\_

Subject \_\_\_\_\_

Assessment \_\_\_\_\_

Visit

Screen Failure ☐

Screening ☐

Admission (Day -2) ☐

Baseline (Day -1) ☐

Baseline (Day 0) ☐

Day 1 ☐

Day 2 ☐

Day 3 ☐

Day 4 ☐

Day 5 ☐

Day 6 ☐

Discharge ☐

Other ☐

Other, Specify \_\_\_\_\_

Timepoint \_\_\_\_\_

Description of Deviation \_\_\_\_\_

Date Deviation Occurred

DD/MMM/YYYY \_\_\_\_\_

**Final version 5.0 (Main CRF): Case Book****Project Name: ZRHR-REXC-03-EU****Form: Deviation****Generated On: 28 Oct 2013 17:39:05**

Date Deviation Reported

DD/MMM/YYYY

Date Deviation Ended

DD/MMM/YYYY

Resolution of the Deviation

Source of the Deviation

CRA ☐Site personnel ☐Sponsor ☐CRO ☐Labs ☐IXRS ☐ePRO ☐

Deviation Category

Violation ☐Mis-randomization ☐Mis-use of product ☐Concomitant medication ☐Time deviation ☐Time missing ☐Assessment missing ☐

Deviation Type

Major ☐Minor ☐



**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: Deviation**  
**Generated On: 28 Oct 2013 17:39:05**

If Major, Evaluation Category

Evaluable ☐  
Non Evaluable ☐



**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: Bio-banking (Biomarkers of exposure and risk markers)**  
**Generated On: 28 Oct 2013 17:39:05**

Was a Bio-banking sample for biomarkers of exposure  
and risk markers taken?

No ☐  
Yes ☐

Time of Sample Collection

Fixed Unit:  
hour:min 24-hour clock

Was the subject fasting for at least 8 hours at time of  
sample collection?

No ☐  
Yes ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Vital Signs

Generated On: 28 Oct 2013 17:39:05

Date of assessment  
DD/MMM/YYYY

Time of assessment  
hour:min 24-hour clock

Has the subject smoked within 15 minutes prior to  
assessment

No ☐

Yes ☐

Pulse rate  
beats per minute

Respiratory rate  
breaths per minute

Blood Pressure (systolic)  
mmHg

Blood Pressure (diastolic)  
mmHg

Vital Signs Position of Subject

Sitting ☐

Standing ☐

Supine ☒





Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: ECG (12-Lead Standard)

Generated On: 28 Oct 2013 17:39:05

Date of assessment  
DD/MMM/YYYY

Position

Sitting ☐  
Standing ☐  
Supine ☒

Heart Rate  
(beats per minute)

QRS Interval  
(msec)

QT Interval  
(msec)

QTcB Interval  
(msec)

PR Interval  
(msec)

Interpretation

Normal ☐  
Abnormal ☐

If Abnormal, Clinical Significance

Not clinically significant ☐  
Clinically significant ☐



**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: ECG (12-Lead Standard)**  
**Generated On: 28 Oct 2013 17:39:05**

---

If Not Clinically significant or clinically Significant, Please  
specify the finding(s) \_\_\_\_\_

---



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Spirometry

Generated On: 28 Oct 2013 17:39:05

Category

With short-acting  
bronchodilator ☐  
Without short-acting  
bronchodilator ☐

Date of assessment:  
DD/MMM/YYYY

Time of assessment:  
hour:min 24-hour clock

Name of bronchodilator

Dose

Fixed Unit:  
MG

Predicted FVC value

Fixed Unit:  
L

Best measured FVC value

Fixed Unit:  
L

Percent of predicted FVC value

Fixed Unit:  
%



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Spirometry  
Generated On: 28 Oct 2013 17:39:05

Best measured FEV1 value Fixed Unit:  
L

Predicted FEV1 value Fixed Unit:  
L

Percent of predicted FEV1 value Fixed Unit:  
%

Interpretation Normal ☐  
Abnormal ☐

If Abnormal, Clinical Significance Not clinically significant ☐  
Clinically significant ☐

If Not Clinically Significant or Clinically Significant, Please  
specify the finding(s)



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination

Generated On: 28 Oct 2013 17:39:05

Date of assessment

Fixed Unit:  
DD/MMM/YYYY

System

General Appearance ☒

HEENT ☐  
(head, eyes, ears, nose,  
throat)

Thyroid Gland ☐

Heart ☐

Chest ☐

Lungs ☐

Gastrointestinal ☐

Cardiovascular System ☐

Neurologic ☐

Skin ☐

Back ☐

Musculoskeletal ☐

Abdomen ☐

Dentition ☐

Other ☐

Other, Specify

Outcome

Normal ☐

Abnormal ☐

Abnormal, please specify:



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination

Generated On: 28 Oct 2013 17:39:05

Clinically significant No ☐  
Yes ☐

Not Done \_\_\_\_\_

Not Done; please specify the reason: \_\_\_\_\_

System General Appearance ☐  
HEENT ☒  
(head, eyes, ears, nose,  
throat)  
Thyroid Gland ☐  
Heart ☐  
Chest ☐  
Lungs ☐  
Gastrointestinal ☐  
Cardiovascular System ☐  
Neurologic ☐  
Skin ☐  
Back ☐  
Musculoskeletal ☐  
Abdomen ☐  
Dentition ☐  
Other ☐

Other, Specify \_\_\_\_\_

Outcome Normal ☐  
Abnormal ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination

Generated On: 28 Oct 2013 17:39:05

Abnormal, please specify: \_\_\_\_\_

Clinically significant

No ☐

Yes ☐

Not Done \_\_\_\_\_

Not Done; please specify the reason: \_\_\_\_\_

System

General Appearance ☐

HEENT ☐

(head, eyes, ears, nose,  
throat)

Thyroid Gland ☒

Heart ☐

Chest ☐

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Gastrointestinal ☐

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Neurologic ☐

Skin ☐

Back ☐

Musculoskeletal ☐

Abdomen ☐

Dentition ☐

Other ☐

Other, Specify \_\_\_\_\_





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Physical Examination  
Generated On: 28 Oct 2013 17:39:05

Outcome Normal ☐  
Abnormal ☐

Abnormal, please specify: \_\_\_\_\_

Clinically significant No ☐  
Yes ☐

Not Done \_\_\_\_\_

Not Done; please specify the reason: \_\_\_\_\_

System General Appearance ☐  
HEENT ☐  
(head, eyes, ears, nose,  
throat)  
Thyroid Gland ☐  
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Gastrointestinal ☐  
Cardiovascular System ☐  
Neurologic ☐  
Skin ☐  
Back ☐  
Musculoskeletal ☐  
Abdomen ☐  
Dentition ☐  
Other ☐



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Generated On: 28 Oct 2013 17:39:05

Other, Specify \_\_\_\_\_

Outcome

Normal ☐

Abnormal ☐

Abnormal, please specify: \_\_\_\_\_

Clinically significant

No ☐

Yes ☐

Not Done \_\_\_\_\_

Not Done; please specify the reason: \_\_\_\_\_



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General Appearance ☐

HEENT ☐

(head, eyes, ears, nose,  
throat)

Thyroid Gland ☐

Heart ☐

Chest ☒

Lungs ☐

Gastrointestinal ☐

Cardiovascular System ☐

Neurologic ☐

Skin ☐

Back ☐

Musculoskeletal ☐

Abdomen ☐

Dentition ☐

Other ☐

Other, Specify

Outcome

Normal ☐

Abnormal ☐

Abnormal, please specify:

Clinically significant

No ☐

Yes ☐

Not Done



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Form: Physical Examination

Generated On: 28 Oct 2013 17:39:05

Not Done; please specify the reason:

System

General Appearance ☐

HEENT ☐

(head, eyes, ears, nose,  
throat)

Thyroid Gland ☐

Heart ☐

Chest ☐

Lungs ☒

Gastrointestinal ☐

Cardiovascular System ☐

Neurologic ☐

Skin ☐

Back ☐

Musculoskeletal ☐

Abdomen ☐

Dentition ☐

Other ☐

Other, Specify

Outcome

Normal ☐

Abnormal ☐

Abnormal, please specify:

Clinically significant

No ☐

Yes ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination

Generated On: 28 Oct 2013 17:39:05

Not Done

Not Done; please specify the reason:

System

General Appearance ☐

HEENT ☐

(head, eyes, ears, nose,  
throat)

Thyroid Gland ☐

Heart ☐

Chest ☐

Lungs ☐

Gastrointestinal ☒

Cardiovascular System ☐

Neurologic ☐

Skin ☐

Back ☐

Musculoskeletal ☐

Abdomen ☐

Dentition ☐

Other ☐

Other, Specify

Outcome

Normal ☐

Abnormal ☐

Abnormal, please specify:



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination

Generated On: 28 Oct 2013 17:39:05

Clinically significant No ☐  
Yes ☐

Not Done \_\_\_\_\_

Not Done; please specify the reason: \_\_\_\_\_

System	General Appearance <input type="checkbox"/>
	HEENT <input type="checkbox"/>
	(head, eyes, ears, nose, throat)
	Thyroid Gland <input type="checkbox"/>
	Heart <input type="checkbox"/>
	Chest <input type="checkbox"/>
	Lungs <input type="checkbox"/>
	Gastrointestinal <input type="checkbox"/>
	Cardiovascular System <input checked="" type="checkbox"/>
	Neurologic <input type="checkbox"/>
	Skin <input type="checkbox"/>
	Back <input type="checkbox"/>
	Musculoskeletal <input type="checkbox"/>
	Abdomen <input type="checkbox"/>
	Dentition <input type="checkbox"/>
	Other <input type="checkbox"/>

Other, Specify \_\_\_\_\_

Outcome Normal ☐  
Abnormal ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination

Generated On: 28 Oct 2013 17:39:05

Abnormal, please specify: \_\_\_\_\_

Clinically significant

No ☐

Yes ☐

Not Done \_\_\_\_\_

Not Done; please specify the reason: \_\_\_\_\_

System

General Appearance ☐

HEENT ☐

(head, eyes, ears, nose,  
throat)

Thyroid Gland ☐

Heart ☐

Chest ☐

Lungs ☐

Gastrointestinal ☐

Cardiovascular System ☐

Neurologic ☒

Skin ☐

Back ☐

Musculoskeletal ☐

Abdomen ☐

Dentition ☐

Other ☐

Other, Specify \_\_\_\_\_





Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination

Generated On: 28 Oct 2013 17:39:05

Outcome Normal ☐  
Abnormal ☐

Abnormal, please specify: \_\_\_\_\_

Clinically significant No ☐  
Yes ☐

Not Done \_\_\_\_\_

Not Done; please specify the reason: \_\_\_\_\_

System General Appearance ☐  
HEENT ☐  
(head, eyes, ears, nose,  
throat)  
Thyroid Gland ☐  
Heart ☐  
Chest ☐  
Lungs ☐  
Gastrointestinal ☐  
Cardiovascular System ☐  
Neurologic ☐  
Skin ☒  
Back ☐  
Musculoskeletal ☐  
Abdomen ☐  
Dentition ☐  
Other ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Physical Examination  
Generated On: 28 Oct 2013 17:39:05

Other, Specify \_\_\_\_\_

Outcome

Normal ☐

Abnormal ☐

Abnormal, please specify: \_\_\_\_\_

Clinically significant

No ☐

Yes ☐

Not Done \_\_\_\_\_

Not Done; please specify the reason: \_\_\_\_\_



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination

Generated On: 28 Oct 2013 17:39:05

System

- General Appearance ☐  
HEENT ☐  
(head, eyes, ears, nose,  
throat)  
Thyroid Gland ☐  
Heart ☐  
Chest ☐  
Lungs ☐  
Gastrointestinal ☐  
Cardiovascular System ☐  
Neurologic ☐  
Skin ☐  
Back ☒  
Musculoskeletal ☐  
Abdomen ☐  
Dentition ☐  
Other ☐

Other, Specify

Outcome

- Normal ☐  
Abnormal ☐

Abnormal, please specify:

Clinically significant

- No ☐  
Yes ☐

Not Done



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination

Generated On: 28 Oct 2013 17:39:05

Not Done; please specify the reason:

System

General Appearance ☐

HEENT ☐

(head, eyes, ears, nose,  
throat)

Thyroid Gland ☐

Heart ☐

Chest ☐

Lungs ☐

Gastrointestinal ☐

Cardiovascular System ☐

Neurologic ☐

Skin ☐

Back ☐

Musculoskeletal ☒

Abdomen ☐

Dentition ☐

Other ☐

Other, Specify

Outcome

Normal ☐

Abnormal ☐

Abnormal, please specify:

Clinically significant

No ☐

Yes ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination

Generated On: 28 Oct 2013 17:39:05

Not Done

Not Done; please specify the reason:

System

General Appearance ☐

HEENT ☐

(head, eyes, ears, nose,  
throat)

Thyroid Gland ☐

Heart ☐

Chest ☐

Lungs ☐

Gastrointestinal ☐

Cardiovascular System ☐

Neurologic ☐

Skin ☐

Back ☐

Musculoskeletal ☐

Abdomen ☒

Dentition ☐

Other ☐

Other, Specify

Outcome

Normal ☐

Abnormal ☐

Abnormal, please specify:



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination

Generated On: 28 Oct 2013 17:39:05

Clinically significant No ☐  
Yes ☐

Not Done \_\_\_\_\_

Not Done; please specify the reason: \_\_\_\_\_

System	General Appearance <input type="checkbox"/>
	HEENT <input type="checkbox"/>
	(head, eyes, ears, nose, throat)
	Thyroid Gland <input type="checkbox"/>
	Heart <input type="checkbox"/>
	Chest <input type="checkbox"/>
	Lungs <input type="checkbox"/>
	Gastrointestinal <input type="checkbox"/>
	Cardiovascular System <input type="checkbox"/>
	Neurologic <input type="checkbox"/>
	Skin <input type="checkbox"/>
	Back <input type="checkbox"/>
	Musculoskeletal <input type="checkbox"/>
	Abdomen <input type="checkbox"/>
	Dentition <input checked="" type="checkbox"/>
	Other <input type="checkbox"/>

Other, Specify \_\_\_\_\_

Outcome Normal ☐  
Abnormal ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination

Generated On: 28 Oct 2013 17:39:05

Abnormal, please specify: \_\_\_\_\_

Clinically significant

No ☐

Yes ☐

Not Done \_\_\_\_\_

Not Done; please specify the reason: \_\_\_\_\_

System

General Appearance ☐

HEENT ☐

(head, eyes, ears, nose,  
throat)

Thyroid Gland ☐

Heart ☐

Chest ☐

Lungs ☐

Gastrointestinal ☐

Cardiovascular System ☐

Neurologic ☐

Skin ☐

Back ☐

Musculoskeletal ☐

Abdomen ☐

Dentition ☐

Other ☒

Other, Specify \_\_\_\_\_





Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination

Generated On: 28 Oct 2013 17:39:05

Outcome Normal ☐  
Abnormal ☐

Abnormal, please specify: \_\_\_\_\_

Clinically significant No ☐  
Yes ☐

Not Done \_\_\_\_\_

Not Done; please specify the reason: \_\_\_\_\_

System General Appearance ☐  
HEENT ☐  
(head, eyes, ears, nose,  
throat)  
Thyroid Gland ☐  
Heart ☐  
Chest ☐  
Lungs ☐  
Gastrointestinal ☐  
Cardiovascular System ☐  
Neurologic ☐  
Skin ☐  
Back ☐  
Musculoskeletal ☐  
Abdomen ☐  
Dentition ☐  
Other ☒



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Physical Examination  
Generated On: 28 Oct 2013 17:39:05

Other, Specify \_\_\_\_\_

Outcome

Normal ☐

Abnormal ☐

Abnormal, please specify: \_\_\_\_\_

Clinically significant

No ☐

Yes ☐

Not Done \_\_\_\_\_

Not Done; please specify the reason: \_\_\_\_\_



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination

Generated On: 28 Oct 2013 17:39:05

System

General Appearance ☐

HEENT ☐

(head, eyes, ears, nose,  
throat)

Thyroid Gland ☐

Heart ☐

Chest ☐

Lungs ☐

Gastrointestinal ☐

Cardiovascular System ☐

Neurologic ☐

Skin ☐

Back ☐

Musculoskeletal ☐

Abdomen ☐

Dentition ☐

Other ☒

Other, Specify

Outcome

Normal ☐

Abnormal ☐

Abnormal, please specify:

Clinically significant

No ☐

Yes ☐

Not Done



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination

Generated On: 28 Oct 2013 17:39:05

Not Done; please specify the reason: \_\_\_\_\_

System

General Appearance ☐

HEENT ☐

(head, eyes, ears, nose,  
throat)

Thyroid Gland ☐

Heart ☐

Chest ☐

Lungs ☐

Gastrointestinal ☐

Cardiovascular System ☐

Neurologic ☐

Skin ☐

Back ☐

Musculoskeletal ☐

Abdomen ☐

Dentition ☐

Other ☒

Other, Specify \_\_\_\_\_

Outcome

Normal ☐

Abnormal ☐

Abnormal, please specify: \_\_\_\_\_

Clinically significant

No ☐

Yes ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Physical Examination

Generated On: 28 Oct 2013 17:39:05

Not Done

Not Done; please specify the reason:

System

General Appearance ☐

HEENT ☐

(head, eyes, ears, nose,  
throat)

Thyroid Gland ☐

Heart ☐

Chest ☐

Lungs ☐

Gastrointestinal ☐

Cardiovascular System ☐

Neurologic ☐

Skin ☐

Back ☐

Musculoskeletal ☐

Abdomen ☐

Dentition ☐

Other ☒

Other, Specify

Outcome

Normal ☐

Abnormal ☐

Abnormal, please specify:



**Final version 5.0 (Main CRF): Case Book**

**Project Name: ZRHR-REXC-03-EU**

**Form: Physical Examination**

**Generated On: 28 Oct 2013 17:39:05**

Clinically significant

No ☐

Yes ☐

Not Done

Not Done; please specify the reason:



**Final version 5.0 (Main CRF): Case Book**

**Project Name: ZRHR-REXC-03-EU**

**Form: Weight**

**Generated On: 28 Oct 2013 17:39:05**

\_\_\_\_\_  
Date of assessment  
DD/MMM/YYYY

\_\_\_\_\_  
Time of assessment  
hour:min 24-hour clock

\_\_\_\_\_  
Weight

Fixed Unit:  
kg





Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: X-Ray  
Generated On: 28 Oct 2013 17:39:05

Category for Examination

Chest X-Ray ☐

Date of assessment  
DD/MMM/YYYY

System

General Appearance ☐  
HEENT ☐  
(head, eyes, ears, nose,  
throat)  
Thyroid Gland ☐  
Heart ☐  
Chest ☒  
Lungs ☐  
Gastrointestinal ☐  
Cardiovascular System ☐  
Neurologic ☐  
Skin ☐  
Back ☐  
Musculoskeletal ☐  
Abdomen ☐  
Dentition ☐  
Other ☐

Interpretation

Normal ☐  
Abnormal ☐

Clinically significant

No ☐  
Yes ☐



**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: X-Ray**  
**Generated On: 28 Oct 2013 17:39:05**

Abnormal, please specify: \_\_\_\_\_



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Urine Drug Screen

Generated On: 28 Oct 2013 17:39:05

Category

- Clinical Chemistry ☐  
Drug Screen ☒  
Haematology ☐  
Serology ☐  
Pregnancy Testing ☐  
Urinalysis ☐  
Cotinine Screening ☐  
Alcohol Breath Test ☐

Date of sample collection

Fixed Unit:  
DD/MMM/YYYY

Time of sample collection

Fixed Unit:  
hour:min 24-hour clock

Drug type

- Amphetamines ☐  
Barbiturates ☐  
Benzodiazepines ☐  
Cannabinoids ☐  
Cocaine ☐  
Opiates ☐

Result

- Negative ☐  
Positive ☐



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Alcohol Breath Test  
Generated On: 28 Oct 2013 17:39:05

Category

Clinical Chemistry ☐  
Drug Screen ☐  
Haematology ☐  
Serology ☐  
Pregnancy Testing ☐  
Urinalysis ☐  
Cotinine Screening ☐  
Alcohol Breath Test ☒

Date of assessment  
DD/MMM/YYYY

Time of assessment  
hour:min 24-hour clock

Result

Negative ☐  
Positive ☐



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Urine Pregnancy Test

Generated On: 28 Oct 2013 17:39:05

Category

- Clinical Chemistry ☐  
Drug Screen ☐  
Haematology ☐  
Serology ☐  
Pregnancy Testing ☒  
Urinalysis ☐  
Cotinine Screening ☐  
Alcohol Breath Test ☐

Date of Test  
DD/MMM/YYYY

Time of Test  
hour:min 24-hour clock

Specify result

- Negative ☐  
Positive ☐  
Unclear ☐

Specify result of FSH test

- < 20 IU/L ☐  
>= 20 IU/L ☐



**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: Blood Samples**  
**Generated On: 28 Oct 2013 17:39:05**

Date  
DD/MMM/YYYY

Time  
hour:min 24-hour clock

Scheduled Time

Sample Type



**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: CO Breath Test**  
**Generated On: 28 Oct 2013 17:39:05**

\_\_\_\_\_  
\_\_\_\_\_  
Date of Assessment  
DD/MMM/YYYY

\_\_\_\_\_  
\_\_\_\_\_  
Actual Time of Assessment  
hour:min 24-hour clock

\_\_\_\_\_  
\_\_\_\_\_  
Result  
ppm





**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: Subject (Site level)**  
**Generated On: 28 Oct 2013 17:39:05**

---

Subject (site level)

---



**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: Site Accountability**  
**Generated On: 28 Oct 2013 17:39:05**

Date of batch dispensed	_____
Batch number	_____
Category	Received <input type="checkbox"/> Returned <input type="checkbox"/>
Batch Expiration Date (only for received event) DD/MMM/YYYY	_____
Number of unused packs returned	_____
Number of unused sticks returned (only for returned event)	_____
Batch number	_____



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: LABSTAT results  
Generated On: 28 Oct 2013 17:39:05

Cohort Number

Kit Number

Vial Number

Day Number

Sample Collection Date

Group No.

Run No.

Port No.

Sample ID

Number of Filters

Extraction Volume (ml)

Date of Extraction

Sample Volume (ml)

Dilution Volume (ml)



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: LABSTAT results  
Generated On: 28 Oct 2013 17:39:05

\_\_\_\_\_  
Total Volume (ml) \_\_\_\_\_  
\_\_\_\_\_  
Date of analysis (UV) \_\_\_\_\_  
\_\_\_\_\_  
Absolute UV Absorbance Mouthpiece part of the Filter \_\_\_\_\_  
\_\_\_\_\_  
Absolute UV Absorbance 'PLA + HAT' part of the Filter \_\_\_\_\_  
\_\_\_\_\_  
Absolute UV Absorbance Full Filter \_\_\_\_\_  
\_\_\_\_\_  
Normalized UV Absorbance Mouthpiece part of the Filter \_\_\_\_\_  
\_\_\_\_\_  
Normalized UV Absorbance 'PLA + HAT' part of the Filter \_\_\_\_\_  
\_\_\_\_\_  
Normalized UV Absorbance Full Filter \_\_\_\_\_  
\_\_\_\_\_  
Date of analysis (Nicotine) \_\_\_\_\_  
\_\_\_\_\_  
Nicotine Amount Mouthpiece part of the Filter (mg/ml) \_\_\_\_\_  
\_\_\_\_\_  
Nicotine Amount 'PLA + HAT' part of the Filter (mg/ml) \_\_\_\_\_  
\_\_\_\_\_  
Nicotine Amount Full Filter (mg/ml) \_\_\_\_\_  
\_\_\_\_\_  
Nicotine Amount Mouthpiece part of the Filter (mg/filter) \_\_\_\_\_  
\_\_\_\_\_  
Nicotine Amount 'PLA + HAT' part of the Filter (mg/filter) \_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_



**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: LABSTAT results**  
**Generated On: 28 Oct 2013 17:39:05**

Nicotine Amount Full Filter (mg/filter)

Comments



Final version 5.0 (Main CRF): Case Book  
Project Name: ZRHR-REXC-03-EU  
Form: Lab-BU  
Generated On: 28 Oct 2013 17:39:05

Experiment Type	
Date of Sample Collection	
Time of Sample Collection	
Analyte Name	
Result	
Unit	
Lower limit	
Upper limit	



Final version 5.0 (Main CRF): Case Book

Project Name: ZRHR-REXC-03-EU

Form: Lab-BU

Generated On: 28 Oct 2013 17:39:05

Flag	Normal <input type="checkbox"/>
	Low <input type="checkbox"/>
	High <input type="checkbox"/>
	Abnormal <input type="checkbox"/>
	Grade 1 high <input type="checkbox"/>
	Grade 2 high <input type="checkbox"/>
	Grade 3 high <input type="checkbox"/>
	Panic high <input type="checkbox"/>
	Panic Low <input type="checkbox"/>
	Exclusion <input type="checkbox"/>
	Test not performed <input type="checkbox"/>
	Grade 1 low <input type="checkbox"/>
	Grade 2 low <input type="checkbox"/>
	Grade 3 low <input type="checkbox"/>
	Grade 1 <input type="checkbox"/>
	Grade 1 abnormal <input type="checkbox"/>
	Grade 2 <input type="checkbox"/>
	Grade 3 <input type="checkbox"/>
	Grade 2 abnormal <input type="checkbox"/>
	Grade 3 abnormal <input type="checkbox"/>

Clinically Significant?	No <input type="checkbox"/>
	Yes <input type="checkbox"/>

Comment	<input type="text"/>
Data Type unique identifier	<input type="text"/>
Random number	<input type="text"/>





**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: Lab-BU**  
**Generated On: 28 Oct 2013 17:39:05**

Sex

Date of Birth-BU

Visit ID

Lab Comments

Site Number

Please document clinically relevant abnormalities in the AE form

Derived Form name(Lab Type-Date)

H\_NOW (Derived):



**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: Biomarker(Blood)**  
**Generated On: 28 Oct 2013 17:39:05**

Sample type	
Sample Barcode	
Analyte	
Result	
Result Unit	
Lab Status	
Sample comment	
Detection method	
Lower limit of quantification	
Planned time point (Hour)	
Day of Visit	
Celerion Study Number	
Date of Collection	
Timepoint-minutes	



**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: Biomarker(Blood)**  
**Generated On: 28 Oct 2013 17:39:05**

Urine Start Day

Urine End Day



**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: Biomarker(Urine)**  
**Generated On: 28 Oct 2013 17:39:05**

Sample type	
Sample Barcode	
Analyte	
Result	
Result Unit	
Lab Status	
Sample comment	
Detection method	
Lower limit of quantification	
Planned time point (Hour)	
Day of Visit	
Celerion Study Number	
Date of Collection	
Timepoint-minutes	



**Final version 5.0 (Main CRF): Case Book**  
**Project Name: ZRHR-REXC-03-EU**  
**Form: Biomarker(Urine)**  
**Generated On: 28 Oct 2013 17:39:05**

Urine Start Day

Urine End Day



## **16.1.2.2 SUBJECT QUESTIONNAIRE ENGLISH**

### **16.1.2.2.1 Cough Assessment**



## Cough assessment

Have you experienced a regular need to cough e.g. coughing several times in the last 24 hrs?

YES / NO

If YES, please answer the following questions:

## First Question: Cough Impact Scale

How much is your cough bothering you?

VAS: Not Bothering Me at All -----Extremely Bothersome

## Second Question: Cough Intensity Scale:

How intense is your cough?

1 = very mild - 2 = mild - 3 = moderate - 4 = severe - 5 = very severe

## Third Question: Cough Frequency Scale:

How frequently do you normally have to cough each day?

1 = rarely - 2 = sometimes - 3 = fairly often - 4 = often - 5 = almost always

## Fourth Question: Sputum Production

To what extent do you produce sputum when coughing?

0 = no sputum - 1 = a moderate amount of sputum - 2 = a large amount of sputum - 3 = a very large amount of sputum

## Fifth Question:

Are there any other important observations that you would like to share with us about you coughing? (open question)





#### **16.1.2.2.2 Fagerström Nicotine Dependence Test**

**Fagerstrom Test for Nicotine Dependence \***

Is smoking "just a habit" or are you addicted? Take this test and find out your level of dependence on nicotine.

1. How soon after you wake up do you smoke your first cigarette?
  - ◆ After 60 minutes (0)
  - ◆ 31-60 minutes (1)
  - ◆ 6-30 minutes (2)
  - ◆ Within 5 minutes (3)
2. Do you find it difficult to refrain from smoking in places where it is forbidden?
  - ◆ No (0)
  - ◆ Yes (1)
3. Which cigarette would you hate most to give up?
  - ◆ The first in the morning (1)
  - ◆ Any other (0)
4. How many cigarettes per day do you smoke?
  - ◆ 10 or less (0)
  - ◆ 11-20 (1)
  - ◆ 21-30 (2)
  - ◆ 31 or more (3)
5. Do you smoke more frequently during the first hours after awakening than during the rest of the day?
  - ◆ No (0)
  - ◆ Yes (1)
6. Do you smoke even if you are so ill that you are in bed most of the day?
  - ◆ No (0)
  - ◆ Yes (1)

\* Heatherton TF, Kozlowski LT, Frecker RC, Fagerstrom KO. The Fagerstrom Test for Nicotine Dependence: A revision of the Fagerstrom Tolerance Questionnaire. British Journal of Addictions 1991;86:1119-27

**Fagerstrom Test for Nicotine Dependence (cont.)**

Your score was: \_\_\_\_\_

Your level of dependence on nicotine is:

0-2 Very low dependence	6-7 High dependence
3-4 Low dependence	8-10 Very high dependence
5 Medium dependence	

Scores under 5: "Your level of nicotine dependence is still low. You should act now before your level of dependence increases."

Score of 5: "Your level of nicotine dependence is moderate. If you don't quit soon, your level of dependence on nicotine will increase until you may be seriously addicted. Act now to end your dependence on nicotine."

Score over 7: "Your level of dependence is high. You aren't in control of your smoking – it is in control of you! When you make the decision to quit, you may want to talk with your doctor about nicotine replacement therapy or other medications to help you break your addiction."



### **16.1.2.2.3 Human Smoking Topography Questionnaire**



How do you agree with the following sentences/affirmations :

1. The smoking of the conventional cigarettes/products is different with the device.
- ☐ Strongly agree
  - ☐ Agree
  - ☐ Neither agree nor disagree
  - ☐ Disagree
  - ☐ Strongly disagree

If you agree or strongly agree, please describe :

2. You enjoy smoking with the device as much as without it.
- ☐ Strongly agree
  - ☐ Agree
  - ☐ Neither agree nor disagree
  - ☐ Disagree
  - ☐ Strongly disagree

If you disagree or strongly disagree, please describe :

3. The taste of the conventional cigarette/products is different with the device.
- ☐ Strongly agree
  - ☐ Agree
  - ☐ Neither agree nor disagree
  - ☐ Disagree
  - ☐ Strongly disagree

If you agree or strongly agree, please describe :

4. The device is easy to use.
- ☐ Strongly agree
  - ☐ Agree
  - ☐ Neither agree nor disagree
  - ☐ Disagree
  - ☐ Strongly disagree

If you disagree or strongly disagree, please describe :

5. Your smoking is disturbed by the device
- ☐ Strongly agree
  - ☐ Agree
  - ☐ Neither agree nor disagree
  - ☐ Disagree



☐ Strongly disagree

If you agree or strongly agree, please describe :



#### **16.1.2.2.4 Modified Cigarette Evaluation Questionnaire**



**Modified Cigarette Evaluation Questionnaire (mCEQ)**

Date and time of assessment (24-hour clock)   /    /        ☐ Tick if same as visit date

:    
hour min

If you have smoked since you last completed this questionnaire, please select what best represents how smoking made you feel

1. Was smoking satisfying?

Not at all	Very little	Little	Moderately	A lot	Quite a lot	Extremely
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

2. Did cigarettes taste good?

Not at all	Very little	Little	Moderately	A lot	Quite a lot	Extremely
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

3. Did you enjoy the sensation in your throat and chest?

Not at all	Very little	Little	Moderately	A lot	Quite a lot	Extremely
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

4. Did smoking calm you down?

Not at all	Very little	Little	Moderately	A lot	Quite a lot	Extremely
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>



Modified Cigarette Evaluation Questionnaire						
5. Did smoking make you feel more awake?						
Not at all	Very little	Little	Moderately	A lot	Quite a lot	Extremely
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. Did smoking make you feel less irritable?						
Not at all	Very little	Little	Moderately	A lot	Quite a lot	Extremely
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. Did smoking help you concentrate?						
Not at all	Very little	Little	Moderately	A lot	Quite a lot	Extremely
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. Did smoking reduce your hunger for food?						
Not at all	Very little	Little	Moderately	A lot	Quite a lot	Extremely
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9. Did smoking make you dizzy?						
Not at all	Very little	Little	Moderately	A lot	Quite a lot	Extremely
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10. Did smoking make you nauseous?						
Not at all	Very little	Little	Moderately	A lot	Quite a lot	Extremely
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>



Modified Cigarette Evaluation Questionnaire						
11. Did smoking immediately relieve your craving for a cigarette?						
Not at all	Very little	Little	Moderately	A lot	Quite a lot	Extremely
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
12. Did you enjoy smoking?						
Not at all	Very little	Little	Moderately	A lot	Quite a lot	Extremely
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>



#### **16.1.2.2.5 Minnesota Nicotine Dependence/Withdrawal Scale**



<b>&lt;VISIT&gt;</b>																																																																													
<b>Minnesota Nicotine Dependence/Withdrawal Scale (MNWS)</b>																																																																													
<b>Behavior Rating Scale Self-Report</b>																																																																													
<p>Date and time of assessment (24-hour clock)      <input type="checkbox"/> Tick if same as visit date</p> <p>    <input type="text"/> <input type="text"/> / <input type="text"/> <input type="text"/> / <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>     D D      M M M      Y Y Y Y</p> <p>    <input type="text"/> <input type="text"/> : <input type="text"/> <input type="text"/>     hour      min</p> <p>Please indicate for each of the items below, how you have been feeling over the past 24 hours.</p> <table><thead><tr><th></th><th>None</th><th>Slight</th><th>Mild</th><th>Moderate</th><th>Severe</th></tr></thead><tbody><tr><td>1. Angry, irritable, frustrated</td><td><input type="checkbox"/></td><td><input type="checkbox"/></td><td><input type="checkbox"/></td><td><input type="checkbox"/></td><td><input type="checkbox"/></td></tr><tr><td>2. Anxious, nervous</td><td><input type="checkbox"/></td><td><input type="checkbox"/></td><td><input type="checkbox"/></td><td><input type="checkbox"/></td><td><input type="checkbox"/></td></tr><tr><td>3. Depressed Mood, sad</td><td><input type="checkbox"/></td><td><input type="checkbox"/></td><td><input type="checkbox"/></td><td><input type="checkbox"/></td><td><input type="checkbox"/></td></tr><tr><td>4. Desire or craving to smoke</td><td><input type="checkbox"/></td><td><input type="checkbox"/></td><td><input type="checkbox"/></td><td><input type="checkbox"/></td><td><input type="checkbox"/></td></tr><tr><td>5. Difficulty concentrating</td><td><input type="checkbox"/></td><td><input type="checkbox"/></td><td><input type="checkbox"/></td><td><input type="checkbox"/></td><td><input type="checkbox"/></td></tr><tr><td>6. Increased appetite, hungry, weight gain</td><td><input type="checkbox"/></td><td><input type="checkbox"/></td><td><input type="checkbox"/></td><td><input type="checkbox"/></td><td><input type="checkbox"/></td></tr><tr><td>7. Insomnia, sleep problems, awakening at night</td><td><input type="checkbox"/></td><td><input type="checkbox"/></td><td><input type="checkbox"/></td><td><input type="checkbox"/></td><td><input type="checkbox"/></td></tr><tr><td>8. Restless</td><td><input type="checkbox"/></td><td><input type="checkbox"/></td><td><input type="checkbox"/></td><td><input type="checkbox"/></td><td><input type="checkbox"/></td></tr><tr><td>9. Impatient</td><td><input type="checkbox"/></td><td><input type="checkbox"/></td><td><input type="checkbox"/></td><td><input type="checkbox"/></td><td><input type="checkbox"/></td></tr><tr><td>10. Constipation</td><td><input type="checkbox"/></td><td><input type="checkbox"/></td><td><input type="checkbox"/></td><td><input type="checkbox"/></td><td><input type="checkbox"/></td></tr><tr><td>11. Dizziness</td><td><input type="checkbox"/></td><td><input type="checkbox"/></td><td><input type="checkbox"/></td><td><input type="checkbox"/></td><td><input type="checkbox"/></td></tr></tbody></table>							None	Slight	Mild	Moderate	Severe	1. Angry, irritable, frustrated	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	2. Anxious, nervous	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	3. Depressed Mood, sad	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	4. Desire or craving to smoke	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	5. Difficulty concentrating	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	6. Increased appetite, hungry, weight gain	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	7. Insomnia, sleep problems, awakening at night	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	8. Restless	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	9. Impatient	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	10. Constipation	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	11. Dizziness	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	None	Slight	Mild	Moderate	Severe																																																																								
1. Angry, irritable, frustrated	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>																																																																								
2. Anxious, nervous	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>																																																																								
3. Depressed Mood, sad	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>																																																																								
4. Desire or craving to smoke	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>																																																																								
5. Difficulty concentrating	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>																																																																								
6. Increased appetite, hungry, weight gain	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>																																																																								
7. Insomnia, sleep problems, awakening at night	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>																																																																								
8. Restless	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>																																																																								
9. Impatient	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>																																																																								
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11. Dizziness	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>																																																																								



<b>&lt;VISIT&gt;</b>					
<b>Minnesota Nicotine Dependence/Withdrawal Scale (MNWS)</b>					
<b>Behavior Rating Scale Self-Report</b>					
12. Coughing	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
13. Dreaming or nightmares	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
14. Nausea	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
15. Sore throat	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Heart Rate	_____				bpm
Weight	_____				Kg



#### **16.1.2.2.6 Questionnaire on Smoking Urges**



**Questionnaire on smoking urges (QSU)**

Date and time of assessment (24-hour clock)   /    /        ☐ Tick if same as visit date

:    
hour min

1. I have a desire for a cigarette right now

Strongly disagree	Disagree	Somewhat disagree	Do not agree or disagree	Somewhat agree	Agree	Strongly agree
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

2. Nothing would be better than smoking a cigarette right now

Strongly disagree	Disagree	Somewhat disagree	Do not agree or disagree	Somewhat agree	Agree	Strongly agree
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

3. If it were possible I would probably smoke now

Strongly disagree	Disagree	Somewhat disagree	Do not agree or disagree	Somewhat agree	Agree	Strongly agree
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>



Questionnaire on smoking urges (QSU)						
4. I could control things better right now if I could smoke						
Strongly disagree						Strongly agree
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. All I want right now is a cigarette						
Strongly disagree						Strongly agree
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. I have an urge for a cigarette						
Strongly disagree						Strongly agree
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. A cigarette would taste good now						
Strongly disagree						Strongly agree
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. I would do almost anything for a cigarette now						
Strongly disagree						Strongly agree
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>



Questionnaire on smoking urges (QSU)						
9. Smoking would make me less depressed						
Strongly disagree						Strongly agree
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10. I am going to smoke as soon as possible						
Strongly disagree						Strongly agree
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>



### **16.1.2.3 SUBJECT QUESTIONNAIRE LOCAL LANGUAGE**

#### **16.1.2.3.1 Cough Assessment**



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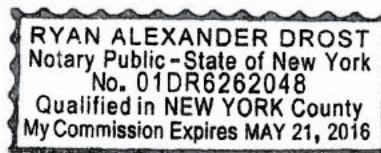
City of New York, State of New York, County of New York

I, Gaby Grijalva, hereby certify that the following is, to the best of my knowledge and belief, a true and accurate translation of the document titled "Cough assessment\_VAS" from English into Poland (Polish) following Covance's process of concept definition, Revisions to existing Polish translations, Covance Review, cognitive interviewing with 5 adult smokers, final proofreading, and formatting.

Gaby Grijalva, Project Coordinator

Sworn to before me this  
Wednesday, April 17, 2013

Signature, Notary Public



Stamp, Notary Public







#### **16.1.2.3.2 Fagerström Nicotine Dependence Test**



City of New York, State of New York, County of New York

I, Gaby Grijalva, hereby certify that the following is, to the best of my knowledge and belief, a true and accurate translation of the document titled "Fagerstrom-Nicotine-Dependence-Test" from English into Poland (Polish) following Covance's process of concept definition, Revisions to existing Polish translations, Covance Review, cognitive interviewing with 5 adult smokers, final proofreading, and formatting.

A handwritten signature in black ink, appearing to read 'Gaby Grijalva'.

Gaby Grijalva, Project Coordinator

Sworn to before me this  
Wednesday, April 17, 2013

A handwritten signature in black ink, appearing to read 'Ryan Alexander Drost'.

Signature, Notary Public



Stamp, Notary Public

### **Test uzależnienia od nikotyny wg Fagerstroma\***

Czy palenie jest „tylko nawykiem”, czy jest Pan/Pani uzależniony/a?

Proszę wykonać ten test i sprawdzić swój poziom uzależnienia od nikotyny.

1. Jak szybko po przebudzeniu zapala Pan/Pani pierwszego papierosa?
  - ♦ Po 60 minutach lub później (0)
  - ♦ 31-60 minut (1)
  - ♦ 6-30 minut (2)
  - ♦ W ciągu 5 minut (3)
2. Czy ma Pan/Pani trudności z powstrzymaniem się od palenia w miejscach, w których jest to zabronione?
  - ♦ Nie (0)
  - ♦ Tak (1)
3. Z którego papierosa byłoby Panu/Pani najtrudniej zrezygnować?
  - ♦ Z pierwszego rano (1)
  - ♦ Z każdego innego (0)
4. Ile papierosów wypala Pan/Pani w ciągu dnia?
  - ♦ 10 lub mniej (0)
  - ♦ 11-20 (1)
  - ♦ 21-30 (2)
  - ♦ 31 lub więcej (3)
5. Czy częściej pali Pan/Pani papierosy w ciągu pierwszych godzin po przebudzeniu niż w pozostałej części dnia?
  - ♦ Nie (0)
  - ♦ Tak (1)
6. Czy pali Pan/Pani papierosy nawet wtedy, gdy jest Pan/Pani tak chory/a, że musi Pan/Pani leżeć w łóżku przez większość dnia?
  - ♦ Nie (0)
  - ♦ Tak (1)

\* Heatherton T.F., Kozłowski L.T., Frecker R.C., Fagerstrom K.O. The Fagerstrom Test for Nicotine Dependence: A revision of the Fagerstrom Tolerance Questionnaire. British Journal of Addictions 1991;86:1119-27

Uzyskany przez Pana/Panią  
wynik: \_\_\_\_\_

Poziom Pana/Pani uzależnienia od  
nikotyny wynosi:

- 0-2 Bardzo słabe uzależnienie
- 3-4 Słabe uzależnienie
- 5 Umiarkowane uzależnienie
- 6-7 Silne uzależnienie
- 8-10 Bardzo silne uzależnienie

**Wyniki poniżej 5:**

„Jest Pan/Pani uzależniony/a od nikotyny, jednak nadal w niewielkim stopniu. Powinien/powinna Pan/Pani już teraz zacząć działać, zanim wzrośnie poziom Pana/Pani uzależnienia.”

**Wynik równy 5:**

„Jest Pan/Pani w umiarkowanym stopniu uzależniony/a od nikotyny. Jeśli szybko nie rzuci Pan/Pani palenia, poziom Pana/Pani uzależnienia wzrośnie i może Pan/Pani stać się poważnie uzależniony/a. Niech Pan/Pani podejmie działania na rzecz uwolnienia się od tego nałogu.”

**Wynik powyżej 7:**

„Jest Pan/Pani silnie uzależniony/a. Nie panuje Pan/Pani nad swoim paleniem – to ono panuje nad Panem/Panią! Gdy postanowi Pan/Pani rzucić palenie, może Pan/Pani porozmawiać z lekarzem na temat terapii substytucyjnej lub innych metod farmakologicznych, które pomagają zerwać z uzależnieniem od nikotyny.”

#### **16.1.2.3.3 Human Smoking Topography Questionnaire**



I, Sumara Aziz of Global Language Solutions, hereby certify that the foregoing document, to the best of our knowledge and belief, is a true, complete and accurate Polish language translation of the attached English language document,

- HST Questionnaire Version 2.0 18/APR/2013

This document was translated by two or more professionals with adequate experience and qualifications in the medical field to properly interpret and translate such documents.

IRVINE, CALIFORNIA  
April 25, 2013

Sumara Aziz  
GLOBAL LANGUAGE SOLUTIONS



W jakim stopniu zgadza się Pan(i) z poniższymi zdaniami/twierdzeniami:

1. Palenie tradycyjnych papierosów/produktów jest inne przy użyciu urządzenia.

- ☐ Zdecydowanie zgadzam się  
☐ Zgadzam się  
☐ Nie mam zdania  
☐ Nie zgadzam się  
☐ Zdecydowanie nie zgadzam się

W przypadku wybrania opcji „zgadzam się” lub „zdecydowanie zgadzam się”, proszę wyjaśnić:

2. Palenie z urządzeniem odpowiada mi w takim samym stopniu jak palenie bez urządzenia.

- ☐ Zdecydowanie zgadzam się  
☐ Zgadzam się  
☐ Nie mam zdania  
☐ Nie zgadzam się  
☐ Zdecydowanie nie zgadzam się

W przypadku wybrania opcji „nie zgadzam się” lub „zdecydowanie nie zgadzam się”, proszę wyjaśnić:

3. Smak tradycyjnych papierosów/produktów jest inne przy użyciu urządzenia.

- ☐ Zdecydowanie zgadzam się  
☐ Zgadzam się  
☐ Nie mam zdania  
☐ Nie zgadzam się  
☐ Zdecydowanie nie zgadzam się

W przypadku wybrania opcji „zgadzam się” lub „zdecydowanie zgadzam się”, proszę wyjaśnić:

4. Urządzenie jest łatwe w użyciu.

- ☐ Zdecydowanie zgadzam się  
☐ Zgadzam się  
☐ Nie mam zdania  
☐ Nie zgadzam się  
☐ Zdecydowanie nie zgadzam się

W przypadku wybrania opcji „nie zgadzam się” lub „zdecydowanie nie zgadzam się”, proszę wyjaśnić:

5. Urządzenie przeszkadza mi w paleniu

HST Questionnaire Version 2.0 18/APR/2013





- ☐ Zdecydowanie zgadzam się
- ☐ Zgadzam się
- ☐ Nie mam zdania
- ☐ Nie zgadzam się
- ☐ Zdecydowanie nie zgadzam się

W przypadku wybrania opcji „zgadzam się” lub „zdecydowanie zgadzam się”, proszę wyjaśnić:



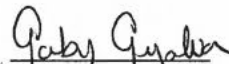
#### **16.1.2.3.4 Modified Cigarette Evaluation Questionnaire**



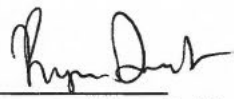
TRANSPERFECT

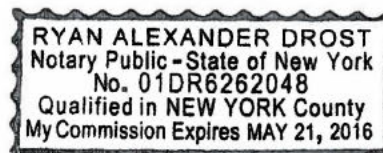
City of New York, State of New York, County of New York

I, Gaby Grijalva, hereby certify that the following is, to the best of my knowledge and belief, a true and accurate translation of the document titled "mCEQ ENG" from English into Poland (Polish) following Covance's process of concept definition, Revisions to existing Polish translations, Covance Review, cognitive interviewing with 5 adult smokers, final proofreading, and formatting.

  
Gaby Grijalva, Project Coordinator

Sworn to before me this  
Wednesday, April 17, 2013

  
Signature, Notary Public



Stamp, Notary Public



<b>&lt;WIZYTA&gt;</b>						
<b>Zmodyfikowany kwestionariusz oceny palenia papierosów (mCEQ)</b>						
Data i godzina badania (format 24-godzinny)		<input type="text"/> / <input type="text"/> / <input type="text"/>			<input type="checkbox"/> Zaznacz, jeśli pokrywa się z datą wizyty	
		D D M M M R R R R				
		<input type="text"/> : <input type="text"/>			godz. min.	
Jeśli palił/a Pan/Pani od czasu ostatniego wypełnienia tego kwestionariusza, proszę zaznaczyć odpowiedzi najlepiej opisujące Pana/Pani odczucia związane z paleniem.						
1. Czy palenie dawało Panu/Pani satysfakcję?						
Wcale	W bardzo małym stopniu	W małym stopniu	W umiarkowanym stopniu	W dużym stopniu	W bardzo dużym stopniu	W najwyższym stopniu
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. Czy papierosy Panu/Pani smakowały?						
Wcale	W bardzo małym stopniu	W małym stopniu	W umiarkowanym stopniu	W dużym stopniu	W bardzo dużym stopniu	W najwyższym stopniu
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Czy odczucia w gardle i klatce piersiowej były dla Pana/Pani przyjemne?						
Wcale	W bardzo małym stopniu	W małym stopniu	W umiarkowanym stopniu	W dużym stopniu	W bardzo dużym stopniu	W najwyższym stopniu
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. Czy palenie działało na Pana/Panią uspokajająco?						
Wcale	W bardzo małym stopniu	W małym stopniu	W umiarkowanym stopniu	W dużym stopniu	W bardzo dużym stopniu	W najwyższym stopniu
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>



<WIZYTA>						
Zmodyfikowany kwestionariusz oceny palenia papierosów						
5. Czy palenie powodowało, że czuł/a się Pan/Pani bardziej rześki/a?						
Wcale	W bardzo małym stopniu	W małym stopniu	W umiarkowanym stopniu	W dużym stopniu	W bardzo dużym stopniu	W najwyższym stopniu
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. Czy palenie powodowało, że był/a Pan/Pani mniej drażliwy/a?						
Wcale	W bardzo małym stopniu	W małym stopniu	W umiarkowanym stopniu	W dużym stopniu	W bardzo dużym stopniu	W najwyższym stopniu
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. Czy palenie pomagało Panu/Pani w skoncentrowaniu się?						
Wcale	W bardzo małym stopniu	W małym stopniu	W umiarkowanym stopniu	W dużym stopniu	W bardzo dużym stopniu	W najwyższym stopniu
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. Czy palenie zmniejszało Pana/Pani głód związany z jedzeniem?						
Wcale	W bardzo małym stopniu	W małym stopniu	W umiarkowanym stopniu	W dużym stopniu	W bardzo dużym stopniu	W najwyższym stopniu
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9. Czy palenie powodowało u Pana/Pani zawroty głowy?						
Wcale	W bardzo małym stopniu	W małym stopniu	W umiarkowanym stopniu	W dużym stopniu	W bardzo dużym stopniu	W najwyższym stopniu
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10. Czy palenie powodowało u Pana/Pani nudności?						
Wcale	W bardzo małym stopniu	W małym stopniu	W umiarkowanym stopniu	W dużym stopniu	W bardzo dużym stopniu	W najwyższym stopniu
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>



<WIZYTA>						
Zmodyfikowany kwestionariusz oceny palenia papierosów						
11. Czy palenie natychmiast zaspokajało u Pana/Pani głód papierosowy?						
Wcale	W bardzo małym stopniu	W małym stopniu	W umiarkowanym stopniu	W dużym stopniu	W bardzo dużym stopniu	W najwyższym stopniu
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
12. Czy palenie sprawiało Panu/Pani przyjemność?						
Wcale	W bardzo małym stopniu	W małym stopniu	W umiarkowanym stopniu	W dużym stopniu	W bardzo dużym stopniu	W najwyższym stopniu
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>



#### **16.1.2.3.5 Minnesota Nicotine Dependence/Withdrawal Scale**





TRANSPERFECT

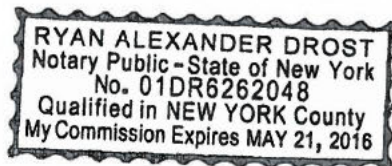
City of New York, State of New York, County of New York

I, Gaby Grijalva, hereby certify that the following is, to the best of my knowledge and belief, a true and accurate translation of the document titled "MNWS ENG SELF" from English into Poland (Polish) following Covance's process of concept definition, Revisions to existing Polish translations, Covance Review, cognitive interviewing with 5 adult smokers, final proofreading, and formatting.

Gaby Grijalva, Project Coordinator

Sworn to before me this  
Wednesday, April 17, 2013

Signature, Notary Public



Stamp, Notary Public



<b>&lt;WIZYTA&gt;</b>					
<b>Minnesocka skala uzależnienia/odstawienia nikotyny (MNWS)</b>					
<b>Samoopisowa skala oceny zachowania</b>					
<p>Data i godzina badania (format 24-godzinny)      <input type="checkbox"/> Zaznacz, jeśli pokrywa się z datą wizyty</p> <p>                                 <u>  </u> <u>  </u> / <u>  </u> <u>  </u> <u>  </u> / <u>  </u> <u>  </u> <u>  </u> <u>  </u>                                  D D        M M M        R R R R</p> <p>                                 <u>  </u> <u>  </u> : <u>  </u> <u>  </u>                                  godz.        min.</p> <p>Dla każdej pozycji przedstawionej poniżej proszę wskazać, co Pan/Pani odczuwał/a w ciągu ostatnich 24 godzin.</p>					
	Brak	Niewielki/e	Łagodny/e	Umiarkowa ny/e	Ciężki/e
1. Gniew, drażliwość, zdenerwowanie	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. Lęk, niepokój	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Obniżony nastrój, smutek	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. Pragnienie zapalenia, czyli głód papierosowy	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. Trudności z koncentracją	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. Wzmożony apetyt, głód, przyrost masy ciała	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. Bezsenność, problemy ze snem, budzenie się w nocy	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. Nerwowość	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9. Zniecierpliwienie	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10. Zaparcia	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
11. Zawroty głowy	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>



<b>&lt;WIZYTA&gt;</b>					
<b>Minnesocka skala uzależnienia/odstawienia nikotyny (MNWS)</b>					
<b>Samoopisowa skala oceny zachowania</b>					
	<b>Brak</b>	<b>Niewielki/e</b>	<b>Łagodny/e</b>	<b>Umiarkowa ny/e</b>	<b>Ciężki/e</b>
12. Kaszel	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
13. Przyjemne sny lub koszmary	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
14. Nudności	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
15. Ból gardła	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Tętno	_____				uderzeń na minutę
Waga	_____				kg



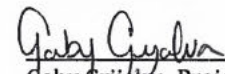
#### **16.1.2.3.6 Questionnaire on Smoking Urges**



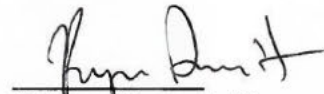
TRANSPERFECT

City of New York, State of New York, County of New York

I, Gaby Grijalva, hereby certify that the following is, to the best of my knowledge and belief, a true and accurate translation of the document titled "QSU-brief\_ORIGINAL.doc" from English into Poland (Polish) following Covance's process of concept definition, Revisions to existing Polish translations, Covance Review, cognitive interviewing with 5 adult smokers, final proofreading, and formatting.

  
Gaby Grijalva, Project Coordinator

Sworn to before me this  
Wednesday, April 17, 2013

  
Signature, Notary Public



Stamp, Notary Public

**Kwestionariusz dotyczący pragnienia zapalenia (QSU)**Data i godzina badania  
(format 24-godzinny)

<input type="text"/>	/	<input type="text"/>	/	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
D		D	M	M	M	R	R R R R

☐ Zaznacz, jeśli  
pokrywa się z  
datą wizyty

<input type="text"/>	:	<input type="text"/>
godz.		min.

1. W tej chwili mam ochotę na papierosa

Zdecydowa  
nie się nie  
zgadzam☐☐☐☐☐☐☐Zdecydowanie  
się zgadzam

2. Nic nie byłoby lepsze niż zapalenie papierosa w tej chwili

Zdecydowa  
nie się nie  
zgadzam☐☐☐☐☐☐☐Zdecydowanie  
się zgadzam

3. Gdyby to było możliwe, prawdopodobnie bym teraz zapalił/a

Zdecydowa  
nie się nie  
zgadzam☐☐☐☐☐☐☐Zdecydowanie  
się zgadzam4. Mógłbym/mogłabym teraz lepiej nad wszystkim panować, gdybym mógł/mogła  
zapalićZdecydowa  
nie się nie  
zgadzam☐☐☐☐☐☐☐Zdecydowanie  
się zgadzam



<b>Kwestionariusz dotyczący pragnienia zapalenia (QSU)</b>							
<b>5. Wszystko, czego teraz chcę to papieros</b>							
<b>Zdecydowa nie się nie zgadzam</b>							<b>Zdecydowanie się zgadzam</b>
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<b>6. Mam ochotę na papierosa</b>							
<b>Zdecydowa nie się nie zgadzam</b>							<b>Zdecydowanie się zgadzam</b>
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<b>7. Papieros by mi teraz posmakował</b>							
<b>Zdecydowa nie się nie zgadzam</b>							<b>Zdecydowanie się zgadzam</b>
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<b>8. Zrobiłbym/zrobiłabym teraz prawie wszystko za papierosa</b>							
<b>Zdecydowa nie się nie zgadzam</b>							<b>Zdecydowanie się zgadzam</b>
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<b>9. Palenie poprawiłoby mi nastrój</b>							
<b>Zdecydowa nie się nie zgadzam</b>							<b>Zdecydowanie się zgadzam</b>
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>



**Kwestionariusz dotyczący pragnienia zapalenia (QSU)**

10. Zapalę, jak tylko będę mógł/mogła

Zdecydowa  
nie się nie  
zgadzam☐☐☐☐☐☐Zdecydowanie  
się zgadzam☐



#### **16.1.2.4 SUBJECT SMOKING DIARY ENGLISH**

Not applicable.



### **16.1.2.5 SUBJECT SMOKING DIARY LOCAL LANGUAGE**

Not applicable.