

MEMO

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Date: 31/Jul/2014

From: Bramley, Alexander

To: Croasdale, Paul; Mulholland, Sarah

Copy to: Hope, Paul; Russum, Kilda; Gaw, Nina; Wilkinson, Alexander Henshaw, Jonathan;
Hossack, Stuart

Re: CCRU Study number: 1001000-8278003 (ZRHR-REXC-03-EU), date: 31/Jul/2014, **PK handover Memo Version 3**

The handover document has been updated to version 3 to correct the reporting of nicotine PK parameters for Subject ~~326~~ (Do not report any NICOTINE PK parameters for Subject 328).
328 28th 31st Jul 2014

The following files are available for use:-

Directory of P:\1001000\8278003\Pharmacometrics\PK\Parameters

09/Jun/2014 09:28	6,809,200	pkmergeV2.xpt
24/Jun/2014 18:14	128,800	fso.xpt

Key

pkmergeV2.xpt	input data for nicotine and cotinine
fso.xpt	output parameters for nicotine and cotinine

WinNonlin/SAS transport file: SAP/TFL naming conventions and definitions

fso.XPT PK parameters

WinNonlin/SAS transport file name	SAP/TFL Parameter	Comments
T _{peak}	t _{peak}	Time to peak concentration
C _{peak}	C _{peak}	Peak nicotine and cotinine plasma concentration
C _{avg2}	C _{avg}	Average concentration calculated over 24 hours for subject 8 and 206
C _{avg}	C _{avg}	Average concentration calculated over 24 hours

Additional Comments for PK data:

- The following nicotine sample results were queried with bioanalytical lab following review by Pharmacokineticist:

SUBJIDN	PARAM	TRTA	Timepoints (reason)
14	Cotinine	THS 2.2	16 hours post dose (high, possible transposition)
22	Cotinine	THS 2.2	16 hours post dose (low, possible transposition)
300	Nicotine	THS 2.2	All timepoints (BLQ with exception of 8 and 10 hours post-dose)

The Bioanalytical lab confirmed the sample results were correct, therefore all data was included in the PK analysis.

- All BLQs have been imputed with $\frac{1}{2}$ LLOQ for PK analysis.
- The bioanalytical result was missing for subject 328 (SVD-nicotine) at nominal 4 hours post-dose. The sample failed to provide reproducible results after investigating the original result is coded as "Failed analytical investigation". In this case the repeat reassay did not confirm the original result within 20% difference. SVD means "Sample Volume Depleted". **Do not report any NICOTINE PK parameters for Subject 328.**
- For subjects 8 and 206 the sampling of the 24 hour sample did not allow for the calculation of C_{avg} out to 24 hours (samples taken at 23:58), for these subjects please present the C_{avg2} value for nicotine and cotinine, flag the results and footnote with 'due to sampling time restrictions C_{avg} calculated as area under the curve from time zero to the last quantifiable concentration divided by the time to the last quantifiable concentration'.

Additional Comments for Medical Writer:

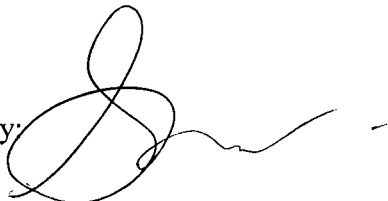
- Phoenix WinNonlin Version 6.2.1 used for PK analysis.

Compiled by:



Date: 31 JUL 2014

Checked by:



Date: 31 JUL 2014