
APPENDIX A3.3-8 (V2)

STABILITY FINAL RESULTS (12 MONTHS) – MENTHOL 1

TABLE OF CHANGES

Document	Summary of Changes
A3.3-8	Original submission STABILITY INTERMEDIATE RESULTS (6 MONTHS) – MENTHOL 1
A3.3-8 (v2)	Amendment: replaces A3.3-8 STABILITY FINAL RESULTS (12 MONTHS) – MENTHOL 1

Confidentiality Statement

Confidentiality Statement: Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris International



Form Number: PMI_RD_FOR_000927

Form Version N°: 1.0

Form Status: Effective

Stability Study Report: STAB-2016_P1_M_1

Form Effective Date: See EDMS

REPORT OF THE STABILITY STUDY FOR DORADO I MINT VINNY LOW THS 2.2 (EXPT004923)

Platform	P1								
Stability Study type	<table border="1"> <tr> <td>Initial Stability Study</td> <td><input type="checkbox"/></td> </tr> <tr> <td>In use</td> <td><input type="checkbox"/></td> </tr> <tr> <td>Post Change</td> <td><input checked="" type="checkbox"/></td> </tr> <tr> <td>Monitoring</td> <td><input type="checkbox"/></td> </tr> </table>	Initial Stability Study	<input type="checkbox"/>	In use	<input type="checkbox"/>	Post Change	<input checked="" type="checkbox"/>	Monitoring	<input type="checkbox"/>
Initial Stability Study	<input type="checkbox"/>								
In use	<input type="checkbox"/>								
Post Change	<input checked="" type="checkbox"/>								
Monitoring	<input type="checkbox"/>								

Name	Role	Justification	Date (dd-Mon yyyy)	Signature
Rita Hajdu Schenk	QC Unit Coordinator	Author	21-Aug-2017	
Samuel Kleinhans <i>P.O: Céline Biès</i>	QC Unit Statistician	Author	21 AUG 2017	
Cristina Llanos Alperi	Quality Assurance	Reviewer	21. AUG-2017	
Shelley Moores	Quality Assurance	Reviewer	21-AUG-2017	
Cyril Jeannet	Head of QC Unit	Approver	21-Aug-2017	



Form Number: PMI_RD_FOR_000927

Form Version N°: 1.0

Form Status: Effective

Stability Study Report: STAB-2016_P1_M_1

Form Effective Date: See EDMS

Table of Contents

1 Purpose	3
2 Batches	3
3 Tests Methods and Specifications	3
3.1 Preparation and Conditioning	3
3.2 Aerosol Generation and Analyses	4
3.3 Visual Inspection	5
3.4 Sensorial Evaluation	6
4 Stability Study Design	6
5 Deviations to Study Protocol	7
5.1 Deviation in Storage Condition	7
5.2 Deviation in Methods	7
5.3 Deviation in Study Design	8
6 Stability Data Evaluation	8
6.1 Storage Condition 22°C 60% RH	10
6.2 Storage Condition 30°C 35% RH	30
6.3 Storage Condition 30°C 75% RH	50
7 Stability Assessment	70
8 Related Documents	70
9 Reference Documents	70
10 Revision History for Stability Report	71
11 Definitions and Abbreviations	71
12 Appendices	72
12.1 Climatic Zones	72
12.2 Equivalence List for Quality Documents	72
12.3 Sample Traceability Matrix	73



Form Number: PMI_RD_FOR_000927

Form Version N°: 1.0

Form Status: Effective

Stability Study Report: STAB-2016_P1_M_1

Form Effective Date: See EDMS

1 Purpose

The objective of this stability study is to demonstrate that the commercial product THS 2.2 Low Menthol (Dorado I Mint Vinny) version (Platform 1) produced at Philip Morris Manufacturing & Technology Bologna (PMMTB) remains within product specifications over the determined shelf life period, when stored under the defined WHO ($30 \pm 2^\circ\text{C}$; $75 \pm 5\%$ RH and $30 \pm 2^\circ\text{C}$ $35 \pm 5\%$ RH) and ISO ($22 \pm 2^\circ\text{C}$; $60 \pm 5\%$ RH) storage conditions.

This report summarizes the results and trend analysis of the stability study STAB-2016_P1_M_1 performed according a protocol [\[1\]](#). The study was performed in 3 production scale Dorado I Mint Vinny Low batches.

(b) (4)

The Evaluation of the stability data was performed according the description in the procedure PMI_RD_SOP_000296 Perform Stability Studies and in line with [ICH Q1\(E\) Evaluation of Stability Data](#).

2 Batches

Table 1 Identification of THS 2.2 Dorado I Vinny Low

Product/ Test item	Consumable Batch Number	Finished Product Code	Manufacturing Date
THS 2.2 Dorado I Vinny Low	B-25900 / 41.2381531	ME000041.01	21 Dec. 2015
	B-25901 / 41.2374718	ME000041.01	22 Dec. 2015
	B-25902 / 41.2379112	ME000041.01	16 Dec. 2015

The samples were stored in the climatic chambers in packs. The packs are polypropylene wrapped and consists of two collation, each collation containing 10 Heat sticks.

3 Tests Methods and Specifications

3.1 Preparation and Conditioning

The 3R4F Reference Cigarette (purchased from the University of Kentucky) or P1 monitor (P1M1) was used as an internal monitor for aerosol chemistry and values were compared to respective upper and lower limit defined in the control charts to verify the correct functioning of the experimental setup.

At each time point before aerosol analyses, in order to perform the testing under normal conditions as on freshly made products, sticks were reconditioned outside of the packs following ISO standard 3402 ([1999](#)), at least 48 hours at $22 \pm 1^\circ\text{C}$, $60 \pm 3\%$ RH prior to aerosol generation. For the determination of the Menthol in the aerosol, sticks were kept in closed packs prior analyses in order to avoid loss of menthol.

Conditioning for physical analyses was performed as described in respective work instruction, inside open packs for at least 24 hours at $22 \pm 2^\circ\text{C}$ and $50 \pm 5\%$ RH.



Form Number: PMI_RD_FOR_000927

Form Version N°: 1.0

Form Status: Effective

Stability Study Report: STAB-2016_P1_M_1

Form Effective Date: See EDMS

Sticks were kept in closed pack at $22^{\circ}\text{C} \pm 2^{\circ}\text{C}$ and $58\% \text{ RH} \pm 5\%$ prior sensorial evaluation.

Visual evaluation was performed on sticks received in close packs without any preliminary preparation.

3.2 Aerosol Generation and Analyses

The atmosphere for aerosol generation was $22 \pm 2^{\circ}\text{C}$, $60 \pm 5\% \text{ RH}$.

Aerosol generation was performed on Borgwaldt linear smoking machines.

The Health Canada Intense (HCI) smoking regimen using bell shaped puff profile was used with the below listed parameters to generate the aerosol for further chemical analyses:

- Puff volume: 55 mL
- Puff duration: 2.0 s
- Puff interval: 30 s
- Number of puffs: 12

All the instruments and material are listed in the relevant work instructions in [Table 2](#).

The tobacco heating device DV.000174 was used to generate aerosol for chemical analyses and device DV.000101.RD was used for sensorial evaluation (b) (4).

Table 2 Tests, Methods and Specifications

Parameter	Method Name	Method Version Planned	Method Version Used T0 / T12	Specifications [2] -[4]
Nicotine mg/stick	PMI_RD_WKI_000530	7.0	7.0 / 8.0	(b) (4)
	PMI_RD_WKI_000953	3.0	3.0 / 3.0	
Glycerin mg/stick	PMI_RD_WKI_000530	7.0	7.0 / 8.0	
	PMI_RD_WKI_000953	3.0	3.0 / 3.0	
CO mg/stick	PMI_RD_WKI_000530	7.0	7.0 / 8.0	
Triacetin mg/stick	PMI_RD_WKI_000530	7.0	7.0 / 8.0	
	PMI_RD_WKI_000953	3.0	3.0 / 3.0	
Menthol mg/stick	PMI_RD_WKI_000530	7.0	7.0 / 8.0	
	PMI_RD_WKI_000953	3.0	3.0 / 3.0	
TPM mg/stick	PMI_RD_WKI_000530	7.0	7.0 / 8.0	
Phenol µg/stick	PMI_RD_WKI_000530	7.0	7.0 / 8.0	
	PMI_RD_WKI_000953	3.0	3.0 / 3.0	
Acrylamide µg/stick	PMI_RD_WKI_000530	7.0	7.0 / 8.0	
	PMI_RD_WKI_000953	3.0	3.0 / 3.0	



Form Number: PMI_RD_FOR_000927

Form Version N°: 1.0

Form Status: Effective

Stability Study Report: STAB-2016_P1_M_1

Form Effective Date: See EDMS

Parameter	Method Name	Method Version Planned	Method Version Used T0 / T12	Specifications [2] -[4]
Acetamide µg/stick	PMI_RD_WKI_000530	7.0	7.0 / 8.0	(b) (4)
	PMI_RD_WKI_000584	7.0	7.0 / 7.0	
Acetaldehyde µg/stick	PMI_RD_WKI_000534	11.0	11.0 / 12.0	
	PMI_RD_WKI_000391	13.0	13.0 / 15.0	
Butyraldehyde µg/stick	PMI_RD_WKI_000534	11.0	11.0 / 12.0	
	PMI_RD_WKI_000391	13.0	13.0 / 15.0	
Acrylonitrile µg/stick	PMI_RD_WKI_000518	7.0	7.0 / 7.0	
	PMI_RD_WKI_000383	15.0	15.0 / 17.0	
Isoprene µg/stick	PMI_RD_WKI_000518	7.0	7.0 / 7.0	
	PMI_RD_WKI_000383	15.0	15.0 / 17.0	
Pyridine µg/stick	PMI_RD_WKI_000518	7.0	7.0 / 7.0	
	PMI_RD_WKI_000383	15.0	15.0 / 17.0	
Ammonia ua/stick	PMI_RD_WKI_000385	10.0	10.0 / 10.0	
	PMI_RD_WKI_001392	1.0	1.0 / 2.0	

(b) (4)

(b) (4)

3.3 Visual Inspection

(b) (4)



Form Number: PMI_RD_FOR_000927

Form Version N°: 1.0

Form Status: Effective

Stability Study Report: STAB-2016_P1_M_1

Form Effective Date: See EDMS

3.4 Sensorial Evaluation

(b) (4)

4 Stability Study Design

Table 3 Testing Matrix

Batch	Storage Conditions	Beginning of the Study *	Analysis Time Points (months)					
			0	2	4	6	9	12
Dorado I Vinny Low (B-25900)	22°C±2°C / 60%RH±5%RH	January 22, 2016	MP S PF		MP S	MP S PF		MP S PF
	30°C±2°C / 75%RH±5%RH			MP S	MP S		C**	C**
	30°C±2°C / 35%RH±5%RH			MP S		MP S PF	MP S PF	MP S PF
Dorado I Vinny Low (B-25901)	22°C±2°C / 60%RH±5%RH	January 22, 2016	MP S PF	MP S	MP S		MP S PF	MP S PF
	30°C±2°C / 75%RH±5%RH			MP S		MP S PF	C**	C**
	30°C±2°C / 35%RH±5%RH				MP S	MP S PF		MP S PF
Dorado I Vinny Low (B-25902)	22°C±2°C / 60%RH±5%RH	January 22, 2016	MP S PF	MP S		MP S PF	MP S PF	MP S PF
	30°C±2°C / 75%RH±5%RH				MP S	MP S PF		C**
	30°C±2°C / 35%RH±5%RH			MP S	MP S		MP S PF	MP S PF

M: Batch release parameters, acrylonitrile, isoprene; **P:** Physical measurements: diameter and visual inspection; **S:** Sensorial analysis; **PF:** All performance parameters

* Beginning of the study corresponds to the date when the packs were put in the climatic chambers.

** Analyses at T9 and T12 for the conditions 30°C 75%RH were cancelled, decision based on visual aspect not acceptable at T4 and T6.

The number of replicates performed per analyses were as follows:

- T0 and T12 aerosol: 6 replicates/batch (b) (4) 50 sticks/batch; Visual evaluation: 100 sticks/batch



Form Number: PMI_RD_FOR_000927

Form Version N°: 1.0

Form Status: Effective

Stability Study Report: STAB-2016_P1_M_1

Form Effective Date: See EDMS

- T2 – T9 - aerosol: 4 replicates/batch; (b) 50 sticks/batch; Visual evaluation: 100 sticks/batch

5 Deviations to Study Protocol

5.1 Deviation in Storage Condition

Due to breakdown of the conditioning system for 22°C 60%RH, the relative humidity was not stable and was out of the tolerance from 24 Dec. 2016 to 30 Dec. 2016 with a mean value of 52.2%RH. The non-conformity is documented in RLS-TIM-17-1. The out of tolerance happened approximately 1 month before T12 time point and represent ~5% below the lower range limit.

5.1.1 Impact on the Study

In dry condition, 30°C 35%RH, the product remain in specification at T12. As the packs are stored in the climatic chambers in polypropylene wrapped packs and as no out of trend was observed as T12, it is considered that the product was not affected by this non-conformity in this period of time.

5.2 Deviation in Methods

The version of some of the methods changed during the study compared to what was described in the study protocol (Table 2). The change in the versions reflects only changes with no impact on the quantification for the all methods, except for Isoprene (PMI_RD_WKI_000383).

The version of the method changed from V15 to V16 between the T0 and the T2 (18 Feb. 2016) due to implementation of Certified Reference Materials. The change was considered at the time as having no impact on the quantification of the compounds of the method, involving Isoprene, Acrylonitrile and Pyridine from the stability studies.

An out of trend investigation was opened for Isoprene at T6 for the conditions 22°C 60%RH and 30°C 35%RH and observed that the 3R4F monitor had similar increasing trend as the samples from the stability study indicating that the increase was not product related. A laboratory investigation [6] was performed and confirmed that switching from V15 to V16 had an impact on the quantification for Isoprene only and that the values generated from 18 Feb. 2016 to 25 Oct. 2016 tend to be overestimated, however no constant bias could be determined.

It was then decided to revert back to the reference material used prior to February 2016 described in PMI_RD_WKI_000383 V15 which provided more consistent results regarding Isoprene quantitation than those used after that date. This change was implemented in PMI_RD_WKI_000383 V17 effective as of 25 Oct. 2016, just prior the analyses for T9 time point.

The method (PMI_RD_WKI_000383) versions per time point are summarized in Table 4.

Table 4 PMI_RD_WKI_000383 Versions per Time Point

STAB-2016_P1_M_1	Time Points (months)					
	0	2	4	6	9	12
Version of the method PMI_RD_WKI_000383	V15.0	V16.0	V16.0	V16.0	V17.0	V17.0



Form Number: PMI_RD_FOR_000927

Form Version N°: 1.0

Form Status: Effective

Stability Study Report: STAB-2016_P1_M_1

Form Effective Date: See EDMS

5.2.1 Impact on the Study

The change in the method during the stability study has an impact on the evaluation of results for Isoprene.

The stability specifications were set by using the T0 values obtained with method V15. As during three intermediate time-points (T2, T4 and T6) the quantification of Isoprene was performed with method V16 and consequently overestimated, the results of these time point cannot be used for the evaluation.

Therefore, for storage conditions 22°C 60%RH and 30°C 35%RH only the reported value from T9 and T12 are used for evaluation. As the degradation of Isoprene was following a linear trend in previous stability studies it is considered covering the worst case by evaluating T9 and T12. Results from T2 to T6 are not reported.

For the storage condition 30°C 75%RH for which analyses were performed only until T6, the reported values from T2 to T6, obtained with the method V16, are checked against the specification, which covers as well the worst case knowing that these values are overestimated.

5.3 Deviation in Study Design

The analyses for T9 and T12 time point for the tropical 30°C 75%RH condition (Climatic Zone IVB) were cancelled, decision based on the visual aspect of the sticks found not acceptable at T4 and T6.

5.3.1 Impact on the Study

The data evaluation for this condition was performed with the results from T0 to T6, trend analyses was not performed when results were available for less than 3 time point. The reported values are checked against the specifications as described in [Chapter 6.3](#).

6 Stability Data Evaluation

The statistical analysis for the chemical and physical characterization is performed according PMI_RD_SOP_000296, following ICH Q1E and is mainly performed by modelling the degradation profile of the test parameters by using regression models. The regression analysis defines the trend of a quantitative stability test parameter for each batch over time on the predetermined stress conditions. The regression analysis is only performed for parameters for which a minimum of 3 time points data is available and data is suitable for trend analyses. For the other parameters having less than 3 data points, the reported value (mean) is compared versus the specification.

The [Tables 5 - 13](#) contain for each batch and for each tested parameter per time point the reported values, together with the specifications. When only Upper specification exists the fields for the Lower specifications are marked in gray. The fields for the "Time points" are marked in gray when no analyses were performed by study design or results are not reported (i.e. Isoprene value -see Deviation in [Chapter 5.2](#)).

The relative degradation rate, the R^2 and the severity scores are provided for information only and for parameters with at least 3 time points available (NA –is written when it's is not applicable).

The [Figures 1 - 48](#) contain the reported values for the 3 batches together with the upper and/or lower specification levels (USL and LSL), the linear regression of the 3 batches if applicable and the upper and lower 95 % confidence intervals for the regression mean (UMCI and LMCI). The Figure titles contain the



Form Number: PMI_RD_FOR_000927

Form Version N°: 1.0

Form Status: Effective

Stability Study Report: STAB-2016_P1_R_1

Form Effective Date: See EDMS

conclusion about the shelf life obtained with (b) [REDACTED] in case of trend analyses or conclusion about shelf life by comparing the reported value with the specification.

The shelf life obtained with (b) [REDACTED] is truncated to whole number. In case the shelf life calculated by () [REDACTED] is longer than the study duration (4) than the shelf life will be equal to the study duration. (4)



Form Number: PMI_RD_FOR_000927

Form Version N°: 1.0

Form Status: Effective

Stability Study Report: STAB-2016_P1_M_1

Form Effective Date: See EDMS

6.1 Storage Condition 22°C 60% RH

Table 5 B-25900 / 41.2381531 at 22°C 60% RH

B-25900 / 41.2381531	Unit	Specifications		Time point (Months)						Degradation Rate	R^2	Severity Score
		Lower	Upper	0	2	4	6	9	12			
Test												
Menthol	mg/stick	(b) (4)		1.25		1.78	1.75		1.79	2.79%	0.57	1.6
Nicotine	mg/stick			1.17		1.12	1.17		1.13	-0.22%	0.26	0.1
Glycerin	mg/stick			4.68		4.67	4.76		4.22	-0.81%	0.64	0.5
CO	mg/stick			0.3		0.6	0.4		0.3	-0.95%	0.03	0.0
Triacetin	mg/stick			0.5		0.5	0.5		0.4	-2.01%	0.94	1.9
Phenol	µg/stick			1.2		1.5	1.4		1.1	-0.71%	0.06	0.0
Acrylamide	µg/stick			1.4		1.5	1.7		1.3	-0.17%	0.01	0.0
Acetamide	µg/stick			3.0			3.0		2.9	-0.21%	0.69	0.1
Acetaldehyde	µg/stick			205			191		199	-0.26%	0.20	0.1
Butyraldehyde	µg/stick			13.9			12.3		12.7	-0.70%	0.48	0.3
Acrylonitrile	µg/stick			0.16		0.16	0.15		0.13	-1.34%	0.89	1.2
Isoprene	µg/stick			1.59					1.46	NA	NA	NA
Pyridine	µg/stick			8.6			8.4		6.6	-1.92%	0.82	1.6
Ammonia	µg/stick			12.3			10.4		9.7	-1.75%	0.94	1.6
TPM	mg/stick			54		53	54		50	-0.63%	0.73	0.5

(b) (4)



Form Number: PMI_RD_FOR_000927

Form Version N°: 1.0

Form Status: Effective

Stability Study Report: STAB-2016_P1_M_1

Form Effective Date: See EDMS

Table 6 B-25901 / 41.2374718 at 22°C 60% RH

B-25901 / 41.2374718	Unit	Specifications		Time point (Months)						Degradation Rate	R^2	Severity Score
		Lower	Upper	0	2	4	6	9	12			
Test		(b) (4)										
Menthol	mg/stick	(b) (4)		1.23	1.85	2.04		2.09	1.87	2.59%	0.35	0.9
Nicotine	mg/stick	(b) (4)		1.23	1.25	1.19		1.16	1.20	-0.38%	0.46	0.2
Glycerin	mg/stick	(b) (4)		4.53	5.08	4.66		4.46	4.60	-0.38%	0.14	0.1
CO	mg/stick	(b) (4)		0.3	0.3	0.6		0.5	0.3	1.00%	0.02	0.0
Triacetin	mg/stick	(b) (4)		0.5	0.6	0.5		0.5	0.5	-1.19%	0.48	0.6
Phenol	µg/stick	(b) (4)		1.2	1.7	1.3		1.4	1.4	0.12%	0.00	0.0
Acrylamide	µg/stick	(b) (4)		1.4	1.6	1.5		1.4	1.5	0.24%	0.05	0.0
Acetamide	µg/stick	(b) (4)		3.2				3.1	3.2	-0.23%	0.58	0.1
Acetaldehyde	µg/stick	(b) (4)		195				186	205	0.21%	0.07	0.0
Butyraldehyde	µg/stick	(b) (4)		13.4				13.1	12.6	-0.46%	0.87	0.4
Acrylonitrile	µg/stick	(b) (4)		0.17	0.16	0.16		0.14	0.15	-0.99%	0.62	0.6
Isoprene	µg/stick	(b) (4)		1.72				1.60	1.70	-0.24%	0.16	0.0
Pyridine	µg/stick	(b) (4)		8.7				8.9	7.2	-1.05%	0.41	0.4
Ammonia	µg/stick	(b) (4)		12.5				11.0	10.4	-1.36%	1.00	1.4
TBM	mg/stick	(b) (4)		56	57	53		53	52	0.72%	0.79	0.6

(b) (4)



Form Number: PMI_RD_FOR_000927

Form Version N°: 1.0

Form Status: Effective

Stability Study Report: STAB-2016_P1_M_1

Form Effective Date: See EDMS

Table 7 B-25902 / 41.2379112 at 22°C 60% RH

B-25902 / 41.2379112	Unit	Specifications		Time point (Months)						Degradation Rate	R^2	Severity Score
		Lower	Upper	0	2	4	6	9	12			
Test		(b) (4)										
Menthol	mg/stick	(b) (4)		1.05	1.68		1.89	1.97	1.76	3.84%	0.51	1.9
Nicotine	mg/stick	(b) (4)		1.22	1.13		1.17	1.10	1.15	-0.40%	0.27	0.1
Glycerin	mg/stick	(b) (4)		4.59	4.60		4.43	4.13	4.08	-1.04%	0.93	1.0
CO	mg/stick	(b) (4)		0.3	0.3		0.4	0.5	0.3	2.26%	0.22	0.5
Triacetin	mg/stick	(b) (4)		0.5	0.5		0.5	0.4	0.4	-1.51%	0.88	1.3
Phenol	µg/stick	(b) (4)		1.3	1.2		1.2	0.9	1.0	-2.15%	0.72	1.6
Acrylamide	µg/stick	(b) (4)		1.4	1.3		1.6	1.3	1.3	-0.60%	0.09	0.1
Acetamide	µg/stick	(b) (4)		3.0			3.0	2.8	2.5	-1.34%	0.75	1.0
Acetaldehyde	µg/stick	(b) (4)		195			200	177	198	-0.21%	0.04	0.0
Butyraldehyde	µg/stick	(b) (4)		13.4			13.1	12.1	12.8	-0.57%	0.52	0.3
Acrylonitrile	µg/stick	(b) (4)		0.16	0.14		0.17	0.13	0.14	-0.97%	0.22	0.2
Isoprene	µg/stick	(b) (4)		1.66				1.49	1.41	-1.21%	1.00	1.2
Pyridine	µg/stick	(b) (4)		8.6			9.1	8.6	7.2	-1.03%	0.36	0.4
Ammonia	µg/stick	(b) (4)		12.0			10.6	10.6	9.2	-1.72%	0.91	1.6
TBM	mg/stick	(b) (4)		56	54		55	53	51	-0.57%	0.72	0.4

(b) (4)



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.1.1 Mainstream Aerosol Evaluation

6.1.1.1 Menthol

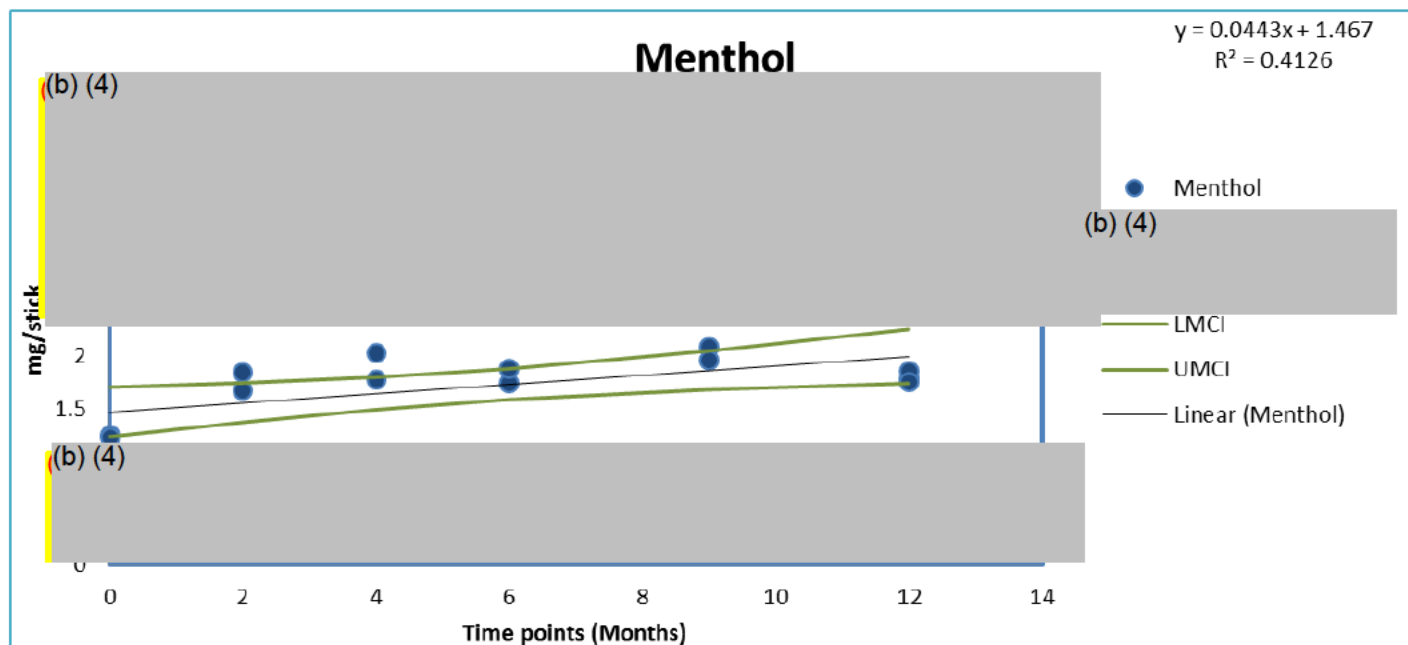


Figure 1 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.1.1.2 Nicotine

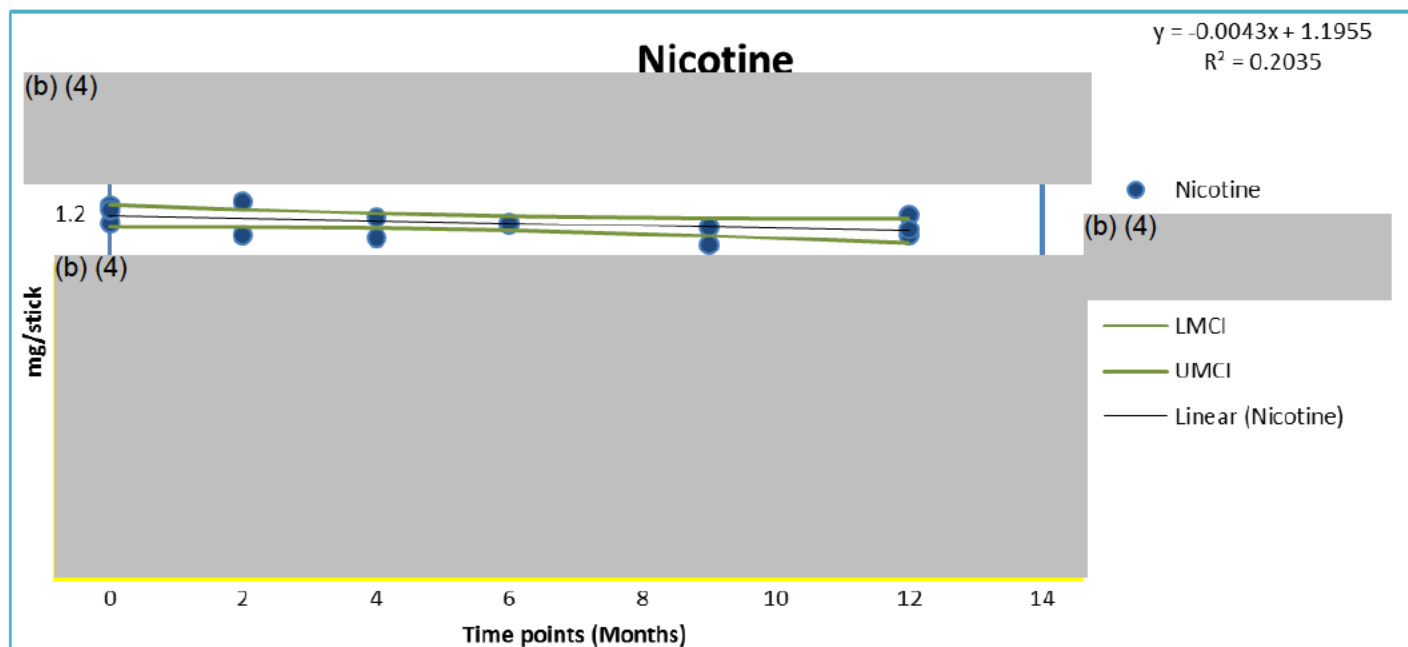


Figure 2 The best model accepted at the significance level of 0.25 has Different intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.1.1.3 Glycerin

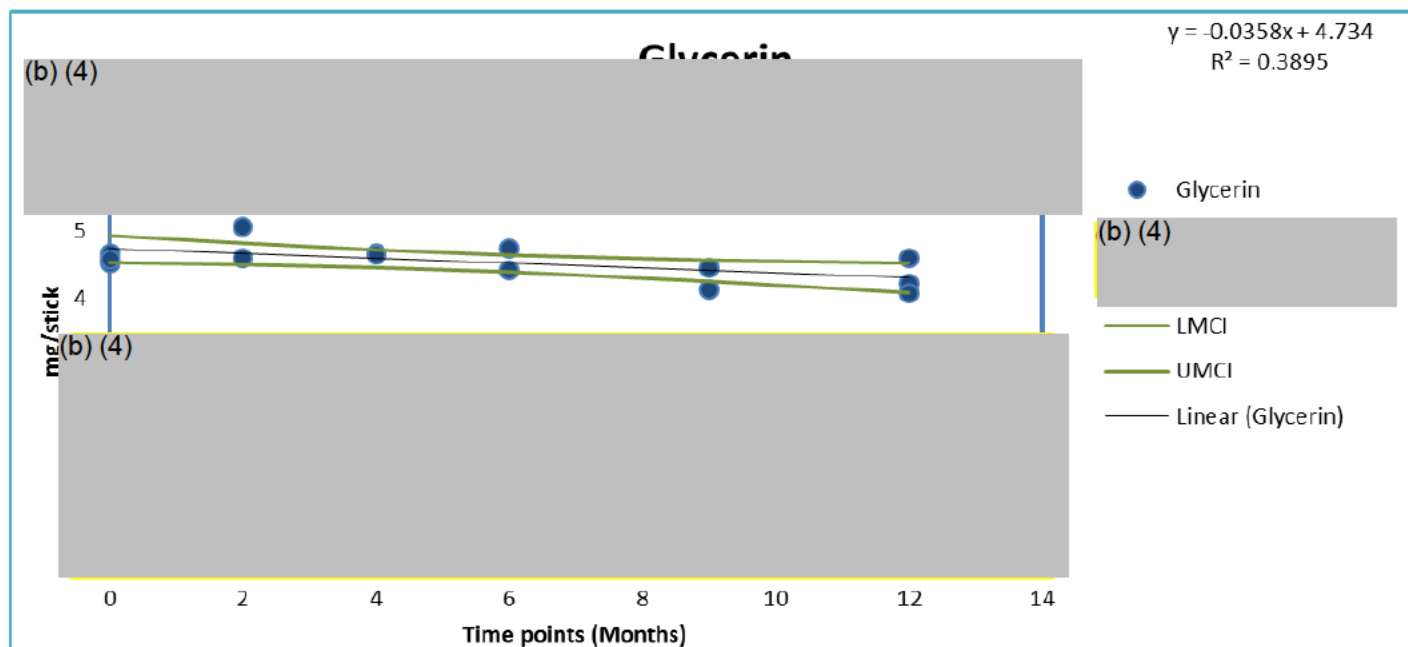


Figure 3 The best model accepted at the significance level of 0.25 has Different intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.1.1.4 CO

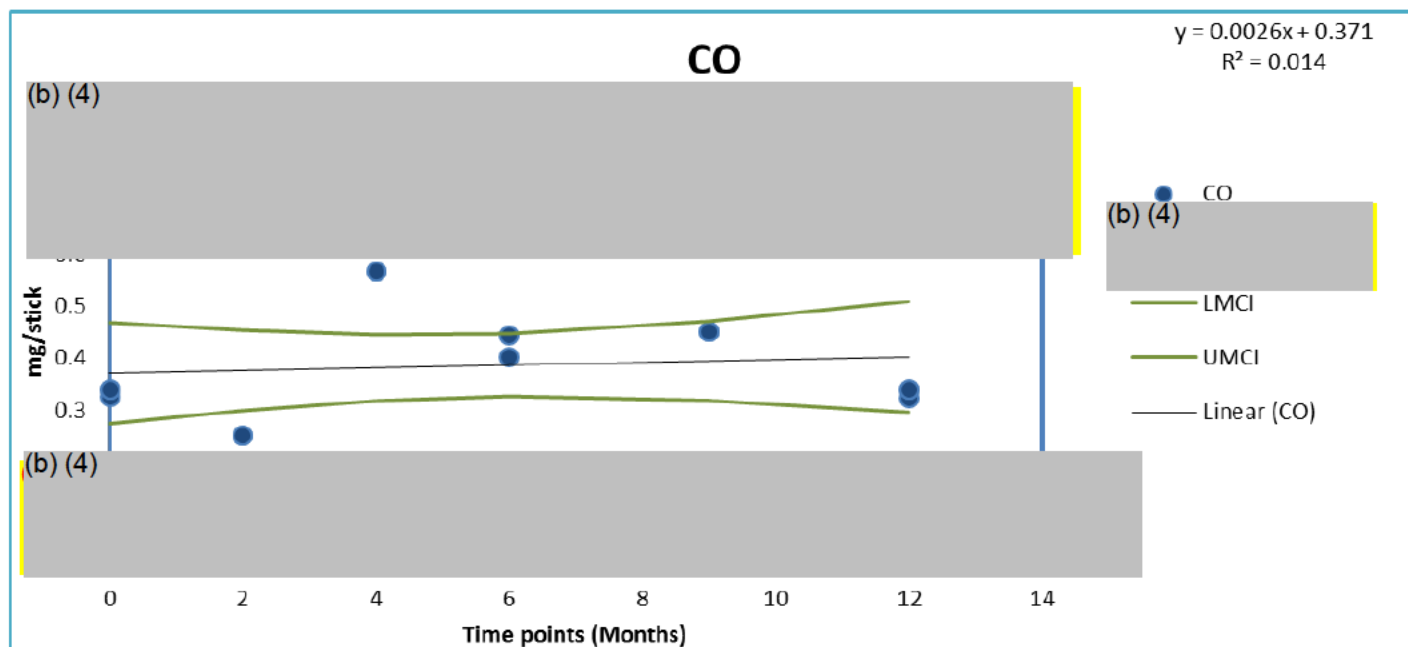


Figure 4 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.1.1.5 Triacetin

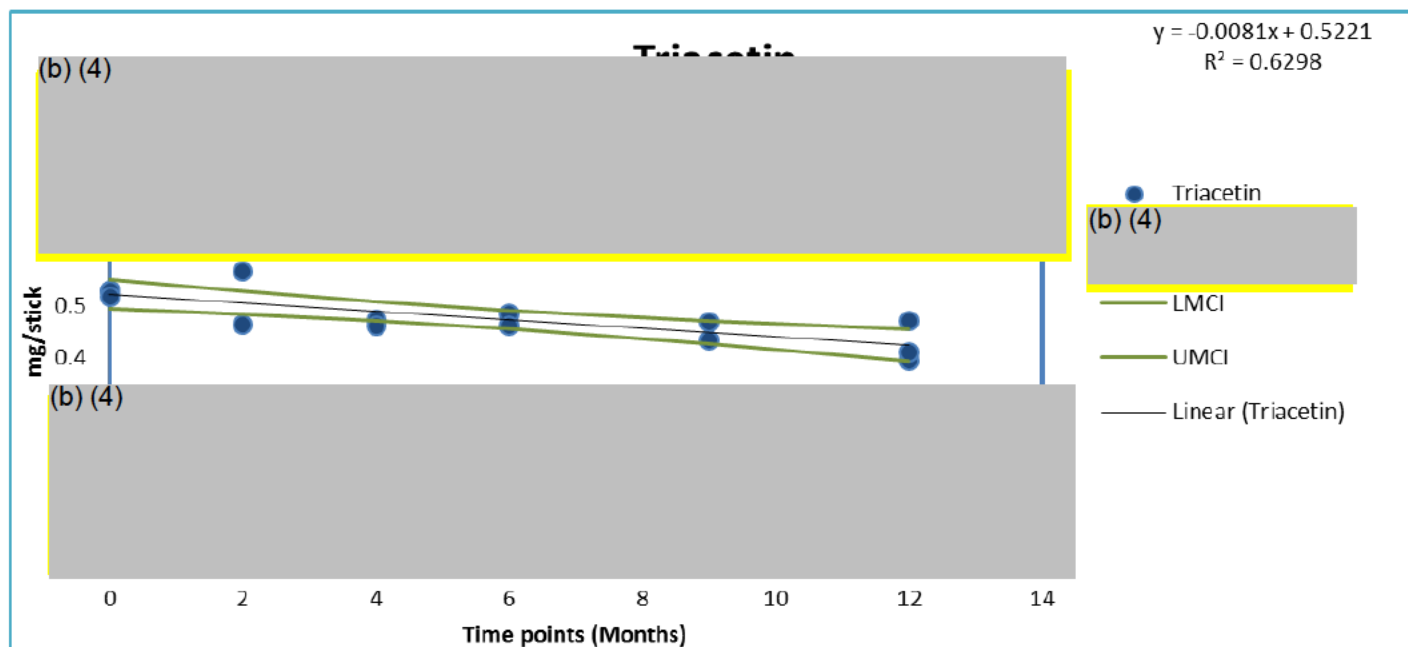


Figure 5 The best model accepted at the significance level of 0.25 has Different intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.1.1.6 TPM

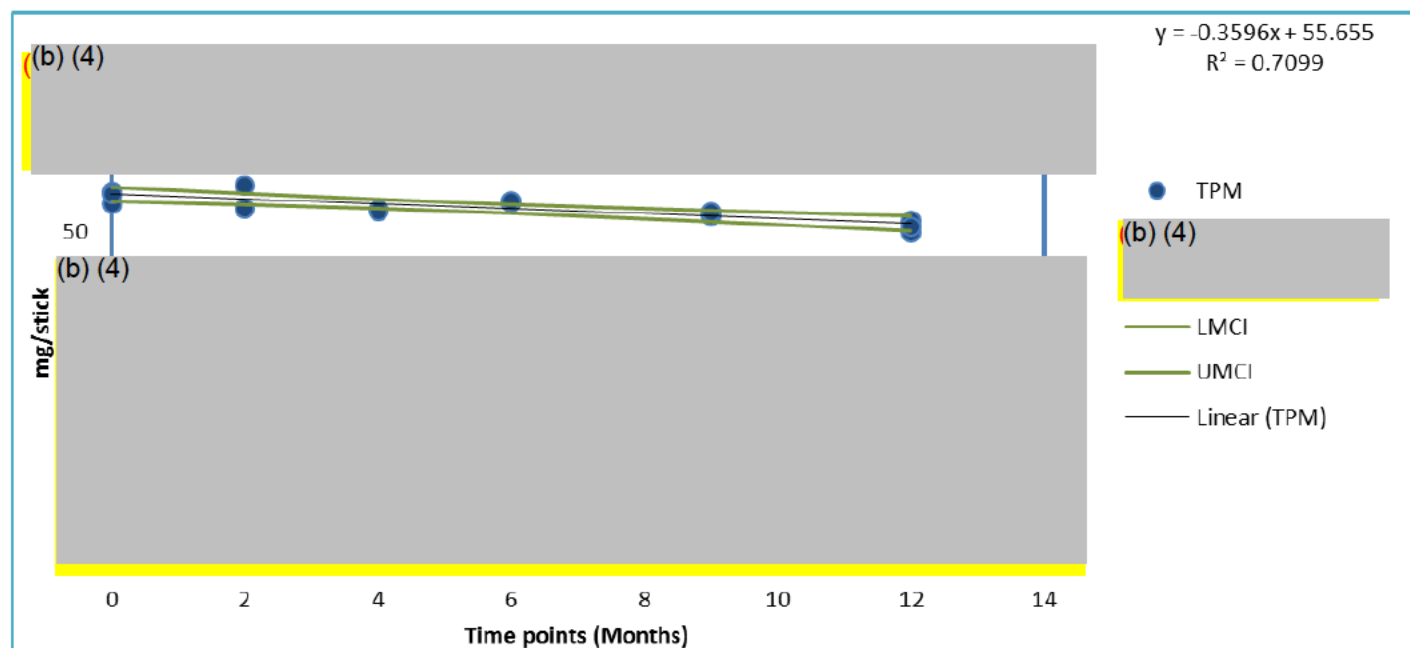


Figure 6 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.1.1.7 Phenol

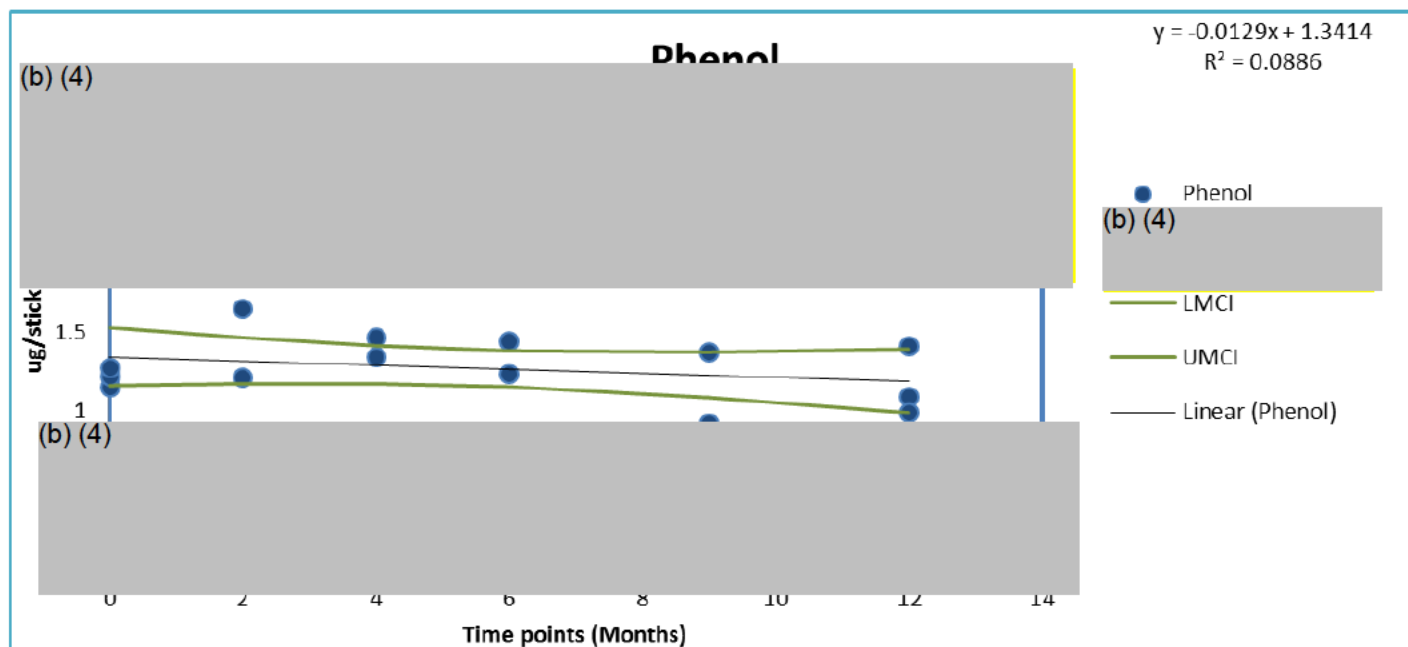


Figure 7 The best model accepted at the significance level of 0.25 has Different intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.1.1.8 Acrylamide

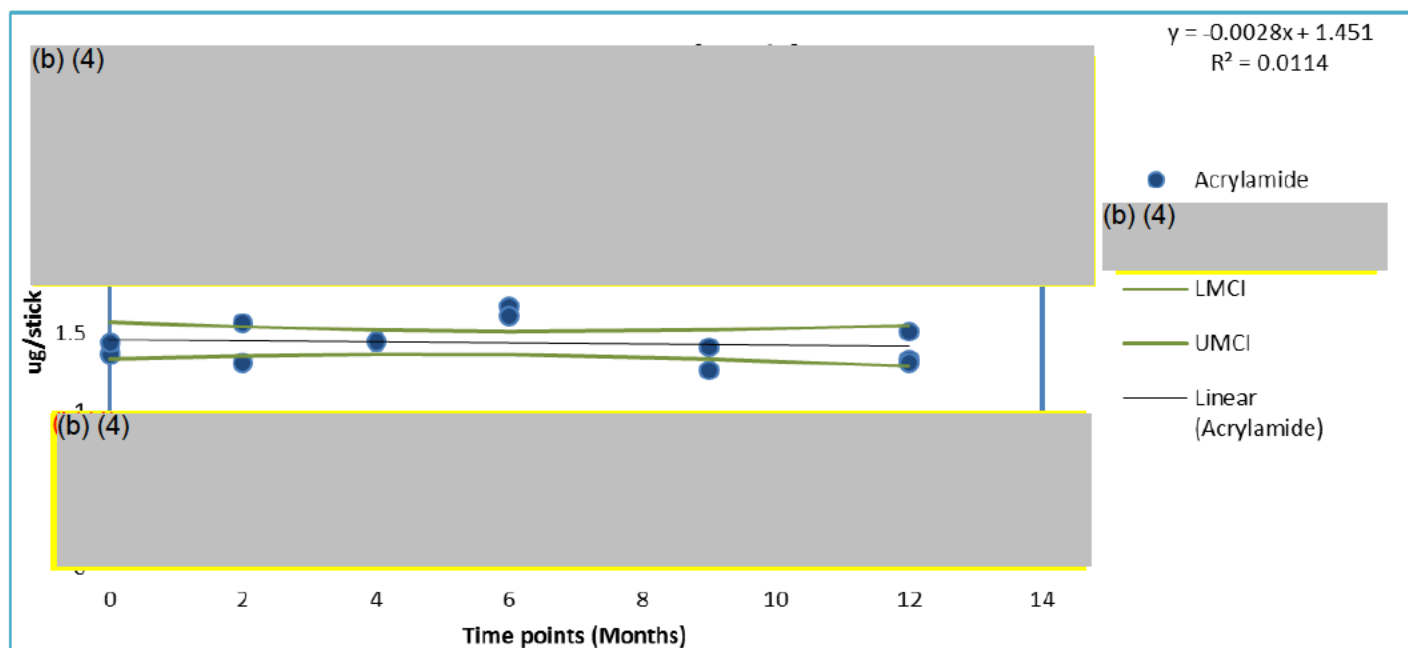


Figure 8 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.1.1.9 Acetamide

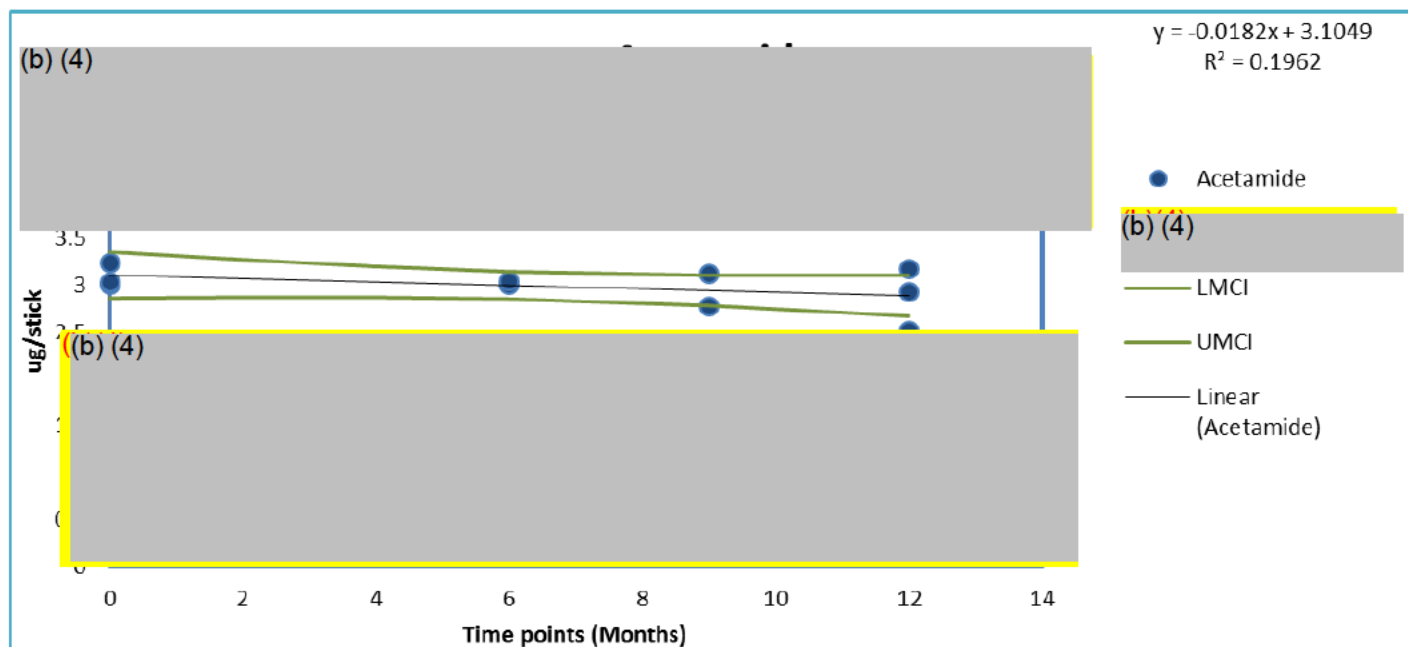


Figure 9 The best model accepted at the significance level of 0.25 has Different intercepts and Different slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.1.1.10 Acetaldehyde

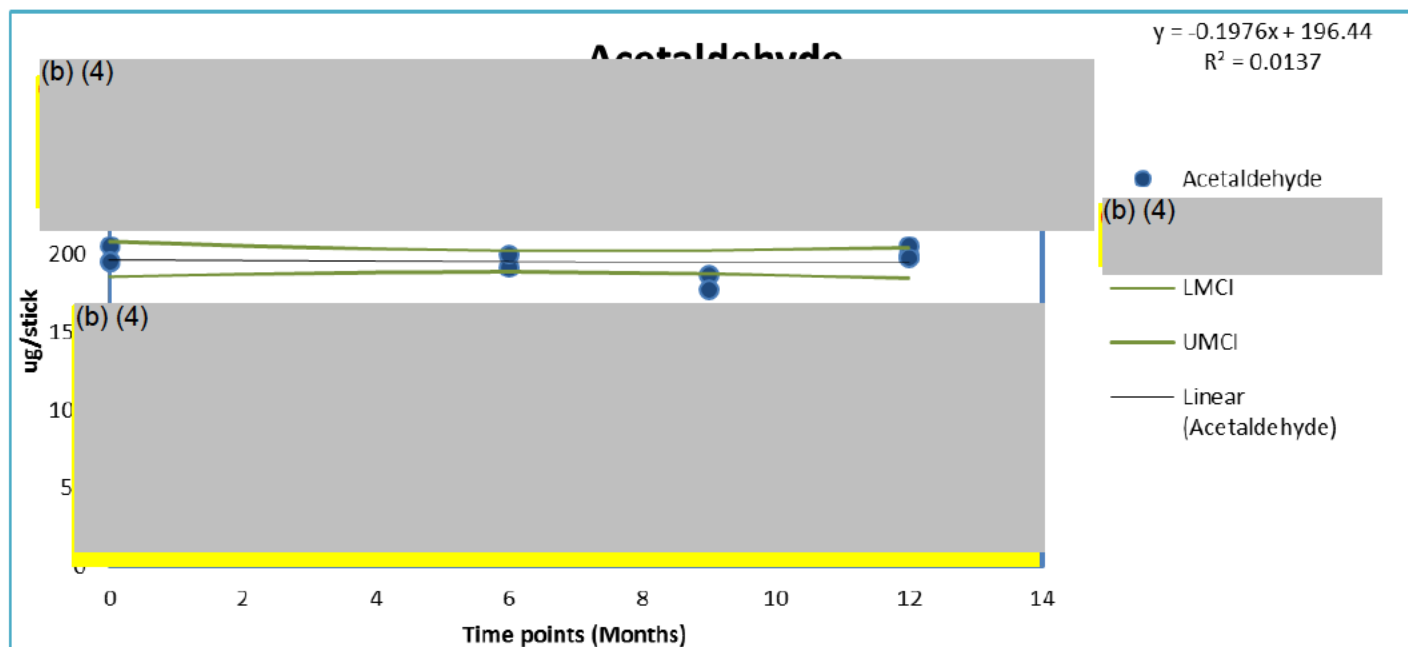


Figure 10 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.1.1.11 Butyraldehyde

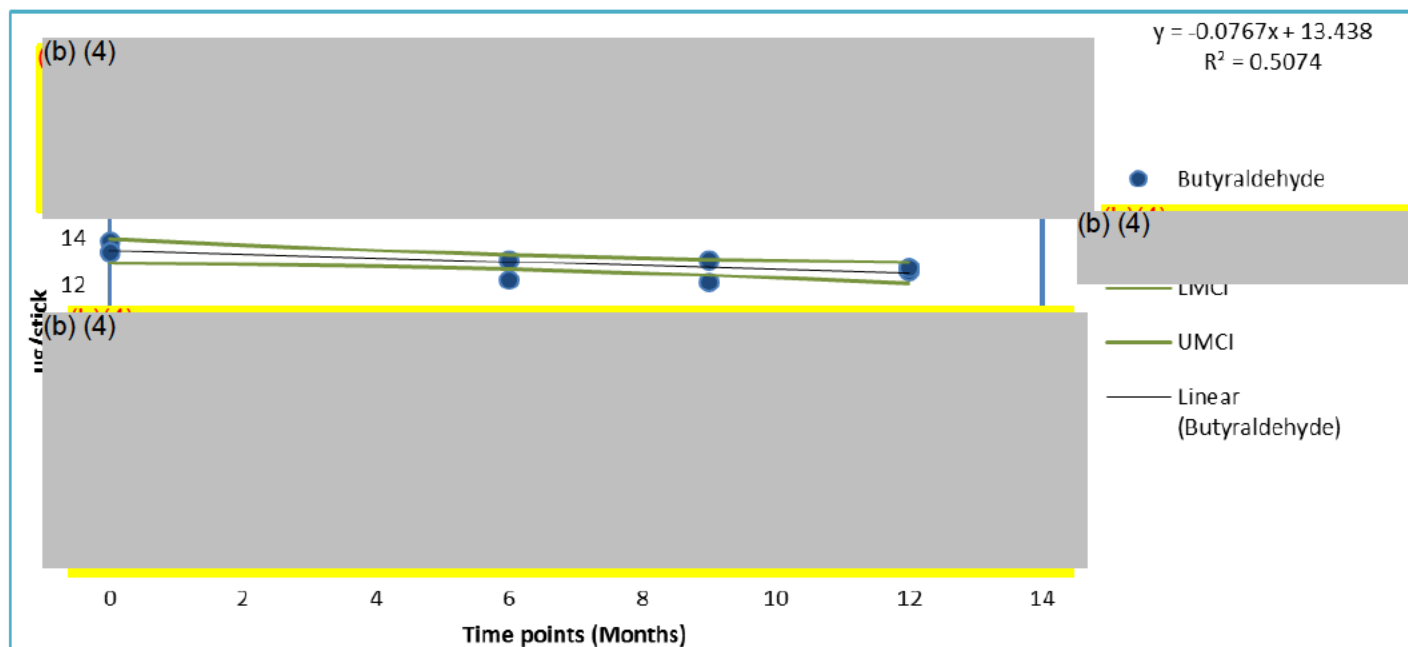


Figure 11 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.1.1.12 Acrylonitrile

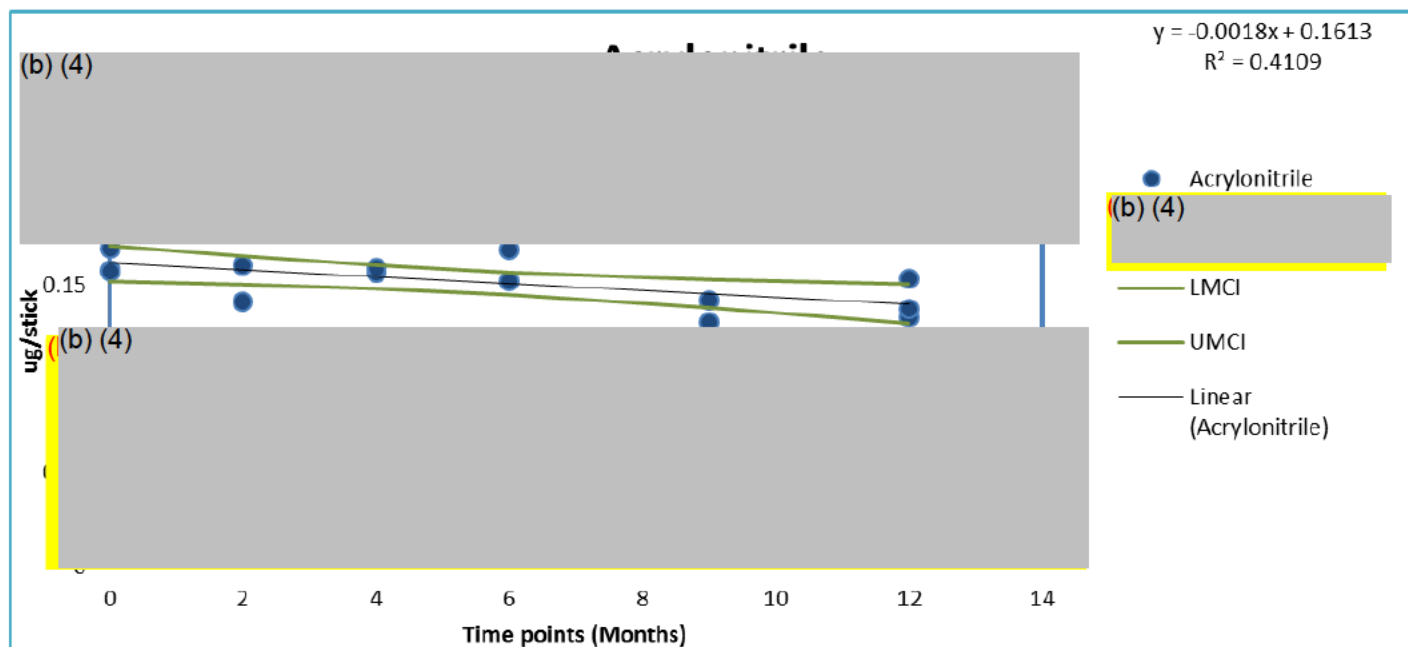


Figure 12 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.1.1.13 Isoprene

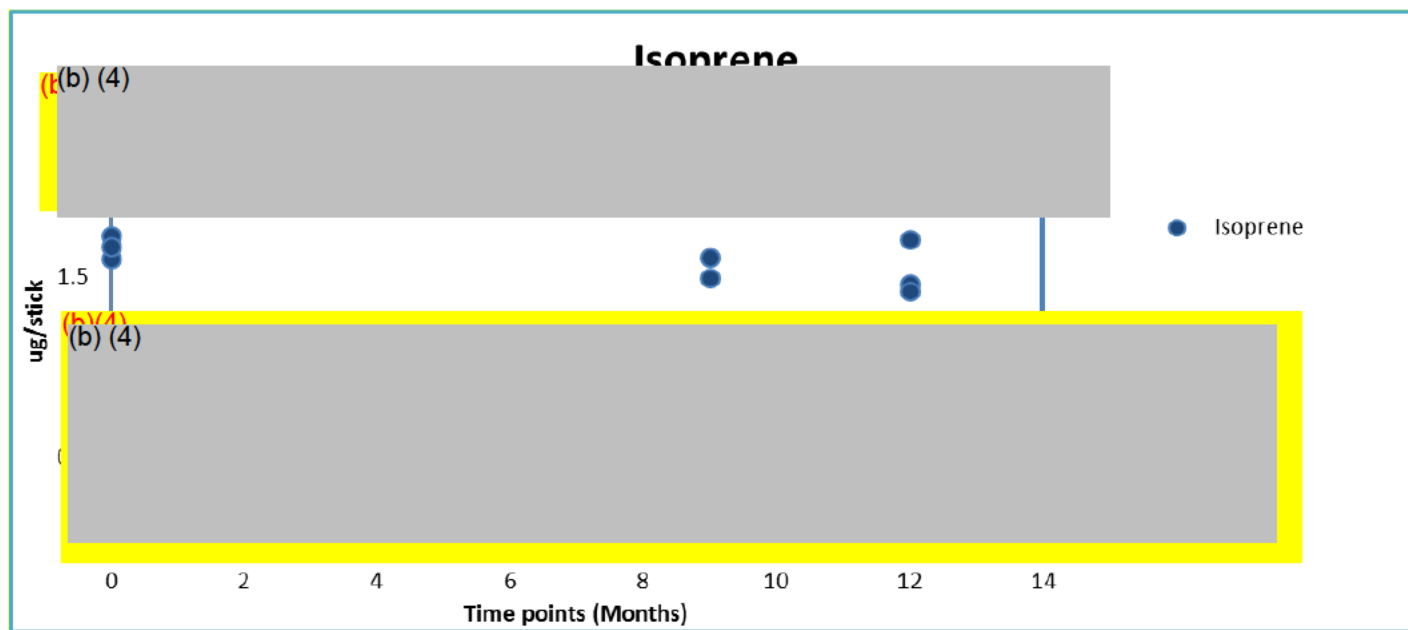


Figure 13 There is no obvious change over time in Isoprene level and all the values are well inside the specifications, therefore Isoprene is considered stable for 12 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.1.1.14 Pyridine

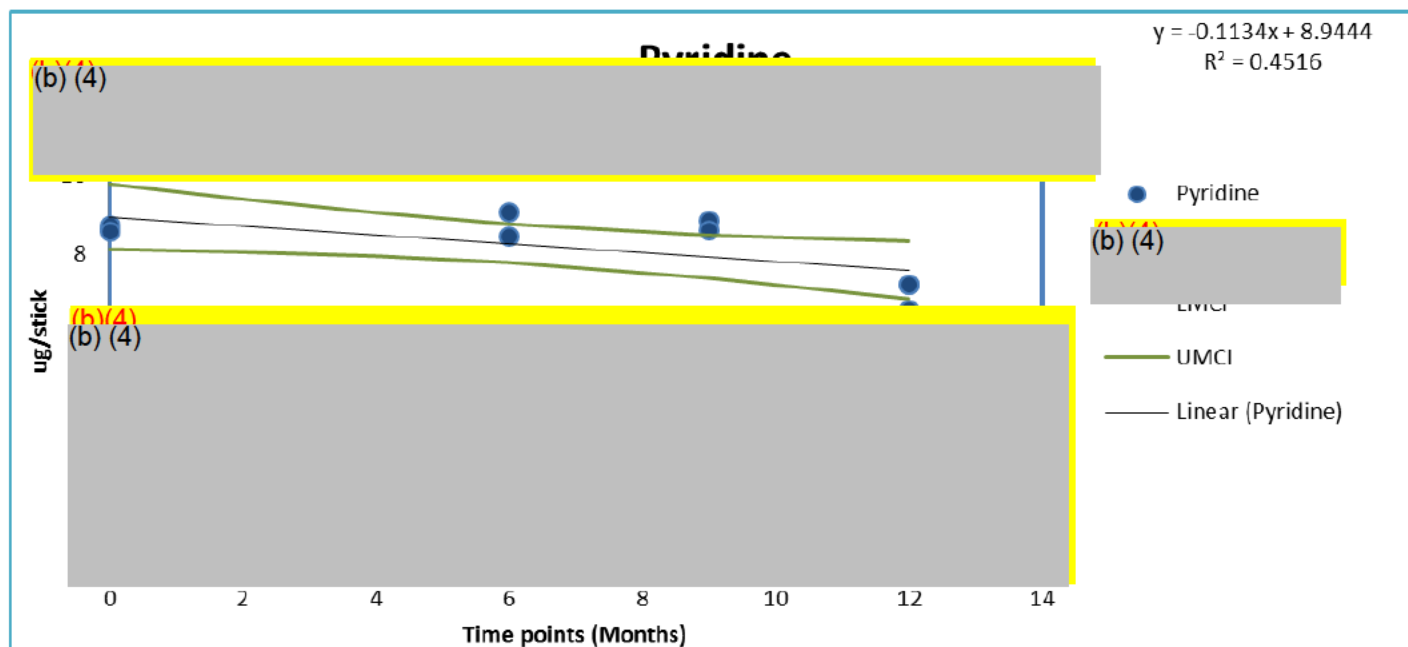


Figure 14 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.1.1.15 Ammonia

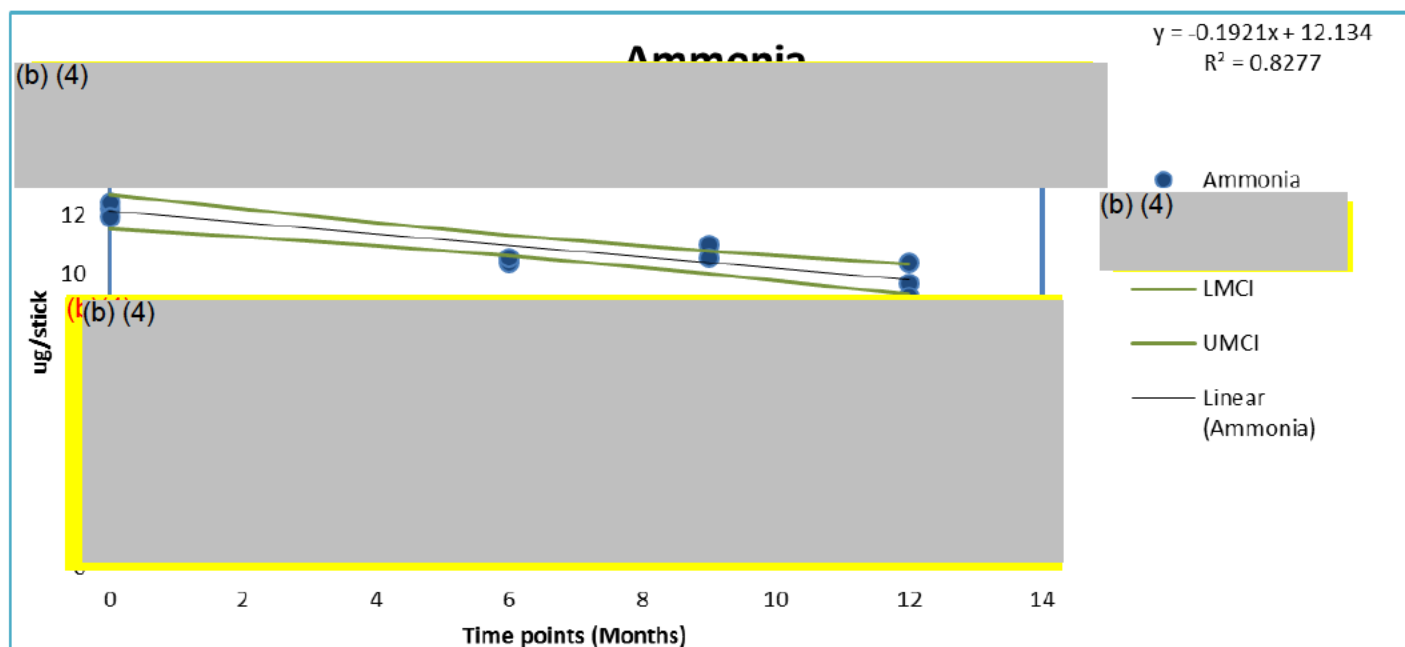


Figure 15 The best model accepted at the significance level of 0.25 has Different intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



Form Number: PMI_RD_FOR_000927

Form Version N°: 1.0

Form Status: Effective

Stability Study Report: STAB-2016_P1_M_1

Form Effective Date: See EDMS

6.1.2 Physical Attributes Evaluation

(b) (4)





Form Number: PMI_RD_FOR_000927

Form Version N°: 1.0

Form Status: Effective

Stability Study Report: STAB-2016_P1_M_1

Form Effective Date: See EDMS

6.1.3 Sensorial Evaluation

Sensorial evaluation results are described in details in a separate report [\[5\]](#).

No drastic sensory changes were observed over the storage time of 12 months at condition 22°C 60%RH. (b) (4)

(b) (4)

Based on t
C 60% RH.

Therefore, a shelf life of 12 months could is considered as acceptable.

6.1.4 Visual inspection

The visual quality of the tobacco sticks was found acceptable from visual point of view after 12 months of storage in 22°C 60%RH.



Form Number: PMI_RD_FOR_000927

Form Version N°: 1.0

Form Status: Effective

Stability Study Report: STAB-2016_P1_M_1

Form Effective Date: See EDMS

6.2 Storage Condition 30°C 35% RH

Table 8 B-25900 / 41.2381531 at 30°C 35% RH

B-25900 / 41.2381531	Unit	Specifications		Time point (Months)						Degradation Rate	R^2	Severity Score
		Lower	Upper	0	2	4	6	9	12			
Test		(b) (4)										
Menthol	mg/stick	(b) (4)		1.25	1.85		1.68	1.74	1.70	1.49%	0.23	0.3
Nicotine	mg/stick			1.17	1.14		1.12	1.09	1.07	-0.70%	0.98	0.7
Glycerin	mg/stick			4.68	4.74		4.49	4.35	3.99	-1.20%	0.90	1.1
CO	mg/stick			0.3	0.3		0.4	0.5	0.3	2.25%	0.17	0.4
Triacetin	mg/stick			0.5	0.5		0.4	0.4	0.4	-1.94%	0.85	1.6
Phenol	µg/stick			1.2	1.3		1.4	1.2	1.1	-0.42%	0.04	0.0
Acrylamide	µg/stick			1.4	1.4		1.5	1.3	1.2	-1.17%	0.45	0.5
Acetamide	µg/stick			3.0			2.9	2.7	2.7	-1.00%	0.87	0.9
Acetaldehyde	µg/stick			205			189	194	197	-0.34%	0.26	0.1
Butyraldehyde	µg/stick			13.9			11.7	12.4	11.3	-1.40%	0.78	1.1
Acrylonitrile	µg/stick			0.16	0.15		0.14	0.13	0.13	-1.70%	0.88	1.5
Isoprene	µg/stick			1.59				1.48	1.32	-1.27%	0.85	1.1
Pyridine	µg/stick			8.6			8.4	8.8	8.3	-0.18%	0.14	0.0
Ammonia	µg/stick			12.3			7.9	8.0	6.8	-3.82%	0.89	3.4
TPM	mg/stick			54	53		52	51	48	-0.88%	0.94	0.8

(b) (4)



Form Number: PMI_RD_FOR_000927

Form Version N°: 1.0

Form Status: Effective

Stability Study Report: STAB-2016_P1_M_1

Form Effective Date: See EDMS

Table 9 B-25901 / 41.2374718 at 30°C 35% RH

B-25901 / 41.2374718	Unit	Specifications		Time point (Months)						Degradation Rate	R^2	Severity Score
		Lower	Upper	0	2	4	6	9	12			
Test												
Menthol	mg/stick	(b) (4)		1.23		2.00	1.97		1.66	1.75%	0.15	0.3
Nicotine	mg/stick			1.23		1.13	1.22		1.15	-0.41%	0.26	0.1
Glycerin	mg/stick			4.53		4.36	4.50		4.17	-0.60%	0.72	0.4
CO	mg/stick			0.3		0.5	0.4		0.3	-0.81%	0.03	0.0
Triacetin	mg/stick			0.5		0.4	0.5		0.4	-1.33%	0.52	0.7
Phenol	µg/stick			1.2		1.6	1.4		1.1	-1.01%	0.12	0.1
Acrylamide	µg/stick			1.4		1.4	1.6		1.3	-0.63%	0.12	0.1
Acetamide	µg/stick			3.2			3.1		2.9	-0.87%	1.00	0.9
Acetaldehyde	µg/stick			195			196		207	0.52%	0.80	0.4
Butyraldehyde	µg/stick			13.4			12.0		11.9	-0.98%	0.83	0.8
Acrylonitrile	µg/stick			0.17		0.16	0.14		0.14	-1.35%	0.80	1.1
Isoprene	µg/stick			1.72					1.39	NA	NA	NA
Pyridine	µg/stick			8.7			8.6		8.5	-0.25%	0.97	0.2
Ammonia	µg/stick			12.5			8.2		6.9	-3.84%	0.91	3.5
TPM	mg/stick			56		52	52		50	-0.88%	0.82	0.7

(b) (4)



Form Number: PMI_RD_FOR_000927

Form Version N°: 1.0

Form Status: Effective

Stability Study Report: STAB-2016_P1_M_1

Form Effective Date: See EDMS

Table 10 B-25902 / 41.2379112 at 30°C 35% RH

B-25902 / 41.2379112	Unit	Specifications		Time point (Months)						Degradation Rate	R^2	Severity Score
		Lower	Upper	0	2	4	6	9	12			
Menthol	mg/stick	(b) (4)		1.05	1.67	1.68		1.65	1.60	2.02%	0.27	0.5
Nicotine	mg/stick			1.22	1.14	1.11	1.11	1.10	1.10	-0.68%	0.64	0.4
Glycerin	mg/stick			4.59	4.66	3.66	4.13	4.13	3.78	-1.34%	0.43	0.6
CO	mg/stick			0.3	0.3	0.5	0.4	0.4	0.3	0.82%	0.02	0.0
Triacetin	mg/stick			0.5	0.4	0.4	0.4	0.4	0.4	-1.57%	0.34	0.5
Phenol	µg/stick			1.3	1.2	0.7	1.1	1.0	0.9	-2.28%	0.33	0.8
Acrylamide	µg/stick			1.4	1.3	1.0	1.4	1.2	1.1	-1.36%	0.25	0.3
Acetamide	µg/stick			3.0				2.8	2.7	-0.88%	0.97	0.9
Acetaldehyde	µg/stick			195				189	206	0.26%	0.13	0.0
Butyraldehyde	µg/stick			13.4				11.9	11.9	-1.02%	0.94	1.0
Acrylonitrile	µg/stick			0.16	0.15	0.15		0.13	0.14	-1.14%	0.63	0.7
Isoprene	µg/stick			1.66				1.48	1.37	-1.39%	0.98	1.4
Pyridine	µg/stick			8.6				8.9	8.4	-0.05%	0.01	0.0
Ammonia	µg/stick			12.0				7.6	6.2	-4.04%	1.00	4.0
TPM	mg/stick			56	54	49	51	51	48	-0.98%	0.68	0.7

(b) (4)



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.2.1 Mainstream Aerosol Evaluation

6.2.1.1 Menthol

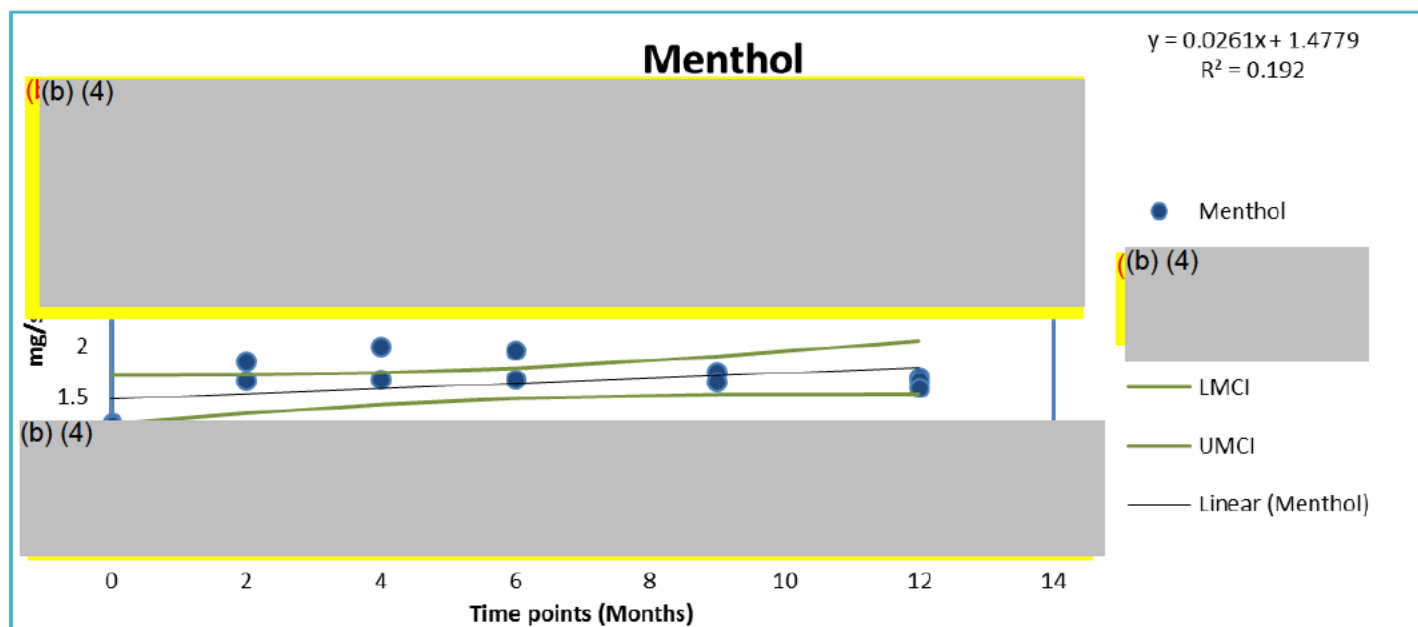


Figure 17 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.2.1.2 Nicotine

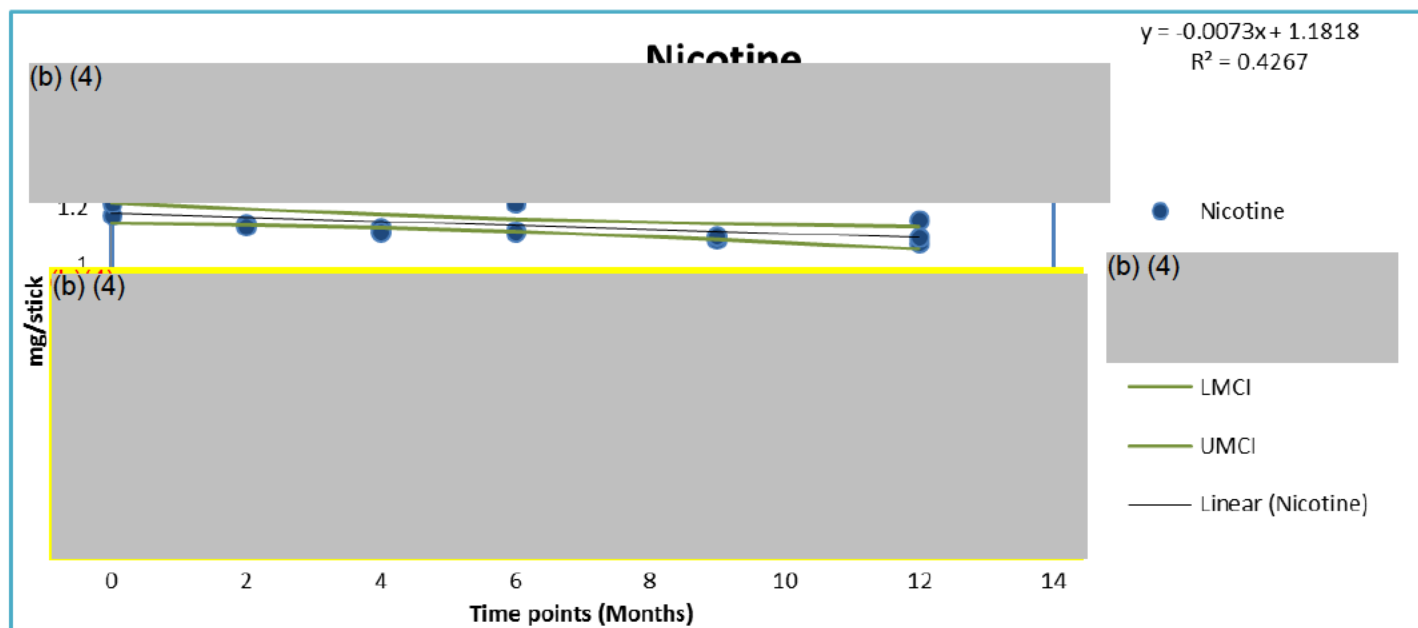


Figure 18 The best model accepted at the significance level of 0.25 has Different intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.2.1.3 Glycerin

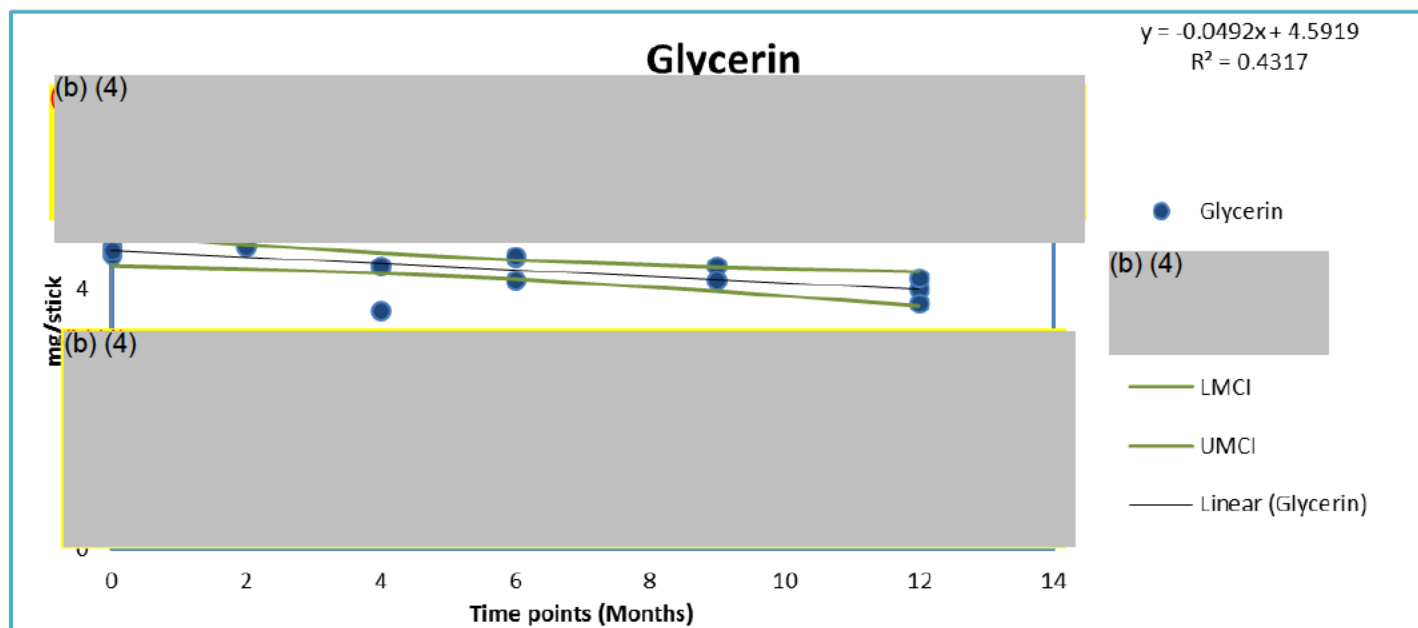


Figure 19 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.2.1.4 CO

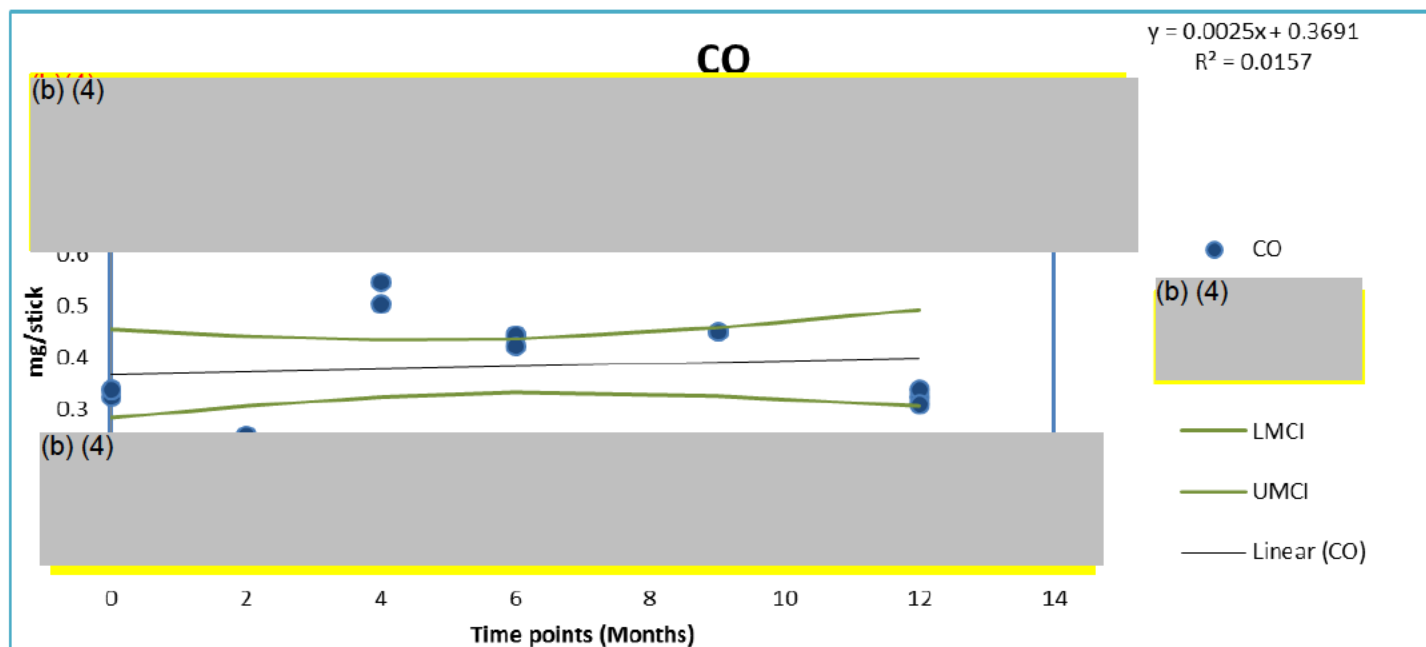


Figure 20 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.2.1.5 Triacetin

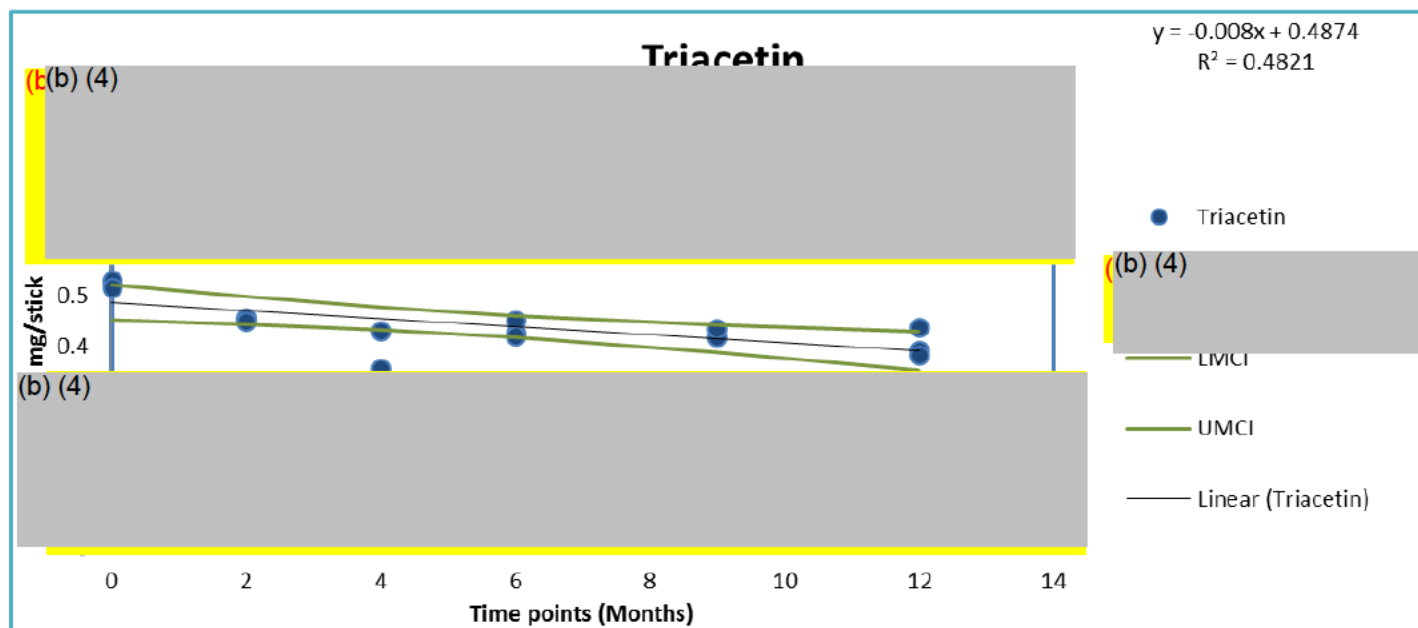


Figure 21 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.2.1.6 TPM

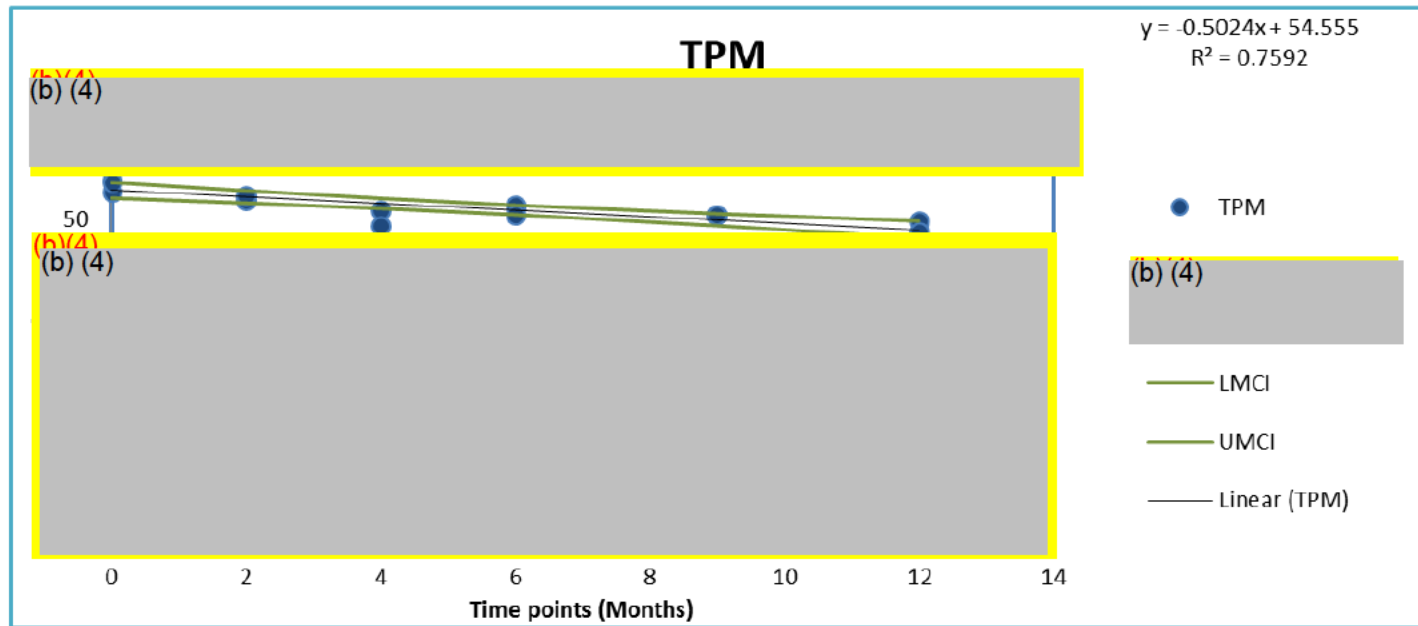


Figure 22 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.2.1.7 Phenol

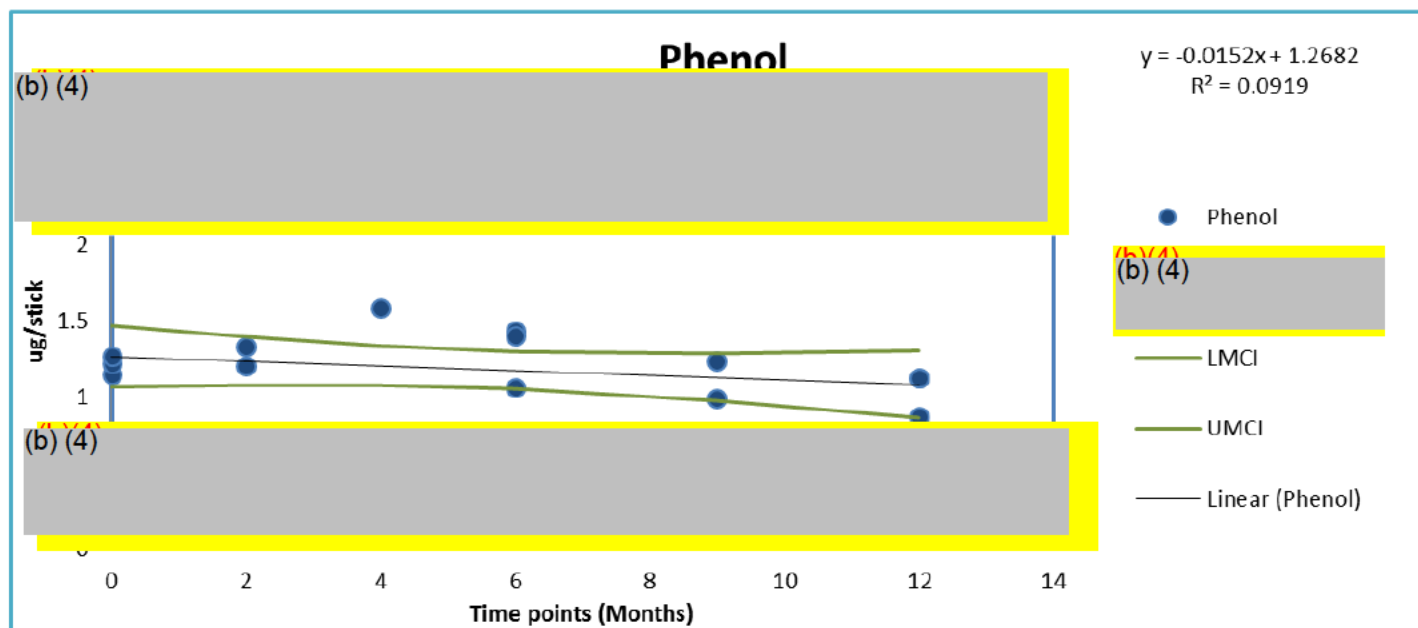


Figure 23 The best model accepted at the significance level of 0.25 has Different intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.2.1.8 Acrylamide

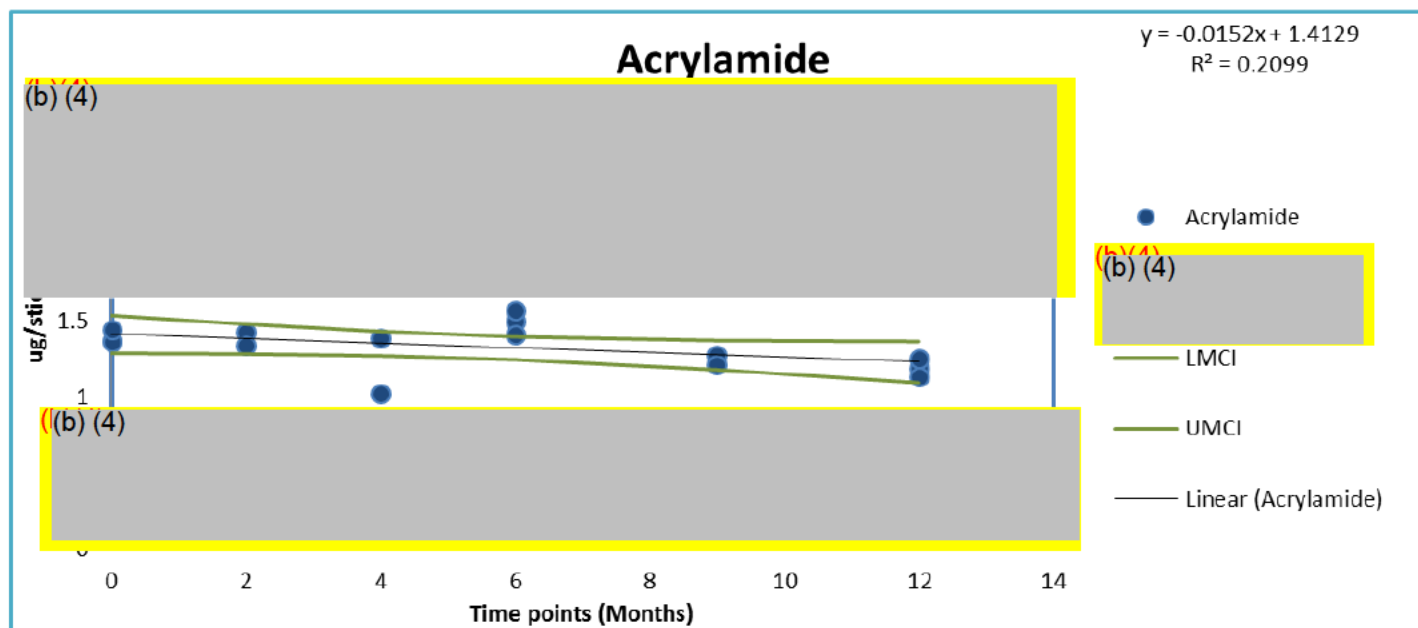


Figure 24 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.2.1.9 Acetamide

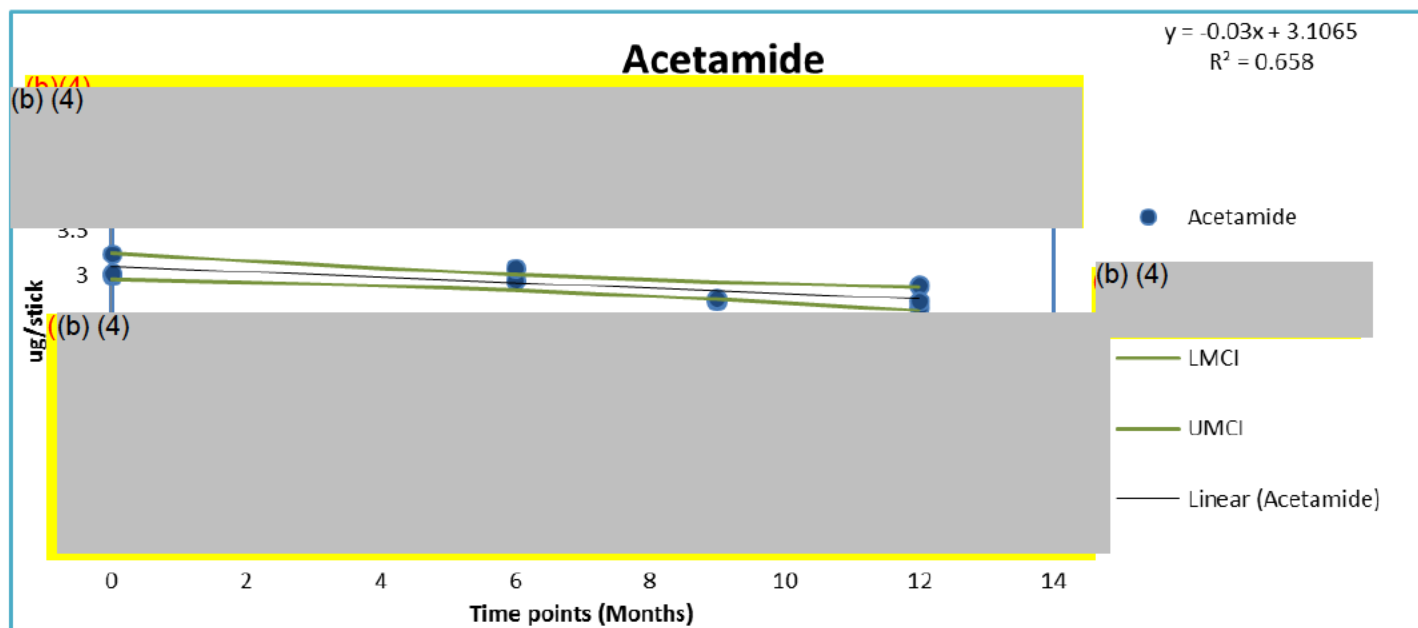


Figure 25 The best model accepted at the significance level of 0.25 has Different intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.2.1.10 Acetaldehyde

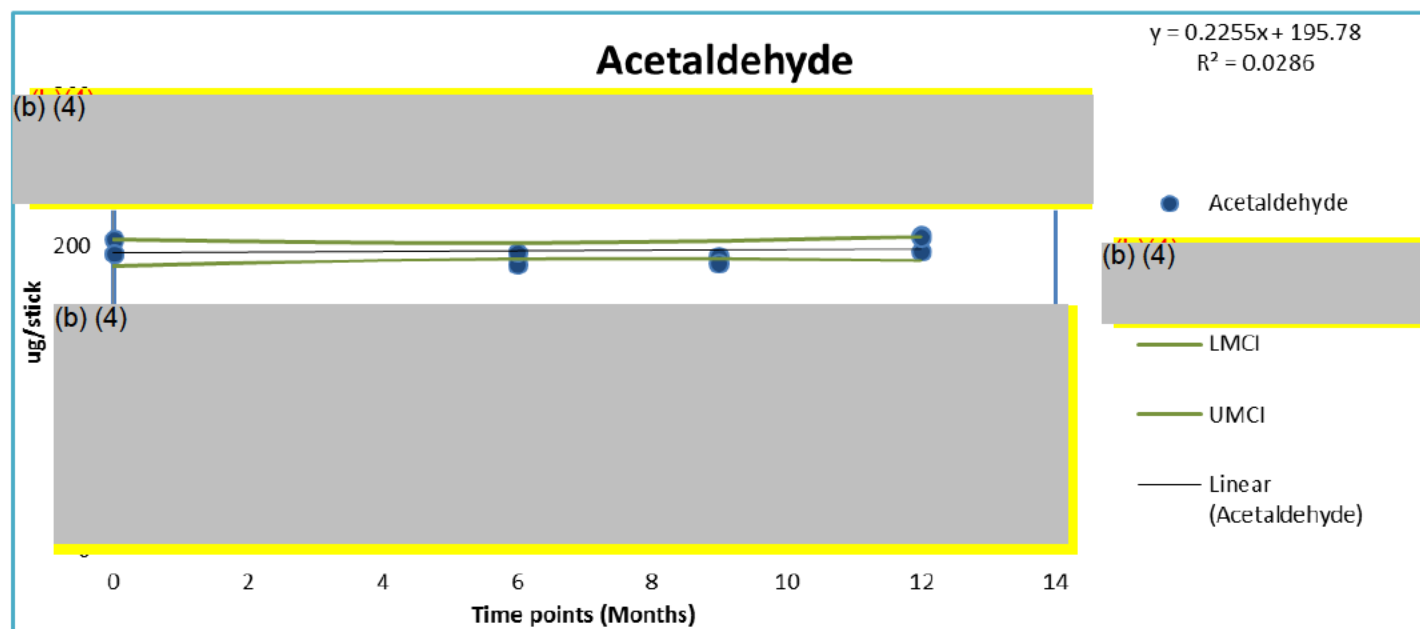


Figure 26 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.2.1.11 Butyraldehyde

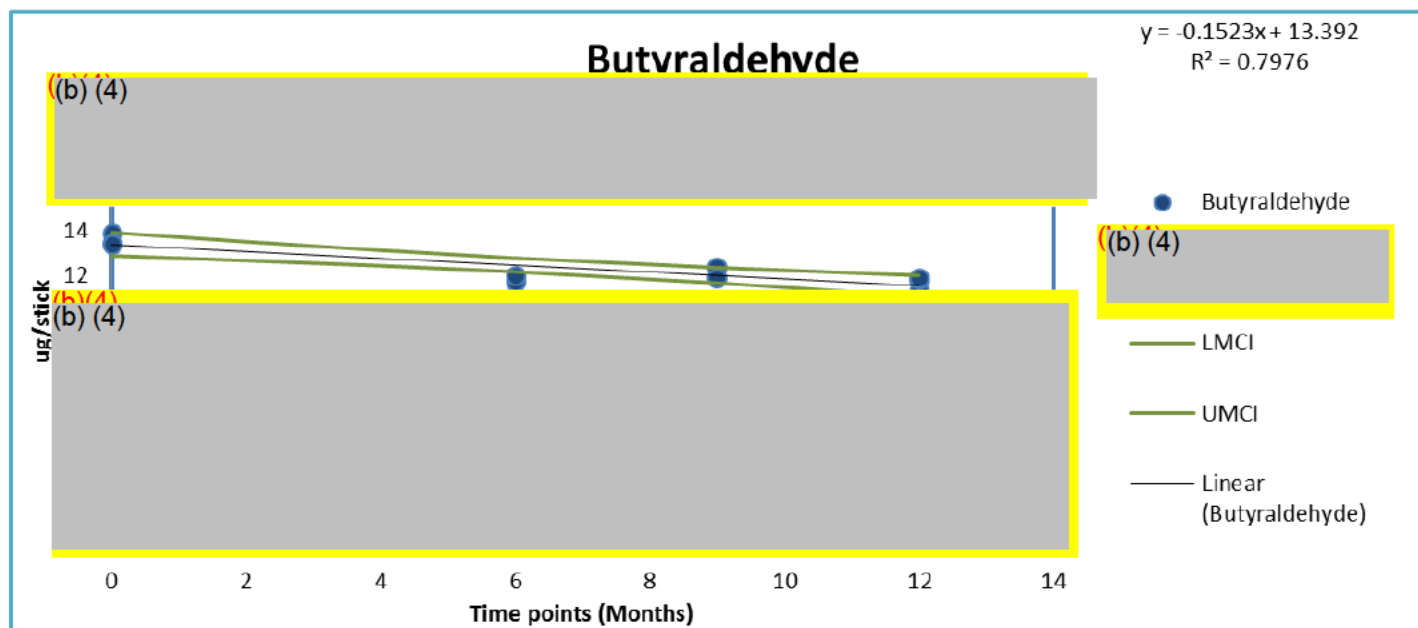


Figure 27 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.2.1.12 Acrylonitrile

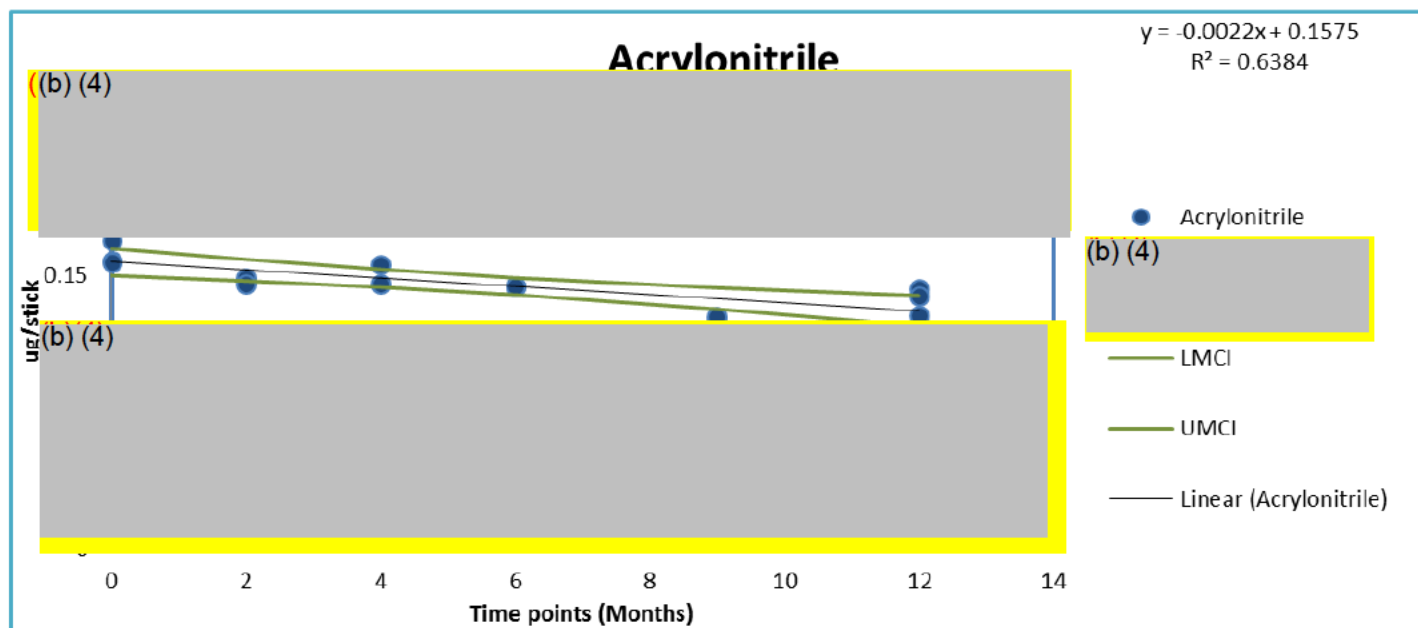


Figure 28 The best model accepted at the significance level of 0.25 has Different intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.2.1.13 Isoprene

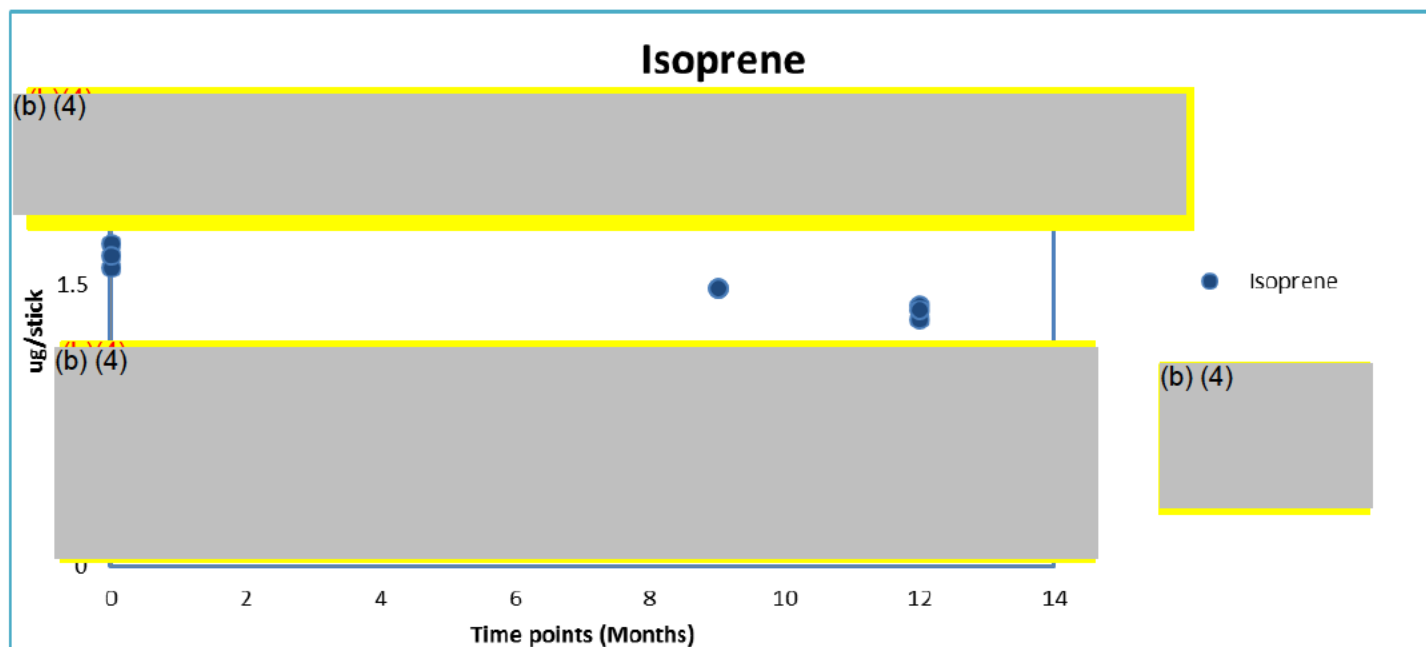


Figure 29 There is no obvious change over time in Isoprene level and all the values are well inside the specifications, therefore Isoprene is considered stable for 12 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.2.1.14 Pyridine

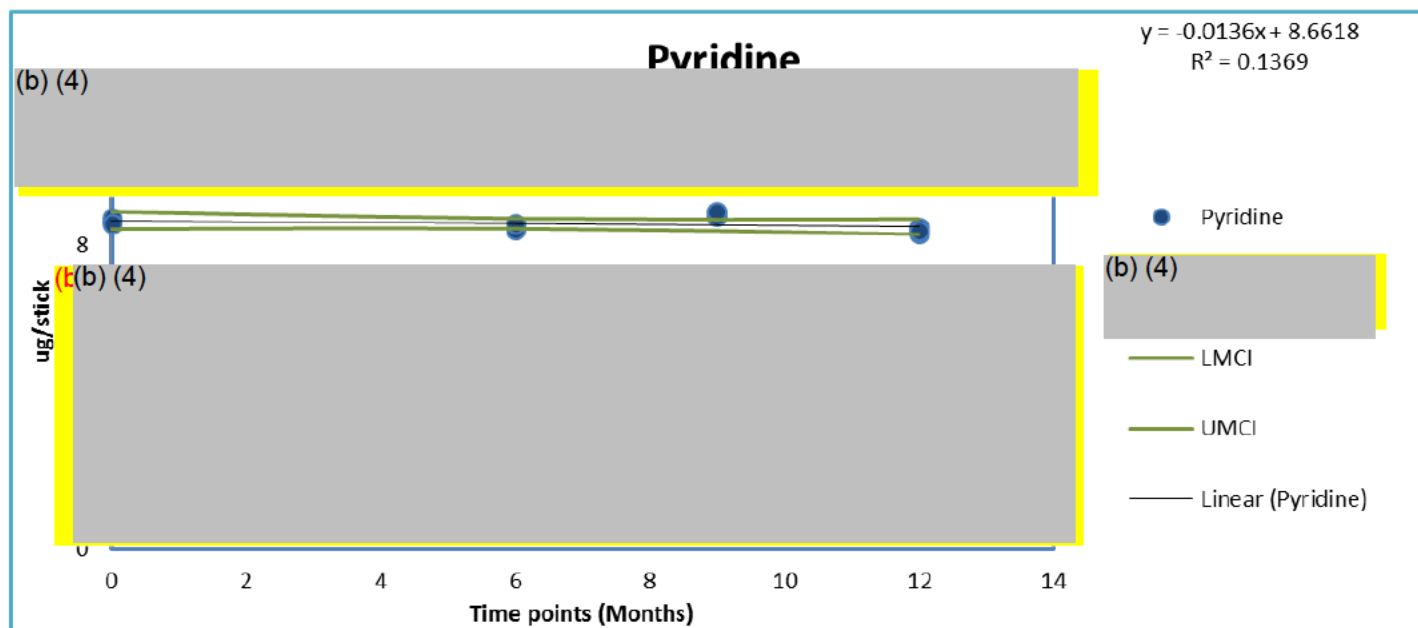


Figure 30 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.2.1.15 Ammonia

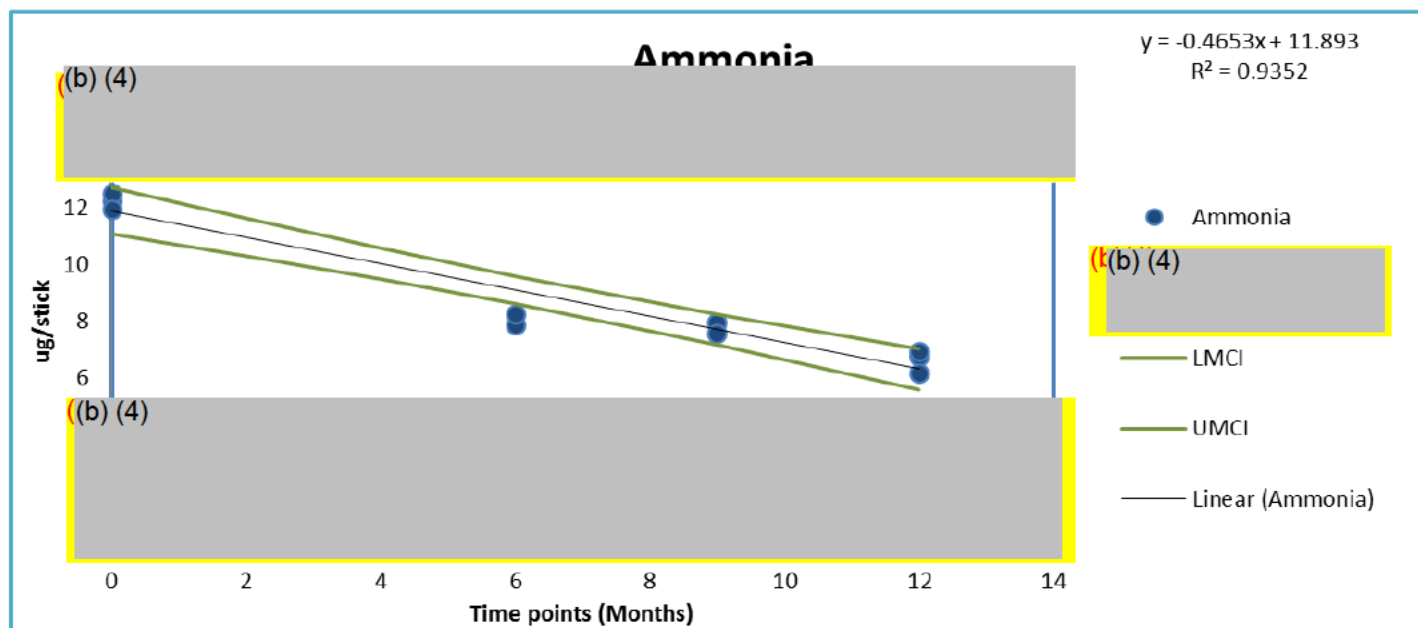


Figure 31 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



Form Number: PMI_RD_FOR_000927

Form Version N°: 1.0

Form Status: Effective

Stability Study Report: STAB-2016_P1_M_1

Form Effective Date: See EDMS

6.2.2 Physical Attributes Evaluation

(b) (4)





Form Number: PMI_RD_FOR_000927

Form Version N°: 1.0

Form Status: Effective

Stability Study Report: STAB-2016_P1_M_1

Form Effective Date: See EDMS

6.2.3 Sensorial Evaluation

Sensorial evaluation results are described in details in a separate report [\[5\]](#).

No drastic sensory changes were observed over the storage time of 12 months at condition 30°C 35%RH. (b) (4)

(b) (4)

Based

is hypothesized that consumers should not reject the product for a period up to 12 month storage in 30°C 35% RH.

Therefore, a shelf life of 12 months could be considered as acceptable.

6.2.4 Visual inspection

The visual quality of the tobacco sticks was found acceptable from visual point of view after 12 months of storage in 30°C 35%RH.



Form Number: PMI_RD_FOR_000927

Form Version N°: 1.0

Form Status: Effective

Stability Study Report: STAB-2016_P1_M_1

Form Effective Date: See EDMS

6.3 Storage Condition 30°C 75% RH

Table 11 B-25900 / 41.2381531 at 30°C 75% RH

B-25900 / 41.2381531	Unit	Specifications	Time point (Months)						Degradation Rate	R^2	Severity Score
			0	2	4	6	9	12			
Test		(b) (4)									
Menthol	mg/stick		1.25	1.88	1.73				8.74%	0.53	4.6
Nicotine	mg/stick		1.17	1.15	1.06				-2.37%	0.91	2.2
Glycerin	mg/stick		4.68	4.67	4.02				-3.46%	0.76	2.6
CO	mg/stick		0.3	0.3	0.5				18.04%	0.56	10.1
Triacetin	mg/stick		0.5	0.4	0.3				-9.28%	0.97	9.0
Phenol	µg/stick		1.2	1.3	1.3				3.93%	0.87	3.4
Acrylamide	µg/stick		1.4	1.4	1.3				-1.91%	0.80	1.5
Acetamide	µg/stick		3.0						NA	NA	NA
Acetaldehyde	µg/stick		205						NA	NA	NA
Butyraldehyde	µg/stick		13.9						NA	NA	NA
Acrylonitrile	µg/stick		0.16	0.14	0.16				-0.36%	0.01	0.0
Isoprene	µg/stick		1.59	1.64*	1.86*				NA	NA	NA
Pyridine	µg/stick		8.6						NA	NA	NA
Ammonia	µg/stick		12.3						NA	NA	NA
TPM	mg/stick		54	53	50				-1.78%	0.96	1.7

(b) (4)

* Isoprene values in T2 and T4 are explained in [Chapter 5.2](#).



Form Number: PMI_RD_FOR_000927

Form Version N°: 1.0

Form Status: Effective

Stability Study Report: STAB-2016_P1_M_1

Form Effective Date: See EDMS

Table 12 B-25901 / 41.2374718 at 30°C 75% RH

B-25901 / 41.2374718	Unit	Specifications	Time point (Months)						Degradation Rate	R ²	Severity Score
Test		(b) (4)	0	2	4	6	9	12			
Menthol	mg/stick	(b) (4)	1.23	1.86		1.88			6.71%	0.60	4.0
Nicotine	mg/stick	(b) (4)	1.23	1.17		1.19			-0.39%	0.21	0.1
Glycerin	mg/stick	(b) (4)	4.53	4.79		4.33			-0.96%	0.35	0.3
CO	mg/stick	(b) (4)	0.3	0.3		0.5			10.39%	0.57	5.9
Triacetin	mg/stick	(b) (4)	0.5	0.5		0.4			-4.50%	0.97	4.4
Phenol	µg/stick	(b) (4)	1.2	1.7		1.6			3.26%	0.35	1.1
Acrylamide	µg/stick	(b) (4)	1.4	1.4		1.6			2.42%	1.00	2.4
Acetamide	µg/stick	(b) (4)	3.2			3.2			NA	NA	NA
Acetaldehyde	µg/stick	(b) (4)	195			212			NA	NA	NA
Butyraldehyde	µg/stick	(b) (4)	13.4			12.2			NA	NA	NA
Acrylonitrile	µg/stick	(b) (4)	0.17	0.14		0.17			0.26%	0.01	0.0
Isoprene	µg/stick	(b) (4)	1.72	1.66*		2.30*			NA	NA	NA
Pyridine	µg/stick	(b) (4)	8.7			8.6			NA	NA	NA
Ammonia	µg/stick	(b) (4)	12.5			8.9			NA	NA	NA
TPM	mg/stick	(b) (4)	56	54		54			-0.60%	0.54	0.3

* Isoprene values in T2 and T4 are explained in [Chapter 5.2](#).



Form Number: PMI_RD_FOR_000927

Form Version N°: 1.0

Form Status: Effective

Stability Study Report: STAB-2016_P1_M_1

Form Effective Date: See EDMS

Table 13 B-25902 / 41.2379112 at 30°C 75% RH

B-25902 / 41.2379112	Unit	Specifications	Time point (Months)						Degradation Rate	R ²	Severity Score
Test		(b) (4)	0	2	4	6	9	12			
Menthol	mg/stick		1.05		1.85	1.93			13.95%	0.94	13.1
Nicotine	mg/stick		1.22		1.07	1.19			-0.73%	0.12	0.1
Glycerin	mg/stick		4.59		4.04	4.41			-1.00%	0.24	0.2
CO	mg/stick		0.3		0.5	0.5			6.88%	0.55	3.8
Triacetin	mg/stick		0.5		0.4	0.4			-5.09%	0.78	4.0
Phenol	µg/stick		1.3		1.1	1.5			2.47%	0.18	0.4
Acrylamide	µg/stick		1.4		1.3	1.6			1.20%	0.10	0.1
Acetamide	µg/stick		3.0			3.3			NA	NA	NA
Acetaldehyde	µg/stick		195			229			NA	NA	NA
Butyraldehyde	µg/stick		13.4			13.7			NA	NA	NA
Acrylonitrile	µg/stick		0.16		0.13	0.14			-1.96%	0.61	1.2
Isoprene	µg/stick		1.66		1.56*	1.82*			NA	NA	NA
Pyridine	µg/stick		8.6			8.2			NA	NA	NA
Ammonia	µg/stick		12.0			8.7			NA	NA	NA

(b) (4)

* Isoprene values in T2 and T4 are explained in [Chapter 5.2](#).



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.3.1 Mainstream Aerosol Evaluation

6.3.1.1 Menthol

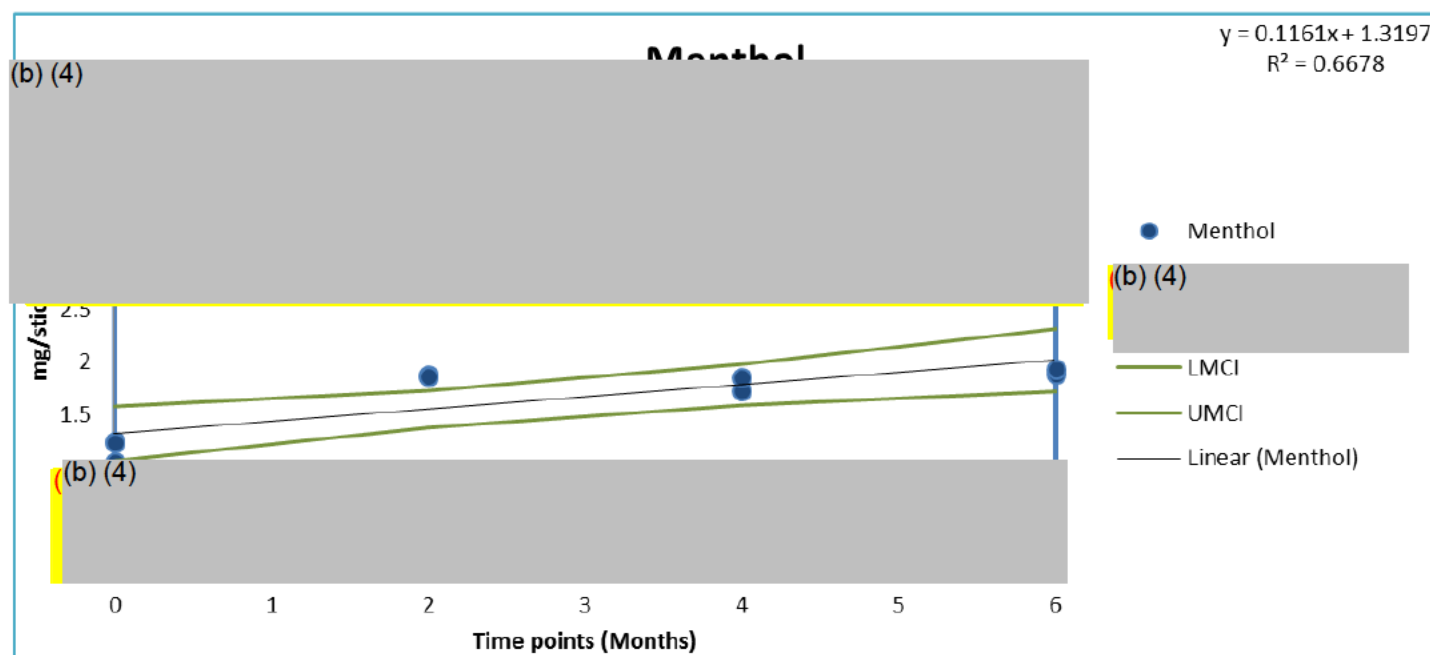


Figure 33 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 6 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 6 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.3.1.2 Nicotine

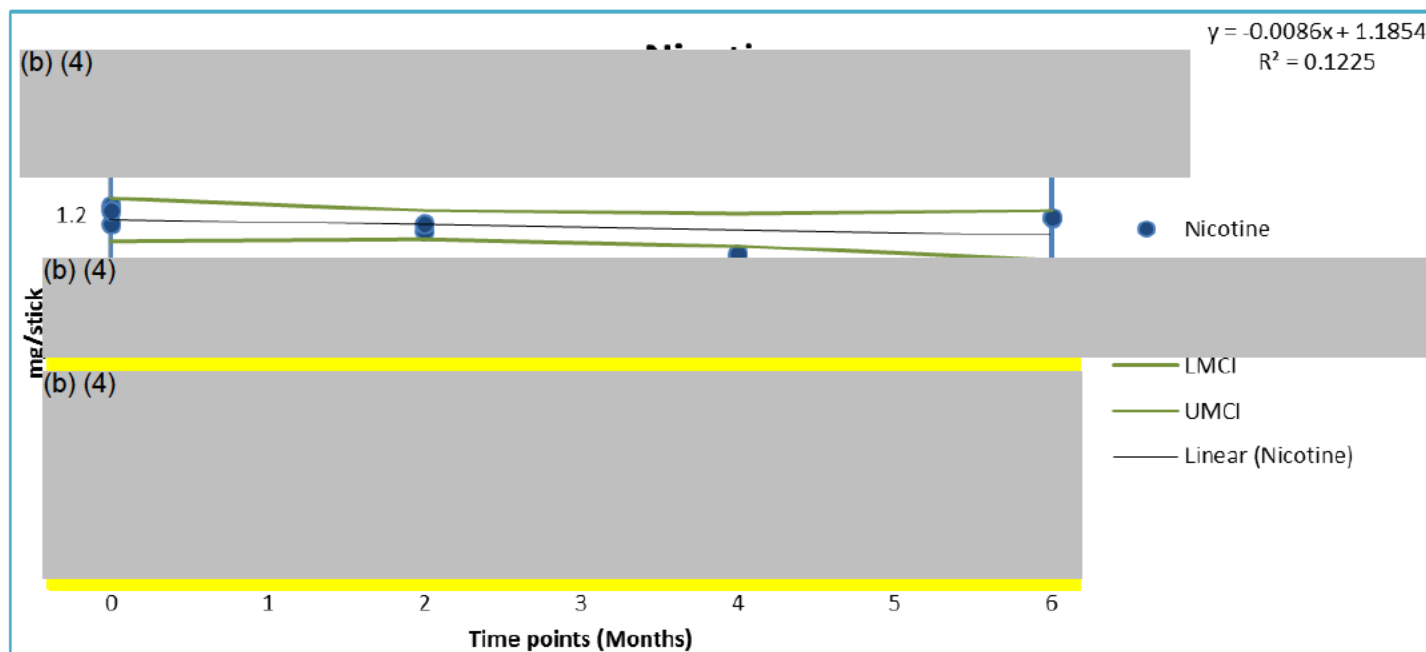


Figure 34 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 6 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 6 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.3.1.3 Glycerin

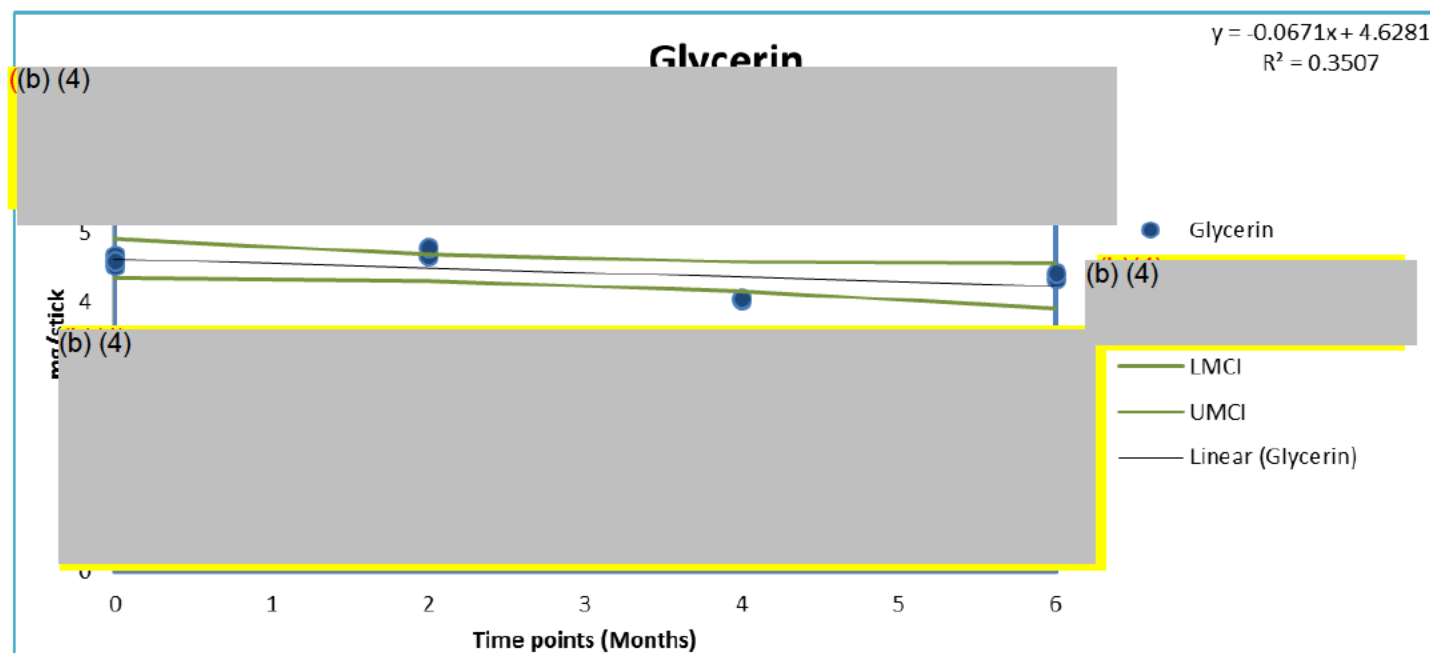


Figure 35 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 6 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 6 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.3.1.4 CO

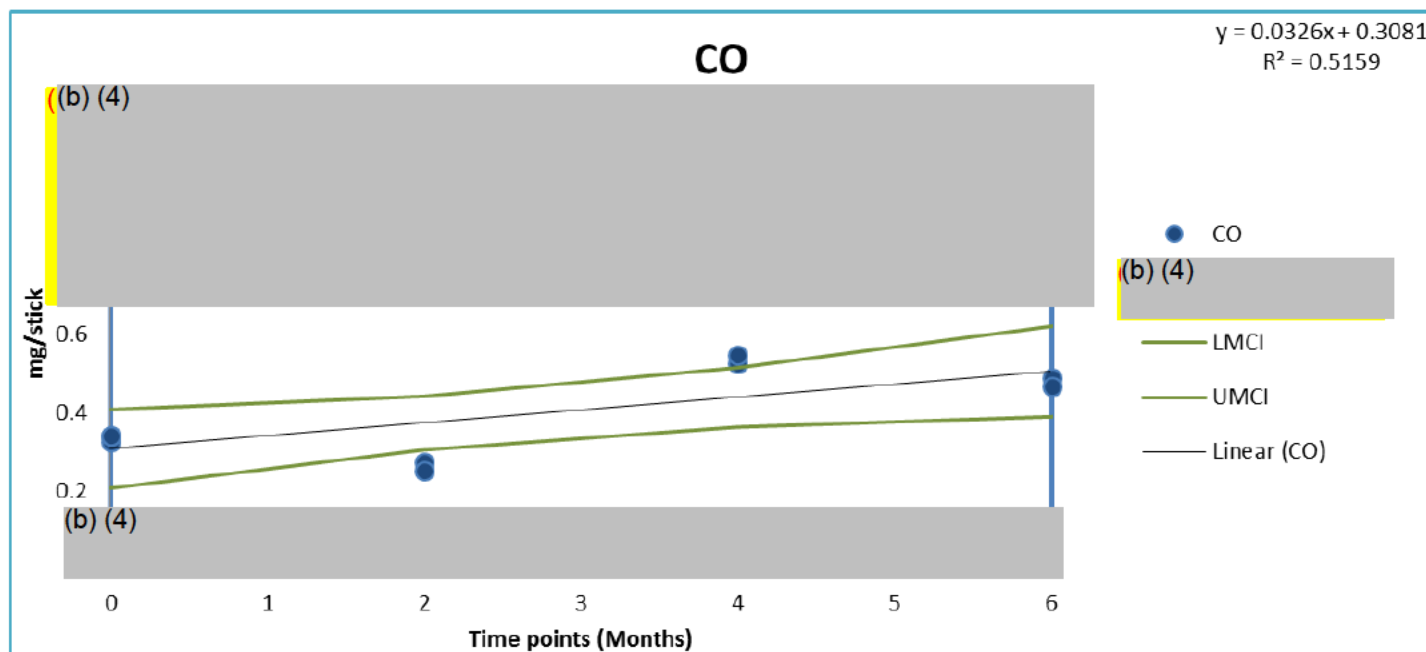


Figure 36 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 6 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 6 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.3.1.5 Triacetin

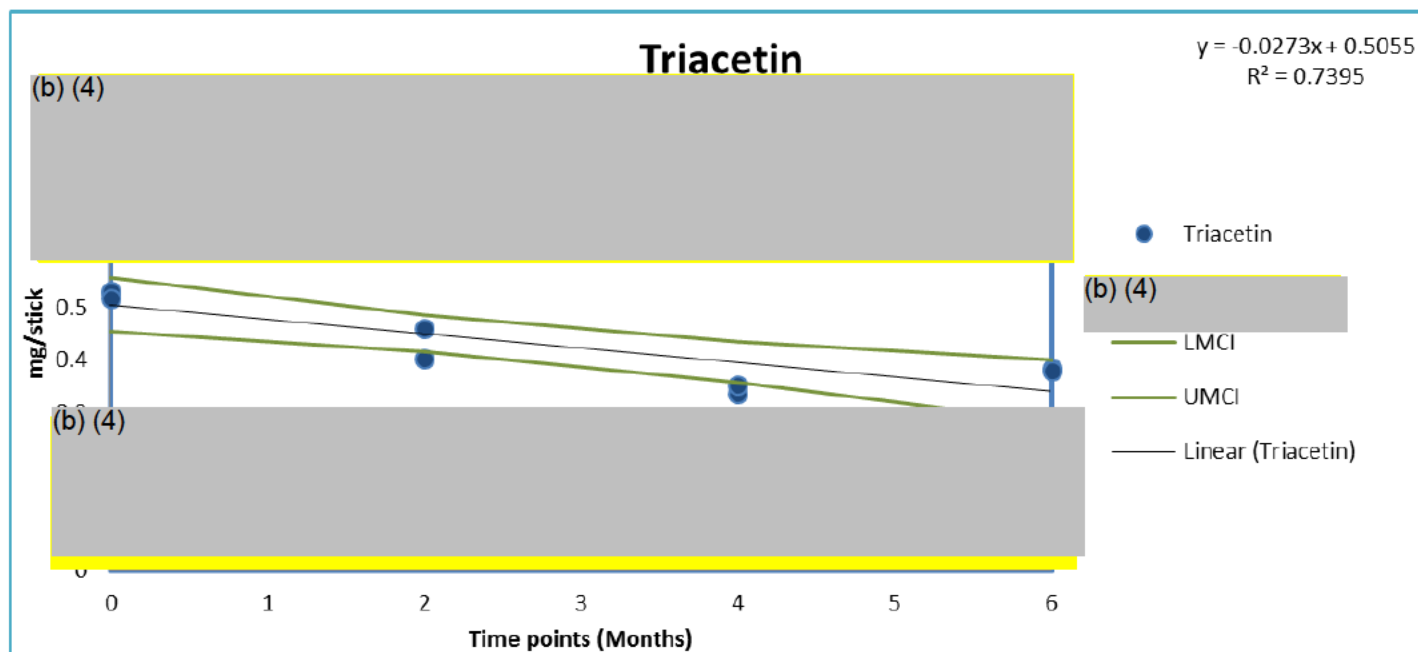


Figure 37 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 6 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 6 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.3.1.6 TPM

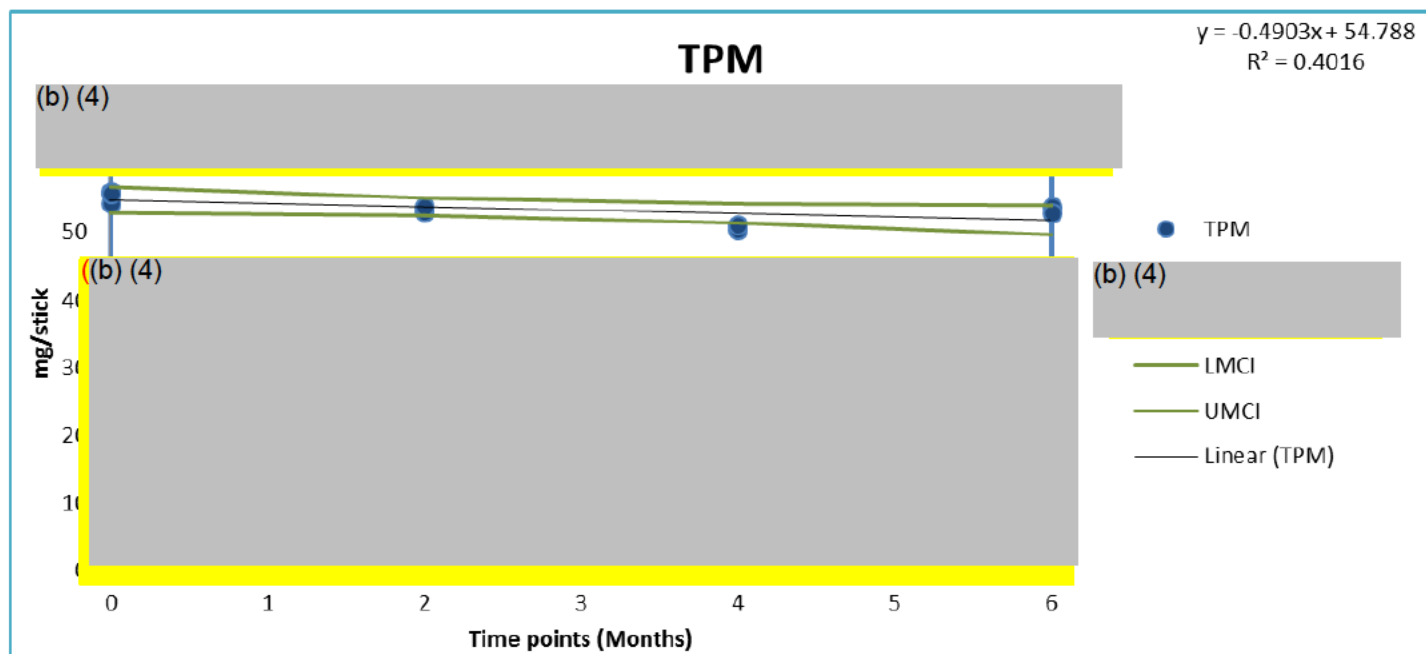


Figure 38 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 6 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 6 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.3.1.7 Phenol

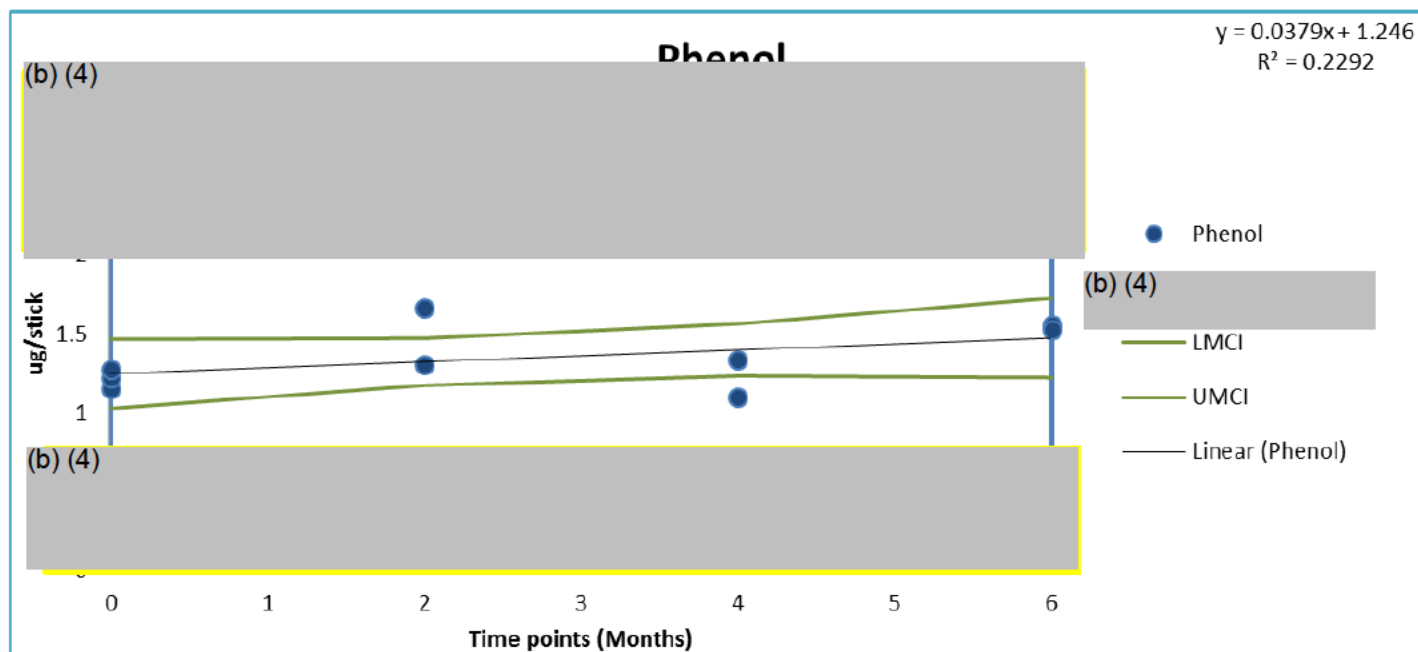


Figure 39 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 6 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 6 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.3.1.8 Acrylamide

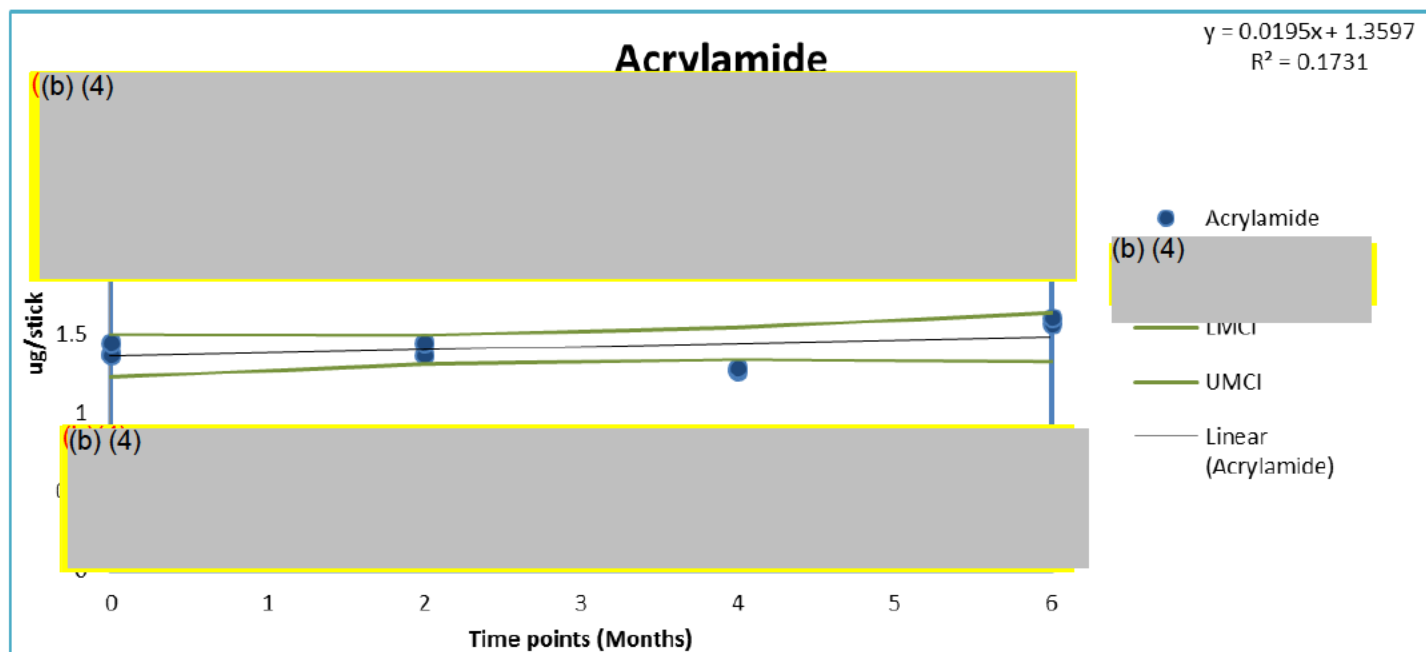


Figure 40 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 6 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 6 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.3.1.9 Acetamide

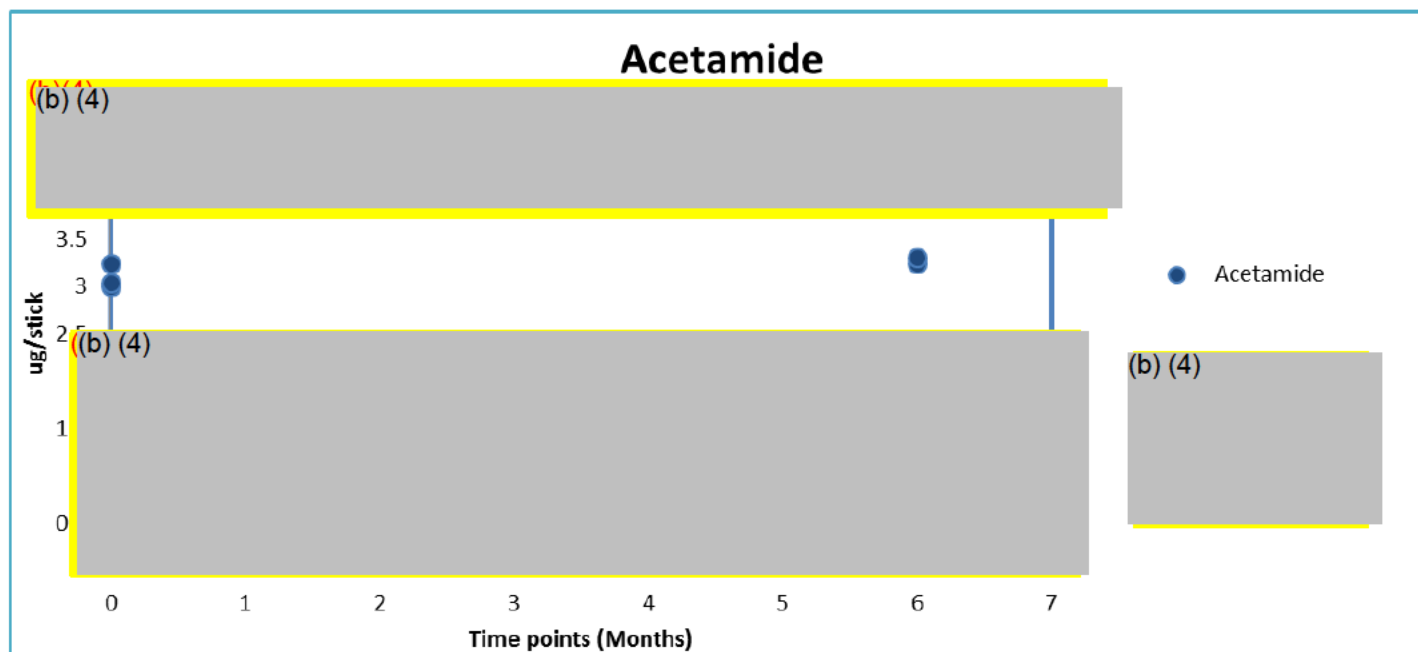


Figure 41 Acetamide is not suitable for trend analysis since it was tested in less than 3 different time points. All the values obtained are inside the specifications and therefore Acetamide is considered stable for 6 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.3.1.10 Acetaldehyde

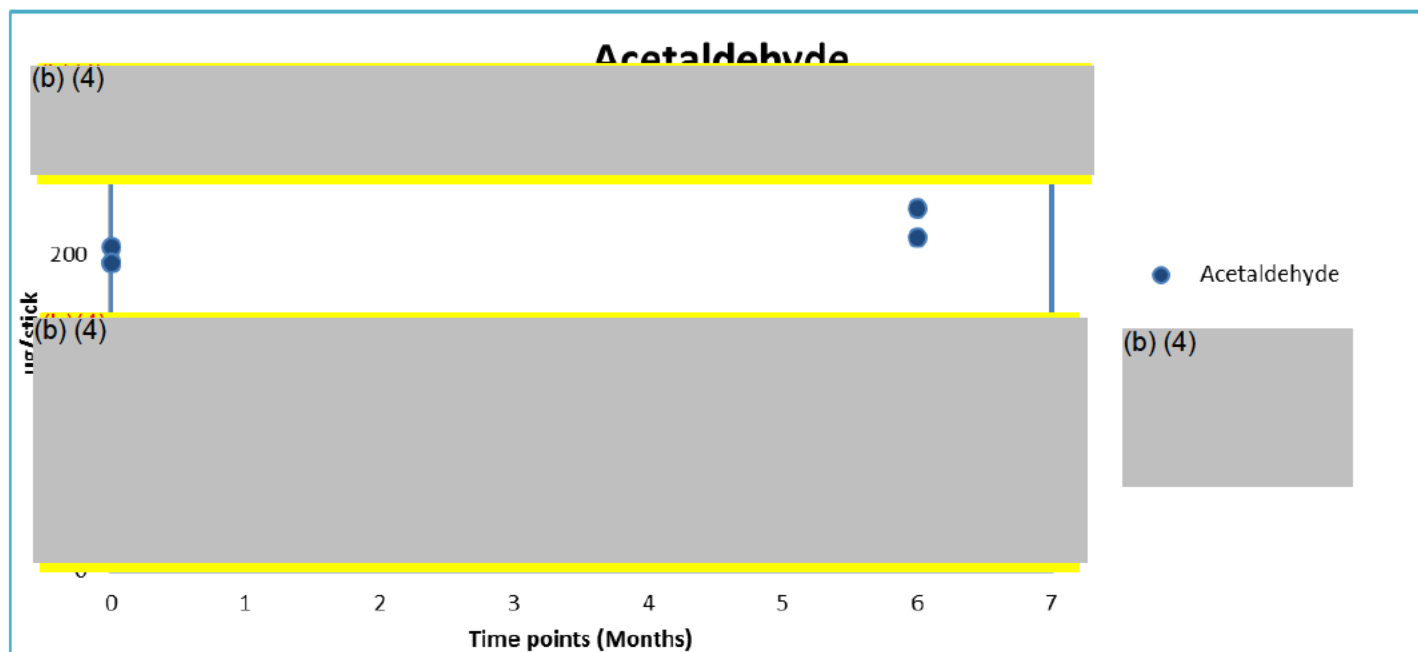


Figure 42 Acetaldehyde is not suitable for trend analysis since it was tested in less than 3 different time points. All the values obtained are inside the specifications and therefore Acetaldehyde is considered stable for 6 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.3.1.11 Butyraldehyde

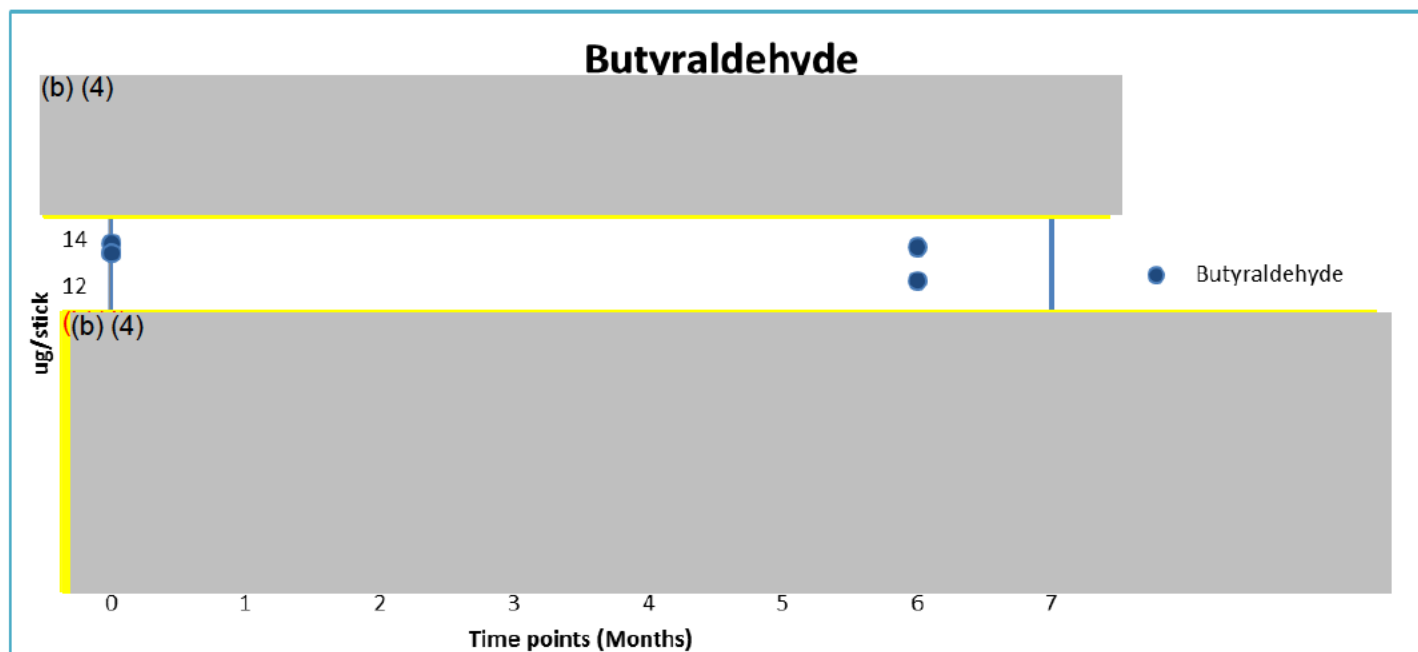


Figure 43 Butyraldehyde is not suitable for trend analysis since it was tested in less than 3 different time points. All the values obtained are inside the specifications and therefore Butyraldehyde is considered stable for 6 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.3.1.12 Acrylonitrile

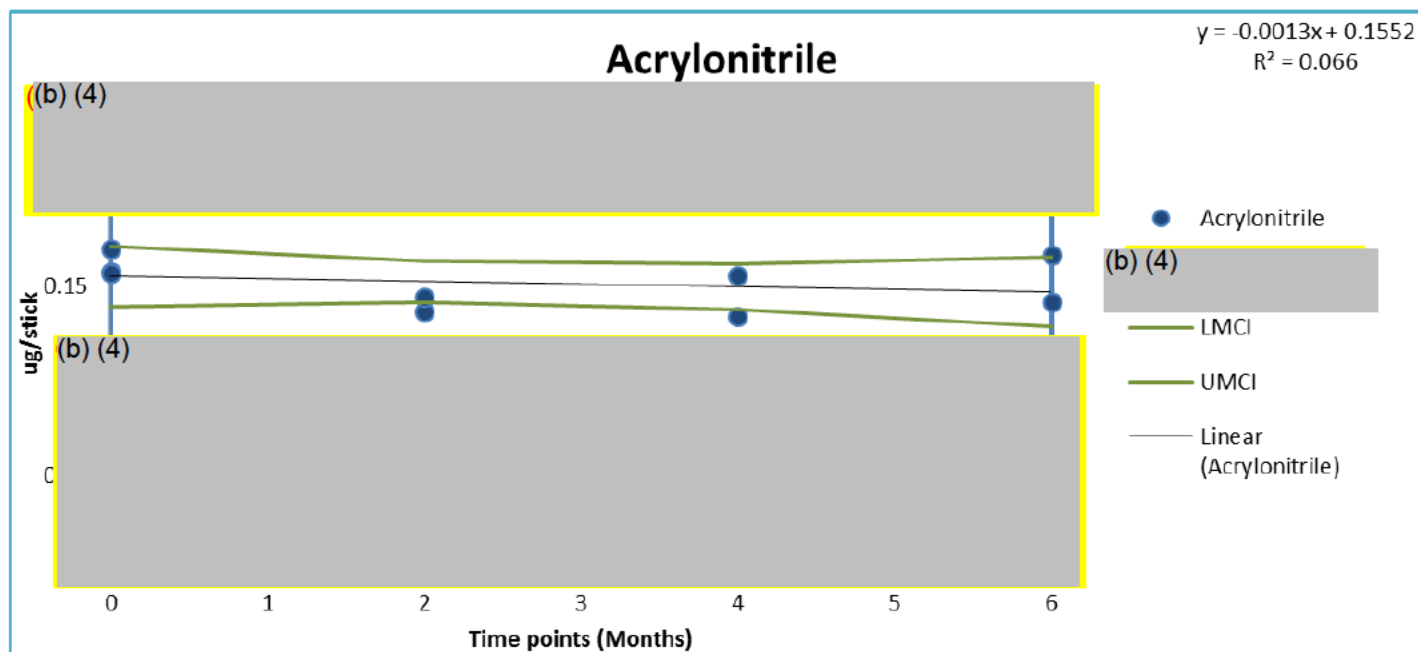


Figure 44 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 6 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 6 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.3.1.13 Isoprene

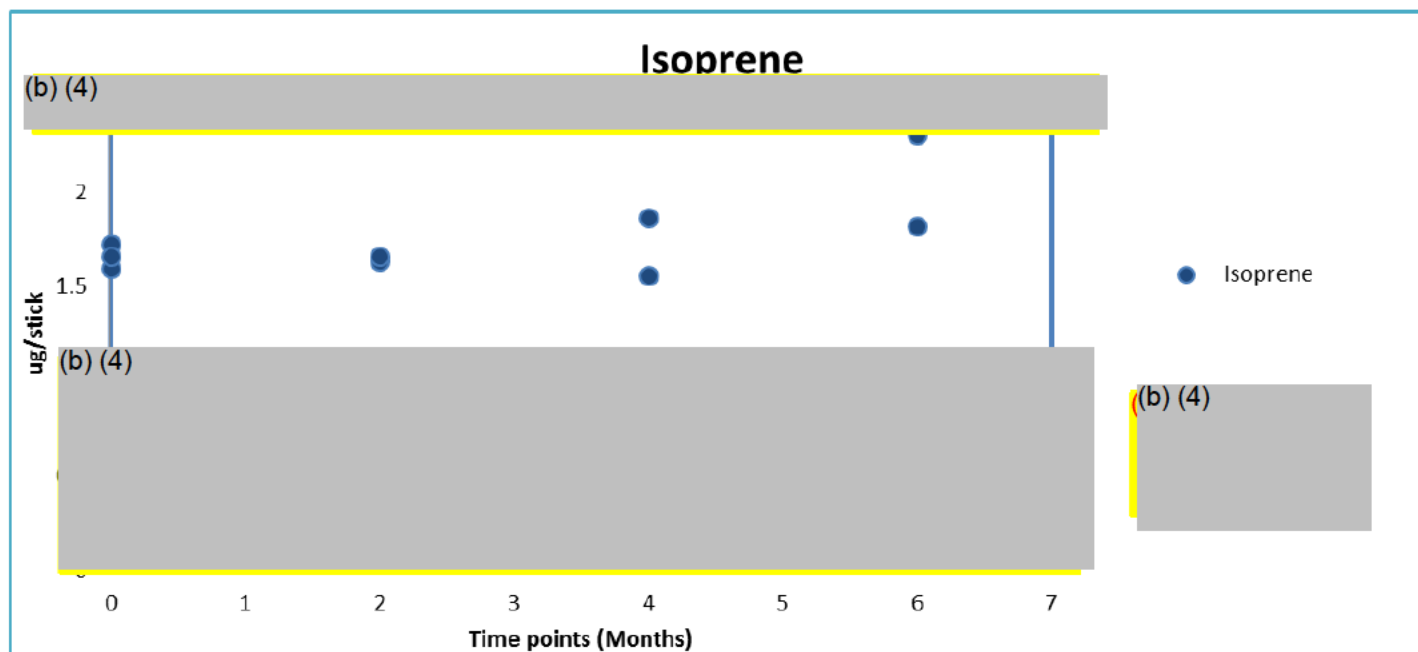


Figure 45 The reported values are well inside the specifications even with the overestimated values in T2 and T4 (see [Chapter 5.2](#)), therefore Isoprene is considered stable for 4 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.3.1.14 Pyridine

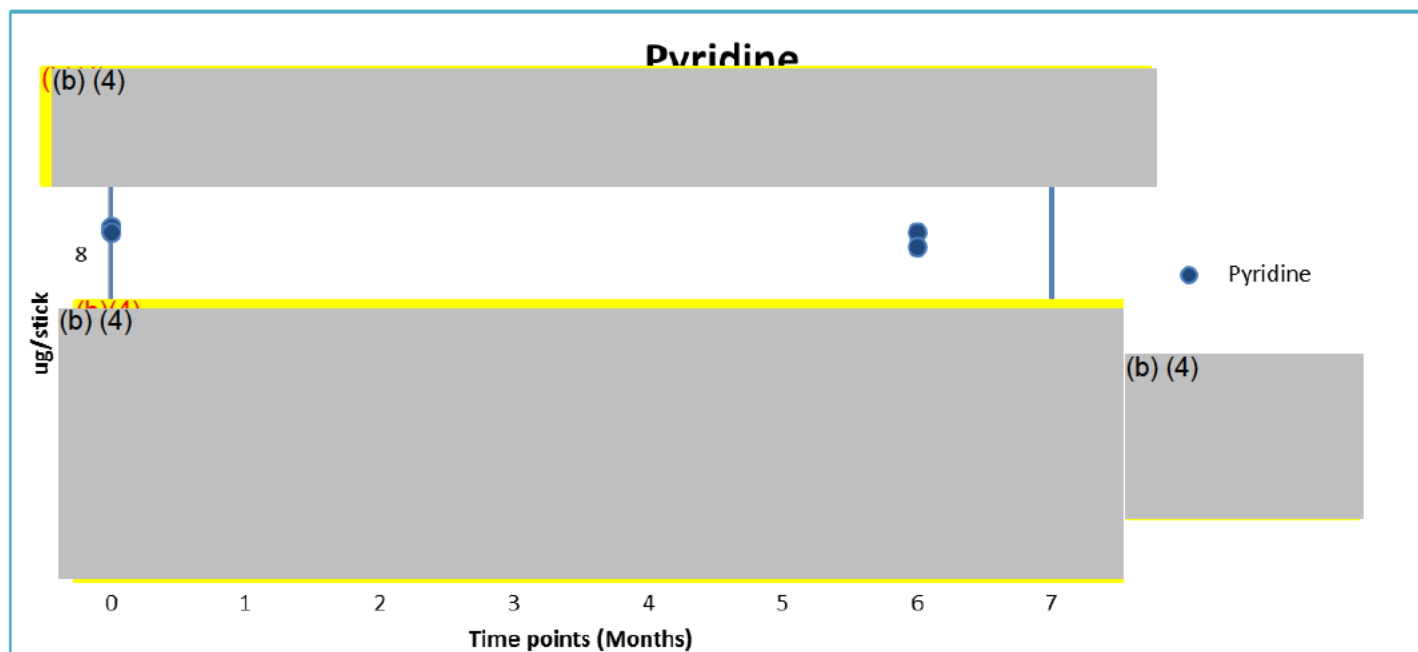


Figure 46 Pyridine is not suitable for trend analysis since it was tested in less than 3 different time points. All the values obtained are inside the specifications and therefore Pyridine is considered stable for 6 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_1

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.3.1.15 Ammonia

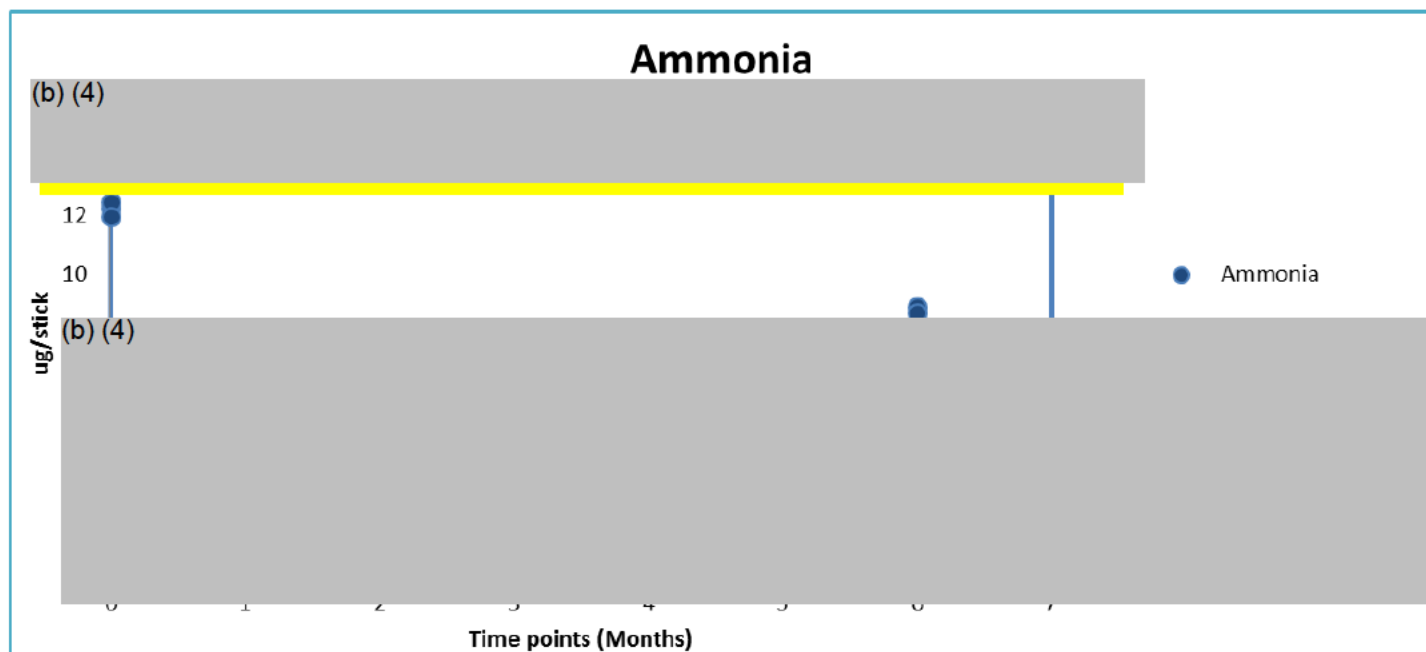


Figure 47 Ammonia is not suitable for trend analysis since it was tested in less than 3 different time points. All the values obtained are inside the specifications and therefore Ammonia is considered stable for 6 months.



Form Number: PMI_RD_FOR_000927

Form Version N°: 1.0

Form Status: Effective

Stability Study Report: STAB-2016_P1_M_1

Form Effective Date: See EDMS

6.3.2 Physical Attributes Evaluation

(b) (4)





Form Number: PMI_RD_FOR_000927

Form Version N°: 1.0

Form Status: Effective

Stability Study Report: STAB-2016_P1_M_1

Form Effective Date: See EDMS

6.3.3 Sensorial Evaluation

Sensorial evaluation results are described in details in a separate report [\[5\]](#).

(b) (4)

A shelf life of 6 months is considered as acceptable.

6.3.4 Visual inspection

(b) (4)

The visual quality of the tobacco sticks can be considered acceptable during 2 months storage in 30°C 75%RH.



Form Number: PMI_RD_FOR_000927

Form Version N°: 1.0

Form Status: Effective

Stability Study Report: STAB-2016_P1_M_1

Form Effective Date: See EDMS

7 Stability Assessment

Overall it can be concluded that the THS 2.2 Dorado I Vinny Low remained within specifications up to 12 months in the 22°C 60%RH and 30°C 35%RH conditions; and up to 4 months in the 30°C 75%RH.

In the conditions 22°C 60%RH all the product parameters were found stable for 12 months.

In the conditions 30°C 35%RH all the product parameters were found stable for 12 months.

In wet and very humid conditions 30°C 75%RH, all the product parameters were found stable for 6 months with the exception of:

- Isoprene was found acceptable up to 4 months. Due to deviation described in [Chapter 5.2](#) the stability until 6 months could not be demonstrated.
- Visual aspect was found acceptable up to 2 months.

8 Related Documents

[1] P1 THS 2 2 EXPT004923_STABILITY STUDY PROTOCOL DORADO I MINT VINNY.doc

<https://disco.app.pmi/disco/drl/objectId/0901d4ec805dd8b4>

[2] P1 Product specifications

<https://disco.app.pmi/disco/drl/objectId/0901d4ec80572517>

[3] P1_PDev_SPE_DI Vinny Low menthol batch release specs.doc

<https://disco.app.pmi/disco/drl/objectId/0901d4ec805e1a89>

[4] P1_PDev_SPE_DI Vinny low Performance Specifications.doc

<https://disco.app.pmi/disco/drl/objectId/0901d4ec805e03a0>

[5] P1_CPD_SWP_Product monitoring__SS_004_2017_02_1_MRTP_DI Vinny Low_T12

<http://rrpplm.app.pmi/Agile/PLMServlet?fromPCCClient=true&module=ActivityHandler&requestUrl=module%3DActivityHandler%26opcode%3DdisplayObject%26classid%3D18387%26objid%3D229288%26tabid%3D%26>

[6] Scientific Report: PT_AL_Isoprene Investigation_PMI_RD_WKI_000383

<https://disco.app.pmi/disco/drl/objectId/0901d4ec806191b5>

9 Reference Documents

WHO Stability testing of active pharmaceutical ingredients and finished pharmaceutical products

ISO 3402:1999 Tobacco and tobacco products -- Atmosphere for conditioning and testing

ICH Q1(E) Evaluation of Stability Data



Form Number: PMI_RD_FOR_000927

Form Version N°: 1.0

Form Status: Effective

Stability Study Report: STAB-2016_P1_M_1

Form Effective Date: See EDMS

10 Revision History for Stability Report

Version Nr	Description of change	Justification
1.0	Initial version.	NA
2.0	<ol style="list-style-type: none"> Alignment of vocabulary for specifications throughout the report. In Chapter 6 Stability Data Evaluation description was clarified regarding conclusion about shelf life and truncation. Correction in Figure titles in Chapter 6 of the earlier crossing time. For all tested parameters evaluated (b) the earliest crossing time was written as 12 months for 22°C 60%RH and 30°C 35%RH and 6 months for 30°C 75% RH. This is now corrected to "over" 12 or 6 months in case the crossing time determined by (b) was longer than the study length. Chapter 7 Stability Assessment has been reviewed in order to conclude about product stability parameters and removed product shelf life recommendation. 	<ol style="list-style-type: none"> Clarification that the specifications used are the product specifications. This is a clarification about how data evaluation was done and reported. The earliest crossing time was wrongly written for attributes where (b) model determined earliest crossing time longer than the study duration. The decision about product shelf life remains to the sponsor of the study.

11 Definitions and Abbreviations

Abbreviation	
CO	Carbon Monoxide
IP	Intermediate Precision
ISO	International Organization for Standardization
LMCI	95% lower mean confidence interval for the predicted values
LSL	Lower Shelf Life specification limit
PDIMS	Product Development Information Management System
PMMTB	Philip Morris Manufacturing & Technology Bologna (Training Center)
QDP	Quantitative Descriptive Profile
RDLIMS	Research Development Laboratory Information Management System
R&D	Research and Development



Form Number: PMI_RD_FOR_000927

Form Version N°: 1.0

Form Status: Effective

Stability Study Report: STAB-2016_P1_M_1

Form Effective Date: See EDMS

Abbreviation	
RH	Relative Humidity
SDMS	Scientific Data Management System
THS	Tobacco Heating System
TO	Testing Order
TPM	Total Particulate Matter
USL	Upper Shelf Life specification limit
UMCI	95% upper mean confidence interval for the predicted values
WHO	World Health Organization

12 Appendices

12.1 Climatic Zones

Table 14 Climatic Zones

Climatic Zone	Definition	Long Term Testing Conditions
I	Temperated climate	21°C / 45% RH
II	Subtropical and Mediterranean Climate	25°C / 60% RH
III	Hot and dry climate	30°C / 35% RH
IVA	Hot and humid climate	30°C / 65% RH
IVB	Hot and very humid climate	30°C / 75% RH

12.2 Equivalence List for Quality Documents

Table 15 CDocs and OMSP References

CDocs number	OMSP number
PMI_RD_FOR_000927	PMI-RRP-FOR-111545
PMI_RD_WKI_000383	PMI-RRP-WKI-111706
PMI_RD_WKI_000391	PMI-RRP-WKI-111709
PMI_RD_WKI_000477	PMI-RRP-WKI-111657
PMI_RD_WKI_000518	PMI-RRP-WKI-111729
PMI_RD_WKI_000530	PMI-RRP-WKI-111801
PMI_RD_WKI_000534	PMI-RRP-WKI-111743
PMI_RD_WKI_000584	PMI-RRP-WKI-111771



Form Number: PMI_RD_FOR_000927

Form Version N°: 1.0

Form Status: Effective

Stability Study Report: STAB-2016_P1_M_1

Form Effective Date: See EDMS

CDocs number	OMSP number
PMI_RD_WKI_000953	PMI-RRP-WKI-111604
PMI_RD_WKI_001392	PMI-RRP-WKI-111823
PMI_RD_SOP_000296	PMI-RRP-SOP-111558

12.3 Sample Traceability Matrix

Analyses have been requested through Testing orders in PDIMS ([Table 16](#)).

Results for aerosol chemistry and physical measurements are stored in SDMS under the corresponding project numbers. Results of sensory evaluation are stored in PDIMS.

Table 16 Sample Traceability Matrix

Time Point	Testing Order	RDLIMS Project Number
T0	TO-10587, TO-10588, TO-10589	RLS-ZRH-2016-18/19
T2	TO-10977, TO-10978, TO-10979	RLS-ZRH-2016-117/118
T4	TO-11414, TO-11416, TO-11419	RLS-ZRH-2016-192/195
T6	TO-11893, TO-11894, TO-11894	RLS-ZRH-2016-301
T9	TO-12683, TO-12684, TO-12742	RLS-ZRH-2016-445/446
T12	TO-13465, TO-13467, TO-13468	RLS-ZRH-2017-28/30