

APPENDIX A3.3-11

STABILITY FINAL RESULTS (12 MONTHS) – MENTHOL 2

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

Platform	P1								
Stability Study type	<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="padding: 2px;">Initial Stability Study</td> <td style="text-align: center; padding: 2px;"><input type="checkbox"/></td> </tr> <tr> <td style="padding: 2px;">In use</td> <td style="text-align: center; padding: 2px;"><input type="checkbox"/></td> </tr> <tr> <td style="padding: 2px;">Post Change</td> <td style="text-align: center; padding: 2px;"><input checked="" type="checkbox"/></td> </tr> <tr> <td style="padding: 2px;">Monitoring</td> <td style="text-align: center; padding: 2px;"><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"/>
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Post Change	<input checked="" type="checkbox"/>								
Monitoring	<input type="checkbox"/>								

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1 Purpose

The objective of this stability study is to demonstrate that the commercial product THS 2.2 High Menthol (Dorado I Mint Vinny 2) 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_5 performed according a protocol [1]. The study was performed in 3 production scale Dorado I Mint Vinny High 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 High

Product/ Test item	Consumable Batch Number	Finished Product Code	Manufacturing Date
THS 2.2 Dorado I Vinny High	B-31061 / 41-2572271	ME000006.01	16 Jul. 2016
	B-31062 / 41-2572272	ME000006.01	16 Jul. 2016
	B-31063 / 41-2572273	ME000006.01	17 Jul. 2016

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.



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Sticks were kept in closed pack at 22°C ± 2°C and 58% RH ± 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 ± 2°C, 60 ± 5% 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(7) was used to generate aerosol for chemical analyses from T0 to T9, DV.000180(5) was used for T12 (see deviation in Chapter 5.6). Device DV.000101.RD(1) 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	



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Parameter	Method Name	Method Version Planned	Method Version Used T0 / T12	Specifications [2] - [4]
Acrylamide µg/stick	PMI_RD_WKI_000530	7.0	7.0 / 8.0	(b) (4)
	PMI_RD_WKI_000953	3.0	3.0 / 3.0	
Acetamide µg/stick	PMI_RD_WKI_000530	7.0	7.0 / 8.0	
	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	16.0	16.0 / 17.0	
Isoprene µg/stick	PMI_RD_WKI_000518	7.0	7.0 / 7.0	
	PMI_RD_WKI_000383	16.0	16.0 / 17.0	
Pyridine µg/stick	PMI_RD_WKI_000518	7.0	7.0 / 7.0	
	PMI_RD_WKI_000383	16.0	16.0 / 17.0	
Ammonia µg/stick	PMI_RD_WKI_000385	10.0	10.0 / 12.0	
	PMI_RD_WKI_001392	2.0	2.0 / 2.0	

(b) (4)

(b) (4)

3.3 Visual Inspection

(b) (4)



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(b) (4)

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 High (B-31061)	22°C±2°C / 60%RH±5%RH	23 August 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 High (B-31062)	22°C±2°C / 60%RH±5%RH	23 August 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 High (B-31063)	22°C±2°C / 60%RH±5%RH	23 August 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 (C), 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



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

5 Deviations to Study Protocol

5.1 Deviation in Storage Condition 1

A deviation (RLS-TIM-16-23) was opened by Test Item Management as the daily check of the data from the climatic chamber 10681 (storage condition 30°C 35%RH) were inside the acceptance criteria, however the datalogger data PMI:7927/SN:81311 were out of specification with a mean value of 29.7%RH from 23 Sep. 2016 till 14 Oct. 2016.

A thermo-mapping test has been initiated by Test Item Management to understand difference between data from the climatic chamber and datalogger. Results showed that the non-conformity was due to datalogger being at the border of the chamber. When datalogger was put on the side of the packs the conditions were in range. The investigation is documented in a separate report [6]. A thermo-mapping of all climatic chambers has been initiated by Test Item Management.

5.1.1 Impact on the Study

This deviation was considered having no impact on the study.

5.2 Deviation in Storage Condition 2

A deviation (RLS-TIM-16-22) was opened as the daily check of the data from the climatic chamber 10680 (storage condition 30°C 75%RH) were inside the acceptance criteria, however the datalogger data PMI:9800/SN:90781 were out of specification with a mean value of 67.4%RH from 23 Sep. 2016-14 Oct. 2016.

A thermo-mapping test has been initiated by Test Item Management to understand difference between data from the climatic chamber and datalogger. Results showed that the non-conformity was due to datalogger being at the border of the chamber. When datalogger was put on the side of the packs the conditions were in range. The investigation is documented in a separate report [6]. A thermo-mapping of all climatic chambers has been initiated by Test Item Management.

5.2.1 Impact on the Study

This deviation was considered having no impact on the study.

5.3 Deviation in Storage Condition 3

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 just one day after the T4 time point and represent ~5% below the lower range limit.



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5.3.1 Impact on the Study

The product remained in specification at T6 in dry condition, 30°C 35%RH. As the packs are stored in the climatic chambers in polypropylene wrapped packs and as no out of trend was observed as T6, it is considered that the product was not affected by this non-conformity in this period of time.

5.4 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 all methods, except for Isoprene (PMI_RD_WKI_000383).

The version of the method changed from V16.0 to V17.0 between the T0 and the T2 time point (25 Oct. 2016). The change during the study could not be avoided as a laboratory investigation (RLS-GC-16-159) lead to the conclusion that the changes implemented in the V16.0 of the method (changes in the standard preparation which included a change of supplier from Fluka to Restek reference material) lead to an increase of the Isoprene values compared to previous version 15.0.

A laboratory investigation [7] was performed and confirmed that switching from V15.0 to V16.0 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 V15.0 which provided more consistent results regarding Isoprene quantitation than those used after that date. This change was implemented in PMI_RD_WKI_000383 V17.0 effective as of 25 Oct. 2016, just prior the analyses for T2 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_5	Time Points (months)					
	0	2	4	6	9	12
Version of the method PMI_RD_WKI_000383	V16.0	V17.0	V17.0	V17.0	V17.0	V17.0

5.4.1 Impact on the Study

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

As the T0 values (obtained with method V16.0) were used to set the specification, this specification cannot be used to assess Isoprene values obtained from T2 to T12 with method version 17.0.

Specification of Isoprene (2.33 µg/stick) used in the stability study STAB-2016_P1_M_1 on Low menthol product, obtained with the method 15.0, will be used for this stability study on the High menthol product (STAB-2016_P1_M_5). Isoprene is not expected to be different between the Low and the High menthol products.

In addition, the T0 value will not be reported and will not be taken into account during the evaluation.



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5.5 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.

5.5.1 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.

5.6 Deviation in Tobacco Heating Device

For analyses of aerosol constituents it was planned to use the device DV.000174(7). This was indeed the case for the analyses of T0 to T9. However, for the analyses of T12 time point, the lab used the DV.000180(5), batch B-34548. This had to be done as the batch of device described in the study protocol (B-23172/ DV.000174(7)) reached the 2 years usage in the laboratory and according to PMI-RRP-WKI-111703 they should be replaced. The non-conformity NC-RRP-NEU-2017-500 was opened by the lab to document the deviation versus the analytical request.

5.6.1 Impact on the Study

The two devices, DV.000174(7) and DV.000180(5), are equivalent and have been released with the same design change request (DCR-000310). Therefore, no impact on the study is expected.

6 Stability Data Evaluation

The statistical analysis for the chemical and physical characterization is performed according PMI_RD_SOP_000296 V4.0, 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.

For Menthol, linear model is used for the degradation profile as no better model was found, even though the evolution of the Menthol in the aerosol is not linear. This is due to migration of the Menthol from the design elements to the tobacco plug in the first months and then reaching a plateau or even loosing Menthol under higher temperature (i.e. 30°C).

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 (b) (4) 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 5.4).

The relative degradation rate, the R² 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 - 49 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



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lower 95 % confidence intervals for the regression mean (UMCI and LMCI). The Figure titles contain the conclusion about the shelf life obtained with (b) (4) in case of trend analyses or conclusion about shelf life by comparing the reported value with the specification.

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

The investigations of OOS or OOT results and their conclusions are available in separate documents ([11]-[16]).



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6.1 Storage Condition 22°C 60% RH

Table 5 B-31061/ 41-2572271 at 22°C 60% RH

B-31061/ 41-2572271	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)		2.81		3.39	3.55		3.86	2.88%	0.91	2.6
Nicotine	mg/stick			1.17		1.20	1.15		1.21	0.22%	0.24	0.1
Glycerin	mg/stick			5.31		5.24	4.63		4.38	-1.56%	0.84	1.3
CO	mg/stick			0.5		0.3	0.5		0.6	1.36%	0.09	0.1
Triacetin	mg/stick			0.7		0.5	0.5		0.5	-2.79%	0.77	2.1
Phenol	µg/stick			1.5		1.0	1.1		1.3	-0.35%	0.01	0.0
Acrylamide	µg/stick			1.9		1.4	1.4		1.3	-2.36%	0.69	1.6
Acetamide	µg/stick			2.9			2.9		3.3	1.10%	0.72	0.8
Acetaldehyde	µg/stick			201			199		201	-0.01%	0.01	0.0
Butyraldehyde	µg/stick			15.3			13.4		14.9	-0.22%	0.04	0.0
Acrylonitrile	µg/stick			0.15		0.15	0.15		0.16	0.68%	0.60	0.4
Isoprene	µg/stick			*		1.75	1.67		2.26	5.26%	0.87	4.6
Pyridine	µg/stick			8.7			8.8		8.9	0.21%	0.99	0.2
Ammonia	µg/stick			11.7			10.2		9.0	-1.98%	1.00	2.0
TPM	mg/stick			59			56		54	-0.69%	0.90	0.6

(b) (4)

* Isoprene value not reported, as explained i



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Table 6 B-31062/ 41-2572272 at 22°C 60% RH

B-31062/ 41-2572272	Unit	Specifications		Time point (Months)						Degradation Rate	R^2	Severity Score
		Lower	Upper	0	2	4	6	9	12			
Menthol	mg/stick	(b) (4)		2.84	3.37	3.45		3.62	3.74	2.01%	0.78	1.6
Nicotine	mg/stick	(b) (4)		1.19	1.23	1.27		1.14	1.19	-0.37%	0.22	0.1
Glycerin	mg/stick	(b) (4)		5.30	4.84	5.48		4.49	4.60	-1.19%	0.52	0.6
CO	mg/stick	(b) (4)		0.5	0.3	0.3		0.4	0.6	2.00%	0.13	0.3
Triacetin	mg/stick	(b) (4)		0.7	0.5	0.5		0.5	0.5	-1.94%	0.70	1.4
Phenol	µg/stick	(b) (4)		1.5	1.3	1.5		1.1	1.4	-0.89%	0.17	0.1
Acrylamide	µg/stick	(b) (4)		1.9	1.5	1.6		1.3	1.3	-2.28%	0.71	1.6
Acetamide	µg/stick	(b) (4)		3.1				2.9	3.5	0.91%	0.23	0.2
Acetaldehyde	µg/stick	(b) (4)		203				205	205	0.06%	0.78	0.0
Butyraldehyde	µg/stick	(b) (4)		14.9				14.5	15.5	0.20%	0.12	0.0
Acrylonitrile	µg/stick	(b) (4)		0.15	0.12	0.15		0.15	0.17	1.51%	0.34	0.5
Isoprene	µg/stick	(b) (4)		*	1.80	1.76		1.80	2.24	2.37%	0.60	1.4
Pyridine	µg/stick	(b) (4)		8.7				9.3	8.7	0.11%	0.04	0.0
Ammonia	µg/stick	(b) (4)		11.7				10.0	9.2	-1.77%	1.00	1.8
TPM	mg/stick	(b) (4)		59				55	57	-0.38%	0.58	0.2

(b) (4)

* Isoprene value not reported, as explained



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Table 7 B-31063/ 41-2572273at 22°C 60% RH

B-31063/ 41-2572273	Unit	Specifications		Time point (Months)						Degradation Rate	R^2	Severity Score
		Lower	Upper	0	2	4	6	9	12			
Menthol	mg/stick	(b) (4)		2.66	3.30		3.60	3.72	3.83	2.98%	0.83	2.5
Nicotine	mg/stick	(b) (4)		1.16	1.22		1.22	1.11	1.26	0.20%	0.04	0.0
Glycerin	mg/stick	(b) (4)		5.09	5.21		4.86	4.58	4.73	-0.88%	0.75	0.7
CO	mg/stick	(b) (4)		0.6	0.4		0.5	0.4	0.6	1.42%	0.11	0.2
Triacetin	mg/stick	(b) (4)		0.6	0.5		0.5	0.5	0.5	-1.91%	0.80	1.5
Phenol	µg/stick	(b) (4)		1.3	1.4		1.3	1.2	1.6	0.96%	0.13	0.1
Acrylamide	µg/stick	(b) (4)		1.8	1.5		1.5	1.3	1.4	-1.73%	0.59	1.0
Acetamide	µg/stick	(b) (4)		3.0			3.0	2.9	3.6	1.15%	0.31	0.4
Acetaldehyde	µg/stick	(b) (4)		194			206	202	218	0.91%	0.78	0.7
Butyraldehyde	µg/stick	(b) (4)		15.3			14.1	14.5	16.5	0.47%	0.12	0.1
Acrylonitrile	µg/stick	(b) (4)		0.14	0.11		0.16	0.15	0.17	2.17%	0.45	1.0
Isoprene	µg/stick	(b) (4)		*	1.70		1.82	1.62	2.08	1.76%	0.35	0.6
Pyridine	µg/stick	(b) (4)		8.3			9.2	9.0	8.3	0.11%	0.01	0.0
Ammonia	µg/stick	(b) (4)		11.5			10.4	10.1	9.6	-1.36%	1.00	1.4
TPM	mg/stick	(b) (4)		58			56	56	58	-0.12%	0.10	0.0

(b) (4)

* Isoprene value not reported, as explained



6.1.1 Mainstream Aerosol Evaluation

6.1.1.1 Menthol

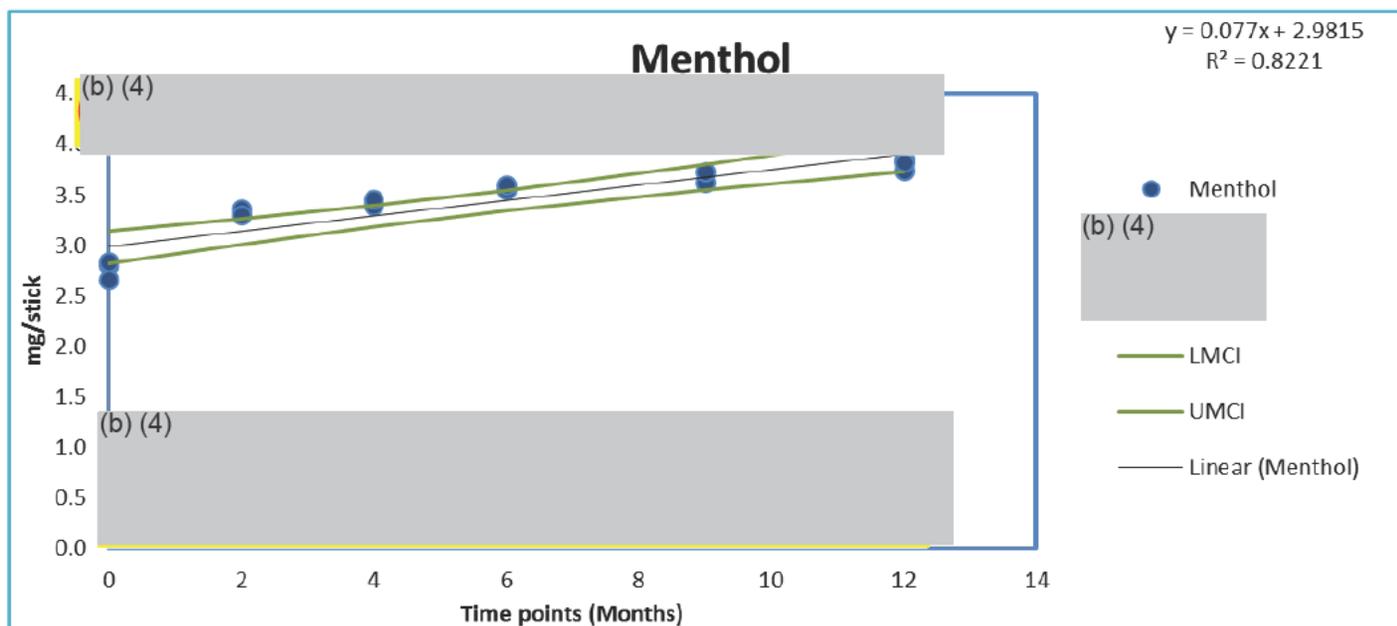


Figure 1 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time at 11 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 11 months.



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Form Effective Date: See EDMS

6.1.1.2 Nicotine

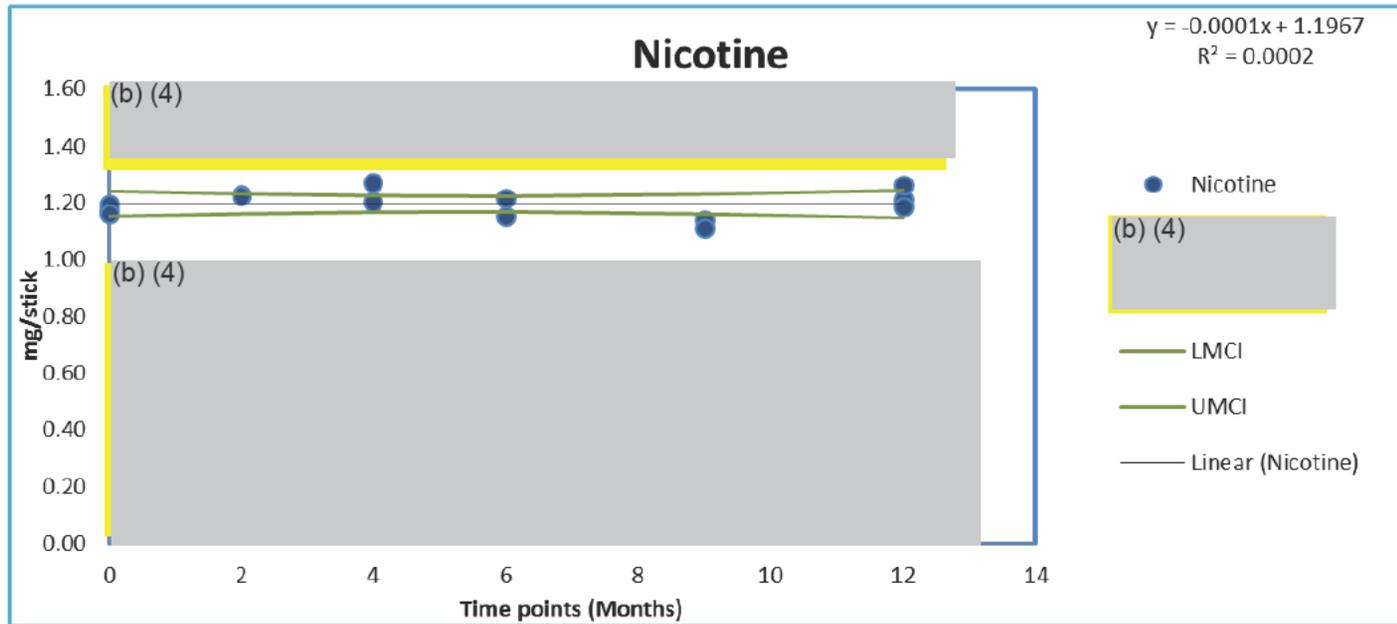


Figure 2 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



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Stability Study Report: STAB-2016_P1_M_5

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.1.1.3 Glycerin

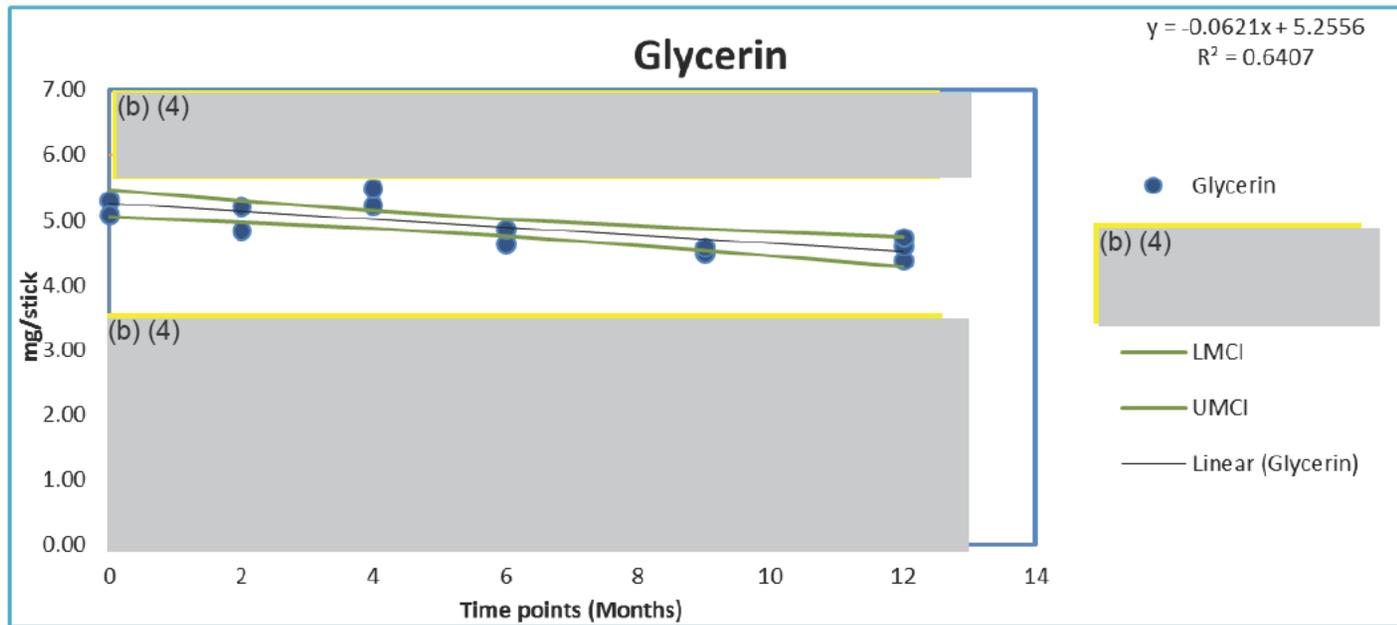


Figure 3 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



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6.1.1.4 CO

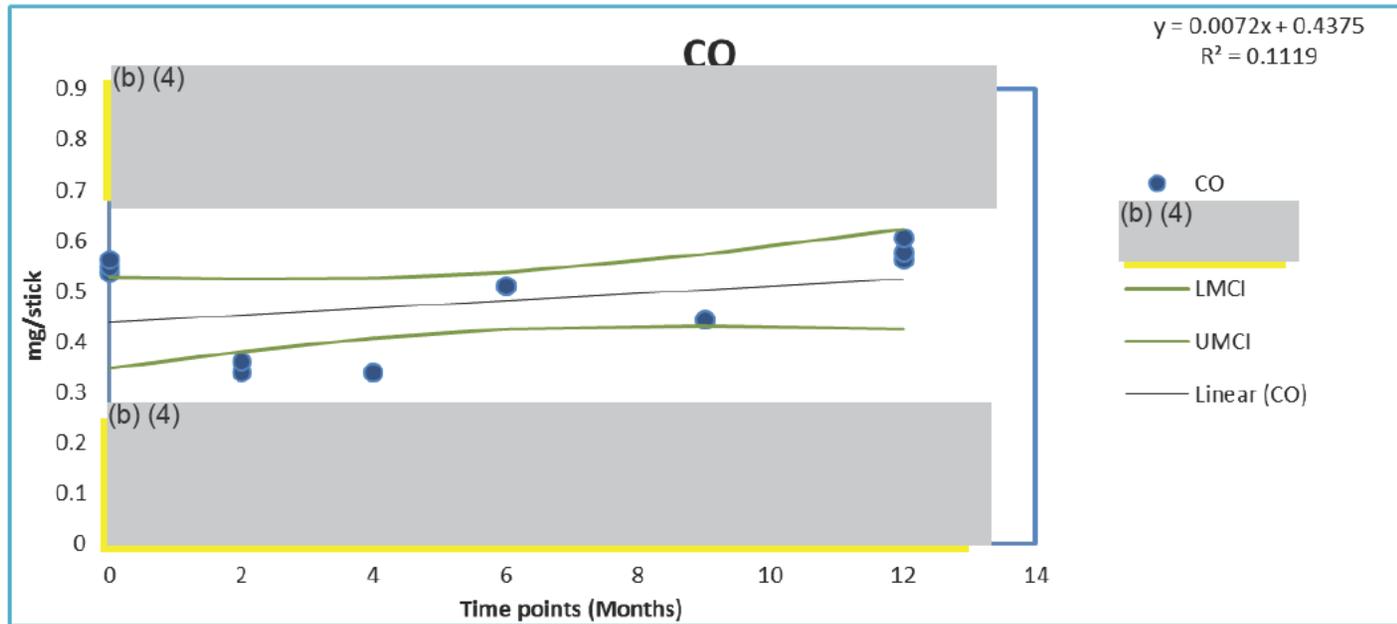


Figure 4 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



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Form Status: Effective
Form Effective Date: See EDMS

6.1.1.5 Triacetin

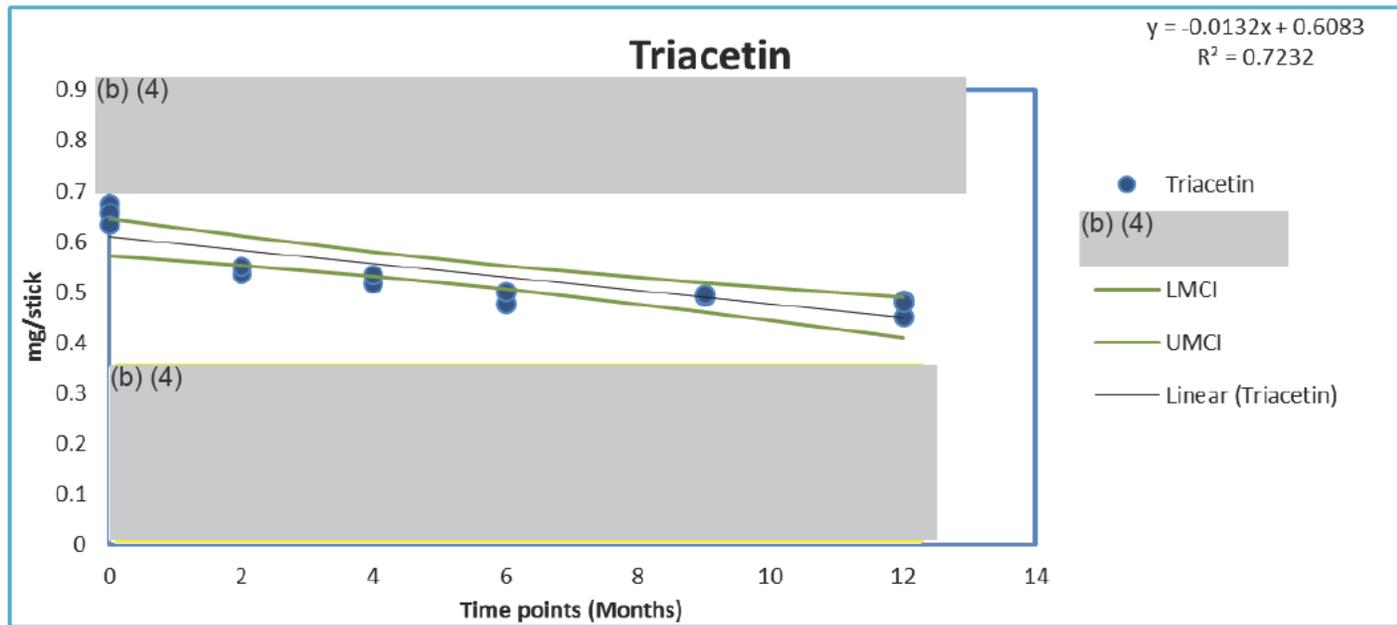


Figure 5 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



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Form Status: Effective
Form Effective Date: See EDMS

6.1.1.6 TPM

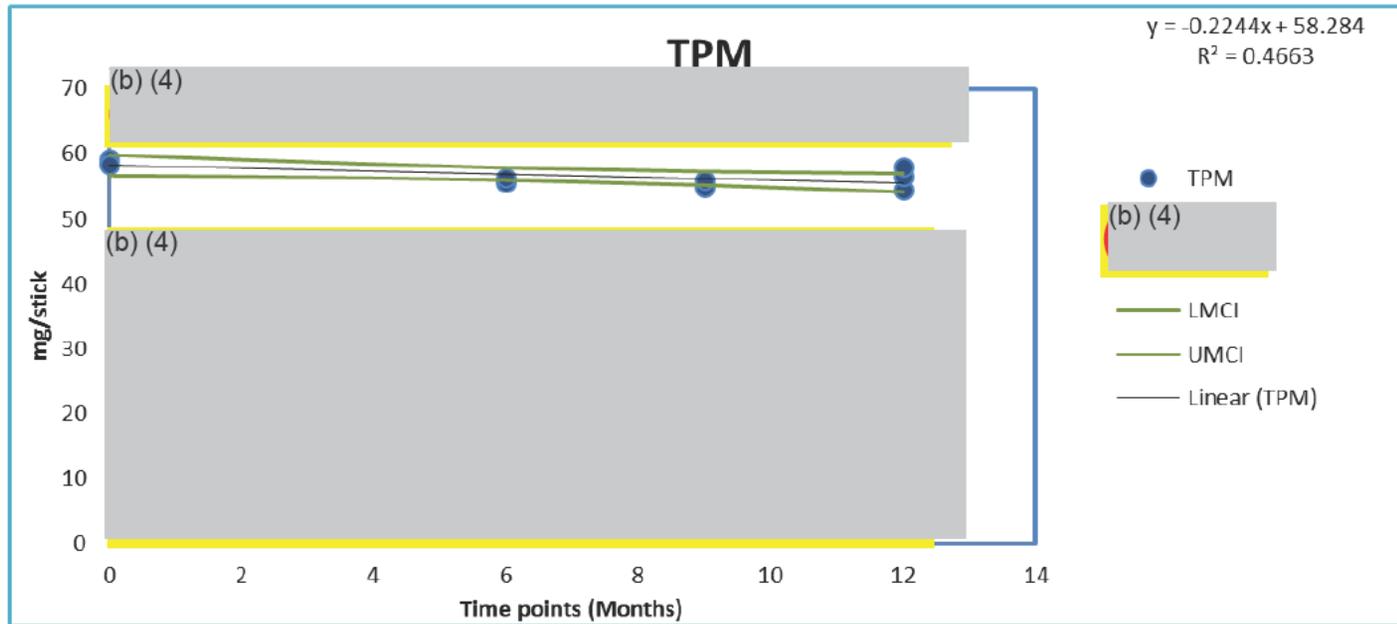


Figure 6 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



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6.1.1.7 Phenol

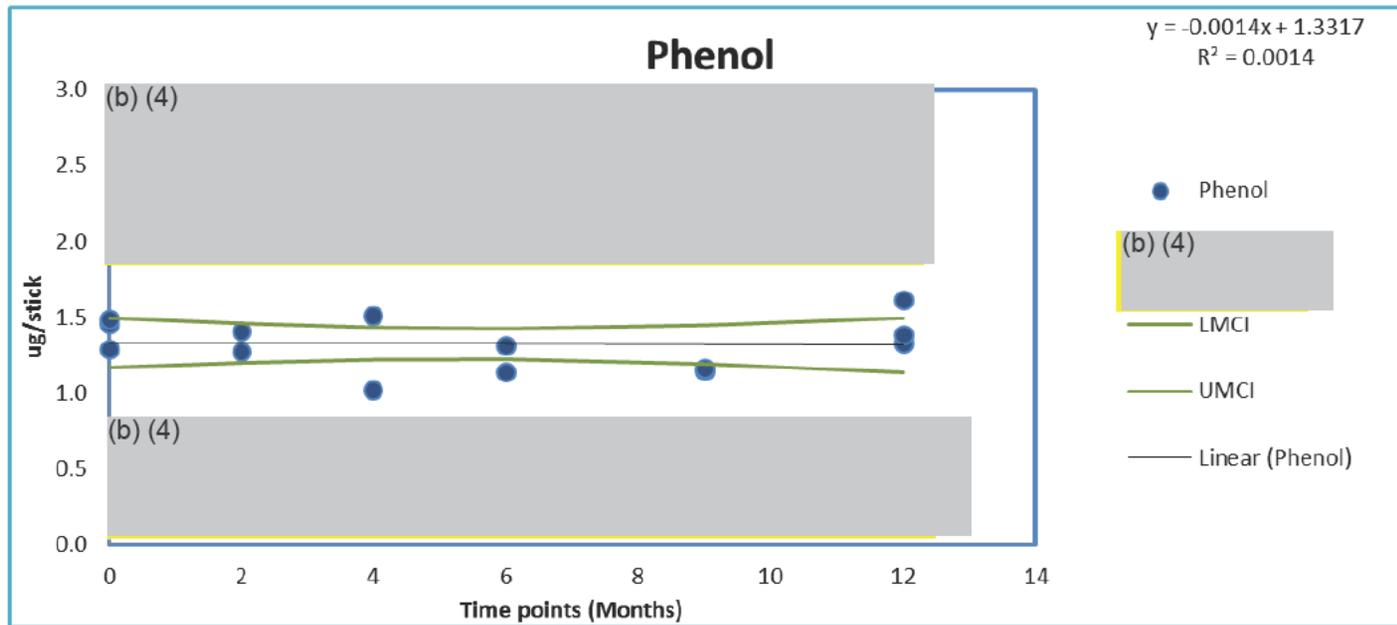


Figure 7 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



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6.1.1.8 Acrylamide

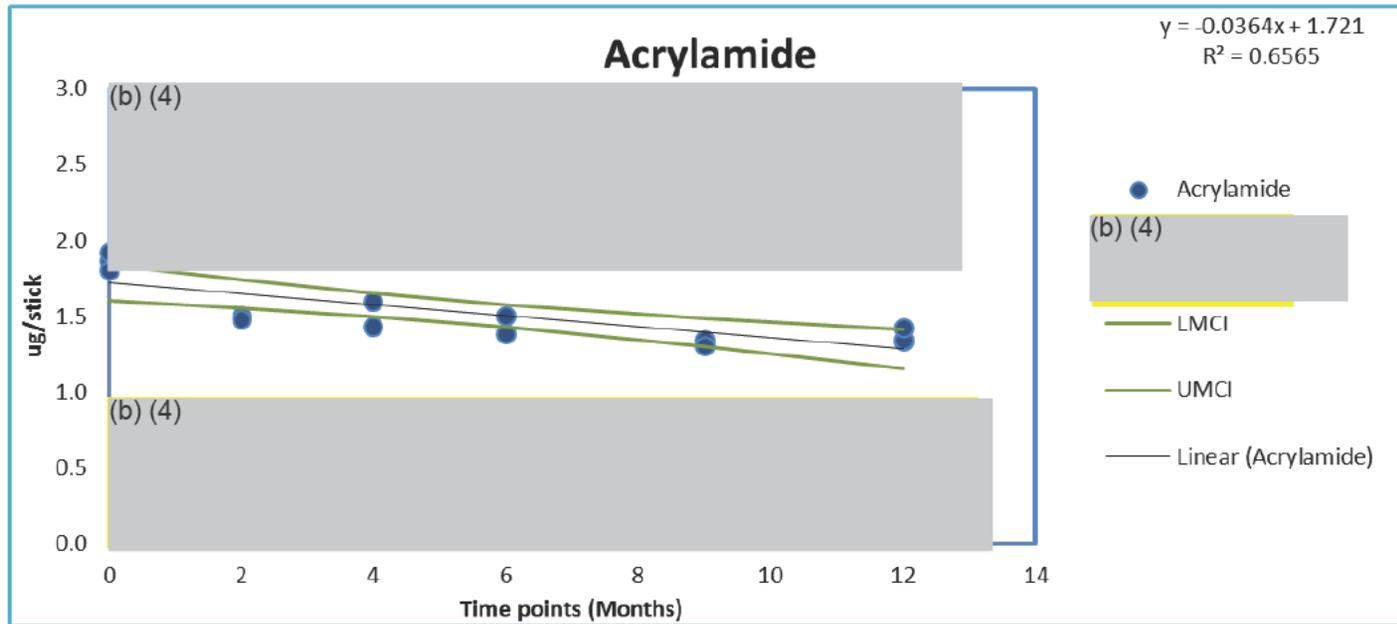


Figure 8 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



6.1.1.9 Acetamide

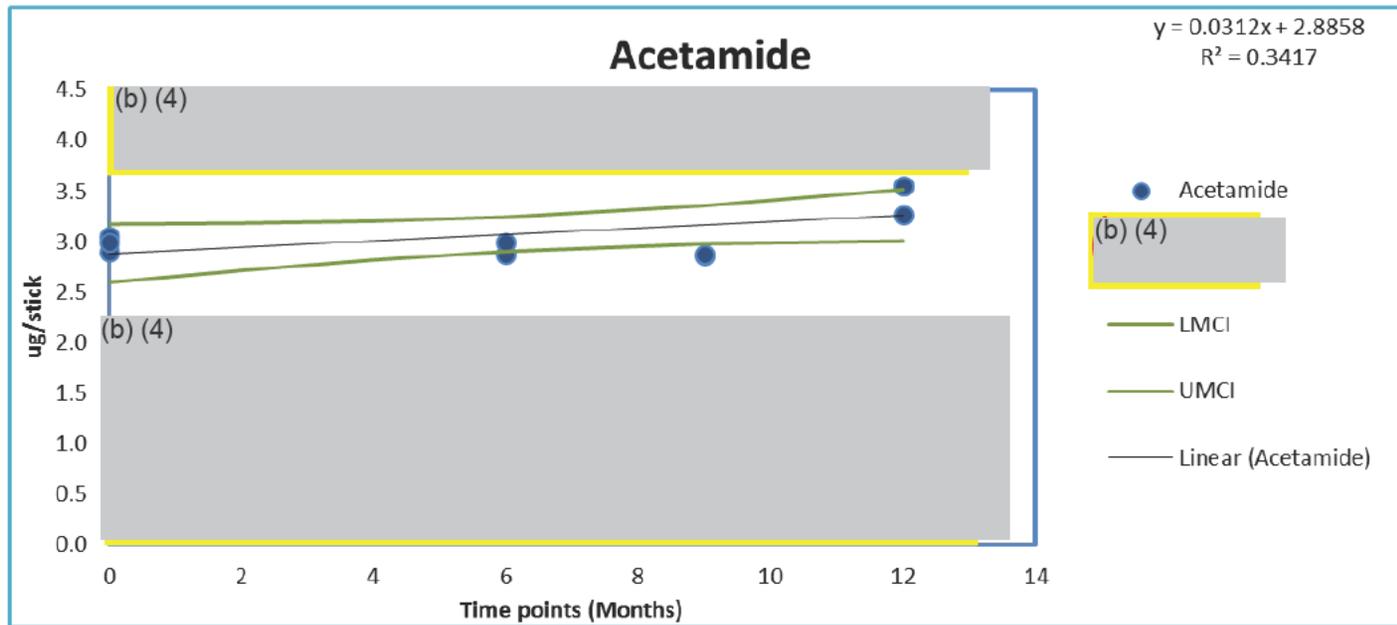


Figure 9 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



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6.1.1.10 Acetaldehyde

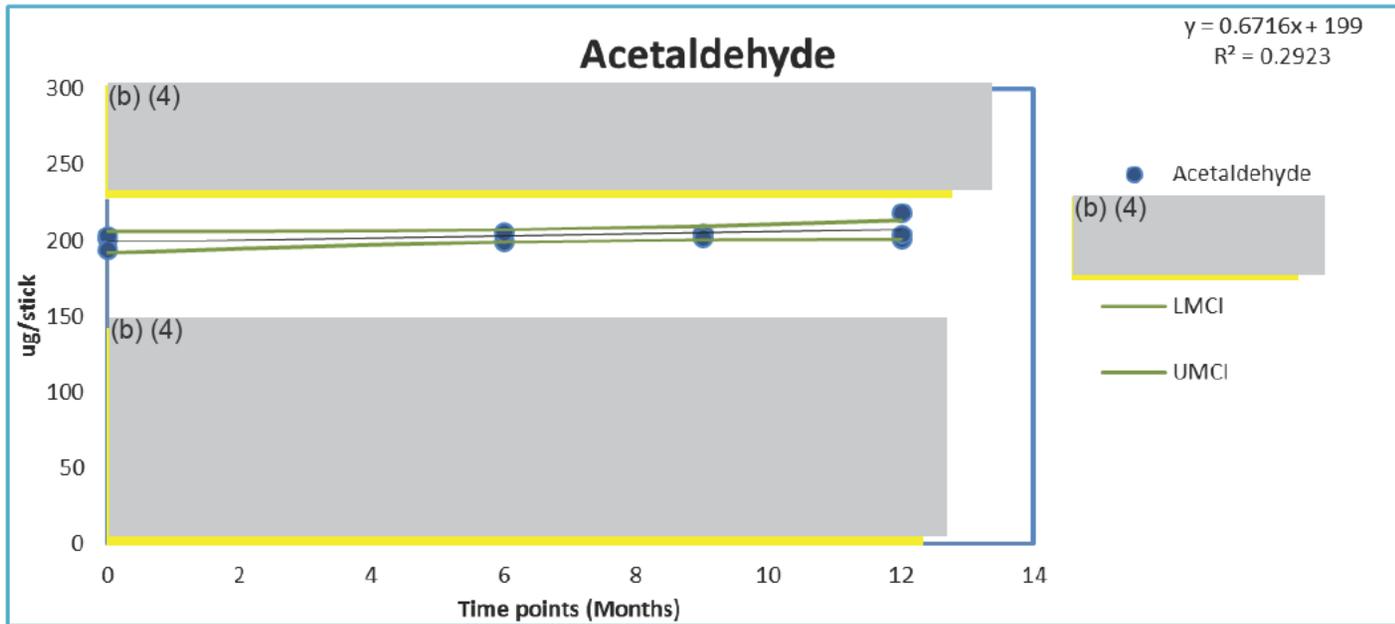


Figure 10 The best model accepted at the significance level of 0.25 has Different intercepts and Different slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



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Form Status: Effective
Form Effective Date: See EDMS

6.1.1.11 Butyraldehyde

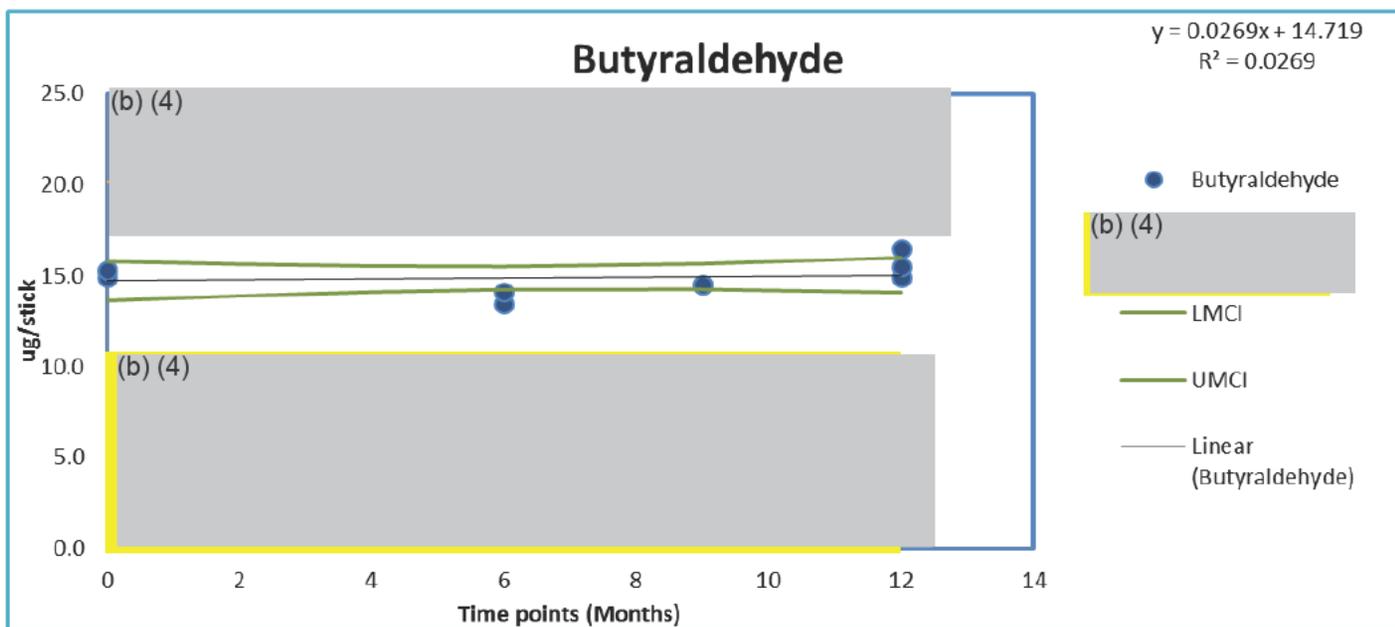


Figure 11 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



6.1.1.12 Acrylonitrile

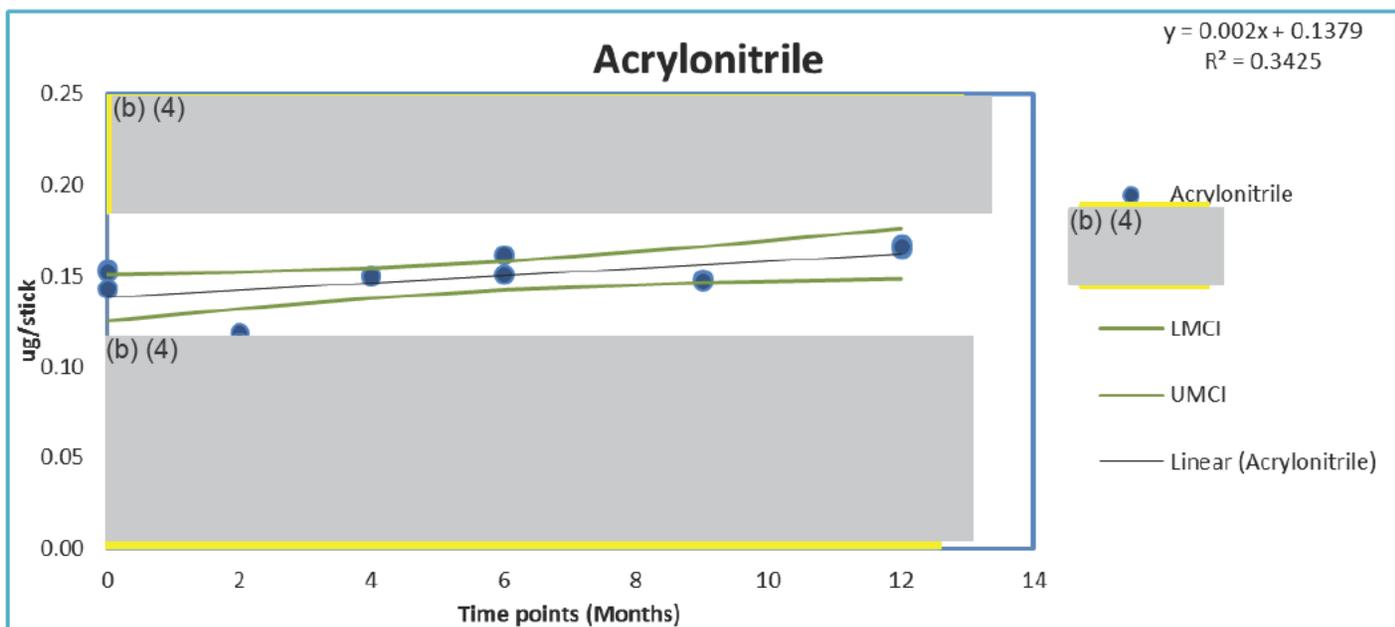


Figure 12 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



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6.1.1.13 Isoprene

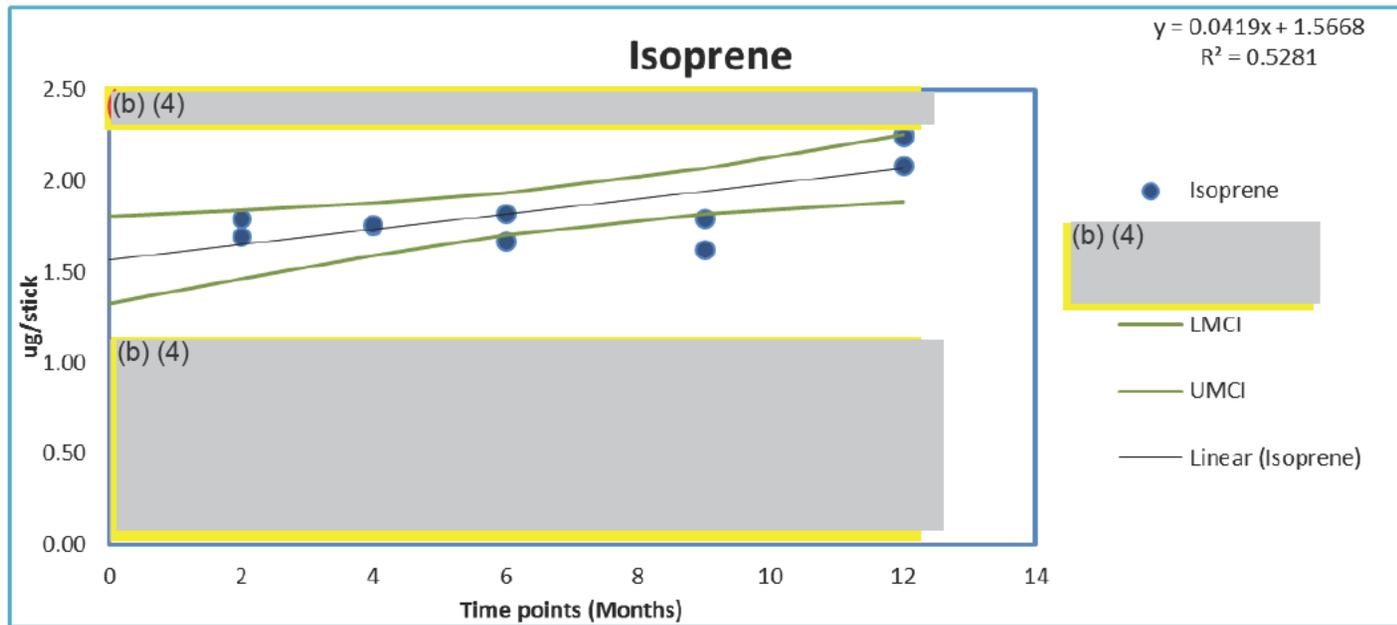


Figure 13 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



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6.1.1.14 Pyridine

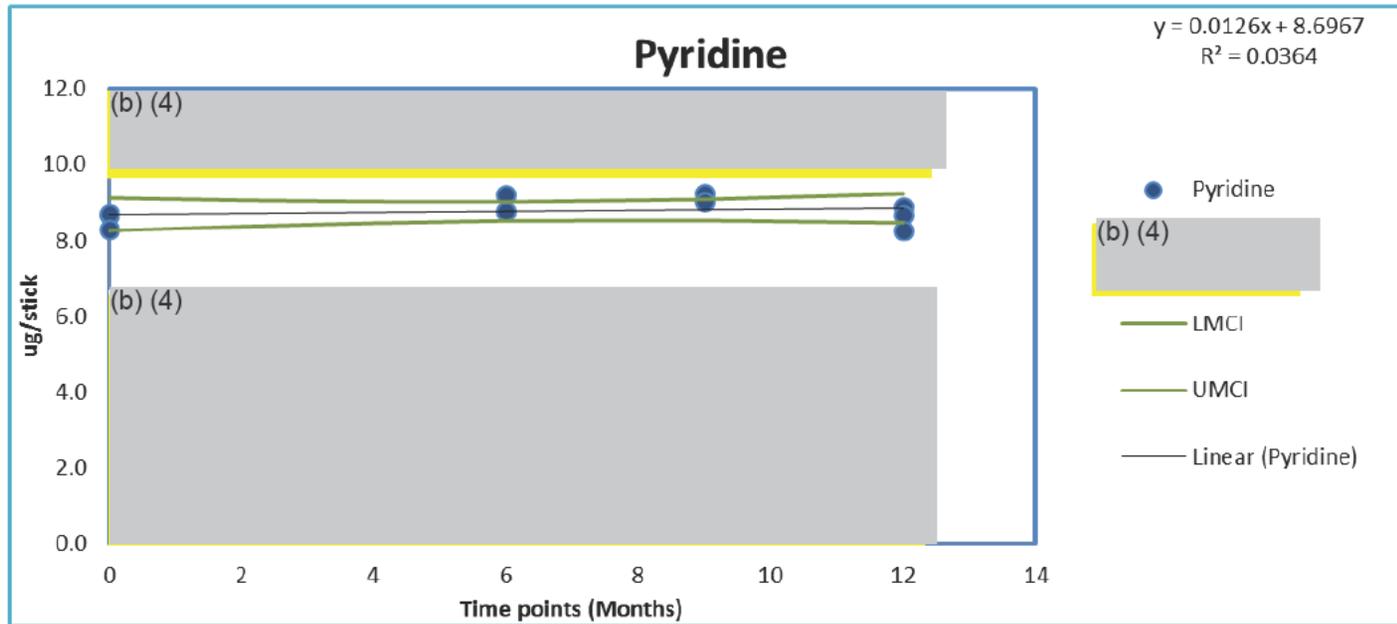


Figure 14 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



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6.1.1.15 Ammonia

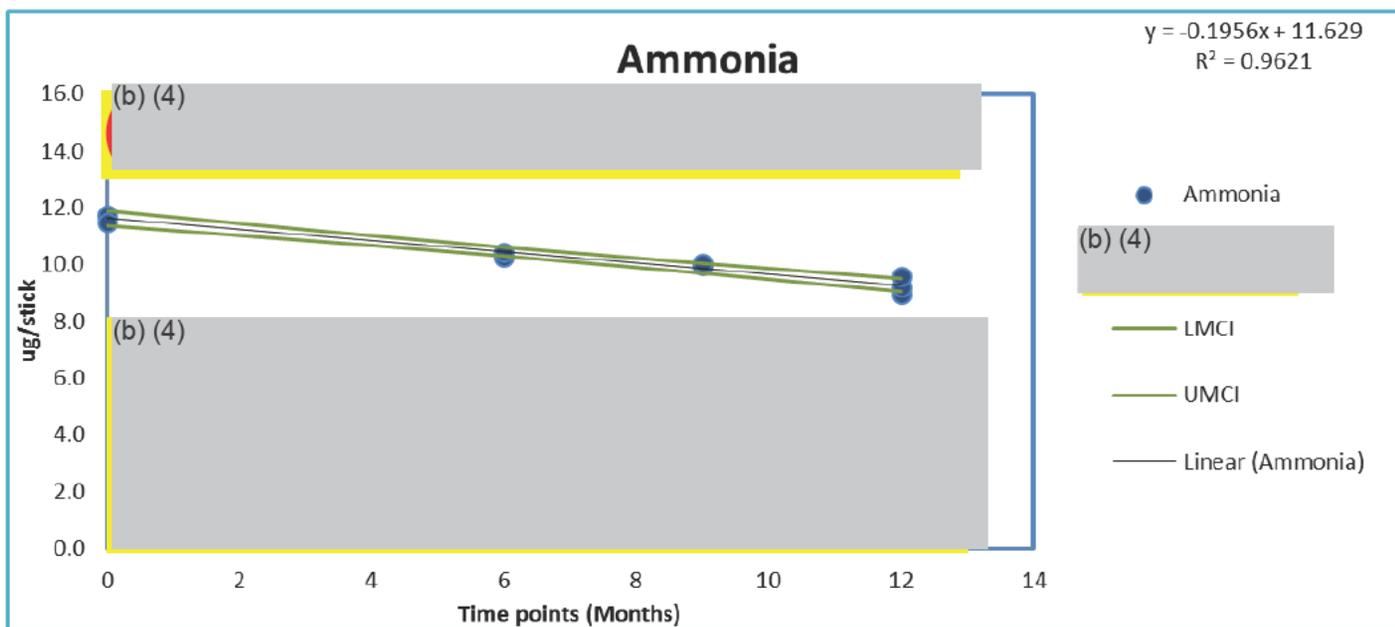


Figure 15 The best model accepted at the significance level of 0.25 has Different intercepts and Different slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



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6.1.2 Physical Attributes Evaluation

(b) (4)





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6.1.3 Sensorial Evaluation

Sensorial evaluation results are described in details in a separate report [4].

Overall, Dorado I Vinny High was relatively stable sensory wise over the 12 month storage period for the conditions 22°C 60%RH.

(b) (4)

A shelf life of 12 months is considered 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.



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6.2 Storage Condition 30°C 35% RH

Table 8 B-31061/ 41-2572271 at 30°C 35% RH

B-31061/ 41-2572271	Unit	Specifications	Time point (Months)						Degradation Rate	R ²	Severity Score
			0	2	4	6	9	12			
Test		(b) (4)	0	2	4	6	9	12			
Menthol	mg/stick		2.81	3.61		3.42	3.29	3.37	0.69%	0.13	0.1
Nicotine	mg/stick		1.17	1.20		1.10	1.08	1.08	-0.82%	0.81	0.7
Glycerin	mg/stick		5.31	4.83		4.34	4.25	3.93	-2.08%	0.94	1.9
CO	mg/stick		0.5	0.3		0.5	0.5	0.6	1.60%	0.16	0.3
Triacetin	mg/stick		0.7	0.5		0.4	0.5	0.4	-2.84%	0.61	1.7
Phenol	µg/stick		1.5	1.2		1.0	1.1	1.1	-1.70%	0.42	0.7
Acrylamide	µg/stick		1.9	1.4		1.2	1.2	1.1	-3.47%	0.81	2.8
Acetamide	µg/stick		2.9			2.7	2.5	3.1	0.10%	0.00	0.0
Acetaldehyde	µg/stick		201			193	210	206	0.33%	0.20	0.1
Butyraldehyde	µg/stick		15.3			12.1	14.0	14.0	-0.65%	0.14	0.1
Acrylonitrile	µg/stick		0.15	0.13		0.15	0.14	0.15	0.44%	0.07	0.0
Isoprene	µg/stick		*	1.95		1.57	1.51	1.83	-0.87%	0.10	0.1
Pyridine	µg/stick		8.7			8.6	8.3	8.1	-0.55%	0.87	0.5
Ammonia	µg/stick		11.7			8.3	7.4	7.0	-3.58%	0.93	3.3

(b) (4)

* Isoprene value not reported, as explained



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Table 9 B-31062/ 41-2572272 at 30°C 35% RH

B-31062/ 41-2572272	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)		2.84		3.55	3.36		3.32	1.00%	0.27	0.3
Nicotine	mg/stick	(b) (4)		1.19		1.15	1.14		1.12	-0.48%	0.82	0.4
Glycerin	mg/stick	(b) (4)		5.30		4.79	4.73		4.23	-1.65%	0.97	1.6
CO	mg/stick	(b) (4)		0.5		0.3	0.5		0.6	1.50%	0.08	0.1
Triacetin	mg/stick	(b) (4)		0.7		0.4	0.5		0.4	-2.65%	0.54	1.4
Phenol	µg/stick	(b) (4)		1.5		1.1	1.2		1.2	-1.53%	0.33	0.5
Acrylamide	µg/stick	(b) (4)		1.9		1.4	1.3		1.2	-3.28%	0.77	2.5
Acetamide	µg/stick	(b) (4)		3.1			2.9		3.2	0.45%	0.19	0.1
Acetaldehyde	µg/stick	(b) (4)		203			202		224	0.86%	0.69	0.6
Butyraldehyde	µg/stick	(b) (4)		14.9			12.7		15.1	0.13%	0.01	0.0
Acrylonitrile	µg/stick	(b) (4)		0.15		0.14	0.15		0.17	1.09%	0.52	0.6
Isoprene	µg/stick	(b) (4)		*		1.59	1.72		2.26	6.87%	1.00	6.9
Pyridine	µg/stick	(b) (4)		8.7			8.9		8.6	-0.11%	0.12	0.0
Ammonia	µg/stick	(b) (4)		11.7			8.4		7.0	-3.46%	0.95	3.3
TPM	ma/stick	(b) (4)		59			53		51	-1.03%	0.94	1.0

* Isoprene value not reported, as explained i



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Table 10 B-31063/ 41-2572273 at 30°C 35% RH

B-31063/ 41-2572273	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)		2.66	3.64	3.67		3.27	3.14	0.19%	0.01	0.0
Nicotine	mg/stick			1.16	1.18	1.15		1.05	1.11	-0.67%	0.57	0.4
Glycerin	mg/stick			5.09	4.73	4.84		4.22	3.96	-1.79%	0.95	1.7
CO	mg/stick			0.6	0.3	0.3		0.5	0.5	1.71%	0.09	0.2
Triacetin	mg/stick			0.6	0.5	0.5		0.4	0.4	-2.62%	0.69	1.8
Phenol	µg/stick			1.3	1.3	1.2		1.1	1.2	-1.08%	0.68	0.7
Acrylamide	µg/stick			1.8	1.4	1.4		1.2	1.1	-2.89%	0.79	2.3
Acetamide	µg/stick			3.0				2.6	3.3	0.27%	0.02	0.0
Acetaldehyde	µg/stick			194				197	192	-0.02%	0.01	0.0
Butyraldehyde	µg/stick			15.3				12.8	12.7	-1.51%	0.95	1.4
Acrylonitrile	µg/stick			0.14	0.12	0.14		0.13	0.16	1.44%	0.36	0.5
Isoprene	µg/stick			*	1.83	1.68		1.47	2.06	0.79%	0.06	0.0
Pyridine	µg/stick			8.3				8.7	8.8	0.51%	1.00	0.5
Ammonia	µg/stick			11.5				7.2	7.0	-3.46%	0.96	3.3
TPM	ma/stick			58				50	53	-0.97%	0.73	0.7

(b) (4)

* Isoprene value not reported, as explained



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6.2.1 Mainstream Aerosol Evaluation

6.2.1.1 Menthol

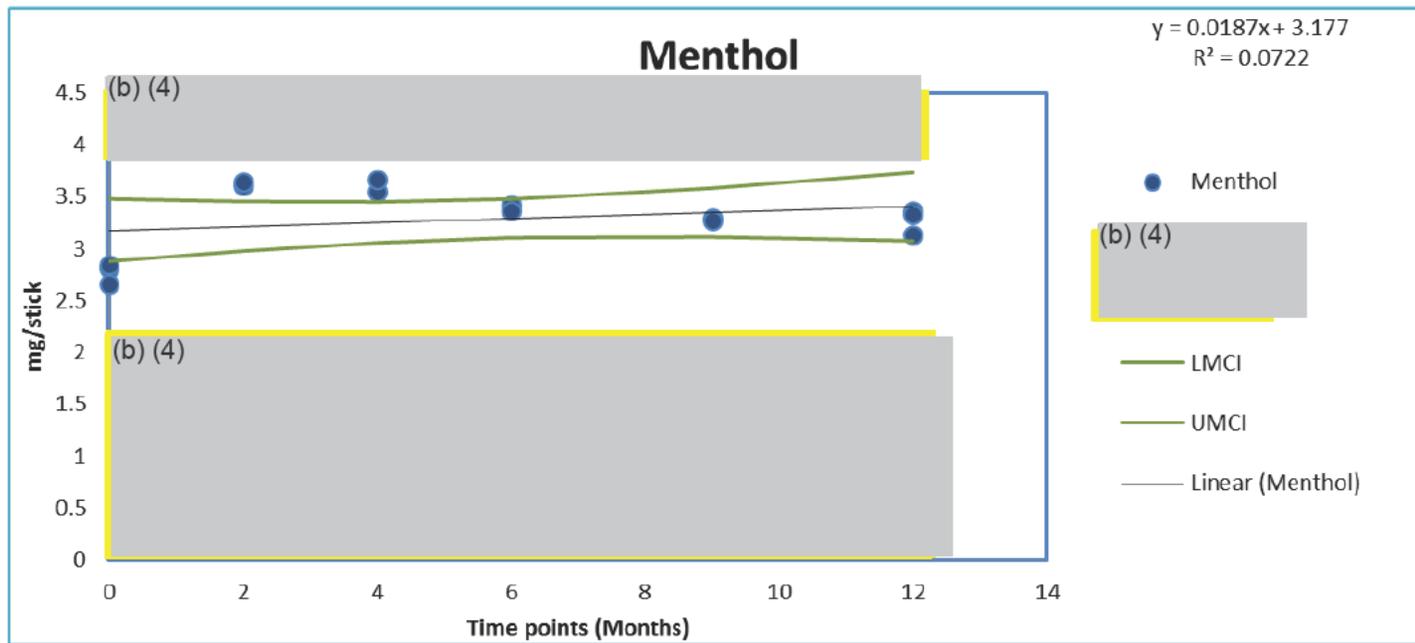


Figure 17 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



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Form Effective Date: See EDMS

6.2.1.2 Nicotine

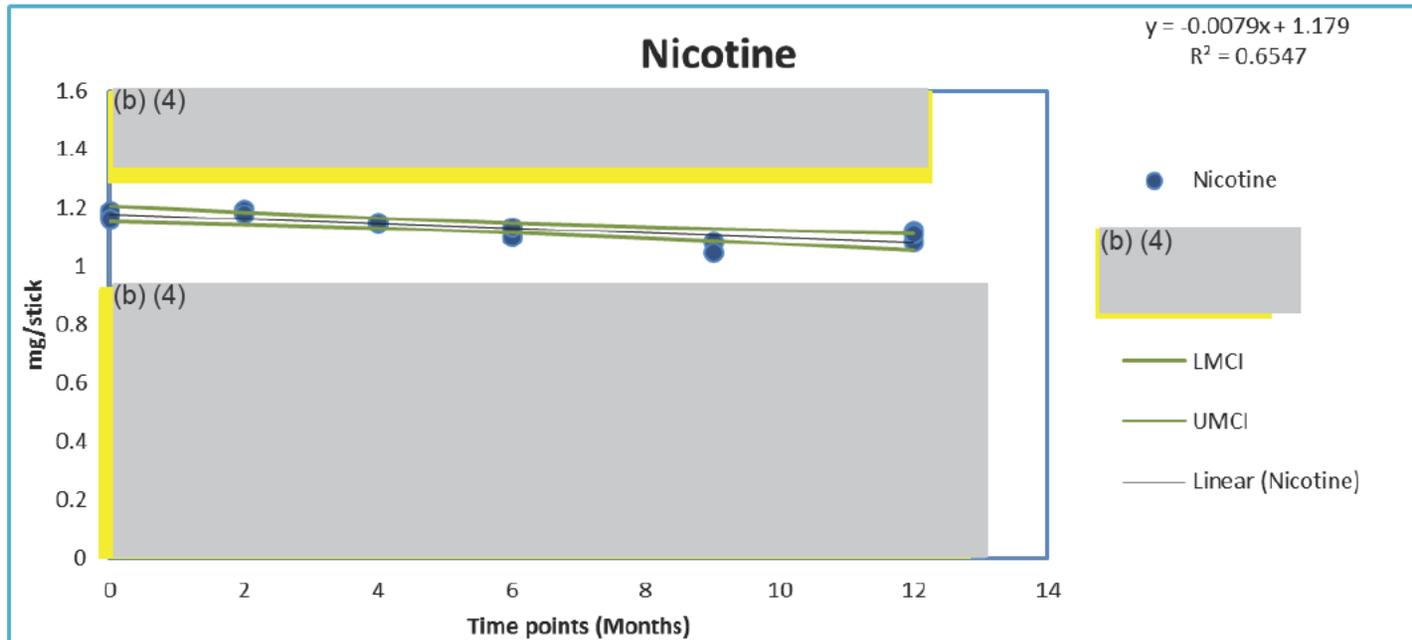


Figure 18 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



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Form Status: Effective
Form Effective Date: See EDMS

6.2.1.3 Glycerin

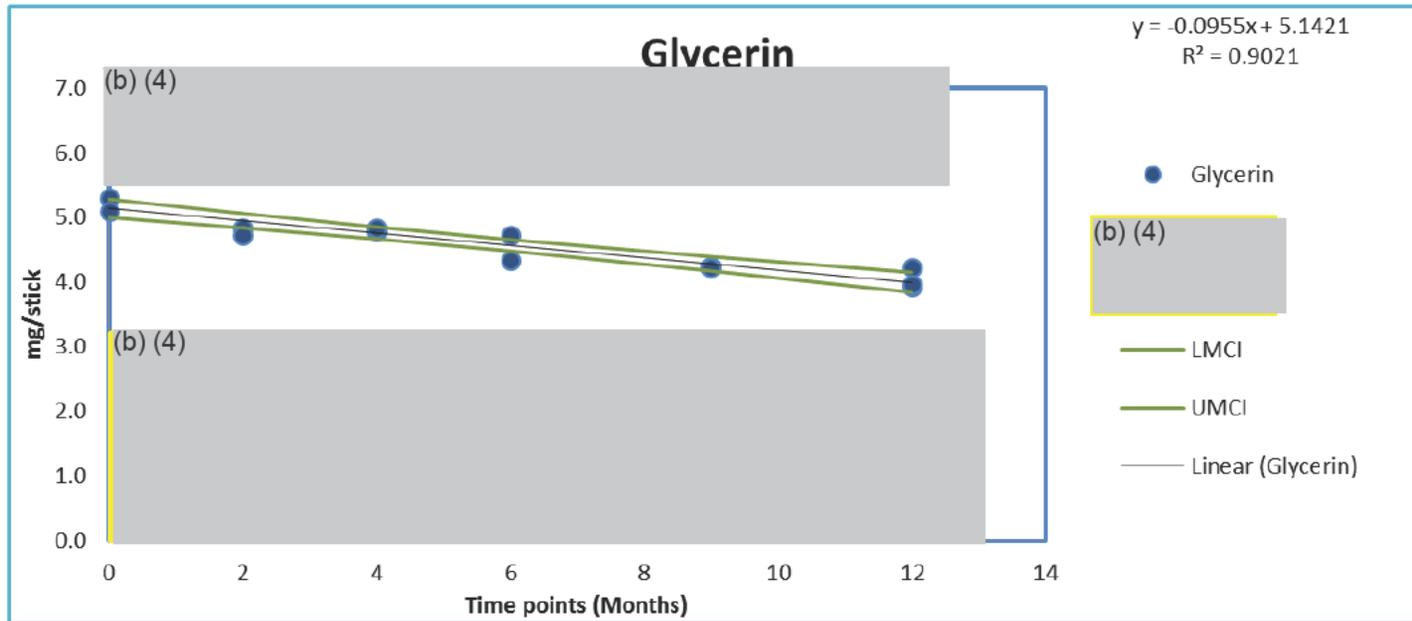


Figure 19 The best model accepted at the significance level of 0.25 has Different intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



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Form Status: Effective
Form Effective Date: See EDMS

6.2.1.4 CO

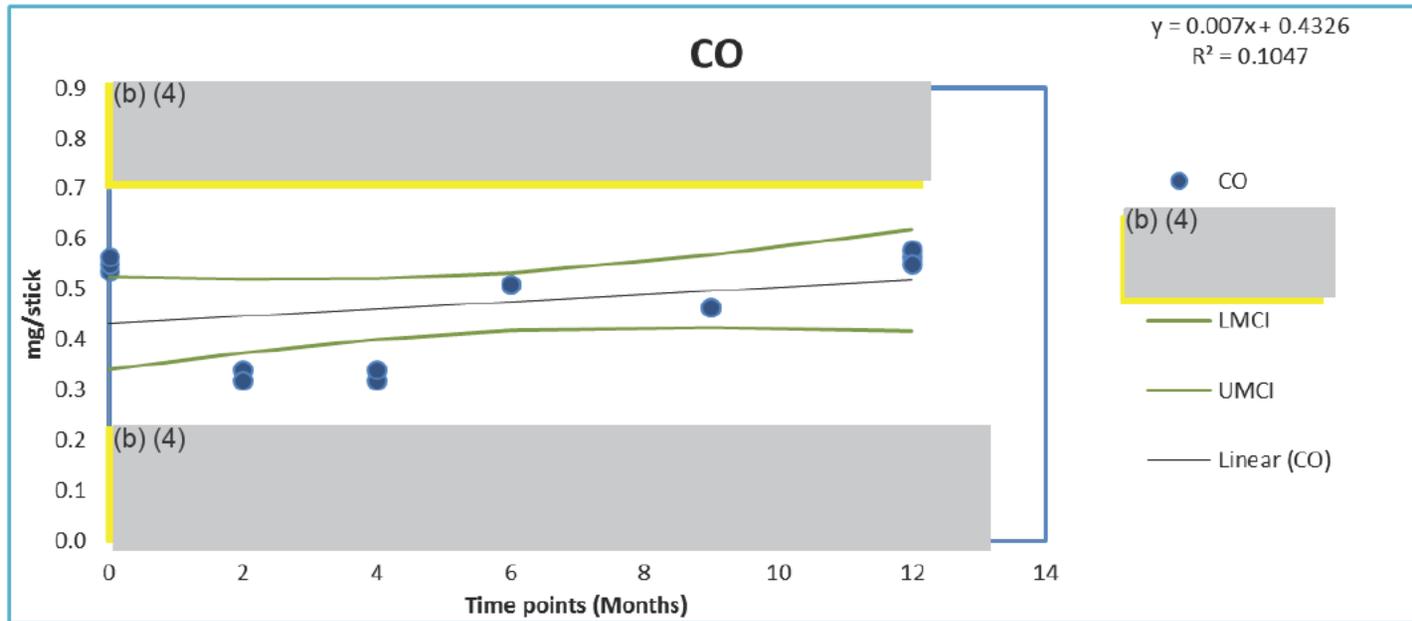


Figure 20 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



6.2.1.5 Triacetin

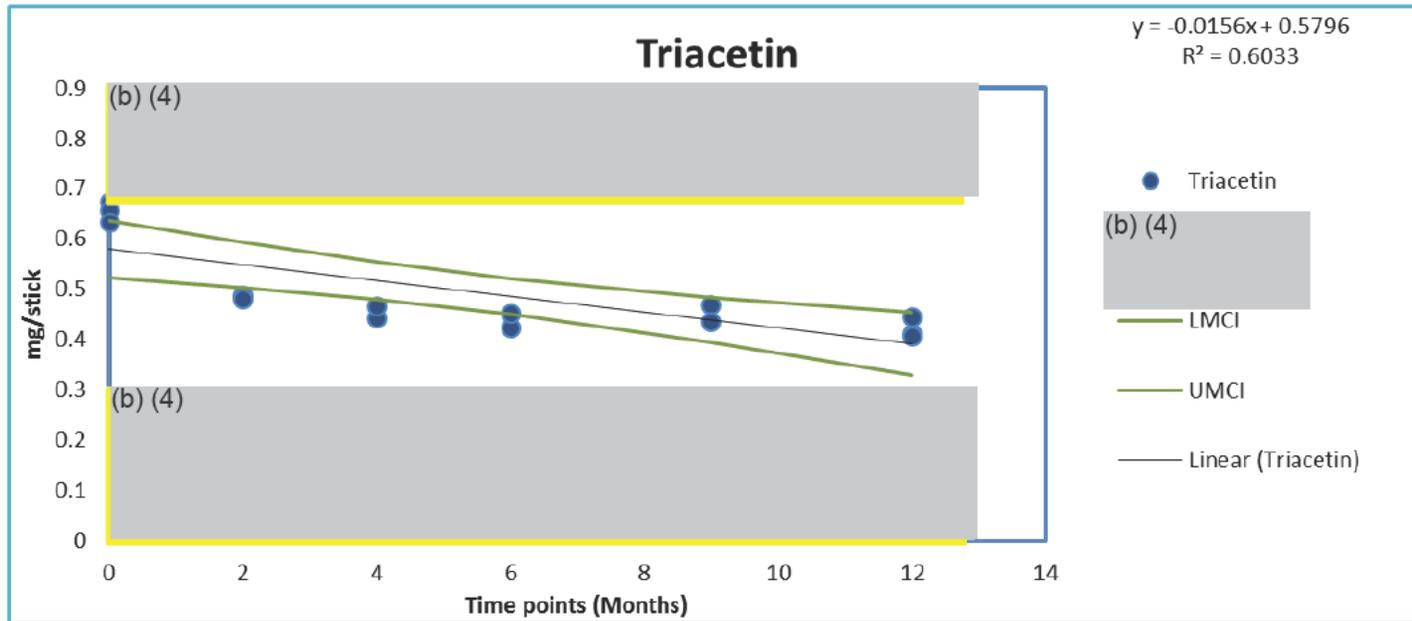


Figure 21 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



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Form Status: Effective
Form Effective Date: See EDMS

6.2.1.6 TPM

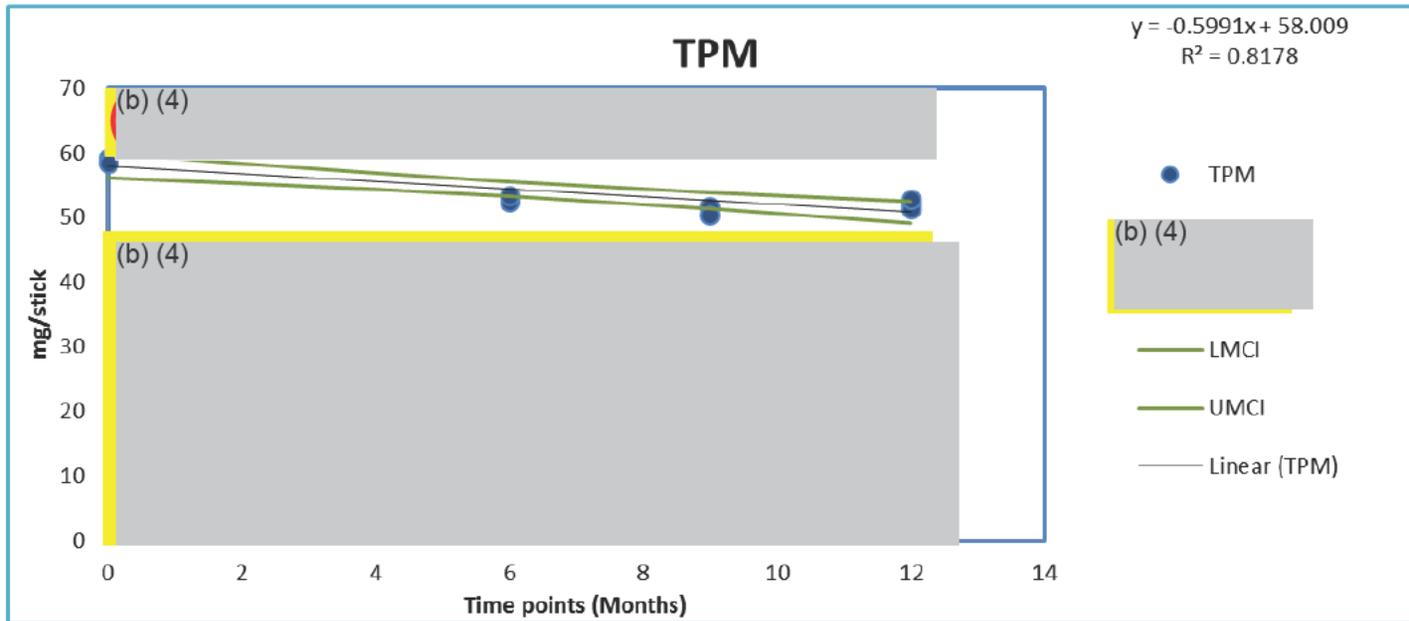


Figure 22 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



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Stability Study Report: STAB-2016_P1_M_5

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.2.1.7 Phenol

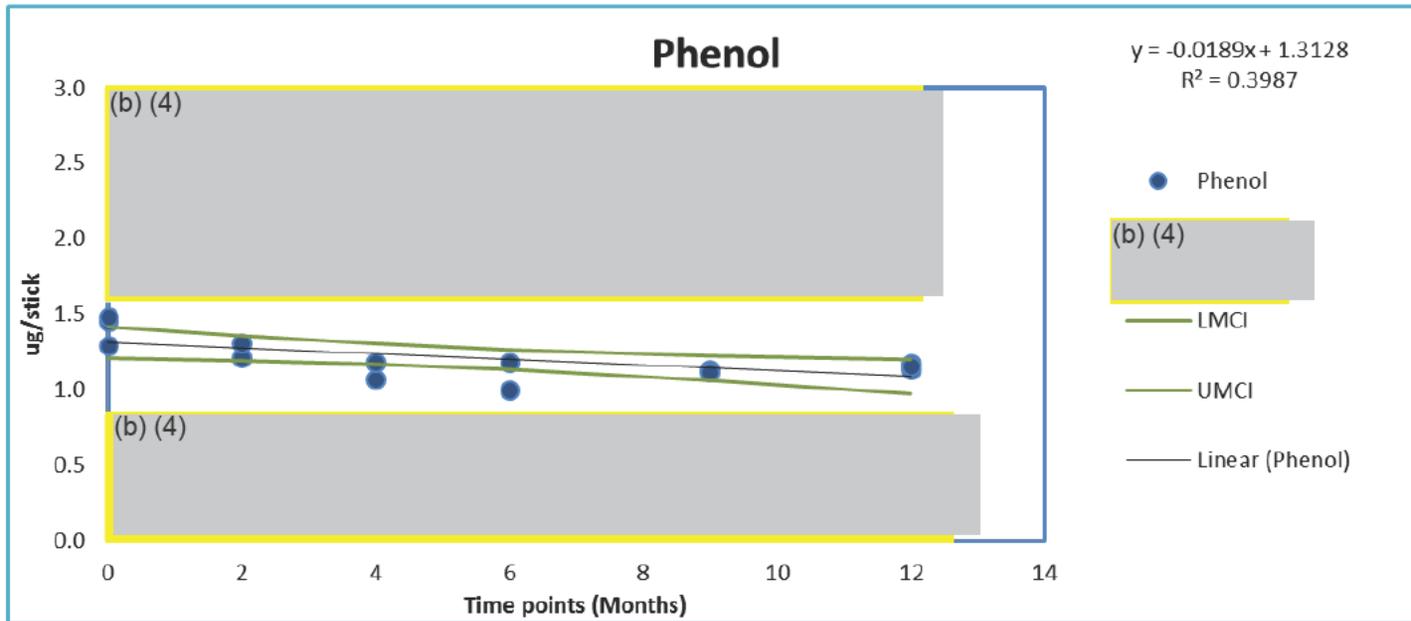


Figure 23 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



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Stability Study Report: STAB-2016_P1_M_5

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.2.1.8 Acrylamide

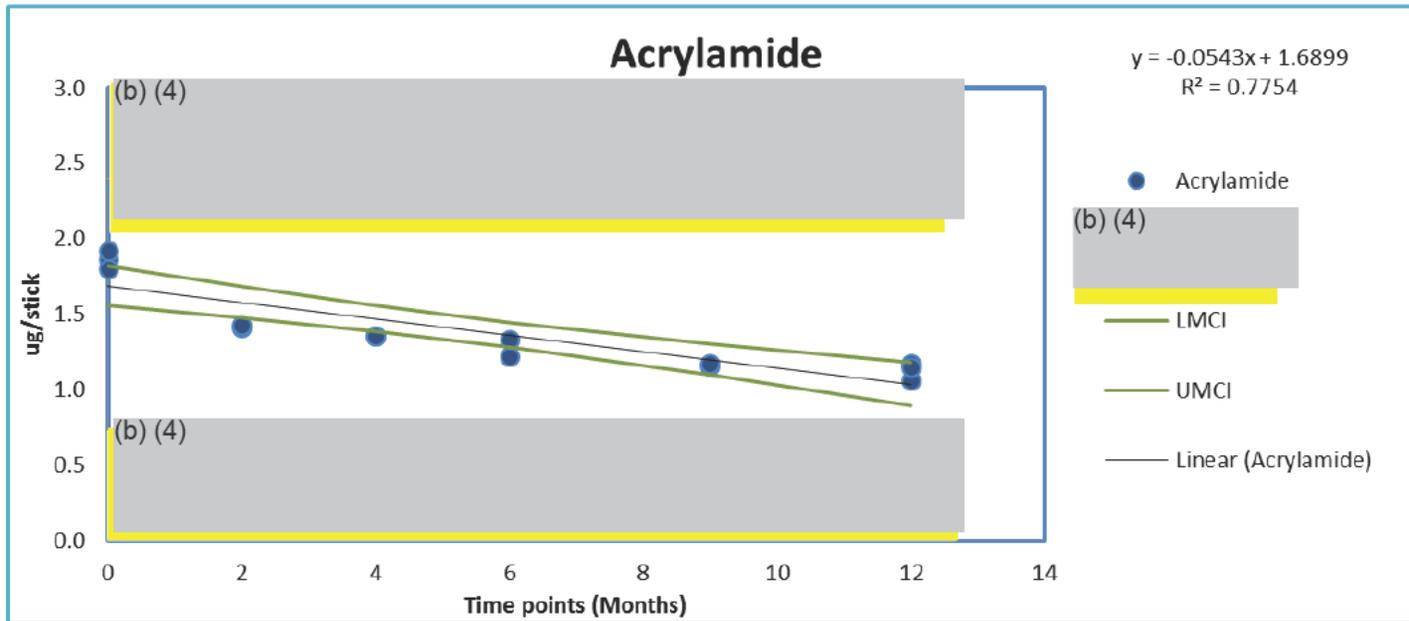


Figure 24 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



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Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.2.1.9 Acetamide

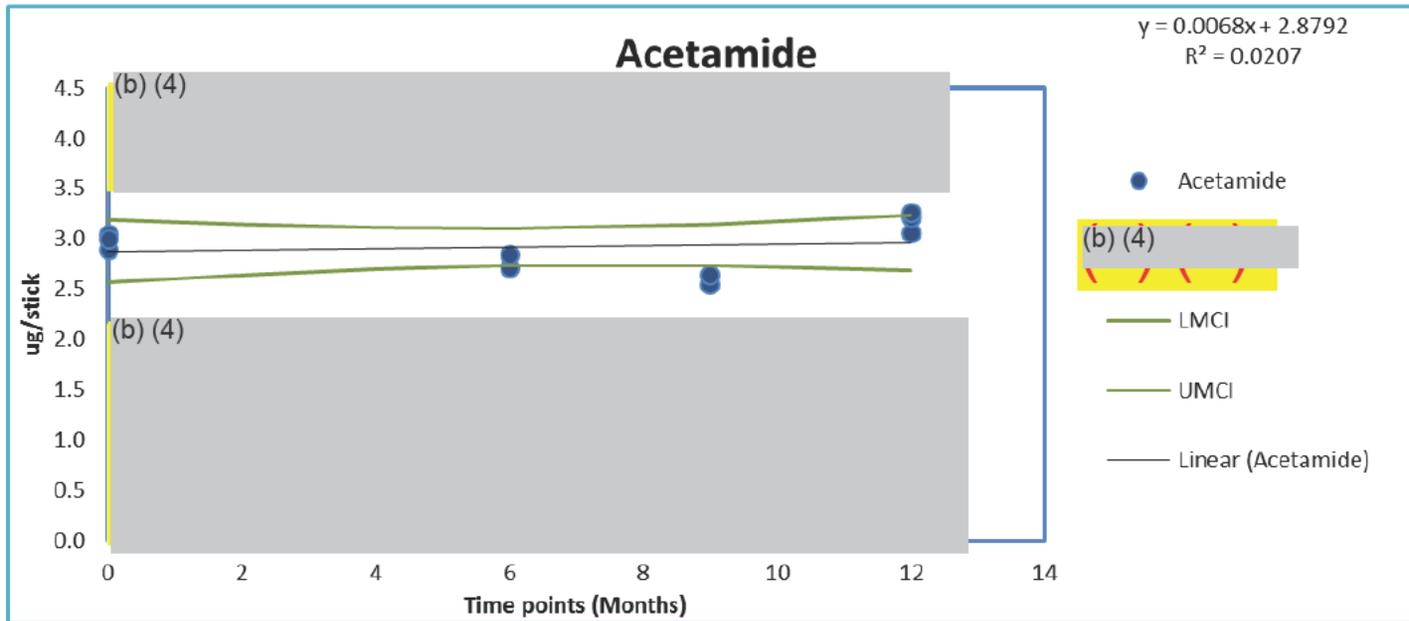


Figure 25 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



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Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.2.1.10 Acetaldehyde

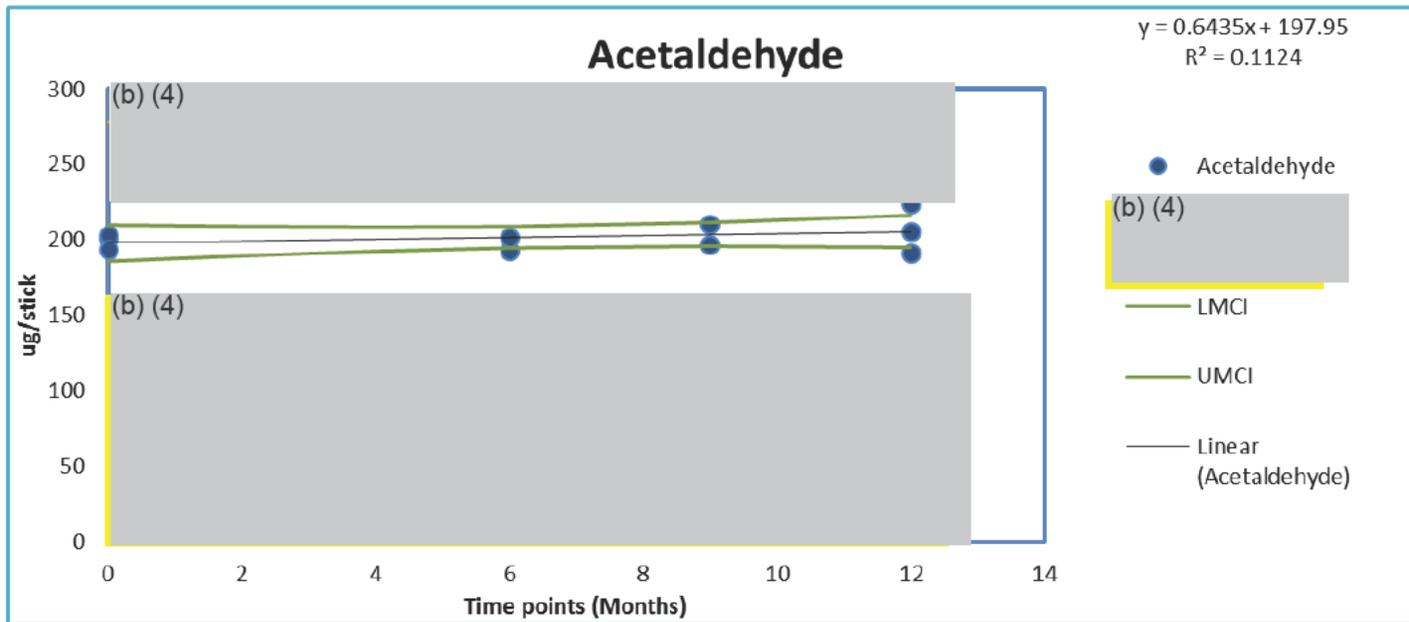


Figure 26 The best model accepted at the significance level of 0.25 has Different intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



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Stability Study Report: STAB-2016_P1_M_5

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.2.1.11 Butyraldehyde

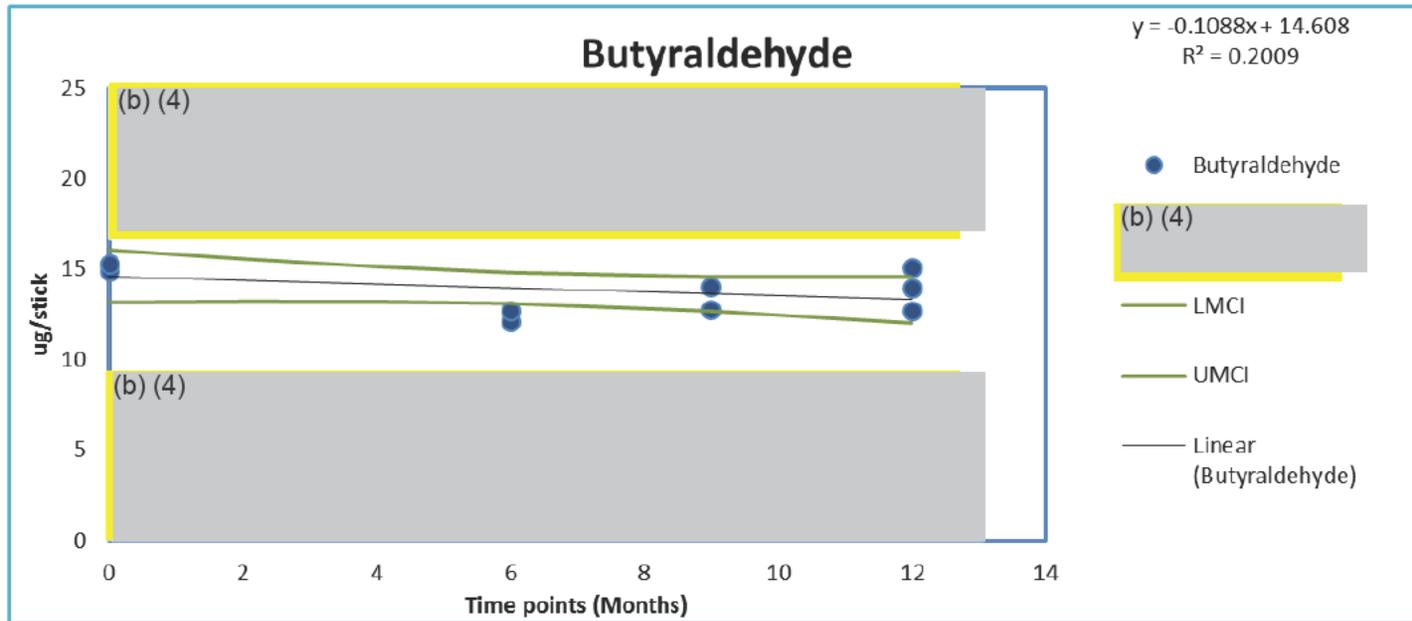


Figure 27 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



6.2.1.12 Acrylonitrile

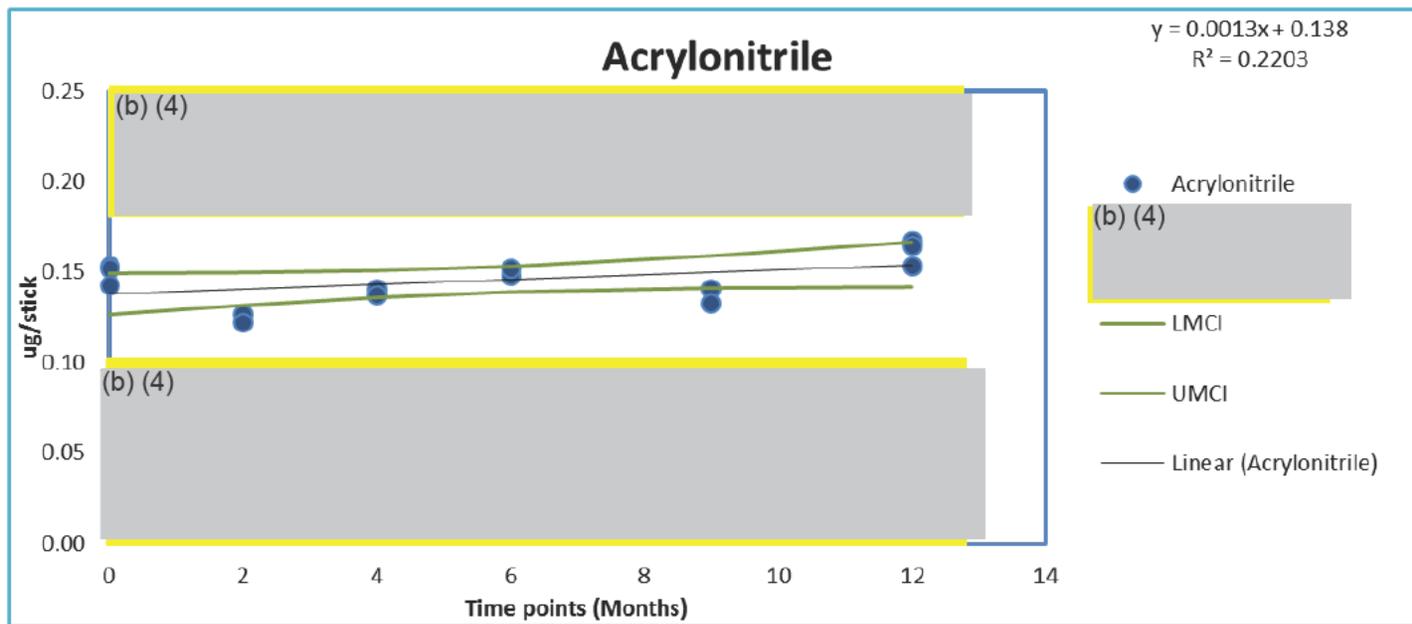


Figure 28 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



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Form Status: Effective
Form Effective Date: See EDMS

6.2.1.13 Isoprene

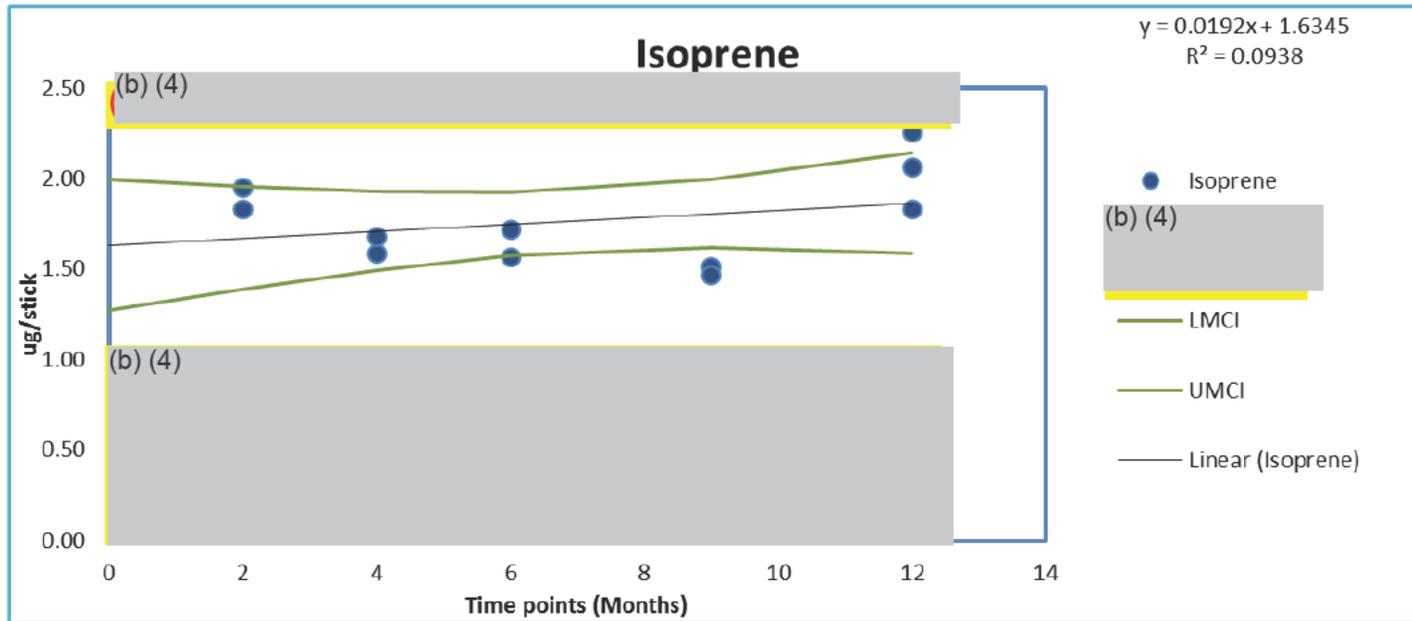


Figure 29 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



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Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.2.1.14 Pyridine

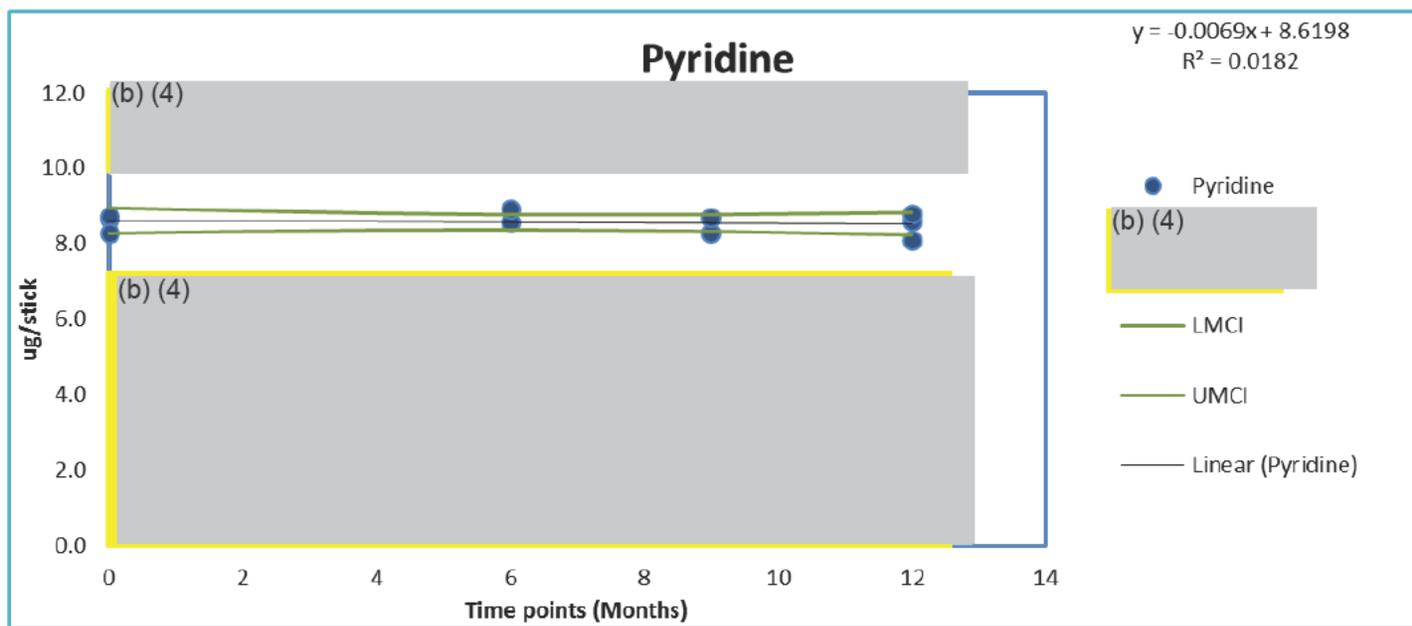


Figure 30 The best model accepted at the significance level of 0.25 has Different intercepts and Different slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



Form Number: PMI_RD_FOR_000927
Stability Study Report: STAB-2016_P1_M_5

Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.2.1.15 Ammonia

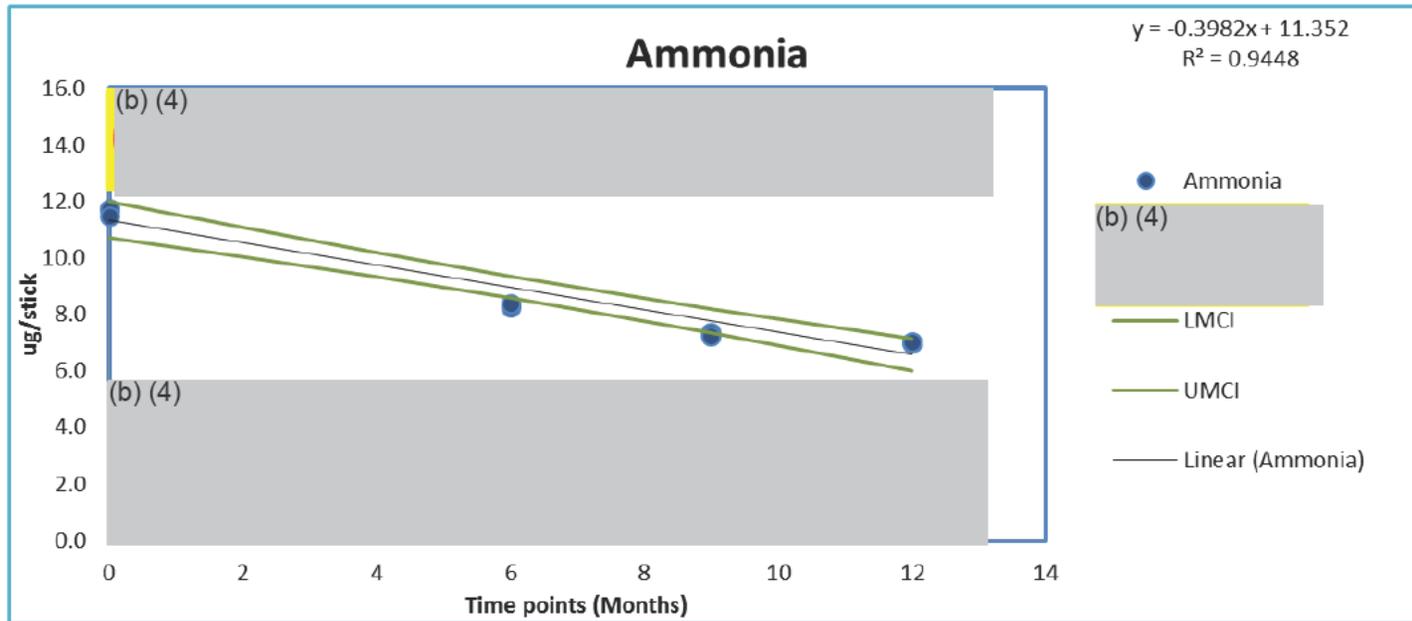


Figure 31 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 12 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 12 months.



Form Number: PMI_RD_FOR_000927

Form Version N°: 1.0

Form Status: Effective

Stability Study Report: STAB-2016_P1_M_5

Form Effective Date: See EDMS

6.2.2 Physical Attributes Evaluation

(b) (4)





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Form Status: Effective

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Form Effective Date: See EDMS

6.2.3 Sensorial Evaluation

Sensorial evaluation results are described in details in a separate report [4].

Overall, Dorado I Vinny High was relatively stable sensory wise over the 12 month storage period for the conditions 30°C 35%RH (b) (4) (b) (4).

A shelf life of 12 months is considered 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.



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Form Status: Effective

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6.3 Storage Condition 30°C 75% RH

Table 11 B-31061/ 41-2572271 at 30°C 75% RH

B-31061/ 41-2572271	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)		2.81	3.65	3.58				6.52%	0.68	4.4
Nicotine	mg/stick			1.17	1.18	1.08				-1.95%	0.73	1.4
Glycerin	mg/stick			5.31	4.79	4.42				-4.22%	0.99	4.2
CO	mg/stick			0.5	0.3	0.3				-9.73%	0.75	7.3
Triacetin	mg/stick			0.7	0.4	0.4				-11.84%	0.92	10.8
Phenol	µg/stick			1.5	1.2	1.0				-7.88%	1.00	7.9
Acrylamide	µg/stick			1.9	1.4	1.2				-8.94%	0.95	8.5
Acetamide	µg/stick			2.9						NA	NA	NA
Acetaldehyde	µg/stick			201						NA	NA	NA
Butyraldehyde	µg/stick			15.3						NA	NA	NA
Acrylonitrile	µg/stick			0.15	0.12	0.12				-5.93%	0.76	4.5
Isoprene	µg/stick			*	1.89	1.46				-9.29%	1.00	9.3
Pyridine	µg/stick			8.7						NA	NA	NA
Ammonia	µg/stick			11.7						NA	NA	NA
TPM	mg/stick			59						NA	NA	NA

(b) (4)



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Form Status: Effective

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Table 12 B-31062/ 41-2572272 at 30°C 75% RH

B-31062/ 41-2572272	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)		2.84	3.58		3.47			2.78%	0.43	1.2
Nicotine	mg/stick			1.19	1.28		1.15			-0.82%	0.23	0.2
Glycerin	mg/stick			5.30	5.03		4.43			-2.75%	1.00	2.7
CO	mg/stick			0.5	0.3		0.5			0.06%	0.00	0.0
Triacetin	mg/stick			0.7	0.5		0.4			-6.83%	0.83	5.7
Phenol	µg/stick			1.5	1.5		1.2			-3.10%	0.94	2.9
Acrylamide	µg/stick			1.9	1.6		1.3			-5.48%	0.95	5.2
Acetamide	µg/stick			3.1			3.1			NA	NA	NA
Acetaldehyde	µg/stick			203			205			NA	NA	NA
Butyraldehyde	µg/stick			14.9			12.5			NA	NA	NA
Acrylonitrile	µg/stick			0.15	0.11		0.16			1.56%	0.08	0.1
Isoprene	µg/stick			*	1.61		1.68			NA	NA	NA
Pyridine	µg/stick			8.7			8.5			NA	NA	NA
Ammonia	µg/stick			11.7			9.1			NA	NA	NA
TPM	mg/stick			59			54			NA	NA	NA

(b) (4)



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Form Status: Effective

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Table 13 B-31063/ 41-2572273 at 30°C 75% RH

B-31063/ 41-2572273	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)		2.66		3.61	3.44			5.29%	0.77	4.1
Nicotine	mg/stick	(b) (4)		1.16		1.10	1.16			-0.25%	0.06	0.0
Glycerin	mg/stick	(b) (4)		5.09		4.51	4.43			-2.26%	0.95	2.1
CO	mg/stick	(b) (4)		0.6		0.3	0.5			-2.45%	0.10	0.3
Triacetin	mg/stick	(b) (4)		0.6		0.4	0.4			-7.83%	0.85	6.7
Phenol	µg/stick	(b) (4)		1.3		1.1	1.3			-0.66%	0.05	0.0
Acrylamide	µg/stick	(b) (4)		1.8		1.2	1.3			-5.08%	0.78	4.0
Acetamide	µg/stick	(b) (4)		3.0			2.9			NA	NA	NA
Acetaldehyde	µg/stick	(b) (4)		194			212			NA	NA	NA
Butyraldehyde	µg/stick	(b) (4)		15.3			12.9			NA	NA	NA
Acrylonitrile	µg/stick	(b) (4)		0.14		0.14	0.15			0.38%	0.10	0.0
Isoprene	µg/stick	(b) (4)		*		1.62	1.78			NA	NA	NA
Pyridine	µg/stick	(b) (4)		8.3			8.4			NA	NA	NA
Ammonia	µg/stick	(b) (4)		11.5			10.0			NA	NA	NA
TPM	mg/stick	(b) (4)		58			55			NA	NA	NA



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Form Status: Effective
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6.3.1 Mainstream Aerosol Evaluation

6.3.1.1 Menthol

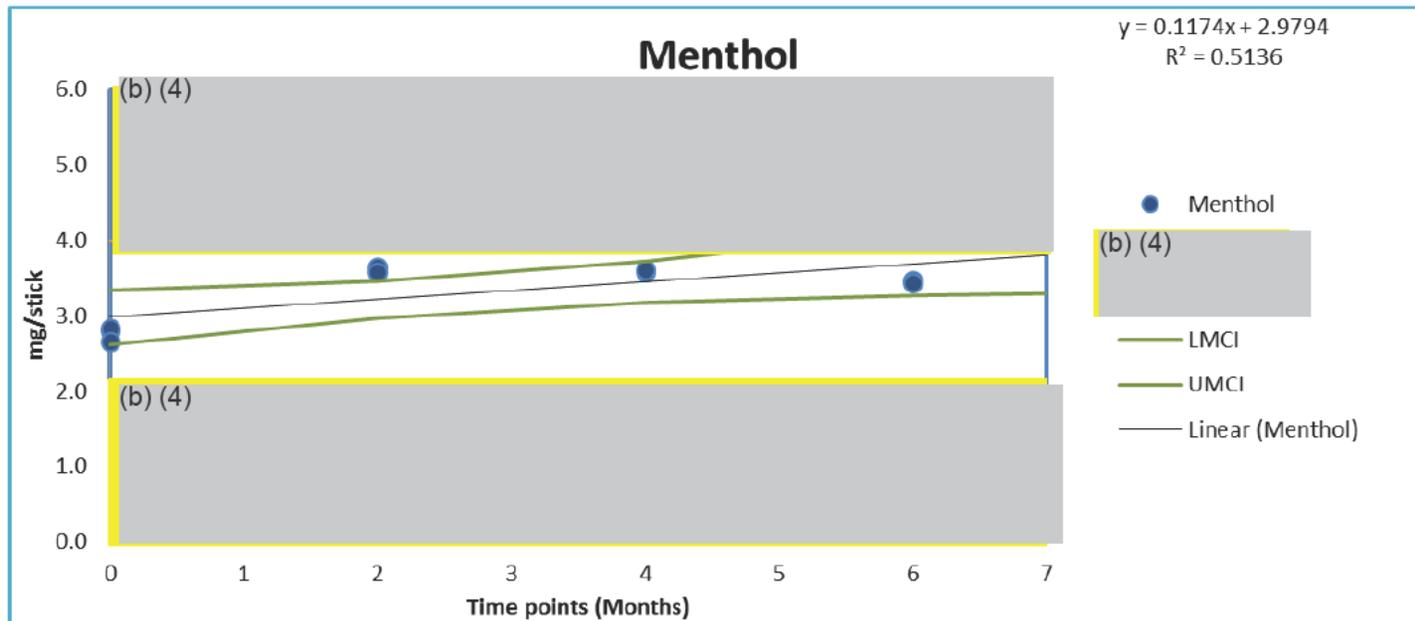


Figure 33 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time at 5 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 5 months.



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Form Status: Effective
Form Effective Date: See EDMS

6.3.1.2 Nicotine

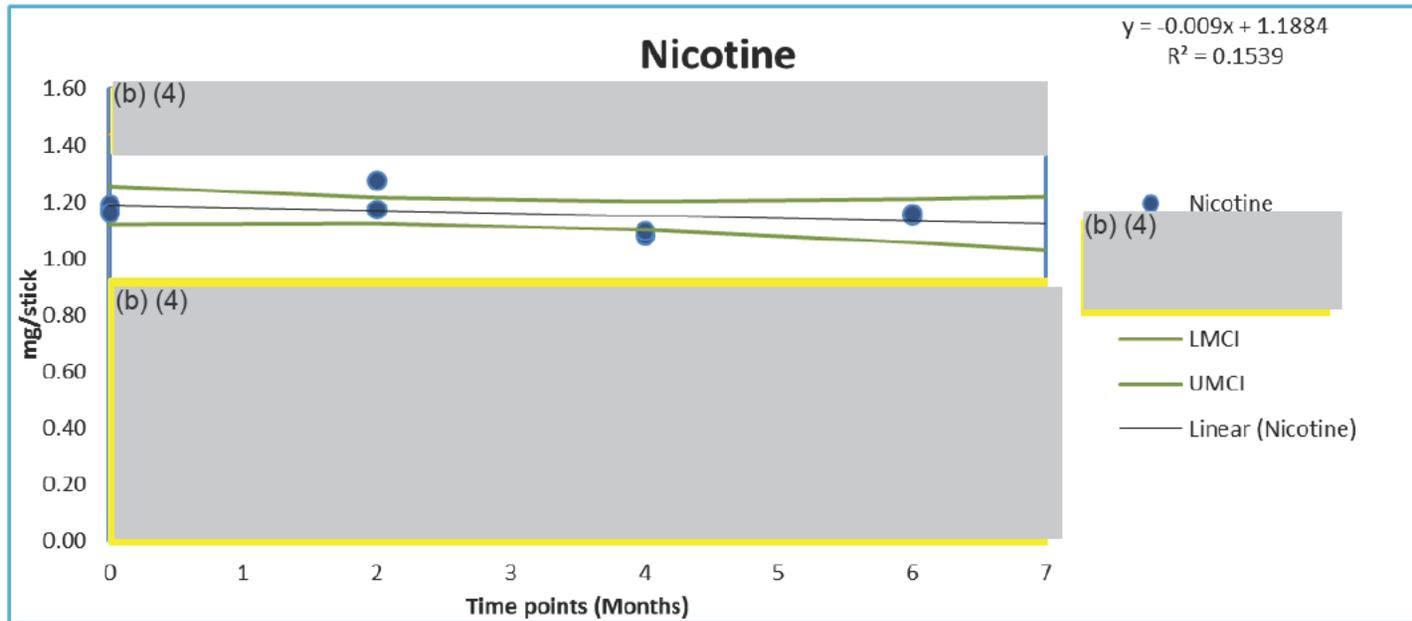


Figure 34 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 6 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 6 months.



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Form Version N°: 1.0

Form Status: Effective
Form Effective Date: See EDMS

6.3.1.3 Glycerin

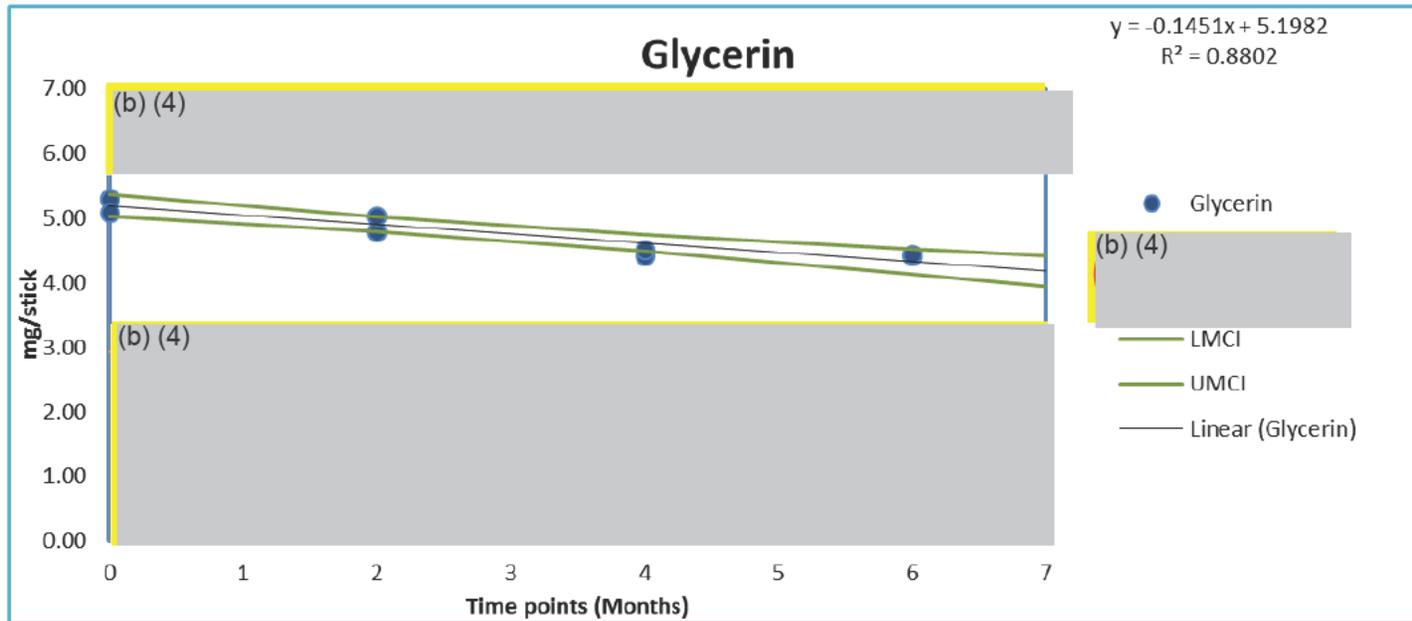


Figure 35 The best model accepted at the significance level of 0.25 has Different intercepts and Different slopes. The model suggests the earliest crossing time over 6 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 6 months.



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Form Effective Date: See EDMS

6.3.1.4 CO

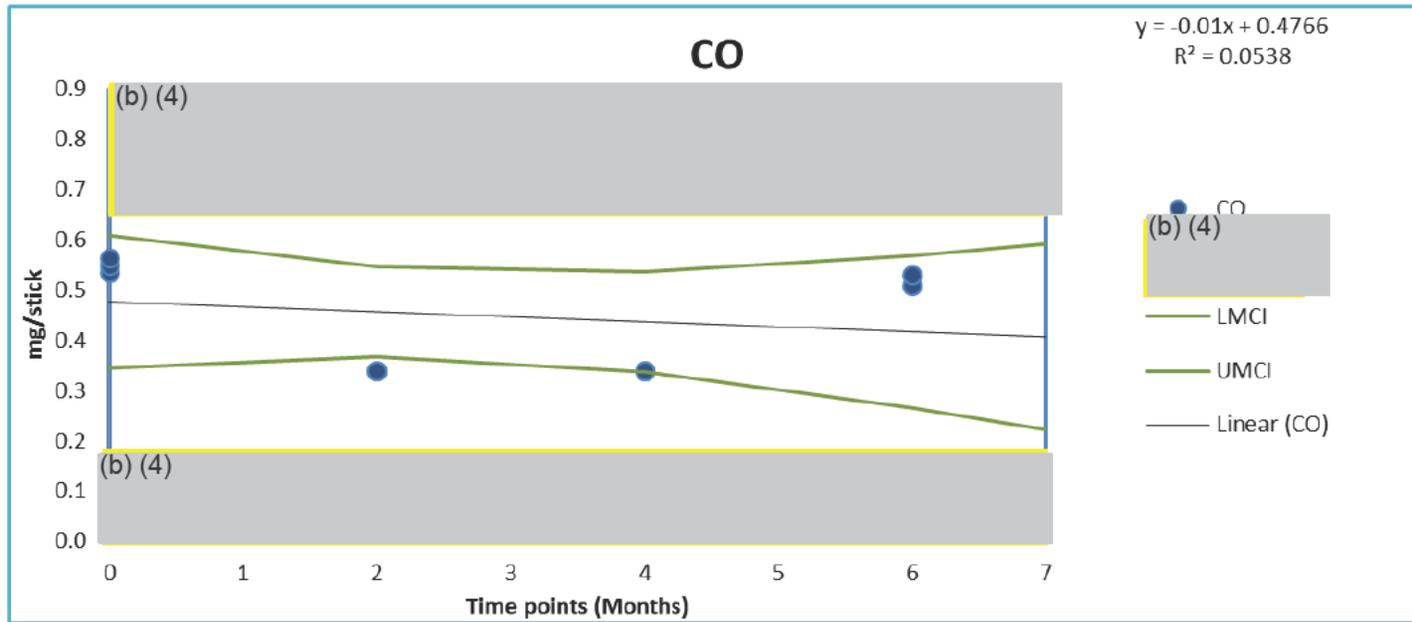


Figure 36 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 6 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 6 months.



6.3.1.5 Triacetin

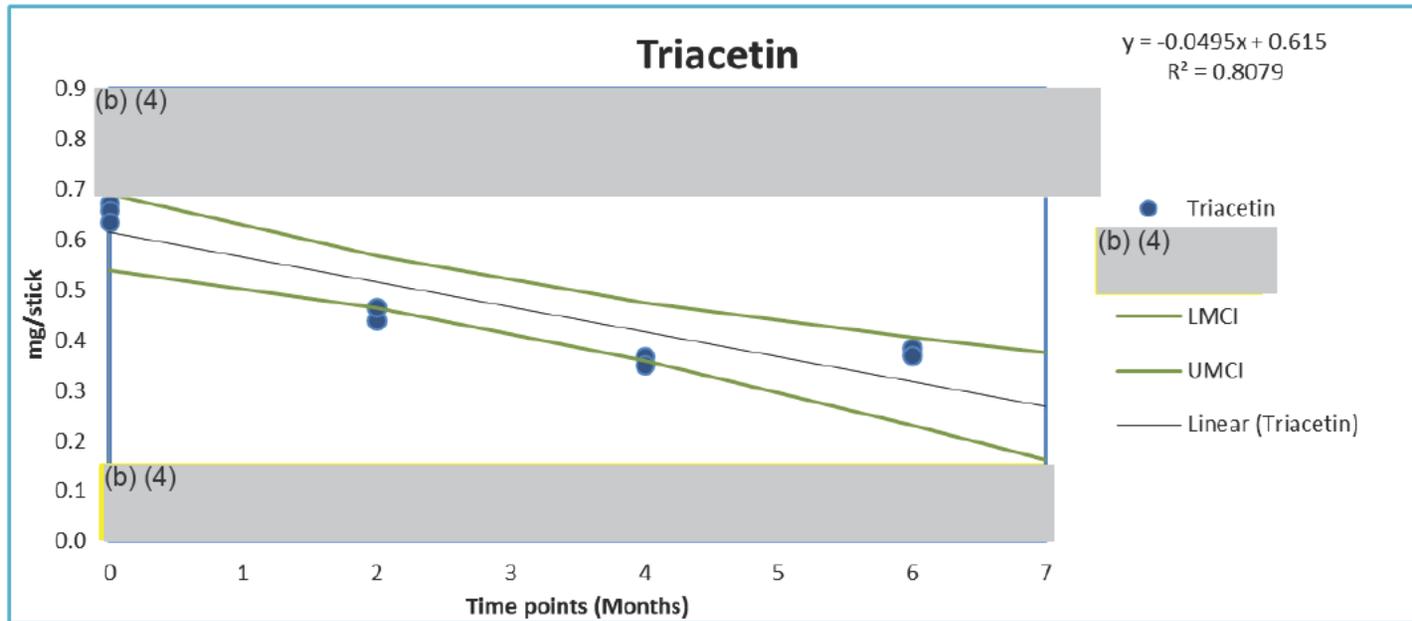


Figure 37 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 6 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 6 months.



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Form Effective Date: See EDMS

6.3.1.6 TPM

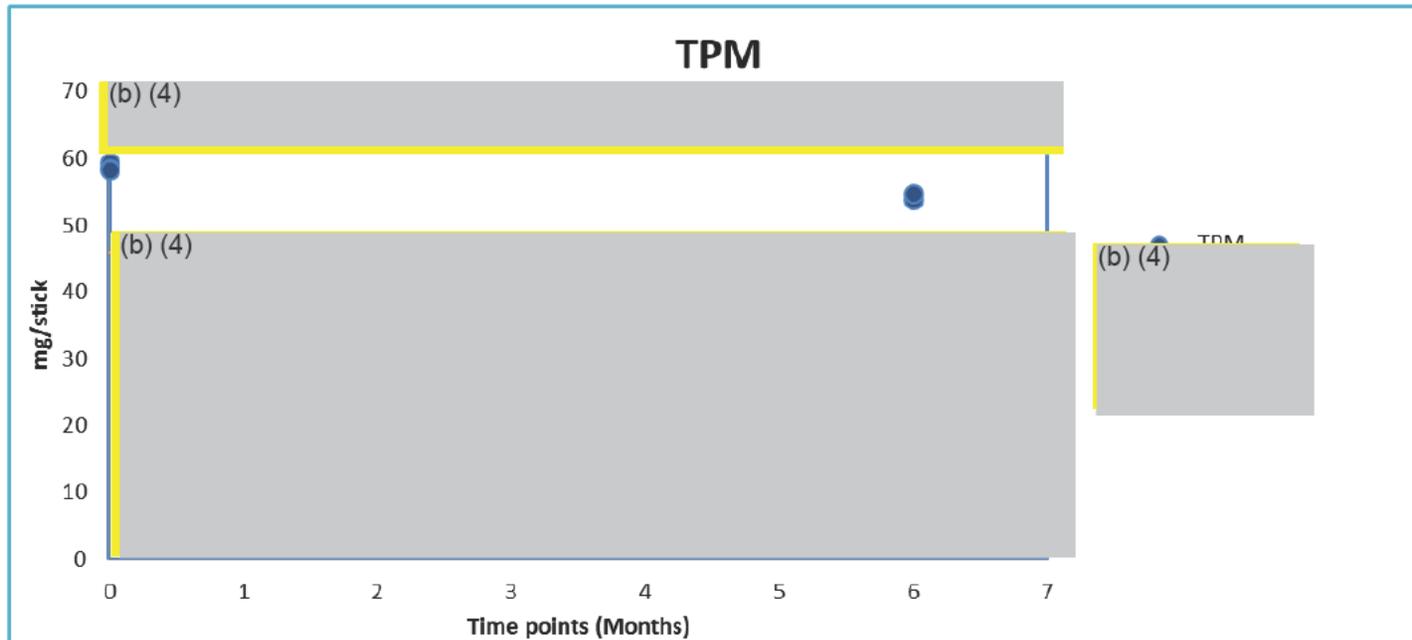


Figure 38 TPM is not suitable for trend analysis since it was tested in less than 3 different time points. All the values obtained are inside the specifications and therefore TPM is considered stable for 6 months.



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Form Status: Effective
Form Effective Date: See EDMS

6.3.1.7 Phenol

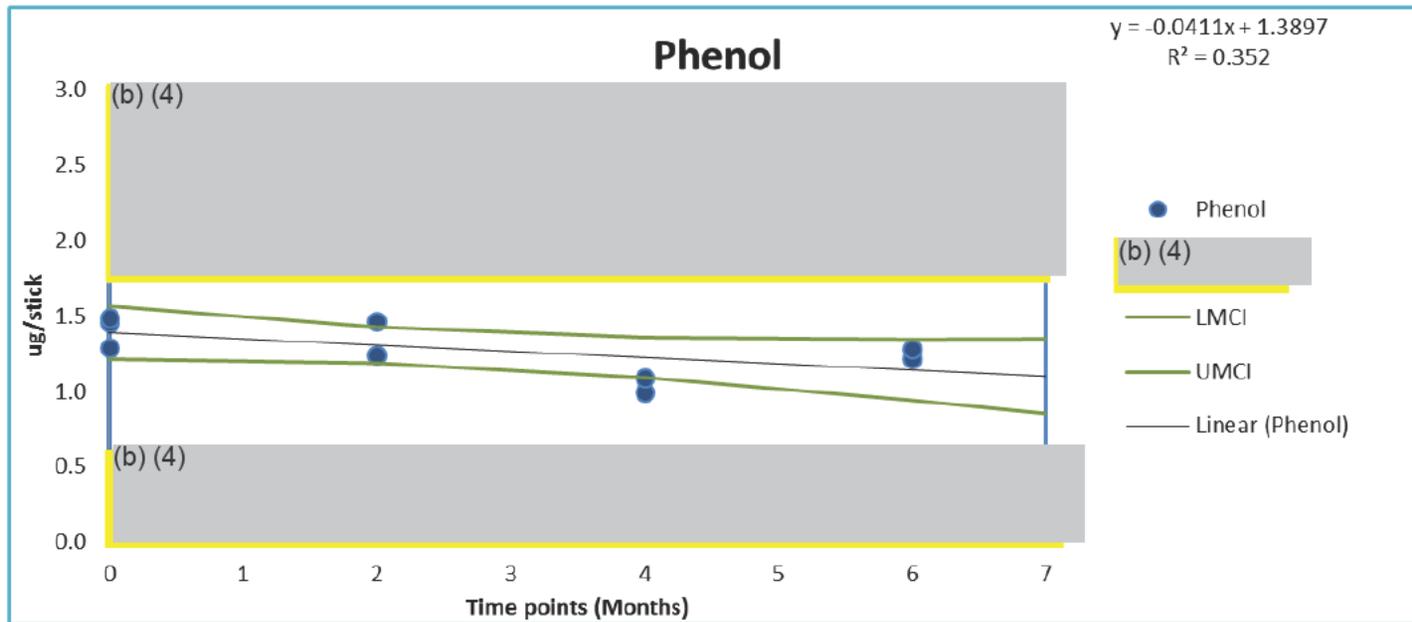


Figure 39 The best model accepted at the significance level of 0.25 has Different intercepts and Different slopes. The model suggests the earliest crossing time over 6 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 6 months.



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Form Status: Effective
Form Effective Date: See EDMS

6.3.1.8 Acrylamide

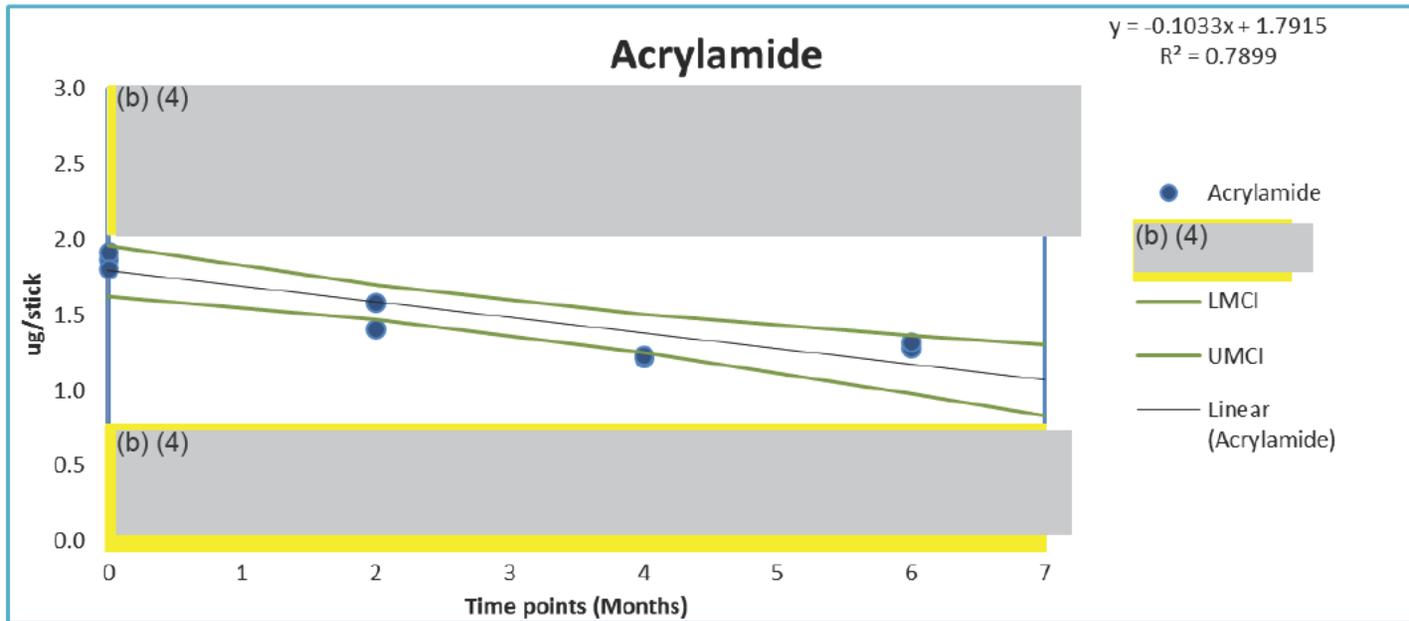


Figure 40 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 6 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 6 months.



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Form Effective Date: See EDMS

6.3.1.9 Acetamide

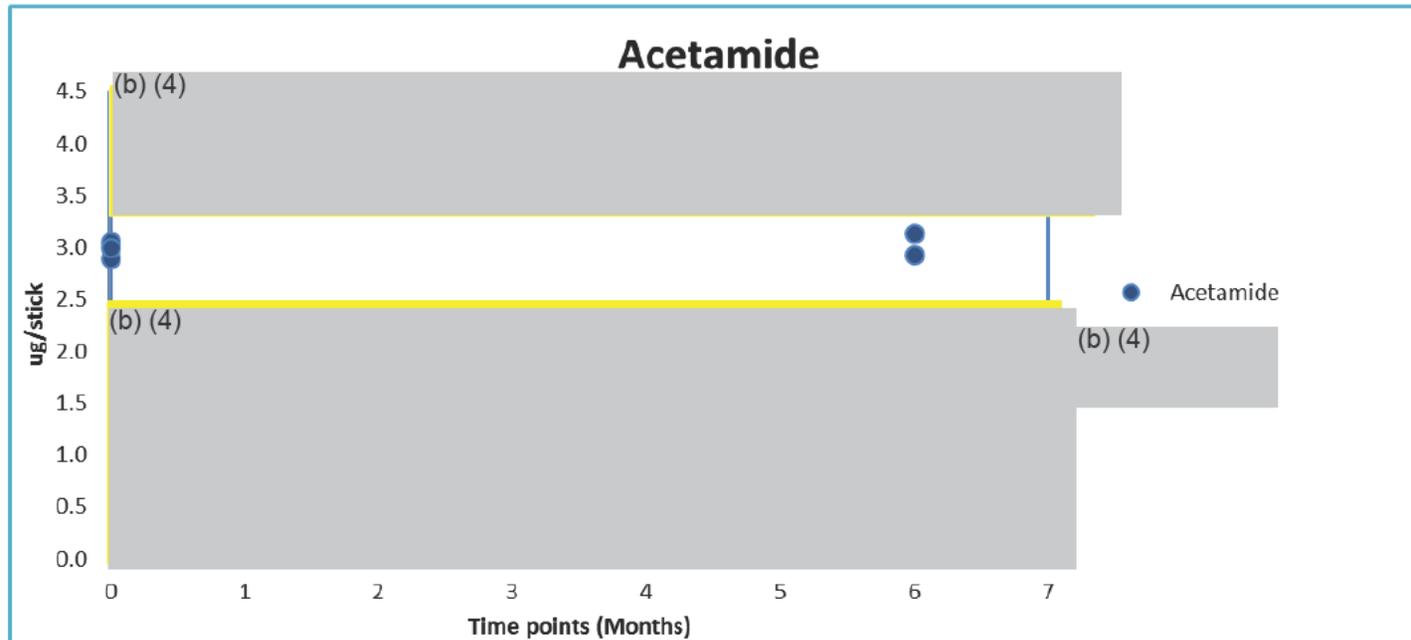


Figure 41 Acetamide is not suitable for trend analysis since it was tested in less than 3 different time points. All the values obtained are inside the specifications and therefore Acetamide is considered stable for 6 months.



6.3.1.10 Acetaldehyde

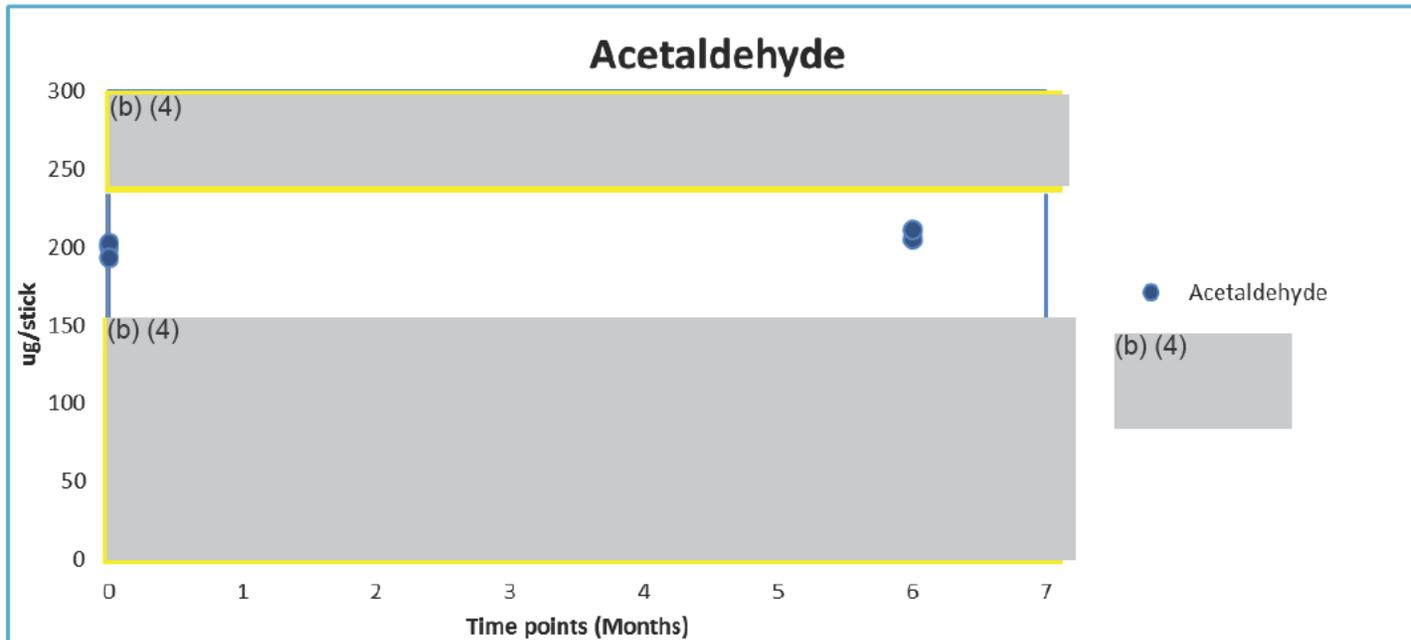


Figure 42 Acetaldehyde is not suitable for trend analysis since it was tested in less than 3 different time points. All the values obtained are inside the specifications and therefore Acetaldehyde is considered stable for 6 months.



6.3.1.11 Butyraldehyde

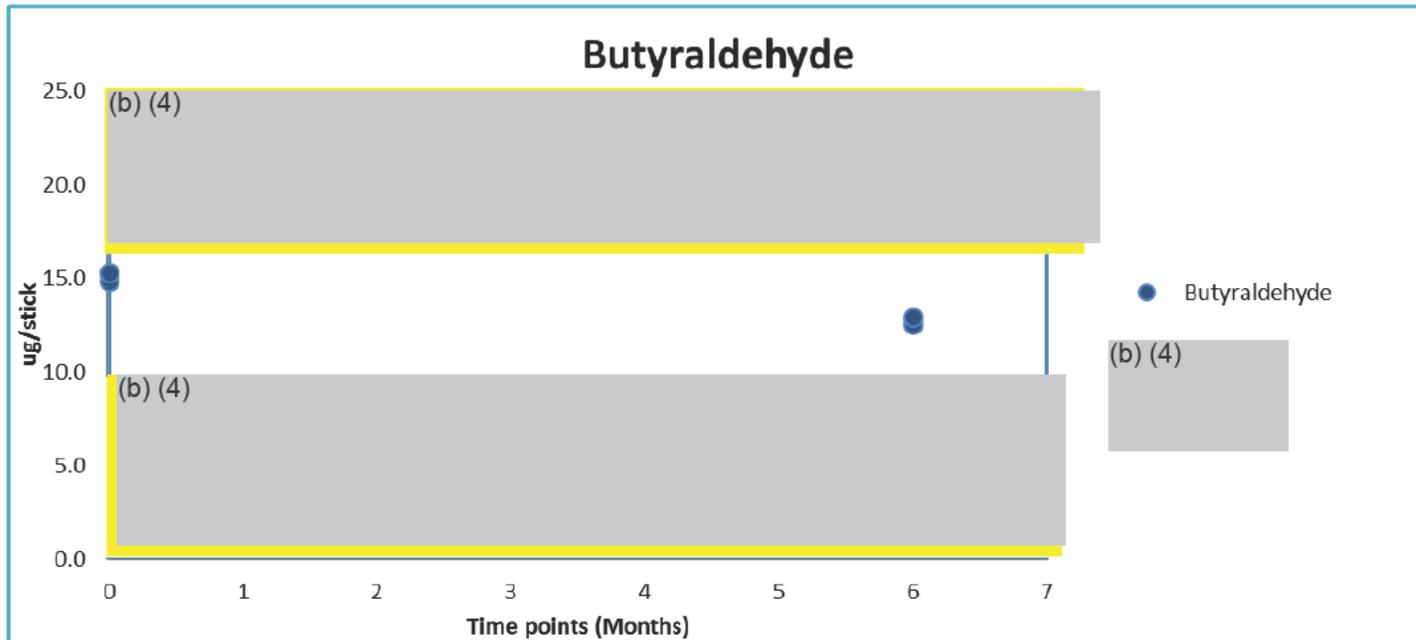


Figure 43 Butyraldehyde is not suitable for trend analysis since it was tested in less than 3 different time points. All the values obtained are inside the specifications and therefore Butyraldehyde is considered stable for 6 months.



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6.3.1.12 Acrylonitrile

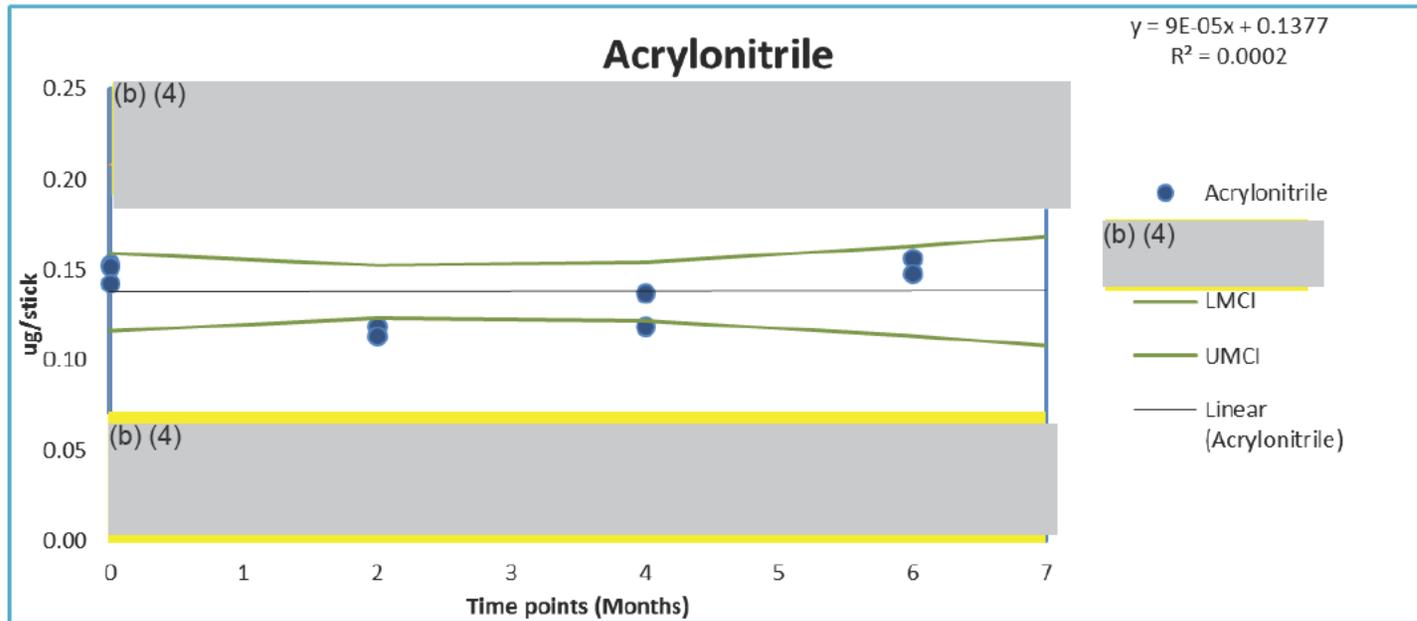


Figure 44 The best model accepted at the significance level of 0.25 has Common intercepts and Common slopes. The model suggests the earliest crossing time over 6 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 6 months.



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Form Status: Effective
Form Effective Date: See EDMS

6.3.1.13 Isoprene

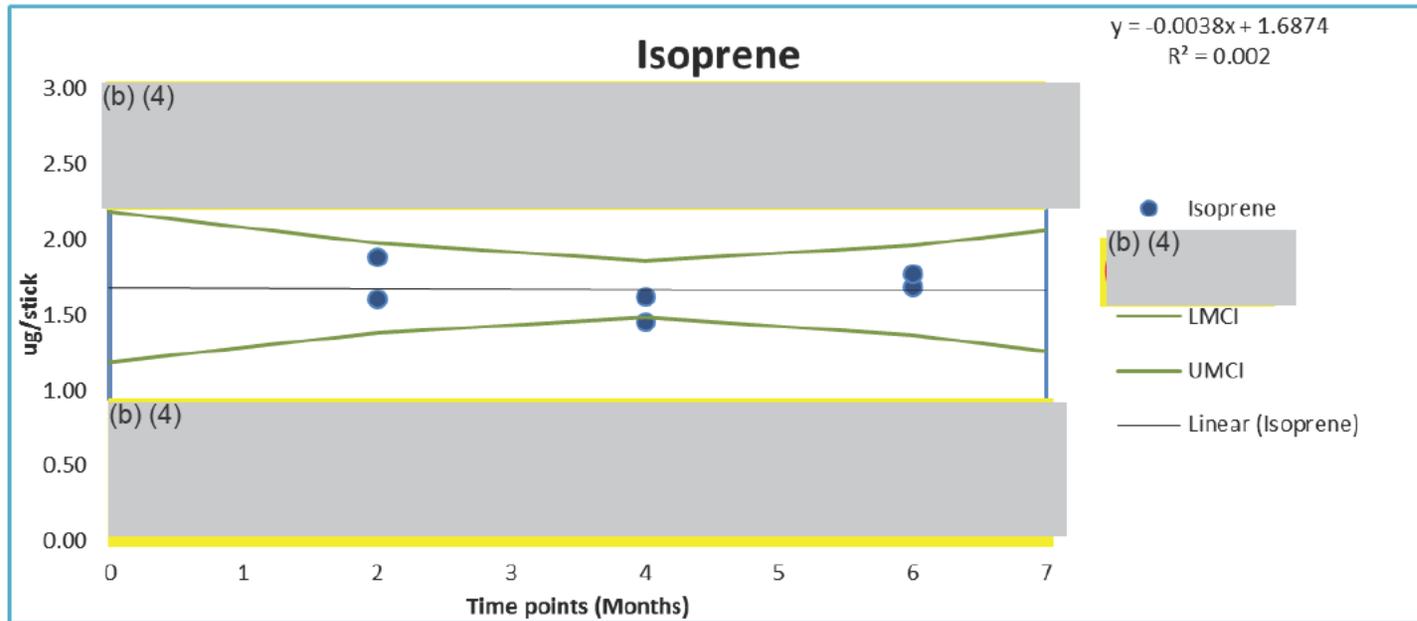


Figure 45 The best model accepted at the significance level of 0.25 has Different intercepts and Different slopes. The model suggests the earliest crossing time over 6 months with 95 percent confidence. ICH Guidelines indicate an expiration time of 6 months.



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6.3.1.14 Pyridine

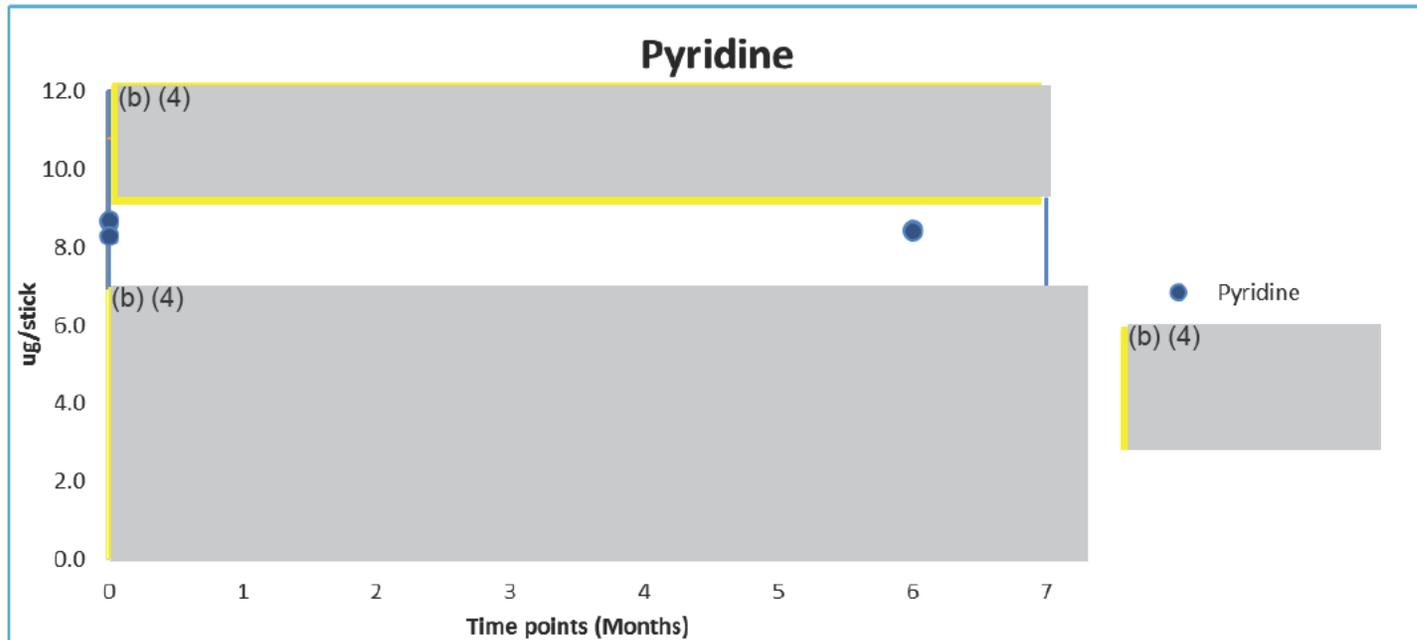


Figure 46 Pyridine is not suitable for trend analysis since it was tested in less than 3 different time points. All the values obtained are inside the specifications and therefore Pyridine is considered stable for 6 months.



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Form Effective Date: See EDMS

6.3.1.15 Ammonia

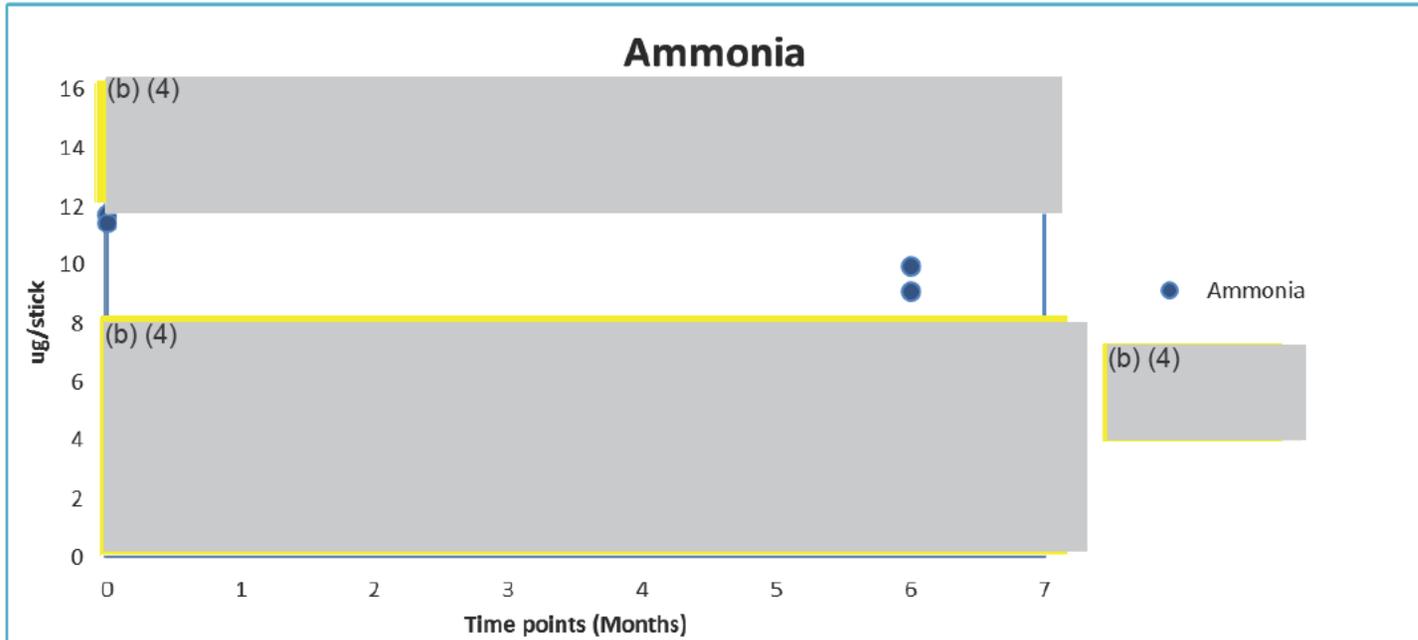


Figure 47 Ammonia is not suitable for trend analysis since it was tested in less than 3 different time points. All the values obtained are inside the specifications and therefore Ammonia is considered stable for 6 months.



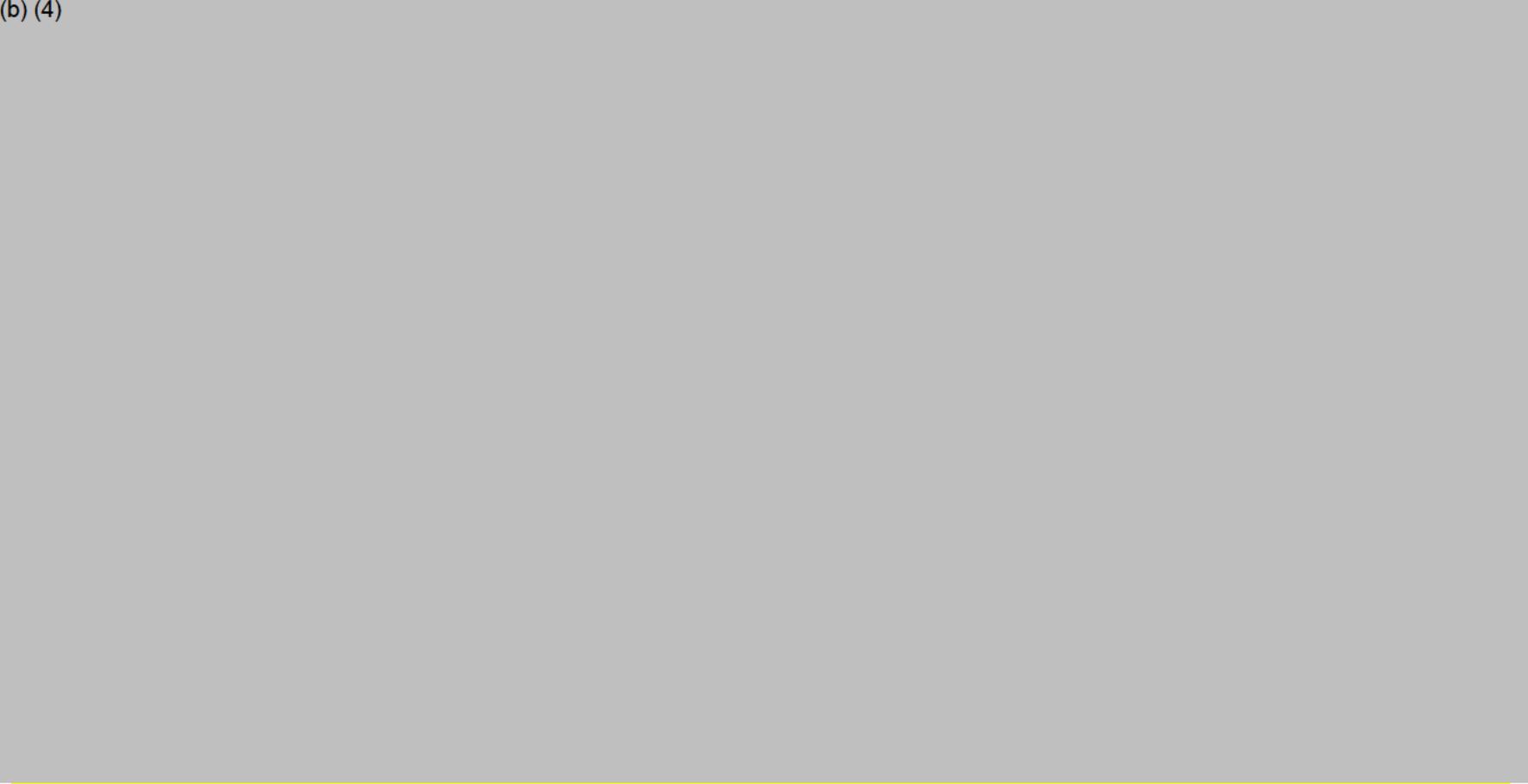
Form Number: PMI_RD_FOR_000927
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6.3.2 Physical Attributes Evaluation

(b) (4)





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(b) (4)



(b) (4)



(b) (4)





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6.3.3 Sensorial Evaluation

Sensorial evaluation results are described in details in a separate report [4].

(b) (4)

(b) (4)

A shelf life of 6 months is considered acceptable for this condition.

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.



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7 Stability Assessment

Overall it can be concluded that the THS 2.2 Dorado I Vinny High remained within specifications up to 11 months in the 22°C 60%RH, up to 12 months in the 30°C 35%RH conditions; and up to 5 months in the 30°C 75%RH.

In the conditions 22°C 60%RH all the product parameters remained with specifications for 12 months, except Menthol.

Menthol increased with time and remained within specification limit until 11 months. However, the product remains within the new toxicological threshold of 4.7 mg/stick [10] for 12 months.

In the storage conditions 30°C 35%RH all the product parameters remained with specifications for 12 months.

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

- Menthol, increased with time and remained within specification up to 5 months. However, the product remains within the new toxicological threshold of 4.7 mg/stick [10] for 6 months.
- 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 2.doc

<https://disco.app.pmi/disco/drl/objectId/0901d4ec8061126d>

[2] P1 Product specifications

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

[3] P1_PDev_SPE_D1 High batch release specification

<https://disco.app.pmi/disco/drl/objectId/0901d4ec805e1a9d>

[4] P1_PDev_SPE_D1 High Performance specification

<https://disco.app.pmi/disco/drl/objectId/0901d4ec805e037c>

[5] P1_CPD_SWP_Product monitoring_SS_035_2017_02_1_MRTP_DI Vinny High_T12

<http://rrpplm.app.pmi/Agile/PLMServlet?action=OpenEmailObject&classid=18387&objid=264907>

[6] Test Thermomapping RLS-TIM-16-22 and RLS-TIM-16-23.doc

<https://disco.app.pmi/disco/drl/objectId/0901d4ec806c6416>

[7] Scientific Report: PT_AL_Isoprene Investigation_PMI_RD_WKI_000383

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

[8] P1 THS 2 2 STABILITY STUDY REPORT DII RON STAB-2014_P1_R_1.doc

<https://disco.app.pmi/disco/drl/objectId/0901d4ec805507ce>



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[9] P1 THS 2 2 STABILITY STUDY REPORT DI VINNY HIGH STAB-2014_P1_M_1.doc

<https://disco.app.pmi/disco/drl/objectId/0901d4ec8055090b>

[10] Menthol Threshold Level in PMI Products, F. Vonmoos, V1.0, 05-Oct-2017

[11] PMI_RD_FOR_000932_STAB-2016_P1_M_5_OOS Triacetin_T0.doc

<https://disco.app.pmi/disco/drl/objectId/0901d4ec805da5f4>

[12] PMI_RD_FOR_000932_STAB-2016_P1_M_5_OOT Menthol_T2.doc

<https://disco.app.pmi/disco/drl/objectId/0901d4ec805ecf79>

[13] PMI_RD_FOR_000932_STAB-2016_P1_M_5_OOT Menthol Phenol Triacetin_T9.doc

<https://disco.app.pmi/disco/drl/objectId/0901d4ec806650ca>

[14] PMI_RD_FOR_000932_STAB-2016_P1_M_5_OOT Menthol_T12.doc

<https://disco.app.pmi/disco/drl/objectId/0901d4ec8069f0ea>

[15] PMI_RD_FOR_000932_STAB-2016_P1_M_5_OOT Acetamide_T12.doc

<https://disco.app.pmi/disco/drl/objectId/0901d4ec8069f0e4>

[16] PMI_RD_FOR_000932_STAB-2016_P1_M_5_OOT Isoprene Acrylonitrile_T12.doc

<https://disco.app.pmi/disco/drl/objectId/0901d4ec8069f0e8>

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

10 Revision History for Stability Report

Version Nr	Description of change	Justification
1.0	Initial version.	NA

11 Definitions and Abbreviations

Abbreviation	
CO	Carbon Monoxide
ICH	International Conference on Harmonization



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Abbreviation	
IP	Intermediate Precision
ISO	International Organization for Standardization
(b) (4)	
FOR	Form
LMCI	95% lower mean confidence interval for the predicted values
LSL	Lower Shelf Life specification limit
OMSP	Operation Management System Portal
OOS	Out of Specification
OOT	Out of Trend
P1	Platform 1
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
RH	Relative Humidity
SDMS	Scientific Data Management System
SOP	Standard Operation Procedure
QC	Quality Control
THS	Tobacco Heating System
TIM	Test Item Management
TO	Testing Order
TPM	Total Particulate Matter
USL	Upper Shelf Life specification limit



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Abbreviation	
UMCI	95% upper mean confidence interval for the predicted values
WHO	World Health Organization
WKI	Work Instruction

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_000385	PMI-RRP-WKI-111707
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
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](#)).



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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-12072, TO-12073, TO-12075	RLS-ZRH-2016-334/335
T2	TO-12688, TO-12690; TO-12741	RLS-ZRH-2016-451/454
T4	TO-13289, TO-13290, TO-13292	RLS-ZRH-2016-570/571
T6	TO-13809, TO-13811, TO-13812	RLS-ZRH-2017-115/117
T9	TO-14658, TO-14661, TO-14662	RLS-ZRH-2017-355/356
T12	TO-15669, TO-15670, TO-15703	RLS-ZRH-2017-844/845