

Module 6: Customer Feedback Regarding PVT



Case 1-a



Apparatus 1 -- 1-stage test for equipment with 7 positions

Acceptance criteria for USP Prednisone Tablets RS, R031Y1

GeoMean, lower	54
GeoMean, upper	84
%CV, upper	11

Run 1 Data		Run 2 Data	
Vessel 1	61.8	Vessel 1	70.8
Vessel 2	59.6	Vessel 2	52.1
Vessel 3	52.4	Vessel 3	46.1
Vessel 4	46.5	Vessel 4	53.7
Vessel 5	49.6	Vessel 5	68.3
Vessel 6	51.6	Vessel 6	44.7
Vessel 7	68.4	Vessel 7	45.8

Test Results		
Combined GeoMean	54	Meets
Combined %CV	17	Does not meet

FAILS

Case 1-b



Apparatus 1 -- 1-stage test for equipment with 7 positions

Acceptance criteria for USP Prednisone Tablets RS, R05990

GeoMean, lower	54
GeoMean, upper	83
%CV, upper	11

Run 1 Data		Run 2 Data	
Vessel 1	54.0	Vessel 1	49.9
Vessel 2	52.6	Vessel 2	53.4
Vessel 3	62.6	Vessel 3	48.3
Vessel 4	53.0	Vessel 4	52.2
Vessel 5	47.2	Vessel 5	50.0
Vessel 6	53.3	Vessel 6	42.1
Vessel 7	57.4	Vessel 7	32.4

Test Results		
Combined GeoMean	50	Does not meet
Combined %CV	14	Does not meet

FAILS

Case 1



- ▶ Clarification was needed regarding the following:
 - Designated vessels in the dissolution apparatus
 - Designated baskets
 - Appearance and cleanliness of the baskets
 - Helium sparging was used for the de-aeration of the medium
 - The volume of medium was measured using 500 ml graduated cylinder
 - Different filter material was used for the filtration of the sample solutions
 - The filter material was neither pre-wetted nor saturated before filtration
- ▶ Response:

“Thank you for your support. We happily passed calibration with different analyst and new tablets lot.”

Case 2



Apparatus 2 -- 2-stage test for equipment with 6 positions

Acceptance criteria for USP Prednisone Tablets RS, R031Y1

▶ PVT App. 2

- Mechanical qualification conducted
- De-aeration of the medium using automated degassing system
- Simultaneous start
- Sampling and filtration manually

	Stage 1	Stage 2
GeoMean, lower	29	27
GeoMean, upper	36	40
%CV, upper	4.7	6.3

Stage 1 (Run 1) data	
Vessel 1	36.202
Vessel 2	37.463
Vessel 3	30.818
Vessel 4	35.057
Vessel 5	39.983
Vessel 6	36.546

Test Results		
1st Stage GeoMean	36	Meets
1st Stage %CV	8.7	Does not meet

Stage 2 necessary; enter Stage 2 data

Case 2 -a



Original vessels were replaced with certified ones.



Apparatus 2 -- 2-stage test for equipment with 6 positions

Acceptance criteria for USP Prednisone Tablets RS, R031Y1

	Stage 1	Stage 2
GeoMean, lower	29	27
GeoMean, upper	36	40
%CV, upper	4.7	6.3

Stage 1 (Run 1) data	
Vessel 1	34.765
Vessel 2	33.754
Vessel 3	35.863
Vessel 4	34.554
Vessel 5	35.862
Vessel 6	34.298

Test Results		
1st Stage GeoMean	35	Meets
1st Stage %CV	2.4	Meets

PASSES

Case 3



Description of the issue:

- ▶ “We are seeing multiple failures in the field especially with USP Apparatus 1 with high variability. We are seeing these failures on an apparatus previously not having any issues, and they are meeting the Enhanced MQ tolerances, vibration is in check, and components are clean and in perfect condition. Also, the analysts are veterans at performing PVT and some of these apparatus are brand new; we have never had a problems passing the PVT in the past.”

After a few weeks later:

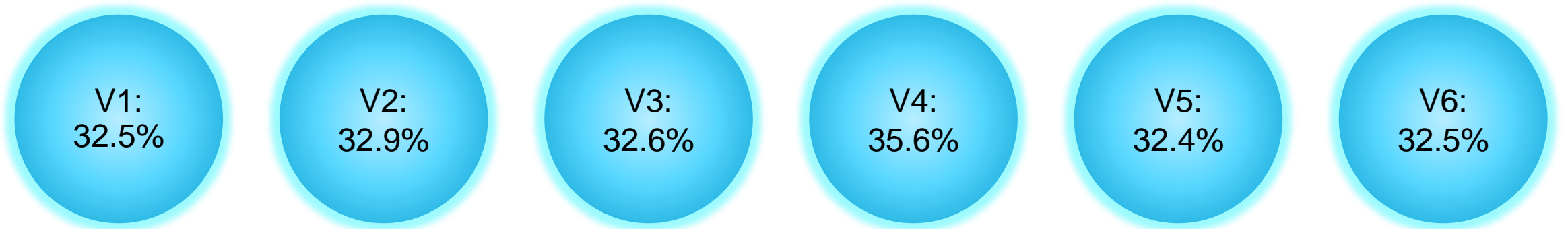
- ▶ “We are not pursuing the complaint at this time. A couple of GMP issues were found at a site that we believe contributed to high variability with the PVT. Issues have been addressed.”

Case 4



“After your training I started to use all the rules that you provided especially for medium degassing, and my results are better and have progressed after having experience in all steps that you recommended during the PVT test. Almost all dissolution tests I meet on the first step from six tablets.

I would like to share with you my results from my last tests are really improved and very precise. Please see below:”



Discussion



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