

Owning Location:	DPDS Analytical Development
Document Type: Subtype	Technical Document:General
Title:	Certificate of Analysis for CNTO 148 Primary Reference Standard Lot 13K03AA

Product	CNTO 148 Primary Reference Standard (PRS)
Material Description: (formulation)	10 mg/mL ¹ in 4.5% Sorbitol, 10 mM Histidine, 0.015% Polysorbate 80, pH 5.5
Material Master No.	306111
Lot No.	13K03AA
Manufacturer	Janssen Research & Development via 3rd party fill site PPD, Inc.
Date of Manufacture	03 October 2013
Batch Size	5022 vials
Volume	1 mL / vial
Expiry and Re-Qualification	This reference standard is subject to annual re-qualification according to TV-SPEC-13521 and can be used until the next re-qualification date = 30Jun2021
Storage and Handling	≤ -60°C protected from light. Before use, the Reference Standard is thawed by incubating the vial for 3 minutes at 37°C in a water bath. Subsequently the vial is rotated gently for 1 minute at room temperature. Store thawed Reference Standard at 2-8°C protected from light. Thawed reference standard may be used for up to 24 hours post-thaw.
Shipping	Frozen on dry ice

¹Note this is targeted concentration; use value from results when testing in method.

TEST	METHOD	SPECIFICATION	RESULTS
Bioburden	TV-SOP-31850	≤ 1 CFU/vial (1 mL) (individual)	Vial 1: 0 CFU/vial (1 mL) Vial 2: 0 CFU/vial (1 mL) Vial 3: 0 CFU/vial (1 mL)
Endotoxin by LAL	TV-TMD-31157 or TV-SOP-28784	≤ 0.21 EU/mg	< 0.20 EU/mg
pH	TV-TMD-31178	5.2-5.8 (individual)	Vial 1: pH 5.3

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TEST	METHOD	SPECIFICATION	RESULTS
			Vial 2: pH 5.3 Vial 3: pH 5.3
Color of Solution (USP)	TV-SOP-33501	Colorless to light yellow	Colorless
Color of Solution (EP)	TV-TMD-07857	Colorless to light yellow	Light yellow
Bioactivity Assay	TV-TMD-08359	All subsequent Primary Reference Standards: 85%-115% mean activity relative to the current Reference Standard	Activity: 100% SD: 3.6% (n=12) Mean +/- 3 SD range activity: 89% to 111% Paired t-test p-value ¹ : 0.884 Normalization Factor (NF) 1.000 ¹ P-value > 0.05: current WRS lot# 08G13AA. % potency does not differ statistically from the new PRS Lot#13K03AA.
SDS-PAGE (reduced)	TV-SOP-34964	Purity ≥ 95.0% (individual) Conforms to current Reference Standard, no new band >0.1% (individual)	Vial 1 97.6% Vial 2 98.1% Vial 3 97.8% Average of Vials 1-3: 97.8% Vials 1, 2, 3: Conforms to current Reference Standard, no new band > 0.1%
SDS-PAGE (non-reduced)	TV-SOP-34964	Conforms to current Reference Standard, no new band >0.1% (individual)	Vials 1, 2, 3: Conforms to current Reference Standard, no new band > 0.1%
IEF	TV-SOP-22051	Conforms to current Reference Standard (individual)	Vials 1, 2, 3: Conforms to current Reference Standard
SE- HPLC	TV-TMD-14206	≥ 95.0% Monomer as main component (individual). Retention time difference between new and previous Reference Standard is ≤ 0.1 minutes (individual).	Vial 1: > 99.5% Vial 2: > 99.5% Vial 3: > 99.5% Average of Vials 1-3: > 99.5% Vials 1, 2, 3: 0.0 minute retention time difference
DRID	TV-TMD-06481	Conforms to current Reference Standard	Conforms to current Reference Standard

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TEST	METHOD	SPECIFICATION	RESULTS	
Protein Concentration by A ₂₈₀	TV-TMD-16093	9.0-11.0 mg/mL (individual)	Average of Vials 1-6: 9.9 mg/mL Vial 1: 10.0 mg/mL (Leiden) Vial 2: 10.2 mg/mL (Leiden) Vial 3: 10.0 mg/mL (Leiden) Vial 4: 9.8 mg/mL (Cork) Vial 5: 9.8 mg/mL (Cork) Vial 6: 9.8 mg/mL (Cork)	
Peptide Map	TV-TEC-63313	No Peak (≥ 8% of the reference peak area for well resolved peaks, ≥ 16% of reference peak area for peaks that are not well resolved) between test article and current Reference Standard	No new peaks added or missing compared to the current Reference Standard.	
Oligosaccharide Map	TV-TMD-18195	Neutral Oligosaccharides ≥ 50% and major species elute within ± 0.6 min of zero, one and two galactose core-fucosylated species in current Reference Standard	Neutral oligosaccharides	
			Total neutral oligosaccharides	86.9%
			G0F (Agalacto, core-fucosylated)	0.0 min difference
			G1F (Mono-galacto, core-fucosylated)	0.0 min difference
		Charged Oligosaccharides ≤ 50% and major species elute within ± 0.6 min of sialylated core-fucosylated species in current Reference Standard	G2F (Di-galacto, core-fucosylated)	0.0 min difference
			Charged oligosaccharides	
			Total charged oligosaccharides	13.1%
			Mono-sialylated	0.0 min difference
			Di-sialylated	0.0 min difference

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TEST	METHOD	SPECIFICATION	RESULTS		
Intact Molecular Mass by mass spectrometry (after carboxypeptidase treatment)	TV-TEC-26293	Masses of 4 major glycoforms within ± 42 Da of the current Reference Standard glycoforms after carboxypeptidase treatment	Masses of 4 major glycoforms compared to current Reference Standard: Glycoform 2: 2 Da difference Glycoform 3: 1 Da difference Glycoform 4: 1 Da difference Glycoform 5: 2 Da difference		
Analytical Ultracentrifugation (AUC)	TV-SOP-33958 v2.0	s ⁰ _{20,w} within ± 0.4 S of current Reference Standard (individual)	Vials 1,2,3: s ⁰ _{20,w} within ± 0.4 S of current Reference Standard		
DW-SE-HPLC	TV-TMD-14206	≥ 99.60% Monomer; ≤ 0.22% Aggregate; ≤ 0.15% Fragment (individual)	Vial	Species	Peak Area (%) ^a
			1	Monomer	≥99.92
				Aggregate	< 0.08
				Fragment	< 0.08
			2	Monomer	≥99.92
				Aggregate	< 0.08
				Fragment	< 0.08
			3	Monomer	≥99.92
				Aggregate	< 0.08
				Fragment	< 0.08
			Average of Vials 1-3	Monomer	≥99.92
				Aggregate	< 0.08
				Fragment	< 0.08
			^a The sum of reported impurity peaks plus monomer may not equal 100% due to rounding differences and to the presence of impurity peaks with areas below 0.08% (LOQ); these peaks are included in the calculations of total peak area but are not reported individually.		

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TEST	METHOD	SPECIFICATION	RESULTS		
cIEF	TV-TMD-07104	Sum of percent area of 4 major peaks (C,1,2,3) ≥ 91%; Area%: Peak 3: 12 to 29% Peak 2: 34 to 42% Peak 1: 20 to 33% Peak C: 6 to 15% Peak B: ≤ 7% 4 major peaks (C,1,2,3) within 0.05 pl units of the corresponding peak in the current Reference Standard (individual)	Peak ^a	Δ pl ^b	Area Percent (%)
			Vial 1		
			Peak 3	0.01	27
			Peak 2	0.01	38
			Peak 1	0.00	23
			Peak C	0.01	8
			Peak B	NR	3
			Sum of % peak area of C, 1, 2, 3		97
			Vial 2		
			Peak 3	0.00	27
			Peak 2	0.00	38
			Peak 1	0.01	23
			Peak C	0.00	8
			Peak B	NR	2
			Sum of % peak area of C, 1, 2, 3		97
			Vial 3		
			Peak 3	0.00	27
			Peak 2	0.00	38
			Peak 1	0.01	23
			Peak C	0.00	8
			Peak B	NR	3
			Sum of % peak area of C, 1, 2, 3		96
			Average of Vials 1-3		
			Peak 3	0.00	27
			Peak 2	0.00	38
			Peak 1	0.01	23
			Peak C	0.00	8
			Peak B	NR	3
			Sum of % peak area of C, 1, 2, 3		97
			^a All peaks with ≥ 2.0% area (limit of quantitation).		
^b pl difference from current Reference Standard.					
^c NR - Not reportable, peak area was < 2.0% (limit of quantitation)					

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TEST	METHOD	SPECIFICATION	RESULTS
cSDS (reduced)	TV-TMD-19833	Purity $\geq 98.3\%$ (individual) No new peak > 0.2% compared to current reference standard	Vial 1: 98.8% purity Vial 2: 98.9% purity Vial 3: 98.8% purity Average of Vials 1-3: 98.8% purity Vials 1, 2, 3: No new peak > 0.2% compared to current reference standard
cSDS (non-reduced)	TV-TMD-11936	Purity $\geq 98.3\%$ (individual) No new peak > 0.2% compared to current reference standard	Vial 1: 98.9% purity Vial 2: 98.8% purity Vial 3: 99.0% purity Average of Vials 1-3: 98.9% purity Vials 1, 2, 3: No new peak > 0.2% compared to current reference standard
Deamidation Assay	TV-TMD-01345	Total deamidated LC Asn93: $\leq 5.8\%$	Vial 1: LC= 2.8% HC= 67% %HC= 26%
		Total deamidated HC Asn43: $\leq 79\%$	Vial 2: LC= 2.9% HC= 67% %HC= 27%
		%HC IsoAsp43: $\leq 30\%$	Vial 3: LC= 3.0% HC= 67% %HC= 26%

END OF DOCUMENT

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Document Revision History			
Version Number	Section	Description of Change	Justification of Change
9.0	All	Formatted document according to the current template and replaced legacy document numbers with current document numbers	Current template harmonization
	Manufacturer	Added Manufacturer: Janssen Research & Development via 3rd party fill site PPD, Inc.	Information required on CofA per TV-SOP-29122
	Expiry and Re-qualification	Changed re-qualification date from 30Jun2020 to 30Jun2021 following annual re-qualification testing. Re-qualification reference: TV-TEC-25058 Version 6.0	Updated re-qualification date based on completed annual testing.
	Deamidation Assay	Correct legacy method number from DS-TMS-4290 to DS-TMD-4290 and then replaced with current document number TV-TMD-01345	Corrected typographical error
8.0	Bioactivity Assay	Activity changed from 99% to 100%. Mean +/- 3SD range activity range changed from "89% to 110%" to "89% to 111%."	Updated statistical report for bioactivity qualification, TV-TEC-108926, version 2.0.
7.0	Expiry and Re-Qualification	Changed re-qualification date from 30Jun2019 to 30Jun2020 following annual re-qualification testing. Re-qualification reference: TV-TEC-25058 Version 5.0	Updated re-qualification date based on completed annual testing.
6.0	Expiry and Re-Qualification	Deleted "Expiry: 30 Jun 2019" and "Re-qualification:" Changed re-qualification date from 22Sep2018 to 30Jun2019 following annual re-qualification testing. Re-qualification reference: TV-TEC-25058 Version 4.0	Updated re-qualification date based on completed annual testing and will reach initial 5-year expiry
	Document Revision History	Added version numbers for past re-qualification references for TV-TEC-25058	Traceability since same document is revised each year

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Document Revision History			
Version Number	Section	Description of Change	Justification of Change
5.0	Expiry and Re-Qualification	Changed re-qualification date from 22Sep2017 to 22Sep2018 following annual re-qualification testing. Re-qualification reference: TV-TEC-25058 Version 3.0	Updated re-qualification date based on completed annual testing.
4.0	Expiry and Re-Qualification	Changed re-qualification date from 22Sep16 to 22Sep2017 following annual re-qualification testing. Re-qualification reference: TV-TEC-25058 Version 2.0	Updated re-qualification date based on completed annual testing.
3.0	Expiry and Re-Qualification	Changed re-qualification date from 22Sep15 to 22Sep16 following annual requalification testing. Changed TV-SOP-29122 to TV-SPEC-13521. Requalification references: TV-TEC-25058 Version 1.0; TV-REF-131483	Updated requalification date based on completed annual testing.
2.0	Expiry and Re-Qualification	Changed re-qualification date from 30June15 to 22Sep15	Updated to appropriate requalification date as per TV-SOP-29122.
1.0	All	New Document	N/A

Document Approvals

Approved Date:

Additional Approval Task Verdict: Approve	Jason Lim, (jlim65@its.jnj.com) Data Verifier Approval 25-Jun-2020 02:43:57 GMT+0000
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