PEPTIDE ANDA

DRUG DELIVERY EXPERTS

Case: Support an ANDA submission of a synthetic polypeptide (generic drug product)

DDE Scientific Team

- Formulation development
- Analytical assay development – Specification establishment
- Development stability study
- Process development
- CCS/device selection & qualification

DDE Consulting group

- CMO qualification & selection support
- Tech transfer (process & analytical)

CMO

- ER batch
- 3 GMP batches

- Method transfer
- Data review
- Oversee testing activity

CRO

- GMP stability studies
- Release testing
- USP method verification

Established Target Product Profile and Critical Quality Attributes

QTPP Elements	Target	Justification
Dosage Form	Sterile solution in a pre-filled syringe	Matches RLD
Route of Administration	Subcutaneous Injection	Matches RLD
Dosage Strength; Label Claim	10 mg/mL, 3 mL per injection	Matches RLD
Appearance	Clear and colorless solution	Matches RLD
pH	5.5	Matches RLD
Osmolality	270 To 350 mOsm/kg	Matches RLD
Container closure/delivery device	Type 1 glass, 3 mL syringe, 25G, 5/8" length needle	Matches RLD
Storage condition	< 25°C	Matches RLD
Stability	24 M	Currently confirmed to be >18M. Need for commercialization

Drug product quality attributes	Physical Attributes	Pharmaceutical equivalence requirement: Must meet the same compendia or other applicable (quality) standards (i.e., identity, assay, purity, and quality).
	Identification	
	Assay	
	Content Uniformity	
	Impurities profile	
	Microbial Limits	

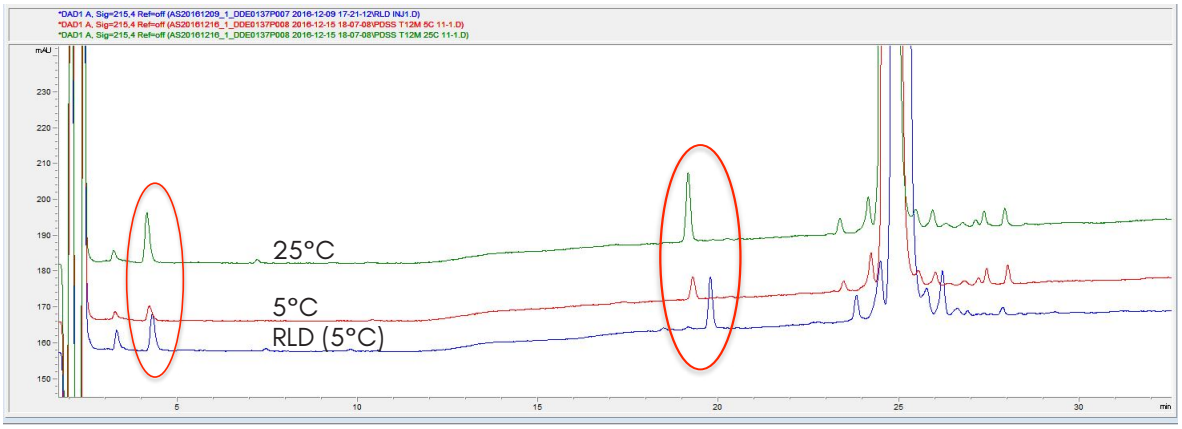
Established Drug Product Specification

Test		Acceptance Criteria	Test method
Appearance:		Colorless、clear solution, Extrinsic Foreign matter is not detected	USP <790>
Identification		The retention time difference between the standard and sample is not more than 2.0%	Test Method: RP-HPLC
pH		pH: 5.5 ± 0.3	Test: USP < 791 >
Particulate Matter		NMT 6,000 counts/container ≥ 10 µm NMT 600 counts/container ≥ 25 µm	Test: USP < 787 >
Osmolality		NLT 270 mOsm/kg NMT 350 mOsm/kg	Test: USP < 785 >
Assay (%)		90.0 - 110.0%	Test Method: RP-HPLC
Purity		NLT 90.0%	Test Method: RP-HPLC
Total Related Impurity (%)		NMT 10.0%	Test Method: RP-HPLC
Specified identified impurity (%)		RRT 0.15 to 0.22 Impurity 1: NMT 1.1% RRT 0.68 to 0.88 Impurity 2: NMT 1.2% RRT 0.91 Impurity 3: NMT 0.1% RRT0.97~1.0 combined impurities: NMT 1.5% RRT 1.03 Impurity 4: NMT 0.1% RRT 1.06 Impurity 5: NMT 0.3% RRT 1.07 Impurity 6: NMT 0.4%	Test Method: RP-HPLC
Non specified, unidentified impurity (%)		NMT 0.2 %	Test Method: RP-HPLC
BET	Sterility	NMT 100 CFU/ml	USP < 71 >
	Endotoxin	NMT 32 EU/dose	USP < 85 >
Glide force		Break Loose force: < 30 N Glide force: <15 N	ISO 11040-2
Volume Delivery		NLT 3.0 mL	USP < 1 >
Uniformity of Dosage Units		Acceptance Values: • L1 ≤ 15 • L2 ≤ 15	USP < 905 >

Characterization of Impurity Profile Over 12 Month Storage Period

Peaks grow in over the storage period

- Impurity profile bench-marked against RLD
- Similar profile was observed
- Two major degradants were observed



For More Information, Please Visit *www.drugdeliveryexperts.com*

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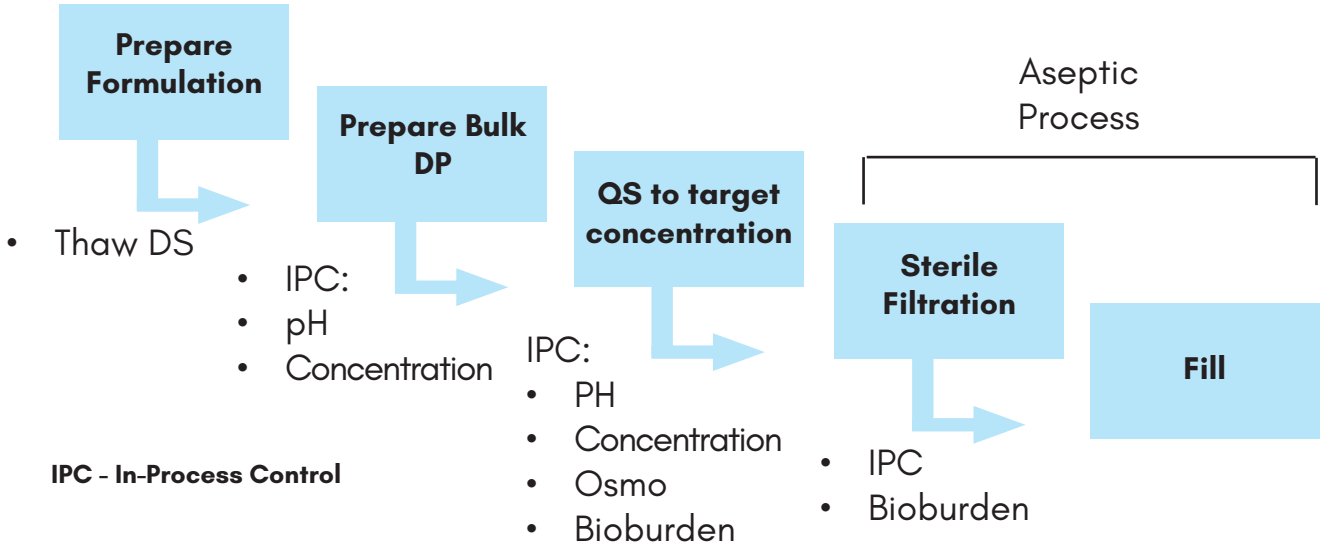
Established Manufacturing Process and Technology Transfer to CMO



IPC - In-Process Control

Quality Control of Drug Product Manufactured by CMO

- DP samples: Manufactured at CMO, aseptic manufacture
- Impurity 1 & 2 were not observed at T0 – Impurity 1 & 2 are susceptible to heat treatment or under ambient storage condition
- Aseptic manufacture process is recommended over the terminal sterilization proess
- RLD: reference listed drug