S.4 CONTROL OF DRUG SUBSTANCE

S.4.1 SPECIFICATION FOR DRUG SUBSTANCE

Test procedure	Acceptance criteria	Method reference
Description	A white to brown powder	Visual inspection
Identification	Conforms with reference	Identification by IR spectroscopy Identification by HPLC
Assay (on water and solvent free basis)	98% to 102% w/w	Assay by LC
Drug Substance Related Organic impurities:		Organic impurities by LC
Impurity 1	NMT 0.5% w/w	
Impurity 2	NMT 0.5% w/w	
Any individual unspecified impurity	NMT 0.10% w/w	
Total impurities	NMT 2.0% w/w	
Mutagenic impurities		ACP-5187 content by LC-MS
Impurity - Mutagenic	NMT 50 ppm	
Enantiomeric purity	NLT 99.6%	Enantiomeric purity by LC
Residual solvents:		Residual solvents by headspace GC
Solvent 1	NMT 0.1% w/w	
Solvent 2	NMT 2.0% w/w	
Water content	NMT 1.0%	USP Karl Fischer titration
Particle size distribution		Laser diffraction
$D_{(v, 0.9)}$	NMT 319 µm	
$D_{(v, 0.5)}$	NMT 145 µm	
$D_{(v, 0.1)}$	NMT 20 µm	
Residue on ignition/sulphated ash	NMT 0.1% w/w	USP

NLT Not more than.
NMT Not less than.

Drug Substance Test procedure
Description
Identification
Assay (on water and solvent free basis)
Organic impurities:
Impurity 1
Impurity 2
Impurity 3
Any individual unspecified impurity
Total impurities
Mutagenic impurities
Impurity - Mutagenic
Enantiomeric purity
Residual solvents:
Methanol
Ethanol
Water content
Particle size distribution $D_{(v, 0.9)}$ $D_{(v, 0.5)}$ $D_{(v, 0.1)}$
Polymorph B
Residue on ignition/sulphated ash

Drug Product Test procedure
Description
Identification
Assay
Degradation products
Impurity 1
Impurity 2
Impurity 3
ACP-5944
Individual unspecified degradation products
Total degradation products
Nitrosamine
Polymorph B
Dissolution
Uniformity of dosage units
Microbiological quality