

Control of residual monomers in the carrier

No organic solvent was used in the preparation process of Arginase, and the main risk was introduced by the polymer epoxy resin carrier used in the immobilization process. According to the information provided by the supplier, the monomer composition of the carrier is Glycidyl methacrylate and ethylene glycol dimethacrylate, the initiator is Azobisisobutyronitrile, and the solvents used in the production of the carrier are toluene, xylene, and methanol. For the above impurities, a determination method of residual solvents in Arginase has been established. Through the detection of several batches of residual solvents in Arginase, it can be seen that the residual solvents in Arginase are far below the residual limit. The risk of monomer and solvent residues in Arginase is small,

Production process control: The conversion process is stirred at low speed to avoid carrier collision and breakage, and the subsequent material liquid is crystallized after precision filtration. The filter membrane can intercept the broken carrier. Avoid residual carriers in the finished product.

Table 1 Control limit and basis of residual monomer and solvent in Arginase

Item	Control Limits	Standard basis
Glycidyl methacrylate	≤27.27mg/kg	ECHA
Azobisisobutyronitrile	≤10.91mg/kg	ICH M7
EGMa	≤500mg/kg	
Toluene	≤20mg/kg	GB/T 24395-2009
O-xylene	≤20mg/kg	
O-xylene		
O-xylene		

Table 3.2.S.2.3.3-7 Test Results of Arginase Residual Solvent

Item	Control standards	Detection limit	G19SM3122022010 1	G19SM3122022050 3
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Jing Jing Pharmaceutical Co., Ltd.

Glycidyl methacrylate	≤27.27mg/k g	1.4 mg/k g	Not detected	Not detected
Azobisisobutyronitrile	≤10.91mg/k g	1.5 mg/k g	Not detected	Not detected
EGMa	≤500 mg/kg	1.5 mg/k g	Not detected	Not detected
Toluene	≤20mg/kg	0.6 mg/k g	Not detected	Not detected
O-xylene	≤20mg/kg	0.3 mg/k g	Not detected	Not detected
O-xylene				
O-xylene				