



100 Majestic Way, Bangor, PA 18013 / www.biospectra.us

ELEMENTAL IMPURITY ASSESSMENT

MATERIAL NAME: BIS-TRIS 2023 E04 VALIDATION

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| Table 1: Elemental Impurity Risk Assessment | | Analytical Method: BSI-ATM-0075 Method Validation Report: BSI-RPT-0803 Galactose Bio Excipient Grade Batch Record DCN: BSI-MPR-0065 Manufacturing Process DCN: BSI-PRL-0603 Degradation and Impurity Protocol: BSI-PRL-0620 Degradation and Impurity Report: BSI-RPT-1316 Parenteral Specifications (10g/day MDD) | |
|----------------------------------------------------|--------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------|
| Element | Class | ¹Limits 1.0J Target ppm (µg/g) | Control Threshold Limits 0.3J Target ppm (µg/g) |
| Cd | 1 | 0.20 | 0.06 |
| Pb | 1 | 0.50 | 0.15 |
| As | 1 | 1.5 | 0.045 |
| Hg | 1 | 0.30 | 0.09 |
| Co | 2A | 0.50 | 0.15 |
| V | 2A | 1.0 | 0.30 |
| Ni | 2A | 2.0 | 0.60 |
| Tl | 2B | 0.80 | 0.24 |
| Au | 2B | 10 | 3.0 |
| Pd | 2B | 1.0 | 0.30 |
| Ir | 2B | 1.0 | 0.30 |
| Os | 2B | 1.0 | 0.30 |
| Rh | 2B | 1.0 | 0.30 |
| Ru | 2B | 1.0 | 0.30 |
| Se | 2B | 8.0 | 2.4 |
| Ag | 2B | 1.0 | 0.30 |

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|----------------------------------------------------|--------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------|
| Element | Class | ¹Limits 1.0J Target ppm (µg/g) | Control Threshold Limits 0.3J Target ppm (µg/g) |
| Pt | 2B | 1.0 | 0.30 |
| Li | 3 | 25 | 7.5 |
| Sb | 3 | 9.0 | 2.7 |
| Ba | 3 | 70 | 21 |
| Mo | 3 | 150 | 45 |
| Cu | 3 | 30 | 9.0 |
| Sn | 3 | 60 | 18 |
| Cr | 3 | 110 | 33 |
| Fe | 4 | 10 | 3.0 |
| K | 4 | 50 | 15 |
| Na | 4 | 50 | 15 |

¹Limits derived from Analytical Method BSI-ATM-0075

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| TABLE 2: ELEMENTAL IMPURITY ASSESSMENT | | | | | Analytical Method: BSI-ATM-0075 Method Validation Report: BSI-RPT-0803 Bis-Tris Bio Excipient Grade Batch Record DCN: BSI-MPR-0065 Manufacturing Process DCN: BSI-PRL-0603 Degradation and Impurity Protocol: BSI-PRL-0620 Degradation and Impurity Report: BSI-RPT-1316 Parenteral Specifications (10g/day MDD) | | |
|-----------------------------------------------|--------------|--------------------------------------|--------------------------------------------------------|--------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------|----------------------------------------------------------------------|
| Element | Class | Limits 1.0J Target ppm (µg/g) | Control Threshold Limits 0.3J Target ppm (µg/g) | Result RM Lot: M155 0705 ppm (µg/g) | Result ML Lot: BTRI-0123-00003-PV ML ppm (µg/g) | Result WC Lot: BTRI-0123-00003-PV WC 1st Basket ppm (µg/g) | Result FG Lot: BTRI-0123-00003-PV Beginning Drum 1 ppm (µg/g) |
| Cd | 1 | 0.20 | 0.06 | <0.06 | <0.06 | <0.06 | <0.06 |
| Pb | 1 | 0.50 | 0.15 | <0.15 | <0.15 | <0.15 | <0.15 |
| As | 1 | 1.5 | 0.045 | <0.45 | <0.45 | <0.45 | <0.45 |
| Hg | 1 | 0.30 | 0.09 | <0.09 | <0.09 | <0.09 | <0.09 |
| Co | 2A | 0.50 | 0.15 | <0.15 | <0.15 | <0.15 | <0.15 |
| V | 2A | 1.0 | 0.30 | <0.30 | <0.30 | <0.30 | <0.30 |
| Ni | 2A | 2.0 | 0.60 | <0.60 | <0.60 | <0.60 | <0.60 |
| Tl | 2B | 0.80 | 0.24 | <0.24 | <0.24 | <0.24 | <0.24 |
| Au | 2B | 10 | 3.0 | <3.0 | <3.0 | <3.0 | <3.0 |
| Pd | 2B | 1.0 | 0.30 | <0.30 | <0.30 | <0.30 | <0.30 |
| Ir | 2B | 1.0 | 0.30 | <0.30 | <0.30 | <0.30 | <0.30 |
| Os | 2B | 1.0 | 0.30 | <0.30 | <0.30 | <0.30 | <0.30 |
| Rh | 2B | 1.0 | 0.30 | <0.30 | <0.30 | <0.30 | <0.30 |
| Ru | 2B | 1.0 | 0.30 | <0.30 | <0.30 | <0.30 | <0.30 |

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| Element | Class | Limits 1.0J Target ppm (µg/g) | Control Threshold Limits 0.3J Target ppm (µg/g) | Result RM Lot: M155 0705 ppm (µg/g) | Result ML Lot: BTRI-0123-00003-PV ML ppm (µg/g) | Result WC Lot: BTRI-0123-00003-PV WC 1st Basket ppm (µg/g) | Result FG Lot: BTRI-0123-00003-PV Beginning Drum 1 ppm (µg/g) |
| Se | 2B | 8.0 | 2.4 | <2.4 | <2.4 | <2.4 | <2.4 |
| Ag | 3 | 1.0 | 0.30 | <0.30 | <0.30 | <0.30 | <0.30 |
| Pt | 3 | 1.0 | 0.30 | <0.30 | <0.30 | <0.30 | <0.30 |
| Li | 3 | 25 | 7.5 | <7.5 | <7.5 | <7.5 | <7.5 |
| Sb | 3 | 9.0 | 2.7 | <2.7 | <2.7 | <2.7 | <2.7 |
| Ba | 3 | 70 | 21 | <21 | <21 | <21 | <21 |
| Mo | 3 | 150 | 45 | <45 | <45 | <45 | <45 |
| Cu | 3 | 30 | 9.0 | <9.0 | <9.0 | <9.0 | <9.0 |
| Sn | 3 | 60 | 18 | <18 | <18 | <18 | <18 |
| Cr | 3 | 110 | 33 | <33 | <33 | <33 | <33 |
| Fe | 4 | 10 | 3.0 | <3.0 | <3.0 | <3.0 | <3.0 |
| K | 4 | 50 | 15 | <15 | <15 | <15 | <15 |
| Na | 4 | 50 | 15 | <15 | <15 | <15 | <15 |

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