

# BIOSPECTRA

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Effective Date:	29-Apr-2021	28-Apr-2024	: Date of Next Review																									
Initiated By:	Yencho, Amy M	N/A	: Supersedes																									
Reason for Print:	MasterControl																											
Approval:	<table border="1"> <thead> <tr> <th>Approvers</th> <th>Date</th> <th>Time</th> <th>Group</th> <th>Name</th> </tr> </thead> <tbody> <tr> <td></td> <td>29-Apr-2021</td> <td>09:46:32 AM</td> <td>EDITOR</td> <td>Yencho, Amy M</td> </tr> <tr> <td></td> <td>29-Apr-2021</td> <td>09:48:09 AM</td> <td>QUALITY</td> <td>Goheen, Joshua</td> </tr> <tr> <td></td> <td>29-Apr-2021</td> <td>10:21:50 AM</td> <td>QUALITY</td> <td>Lippman, Jason C</td> </tr> <tr> <td></td> <td>29-Apr-2021</td> <td>10:23:37 AM</td> <td>MANAGEMENT</td> <td>Uhlig, Mark W</td> </tr> </tbody> </table>			Approvers	Date	Time	Group	Name		29-Apr-2021	09:46:32 AM	EDITOR	Yencho, Amy M		29-Apr-2021	09:48:09 AM	QUALITY	Goheen, Joshua		29-Apr-2021	10:21:50 AM	QUALITY	Lippman, Jason C		29-Apr-2021	10:23:37 AM	MANAGEMENT	Uhlig, Mark W
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## ELEMENTAL IMPURITY ASSESSMENT

MATERIAL NAME:

TROMETHAMINE (TRIS)

BioFUISA/BIOACTIVE GRADE

2020

Printed On:	24-Nov-2021 10:15:42 AM	Gathagan, Danielle E	: Printed By
Print Expiration:	Not Applicable		
Notice:	The Information contained herein is the property of BioSpectra and is Confidential.		

<b>TABLE 1: ELEMENTAL IMPURITY RISK ASSESSMENT</b>					Manufacturing Process DCN: 16-000000 Method Validation Protocol: 20-003543 Method Validation Report: 20-003551 Parenteral Specifications: 126 g/day MDD			
<b>Element</b>	<b>Class</b>	<b>Intentionally Added</b>	<b>Potential Sources?</b>	<b>Manufacturing Equipment Risk?</b>	<b>Method LOQ ppm (µg/g)</b>	<b>Limits 1.0J 126 g/day MDD Target ppm (µg/g)</b>	<b>30% Control Threshold Limits Target ppm (µg/g)</b>	<b>50% Control Threshold Limits Target ppm (µg/g)</b>
Cd	1	No	None	None	0.002	0.016	0.005	0.008
Pb	1	No	None	None	0.005	0.040	0.012	0.020
As	1	No	None	None	0.015	0.119	0.036	0.060
Hg	1	No	None	None	0.003	0.024	0.007	0.012
Co	2A	No	None	None	0.005	0.040	0.012	0.020
V	2A	No	None	None	0.01	0.079	0.024	0.040
Ni	2A	No	Raw Material Catalyst	Stainless Steel	0.02	0.159	0.048	0.079
Tl	2B	No	None	None	0.008	0.063	0.019	0.032
Au	2B	No	None	None	0.10	0.794	0.238	0.397
Pd	2B	No	None	None	0.01	0.079	0.024	0.040
Ir	2B	No	None	None	0.01	0.079	0.024	0.040
Os	2B	No	None	None	0.01	0.079	0.024	0.040
Rh	2B	No	None	None	0.01	0.079	0.024	0.040
Ru	2B	No	None	None	0.01	0.079	0.024	0.040

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Element	Class	Intentionally Added	Potential Sources?	Manufacturing Equipment Risk?	Method LOQ ppm (µg/g)	Limits 1.0J 126 g/day MDD Target ppm (µg/g)	30% Control Threshold Limits Target ppm (µg/g)	50% Control Threshold Limits Target ppm (µg/g)
<sup>1</sup> Se	2B	No	None	None	0.05	0.397	0.119	0.198
Ag	2B	No	None	None	0.01	0.079	0.024	0.040
Pt	2B	No	None	None	0.01	0.079	0.024	0.040
Li	3	No	None	None	0.25	1.984	0.595	0.992
Sb	3	No	None	None	0.09	0.714	0.214	0.357
Ba	3	No	None	None	0.70	5.556	1.667	2.778
<sup>1</sup> Mo	3	No	None	Stainless Steel	0.05	0.397	0.119	0.198
<sup>1</sup> Cu	3	No	None	None	0.025	0.198	0.060	0.099
Sn	3	No	None	None	0.60	4.762	1.429	2.381
<sup>1</sup> Cr	3	No	None	Stainless Steel	0.05	0.397	0.119	0.198
Additional Elements								
Al	4	No	Raw Material	None	0.40			
Fe	4	No	None	Stainless Steel	0.20			
Mn	4	No	None	Stainless Steel	0.025			

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Zn	4	No	None	Stainless Steel	0.20			

<sup>1</sup>More stringent target specification than USP.

TABLE 2: ELEMENTAL IMPURITY RISK ASSESSMENT				Manufacturing Process DCN: 16-000000 Method Validation Protocol: 20-003543 Method Validation Report: 20-003551 Parenteral Specifications: 126 g/day MDD			
Element	30% Control Threshold Target ppm (µg/g)	50% Control Threshold Target ppm (µg/g)	Result Batch 1 Lot: TR1200-016-0220-PV ppm (µg/g)	Result Batch 2 Lot: TR1200-017-0220-PV ppm (µg/g)	Result Batch 3 Lot: TR1200-018-0220-PV ppm (µg/g)	Meets 30% Control Threshold (Yes or No)	Meets 50% Control Threshold (Yes or No)
Cd	0.005	0.008	<0.002	<0.002	<0.002	Yes	Yes
Pb	0.012	0.020	<0.005	<0.005	<0.005	Yes	Yes
As	0.036	0.060	<0.015	<0.015	<0.015	Yes	Yes
Hg	0.007	0.012	<0.003	<0.003	<0.003	Yes	Yes
Co	0.012	0.020	<0.005	<0.005	<0.005	Yes	Yes
V	0.024	0.040	<0.01	<0.01	<0.01	Yes	Yes

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<b>TABLE 2: ELEMENTAL IMPURITY RISK ASSESSMENT</b>			Manufacturing Process DCN: 16-000000 Method Validation Protocol: 20-003543 Method Validation Report: 20-003551 Parenteral Specifications: 126 g/day MDD				
<b>Element</b>	<b>30% Control Threshold Target ppm (µg/g)</b>	<b>50% Control Threshold Target ppm (µg/g)</b>	<b>Result Batch 1 Lot: TR1200-016-0220-PV ppm (µg/g)</b>	<b>Result Batch 2 Lot: TR1200-017-0220-PV ppm (µg/g)</b>	<b>Result Batch 3 Lot: TR1200-018-0220-PV ppm (µg/g)</b>	<b>Meets 30% Control Threshold (Yes or No)</b>	<b>Meets 50% Control Threshold (Yes or No)</b>
Ni	0.048	0.079	0.053	0.064	0.045	No	Yes
Tl	0.019	0.032	<0.008	<0.008	<0.008	Yes	Yes
Au	0.238	0.397	<0.10	<0.10	<0.10	Yes	Yes
Pd	0.024	0.040	<0.01	<0.01	<0.01	Yes	Yes
Ir	0.024	0.040	<0.01	<0.01	<0.01	Yes	Yes
Os	0.024	0.040	<0.01	<0.01	<0.01	Yes	Yes
Rh	0.024	0.040	<0.01	<0.01	<0.01	Yes	Yes
Ru	0.024	0.040	<0.01	<0.01	<0.01	Yes	Yes
Se	0.119	0.198	<0.05	<0.05	<0.05	Yes	Yes
Ag	0.024	0.040	<0.01	<0.01	<0.01	Yes	Yes
Pt	0.024	0.040	<0.01	<0.01	<0.01	Yes	Yes
Li	0.595	0.992	<0.25	<0.25	<0.25	Yes	Yes
Sb	0.214	0.357	<0.09	<0.09	<0.09	Yes	Yes
Ba	1.667	2.778	<0.70	<0.70	<0.70	Yes	Yes

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Element	30% Control Threshold Target ppm (µg/g)	50% Control Threshold Target ppm (µg/g)	Result Batch 1 Lot: TR1200-016-0220-PV ppm (µg/g)	Result Batch 2 Lot: TR1200-017-0220-PV ppm (µg/g)	Result Batch 3 Lot: TR1200-018-0220-PV ppm (µg/g)	Meets 30% Control Threshold (Yes or No)	Meets 50% Control Threshold (Yes or No)
Mo	0.119	0.198	<0.05	<0.05	<0.05	Yes	Yes
Cu	0.060	0.099	<0.025	<0.025	<0.025	Yes	Yes
Sn	1.429	2.381	<0.60	<0.60	<0.60	Yes	Yes
Cr	0.119	0.198	<0.05	<0.05	<0.05	Yes	Yes
Additional Elements							
Al			<0.40	<0.40	<0.40		
Fe			<0.20	<0.20	<0.20		
Mn			<0.025	<0.025	<0.025		
Zn			<0.20	<0.20	<0.20		

TABLE 3: ELEMENTAL IMPURITY RISK ASSESSMENT		Manufacturing Process DCN: 16-000000 Method Validation Protocol: 20-003543 Method Validation Report: 20-003551 Parenteral Specifications: 126g/day MDD	
Element	Raw Material Result Lot: D609JBI032 ppm (µg/kg)	Raw Material Result Lot: D609JBK032 ppm (µg/kg)	Raw Material Result Lot: D609JCB032 ppm (µg/kg)

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<b>Element</b>	<b>Raw Material Result Lot: D609JBI032 ppm (µg/kg)</b>	<b>Raw Material Result Lot: D609JBK032 ppm (µg/kg)</b>	<b>Raw Material Result Lot: D609JCB032 ppm (µg/kg)</b>
Cd	<0.002	<0.002	<0.002
Pb	<0.005	<0.005	<0.005
As	<0.015	<0.015	<0.015
Hg	<0.003	<0.003	<0.003
Co	<0.005	<0.005	<0.005
V	<0.01	<0.01	<0.01
Ni	1.018	0.677	0.720
Tl	<0.008	<0.008	<0.008
Au	<0.10	<0.10	<0.10
Pd	<0.01	<0.01	<0.01
Ir	<0.01	<0.01	<0.01
Os	<0.01	<0.01	<0.01
Rh	<0.01	<0.01	<0.01
Ru	<0.01	<0.01	<0.01
Se	<0.05	<0.05	<0.05

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<b>Element</b>	<b>Raw Material Result Lot: D609JBI032 ppm (µg/kg)</b>	<b>Raw Material Result Lot: D609JBK032 ppm (µg/kg)</b>	<b>Raw Material Result Lot: D609JCB032 ppm (µg/kg)</b>
Ag	<0.01	<0.01	<0.01
Pt	<0.01	<0.01	<0.01
Li	<0.25	<0.25	<0.25
Sb	<0.09	<0.09	<0.09
Ba	<0.70	<0.70	<0.70
Mo	<0.05	<0.05	<0.05
Cu	<0.025	<0.025	<0.025
Sn	<0.60	<0.60	<0.60
Cr	<0.05	<0.05	<0.05
<b>Additional Elements</b>			
Al	<0.40	<0.40	<0.40
Fe	<0.20	<0.20	<0.20
Mn	<0.025	<0.025	<0.025
Zn	<0.20	<0.20	<0.20

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