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# ELEMENTAL IMPURITY ASSESSMENT

## MATERIAL NAME: HEPES ZONE E 2022

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<b>TABLE 1: ELEMENTAL IMPURITY ASSESSMENT</b>		Analytical Method: BSI-ATM-0054, Method Validation Report: BSI-RPT-0544 Degradation and Impurity Protocol: BSI-PRL-0558 Manufacturing Process: BSI-PRL-0539 Parenteral Specifications (10g/day MDD)	
<b>Element</b>	<b>Class</b>	<b>1Limits 1.0J Target ppm (µg/g)</b>	<b>Limits 0.3J ppm (µg/g)</b>
Cadmium (Cd)	1	0.20	0.06
Lead (Pb)	1	0.50	0.15
Arsenic (As)	1	1.5	0.45
Mercury (Hg)	1	0.30	0.09
Cobalt (Co)	2A	0.50	0.15
Vanadium (V)	2A	1.0	0.30
Nickel (Ni)	2A	2.0	0.60
Thallium (Tl)	2B	0.80	0.24
Gold (Au)	2B	10	3.0
Palladium (Pd)	2B	1.0	0.30
Iridium (Ir)	2B	1.0	0.30
Osmium (Os)	2B	1.0	0.30
Rhodium (Rh)	2B	1.0	0.30
Ruthenium (Ru)	2B	1.0	0.30
Selenium (Se)	2B	8.0	2.4
Silver (Ag)	2B	1.0	0.30
Platinum (Pt)	2B	1.0	0.30
Lithium (Li)	3	25	7.5

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<b>Element</b>	<b>Class</b>	<b><sup>1</sup>Limits 1.0J Target ppm (µg/g)</b>	<b>Limits 0.3J ppm (µg/g)</b>
Antimony (Sb)	3	9.0	2.7
Barium (Ba)	3	70	21
Molybdenum (Mo)	3	15	4.5
Copper (Cu)	3	5.0	1.5
Tin (Sn)	3	60	18
Chromium (Cr)	3	5.0	1.5
Iron (Fe)	4	5.0	1.5
Manganese (Mn)	4	5.0	1.5
Zinc (Zn)	4	5.0	1.5
Calcium (Ca)	4	50	15
Potassium (K)	4	50	15
Magnesium (Mg)	4	5.0	1.5

<sup>1</sup>Limits derived from Analytical Method BSI-ATM-0054

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<b>TABLE 2: ELEMENTAL IMPURITY ASSESSMENT</b>				Analytical Method: BSI-ATM-0054 Degradation and Impurity Protocol: BSI-PRL-0558 Manufacturing Process: BSI-PRL-0539 Parenteral Specifications (10g/day MDD)	
<b>Element</b>	<b>Class</b>	<b>Limits 1.0J Target ppm (µg/g)</b>	<b>RM Result Lot: RMAT-1021-0038 ppm (µg/g)</b>	<b>RM Result Lot: RMAT-1021-0042 ppm (µg/g)</b>	<b>ML Result Lot: HEPE-0122-00036-PV ppm (µg/g)</b>
Cd	1	0.20	<0.06	<0.06	<0.06
Pb	1	0.50	<0.15	<0.15	<0.15
As	1	1.5	<0.45	<0.45	<0.45
Hg	1	0.30	<0.09	<0.09	<0.09
Co	2A	0.50	<0.15	<0.15	<0.15
V	2A	1.0	<0.30	<0.30	<0.30
Ni	2A	2.0	<0.60	<0.60	<0.60
Tl	2B	0.80	<0.24	<0.24	<0.24
Au	2B	10	<3.0	<3.0	<3.0
Pd	2B	1.0	<0.30	<0.30	<0.30
Ir	2B	1.0	<0.30	<0.30	<0.30
Os	2B	1.0	<0.30	<0.30	<0.30
Rh	2B	1.0	<0.30	<0.30	<0.30
Ru	2B	1.0	<0.30	<0.30	<0.30
Se	2B	8.0	<2.4	<2.4	<2.4
Ag	2B	1.0	<0.30	<0.30	<0.30
Pt	2B	1.0	<0.30	<0.30	<0.30

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<b>TABLE 2: ELEMENTAL IMPURITY ASSESSMENT</b>				Analytical Method: BSI-ATM-0054 Degradation and Impurity Protocol: BSI-PRL-0558 Manufacturing Process: BSI-PRL-0539 Parenteral Specifications (10g/day MDD)	
<b>Element</b>	<b>Class</b>	<b>Limits 1.0J Target ppm (µg/g)</b>	<b>RM Result Lot: RMAT-1021-0038 ppm (µg/g)</b>	<b>RM Result Lot: RMAT-1021-0042 ppm (µg/g)</b>	<b>ML Result Lot: HEPE-0122-00036-PV ppm (µg/g)</b>
Li	3	25	<7.5	<7.5	<7.5
Sb	3	9.0	<2.7	<2.7	<2.7
Ba	3	70	<21	<21	<21
Mo	3	15	<4.5	<4.5	<4.5
Cu	3	5.0	<1.5	<1.5	<1.5
Sn	3	60	<18	<18	<18
Cr	3	5.0	<1.5	<1.5	<1.5
Fe	4	5.0	<1.5	<1.5	<1.5
Mg	4	5.0	<1.5	<1.5	<1.5
Mn	4	5.0	<1.5	<1.5	<1.5
Zn	4	5.0	<1.5	<1.5	<1.5
Ca	4	50	<15	<15	<15
K	4	50	<15	<15	<15

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TABLE 3: ELEMENTAL IMPURITY ASSESSMENT				Analytical Method: BSI-ATM-0054 Manufacturing Process: BSI-PRL-0539 Parenteral Specifications (10g/day MDD)	
Element	Class	Limits 1.0J Target ppm (µg/g)	WC Result Lot: HEPE-0122-00036-PV Top ppm (µg/g)	WC Result Lot: HEPE-0122-00036-PV Bottom ppm (µg/g)	FG Result Lot: HEPE-0122-00036-PV Beginning ppm (µg/g)
Cd	1	0.20	<0.06	<0.06	<0.06
Pb	1	0.50	<0.15	<0.15	<0.15
As	1	1.5	<0.45	<0.45	<0.45
Hg	1	0.30	<0.09	<0.09	<0.09
Co	2A	0.50	<0.15	<0.15	<0.15
V	2A	1.0	<0.30	<0.30	<0.30
Ni	2A	2.0	<0.60	<0.60	<0.60
Tl	2B	0.80	<0.24	<0.24	<0.24
Au	2B	10	<3.0	<3.0	<3.0
Pd	2B	1.0	<0.30	<0.30	<0.30
Ir	2B	1.0	<0.30	<0.30	<0.30
Os	2B	1.0	<0.30	<0.30	<0.30
Rh	2B	1.0	<0.30	<0.30	<0.30
Ru	2B	1.0	<0.30	<0.30	<0.30
Se	2B	8.0	<2.4	<2.4	<2.4
Ag	2B	1.0	<0.30	<0.30	<0.30
Pt	2B	1.0	<0.30	<0.30	<0.30

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Element	Class	Limits 1.0J Target ppm (µg/g)	WC Result Lot: HEPE-0122-00036-PV Top ppm (µg/g)	WC Result Lot: HEPE-0122-00036-PV Bottom ppm (µg/g)	FG Result Lot: HEPE-0122-00036-PV Beginning ppm (µg/g)
Li	3	25	<7.5	<7.5	<7.5
Sb	3	9.0	<2.7	<2.7	<2.7
Ba	3	70	<21	<21	<21
Mo	3	15	<4.5	<4.5	<4.5
Cu	3	5.0	<1.5	<1.5	<1.5
Sn	3	60	<18	<18	<18
Cr	3	5.0	<1.5	<1.5	<1.5
Fe	4	5.0	<1.5	<1.5	<1.5
Mg	4	5.0	<1.5	<1.5	<1.5
Mn	4	5.0	<1.5	<1.5	<1.5
Zn	4	5.0	<1.5	<1.5	<1.5
Ca	4	50	<15	<15	<15
K	4	50	<15	<15	<15

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