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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><sup>1</sup>Limits 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>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><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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TABLE 2: ELEMENTAL IMPURITY ASSESSMENT				Analytical Method: BSI-ATM-0054 Degradation and Impurity Protocol: BSI-PRL-0558 Manufacturing Process: BSI-PRL-0539 Parenteral Specifications (10g/day MDD)	
Element	Class	Limits 1.0J Target ppm (µg/g)	RM Result Lot: RMAT-1021-0038 ppm (µg/g)	RM Result Lot: RMAT-1021-0042 ppm (µg/g)	ML Result Lot: HEPE-0122-00036-PV 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	3	1.0	<0.30	<0.30	<0.30
Pt	3	1.0	<0.30	<0.30	<0.30

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TABLE 2: ELEMENTAL IMPURITY ASSESSMENT				Analytical Method: BSI-ATM-0054 Degradation and Impurity Protocol: BSI-PRL-0558 Manufacturing Process: BSI-PRL-0539 Parenteral Specifications (10g/day MDD)	
Element	Class	Limits 1.0J Target ppm (µg/g)	RM Result Lot: RMAT-1021-0038 ppm (µg/g)	RM Result Lot: RMAT-1021-0042 ppm (µg/g)	ML Result Lot: HEPE-0122-00036-PV 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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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	3	1.0	<0.30	<0.30	<0.30
Pt	3	1.0	<0.30	<0.30	<0.30

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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)
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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# ELEMENTAL IMPURITY ASSESSMENT MATERIAL NAME: HEPES N02 2021

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<b>TABLE 1: ELEMENTAL IMPURITY ASSESSMENT</b>	Analytical Method: BSI-ATM-0054, Method Validation Report: BSI-RPT-0544 Manufacturing Process: BSI-PRL-0400 Degradation and Impurity Protocol: BSI-PRL-0436, Report: BSI-RPT-1029 Parenteral Specifications (10g/day MDD)	
<b>Element</b>	<b>Class</b>	<b><sup>1</sup>Limits 1.0J Target ppm (µg/g)</b>
Cd	1	0.20
Pb	1	0.50
As	1	1.5
Hg	1	0.30
Co	2A	0.50
V	2A	1.0
Ni	2A	2.0
Tl	2B	0.80
Au	2B	10
Pd	2B	1.0
Ir	2B	1.0
Os	2B	1.0
Rh	2B	1.0
Ru	2B	1.0
Se	2B	8.0
Ag	2B	1.0
Pt	2B	1.0
Li	3	25

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<b>TABLE 1: ELEMENTAL IMPURITY ASSESSMENT</b>	Analytical Method: BSI-ATM-0054, Method Validation Report: BSI-RPT-0544 Manufacturing Process: BSI-PRL-0400 Degradation and Impurity Protocol: BSI-PRL-0436, Report: BSI-RPT-1029 Parenteral Specifications (10g/day MDD)	
<b>Element</b>	<b>Class</b>	<b><sup>1</sup>Limits 1.0J Target ppm (µg/g)</b>
Sb	3	9.0
Ba	3	70
Mo	3	15
Cu	3	5.0
Sn	3	60
Cr	3	5.0
Fe	4	5.0
Mn	4	5.0
Zn	4	5.0
Ca	4	50
K	4	50
Mg	4	5.0

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

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TABLE 2: ELEMENTAL IMPURITY ASSESSMENT				Manufacturing Process: BSI-PRL-0400 Degradation and Impurity Protocol: BSI-PRL-0436, Report: BSI-RPT-1029 Parenteral Specifications (10g/day MDD)		
Element	Class	Limits 1.0J Target ppm (µg/g)	Result Lot: HEPE-0121-00154-PV Beginning ppm (µg/g)	Result Lot: HEPE-0121-00154-PV Middle ppm (µg/g)	Result Lot: HEPE-0121-00154-PV End ppm (µg/g)	Result Lot: HEPE-0121-00154-PV Composite ppm (µg/g)
Cd	1	0.20	<0.06	<0.06	<0.06	<0.06
Pb	1	0.50	<0.15	<0.15	<0.15	<0.15
As	1	1.5	<0.45	<0.45	<0.45	<0.45
Hg	1	0.30	<0.09	<0.09	<0.09	<0.09
Co	2A	0.50	<0.15	<0.15	<0.15	<0.15
V	2A	1.0	<0.30	<0.30	<0.30	<0.30
Ni	2A	2.0	<0.60	<0.60	<0.60	<0.60
Tl	2B	0.80	<0.24	<0.24	<0.24	<0.24
Au	2B	10	<3.0	<3.0	<3.0	<3.0
Pd	2B	1.0	<0.30	<0.30	<0.30	<0.30
Ir	2B	1.0	<0.30	<0.30	<0.30	<0.30
Os	2B	1.0	<0.30	<0.30	<0.30	<0.30
Rh	2B	1.0	<0.30	<0.30	<0.30	<0.30
Ru	2B	1.0	<0.30	<0.30	<0.30	<0.30
Se	2B	8.0	<2.4	<2.4	<2.4	<2.4
Ag	3	1.0	<0.30	<0.30	<0.30	<0.30
Pt	3	1.0	<0.30	<0.30	<0.30	<0.30

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TABLE 2: ELEMENTAL IMPURITY ASSESSMENT				Manufacturing Process: BSI-PRL-0400 Degradation and Impurity Protocol: BSI-PRL-0436, Report: BSI-RPT-1029 Parenteral Specifications (10g/day MDD)		
Element	Class	Limits 1.0J Target ppm (µg/g)	Result Lot: HEPE-0121-00154-PV Beginning ppm (µg/g)	Result Lot: HEPE-0121-00154-PV Middle ppm (µg/g)	Result Lot: HEPE-0121-00154-PV End ppm (µg/g)	Result Lot: HEPE-0121-00154-PV Composite ppm (µg/g)
Li	3	25	<7.5	<7.5	<7.5	<7.5
Sb	3	9.0	<2.7	<2.7	<2.7	<2.7
Ba	3	70	<21	<21	<21	<21
Mo	3	15	<4.5	<4.5	<4.5	<4.5
Cu	3	5.0	<1.5	<1.5	<1.5	<1.5
Sn	3	60	<18	<18	<18	<18
Cr	3	5.0	<1.5	<1.5	<1.5	<1.5
Fe	4	5.0	<1.5	<1.5	<1.5	<1.5
Mg	4	5.0	<1.5	<1.5	<1.5	<1.5
Mn	4	5.0	<1.5	<1.5	<1.5	<1.5
Zn	4	50	<15	<15	<15	<15
Ca	4	50	<15	<15	<15	<15
K	4	5.0	<1.5	<1.5	<1.5	<1.5

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TABLE 3: ELEMENTAL IMPURITY ASSESSMENT			Manufacturing Process: BSI-PRL-0400 Degradation and Impurity Protocol: BSI-PRL-0436, Report: BSI-RPT-1029 Parenteral Specifications (10g/day MDD)		
Element	Class	Limits 1.0J Target ppm (µg/g)	Result RM Lot: RMAT-1021-0028 ppm (µg/g)	Result RM Lot: RMAT-1021-0030 ppm (µg/g)	Result RM Lot: RMAT-1021-0033 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	3	1.0	<0.30	<0.30	<0.30
Pt	3	1.0	<0.30	<0.30	<0.30

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TABLE 3: ELEMENTAL IMPURITY ASSESSMENT			Manufacturing Process: BSI-PRL-0400 Degradation and Impurity Protocol: BSI-PRL-0436, Report: BSI-RPT-1029 Parenteral Specifications (10g/day MDD)		
Element	Class	Limits 1.0J Target ppm (µg/g)	Result RM Lot: RMAT-1021-0028 ppm (µg/g)	Result RM Lot: RMAT-1021-0030 ppm (µg/g)	Result RM Lot: RMAT-1021-0033 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	50	<15	<15	<15
Ca	4	50	<15	<15	<15
K	4	5.0	<1.5	<1.5	<1.5

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TABLE 4: ELEMENTAL IMPURITY ASSESSMENT				Manufacturing Process DCN: BSI-PRL-0400 Degradation and Impurity Protocol: BSI-PRL-0436, Report: BSI-RPT-1029 Parenteral Specifications (10g/day MDD)	
Element	Class	Limits 1.0J Target ppm (µg/g)	Result ML Lot: HEPE-0121-00154-PV ML ppm (µg/g)	Result WC Lot: HEPE-0121-00154-PV WC Drum #1 ppm (µg/g)	Result FG Lot: HEPE-0121-00154-PV FG Drum #1 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	3	1.0	<0.30	<0.30	<0.30
Pt	3	1.0	<0.30	<0.30	<0.30

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TABLE 4: ELEMENTAL IMPURITY ASSESSMENT				Manufacturing Process DCN: BSI-PRL-0400 Degradation and Impurity Protocol: BSI-PRL-0436, Report: BSI-RPT-1029 Parenteral Specifications (10g/day MDD)	
Element	Class	Limits 1.0J Target ppm (µg/g)	Result ML Lot: HEPE-0121-00154-PV ML ppm (µg/g)	Result WC Lot: HEPE-0121-00154-PV WC Drum #1 ppm (µg/g)	Result FG Lot: HEPE-0121-00154-PV FG Drum #1 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	50	<15	<15	<15
Ca	4	50	<15	<15	<15
K	4	5.0	<1.5	<1.5	<1.5

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