!" #&/
4;O <548G=>3> 70AB>AC20==O ?@5?0@0BC

&□$□ ®
(CEFOBID®)

!:;04:
4VNG0 @5G>28=0: cefoperazone;
1 D;0:>= F5D>?5@07>= C 283;O4V F5D>?5@07>=C =0B@VN 1 3.

V:0@AL:0 D>@<0. >@>H>: 4;O ?@83>BC20==O @>7G8=C 4;O V=T:FV9.

$0@<0:>B5@0?52B8G=0 3@C?0. ?>A?>@8=8 ?>:>;V==O. >4 ATC J01DD12.

;V=VG=V E0@0:B5@8AB8:8.
>:070==O.
;O ;V:C20==O V=D5:FV9, A?@8G8=5=8E GCB;828<8 4> &5D>1V4C >@30=V7<0<8:
- V=D5:FVW 25@E=VE B0 =86=VE 48E0;L=8E H;OEV2;
- V=D5:FVW 25@E=VE B0 =86=VE 2V44V;V2 A5G>282V4=8E H;OEV2;
- ?5@8B>=VB, E>;5F8AB8B, E>;0=3VB B0 V=HV V=B@0014>
- A5?B8F5
- <5=V=3VB;
- V=D5:FVW H:V@8 B0 <O:8E B:0=8=;
- V=D5:FVW :VAB>: B0 AC3;>1V2;
- 70?0;L=V 70E2>@N20==O B07>28E >@30=V2, 5=4><5B@8B, 3>=>@5O B0 V=HV V=D5:FVW AB0B528E H;OEV2.

@>DV;0:B8:0.
&5D>1V4 <>6=0 ?@87=0G0B8 4;O ?@>DV;0:B8:8 ?VA;O>?5@0FV9=8E CA:;04=5=L ?V4 G0A 014> ;>3VG=8E, A5@F52>-AC48==8E B0 >@B>?548G=8E >?5@0FV9.

@>B8?>:070==O. V?5@GCB;82VABL 4> F5D>?5@07>=C 01> 1C4L-O:>3> 7 0=B81V>B8:V2 F5D0;>A?>@8=>2>3> @O4C.

!?>AV1 70AB>AC20==O B0 4>78.
@5?0@0B ?@87=0G0NBL 4;O 2=CB@VH=L>25==3> 01> 2=CB@VH=L><O7>2>3> 70AB>AC20==O.
>@>A;V.
0728G09 4>70 4;O 4>@>A;8E AB0=>28BL 2-4 3 =0 4>1C, O:C 22>4OBL :>6=V 12 3>48= C @V2=> @>7?>4V;5=8E 4>70E. @8 >A>1;82> BO6:8E V=D5:FVOE 4>7C <>6=0 71V;LH8B8 4> 8 3/4>1C, O:C 22>4OBL :>6=V 12 3>48= C @V2=> @>7?>4V;5=8E 4>70E. @8 22545==V &5D>1V4C C 4>1>2V9 4>7V 12-16 3, @>7?>4V;5=V9 =0 3 @V2=V 4>78 (7 V=B5@20;>< 8 3>48=), =5 1C;> 28O2;5=> 6>4=8E CA:;04=5=L. V:C20==O ?@5?0@0B>< <>6=0 @>7?>G0B8 4> >45@60==O @57C;LB0BV2 4>A;V465==O GCB;82>ABV >@30=V7

5:><5=4>20=0 4>70 ?@8 =5CA:;04=5=>=>:>:>2>28BL 500 <3 >4=>@07>2>, 2=CB@VH=L><□O7>2>. =CB@VH=L><O7>25 22545==O 74V9A=NTBLAO 3;81>:> C 25;8:89 AV4=8G=89<O7 01> C ?5@54=N ?>25@E=N AB53=0.
><1V=>20=0 B5@0?VO.
(8@>:89 A?5:B@ 4VW &5D>1V4C 40T 7<>3C 74V9A=N20B8 <>=>B5@0?VN 1V;LH>ABV V=D5:FV9. 4=0: &5D>1V4® <>6=0 70AB>A>2C20B8 V 4;O :><1V=>20=>3> ;V:C20==O C ?>T4=0==V 7 V=H8<8 0=B81V>B8:0<8, O:I> B0:5 ?>:070=5. @8 >4=>G0A=>3;V:>7840<8 @5:><5=4CTBLAO :>=B@>;N20B8 DC=:FVN =8@>:. !;V4 1@0B8 4> C2038 >DVFV9=V @5:><5=40FVW 7 28:>@8AB0==O 0=B81V>B8:V2.
0AB>AC20==O ?0FVT=B0< 7 ?>@CH5==O< DC=:FVW ?5GV=:8.
>@83C20==O 4>78 <>65 1CB8 =5>1EV4=8< C 28?04:0E 70:C?>@N20==O 6>2G=8E ?@>B>:V2, BO6:8E 70E2>@N20=L ?5GV=:8 01> AC?CB=L>3> C@065==O =8@>:. /:I> :>=B@>;L :>=F5=B@0FVW ?@5?0@0BC C A8@>20BFV :@>2V =5 ?@>2>4OBL, 4>70 =5 ?>28==0 ?5@528IC20B8 2 3 =0 4>1C.
0AB>AC20==O ?0FVT=B0< 7 ?>@CH5==O< DC=:FVW =8@>:.

A:V;L:8 =8@:8 =5 T 3>;>2=8< H;OE>< 282545==O &5D>1V4C, E2>@8< 7 C@065==O< =8@>: 728G09=C 4>1>2C 4>7C (2-4 3) <>6=0 ?@87=0G0B8 157 :>@83C20==O. ;O ?0FVT=BV2, C O:8E H284:VABL ::C1>G:>2>W DV;LB@0FVW =86G0 70 18 <;/E2 01> A8@>20B:>289 @V25=L :@50B8=V=C ?5@528ICT 3,5 <3/100 <;, <0:A8<0;L=0 4>1>20 4>70 AB0=>28BL 4 3.

5@V>4 =0?V2282545==O &5D>1V4C V7 A8@>20B:8 :@>2V 45I> 7=86CTBLAO ?V4 G0A 35<>4V0;V7C. 2545==O ?@5?0@0BC A;V4 74V9A=N20B8 ?VA;O 70:V=G5==O 4V0;V7C.

0AB>AC20==O ?0FVT=B0< 7 ?>@CH5==O< DC=:FVW ?5GV=:8 V AC?CB=V< ?>@CH5==O< DC=:FVW =8@>:.

?0FVT=BV2 7 ?>@CH5==O< DC=:FVW ?5GV=:8 B0 AC?CB=V< C@065==O< =8@>: =5>1EV4=> ?@>2>48B8 A?>AB5@565==O 70 :>=F5=B@0FVTN ?@5?0@0BC C A8@>20BFV :@>2V B0 :>@83C20B8 4>7C 2 @07V =5>1EV4=>ABV. /:I> :>=B@>;L :>=F5=B@0FVW ?@5?0@0BC C A8@>20BFV :@>2V =5 ?@>2>4OBL, 4>70 =5 ?>28==0 ?5@528IC20B8 2 3 =0 4>1C.

VB8.

V4 G0A ;V:C20==O =5<>2;OB B0 4VB59 &5D>1V4® A;V4 ?@87=0G0B8 C 4>1>28E 4>70E 2V4 50 <3 4> 200 <3 =0 1 :3 <0A8 BV;0; 4>7C 22>4OBL C 2 ?@89><8 (:>6=V 8-12 3>48=). 0:A8<0;L=0 4>70 =5 ?>28==0 ?5@528IC20B8 12 3 =0 4>1C. >1>2V 4>78 4> 300 <3/:3 1C;8 70AB>A>20=V 4;O ;V:C20==O =5<>2;OB B0 C 4VB59 7 BO6:8<8 V=D5:FVO<8, 2:;NG0NG8 :V;L:>E ?0FVT=BV2 7 10:B5@V0;L=8< <5=V=3VB><, B0 =5 A?@8G8=O;8 CA:;04=5=L.

0AB>AC20==O =>2>=0@>465=8

>2>=0@>465=8< (4> 8 4=V2) ?@5?0@0B A;V4 22>48B8 G5@57 :>6=V 12 3>48=.

=CB@VH=L>25==5 70AB>AC20==O 4VBO< B0 4>@>A;8

;O ?5@5@82G0AB>W 2=CB@VH=L>25==>W V=DC7VW 1 3 &5D>1V4C (2=0) A;V4 @>7G8=8B8 C 20-100 <; AC3> AB5@8;L=>3> @>7G8=C 4;O 2=CB@VH=L>25==8E V=T:FV9 V 22>48B8 ?@>BO3>< 15 E28;8= - 1 3>48=8. /:I> @>7G8==8:>< T AB5@8;L=0 2>40, B> C D;0:>= V7 ?@5?0@0B>< 4>40NBL =5 1V;LH =V6 20 <;.

;O 157?5@5@2=>W 2=CB@VH=L>25==>W V=DC7VW :>65= 3@0< &5D>1V4C 2V4=>2;NNBL 01> C 5 <; AB5@8;L=>W 2>48 4;O V=`T:FV9, 01> C 5 <; 10:B5@V>AB0B8G=>W 2>48 4;O V=T:FV9; F59 @>7G8= 4>40NBL 4> 2V4?>2V4=>3> @>7G8==8:0 4;O 2=CB@VH=L>25==>3> 22545==O.

;O 157?>A5@54=L>W 2=CB@VH=L>25==>W V=`T:FVW <0:A8<0;L=0 @07>20 4>70 &5D>1V4C 4;O 4>@>A;8E ?0FVT=BV2 AB0=>28BL 2 3, 4;O 4VB59 50 <3/:3 <0A8 BV;0. @5?0@0B @>7G8=ONBL C 2V4?>2V4=>7G8==8:C 4;O 4>AO3=5==O :V=F52>W :>=F5=B@0FVW 100 <3/<; V 22>4OBL ?@>BO3>< =5 <5=H5

3-5 E28;8=.

;O 0=B810:B5@V0;L=>W ?@>DV;0:B8:8 ?VA;O>?5@0FV9=8E CA:;04=5=L ?@87=0G0NBL ?>1 3 01> 2 3 ?@5?0@0BC 2=CB@VH=L>25==> 70 30-90 E28;8= 4> ?>G0B:C >?5@0FVW. >7C <>6=0 ?>2B>@N20B8 G5@57 :>6=V 12 3>48=, >4=0: C 1V;LH>ABV 28?04:V2 ?@>BO3>< =5 1V;LH 24 3>48=8. @8 >?5@0FVOE 7 ?V428I5=8< @878:>< V=DV:C20==O (=0?@8:;04, >?5@0FVW C :>;>@5:B0;L=V9 7>=V) B0 :>;8 V=DV:C20==O <>65 70240B8 >A>1;82> 25;8:>W H:>48 (=0?@8:;04, ?@8 >?5@0FVOE =0 2V4:@8B> ?@>B57C20==V AC3;>1V2), ?@>DV;0:B8G=5 70AB>AC20==O &5D>1V4C<>65 B@820B8 ?@>BO3>< 72 3>48=8 ?VA;O 70:V=G5==O >?5@0FVW.

=CB@VH=L>25==5 22545==O

!B5@8;L=89 ?>@>H>: &5D>1V4® <>6=0 A?>G0B:C @>7G8=8B8 70 4>?><>3>N 1C4L-O:>3> AC3> @>7G8==8:0 (2,8 <;/3 F5D>?5@07>=C), ?@840B=>3> 4;O 2=CB@VH=L>25==>3> 22545==O (B01;8FO 1). <5B>N ?>;53H5==O 2V4=>2;5==O @5:><5=4CTBLAO 70AB>A>2C20B8 5 <; @>7G8==8:0 =0 1 3 &5D>1V4C.

>7G8=8, @5:><5=4>20=V 4;O 2V4=>2;5==O ?>@>H:C F5D>?5@07>=C =0B@VN "01;8FO 1

5 % 3;N:>70 4;O V=T:FV9	10 % 3;N:>70 4;O V=T:FV9
5 % 3;N:>70 B0 0,9 % =0B@VN E;>@84 4;O V=`T:FV9	0,9 % =0B@VN E;>@84 4;O V=`T:FV9
5 % 3;N:>70 B0 0,2 % =0B@VN E;>@84 4;O V=`T:FV9	AB5@8;L=0 2>40 4;O V=`T:FV9
Normosol M B0 5 % 3;N:>70 4;O V=T:FV9	Normosol R

VA;O FL>3> C25AL >1T< >45@60=>3> @>7G8=C A;V4 @>725AB8 >4=8< V7 AB0=40@B=8E @>7G8==8:V2 4;O 2=CB@VH=L>25==>3> 22545==O (B01;8FO 2).

>7G8==8:8 4;O 2=CB@VH=L>25==8E V=DC7V9 "01;8FO 2

5 % 3;N:>70 4;O V=T:FV9	10 % 3;N:>70 4;O V=T:FV9
5 % 3;N:>70 B0 @>7G8= V=35@0 ;0:B0B=89 4;O V=`T:FV9	@>7G8= V=35@0 ;0:B0B=89
5 % 3;N:>70 B0 0,9 % =0B@VN E;>@84 4;O V=`T:FV9	0,9 % =0B@VN E;>@84 4;O V=`T:FV9
Normosol M B0 5 % 3;N:>70 4;O V=T:FV9	Normosol R
5 % 3;N:>70 B0 0,2 % =0B@VN E;>@84 4;O V=`T:FV9	

=CB@VH=L><O7>25 22545==O

;O ?@83>BC20==O @>7G8=C, ?@87=0G5=>3> 4;O 2=CB@VH=L><O7>2>3> 22545==O, <>6=0 28:>@8AB>2C20B8 AB5@8;L=C 01> 10:B5@V>AB0B8G=C 2>4C 4;O V=T:FV9. # 28?04:0E, :>;8 ?5@5410G0TBLAO 22545==O @>7G8=C 7 :>=F5=B@0FVTN 250 <3/<; 01> 28I5, 4;O ?@83>BC20==O @>7G8=C @5:><5=4CTBLAO 28:>@8AB0B8 @>7G8= ;V4>:0W=C. "0:89 @>7G8= <>6=0 ?@83>BC20B8, 28:>@8AB>2CNG8 AB5@8;L=C 2>4C 4;O V=`T:FV9 B0 2 % @>7G8= ;V4>:0W=C, :V=F520 :>=F5=B@0FVO ;V4>:0W=C <0T 1CB8
0,5 %.
5:><5=4CTBLAO A?>AV1 @>7G8=5==O C 2 5B0?8: A?>G0B:C A;V4 4>40B8 =5>1EV4=C :V;L:VABL AB5@8;L=>W 2>48 4;O V=`T:FV9 V 71>2BC20B8 4> ?>2=>3> @>7G8=5==O ?>@>H:C &5D>1V4®, ?VA;O FL>3> 4>40B8 =5>1EV4=C :V;L:VABL 2 % @>7G8=C ;V4>:0W=C B0 7

	V=F520 :>=F5=B@0FVO F5D>?5@07>=C	I 5B0?, >1□T< AB5@8;L=>W 2>48	II 5B0?, >1□T< 2 % ;V4>:0W=C	1□T< 4;O 22545==O *
$;0:>= 1 3	250 <3/<;	2,6 <;	0,9 <;	4 <;
	333 <3/<;	1,8 <;	0,6 <;	3 <;

* @54AB02;5=0 =04;8H:>20 :V;L:VABL, O:0 T 4>AB0B=L>N 4;O >B@8<0==O B0 70AB>AC20==O 70O2;5=8E >1T
=CB@VH=L><O7>25 22545==O 74V9A=NTBLAO 3;81>:> C 25;8:89 AV4=8G=89<O7 01> C ?5@54=N ?>25@E=N AB53=0.

15@V30==O @>7G8=V2

!B01V;L=VABL

%V7G8=V2 F5D>?5@07>=C, ?@83>B>2;5=8E 70 4>?><>3>N =02545=8E =86G5 ?0@5=B5@0;L=8E @>7G8==8:V2 B0 7 ?@81;87=8<8 :>=F5=B@0FVO<8 F5D>?5@07>=C, 70157?5GCT ABV9:VABL @>7G8=C 70 C<>28 4>45@60==O 2:070=8E B53> ?@>@8AB0=89 @>7G8= ?V4;O30T 7=8I5==N. !B01V;L=0 :V<=0B=0 B5□!), 24 3>48=8

>7G8=8	@81;87=V :>=F5=B@0FVW
0:B5@V>AB0B8G=0 2>40 4;O V=T:FV9	300 <3/<;
5 % 3;N:>70 4;O V=T:FV9	2 <3 4> 50 <3/<;
5 % 3;N:>70 4;O V=`T:FV9 B0 @>7G8= V=35@0 ;0:B0B=89 4;O V=T:FV9	2 <3 4> 50 <3/<;
5 % 3;N:>70 B0 0,9 % =0B@VN E;>@84 4;O V=T:FV9	2 <3 4> 50 <3/<;
5 % 3;N:>70 B0 0,2 % =0B@VN E;>@84 4;O V=T:FV9	2 <3 4> 50 <3/<;
10 % 3;N:>70 4;O V=T:FV9	2 <3 4> 50 <3/<;
>7G8= V=35@0 ;0:B0B=89 4;O V=T:FV9	2 <3/<;
0,5 % ;V4>:0W= 4;O V=T:FV9	300 <3/<;
0,9 % =0B@VN E;>@84 4;O V=T:FV9	2 <3 4> 300 <3/<;
!B5@8;L=0 2>40 4;O V=T:FV9	300 <3/<;
Normosol M B0 5 % 3;N:>70 4;O V=T:FV9	2 <3 4> 50 <3/<;
Normosol R	2 <3 4> 50 <3/<;

CB5@8;L=0 2>40 4;O V=T:FV9	300 <3/<;

V4=>2;5=V @>7G8=8 &5D>1V4C <>6=0 715@V30B8 C A:;O=8E 01> ?;0AB<0A>28E H?@8F0E, A:;O=8E 01> 3=CG:8E ?;0AB<0A>28E TABOE, I> ?@87=0G5=V 4;O ?0@5=B5@0;L=8E @>7G8=V2, ?@>BO3>< 5 4=V2 C E>;>48;L=8:C (2-8 □!).

>7G8=8	@81;87=V :>=F5=B@0FVW
0:B5@V>AB0B8G=0 2>40 4;O V=T:FV9	300 <3/<;
5 % 3;N:>70 4;O V=T:FV9	2 <3 4> 50 <3/<;
5 % 3;N:>70 B0 0,9 % =0B@VN E;>@84 4;O V=`T:FV9	2 <3 4> 50 <3/<;
5 % 3;N:>70 B0 0,2 % =0B@VN E;>@84 4;O V=`T:FV9	2 <3 4> 50 <3/<;
>7G8= V=35@0 ;0:B0B=89 4;O V=`T:FV9	2 <3/<;
0,5 % ;V4>:0W= 4;O V=`T:FV9	300 <3/<;
0,9 % =0B@VN E;>@84 4;O V=T:FV9	2 <3 4> 300 <3/<;
Normosol M B0 5 % 3;N:>70 4;O V=T:FV9	2 <3 4> 50 <3/<;
Normosol R	2 <3 4> 50 <3/<;
!B5@8;L=0 2>40 4;O V=T:FV9	300 <3/<;

V4=>2;5=V @>7G8=8 &5D>1V4C <>6=0 715@V30B8 C A:;O=8E 01> ?;0AB<0A>28E H?@8F0E, A:;O=8E 01> 3=CG:8E ?;0AB<0A>28E TABOE, I> ?@87=0G5=V 4;O ?0@5=B5@0;L=8E @>7G8=V2, ?@>BO3>< 3 01>

5 B86=V2 C <>@>78;L=V9 :0<5@V (2V4 -20 4> -10 □!):

>7G8=8	@81;87=V :>=F5=B@0FVW
3 B86=V	
5 % 3;N:>70 4;O V=T:FV9	50 <3/<;
5 % 3;N:>70 B0 0,9 % =0B@VN E;>@84 4;O V=`T:FV9	2 <3/<;
5 % 3;N:>70 B0 0,2 % =0B@VN E;>@84 4;O V=`T:FV9	2 <3/<;
5 B86=V2	
0,9 % =0B@VN E;>@84 4;O V=T:FV9	300 <3/<;
!B5@8;L=0 2>40 4;O V=T:FV9	300 <3/<;

V4=>2;5=V @>7G8=8 &5D>1V4C <>6=0 715@V30B8 C A:;O=8E 01> ?;0AB<0A>28E H?@8F0E, A:;O=8E 01> 3=CG:8E ?;0AB<0A>28E TABOE, I> ?@87=0G5=V 4;O ?0@5=B5@0;L=8E @>7G8=V2.
>7<>@>6C20B8 ?@5?0@0B ?5@54 70AB>AC20==O< ?>B@V1=> ?@8 :V<=0B=V9 B57<>@>6C20==O =528:>@8AB0=89 @>7G8= ?V4;O30T 7=8I5==N. >7G8= =5 <>6=0 ?>2B>@=> 70<>@>6C20B8. 1V>;>3VG=>W B>G:8 7>@C ?@5?0@0B A;V4 28:>@8AB0B8 =5309=>. /:I> ?@5?0@0B =5 28:>@8AB0B8 >4@07C, G0A 715@V30==O B0 4>B@8<0==O C<>2 ?5@54 28:>@8AB0==O< ?@5?0@0BC, T 2V4?>2V40;L=VABN :>@8ABC20GV2 V, O: ?@028;>, =5<>65 ?5@528IC20B8 24 3>48=8 70 B5 BV;L:8 2V4=>2;5==O/@>72545==O =5 2V41C;>AO 2 :>=B@>;L>20=8E V ?5@52V@5=8E 0A5?B8G=8E C<>20E

>1VG=V @50:FVW.
86G5 =02545=V ?>1VG=V @50:FVW, I> 1C;8 28O2;5=V B0 ?@> O:V ?>2V4><;O;>AO ?@>BO3>< B5@0?VW F5D>?5@07>=>B0 ?>1VG=8E @50:FV9 2V4>1@065=0 O:: 4C65 G0AB> (≥ 1/10); G0AB> (2V4 ≥ 1/100 4> < 1/10); =5G0AB> (2V4 ≥ 1/1000 4> < 1/100); @V4:> (2V4 ≥ 1/10 000 4> < 1/1000); 4C65 @V4:> (< 1/10 000); =52V4><> (G0AB>B0 =5 <>65 1CB8 2AB0=>2;5=0, 28E>4OG8 7 =0O2=8E 40=8E).

!8AB5<0->@30=-:;0A	>1VG=0 @50:FVO	'0AB>B0
=D5:FVW B0 V=207VW	?A524><5<1@0=>7=89 :>;VB	=52V4><>
>7;048 7 1>:C A8AB5<8 :@>2V B0 ;VW A8AB5<8	5>78=>DV;VO	4C65 G0AB>

	=59B@>?5=VO[1], 7=865==O @V2=O =59B@>DV;V2, ?>78B82=0 ?@O<0 0=B83;>1C;V=>20 ?@>10 C<1A0, 7=865==O @V2=O 35<>3;>1V=C, 7=865==O @V2=O 35 <0B>:@8BC	G0AB>
	3V?>?@>B@><1V=5	@V4:>
	B@><1>F8B>?5=VO	=52V4><>
>7;048 7 1>:C VW A8AB5 <8[2]	3V?5@GCB;82VABL	G0AB>
	0=0DV;0:B>W4=0 @50:FVO	=52V4><>
>7;048 7 1>:C AC48=	:0@4V>35==89 H>:, 35<>@03VO	=52V4><>
>7;048 7 1>:C H;C=:>2>-:8H:>2>3> B@0:BC[3]	4V0@5O	G0AB>
	1;N20==O	=5G0AB>
5?0B>1V;V0@=V @>7;048	?V428I5==O @V2=O ", !" B0 ;C6=>W D>AD0B078	G0AB>
	6>2BO=8FO	=52V4><>
>7;048 7 1>:C H:V@8 B0 ?V4H:V@=>W :;VB:>28=8	<0:C;>?0?C;L>7=V 28A8?0==O, :@>?82O=:0	G0AB>
	B>:A8G=89 5?V45@<0;L=89 =5:@>;V7, A8=4@>< !BV25=A0-6>=A>=0, A2V@1V6	=52V4><>
030;L=V @>7;048 B0 @50:FVW 2	1V;L C	G0AB>
	D;51VB C	=5G0AB>

1 ?>2O70=> 7 B@820;8< 70AB>AC20==O<, >1>@>B=>3> E0@0:B5@C.
2 1V;LH0 2V@>3V4=VABL 28=8:=5==O C ?0FVT=BV2, 2 0=0<=57V O:8E 2V47=0G5=> AE8;L=VABL 4> 0;5@3VG=8E @50:FV9, >A>1;82> =0 ?5=VF8;V=.
3 ?5@5206=> ;53:>3> B0 ?>3> ABC?5=O BO6:>ABV.

>2V4><;5==O ?@> ?V4>7@N20=V ?>1VG=V @50:FVW.
06;82> ?>2V4><;OB8 ?@> ?V4>7@N20=V ?>1VG=V @50:FVW ?VA;O @5TAB@0FVW ;V:0@AL:>3> 70A>1C. &5 4>72>;OT ?@>4>26C20B8 <>=VB>@8=3 A?V22V4=>H5==O @878:/:>@8ABL ;V:0@AL:>3> 70A>1C. @>E0==O 4> <548G=8E ?@0FV2=8:V2 ?>2V4><;OB8 ?@> 1C4L-O:V ?V4>7@N20=V ?>1VG=V @50:FVW 70 4>?><>3>N =0FV>=0;L=>W A8AB5<8 72VB=>ABV.

5@54>7C20==O. 0=V I>4> 3>AB@>W B>:A8G=>ABV =0B@VN F5D>?5@07>=C >1<565=V. GV:C20=8<8 ?@>O20<8 ?5@54>7C20==O ;V:0@AL:8< 70A>1>< T, ?5@54CAV<, ?>A8;5==O E0@0:B5@=8E 4;O ?@5?0@0BC ?>1VG=8E @50:FV9. !;V4 27OB8 4> C2038 B>9 D0:B, I> 28A>:V :>=F5=B@0FVW 15B0-;0:B0 <=8E 0=B81V>B8:V2 C A?8==><>7:>2V9 @V48=V <>6CBL A?@8G8=8B8 =52@>;>3VG=V 5D5:B8 V AC4> <8. A:V;L:8 F5D>?5@07>= 282>48BLAO 7 >@30=V7

0AB>AC20==O C ?5@V>4 203VB=>ABV 01> 3>4C20==O 3@C44N.
<u>03VB=VABL</u>
45:20B=8E V =0;56=8< G8=>< :>=B@>;L>20=8E 4>A;V465=L 70 CG0ABN 203VB=8E 6V=>: =5 ?@>2>48;8, B>A>2C20B8 C ?5@V>4 203VB=>ABV ;8H5 70 :@09=L>W ?>B@518.
<u>>4C20==O 3@C44N</u>
8H5 =525;8:V :V;L:>ABV F5D>?5@07>=C ?@>=8:0NBL C 3@C4=5 <>;>:>. %>G0 F5D>?5@07>= ?>30=> ?@>=8:0T C 3@C4=5 <>;>:>, A;V4 7 >15@56=VABN ?@87=0G0B8 ?@5?0@0B C ?5@V>4 3>4C20==O 3@C44N.

VB8.
&5D>?5@07>= 5D5:B82=> 70AB>A>2CNBL =5<>2;OB0A;V465==O 70 CG0ABN =54>=>H5=8E =5 <>2;OB V =>2>=0@>465=8E =5 ?@>2>48;8AO. ">
=>2>=0@>465=8E 7 O45@=>N 6>2BO=8F5N F5D>?5@07>= =5 28BVA=OT 1V;V@C1V= V7 4V;O=>: 9>3> 72O7C20==O 7 1V;:0<8 ?;07<8 :@>2V.

A>1;82>ABV 70AB>AC20==O.
<u>V?5@GCB;82VABL</u>

!5@9>7=V @50:FVW 3V?5@GCB;82>ABV (0=0DV;0:B8G=V @50:FVW), V=:>;8 7 ;5B0;L=8< =0A;V4:><, 1C;8 70@5TAB@>20=V C ?0FVT=BV2, O:V >B@8 28=8:0;8 C ?0FVT=BV2, 2 0=0<=57V O:8E =0O2=V @50:FVW 3V?5@GCB;82>ABV 4> 45:V;L:>E 0;5@35=V2.
5@54 ?@87=0G5==O< B5@0?VW F5D>?5@07>=>< A;V4 @5B5;L=> 7V1@0B8 0=0<=57, I>1 7OAC20B8, G8 28=8:0;8 C E2>@>3> @0=VH5 @50:FVW 3V?5@GCB;82>ABV 4> F5D0;>A?>@8=V2, ?5=VF8;V=V2 G8 4> V=H8E ;V:0@AL:8E 70A>1V2. !;V4 7 >15@56=VABN ?@87=0G0B8 F59 ?@5?0@0B ?0FVT=B0<, GCB;828< 4> ?5=VF8;V=C. =B81V>B8:8 A;V4 7 >15@56=VABN ?@87=0G0B8 1C4L-O:>3> @0=VH5 1C;8 ?@>O28 1C4L-O:>W D>@<8 0;5@3VW, >A>1;82> 0;5@3VW =0 ;V:0@AL:V 70A>18.
/:I> 28=8:0T 0;5@3VG=0 @50:FVO, A;V4 2V47=V 0=0DV;0:B8G=V @50:FVW 28<030NBL =5309=>3> =52V4:;04=>3> 22545==O 04@5=0;V=C. @8 =5>1EV4=>ABV A;V4 70AB>A>2C20B8 :8A5=L, 2=CB@VH=L>25==V :>@B8:>AB5@>W48, 0 B0:>6 ?V4B@8EV4=VABL 48E0;L=8E H;OEV2, C B>?> <>3>N V=BC10FVW.
0AB>AC20==O E2>@8< 7 ?>@CH5==O< DC=:FVW ?5GV=:8
&5D>?5@07>= 7=0G=>N N 5:A:@5BCTBLAO 7 6>2GN. # ?0FVT=BV2 V7 70E2>@N20==O<8 ?5GV=:8 B0 /01> >1AB@C:FVTN 6>2G=8E H;OEV2 ?>4>26CTBLAO ?5@V>4 =0?V2282545==O F5D>?5@07>=C V7 A8@>20B:8 :@>2V V 71V;LHCTBLAO =8@:>20 5:A:@5FVO ?@5?0@0BC 7 A5G5N. 02VBL ?@8 BO6:8E ?>@CH5==OE DC=:FVW ?5GV=:8 C 6>2GV 4>AO30NBLAO B5@0?52B8G=V :>=F5=B@0FVW F5D>?5@07>=C, 0 ?5@V>4 =0?V2282545==O 7@>AB0T ;8H5 C 2-4 @078.
030;L=V 70AB5@565==O
45O:8E ?0FVT=BV2 ;V:C20==O F5D>?5@07>=><, O: V V=H8<8 0=B81V>B8:0<8, ?@872>48BL 4> 45DVF8BC 2VB0D;>@8, O:0 C =>@ 3@C?8 @878:C =0;560BL ?0FVT=B8 7 ?>30=8< E0@GC20==O<, 7 @>7;040<8 2A<>:BC20==O (=0?@8:;04 2VAF84>7><) B0 ?0FVT=B8, O:V B@820;89 G0A ?5@51C20NBL =0 ?0@5=B5@0;L=>=B@>;N20B8 ?@>B@><1V=>289 G0A V C @07V =5>1EV4=>ABV ?@87=0G0B8 5:7>35==89 2VB0
/: V V=HV 0=B81V>B8:8, ?@8 B@820;>AC20==V F5D>?5@07>= <>65 ?@872>48B8 4> ?>A8;5=>3> @>ABC @578AB5=B=>W D;>@8, C 72O7:C 7 G8< ?V4 G0A ;V:C20==O 70 ?0FVT=B0<8 A;V4 @5B5;L=> A?>AB5@V30B8. /: V ?@8 ;V:C20==V 1C4L-O:8< ?>BC6=8< A8AB5<=8< ?@5?0@0B><, ?V4 G0A B@820;>W B5@0?VW F5D>?5@07>=>< @5:><5=4>20=> ?@>2>48B8 ?5@V>48G=V >1AB565==O 7 <5B>N 28O2;5==O <>6;828E DC=:FV>=0;L=8E ?>@CH5=L 7 1>:C A8AB5< >@30=V7:@5<0 =8@>:, ?5GV=:8 V A8AB5<8 :@>2>B2>@5==O. A>1;82> 206;82V B0:V >1AB565==O C =>2>=0@>465=8E, 7>:@5 <0 C =54>=>H5=8E, B0 V=H8E =5<>2;OB.
V4 G0A 70AB>AC20==O <0965 2AVE 0=B810:B5@V0;L=8E ?@5?0@0BV2, 2:;NG0NG8 F5D>?5@07>=, ?>2V4><;O;>AO ?@> 28?04:8 4V0@5W, A?@8G8=5=>W *Clostridium difficile*[*Clostridium difficile*associated diarrhea] (CDAD), O:V 70 ABC?5=5< BO6:>ABV 20@VN20;8 2V4 ;53:>W 4V0@5W 4> ;5B0;L=>3> :>;VBC. V:C20==O 0=B810:B5@V0;L=8<8 ?@5?0@0B0<8 ?>@CHCT =>@<0;L=C D;>@C B>2AB>3> :8H5G=8:C, I> ?@872>48BL 4> ?>A8;5=>3> @>ABC *C. difficile.*
C. difficile A8=B57CT B>:A8=8 A V B, I> A?@8ONBL @>728B:C CDAD. (B0<8 *C. difficile* 7 3V?5@?@>4C:FVTN B>:A8=V2 >1C<>2;NNBL ?V428I5=C 70E2>@N20=VABL V A<5@B=VABL, >A:V;L:8 V=D5:FVW, O:V 2>=8 A?@8G8=NNBL,<>6CBL 1CB8 ABV9:8<8 4> B5@0?VW 0=B81=8<8 ?@5?0@0B0<8 V <>6CBL ?>B@51C20B8 :>;5:B>728B>: CDAD A;V4 70?V4>7@N20B8 2 CAVE ?0FVT=BV2, C O:8E A?>AB5@V30;8AO ?@>O28 4V0@5W ?VA;O 70AB>AC20==O 0=B81V>B8:V2. 5>1EV4=5 @5B5;L=5 282G5==O 0=0<=57C, >A:V;L:8 ?>2V4><;O;>AO, I> CDAD 28=8:0;0 1V;LH =V6 G5@57 2
/:I> ?0FVT=B 4>B@8< =0B@VN, B> A;V4 27OB8 4> C2038, I> &5D>1V4®

40B=VABL 2?;820B8 =0 H284:VABL @50:FVW ?@8 :5@C20==V 02B>B@0=A?>@B>< 01> @>1>BV 7 V=H8<8 <5E0=V7<0<8.
>A2V4 :;V=VG=>3> 70AB>AC20==O F5D>?5@07>=C 2:07CT =0 B5, I> 2?;82 ?@5?0@0BC =0 740B=VABL ?0FVT=B0 :5@C20B8 B@0=A?>@B=8<8 70A>10<8 01> ?@0FN20B8 7 <5E0=V7<0<8 T <0;>9<>2V@=8

70T<>4VO 7 V=H8<8 ;V:0@AL:8<8 70A>10<8 B0 V=HV 2848 270T<>4V9.
;:>3>;L

>2V4><;O;>AO, I> ?@8 26820==V 0;:>3>;N ?V4 G0A ;V:C20==O ?@5?0@0B>< V =02VBL G5@57 5 4V1 ?VA;O >AB0==L>3> 22545==O F5D>?5@07>=C 28=8:0;0 48AC;LDV@0<>?>4V1=0 @50:FVO, I> E0@0:B5@87C20;0AO ?@8?;820<8, ?VB;82VABN, 3>;>2=8< 1>;5< V B0EV:0@4VTN. >4V1=V @50:FVW 28=8:0;8 V ?VA;O ?@89>A?>@8=V2, B>3>;L=8E =0?>W2 C ?5@V>4 ;V:C20==O F5D>?5@07>=>;.
70T<>4VW, I> 2?;820NBL =0 @57C;LB0B8 ;01>@0B>@=8E 4>A;V465=L
>65 28=8:0B8 E81=>?>78B82=0 @50:FVO A5GV =0 3;N:>7C ?@8 ?@>2545==V B5ABV2 7 @>7G8=0<8 5=548:B0 01> $5;V=30.

$0@<0:>;>3VG=V 2;0AB82>ABV.

$0@<0:>48=0

0:B5@8F84=0 4VO ?5=0 C?>2V;L=5==O< A8=B57C ABV=:8 :;VB8=8 10:B5@VW.
&5D>1V4® 0:B82=89 *in vitro* 2V4=>A=> 25;8:>W :V;L:>ABV :;V=VG=> 7=0GCI8E >@30=V79 65 G0A 2V= 28O2;OT @578AB5=B=VABL 4> 4VW 1030BL>E 15B0-;0:B0<07.
07=0G5=V =86G5 >@30=V7<8 T GCB;828<8 4> &5D>1V4C.

@078B82=V >@=0=V7<8:

Staphylococcus aureus (HB0<8, I> ?@>4C:CNBL B0 HB0<8, I> =5 ?@>4C:CNBL ?5=VF8;V=07C), *Staphylococcus epidermidis, Streptococcus pneumoniae* (>?5@54=O =0720 *Diplococcus pneumoniae), Streptococcus pyogenes* (15B0-35<>;VB8G=89 AB@5?B>:>: 3@C?8), *Streptococcus agalactiae* (15B0-35 <>;VB8G=89 AB@5?B>:>: 3@C?8 B), *Streptococcus faecalis* (5=B5@>:>:), 15B0-35<>;VB8G=V AB@5?B>:>:8.

@0<=530B82=V >@30=V7<8:

Escheria coli, @V4 *Klebsiella,* @V4 *Enterobacter,* @V4 *Citrobacter, Hæmophilus influenzae, Proteus mirabilis, Proteus vulgaris, Morganella morganii* (@0=VH5 *Proteus morganii*), *Providencia rettgeri* (@0=VH5 *Proteus rettgeri*), @V4 *Providenci0,* @V4 *Serratia* (2:;NG0NG8 *S. Marcescens*), @V4 *Salmonella* B0 *Shigella, Pseudomonas aeruginosa* B0 45O:V V=HV *Pseudomonas, Acinetobacter calcoaceticus, Neisseria gonorrhœae* (HB0<8, I> ?@>4C:CNBL V =5 ?@>4C:CNBL 15B0-;0:B0<078), *Neisseria meningitidis, Bordetella pertussis, Yersinia enterocolitica.*

=05@>1=V >@30=V7<8:

3@078B82=V B0 3@0<=530B82=V :>:8 (2:;NG0NG8 @V4 *Peptococcus, Peptostreptoccus* B0 *Velionella*);
3@078B82=V ?0;8G:8 (2:;NG0NG8 @V4 *Clostridium, Eubacterium* B0 *Lactobacillus*);
3@0<=530B82=V ?0;8G:8 (2:;NG0NG8 @V4 *Fusobacterium*, 1030B> HB0 *Bacteroides fragilis* B0 V=H8E ?@54AB02=8:V2 @>4C *Bacteroides*).

$0@<0:>:V=5B8:0.

8A>:V @V2=V C :@>2V, 6>2GV B0 A5GV 4>AO30NBLAO ?VA;O @07>2>3> 22545==O ?@5?0@0BC. # B01;8FV 3 =02545=> :>=F5=B@0FVW ?@5?0@0BC C A8@>20BFV :@>2V 4>@>A;8E 74>@>28E >AV1. &V 40=V 1C;> >45@60=> ?VA;O 15-E28;8==>3> 2=CB@VH=L>25==>3> 22545==O 1, 2, 3 01> 4 3 ?@5?0@0BC 01> @07>2>3> 2=CB@VH=L><□O7>2>3> 22545==O 1 01> 2 3 ?@5?0@0BC. @>15=5F84 =5 <0T 2?;82C =0 @V25=L :>=F5=B@0FVW F5D>?5@07>=C C :@>2V.

>=F5=B@0FVW F5D>?5@07>=C C A8@>20BFV :@>2V "01;8FO 3

!5@54=V :>=F5=B@0FVW C A8@>20BFV :@>2V (							
>70, A?>AV1 22545==O	0*	30 E28;8=	1 3>48=0	2 3>48=8	4 3>48=8	8 3>48=	12 3>48=
1 3 2=CB@VH=L>25==>	153	114	73	38	16	4	0,5
2 3 2=CB@VH=L>25==>	252	153	114	70	32	8	2
3 3 2=CB@VH=L>25==>	340	210	142	89	41	9	2
4 3 2=CB@VH=L>25==>	506	325	251	161	71	19	6
1 3 2=CB@VH=L> <□O7>2>	32**	52	65	57	33	7	1
2 3 2=CB@VH=L> <□O7>2>	40**	69	93	97	58	14	4

* '0A, I> <8=C2 ?VA;O 22545==O ?@5?0@0BC (2V4;V: >4@07C ?VA;O 7025@H5==O V=DC7VW).

** 57C;LB0B8, O:V 1C;> >B@8<0=> G5@57 15 E28;8= ?VA;O 22545==O ?@5?0@0BC.
5@V>4 =0?V2282545==O &5D>1V4C V7 A8@>20B:8 :@>2V 4>@V2=NT ?@81;87=> 2 3>48=8, =570;56=> 2V4 A?>A>1C 9>3> 22545==O.
&5D>1V4® 4>AO30T B5@0?52B8G=8E @V2=V2 C 2AVE @V48=0E B0 B:0=8=0E >@30=V7 4>A;V46C20;8AO. !5@54 =8E T 0AF8B8G=0 B0 F5@51@>A?V=0;L=0 (?V4 G0A <5=V=3VBC) @V48=8, A5G0, 6>2G B0 ABV=:0 6>2G=>3>
&5D>1V4® 282>48BLAO 7 6>2GN B0 A5G5N. >=F5=B@0FVO ?@5?0@0BC C 6>2GV 4>AO30T 4C65 28A>:8E @V2=V2 (O: ?@028;>, G5@57 1-3 3>48=8 ?VA;O 22545==O) B0 ?5@528ICT 0=0;>3VG=V :>=F5=B@0FVW C A8@>20BFV :@>2V C 100 @07V2.
C;> 70@5TAB@>20=> B0:V :>=F5=B@0FVW C 6>2GV: 2V4 66
'5@57 12 3>48= ?VA;O 22545==O C @V7=8E 4>70E B0 @V7=8<8 A?>A>10<8 ?V428I5==O :>=F5=B@0FVW F5D>?5@07>=C C A5GV ?0FVT=BV2 7 =>@<0;L=>N DC=:FVTN =8@>: 4>AO30T C A5@54=L> 30 %. >=F5=B@0FVW ?@5?0@0BC C A5GV ?>=04 2200®. VA;O 2=CB@VH=L><O7>2>3> 22545==O 2 3 ?@5?0@0BC <0:A8<0;L=V :>=F5=B@0FVW C A5GV AB0=>28;8 ?@81;87=> 1000 >2B>@=5 22545==O &5D>1V4C® =5 ?@872>48BL 4> :C@>28E 4>1@>2>;LFV2.
?0FVT=BV2 7 ?>@CH5==O< DC=:FVW ?5GV=:8 ?5@V>4 =0?V2282545==O ?@5?0@0BC V7 A8@>20B:8 :@>2V 7@>AB0T, 0;5 7@>AB0T V 2840;5==O 7 A5G5N. # ?0FVT=BV2 7 =8@:>2>N B0 ?5GV=:>2>N =54>AB0B=VABN &5D>1V4® <>65 :C20BFV :@>2V.
E2>@8E 7 =8@:>2>N =54>AB0B=VABN<0:A8<0;L=0 :>=F5=B@0FVO C A8@>20BFV :@>2V, ?;>I0 ?V4 D0@<0:>:V=5B8G=>N :@82>N, 0 B0:>6 ?5@V>4 =0?V2282545==O V7 A8@>20B:8 :@>2V B0:V 6, O: V C 74>@>28E 4>1@>2>;LFV2.

$0@<0F52B8G=V E0@0:B5@8AB8:8.
A=>2=V DV78:>-EVABV: 2V4 1V;>3> 4> <0965 1V;>3> :>;L>@C :@8AB0;VG=89 ?>@>H>:.

5AC
>7G8=8 &5D>1V4C® B0 03;V:>784V2 =5 A;V4 22>48B8 >4=>G0A=>, >A:V;L:8 ?5@5410G0TBLAO ?@>2545==O :><1V=>20=>3> ;V:C20==O &5D>1V4><® B0 03;V:>784><, B> F5 <>6=0 7@>18B8 H;OE>< G5@3C20==O 2=CB@VH=L>25==8E V=DC7V9 70 C<>28 28:>@8AB0==O >:@5<>W A8AB5<8 4;O 2=CB@VH=L>25==>3> 22545==O. 5:><5=4CTBLAO 22>48B8 &5D>1V4® ?5@54 03;V:>7840<8. 5@54 ?>40;LH8< 22545==O< 03;V:>784C A;V4 ?@><8B8 CAN A8AB52V4=8< @>7G8=>

"5@ABV. **2 @>:8.**

#<>28 715@V30==O.
15@V30B8 2 =54>ABC?=>

#?0:>2:0.
>@>H>: C D;0:>=V. > 1 D;0:>=C 2 :0@B>==V9 C?0:>2FV.

0B53>@VO 2V4?CA:C. 0 @5F5?B>

8@>1=8:.
%0C?B $0@<0 0BV=0 !.@.;./
Haupt Pharma Latina S.r.l.

VAF57=0E>465==O.
>@3> !0= VH5;L !.!. 156 . 47.600 04100 0BV=0 (''), B0;VO/
Borgo San Michele S.S. 156 KM. 47.600 04100 Latina (LT), Italy.