

!" #&/

4;O <548G=>3> 70AB>AC20==O ;V:0@AL:>3> 70A>1C

(LEBEL)

!::04:

4VNG0 @5G>28=0: levofloxacin;

1 B01;5B:0 D;>:A0F8=C 500 <3 (C 283;O4V ;52>D;>:A0F8=C 35

4>?>28=8: F5;N;>70 :@8AB0;VG=0, 3V?@<5;>70, :@>A?>2V4>=, =0B@VN AB50@8;DC<0@0B; ?>:@8BBO Opadry Y1 7000 White: 3V?@<5;>70, B8B0=C 4V>:A84 (171), ?>;V5B8;5=3;V:>;L 400.

V:0@AL:0 D>@<0. "01;5B:8, 2:@8BV >1>;>=:>N.

A=>2=V DV78:>-EVABV: ?@>4>23C20BV B01;5B:8, 2:@8BV >1>;>=:>N, 1V;>3> :>;L>@C, 7 ;V=VTN @>7;>4=>3> 1>:C.

\$0@<0:>B5@0?52B8G=0 3@C?0.

=B810:B5@V0;L=V 70A>18 3@C?8 EV=>;>=V2. \$B>@EV=>;>=8. >4 "% J01M 12.

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

\$0@<0:>48=0

52>D;>:A0F8= F5 A8=B5B8G=89 0=B810:B5@V0;L=89 70AV1 V7 3@C?8 DB>@EV=>;>=V2, S-5=0=BV>

<5@ @0F5W AC3> 70A>1C >D;>:A0F8=C. /: 0=B810:B5@V0;L=89 ?@5?0@0B V7 3@C?8

DB>@EV=>;>=V2 ;52>D;>:A0F8= 4VT =0 :>?>V7><5@07C V.

!BC?V=L 10:B5@V0;L=>W 0:B82=>ABV ;52>D;>:A0F8=C 70;568BL 2V4 A?V22V4=>H5==O<0:A8

<0;L=>W :>=F5=B@0FVW C A8@>20BFV :@>2V (l_{max}) 01> ?>;IV ?V4 :@82>N «:>=F5=B@0FVO-G0A» (UC) B0

A=>2=89 <5E0=V7< @578AB5=B=>ABV T =0A;V4:< In vitro VA=CT ?5@5E@5A=0 @578AB5=B=VABL D;>:A0F8=>< B0 V=H8<8 DB>@EV=>;>=0<8.

0728G09 =5 VA=CT ?5@5E@5A=>W @578AB5=B=>ABVD;>:A0F8=>< B0 V=H8<8 ;:0A0<8

0=B810:B5@V0;L=8E 70A>1V2, I> ?>OA=NTBLAO <5E0=V7<<< 4VW.

5:><5=4>20=V 2@>?59AL:8< :< 7 B5ABC20==O 0=B81=>W GCB;82>ABV (EUCAST) 3@0=8G=V

7=0G5==O ;52>D;>:A0F8=C, I> 2V44V;ONBL GCB;82V>@30=V7<8 2V4 >@30=V7 GCB;828E (?>

@578AB5=B=8E) B0 ?@> GCB;82V 2V4 @578AB5=B=8E >@30=V7

;V=VG=V 3@0=8G=V 7=0G5==O ;52>D;>:A0F8=C (20.06.2006)

0B>35=

'CB;82V

578AB5=B=V

Enterobacteriaceae

≤ 1 <3/;

> 2 <3/;

Pseudomonas spp.

≤ 1 <3/;

> 2 <3/;

Acinetobacter spp.

≤ 1 <3/;

> 2 <3/;

Staphylococcus spp.

≤ 1 <3/;

> 2 <3/;

*S. pneumoniae*¹

≤ 2 <3/;

> 2 <3/;

Streptococcus A, B, C, G

≤ 1 <3/;

> 2 <3/;

H. influenzae,

≤ 1 <3/;

> 1 <3/;

*M. catarrhalis*²

56>2V 7=0G5==O, =5

≤ 1 <3/;

> 2 <3/;

?>2O70=V 7 2840<8³

¹ @0=8G=5 7=0G5==O GCB;828<8 (?> @578AB5=B=8<8) HB0<0<8 1C;> 71V;LH5=> 7 1 4> 2 7 <5B>N AB@8 ABC 48:8E HB03> >@30=V7 45<=>=AB@CT 20@V015;L=VABL 707=0G5=>3> ?0@0=5B@0. @0=8G=V 7=0G5==O AB>ACNBLAO B5@0?VW 28A>:8E 4>7.

² (B0<8 7 25;8G8=0<8 , 28I8<8 2V4 3@0=8G=>3> 7=0G5==O GCB;828<8 (?> @578AB5=B=8<8) HB0<0<8, T 4C65 @V4:VA=8<8 01> ?@> =8E I5 =5 ?>2V4><;O;>AO. "5AB8 =0 V45=B8DV:0FVN B0 ?@>B81=C GCB;82VABL =0 1C4L-O:>;OBV A;V4 ?>2B>@8B8, V, O:I> @57C;LB0B 1C45 ?V4B25@465=>, =04VA;0B8 V7>;OB C 4>2V4:>2C ;01>@0B>@VN.

³ @0=8G=V 7=0G5==O , =5 ?>2O70=V 7 2840<8, 1C;8 287=0G5=V ?5@5206=> 70 40=8<8 D0@<0:>:V=5B8:8 /D0@<0:>48=0Enterococcus, Neisseria, 3@0<=530B82=V 0=05@>18).

5:;<5=4>20=V CLSI (=AB8BCB<< ;V=VG=8E B0 ;01>@0B>@=8E AB0=40@BV2, @0=VH5 NCCLS) 3@0=8G=V
7=0G5==O ;52>D;>:A0F8=C, I> 2V44V;ONBL GCB;82V 2V4 ?@>GCB;828E >@30=V7 GCB;82V 2V4
@578AB5=B=8E >@30=V7 C B01;8FV 4;O B5ABC20==O (

5:;<5=4>20=V CLSI 3@0=8G=V 7=0G5==O B0 48A:>-48DC7=>3> <5B>4C ;52>D;>:A0F8=C (100-S17,
2007)

0B>35=	'CB;82V	578AB5=B=V
<i>Enterobacteriaceae</i>	≤ 2 ≥ 17 <<	≥ 8 ≤ 13 <<
5 <i>Enterobacteriaceae</i>	≤ 2 ≥ 17 <<	≥ 8 ≤ 13 <<
<i>Acinetobacter spp.</i>	≤ 2 ≥ 17 <<	≥ 8 ≤ 13 <<
<i>Stenotrophomonas maltophilia</i>	≤ 2 ≥ 17 <<	≥ 8 ≤ 13 <<
<i>Staphylococcus spp.</i>	≤ 1 ≥ 19 <<	≥ 4 ≤ 15 <<
<i>Enterococcus spp.</i>	≤ 2 ≥ 17 <<	≥ 8 ≤ 13 <<
<i>H. influenzae</i>	≤ 2	
<i>M. catarrhalis</i>	≥ 17 <<	
<i>Streptococcus pneumoniae</i>	≤ 2 ≥ 17 <<	≥ 8 ≤ 13 <<
5B0-35<>;VB8G=89	≤ 2	≥ 8
<i>Streptococcus</i>	≥ 17 <<	≤ 13 <<

1 V4ACB=VABL G8 @V4:VA=5 ?>H8@5==O @578AB5=B=8E HB05@54=L > 28;;NG0T 287=0G5==O
1C4L-O:8E :0B53>@V9 @57C;LB0BV2, V=H8E, =V6 «GCB;82V». ;O HB0 40NBL @57C;LB0B8, O:V
A2V4G0BL ?@> «=5GCB;82C» :0B53>@VN, V45=B8DV:0FVO >@30=V7B81=C GCB;82VABL ?>28==V
1CB8 ?V4B25@465=V 4>2V4:>2>N ;01>@0B>@VTN 7 28:>@8AB0==O< 5B0;>==>3> <5B>4C
@>72545=L CLSI.

=B810:B5@V0;L=89 A?5:B@
>H8@5=VABL @578AB5=B=>ABV 4;O 281@0=8E 284V2<>65 20@VN20B8 35>3@0DVG=> B0 7 G0A>
060=> >B@8<0B8 ;>:0;L=C V=D>@<0FVN ?@> @578AB5=B=VABL, >A>1;82> ?@8 ;V:C20==V BO6:8E
V=D5:FV9. @8 =5>1EV4=>ABV A;V4 725@=CB8AO 70 ?>@04>N 4> A?5FV0;VAB0, :>;8H8@5=VABL
@578AB5=B=>ABV T B0:>N, I> :>@8A=VABL 035=B0 I>=09<5=H5 ?@8 45O:8E B8?0E V=D5:FV9 T AC
<=V2=>N.

0728G09 GCB:82V 2848

5@>1=V 3@078B82=V 10:B5@VW

*Staphylococcus aureus** <5B8F8;V=GCB;8289, *Staphylococcus saprophyticus*, *Streptococci*3@C?0 ! V G,
Streptococcus agalactiae, *Streptococcus pneumoniae**, *Streptococcus pyogenes**

5@>1=V 3@0<=530B82=V 10:B5@VW

*Burkholderia cepacia*** , *Eikenella corrodens*, *Haemophilus influenzae**, *Haemophilus para- influenzae**,
Klebsiella oxytoca, *Klebsiella pneumoniae**, *Moraxella catarrhalis**, *Pasteurella multocida*, *Proteus vulgaris*,
Providencia rettgeri.

=05@>1=V 10:B5@VW

Peptostreptococcus

=HV

*Chlamydophila pneumoniae**, *Chlamydophila psittaci*, *Chlamidia trachomatis*, *Legionella pneumophila**,
*Mycoplasma pneumoniae**, *Mycoplasma hominis*, *Ureaplasma urealyticum*.

848, 4:O O:8E =01CB0 (2B>@8==0) @578AB5=B=VABL <>65 1CB8 ?@>1;5<0B8G=>N

5@>1=V 3@078B82=V 10:B5@VW

*Enterococcus faecalis**, *Staphylococcus aureus* <5B8F8;V=@578AB5=B=89, *Staphylococcus coagulase spp.*

5@>1=V 3@0<=530B82=V 10:B5@VW

*Acinetobacter baumannii**, *Citrobacter freundii**, *Enterobacter aerogenes*, *Enterobacter agglomerans*,
*Enterobacter cloacae**, *Escherichia coli**, *Morganella morganii**, *Proteus mirabilis**, *Providencia stuartii*
*Pseudomonas aeruginosa**, *Serratia marcescens**

=05@>1=V 10:B5@VW

Bacteroides fragilis *Bacteroides ovatus*** , *Bacteroides thetaiotamicron*** , *Bacteroides vulgatus*** , *Clostridium difficile***

* ;V=VG=0 5D5:B82=VABL ?@>45<=>=AB@>20=0 4;O GCB;828E V7>;OBV2 C 70B25@465=8E ;;V=VG=8E ?>:070==OE.

** @8@>4=0 ?@>.

=HV 40=V

>A?VB0;L=V V=D5:FVW, A?@8G8=5=VP. *aeruginosa*, <>6CBL ?>B@51C20B8 :<>1V=>20=>W B5@0?VW.

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

IA>@IFVO

52>D;>:A0F8= ?@8 ?5@>@0;L=> B0 <0965 ?>2=VABN 2A<>:BCTBLAO, ?@8 FL>2V :>=F5=B@0FVW C ?;072V 4>AO30NBLAO ?@>BO3<< 1 3>48=8. 1A>;NB=0 1V>4>ABC?=VABL AB0=>28BL ?@81;87=> 100 %.

60 <0965 =5 2?;820T =0 2A<>:BC20==O ;52>D;>:A0F8=C.

>7?>4V:

@81;87=> 30-40 % ;52>D;>:A0F8=C 72O7CTBLAO 7 ?@>B5W=>< A8@>20B:8 :@>2V. C@07>2> AC20==V ;52>D;>:A0F8=C C 4>7V 500 <3 1 @07 =0 4>1C ?@0:B8G=> 2V4ACB=V9. A=CT =57=0G=89, 0;5 ?5@5410GC20=89 :CAC20==O 4>7 ?> 500 <3 42VGV =0 4>1C. !B01V;L=89 AB0= 4>AO30TBLAO ?@>BO3<< 3 4=V2.

@>=8:=5==O C B:0=8=8 B0 @V48=8 >@30=V7

@>=8:=5==O C A;87>2C >1>;>=:C 1@>=EV2, 1@>=EV0;L=89 A5:@5B B:0=8= ;535=L (!") 0:A8<0;L=0 :>=F5=B@0FVO ;52>D;>:A0F8=C C A;87>2V9 >1>;>=FV 1@>=EV2 B0 1@>=EV0;L=> AC20==O 500 <3 ?5@>@0;L=> AB0=>28BL 8,3

@>=8:=5==O C B:0=8=8 ;535=L

0:A8<0;L=0 :>=F5=B@0FVO ;52>D;>:A0F8=C C B:0=8=0E ;535=L ?VA;O 70AB>AC20==O 500 <3 ?5@>@0;L=> AB0=>28BL ?@81;87=> 11,3 AO30TBLAO G5@57 4-6 3>48= ?VA;O 70AB>AC20==O ?@5?0@0BC. >=F5=B@0FVO C ;535=OE ?5@528ICT B0:C C ?;072V.

@>=8:=5==O C 2@>6=8=8 A5G>2>3>

0:A8<0;L=0 :>=F5=B@0FVO ;52>D;>:A0F8=C 4-6,7 AO30TBLAO G5@57 2-4 3>48=8 ?VA;O ?@89>BO3> <3 4=V2 70AB>AC20==O C 4>70E 500 <3 1 @07 01> 2 @078 =0 4>1C 2V4?>2V4=>.

@>=8:=5==O C F5@51@>A?V=0;L=C (A?8==><>7:>2C) @V48=C

52>D;>:A0F8= ?>30=> ?@>=8:OT C F5@51@>A?V=0;L=C @V48=C.

@>=8:=5==O C B:0=8=8 ?@>AB0B8

VA;O 70AB>AC20==O 500 <3 ;52>D;>:A0F8=C 1 @07 =0 4>1C ?@>BO3<< 3 4=V2 A5@54=V :>=F5=B@0FVW C B:0=8=V ?@>AB0B8 4>AO30NBL 8,7 2V4=> G5@57 2 3>48=8, 6 3>48= B0 24 3>48=8; A5@54=V9 :>5DVVVT=B :>=F5=B@0FV9 ?@>AB0B0/?;07<0 AB0=>28BL 1,84.

>=F5=B@0FVO C A5GV

15@54=O :>=F5=B@0FVO C A5GV G5@57 8-12 3>48= ?VA;O >4=>@07>2>3> ?@89>@0;L=> 4>78 150 <3, 300 <3 G8 500 <3 ;52>D;>:A0F8=C AB0=>28BL 44 <3/;, 91 <3/; B0 200 <3/; 2V4?>2V4=>.

V>B@0=AD>@<0FVO

52>D;>:A0F8= <5B01>;V7CTBLAO =57=0G=>N N, <5B01>;VB0<8 T 48A<5B8;-;52>D;>:A0F8= B0 ;52>D;>:A0F8= N->:A84. &V <5B01>;VB8 AB0=>2;OBL <5=H5 5 % :V;L:>ABV ?@5?0@0BC, I> 284V;OTBLAO 7 A5G5N. 52>D;>:A0F8= T AB5@5>EVAB01V;L=8< B0 =5 ?V4;O30T V=25@AVW E>@0;L=>W AB@C:BC@8.

82545==O

VA;O ?5@>@0;L=>3> B0 2=CB@VH=L>25==>3> 22545==O ;52>D;>:A0F8= 282>48BLAO 7 ?;07<8 :@>2V 2V4=>A=> ?>2V;L=> (?5@V>4 =0?V2282545==O AB0=>28BL 6-8 3>48=). 82545==O 2V41C20TBLAO 70728G09 =8@:0<8 (?=>04 85 % 22545=>W 4>78).

5<0T ACBBT2>W @V7=8FV C D0@<0:>:V=5B8FV ;52>D;>:A0F8=C ?VA;O 2=CB@VH=L>25==>3> B0 ?5@>@0;L=>3> 70AB>AC20==O, I> A2V4G8BL ?@> B5, I> FV H;OE8 (?5@>@0;L=89 B0 2=CB@VH=L>25==89) T 270T<>70

V=V9=VABL

52>D;>:A0F8= <0T ;V=V9=C D0@<0:>:V=5B8:C C 4V0?07>=V 50-600 <3.

0FVT=B8 7 =8@:>2>N =54>AB0B=VABN

0 D0@<0:>:V=5B8:C ;52>D;>:A0F8=C 2?;820T =8@:>20 =54>AB0B=VABL. @8 7=865==V DC=:FVW =8@>: 7=86CTBLAO =8@:>25 282545==O B0 ;;V@5=A, 0 ?5@V>48 =0?V2282545==O 71V;LHCNBLAO, O: 284=> 7 B01;8FV.

;V@5=A :@50B8=V=C (</E2)	< 20	20-40	50-80	0FVT=B8
8@:>289 ;;V@5=A (</E2)	13	26	57	;VB=L>3>
5@V>4 =0?V2282545==O (3>48=8)	35	27	9	2V:C

5<0T 7=0G=8E 2V4AB59 C D0@<0:>:V=5B8FV ;52>D;>:A0F8=C C <>;>48E ?0FVT=BV2 B0 ?0FVT=BV2 ;VB=L>3> 2V:C, :@V< 2V4AB59, ?>2O70=8E V7 ;;V@5=A< :@50B8=V=C.

5=45@=V 2V4ABV

V4><>, I> >:@5<89 0=0;V7 I>4> ?0FVT=BV2 6V=>G>W B0 G>;>2VG>W AB0BV ?@>45<>=AB@C202 =57=0G=V 2V4ABV C D0@<0:>:V=5B8FV ;52>D;>:A0F8=C 70;56=> 2V4 AB0BV. 5 VA=CT 4>:07V2 B>3>, I> FV 35=45@=V 2V4ABV T ;;V=VG=> 7=0GCI8<8.

;V=VG=V E0@0:B5@8AB8:8.

>:070==O.

>@>A;8< 7 V=D5:FVO<8 ;53:>3> 01> ?>3> ABC?5=O B06:>ABV ?@5?0@0B ?@87=0G0B8 4;O ;V:C20==O B0:8E V=D5:FV9, A?@8G8=5=8E GCB;828<8 4> ;52>D;>:A0F8=C >@30=V7<0<8: 3>AB@V A8=CA8B8, 703>AB@5==O E@>=VG=8E 1@>=EVBV2, ?=52<>=VW, CA::04=5=V B0 =5CA::04=5=V V=D5:FVW A5G>282V4=>3> B@0:BC (C B>=5D@8B8), V=D5:FVW H:V@8 V<'O:8E B:0=8=, E@>=VG=89 10:B5@V0;L=89 ?@>AB0B8B.

@>B8?>:070==O.

V428I5=0 GCB;82VABL 4> ;52>D;>:A0F8=C, V=H8E :>5=BV2 ?@5?0@0BC 01> 4> V=H8E EV=>;>=V2. ?V;5?AVO, =0O2=VABL ?>1VG=8E @50:FV9 7 1>:C ACE>68;L ?VA;O ?>?5@54=L>3> 70AB>AC20==O EV=>;>=V2.

70T<>4V0 7 V=H8<8 ;V:0@AL:8<8 70A>10<8 B0 V=HV 2848 270T<>4V9.

?;82 V=H8E ;V:0@AL:8E 70A>1V2 =0 ;52>D;>:A0F8=.

!>;V 70;V70, A>;V F8=:C, 0=B0F848, I> 78=.

A<>:BC20==O ;52>D;>:A0F8=C 7=0G=> 7=86CTBLAO ?@8 70AB>AC20==V A>;59 70;V70, <03=V9- 01> 0;N 4840=>78=C (F5 AB>ACTBLAO ;8H5 ;V:0@AL:8E D>@< 4840=>78=C 7 0;N <03=V92 @1FVN ?VA;O ?5@>@0;L=>3> ?@89><5=4CTBLAO =5 70AB>A>2C20B8 ?@5?0@0B8, O:V 20;5=B=V G8

B@820;5=B=V :0BV>=8, B0:V O: A>;V 70;V70, A>;V F8=:C, <03=V9- 01> 0;N 4840=>78= (F5 AB>ACTBLAO ;8H5 ;V:0@AL:8E D>@< 4840=>78=C 7 0;N <03=V92D;>:A0F8=C (482. @>74V; «!>AV1 70AB>AC20==O B0 4>78»). !>;V :0;L FVN <0NBL

!C:@0;LD0B

V>4>ABC?=VABL B01;5B>; ;52>D;>:A0F8=C 7=0G=> 7<5=HCTBLAO ?@8 >4=>G0A=>AC20==V ?@5?0@0BC 7 AC:@0;LD0B> ?0FVT=B>2V =5>1EV4=> >B@8 AC:@0;LD0B, B0: V ;52>D;>:A0F8=, :@0I5 ?@89<0B8 AC:@0;LD0B G5@57 2 3>48=8 ?VA;O ?@89>D;>:A0F8=C (482. @>74V; «!>AV1 70AB>AC20==O B0 4>78»).

"5>DV;V=, D5=1CD5= 01> V=HV ?>4V1=V =5AB5@>W4=V ?@>B870?0;L=V ;V:0@AL:V 70A>18 5 28O2;5=> D0@<0:>:V=5B8G=>W 270T<>4VW ;52>D;>:A0F8=C 7 B5>DV;V=>B5 <>6;825 ACBBT25 7=865==O AC4<=>3> ?>@>30 ?@8 >4=>G0A=>AC20==V EV=>;>=V2 7 B5>DV;V=>B5 =5AB5@>W4=8 <8 ?@>B870?0;L=8<8 ?@5?0@0B0<8 B0 V=H8<8 ;V:0@AL:8<8 70A>10<8, O:V 7<5=HCNBL AC4<=>89 ?>@V3. V4><>, I> :=F5=B@0FVO ;52>D;>:A0F8=C C ?@8ACB=>ABV D5=1CD5=C ?@81;87=> =0 13 % 28I0, =V6 ?@8 ?@89>D;>:A0F8=C.

@>15=5F84 V F8<5B848=

@>15=5F84 B0 F8<5B848= AB0B8AB8G=> 4>AB>2V@=> 2?;820NBL =0 282545==O ;52>D;>:A0F8=C.

8@>:289 ;V@5=A ;52>D;>:A0F8=C 7=86CTBLAO C ?@8ACB=>ABV F8<5B848=C =0 24 % B0
?@>15=5F84C =0 34 % . &5 ?>OA=NTBLAO B8<, I> >18420 ?@5?0@0B8 740B=V 1;>:C20B8 :0=0;LF52C
A5:@5FVN ;52>D;>:A0F8=C. !;V4 7 >15@56=VABN 70AB>A>2C20B8 ;52>D;>:A0F8=>4=>G0A=> 7
;V:0@AL:8<8 70A>10<8, I> 2?;820NBL =0 :0=0;LF52C A5:@5FVN, B0:8<8 O: ?@>15=5F84 B0 F8
<5B848=, >A>1;82> ?0FVT=B0< 7 =8@>2>N =54>AB0B=VABN.
=HV ;V:0@AL:V 70A>18
0 D0@<0:>:V=5B8:C ;52>D;>:A0F8=C ?@8 >4=>G0A=>

?;82 ?@5?0@0BC =0 V=HV ;V:0@AL:V 70A>18

?>A?>@8=

5@V>4 =0?V2282545==O F8;>A?>@8=C 71V;LHCTBLAO =0 33 % ?@8 >4=>G0A=>;52>D;>:A0F8=>
=B03>=VAB8 2VB0

@8 >4=>G0A=>AC20==V 7 0=B03>=VAB0<8 2VB0<) <>6CBL ?V428IC20B8AO ?>:07=8:8
>:03C;OFV9=8E B5ABV2 ('/4=5 =>@<0;V70FV9=5 A?V22V4=>H5==O) B0/01> 7 O2;OB8AO
:@>2>B5GV, O:V <>6CBL 1CB8 28@065=8<8. 2060NG8 =0 F5, C ?0FVT=BV2, O:V >B@8 0=B03>=VAB8
2VB01EV4=> :>=B@>;N20B8 ?>:07=8:8 :>03C;OFVW (482. @>74V; «A>1;82>ABV 70AB>AC20==O»
V:0@AL:V 70A>18, I> ?>4>26CNBL V=B5@20; Q"

52>D;>:A0F8=, O: V V=HV DB>@EV=>;>=8, A;V4 70AB>A>2C20B8 7 >15@56=VABN ?0FVT=B0<, O:V
>B@818, 2V4>TN 740B=VABN ?>4>26C20B8 V=B5@20; Q" (=0?@8::04 ?@>B80@8B18 ;:0AC B0 III,
B@8F8;;VG=V 0=B845?@5A0=B8 B0 <0:@>;V48) (482. @>74V; «A>1;82>ABV 70AB>AC20==O»
(«>4>265==O V=B5@20;C Q"»)).

=HVD>@<8 270T<>4VW

@89>< W6V

5 A?>AB5@V30;>AO ;:V=VG=> 7=0GCI>W 270T<>4VW 7 E0@G>28<8 ?@>4C:B0<8. "01;5B:8
;52>D;>:A0F8=C B0:8< G8=><>6=0 ?@89<0B8 =570;56=> 2V4 ?@89>

A>1;82>ABV 70AB>AC20==O.

5B8F8;V=-@578AB5=B=89 S.Aureus.

;O <5B8F8;V=-@578AB5=B=>3> S. Aureus (MRSA) VA=CT 4C65 28A>:0 V<>2V@=VABL
:>@578AB5=B=>ABV 4> DB>@EV=>;>=V2, C B> ;52>D;>:A0F8=C. # 7207:C 7 F8< ;52>D;>:A0F8= =5
@5:><5=4>20=89 4;O ;V:C20==O V=D5:FV9, 2V4<8< G8 ?V4>7@N20=8< 71C4=8:>< O:8E T MRSA, 70
28=OB:>< 28?04:V2, :>;8 @57C;LB0B8 ;01>@0B>@=8E B5ABV2 ?V4B25@48;8 GCB;82VABL 71C4=8:0
4> ;52>D;>:A0F8=C.

52>D;>:A0F8= <>6=0 70AB>A>2C20B8 4;O ;V:C20==O 3>AB@>3> 10:B5@V0;L=>3> A8=CA8BC B0
3>AB@>3> 703>AB@5==O E@>=VG=>3> 1@>=EVBC, O:I> FV V=D5:FVW 1C;8 4V03=>AB>20=>
2V4?>2V4=8< G8=>

578AB5=B=VABL 4> DB>@EV=>;>=V2 C E. coli (=091V;LH G0AB>3> 71C4=8:0 V=D5:FV9
A5G>282V4=8E H;OEV2) 20@VNT C @V7=8E :@0W=0E. @8 ?@87=0G5==V DB>@EV=>;>=V2 A;V4
2@0E>2C20B8 H8@5=VABL @578AB5=B=>ABV E. Aoli 4> DB>@EV=>;>=V2.

@8 4C65 B06:>

>A?VB0;L=V V=D5:FVW, A?@8G8=5=VP. aeruginosa, <>6CBL ?>B@51C20B8 :><1V=>20=>W
B5@0?VW.

"5=48=VB B0 @>7@828 ACE>68;L

V4:> <>6CBL B@0?;OB8AO 28?04:8 B5=48=VBC. 09G0ABVH5 F5 AB>ACTBLAO 0EV;;>2>3> ACE>68;;O
B0 <>65 ?@8725AB8 4> @>7@82C ACE>68;;O. &59 =51060=89 5D5:B <>65 28=8:0B8 ?@>B03<< 48
3>48= ?VA;O ?>G0B:C ;V:C20==O B0<>65 1CB8 42>1VG=87@82C ACE>68;;O 71V;LHCTBLAO C
?0FVT=BV2 ;VB=L>3> 2V:C, C ?0FVT=BV2, O:V >B@870E 1000 <3 =0 4>1C, B0 C ?0FVT=BV2, O:V
?@89<0NBL :>@B8:>AB5@>W48. # ?0FVT=BV2 ;VB=L>3> 2V:C A;V4 :>@83C20B8 4>1>2C 4>7C
?@5?0@0BC 70;56=> 2V4 ;:V@5=AC :@50B8=V=C (482. @>74V; «!>AV1 70AB>AC20==O B0 4>78»)." >
1EV4=5 @5B5;L=5 A?>AB5@565==O 70 B0:8<8 ?0FVT=B0<8, O:I> W< ?@87=0G0NBL ;52>D;>:A0F8=
0FVT=B0< A;V4 ?@>:>=AC;LBC20B8AO 7 ;V:0@5<, O:I> C =8E 7 O28;8AO A8<8 B5=48=VBC. @8
?V4>7@V =0 B5=48=VB B5@0?VN ?@5?0@0B<< ?>B@V1=> =5309=> ?@8?8=8B8 B0 @>7?>G0B8
=0;56=5 ;V:C20==O (=0?@8::04 70157?5G8B8 V<<>1V;V70FVN ACE>68;;O).

0E2>@N20==O, A?@8G8=5=V Clostridium difficile

V0@5O, >A>1;82> C BO6:8E 28?04:0E, ?5@A8ABCNG0 B0/01> 35<>@03VG=0, ?V4 G0A G8 ?VA;O ;V:C20==O ?@5?0@0B<< <>65 1CB8 A8<<< E2>@>18, A?@8G8=5=>W Clostridium difficile =091V;LH BO6:>N D>@<>N O:>W T ?A524<<5<1@0=>7=89 :>;VB. /:I> 28=8:0NBL ?V4>7@8 =0 ?A524<<5 <1@0=>7=89 :>;VB, A;V4 =5309=> ?@8?8=8B8 70AB>AC20==O ?@5?0@0BC, 0 ?0FVT=V2 =5>1EV4=> B5@2> ;V:C20B8 ?V4B@8 A?5F8DVG=>W B5@0?VW (=0?@8::04 ?5@>@0;L=89 ?@89<< 20=:>18, I> ?@83=VGCNBL <>B>@8:C :8H5G=8:C, ?@>B8?>:070=V C FV9 ;;V=VG=V9 A8BC0FVW.

0FVT=B8, AE8;L=V 4> AC4<<

@5?0@0B ?@>B8?>:070=89 ?0FVT=B0< 7 5?V;5?AVTN 2 0=0=57V. /: V C 28?04:C 7 V=H8<8 EV=>;>=0 <8, ;52>D;>:A0F8= A;V4 70AB>A>2C20B8 7 =04728G09=>N >15@56=VABN ?0FVT=B0<, AE8;L=8< 4> AC4<<, 7>:@5<0 ?0FVT=B0< 7 ?>?5@54=V<8 C@065==O<8 F5=B@0;L=>W =5@2>2>W A8AB5<8, ?@8 >4=>G0A=V9 B5@0?VW D5=1CD5=<< B0 ?>4V1=8<8 4> =L>3> =5AB5@>W4=8<8 ?@>B870?0;L=8<8 ;V:0@AL:8<8 70A>10<8 G8 ?@5?0@0B0<8, I> ?V428ICNBL AC4<<=C 3>B>2=VABL (7=86CNBL AC4 <=<89 ?>@V3), =0?@8::04 B5>DV;V=<< (482. @>74V; <<□70T<>4VO 7 V=H8<8 ;V:0@AL:8<8 70A>10<8 B0 V=HV 2848 270T<>4V9)). # @07V ?>O28 AC4<< ;V:C20==O ;52>D;>:A0F8=<< =5>1EV4=> ?@8?8=8B8.

0FVT=B8 7 =54>AB0B=VABN 3;N:>7>-6-D>AD0B453V4@>35=078

0FVT=B8 7 ;0B5=B=8<8 G8 =0O2=8<8 45D5:B0<8 0:B82=>ABV 3;N:>7>-6-D>AD0B453V4@>35=078 AE8;L=V 4> 35<>;VB8G=8E @50:FV9 ?@8 ;V:C20==V 0=B810:B5@V0;L=8<8 70A>10<8 3@C?8 EV=>;>=V2 V B>D;>:A0F8= W< A;V4 70AB>A>2C20B8 7 >15@56=VABN.

0FVT=B8 7 =8@:>2>N =54>AB0B=VABN

A;V;L:8 ;52>D;>:A0F8= 282>48BLAO ?5@5206=> =8@:0<8, ?>B@V1=0 :>@5:FVO 4>78 4;O E2>@8E 7 >A;01;5=>N DC=:FVTN =8@: (=8@:>2>N =54>AB0B=VABN) (482. @>74V;«!>AV1 70AB>AC20==O B0 4>78»).

50:FVW ?V428I5=>W GCB;82>ABV (3V?5@GCB;82>ABV)

52>D;>:A0F8= <>65 G0A 2V4 G0AC A?@8G8=OB8 A5@9>7=V, ?>B5=V9=> ;5B0;L=V @50:FVW ?V428I5=>W GCB;82>ABV (=0?@8::04 0=3V=>52@>B8G=89 =01@O: 06 4> 0=0DV;0:B8G=>3> H>:C) ?VA;O 70AB>AC20==O ?>G0B:>2>W 4>78 (482. @>74V; «1VG=V @50:FVW»). # B0:> ;V:0@O.

06:V 1C;L>7=V @50:FVW.

@8 70AB>AC20==V ;52>D;>:A0F8=C ?>2V4<<;O;>AO ?@> 28=8:=5==O 206:8E 1C;L>7=8E @50:FV9, B0:8E O: A8=4@<< !BV25=A0-6=>A=>0 01> B>:A8G=89 5?V45@<0;L=89 =5:@>;V7 (482. @>74V; <<>1VG=V @50:FVW»). @8 28=8:=5==V 1C4L-O:8E @50:FV9 7 1>:C H:V@8 B0/01> A;87>28E >1>;>=: A;V4 =5309=> ?@8?8=8B8 ?@89<< ;52>D;>:A0F8=C, 725@=CB8AO 4> ;V:0@O V, ?@8 =5>1EV4=>ABV, @>7?>G0B8 2V4?>2V4=5 ;V:C20==O.

78 2 :@>2V.

/: V ?@8 70AB>AC20==V CAVE EV=>;>=V2, ?>2V4<<;O;>AO ?@> 28?04:8 7:C @V2=O 3;N:>78 2 :@>2V, A5@54 O:8E 1C;8 28?04:8 3V?>3;V:5 A?>AB5@V30;8AO, O: ?@028;>, C ?0FVT=V2 7 FC:@>28< 4V015B<<, O:V >B@8 ?5@>@0;L=8< FC:@>7=86C20;L=8< ?@5?0@0B<< (=0?@8::04, 3;V15=:<0) 01> V=AC;V=>2V4<<;O;>AO ?@> 28?04:8 3V?>3;V:5W :<<8. # ?0FVT=V2 7 FC:@>28< 4V015B<< @5:> <5=4CTBLAO @5B5;L=> :>=B@>;N20B8 @V25=L 3;N:>78 FC:@C 2 :@>2V (482. @>74V; «>1VG=V @50:FVW»).

@>DV;0:B8:0 D>B>A5=A81V;V70FVW

%>G0 D>B>A5=A81V;V70FVO 28=8:0T 4C65 @V4:> ?@8 ?@89>D;>:A0F8=C, 7 <5B>N WW C=8:=5==O ?0FVT=B0< =5 @5:><5=4CTBLAO 157 >A>1;82>W ?>B@518 ?V44020B8AO 4VW A8;L=8E A=>OG=8E ?@><5=V2 G8 HBCG=>3> # \$-28?@> C;LB@0DV>;5B>2>3> 28?@>;O@VN).

0FVT=B8, O:V >B@8=VAB8 2VB0

7207:C 7 <>6;828< 71V;LH5==O< ?>:07=8:V2 :>03C;OFV9=8E B5ABV2 (1/4=5 =>@<0;V70FV9=5 A?V22V4=>H5==O) V/01> :@>2>B5GV C ?0FVT=V2, O:V ?@89<0;8 ;52>D;>:A0F8= C ?>T4=0==V 7 0=B03>=VAB<< 2VB0<), A;V4 A?>AB5@V30B8 70 ?>:07=8:0<8 :>03C;OFV9=8E B5ABV2 (482. @>74V; « 70T<>4VO 7 V=H8<8 ;V:0@AL:8<8 70A>10<8 B0 V=HV 2848 270T<>4V9»).

A8E>B8G=V @50:FVW

V4><> ?@> ?A8E>B8G=V @50:FVW C ?0FVT=V2, O:V ?@89<0NBL EV=>;>=8, 2;;NG0NG8 ;52>D;>:A0F8=. # @V4:VA=8E 28?04:0E B0:V @50:FVW ?@>3@5AC20;8 4> ACWF840;L=8E 4C<<: B0 A0 <>45AB@C:B82=>W ?>254V=:8, V=>4V =02VBL ?VA;O ?@89=4=VTW 4>78 ;52>D;>:A0F8=C (482.

@>74V; <>1VG=V @50:FVW». # @07V, O:I> C ?0FVT=B0 28=8:0NBL FV @50:FVW, ?@89<
>52>D;>:A0F8=C A;V4 ?@8?8=8B8 B0 240B8AO 4> 2V4?>2V4=8E 70E>4V2. 5:><5=4CTBLAO 7
>15@56=VABN 70AB>A>2C20B8 ;52>D;>:A0F8= ?0FVT=B0< V7 ?A8E>B8G=8<8 @>7;040<8 B0
?0FVT=B0< V7 ?A8E>B8G=8<8 70E2>@N20==O<8 2 0=0<=57V.
>4>265==O V=B5@20;C QT
!;V4 7 >15@56=VABN 70AB>A>2C20B8 DB>@EV=>;>=8, 2::NG0NG8 ;52>D;>:A0F8=, ?0FVT=B0< 7
2V4><8<8 D0:B>@0<8 @878:C ?>4>265==O V=B5@20;C QT, B0:8<8 O::
2@>465=89 A8=4@<< ?>4>265==O V=B5@20;C QT;
AC?CB=T 70AB>AC20==O ;V:0@AL:8E 70A>1V2, 2V4><8E A2>TN 740B=VABN ?>4>26C20B8
V=B5@20; QT (B0:8E O: ?@>B80@8B18 ;:0AC B0 , B@8F8;;VG=V 0=B845?@5A0=B8, <0:@>;V48);
=5A:>@83>20=89 5;5:B@>;VB=89 48A10;0=A (=0?@8;;04 3V?>:0;VT<03=VT
;VB=V9 2V;;
E2>@>10 A5@FO (=0?@8;;04 A5@F520 =54>AB0B=VABL, V=D0@:B:0@40, 1@048:0@4VO) (482.
@>74V;8 «!>AV1 70AB>AC20==O B0 4>78» («0FVT=B8 ;VB=L>3> 2V:C»), «□70T<>4VO 7 V=H8<8
;V:0@AL:8<8 70A>10<8 B0 V=HV 2848 270T<>4V9», «>1VG=V @50:FVW», «5@54>7C20==O»).
5@8D5@8G=0 =59@>?0BVO
V4><> ?@> A5=A>@=C G8 A5=A<>B>@=C ?5@8D5@8G=C =59@>?0BVN, I> <>65 28=8:0B8
@0?B>2>, C ?0FVT=BV2, O:V ?@89<0;8 DB>@EV=>;>=8, 2::NG0NG8 ;52>D;>:A0F8=. @89<<
>52>D;>:A0F8=C A;V4 ?@8?8=8B8, O:I> C ?0FVT=B0 A?>AB5@V30NBLAO A8<8 =59@>?0BVW, I>1
?>?5@548B8 28=8:=5==O =5>1>@>B=>3> AB0=C.
5?0B>1V;V0@=V ?>@CH5==O
V4><> ?@> 28?04:8 =5:@>B8G=>3> 35?0B8BC, 06 4> ?5GV=:>2>W =54>AB0B=>ABV, I> 703@>6C20;0
68BBN, ?@8 ?@89>D;>:A0F8=C, ?5@5206=> C ?0FVT=BV2 7 BO6:8<8 >A=>2=8<8 70E2>@N20==O<8,
=0?@8;;04 A5?A8A<< (482. @>74V; <>1VG=V @50:FVW»). 0FVT=B0< A;V4 ?>@5:><5=4C20B8
?@8?8=8B8 ;V:C20==O B0 725@=CB8AO 4> ;V:0@O, O:I> 28=8:0NBL B0:V A8<8 E2>@>18 ?5GV=:8 O:
0=>@5:AVO, 6>2BO=8FO, G>@=0 A5G0, A25@1V6 01> 1V;L C 4V;O=FV 682>B0
03>AB@5==O myasthenia gravis.
\$B>@EV=>;>=8, 2::NG0NG8 ;52>D;>:A0F8=, <0NBL 5D5:B =5@2>2><O7>2>W 1;>:048 B0 <>6CBL
703>AB@N20B8 <O7>2C A;01:VABL C ?0FVT=BV2 7 myasthenia gravis. # ?VA;O@5TAB@0FV9=4V C
?0FVT=BV2 7 myasthenia gravis V7 70AB>AC20==O< DB>@EV=>;>=V2 1C;8 0A>FV9>20=V A5@9>7=V
?>1VG=V @50:FVW, 2::NG0NG8 ;5B0;L=V 28?04:8 B0 AB0=8, I> ?>B@51C20;8 70E>48 7 ?V4B@8
D;>:A0F8= =5 @5:><5=4>20=> 70AB>A>2C20B8 ?0FVT=B0< 7 myasthenia gravis 2 0=0<=57V.
>@CH5==O 7>@C.
/I> ?@8 ?@89>D;>:A0F8=C 28=8:0NBL 1C4L-O:V ?>@CH5==O 7>@C 01> ?>1VG=V @50:FVW 7 1>:C
>@30=V2 7>@C, A;V4 =5309=> 725@=CB8AO 4> >DB0;L<>;>30 (482. @>74V;8 <>1VG=V @50:FVW» B0
«40B=VABL 2?;820B8 =0 H284:VABL @50:FVW ?@8 :5@C20==V 02B>B@0=A?>@B× 01> V=H8<8
<5E0=V7<0<8»).
!C?5@V=D5:FVO.
0AB>AC20==O ;52>D;>:A0F8=C, >A>1;82> B@820;5, <>65 ?@872>48B8 4> =043> @>ABC =5GCB;828E
(@578AB5=B=8E) 4> ?@5?0@0BC >@30=V7 =0 B;V B5@0?VW @>72820TBLAO AC?5@V=D5:FVO,
=5>1EV4=> 70AB>AC20B8 =0;56=V 70E>48.
?;82 =0 @57C;LB0B8 ;01>@0B>@=8E 4>A;V465=L.
?0FVT=BV2, O:V >B@8D;>:A0F8=, 287=0G5==O >?V0BV2 C A5GV <>65 40B8 E81=>-?>78B82=89
@57C;LB0B. >65 28=8:=CB8 =5>1EV4=VABL ?V4B25@465==O ?>78B82=8E @57C;LB0BV2 =0 >?V0B8
70 4>?><>3>N A?5F8DVG=8E <5B>4V2.
52>D;>:A0F8= <>65 ?@83=VGC20B8 @VAB Mycobacterium tuberculosis V C 7207:C 7 F8< ?@872>48B8
4> E81=>-530B82=8E @57C;LB0BV2 ?@8 10:B5@V>;>3VG=V9 4V03=>AB8FV BC15@:C;L>7C.
5>1EV4=> 1@0B8 4> C2038 >DVFV9=V =0AB0=>28 I>4> 4>FV;L=>3> 70AB>AC20==O
0=B810:B5@V0;L=8E 70A>1V2.
0AB>AC20==O C ?5@V>4 203VB=>ABV 01> 3>4C20==O 3@C44N.

'5@57 2V4ACB=VABL 4>A;V465=L B0<>6;825 CH:>465==O EV=>;>=0<8 AC3;>1>2>3> E@OI0 2
 >@30=V7AB5, ?@5?0@0B ?@>B8?>:070=> ?@87=0G0B8 203VB=8< B0 6V=:0<, O:V 3>4CNBL 3@C44N.
 /:I> ?V4 G0A ;V:C20==O ?@5?0@0B< 4V03=>ABCTBLAO 203VB=VABL, ?@> F5 A;V4 ?>2V4<8B8
 ;V:0@O.
 52>D;>:A0F8= =5 ?@872>482 4> ?>@CH5=L D5@B8;L=>ABV 01> @5?@>4C:B82=>W DC=:FVW C
 IC@V2.

**40B=VABL 2?;820B8 =0 H284:VABL @50:FVW ?@8 :5@C20==V 02B>B@0=A?>@B< 01> V=H8<8
 <5E0=V7<0<8.**

0FVT=B0<, O:V :5@CNBL B@0=A?>@B=8<8 70A>10<8, ?@0FNNBL 7 <0H8=0<8 B0 <5E0=V7<0<8,
 A;V4 2@0EC20B8 <>6;82V =51060=V @50:FVW 7 1>:C =5@2>2>W A8AB5<8 (70?0<>@>G5==O,
 A>=:82VABL, A?;CB0=VABL A2V4<8>ABV, @>7;048 7>@C B0 A;CEC, @>7;048 ?@>F5AV2 @CEC, C B.
 G. ?V4 G0A E>4L18), O:V ?>@CHCNBL 740B=VABL ?0FVT=B0 4> :>=F5=B@0FVW C2038 G8
 H284:>ABV 9>3> @50:FVW.

!>AV1 70AB>AC20==O B0 4>78.

"01;5B:8 ?@89<0B8 1 01> 2 @078 =0 4>1C. >70 70;568BL 2V4 B8?C V BO6:>ABV V=D5:FVW.
 "@820;VABL ;V:C20==O 70;568BL 2V4 ?5@51V3C E2>@>18. 5:<5=4>20=> ?@>4>26C20B8 ;V:C20==O
 ?@5?0@0B<< ?@8=09<=V ?@>BO3<< 48-72 3>48= ?VA;O =>@<0;V70FVW B5 ?V4B25@465=>3>
 1V>;>3VG=8<8 B5AB0<8 7=8I5==O 71C4=8:V2.
 "01;5B:8 A;V4 :>2B0B8, =5 @>76>2CNG8, 70?820NG8 4>AB0B=L>N :V;L:VABN @V48=8. ;O
 7@CG=>ABV 4>7C20==O B01;5B:C <>6=0 @>74V;8B8 70 4>?<>3>N @8A:8 4;O @>7?>4V;C. @89<0B8
 WE <>6=0 O: @07<< 7 W65N, B0: V 2 V=H89 G0A.
 >@>A;8< ?0FVT=B0< V7 =>@<0;L=>N DC=:FVTN =8@>: (:;V@5=A :@50B8=V=C ?>=04 50<;/E2)
 A;V4 4>B@8<5=40FV9:

>:070==O	>1>20 4>70	V;L:VABL ?@89>1C	"@820;VABL ;V:C20==O
>AB@V A8=CA8B8	500 <3	1 @07	10-14 4=V2
03>AB@5==O E@>=VG=>3> 1@>=EVBC	250-500 <3	1 @07	7-10 4=V2
53>A?VB0;L=V ?=52<>=VW	500 <3	1-2 @078	7-14 4=V2
5CA::04=5=V V=D5:FVW A5G>282V4=8E H;OEV2	250 <3	1 @07	3 4=V
%@>=VG=89 10:B5@V0;L=89 ?@>AB0B8B	500 <3	1 @07	28 4=V2
#A::04=5=V V=D5:FVW A5G>282V4=8E H;OEV2 2::NG=> 7 ?VT;>=5D@8B<	250 <3	1 @07	7-10 4=V2
=D5:FVW H:V@8 V <O:8E B:0=8=	250-500 <3	1-2 @078	7-14 4=V2

>7C20==O 4;O ?0FVT=BV2 7 ?>@CH5=>N DC=:FVTN =8@>;, C O:8E ;;V@5=A :@50B8=V=C <5=H5
 50 <;/E2:

;V@5=A :@50B8=V=C	568< 4>7C20==O (70;56=> 2V4 BO6:>ABV V=D5:FVW B0 =>7>;>3VG=>W D>@<8)		
	250 <3/24 3>4	500 <3/24 3>4	500 <3/12 3>4

	?5@H0 4>70:	?5@H0 4>70:	?5@H0 4>70:
50-20 <:/E2	250 <3 =0ABC?=V: 125* <3/24 3>4	500 <3 =0ABC?=V: 250 <3/24 3>4	500 <3 =0ABC?=V: 250 <3/12 3>4
19-10 <:/E2	?5@H0 4>70: 250 <3 =0ABC?=V: 125* <3/ 48 3>4	?5@H0 4>70: 500 <3 =0ABC?=V: 125* <3/24 3>4	?5@H0 4>70: 500 <3 =0ABC?=V: 125* <3/12 3>4
□ 10 <:/E2, (0 B0:>6 ?@8 35<>4V0;V7V B0 %1)	?5@H0 4>70: 250 <3 =0ABC?=V: 125* <3/48 3>4	?5@H0 4>70: 500 <3 =0ABC?=V: 125* <3/24 3>4	?5@H0 4>70: 500 <3 =0ABC?=V: 125* <3/24 3>4

* - 70AB>A>2C20B8 C 2V4?>2V4=>7C20==V.

1VA;O 35<>4V0;V7C 01> E@=>VG=>3> 0<1C;0B>@=>3> ?5@8B>=50;L=>3> 4V0;V7C (%) 4>40B:>2V
4>78 =5 ?>B@V1=V.

>7C20==O 4;O ?0FVT=BV2 7 ?>@CH5=>N DC=:FVTN ?5GV=:8. >@5:FVO 4>78 =5 ?>B@V1=0,
>A;V;L:8 ;52>D;>:A0F8= =57=0G=>N N <5B01>;V7CTBLAO C ?5GV=FV B0 282>48BLAO ?5@5206=>
=8@:0<8.

>7C20==O 4;O ?0FVT=BV2 ;VB=L>3> 2V:C. /:I> =8@:>20 DC=:FVO =5 ?>@CH5=0, =5<0T ?>B@518 C
:>@5:FVW 4>78.

VB8.

0AB>AC20==O ?@5?0@0BC ?@>B8?>:070=> 4VBO<, >A;V;L:8 =5 28;;NG5=> CH:>465==O
AC3;>1>2>3> E@OI0.

5@54>7C20==O.

09206;82VHV ?5@5410GC20=V A8<8 ?5@54>7C20==O ?@5?0@0BC AB>ACNBLAO F5=B@0;L=>W
=5@2>2>W A8AB5<8 (70?0<>@>G5==O, ?>@CH5==O A2V4<>ABV B0 AC4<=>V =0?048); @50:FVW 7
1>:C H;C=:>2>.:8H:>2>W A8AB5<8, B0:V O: =C4>B0 B0 5@>7VO A;87>28E >1>;>=: @8

70AB>AC20==V 4>7 28I8E 70 B5@0?52B8G=V 2V41C20TBLAO ?>4>265==O QT-V=B5@20;C. # @07V
?5@54>7C20==O =5>1EV4=> ?@>2>48B8 @5B5;L=5 A?>AB5@565==O 70 ?0FVT=B<, 2;;NG0NG8 .
V:C20==O: B5@0?VO A8<0B8G=0. # @07V 3>AB@>3> ?5@54>7C20==O ?@87=0G0B8 ?@<820==O
H;C=:0. ;O 70E8ABC A;87>2>W H;C=:0 70AB>A>2C20B8 0=B0F84=V 70A>18.

5<>4V0;V7, C B>=50;L=89 4V0;V7 01> %, =5 T 5D5:B82=8< 4;O 282545==O ;52>D;>:A0F8=C 7 >@30=V7
4=8E A?5F8DVG=8E 0=B84>BV2.

>1VG=V @50:FVW.

=D5:FVW B0 V=207VW: 3@81:>2V V=D5:FVW, 2;;NG0NG8 3@818 @>4C Candida, ?@>;VD5@0FVO
V=H8E @578AB5=B=8E >@30=V7, ?>@CH5==O =>@<0;L=>W D;>@8 :8H5G=8:C B0 @>728B:C
2B>@8==>W V=D5:FVW.

I>:C A8AB5<8 :@>2V B0 ;VW A8AB5<8 :;59:>?5=VO, 5>78=>DV;VO, =59B@>?5=VO, 03@0=C;>F8B>7,
?0=F8B>?5=VO, 35<>;VB8G=0 0=5<1>F8B>?5=VO, O:0 <>65 A?@8G8=8B8 ?V428I5=C AE8;L=VABL 4>
:@>2>28;82V2 01> :@>2>B5G.

I>:C VW A8AB5<8: @50:FVW 3V?5@GCB;82>ABV, 2;;NG0NG8 0=0DV;0:B8G=89/ 0=0DV;0:B>W4=89
H>;, <>6CBL A?>AB5@V30B8AO =02VBL ?VA;O ?5@H>W 4>78 ?@>BO3< :V;L:>E E28;8= 01> 3>48=
?VA;O 70AB>AC20==O (482. @>74V; «A>1;82>ABV 70AB>AC20==O»); 0=3V>=52@>B8G=89 =01@O.;
:@>?82O=:C, A?07< 1@>=EV2, O4CEC, =01@O: H:V@8 B0 A;87>28E, @0?B>25 7=865==O
0@B5@V0;L=>3> B8A:C, H>:.

I>:C <5B01>;V70=>@5:AVO, 2V4ACB=VAB 0?5B8BC, 3V?>3;V:5A>1;82> C ?0FVT=BV2, E2>@8E =0
4V015B (482. @>74V; «A>1;82>ABV 70AB>AC20==O»), 3V?5@3;V:53;V:5<0. 7=0:0<8 3V?>3;V:5:.

I>:C ?A8EV:8: 157A>==O, =5728G09=V A=>284V==O, =VG=V :>H<0@8, 068B0FVO, =5@2>2VABL, =5A?>:V9, 2V4GCBBO AB@0EC, ?A8E>B8G=V @>7;048 (C B.G. ?0@0=>O, 30;NF8=0FVW), 45?@5AVO, B@82>6=VABL, AB0=8 AB@0EC, ?A8E>B8G=V @50:FVW 7 A@>45AB@C:B82=>N ?>254V=>N, 2;;NG0NG8 ACWF840;L=C A?@O<>20=VABL<8A;5==O G8 4V9 (482. @>74V; «A>1;82>ABV 70AB>AC20==O»).

I>:C =5@2>2>W A8AB5<8: 3>;>2=89 1V;L, 70?0<>@>G5==O, A?;CB0=VABL A2V4<>ABV, 70FV?5=V==O, @>7;048 A=C, A=>;82VABL, ?0@5AB57VO, B@5<>@, AC4<8, :=>2C;LAVO, ?5@8D5@8G=0 A5=A>@=0 G8 A5=A<>B>@=0 =59@>?0BVO, 7=865=5 2V4GCBBO 4>B8:C; 48A3527VO (AC1T:B82=89 @>7;04 A<0:C), 2;;NG0NG8 03527VN (2B@0BC A<0:C); ?0@>A@CH5==O =NEC), 2;;NG0NG8 0=>A7;048, 48A:V=57VO (?>@CH5==O :>>@48=0FVW @CEV2), A8=>?5 (=5?@8B> <=VABL), 4>1@>O:VA=0 2=CB@VH=L>G5@5?>0 3V?5@B5=7VO.

I>:C >@30=V2 7>@C: 7>@>2V ?>@CH5==O, 70BC<0=5==O 7>@C, =5GVB:VABL 7>@C, B820 2B@0B0 7>@C.

I>:C >@30=V2 A;CEC B0 @V2=>2038: 25@B83>, ?>@CH5==O A;CEC, 472V= C 2CE0E, ?>@CH5==O A;CEC, 2B@0B0 A;CEC.

I>:C A5@F52>-AC48==>W A8AB5<8: B0EV:0@4VO, 2V4GCBBO A5@F518BBO, H;C=>G:>20 0@8B G:>2V B0EV:0@4VO V ?>;V<>@D=0 H;C=>G:>20 B0EV:0@4VO B8?C torsade de pointes (?5@5206=> C ?0FVT=BV2 7 D0:B>@<< @878:C ?>4>265==O V=B5@20;C QT), I> <>65 ?@872>48B8 4> 7C?8=:8 A5@FO, ?>4>265==O V=B5@20;C QT =0 5;5:B@>:0@4V>3@074V;8 «A>1;82>ABV 70AB>AC20==O» («>4>265==O V=B5@20;C QT») B0 «5@54>7C20==O»), 0@B5@V0;L=0 3V?>B5=7VO, :>;0?A, ?>4V1=89 4;O H>:C; 0;5@3VG=89 20A:C;VB.

I>:C 48E0;L=>W A8AB5<8: 7048H:0 (48A?=>5), 1@>=E>A?07<, 0;5@3VG=89 ?=52<>=VB.

I>:C B@02=>3> B@0:BC: 2V4ACB=VABL 0?5B8BC, 4V0@5O, =C4>B0, 1;N20==O, 1V;L C 682>BV, 48A?5?AVO, @>7;048 B@02;5==O, 74CBBO 682>B0, 70?>@8, 35<>@03VG=0 4V0@5O, I> <>65 A2V4G8B8 ?@> 5=B5@>:>;VB, 2;;NG0NG8 ?A524<>5<1@0=>7=89 :>;VB (482. @>74V; «A>1;82>ABV 70AB>AC20==O»), ?0=:@50B8B.

I>:C 35?0B>1V;V0@=>W A8AB5<8: ?V428I5==O ?>:07=8:V2 ?5GV=>28E 5=78W D>AD0B078, "), ?V428I5==O 1V;V@C1V=C, 35?0B8B, 6>2BO=8FO, BO6:5 C@065==O ?5GV=:8, 2;;NG0NG8 28?04:8 3>AB@>W ?5GV=>2>W =54>AB0B=>ABV (V=>4V ;5B0;L=V), ?5@5206=> C ?0FVT=BV2 7 BO6:8<8 >A=>2=8<8 70E2>@N20==O<8 (482. @>74V; «A>1;82>ABV 70AB>AC20==O»).

I>:C H:V@8 B0 ?V4H:V@=8E B:0=8=: ?>G5@2>=V==O H:V@8, CB2>@5==O ?CE8@V2, 28A8?0==O, A25@1V6, :@>?82□O=:0, 3V?5@3V4@>7, 5:AC40B82=0 @<=0 5@8B5<0, B>:A8G=89 5?V45@<0;L=89 =5:@>;V7 (A8=4@<< 09T;;0), A8=4@< !BV25=A0-6=>A>=0, @50:FVW D>B>GCB;82>ABV, ?V428I5=0 GCB;82VABL 4> A>=OG=>3> B0 C;LB@0DV>;5B>2>3> 28?@F8B>?;0AB8G=89 20A:C;VB, AB<0B8B.

I>:C :VAB:>2>-<O7>2>W A8AB5<8 B0 A?>;CG=>W B:0=8=8: 0@B@0;3VO, C@065==O ACE>68;L (482. @>74V; «A>1;82>ABV 70AB>AC20==O»), C B>2>3> ACE>68;;O); <O7>20 A;01:VABL, O:0<>65 <0B8 >A>1;825 7=0G5==O 4;O E2>@8E =0 BO6:C gravis (482. @>74V; «A>1;82>ABV 70AB>AC20==O»), @014>;V7, @>7@82 72O7>;, @>728: <O7V2, @>7@82 ACE>68;;O (=0?@8;;04 0EV;>2>3>) (482. @>74V; «A>1;82>ABV 70AB>AC20==O»), 0@B@8B.

I>:C =8@>: B0 A5G>284V;L=>W A8AB5<8: ?V428I5=V ?>:07=8:8 :@50B8=V=C 2 A8@>20BFV :@>2V, 3>AB@0 =8@>20 =54>AB0B=VABL (=0?@8;;04, 2=0A;V4>: V=B5@AB8FV0;L=>3> =5D@8BC).

030;L=V @>7;048: 0AB5=VO, 7030;L=0 A;01:VABL, ?V428I5=0 B5AC20==V V=H8E DB>@EV=>;>=V2, <>6;82V=0?048 ?>@DV@VW C ?0FVT=BV2 7 =0O2=VABN ?>@DV@VW.

"5@ABV.

4 @>:8.

#<>28 715@V30==O.

15@V30B8 ?@8 B5□ 2 >@83V=0;L=V9 C?0:>2FV.

15@V30B8 C =54>ABC?=>

#?0:>2:0.

> 7 B01;5B>: C 1;VAB5@V, ?> 1 1;VAB5@C C :0@B>==V9 C?0:>2FV.

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

0 @5F5?B>

8@>1=8:.

'!' .(.

VAF57=0E>465==O 28@>1=8:0 B0 9>3> 04@5A020465==O 4VO;L=>ABV.

!0=:0:;0@ >CW 81100 <. N7465, "C@5GG8=0.