

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

\$&®
(IFICIPRO®)

!;:04:

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

1 B01;5B:0 ?> 250 <3

1 B01;5B:0 ?> 500 <3

4>?>28=8: F5;N;>70 :@8AB0;VG=0, :@5<=VN 48>:A84 :>;>W4=89 1572>4=89, =0B@VN :@>E

<0;L3;V:>;OB (B8?), :@>E<0;L :C:C@C47O=89, <03=VN AB50@0B, B0;L:, ?0@V 1V;89 33G28707.

V:0@AL:0 D>@<0. "01;5B:8 2:@8BV ?;V2:>2>N >1>;>=:>N.

\$0@<0:>B5@0?52B8G=0 3@C?0. =B810:B5@V0;L=V 70A>18 4;O A8AB5<=>3> 70AB>AC20==O.

@C?0 DB>@EV=>;>=V2. >4 " J01M A02.

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

>:070==O.

5CA:;04=5=V B0 CA:;04=5=V V=D5:FVW, A?@8G8=5=V 71C4=8:0<8, GCB;828<8 4> F8?@>D;>:A0F8=C.

□ =D5:FVW 48E0;L=8E H;OEV2: F8?@>D;>:A0F8= <>65 @5:><5=4C20B8AO 4;O ;V:C20==O ?=52
<>=V9, A?@8G8=5=8E *Klebsiella spp.*, *Enterobacter spp.*, *Proteus spp.*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Haemophilus spp.*, *Moraxella catarrhalis*, *Legionella*B0 AB0DV;>:>:0<8.

□ =D5:FVW A5@54=L>3> 2CE0 (A5@54=V9 >B8B) B0 ?@840B:>28E ?07CE =>A0 (A8=CA8B),
>A>1;82> V=D5:FVW, A?@8G8=5=V 3@0<=530B82=8<8 >@30=V7<0<8, 7>:@5<0 *Pseudomonas aeruginosa*, 01> AB0DV;>:>:0<8.

□ =D5:FVW >G59.

□ =D5:FVW =8@>: V A5G>282V4=8E H;OEV2.

□ =D5:FVW AB0B528E >@30=V2, 2;:NG0NG8 04=5:A8B, 3>=>@5N B0 ?@>AB0B8B.

□ =D5:FVW >@30=V2 G5@52=>W ?>@>6=8=8 (V=D5:FVW B@02=>3> B@0:BC, 6>2G>282V4=8E H;OEV2, ?5@8B>=VB).

□ =D5:FVW H:V@8 B0 <'O:8E B:0=8=.

□ =D5:FVW :VAB>: B0 AC3;>1V2.

□ !5?A8A.

□ =D5:FVW 01> 28A>:89 @878: V=D5:FV9 (?@>DV;0:B8:0) C E2>@8E 7 >A;01;5=>N VN A8AB5<>N
(C B>45?@5A0=B0<8 B0 ?@8 =59B@>?5=VW).

□ 81V@:>20 45:>=B045?@5A0=B0<8.

□ @>DV;0:B8:0 V=20782=8E V=D5:FV9, A?@8G8=5=8E *Neisseria meningitides*.

@>B8?>:070==O.

V?5@GCB;82VABL 4> F8?@>D;>:A0F8=C 01> 4> V=H8E :>5=BV2 ?@5?0@0BC, 0 B0:>6 4> V=H8E
?@5?0@0BV2 3@C?8 DB>@EV=>;>=V2;

=0O2=VABL 2 0=0<=57V B5=48=VBC, A?@8G8=5=>3> 70AB>AC20==O< EV=>;>=V2;

>4=>G0A=5 70AB>AC20==O F8?@>D;>:A0F8=C B0 B870=V48=C;

7=0G=V ?>@CH5==O DC=:FVW =8@>: B0 ?5GV=:8;

203VB=VABL 01> ?5@V>4 3>4C20==O 3@C44N.

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

568< 4>7C20==O

/:I>=5 ?@87=0G5=> V=H5, @5:><5=4CNBLAO =0ABC?=V 4>1>2V 4>78:

4;O 4>@>A;8E

=D5:FVW	568< 4>7C20==O
=D5:FVW 48E0;L=8E H;OEV2 (70;56=> 2V4 BO6:>ABV 70E2>@N20==O V 71C4=8:0)	2 × 500 <3 4> 2 × 750 <3

=D5:FVW A5G>282V4=8E H;OE2: 3>AB@V, =5CA::04=5=V; F8AB8B C 6V=>: (4> <5=>?0C78); CA::04=5=V. >=>@5O: 5:AB@035=VB0;L=0; 3>AB@0 =5CA::04=5=0.	2 × 250 <3 4> 2 × 500 <3 @07>20 4>70 500 <3 2 × 500 <3 4> 2 × 750 <3 2 × 250 <3 @07>20 4>70 500 <3
=D5:FVW AB0B528E >@30=V2: =5CA::04=5=0 3>=>@5O (2::;NG0NG8 5:AB@035=VB0;L=V 2>3=8I0 V=D5:FVW); 04=5:A8B, ?@>AB0B8B, >@E>5?V4848	1 × 500 <3 2 × 500 <3 4> 2 × 750 <3
V0@5O	2 × 500 <3
=HV V=D5:FVW (482. @>74V; «>:070==O»)	2 × 500 <3
@8 >A>1;82> BO6:8E, =5157?5G=8E 4;O 68BBO V=D5:FVOE, =0?@8::04, ?@8 @5F8482CNG8E V=D5:FVOE C E2>@8E =0 2VAF84>7; ?@8 V=D5:FVOE :VAB>: V AC3;>1V2, A5?B8F5 =VBV, 7>:@5<0, 70 =002=>ABV <i>Pseudomonas</i> , <i>Staphylococcus</i> 01> <i>Streptococcus</i>	2 × 750 <3
@>DV;0:B8:0 V=20782=8E V=D5:FV9, A?@8G8=5=8E <i>Neisseria meningitides</i>	1 × 500 <3

>40B:>20 V=D>@<0FVO I>4> >:@5<8E 3@C? E2>@8E

VB8 V ?V4;VB:8

□ #A::04=5==O 2VAF84>7C

002=V ::V=VG=V V D0@<0:>:V=5B8G=V 40=V A2V4G0BL =0 :>@8ABL 70AB>AC20==O
F8?@>D;>:A0F8=C 4;O ;V:C20==O ;535=528E 703>AB@5=L, A?@8G8=5=8E *Pseudomonas aeruginosa* C
4VB59 B0 ?V4;VB:V2 7 2VAF84>7< ;535=L (2V:< 2V4 5 4> 17 @>:V2), 4;O ;V:C20==O CA::04=5=L
2VAF84>7C ;535=L, A?@8G8=5=8E *Pseudomonas aeruginosa* (4>A2V4 70AB>AC20==O BV;L:8 C 4VB59
2V:< 2V4 5 4> 17 @>:V2), C 4>7V 20 <3 F8?@>D;>:A0F8=C/:3 <0A8 BV;0 ?5@>@0;L=> 42VGV =0 4>1C
(<0:A8<0;L=0 4>1>20 4>70 1500 <3 F8?@>D;>:A0F8=C) 01> 10 <3 F8?@>D;>:A0F8=C/:3 <0A8 BV;0
2=CB@VH=L>25==> B@8 @078 =0 4>1C (<0:A8<0;L=0 4>1>20 4>70 1200 <3 F8?@>D;>:A0F8=C).

□ #A::04=5=V V=D5:FVW A5G>282V4=8E H;OE2 B0 ?VT;=>5D@8B

@8 CA::04=5=8E V=D5:FVOE A5G>282V4=8E H;OE2 B0 ?VT;=>5D@8BV 4>70 AB0=>28BL 6-10<3
?>:A0F8=C/:3 <0A8 BV;0 2=CB@VH=L>25==> :>6=V 2VAV 3>48=, 0;5 =5 1V;LH5 <0:A8<0;L=>W 4>78
400 <3, 01> 10-20 <3 F8?@>D;>:A0F8=C/:3 <0A8 BV;0 ?5@>@0;L=> :>6=V 12 3>48=, 0;5 =5 1V;LH5<0:A8
<0;L=>W 4>78 750 <3.

568< 4>7C20==O 4;O ;VB=VE ?0FVT=BV2 (> 65 @>:V2)

@8 ;V:C20==V ?0FVT=BV2 ;VB=L>3> 2V:C A;V4 70AB>A>2C20B8 O:>>30 =86GV 4>78
F8?@>D;>:A0F8=C, 70;56=> 2V4 ABC?5=O BO6:>ABV 70E2>@N20==O V ::V@5=AC :@50B8=V=C.

568< 4>7C20==O ?@8 ?>@CH5==V DC=:FVW =8@>: 01> ?5GV=:8.

4>@>A;8E

□ >@CH5==O DC=:FVW =8@>::

?@8 ::V@5=AV :@50B8=V=C 2V4 30 4> 60<;/E2/1,73 <2 (?>20 =54>AB0B=VABL) 01> 9>3>
:=F5=B@0FVW C ?;072V 2V4 1,4 4> 1,9 <3/100 <; <0:A8<0;L=0 4>1>20 4>70 F8?@>D;>:A0F8=C ?>28==O
AB0=>28B8 1000 <3 =0 4>1C 4;O ?5@>@0;L=>3> 70AB>AC20==O;

?@8 ::V@5=AV :@50B8=V=C <5=H5 30 <;/E2/1,73 <2 (BO6:0 =8@>:20 =54>AB0B=VABL) G8 9>3>
:=F5=B@0FVW C ?;072V 5:2V20;5=B=V 01> ?>=04 2 <3/100 <; <0:A8<0;L=0 4>1>20 4>70
F8?@>D;>:A0F8=C <0T AB0=>28B8 500 <3 =0 4>1C 4;O ?5@>@0;L=>3> 70AB>AC20==O.

□ >@CH5==O DC=:FVW =8@>: B0 35<>4V0;V7:

?@8 ;:V@5=AV :@50B8=V=C 2V4 30 4> 60<;/E2/1,73 <2 (?>20 =54>AB0B=VABL) 01> 9>3>
:=F5=B@0FVW C ?;072V 2V4 1,4 4> 1,9 <3/100 <; <0:A8<0;L=0 4>1>20 4>70 F8?@>D;:>:A0F8=C <0T
AB0=>28B8 1000 <3 =0 4>1C 4;O ?5@>@0;L=>3> 70AB>AC20==O;
?@8 ;:V@5=AV :@50B8=V=C<5=H5 30 <;/E2/1,73 <2 (BO6:0 =8@:>20 =54>AB0B=VABL) G8 9>3>
:=F5=B@0FVW C ?;072V 5:2V20;5=B=V 01> ?>=04 2 <3/100 <; <0:A8<0;L=0 4>1>20 4>70
F8?@>D;:>:A0F8=C <0T AB0=>28B8 500 <3 =0 4>1C 4;O ?5@>@0;L=>3> 70AB>AC20==O.
□ >@CH5==O DC=:FVW =8@>: B0 E@>=VG=89 ?5@8B=>50;L=89 4V0;V7 2 0<1C;0B>@=8E C<>20E:
?5@>@0;L=5 70AB>AC20==O F8?@>D;:>:A0F8=C C D>@.: 2:@8B8E ?;V2:>2>N >1>;>=:>N, C 4>7V 1
B01;5B:0 ?> 500 <3 F8?@>D;:>:A0F8=C.

□ >@CH5==O DC=:FVW ?5GV=:8:
:>@5:FVO 4>78 =5 ?>B@V1=0.

□ >@CH5==O DC=:FVW =8@>: B0 ?5GV=:8:

?@8 ;:V@5=AV :@50B8=V=C 2V4 30 4> 60<;/E2/1,73 <2 (?>20 =54>AB0B=VABL) 01> 9>3>
:=F5=B@0FVW C ?;072V 2V4 1,4 4> 1,9 <3/100 <; <0:A8<0;L=0 4>1>20 4>70 F8?@>D;:>:A0F8=C <0T
AB0=>28B8 1000 <3 =0 4>1C 4;O ?5@>@0;L=>3> 70AB>AC20==O;
?@8 ;:V@5=AV :@50B8=V=C<5=H5 30 <;/E2/1,73 <2 (BO6:0 =8@:>20 =54>AB0B=VABL) G8 9>3>
:=F5=B@0FVW C ?;072V 5:2V20;5=B=V 01> ?>=04 2 <3/100 <; <0:A8<0;L=0 4>1>20 4>70
F8?@>D;:>:A0F8=C <0T AB0=>28B8 500 <3 =0 4>1C 4;O ?5@>@0;L=>3> 70AB>AC20==O.
5<0T 4>A2V4C 70AB>AC20==O ?@5?0@0BC 4VBO< 7 ?>@CH5==O< DC=:FVW =8@>: 01> ?5GV=:8.

!/?>AV1 70AB>AC20==O.

"01;5B:8 =DVF8?@>®, 2:@8BV ?;V2:>2>N >1>;>=:>N, A;V4 :>2B0B8, =5 @>76>2CNG8, V 70?820B8
=525;8:>N :V;L:VABN @V48=8. "01;5B:8 <>6=0 ?@89<0B8 =570;56=> 2V4 26820==O W6V.
@89<< ?@5?0@0BC =0BI5A5@F5 ?@8A:>@NT 70A2>T==O 0:B82=>W @5G>28=8. # B0:>D;:>:A0F8=C,
2:@8BV ?;V2:>2>N >1>;>=:>N, =5 A;V4 ?@89<0B8 >4=>G0A=> 7 26820==O< <>;>G=8E ?@>4C:BV2 01>
=0?>W2, 71030G5=8E =V, ACBBT2> =5 2?;820T =0 2A<>:BC20==O F8?@>D;:>:A0F8=C.
/:I> BO6:VABL 70E2>@N20==O ?0FVT=B0 01> V=HV ?@8G8=8 (=0?@8;:04, O:I> E2>@89 >B@8
72>;ONBL ?@89<0B8 B01;5B:8 F8?@>D;:>:A0F8=C, 2:@8BV ?;V2:>2>N >1>;>=:>N, @5:<5=4CTBLAO
?5@59B8 =0 B5@0?VN 2=CB@VH=L>25==>N ;V:0@AL:>N D>@<>N F8?@>D;:>:A0F8=C. VA;O
2=CB@VH=L>25==>3> 22545==O <>6=0 ?@>4>268B8 ;V:C20==O ?5@>@0;L=8< A?>A>1>
"@820;VABL ;V:C20==O.

"@820;VABL ;V:C20==O 70;568BL 2V4 BO6:>ABV 70E2>@N20==O, ;:V=VG=>3> ?5@51V3C B0
10:B5@V>;>3VG=>3> ?@>DV;N. 06;82> ?@>4>26C20B8 ;V:C20==O ?@>BO3<, ?@8=09<=V, 3 4=V2 7
<<5=BC 7=8:=5==O 30@OG:8 01> ;:V=VG=8E A8

1 45=L ?@8 3>AB@V9 =5CA:;04=5=V9 3>=>@5W B0 F8AB8BV;
4> 7 4=V2 ?@8 V=D5:FVOE =8@>:, A5G>282V4=8E H;OEV2 B0 >@30=V2 G5@52=>W ?>@>6=8=8;
C E2>@8E 7V 7=865=8< V< ;V:C20==O ?@>2>4OBL ?@>BO3< CAL>3> ?5@V>4C =59B@>?5=VW;
?@8 >AB5>

7-14 4=V2 ?@8 2AVE V=H8E V=D5:FVOE.

@8 V=D5:FVOE, A?@8G8=5=8E AB@5?B>:>:0<8, ;V:C20==O A;V4 ?@>4>268B8 O:4V.

@8 V=D5:FVOE, A?@8G8=5=8E *Chlamydia*, :C@A ;V:C20==O B0:>6<0T B@820B8 I>=09<5=H5 10 4=V2.
VB8 B0 ?V4;VB:8

#A:;04=5==O 2VAF84>7C

@8 CA:;04=5==OE 2VAF84>7C ;535=L, A?@8G8=5=>3> *Pseudomonas aeruginosa*, C 4VB59 (2V:< 2V4 5
4> 17 @>:V2) B@820;VABL ;V:C20==O AB0=>28BL 10-14 4=V2.

#A:;04=5=V V=D5:FVW A5G>282V4=8E H;OEV2 01> ?VT;=>5D@8B

@8 CA:;04=5=8E V=D5:FVOE A5G>282V4=8E H;OEV2 01> ?VT;=>5D@8BV, A?@8G8=5=8E *Escherichia coli*, :C@A ;V:C20==O AB0=>28BL 10-21 4=V2.

>1VG=V @50:FVW.

51060=V ?>1VG=V @50:FVW ;:0A8DV:>20=V 70 :0B53>@VO<8 G0AB>B8: 4C65 G0ABV (≥ 1/10),
G0ABV (≥ 1/100, < 1/10), =5G0ABV (≥ 1/1000, ≤ 1/100), @V4:V (≥ 1/10000, ≤ 1/1000), 4C65 @V4:V (≤ 1
/10000), =52V4><> (=5 <>6=0 >FV=8B8 =0 >A=>2V =0O2=8E 40=8E).

=D5:FVW B0 V=207VW: =5G0ABV 3@81:>2V AC?5@V=D5:FVW; @V4:V 0=B81V>B8:>-0A>FV9>20=89
:>;VB (4C65 @V4:> 7 <>6;828< ;5B0;L=8< =0A;V4:<<).

I>:C :@>2>B2>@=>W B0 ;VW A8AB5 =5G0ABV 5>78=>DV;VO; @V4:V ;59:>?5=VO, 0=5?5=VO,
;59:>F8B>7, B@><1>F8B>?5=VO, B@><1>F8B>7; 4C65 @V4:V 35<>;VB8G=0 0=5F8B>7, ?0=F8B>?5=VO
(B0:0, I> 703@>6CT 68BBN), ?@83=VG5==O DC=:FVW :VAB:>2>3><>7:C (B0:5, I> 703@>6CT 68BBN).
I>:C VW A8AB5<8: @V4:V 0;5@3VG=V @50:FVW, 0;5@3VG=89/0=3V=>52@>B8G=89 =01@O:; 4C65
@V4:V 0=0DV;0:B8G=V @50:FVW, 0=0DV;0:B8G=89 H>: (B0:89, I> 703@>6CT 68BBN) V @50:FVW,
?>4V1=V 4> A8@>20B:>2>W E2>@>18.

5B01>;VG=V ?>@CH5==O: =5G0ABV 0=>@5:AVO; @V4:V 3V?5@3;V:5
A8EVG=V @>7;048: =5G0ABV ?A8E><>B>@=0 71C4;82VABL/B@82>6=VABL; @V4:V A?;CB0=VABL
A2V4><>ABV, 457>@VT=B0FVO, =5A?>:V9, ?V428I5=0 A>=;82VABL, 45?@5AVO, 30;NF8=0FVW; 4C65
@V4:V ?A8E>78.

I>:C F5=B@0;L=>W =5@2>2>W A8AB5<8: =5G0ABV 3>;>2=89 1V;L, 70?0<>@>G5==O, @>7;048 A=C,
?>@CH5==O A<0:C; @V4:V ?0@5AB57VW, 4875AB57VW, 3V?5AB57VW, B@5<>@, AC4><8, 25@B83>;
4C65 @V4:V @CH5==O :>@48=0FVW, ?>@CH5==O =NEC, 3V?5@5AB57VO, 2=CB@VH=L>G5@5?>=0
3V?5@B5=7VO; =52V4><> ?5@8D5@8G=0 =52@>?0BVO, ?>;V=59@>?0BVO.

I>:C >@30=0 7>@C: @V4:V ?>@CH5==O 7>@C; 4C65 @V4:V ?>@CH5==O :>;L>@>2>3>
A?@89=OBBO.

I>:C >@30=0 A;CEC: @V4:V 472V= C 2CE0E, 3;CE>B0; 4C65 @V4:V ?>@CH5==O A;CEC.

I>:C A5@F52>-AC48==>W A8AB5<8: @V4:V B0EV:0@4VO, 207>48;0B0FVO, 7=865==O
0@B5@V0;L=>3> B8A:C, =5?@8B><=VABL; 4C65 @V4:V 20A:C;VB; =52V4><> ?>4>265==O
V=B5@20;C QT, H;C=>G:>20 0@8BA?@O<>20=0 H;C=>G:>20 B0EV:0@4VO (FV @50:FVW
A?>AB5@V30;8AO ?5@5206=> C ?0FVT=BV2 7 4>40B:>28<8 D0:B>@0<8 @878:C ?@>;>=30FVW
V=B5@20;C QT (482. @>74V; «A>1;82>ABV 70AB>AC20==O»).

I>:C 48E0;L=>W A8AB5<8: @V4:V 48A?=>5 (2;;NG0NG8 0AB<0B8G=V AB0=8).

I>:C B@02=>3> B@0:BC: G0ABV =C4>B0, 4V0@50; =5G0ABV 1;N20==O, 1V;L C 4V;O=FV H;C=:0 V
:8H5G=8:C, 48A?5?B8G=V @>7;048, <5B5>@87<; 4C65 @V4:V ?0=:@50B8B.

I>:C 35?0B>1V;V0@=>W A8AB5<8: =5G0ABV ?V428I5==O @V2=O B@0=A0@CH5==O DC=:FVW
?5GV=:8, 6>2BO=8FO, 35?0B8B (=5V=D5:FV9=89); 4C65 @V4:V =5:@>7 ?5GV=:8 (4C65 @V4:>
?@>3@5ACT 4> ?5GV=:>2>W =54>AB0B=>ABV, I> 703@>6CT 68BBN).

I>:C H:V@8 B0 ?V4H:V@=>W ;;VB:>28=8: =5G0ABV 28A8?0==O, A25@1V6, :@>?82O=:0; @V4:V
@50:FVW D>B>GCB;82>ABV, ?>O20 =5A?5F8DVG=8E ?CE8@V2; 4C65 @V4:V ?5B5EVW,@<=0 5@8B5
<0, 2C7;8:>20 5@8B5<0, A8=4@< !BV25=A0-6>=A>=0 (7 ?>B5=FV9=>N 703@>7>N 68BBN) V
B>:A8G=89 5?V45@<0;L=89 =5:@>;V7 (7 ?>B5=FV9=>N 703@>7>N 68BBN).

I>:C :VAB:>2>-<O7>2>W A8AB5<8: =5G0ABV 0@B@0;3VW; @V4:V

I>:C A5G>284V;L=>W A8AB5<8: =5G0ABV ?>@CH5==O DC=:FVW =8@>; @V4:V =8@>20
=54>AB0B=VABL, :@8AB0;C@VO, 35<0BC@VO, BC1C;>V=B5@AB8FV0;L=89 =5D@8B.

@30=V7< 2 FV;=>5G0ABV =5A?5F8DVG=89 1>;L>289 A8=4@<, =574C60==O, 30@OG:0; @V4:V
=01@O:8, ?V428I5=0 ?VB;82VABL (3V?5@3V4@>7); 4C65 @V4:V ?>@CH5==O E>48.

01>@0B>@=V ?>:07=8:8: =5G0ABV ?V428I5==O @V2=O ;C6=>W D>AD0B078 C :@>2V; @V4:V
2V4E8;5==O 2V4 =>@<8 @V2=O ?@>B@><1V=C, ?V428I5==O @V2=O 0

0ABC?=V =51060=V ?>1VG=V O28I0 =0;560BL 4> :0B53>@VW ?V428I5=>W G0AB>B=>ABV C
?V43@C?0E ?0FVT=BV2, O:V >B@825==> 01> ?>A;V4>2=> (?VA;O 2=CB@VH=L>25==>3> 22545==O
?5@>@0;L=89 @568<): G0ABV 1;N20==O, B@0=78B>@=5 71V;LH5==O 0:B82=>ABV B@0=A0B@>
<1>F8B>?5=VO, B@><1>F8B>7, A?;CB0=VABL A2V4><>ABV V 457>@VT=B0FVO, 30;NF8=0FVW,
?0@5AB57VW, 4875AB57VW, AC4><8, 25@B83>, 70?0<>@>G5==O, ?>@CH5==O 7>@C, ?>@CH5==O
A;CEC, B0EV:0@4VO, 207>48;0B0FVO, 7=865==O 0@B5@V0;L=>3> B8A:C, B@0=78B>@=0 ?5GV=:>20
=54>AB0B=VABL, 6>2BO=8FO, =8@>:20 =54>AB0B=VABL, =01@O:; @V4:V ?0=F8B>?5=VO,
?@83=VG5==O :VAB:>2>3><>7:C, 0=0DV;0:B8G=89 H>;, ?A8E>B8G=V @50:FVW, ?>@CH5==O =NEC,
?>@CH5==O A;CEC, 20A:C;VB, ?0=:@50B8B, =5:@>7 ?5GV=:8, ?5B5EVW, @>7@82 ACE>68;;O

0AB>AC20==O 4VBO<

'0AB>B0 28?04:V2 0@B@>?0BVW, 707=0G5=0 28I5, 70A=>2CTBLAO =0 40=8E, >45@60=8E ?@8
4>A;V465==OE 4>@>A;8E ?0FVT=BV2. # 4VB59 0@B@>?0BVO A?>AB5@V30TBLAO G0AB> (482.
@>74V; «A>1;82>ABV 70AB>AC20==O»).

5@54>7C20==O.

#=0A;V4>: ?5@54>7C20==O <>65 28=8:=CB8 >1>@>B=0 B>:A8G=0 4VO =0 ?0@5=EV:, 0 B0:>6
@>728=CB8AL 3>AB@0 =8@:>20 =54>AB0B=VABL (:>=F5=B@0FVO C ?;072V 12 : B0 ?@89<0B8
0=B0F848, I>
@V< B>3>, C 28?04:C ?5@54>7C20==O =5>1EV4=> 28::;8:0B8 1;N20==O 01> ?@>25AB8 ?@><820==O
H;C=:0 V 70157?5G8B8 26820==O ?0FVT=B0<8 4>AB0B=L>W :V;L:>ABV @V48=8 7<5B>N 725AB8 4>
728B:C :@8AB0;C@VW, AB2>@8B8 :8A;C @50:FVN A5GV, ?@87=0G8B8 A&0B8G=C V ?V4B@8
0 4>?><3>N 35<>4V0;V7C 01> ?5@8B>=50;L=>3> 4V0;V7C 282>48BLAO BV;L:8 =525;8:0 :V;L:VABL
F8?@>D;>:A0F8=C (< 10 %).
!75F8DVG=89 0=B84>B =52V4><89.

0AB>AC20==O C ?5@V>4 203VB=>ABV 01> 3>4C20==O 3@C44N.

0AB>AC20==O □DVF8?@>® ?@>B8?>:070=5 C ?5@V>4 203VB=>ABV.

?>:A0F8= ?@>=8:0T C 3@C4=5 <>;>:, B>AC20==O ?@5?0@0BC A;V4 ?@8?8=8B8 3>4C20==O 3@C44N.

VB8.

?>:A0F8= =5 @5:><5=4>20=> 70AB>A>2C20B8 4VBO< 4;O ;V:C20==O V=H8E V=D5:FV9=8E
70E2>@N20=L, >:@V< ?5@5@0E>20=8E =86G5: F8?@>D;>:A0F8= <>6=0 70AB>A>2C20B8 4VBO< O:
?@5?0@0B 4@C3>W B0 B@5BL>W ;V=VW 4;O ;V:C20==O CA:;04=5=8E V=D5:FV9 A5G>282V4=8E
H;OEV2 B0 ?VT;>=5D@8BC, A?@8G8=5=8E . coli (C ;V=VG=8E 4>A;V465==OE 2V: 4VB59, O:V
>45@6C20;8 ;V:C20==O, AB0=>282 2V4 1 4> 17 @>:V2), 0 B0:>6 4;O ;V:C20==O ;535=528E
703>AB@5=L, A?@8G8=5=8E Pseudomonas aeruginosa C 4VB59 7 2VAF84>7< ;535=L (C ;V=VG=8E
4>A;V465==OE 2V: 4VB59, O:V >45@6C20;8 ;V:C20==O, AB0=>282 2V4 5 4> 17 @>:V2).
V:C20==O F8?@>D;>:A0F8=< <>6=0 ?@87=0G8B8 BV;L:8 ?VA;O @5B5;L=>W >FV=:8
A?V22V4=>H5==O @878:->@8ABL G5@57 V<>2V@=VABL @>728B:C ?>1VG=8E 5D5:BV2 7 1>:C
AC3;>1V2 B0/01> =02:>;8H=VE B:0=8=.

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

;O ;V:C20==O BO6:8E V=D5:FV9 B0 V=D5:FV9, A?@8G8=5=8E AB0DV;>:>:08 01> 0=05@>1=8<8 10:B5@V0
<8, F8?@>D;>:A0F8= A;V4 70AB>A>2C20B8 C :<1V=0FVW 7 2V4?>2V4=8<8 0=B810:B5@V0;L=8<8 70A>10
<8.

0FVT=B0< ;VB=L>3> 2V:C B0 ?0FVT=B0< V7 ?>@CH5==O< DC=:FVW F5=B@0;L=>W =5@2>2>W
A8AB5<8 (5?V;5?AVO, 7=865==O AC4<=>3> ?>@>30, AC4<8 2 0=0<=57V, 7=865==O <>7:>2>3>
:@>2>>1V3C, 0?>?;5:AVO, ?A8EVG=V ?>@CH5==O)DVF8?@>® A;V4 ?@87=0G0B8 ;8H5 70 68BBT28<8
?>:070==O<8 G5@57 =5157?5:C @>728B:C ?>1VG=8E @50:FV9 7 1>:C F5=B@0;L=>W =5@2>2>W
A8AB5<8.

45O:8E 28?04:0E ?>1VG=V @50:FVW 7 1>:C F5=B@0;L=>W =5@2>2>W A8AB5<8

A?>AB5@V30NBLAO 265 ?VA;O ?5@H>3> 70AB>AC20==O F8?@>D;>:A0F8=C. # ?>>48=>:8E 28?04:0E
<>6CBL ?@>3@5AC20B8 45?@5AVO 01> ?A8E>7, 01> 28=8:=CB8=52@>;>3VG=V ?>@CH5==O,
30;NF8=0FVW. # B0:>AC20==O F8?@>D;>:A0F8=C A;V4 ?@8?8=8B8 B0 =5309=> 725@=CB8AO 4>
>V:0@O.

?>:A0F8= 0A>FVNTBLAO 7 ?>4>265==O< V=B5@20;C QT. 0FVT=B8 7 4>40B:>28<8 D0:B>@0<8
@878:C ?@>;>=30FVW V=B5@20;C QT (?0FVT=B8 ;VB=L>3> 2V:C, ?@>;>=30FVO QT 2 0=0<=57V,
=5:>@53>20=0 3V?>:0;VT).

%2>@8< 7 C@065==O<8 ?5GV=:8 G8 1C4L-O:8< B8?>< ?5GV=:>2>W =54>AB0B=>ABV B0 45DVF8B<
3;N:>7>-6-D>AD0B453V4@>35=078 DVF8?@>® A;V4 ?@87=0G0B8 ;8H5 70 68BBT28<8 ?>:070==O<8.

%2>@8< V7 ?>@CH5==O< DC=:FVW ?5GV=:8 =5>1EV4=> :=B@>;N20B8 :=F5=B@0FVN
F8?@>D;>:A0F8=C C ?;072V.

>65 A?>AB5@V30B8AO <8=CI5 7@>AB0==O 0:B82=>ABV B@0=A0W D>AD0B078 B0 28=8:=CB8
E>;5AB0B8G=0 6>2BO=8FO, >A>1;82> C ?0FVT=V2 7 ?>?5@54=V< CH:>465==O< ?5GV=:8.

@8 28=8:=5==V ?V4 G0A 01> ?VA;O ;V:C20==ODVF8?@>® BO6:>W V ABV9:>W 4V0@5W =5>1EV4=>
?@>:=AC;LBC20B8AO 7 ;V:0@5<, 0465 FV A8<8 <>6CBL <0A:C20B8 ?A524><5<1@0=>7=89 :>;VB,
O:89 28<030T =5309=>3> ;V:C20==O. # B0:8E 28?04:0E 70AB>AC20==O F8?@>D;>:A0F8=C =5>1EV4=>
?@8?8=8B8 V @>7?>G0B8 70AB>AC20==O 2V4?>2V4=>W B5@0?VW. @5?0@0B8, I> V=3V1CNBL
?5@8AB0;LB8:C, ?@>B8?>:070=V.

@8 1C4L-O:8E >7=0:0E B5=48=VBC (=0?@8:;04, 1>;NG0 ?@8?CE;VABL, 70?0;5==O) =5>1EV4=>
7C?8=8B8 ?@89>< F8?@>D;>;:A0F8=C, C=8:0B8 DV78G=>3> =020=B065==O B0 ?@>:=AC;LBC20B8AO
7 ;V:0@57@82 ACE>68;L (?5@5206=> 0EV;;>28E) A?>AB5@V30TBLAO ?5@5206=> ?@8 ;V:C20==V
>AV1 ;VB=L>3> 2V:C 01> C 7207:C 7 ?>?5@54=V< ;V:C20==O< 3;N:>:@B8:>W40<8.
?>:A0F8= A;V4 7 >15@56=VABN 70AB>A>2C20B8 ?0FVT=B0< V7 ?>@CH5==O<8 7 1>:C ACE>68;L 2
0=0<=57V, 0A>FV9>20=8<8 7 ;V:C20==O< EV=>;>=0<8.

C6=0 @50:FVO A5GV <>65 A?@8OB8 CB2>@5==N A5G>28E :=:@5<5=BV2, B>D;>;:A0F8=><0<8
?@5?0@0BC 70;56=> 2V4 B06:>ABV =8@:>2>W =54>AB0B=>ABV. # E2>@8E V7 ?>@CH5==O<
DC=:FVW =8@:= =5>1EV4=> :=B@>;N20B8 :=F5=B@0FVN F8?@>D;>;:A0F8=C C ?;072V.

@8 :C@A>2>@0B>@=8E ?>.07=8:V2: ?>O20 >A04C C A5GV, B825 ?V428I5==O :=F5=B@0FVW
A5G>28=8, :@50B8=V=C, 1V;V@C1V=C, C 45O:8E 28?04:0E 3V?5@3;V:535<0BC@VO, 7B@>
<1V=>2>3> V=45:AC.

45O:8E 28?04:0E @50:FVW ?V428I5=>W GCB;82>ABV B0 B06:V 0;5@3VG=V @50:FVW
(0=0DV;0:B8G=V/0=0DV;0:B>W4=V @50:FVW, 4> H>:C)<>6CBL 28=8:=CB8 265 ?VA;O ?5@H>3>
70AB>AC20==O F8?@>D;>;:A0F8=C. # B0:> ?@8?8=8B8 ?@89>< ?@5?0@0BC V @>7?>G0B8
?@>2545==O <548:0<5=B>7=>3> ;V:C20==O.

0FVT=B0<, O:V ;V:CNBLAO F8?@>D;>;:A0F8=><, A;V4 C=8:0B8 4VW C;LB@0DV>;5B>2>3> >?@>
V4><>, I> F8?@>D;>;:A0F8= T ?>E@>B@815@56=>ABV ?@8 >4=>G0A=>AC20==V F8?@>D;>;:A0F8=C
V ?@5?0@0BV2, I> <5B01>;V7CNBLAO F8<8 5=78<0<8, B0:8<8 O: B5>DV;V=, <5B8;;A0=B8=, :>D5W=,
4C;>;:A5B8= B0 V=HV G5@57 B5, I> 71V;LH5==O :=F5=B@0FVW F8E ?@5?0@0BV2 C A8@>20BFV
:@>2V <>65 28;;8:0B8 A?5F8DVG=V ?>1VG=V 5D5:B8.

?>:A0F8= *in vitro* <>65 2?;820B8 =0 @57C;LB0B8 ?>AV2C =0 D;>@C *Mycobacterium spp.* H;OE><
?@83=VG5==O @>ABC C :C;LBC@V 10:B5@V9, ?@872>4OG8 4> E81=>=530B82=8E @57C;LB0BV2
0=0;V7C ?>AV2C 2V4 ?0FVT=V2, O:V ?@89<0NBL F8?@>D;>;:A0F8=.

?>:A0F8= =5 @5:><5=4CTBLAO 4;O ;V:C20==O ?=52<>:=>28E V=D5:FV9 G5@57 =54>AB0B=N
5D5:B82=VABL I>4> 10:B5@V9 3@C?8 *Streptococcus pneumoniae*

=D5:FVW AB0B528E H;OEV2 <>6CBL 1CB8 A?@8G8=5=V @578AB5=B=8<8 4> DB>@EV=>;>=V2
V7>;OB0<8 *Neisseria gonorrhoeae*. /:I> ?V4>7@NTBLAO 01> 2V4><>, I> V=D5:FVW AB0B528E H;OEV2
A?@8G8=5=V *N. gonorrhoeae*, >A>1;82> 206;82> >B@8<0B8 V=D>@<0FVN ?@> ABC?V=L
@578AB5=B=>ABV 4> F8?@>D;>;:A0F8=C V ?V4B25@48B8 GCB;82VABL 4> ?@5?0@0BC =0 >A=>2V
@57C;LB0BV2 ;01>@0B>@=8E 4>A;V465=L.

?5@V>4 ;V:C20==O F8?@>D;>;:A0F8=>< =5 A;V4 26820B8 0;>3>;L.
>@>A;V B0 4VB8.

=865==O @878:C 28=8:=5==O 01> ?@>3@5AC20==O A81V@AL:>W 28@07:8 ?VA;O 05@>35==>3>
:=B0:BC 7 *Bacillus anthracis*

**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.**

?>:A0F8= <>65 2?;820B8 =0 H284:VABL @50:FVW, B> DVF8?@>® ?0FVT=B0< A;V4 CB@8
B@0=A?>@B>< B0 @>1>B8 7 ?>B5=FV9=> =5157?5G=8<8 <5E0=V7<0<8.

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

!;V4 4>B@815@56=>ABV ?@8 >4=>G0A=>AC20==V F8?@>D;>;:A0F8=C V 0=B80@8B , >A:V;L:8
F8?@>D;>;:A0F8= <>65 ?>A8;N20B8 ?@>;>=30FVN V=B5@20;C QT.

@8 >4=>G0A=>D;>;:A0F8=C 7 0=B0F840<8 (I> 2(=0?@8:;04, A525;0<@><, ;0=B0=C :0@1>=0B><) 01>
AC:@0;LD0B><, 0 B0:>6 ?@5?0@0B0<8 7 25;8>;N 1CD5@=>N T<=VABN (=0?@8:;04, B01;5B:8
484>=078=C) 2V41C20TBLAO 7=865==O 01A>@1FVW F8?@>D;>;:A0F8=C. "><5=4CTBLAO
70AB>A>2C20B8 F8?@>D;>;:A0F8= 70 4 3>48=8 4> 70AB>AC20==O 0=B0F84V2 01> AC:@0;LD0BC G8
G5@57 2-4 3>48=8 ?VA;O =L>3>.

0=5 >1<565==O =5 AB>ACTBLAO 0=B0F84V2, I> =0;560BL 4> ;:0AC 1;>;:0B>@V2_2-@5F5?B>@V2.

!;V4 C=8:0B8 >4=>G0A=>3> ?@89>® V <>;>G=8E 01> 71030G5=8E :0;LFVT< ?@>4C:BV2 (=0?@8:;04,
<>;>;:0, 9>3C@BV2, A>:V2 7 ?V428I5=8< 2< :0;LFVN) C 7=0G=8E :V;L:>ABOE. =HV ?@>4C:B8, 4>
A:;04C O:8E 2E>48BL :0;LFV9, =5 2?;820NBL =0 2A<>:BC20==O F8?@>D;>;:A0F8=C.

@5?0@0B8, I> 270;V7> 01> F8=.;, 7=86CNBL 01A>@1FVN F8?@>D;>;:A0F8=C.

!CAC20==O 28A>:8E 4>7 F8?@>D;>:A0F8=C V B5>DV;V=C?@872>48BL 4> =51060=>3> ?V428I5==O
:=F5=B@0FVW B5>DV;V=C C ?;072V B0 ?>4>265==O ?5@V>4C 9>3> =0?V2282545==O (I>1 C=8:=CB8
?>O28 B>:A8G=>ABV B5>DV;V=C, 4>7C B5>DV;V=C =5>1EV4=> 7<5=H8B8).
><1V=>20=5 70AB>AC20==O 4C65 28A>:8E 4>7 EV=>;V=V2 (V=3V1VB>@V2 3V@078) V 450:8E
=5AB5@>W4=8E ?@>B870?0;L=8E ?@5?0@0BV2 (2;;NG0NG8 0F5B8;A0;VF8;>2C :8A;>BC) <>65
?@>2>:C20B8 AC4<<8.
@8 >4=>G0A=>D;>:A0F8=C <>6;825 C?>2V;L=5==O BC1C;O@=>3> B@0=A?>@BC (=8@:>289
<5B01>;V7<) <5B>B@5:A0BC, I> <>65 AC?@>2>46C20B8AL ?V428I5==O< :=F5=B@0FVW
<5B>B@5:A0BC C ?;072V. @8 FL>
5B>.:;>?@0 ?@8A:>@NT 01A>@1FVN F8?@>D;>:A0F8=C, 2=0A;V4>: G>3> A:>@>GCTBLAO ?5@V>4
4>AO3=5==O <0:A8<0;L=>W :=F5=B@0FVW F8?@>D;>:A0F8=C C ?;072V (=0 1V>4>ABC?=VABL
>AB0==L>3> F5 =5 2?;820T).
4=>G0A=5 70AB>AC20==O F8?@>D;>:A0F8=C B0 ;V:0@AL:8E 70A>1V2, I> ><5?@07>;, ?@872>48BL
4> =57=0G=>3> 7=865==O <0:A8<0;L=>W :=F5=B@0FVW C ?;072V (!_max) V 7<5=H5==O ?>:07=8:0
?;>IV ?V4 :@82>N <:=F5=B@0FVO-G0A> (AUC) F8?@>D;>:A0F8=C.
@8 >4=>G0A=>AC20==V F8?@>D;>:A0F8=C V B870=V48=C 28O2;5=> 71V;LH5==O :=F5=B@0FVW
B870=V48=C C ?;072V: 71V;LH5==O !_max C 7 @07V2, 71V;LH5==O ?>:07=8:0 AUC C 10 @07V2. V
71V;LH5==O< :=F5=B@0FVW B870=V48=C C A8@>20BFV :@>2V ?>2O70=V 3V?>B5=782=V B0
A540B82=V ?>1VG=V O28I0. "0:8< G8=><, >4=>G0A=5 70AB>AC20==O F8?@>D;>:A0F8=C V
B870=V48=C ?@>B8?>:070=5.
@8 >4=>G0A=>AC20==V F8?@>D;>:A0F8=C B0 4C;>:A5B8=C <>6;825 71V;LH5==O :=F5=B@0FVW
4C;>:A5B8=C C ?;072V.
?>:A0F8=C <>6=0 70AB>A>2C20B8 C :><1V=0FVOE 7 07;>F8;V=>< B0 F5DB07848<>< ?@8
V=D5:FVOE, A?@8G8=5=8E Pseudomonas; 7 <57;>F8;V=><, 07;>F8;V=>< B0 V=H8<8 5D5:B82=8<8 β-
;0:B0<=8<8 0=B81V>B8:0<8 ?@8 AB@5?B>:>:28E V=D5:FVOE; 7 V7>:A07>;?5=VF8;V=0<8, 20=:><
?@8 AB0DV;>:>:28E V=D5:FVOE; 7 <5B@>=V407>;><, ;:V=40< ?@8 0=05@>1=8E V=D5:FVOE.
4=>G0A=89 ?@89>< F8.;>A?>@8=C V F8?@>D;>:A0F8=C ?@872>48BL 4> ?V428I5==O @V2=O
:@50B8=V=C C ?;072V, C 7207:C 7 F8< =5>1EV4=89 :=B@>;L FL>3> ?>:07=8:0 (2 @078 =0 B8645=L).
@8 >4=>G0A=>AC20==V F8?@>D;>:A0F8=C B0 20@D0@8=C <>6;825 ?V4A8;5==O 4VW 20@D0@8=C.
@>15=5F84 ?@8 >4=>G0A=>D;>:A0F8=>< C?>2V;L=NT 9>3> 282545==O 7 >@30=V7
V4 G0A ;V:C20==O F8?@>D;>:A0F8=>< VA=CT ?V428I5=89 @878: @>7@82C ACE>68;L C E2>@8E, O:V
?0@0;5;L=> >B@8
>T4=0=5 ?@87=0G5==O F8?@>D;>:A0F8=C B0 D5=VB>W=C <>65 ?@8725AB8 4> 7=F5=B@0FVW
D5=VB>W=C C ?;072V.
4=>G0A=5 70AB>AC20==O =5AB5@>W4=8E ?@>B870?0;L=8E 70A>1V2 (=0?@8;:04, D5=1CD5=C) V
4C65 28A>:8E 4>7 EV=>;V=V2 <>65 A?@8G8=OB8 AC4<<8.
?>:A0F8= ?>B5=VNT 4VN 0=B8:>03C;O=BV2 :C<0@8=>2>3> @O4C. "><5=4CTBLAO ?5@V>48G=>
:=B@>;N20B8 ?@>B@><1V=>289 G0A.
@8 >4=>G0A=>D;>:A0F8=>< V 10@1VBC@0B0<8 =5>1EV4=> ?>ABV9=> 74V9A=N20B8 :=B@>;L
G0AB>B8 A5@F528E A:>@>G5=L, 0@B5@V0;L=>3> B8A:C, .
A:V;L:8 70AB>AC20==O F8?@>D;>:A0F8=C A?@8OT 7=865==N ?@>F5AV2A><0;L=>3> >:8A=5==O C
35?0B>F8B0E, F5 2545 4> ?V428I5==O :=F5=B@0FVW B0 71V;LH5==O =0?V2282545==O :A0=B8=V2
(=0?@8;:04, :=D5W=C).
@8 >4=>G0A=>AC20==V 7 3;VIC@84>< <>6;820 28@065=0 3V?>3;V:5
>A>1;82>N >15@56=VABN A;V4 ?@87=0G0B8 F8?@>D;>:A0F8= ?@8 ;V:C20==V E2>@8E FC:@>28<
4V015B><, >A:V;L:8 4VO ?5@>@0;L=8E 3V?>3;V:5 (3;V15=.;0 <>65 ?>A8;8B8AO V 28;;8:0B8 3V?>3;V:5
4=>G0A=5 70AB>AC20==O @>?V=V@>;C 7 F8?@>D;>:A0F8=>< ?@872>48BL 4> 71V;LH5==O AUCV !
max @>?V=V@>;C =0 60 % V 84 % 2V4?>2V4=>. :=VB>@8=3 ?>1VG=8E 5D5:BV2 @>?V=V@>;C B0
2V4?>2V4=5 :=@83C20==O 4>78 @5:><5=4CTBLAO 74V9A=N20B8 ?V4 G0A V >4@07C ?VA;O AC>
70AB>AC20==O 7 F8?@>D;>:A0F8=>
4=>G0A=5 70AB>AC20==O ;V:0@AL:8E 70A>1V2, I> ;V4>:0W=, B0 F8?@>D;>:A0F8=C 7<5=HCT
;V@5=A ;V4>:0W=C, 22545=>3> 2=CB@VH=L>25==>, =0 22 %. %>G0 ;V:C20==O 7 ;V4>:0W=>< 4>1@5
?5@5=>A8BLAO, ?VA;O >4=>G0A=>3> 70AB>AC20==O 7 F8?@>D;>:A0F8=>< <>65
A?>AB5@V30B8AO ?52=0 270T<>4VO, I> <>65 AC?@>2>46C20B8AO ?>1VG=8<8 @50:FVO<8.

;V=VG=89 =03;O4 B0 2V4?>2V4=5 :>@53C20==O 4>78 ;;>70?V=C @5:><5=4CTBLAO 74V9A=N20B8 ?V4 G0A V >4@07C ?VA;O AC3> 22545==O 7 F8?@>D;>:A0F8=>< C 7207:C 7 <>6;828< ?V428I5==O< A8@>20B:>28E :=F5=B@0FV9 ;;>70?V=C.

VA;O ?5@>@0;L=>3> 70AB>AC20==O 50<3 A8;45=0DV;C>4=>G0A=> 7 500 <3 F8?@>D;>:A0F8=C ?V428IC20;8AO AUC V !_{max} A8;45=0DV;C?@81;87=> 242VGV. ">15@56=VABN >4=>G0A=> 70AB>A>2C20B8 F8?@>D;>:A0F8= B0 A8;45=0DV; , @5B5;L=> 7206CNG8 @878: B0 :>@8ABL. @8 >4=>G0A=>AC20==V F8?@>D;>:A0F8=C B0 0=B03>=VAB0 2VB0>FV=8B8 B>G=89 2?;82 F8?@>D;>:A0F8=C =0 ?V428I5==O 7=0G5==O V6=0@>4=>3> =>@<0;V7>20=>3> 2V4=>H5==O (INR). !;V4 74V9A=N20B8 G0AB89 :=B@>;L INR ?V4 G0A V >4@07C ?VA;O AC3> 70AB>AC20==O F8?@>D;>:A0F8=C B0 0=B03>=VAB0 2VB0:C<0@>;C, D5=?@>:C<>=C 01> D;CW=4V>=C).

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

$\$0@<0:>48=0$

?>:A0F8= *in vitro* 28O2;OT 5D5:B82=VABL I>4> H8@>:>3> A?5:B@0 3@0<=530B82=8E V 3@078B82=8E 71C4=8:V2. 5E0=V7< 0=B810:B5@V0;L=>W 4VW >1C<>2;5=89 740B=VABN F8?@>D;>:A0F8=C ?@83=VGC20B8 B>?>V7><5@078 B8?C (-3V@07C B0 B>?>V7><5@07C IV), =5>1EV4=V C 1030BL>E ?@>F5A0E, ?>2'O70=8E 7 , B0:8E O: @5?;V:0FVO, B@0=A:@8?FVO, @5?0@0FVO V @5:><1V=0FVO. 5E0=V7<8 @578AB5=B=>ABV, O:V V=0:B82CNBL V=HV 0=B81V>B8:8, B0:V O: 7=865==O ?@>=8:=>ABV 7>2=VH=L>W ABV=:8 10:B5@VW (?@8B0<0==> 4;O *Pseudomonas aeruginosa*) B0 0:B82=5 282545==O ?@5?0@0BC 7 ;:VB8=8 (5D;N:A), <>6CBL 2?;8=CB8 =0 GCB;82VABL 4> F8?@>D;>:A0F8=C. 5E0=V7<8 @578AB5=B=>ABV, O:8<8 V=0:B82CNBLAO ?5=VF8;V=8, F5D0;>A?>@8=8, 03;V:>7848, <0:@>;VB8 V B5B@0F8;:V=8, <>6CBL =5 2?;820B8 =0 0=B810:B5@V0;L=C 0:B82=VABL F8?@>D;>:A0F8=C. @30=V7<8, ABV9:V 4> F8E ?@5?0@0BV2, <>6CBL 1CB8 GCB;82V 4> F8?@>D;>:A0F8=C. > F8?@>D;>:A0F8=C 7030;>< GCB;82V *in vitro*=0ABC?=V @>48 B0 2848 10:B5@V9:

5@>1=V 3@078B82=V >@30=V7<8: *Bacillus anthracis*, *Staphylococcus aureus*(<5B8F8;V=GCB;82V V7>;OB8), *Staphylococcus saprophyticus*, *Streptococcus spp.*

5@>1=V 3@0<=530B82=V >@30=V7<8: *Aeromonas spp.*, *Brucella spp.*, *Citrobacter koseri*, *Francisella tularensis*, *Haemophilus ducreyi*, *Haemophilus influenzae*, *Legionella spp.*, *Moraxella catarrhalis*, *Neisseria meningitidis*, *Pasteurella spp.*, *Salmonella spp.**, *Shigella spp.*, *Vibrio spp.*, *Yersinia pestis*

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

=HV >@30=V7<8: *Chlamydia trachomatis*, *Chlamydia pneumoniae*, *Mycoplasma hominis*, *Mycoplasma pneumoniae*.

V7=C GCB;82VABL 4> F8?@>D;>:A0F8=C 28O2;ONBL: *Acinetobacter baumann*, *Burkholderia cepacia*, *Campylobacter spp.*, *Citrobacter freundii*, *Enterococcus faecalis*, *Enterobacter aerogenes*, *Enterobacter cloacae*, *Escherichia coli*, *Klebsiella pneumoniae*, *Klebsiella oxytoca*, *Morganella morganii*, *Neisseria gonorrhoeae*, *Proteus mirabilis*, *Proteus vulgaris*, *Providencia spp.*, *Pseudomonas aeruginosa*, *Pseudomonas fluorescens*, *Serratia marcescens*, *Streptococcus pneumoniae*, *Peptostreptococcus spp.*, *Propionibacterium acnes*

0ABC?=V >@30=V7<8 28O2;ONBL A?04:>2C @578AB5=B=VABL 4> F8?@>D;>:A0F8=C *Staphylococcus aureus* (<5B8F8;V=@578AB5=B=V) B0 *Stenotrophomonas maltophilia*, *Actinomyces*, *Enterococcus faecium*, *Listeria monocytogenes*, *Mycoplasma genitalium*, *Ureaplasma urealitycum*, 0=05@>1=V >@30=V7<8 (70 28=OB:>< *Mobiluncus*, *Peptostreptococcus*, *Propionibacterium acnes*)

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

IA>@1FVO. VA;O ?5@>@0;L=>3> 70AB>AC20==O F8?@>D;>:A0F8= H284:> B0 4>1@5 2A <>:BCTBLAO, ?5@5206=> 7 25@E=L>3> 2V44V;C B>=>3> :8H5G=8:C. 0:A8<0;L=V :=F5=B@0FVW C A8@>20BFV :@>2V 4>AO30NBLAO G5@57 1-2 3>48=8. 1A>;NB=0 1V>4>ABC?=VABL ?@5?0@0BC AB0=>28BL 1;87L:> 70-80 %.

>7?>4V;. 2'O7C20==O F8?@>D;>:A0F8=C 7 1V;:0<8 T =57=0G=8< (20-30 %), 0 @5G>28=0 7=0E>48BLAO
2 ?;072V ?5@5206=> 2 =5V>=V7>20=V9 D>@D;>:A0F8= <65 2V;L=> 48DC=4C20B8 C ?>70AC48==89
?@>ABV@. ?>:A0F8= ?@>=8:0T C B:0=8=8 C :>=F5=B@0FVOE, O:V <>6CBL C 1030B> @07V2
?5@528IC20B8 @V25=L ?@5?0@0BC C A8@>20BFV :@>2V.
82545==O. ?>:A0F8= 284V;OTBLAO 7451V;LH>3> C =57
VB8. # 4>A;V465==V 70 CG0ABN 4VB59 =5 A?>AB5@V30;>AO 2V:>2>W 70;56=>ABV C_{max} V ?>:07=8:0
AUC. VA;O 1030B>@07>2>3> 70AB>AC20==O ?@5?0@0BC (10<3/:3/B@8GV =0 45=L) 7=0G=>3>
?V428I5==O C_{max} V AUC =5 A?>AB5@V30;>AO. !5@54=V9 ?5@V>4 =0?V2@>7?04C C 4VB59
AB0=>28BL ?@81;87=> 4-5 3>48=.

\$0@<0F52B8G=V E0@0:B5@8AB8:8.

A=>2=V DV78:>-EVABV: :@C3;V 42>>?C;:V B01;5B:8, 2:@8BV ?;V2:>2>N >1>;>=:>N 2V4 1V;>3> 4>
6>2BC20B>-1V;>3> :>;L>@C (?> 250 <3); B01;5B:8 C D>@2>N >1>;>=:>N, 7 @8A:>N 7 >4=>3> 1>:C, 2V4
1V;>3> 4> 6>2BC20B>-1V;>3> :>;L>@C (?> 500 <3).

"5@ABV. 3 @>:8.

#<>28 715@V30==O.

15@V30B8 ?@8 B5
15@V30B8 C =54>ABC?=>

#?0:>2:0. > 10 B01;5B>: C 1;VAB5@V; ?> 1 01> ?> 10 1;VAB5@V2 C :0@B>==V9 :>@>1FV.

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

8@>1=8:.

«. =V: \$0@<0ALNB8:0; 01>@0B>@V7» (2V44V;5==O DV@<8 «6. . 5

VAF57=0E>465==O.

V;O=:0 218-219, 6V. 9. V. !V. =40AB@V0; @V0, 0=>;V394 116, C460@0B, =4VO.