

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

\$!."®
(FLEMOCLAV SOLUTAB®)

!.;04:
4VNGV @5G>28=8: 0<>:A8F8;V=, ::02C;0=>20 :8A;>B0;
1 B01;5B:0 125/31,25
31,25 <3 ::02C;0=>2>W :8A;>B8 (C 283;O4V :0;VN ::02C;0=0BC);
1 B01;5B:0 250/62,5 <3 250 <3 0<>:A8F8;V=C (C 283;O4V 0<>:A8F8;V=C B@83V4@0BC), 62,5 <3
::02C;0=>2>W :8A;>B8 (C 283;O4V :0;VN ::02C;0=0BC);
1 B01;5B:0 500/125 <3 500 <3 0<>:A8F8;V=C (C 283;O4V 0<>:A8F8;V=C B@83V4@0BC),
125 <3 ::02C;0=>2>W :8A;>B8 (C 283;O4V :0;VN ::02C;0=0BC);
4>?>28=8: F5;N;>70 :@8AB0;VG=0, :@>A?>2V4>=, 20=V;V=, 0@><0B870B>@ 01@8:>A>289,
A0E0@8=, <03=VN AB50@0B.

V:0@AL:0 D>@<0. "01;5B:8, I> 48A?5@3CNBLAO.
A=>2=V DV78:>-EVABV: B01;5B:8 125/31,25 <3 4>230AB>W D>@<8 1V;>3> 01> <0965 1V;>3> :>;L>@C,
157 @8A:8, <0NBL <0@:C20==O 421 B0 ;
B01;5B:8 250/62,5 <3 4>230AB>W D>@<8 1V;>3> 01> <0965 1V;>3> :>;L>@C, 157 @8A:8, <0NBL
<0@:C20==O 422 B0 ;
B01;5B:8 500/125 <3 4>230AB>W D>@<8 1V;>3> 01> <0965 1V;>3> :>;L>@C, 157 @8A:8, <0NBL
<0@:C20==O 424 B0 .
@8 715@V30==V B01;5B:8 2V4 1V;>3> 4> 6>2B>3> :>;L>@C; <>6;825 CB2>@5==O :>@8G=528E
:@0?G0AB8E ?;O

\$0@<0:>B5@0?52B8G=0 3@C?0. =B810:B5@V0;L=V 70A>18 4;O A8AB5<=>3> 70AB>AC20==O. >
<1V=0FVW ?5=VF8;V=V2 7 V=3V1VB>@0<8 15B0-;0:B0<07. >4 "% J01C R02.

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

\$0@<0:>48=0
<>:A8F8;V= =0?V2A8=B5B8G=89 0=B81V>B8: 7 H8@>:8< A?5:B@< 0=B810:B5@V0;L=>W
0:B82=>ABV ?@>B8 1030BL>E 3@078B82=8E V 3@0<=530B82=8E >@30=V7ABV 0<>:A8F8;V=C =5
2;;NG0T>@30=V7<8, I> A8=B57CNBL F59 D5@<5=B. ;02C;0=>20 :8A;>B0 <0T β-;0:B0<=C AB@C:BC@C,
?>4V1=C 4> ?5=VF8;V=V2, 0 B0:>6 740B=VABL V=0:B82C20B8 β-;0:B0<07=V D5@<5=B8, 2;0AB82V
>@30=V7<0<, O:V @578AB5=B=V 4> ?5=VF8;V=V2 V F5D0;>A?>@8=V2. >:@5<0, 2>=0 <0T 28@065=C
0:B82=VABL I>4> 206;828E 7 ;V=VG=>W B>G:8 7>@C ?;07>@30=V7 0<>:A8F8;V=C B0 4> V=H8E
?5=VF8;V=V2 V F5D0;>A?>@8=V2.
V:@>>@30=V7<8, 707=0G5=V =86G5, ::0A8DV:>20=V 2V4?>2V4=> 4> GCB;82>ABV 4> 0<>:A8F8;V=C
/;02C;0=0BC in vitro.
'CB;82V >@30=V7<8
@078B82=V 05@>18: *Bacillus anthracis*, *Enterococcus faecalis*, *Listeria monocytogenes*, *Nocardia asteroides*,
Streptococcus pneumoniae, *Streptococcus pyogenes*, *Streptococcus agalactiae*, *Streptococcus viridans* V=HV β-35
<>;VB8G=V 2848 *Streptococcus*, *Staphylococcus aureus* (<5B8F8;V=GCB;82V HB0<8), *Staphylococcus*
saprophyticus (<5B8F8;V=GCB;82V HB0<8), :>03C;07>=530B82=V AB0DV;>:>:8 (<5B8F8;V=GCB;82V
HB0<8).
@0<=530B82=V 05@>18: *Bordetella pertussis*, *Haemophilus influenza*, *Haemophilus parainfluenzae*,
Helicobacter pylori, *Moraxella catarrhalis*, *Neisseria gonorrhoeae*, *Pasteurella multocida*, *Vibrio cholera*.
=HV: *Borrelia burgdorferi*, *Leptospira icterohaemorrhagiae*, *Treponema pallidum*.
@078B82=V 0=05@>18: 2848 *Clostridium*, *Peptococcus niger*, *Peptostreptococcus magnus*, *Peptostreptococcus*
micros, 2848 *Peptostreptococcus*
@0<=530B82=V 0=05@>18: 2848 *Bacteroides* (2;;NG0NG8 *Bacteroides fragilis*), 2848 *Capnocytophaga*,
Eikenella corrodens, 2848 *Fusobacterium*, 2848 *Porphyromonas*, 2848 *Prevotella*
(B0<8 7 <>6;82>N =01CB>N @578AB5=B=VABN

@0<=530B82=V 05@>18: *Escherichia coli*, *Klebsiella oxytoca*, *Klesiella pneumonia*, 2848 *Klebsiella*, *Proteus mirabilis*, *Proteus vulgaris*, 2848 *Proteus*, 2848 *Salmonella*, 2848 *Shigella*.
@078B82=V 05@>18: 2848 *Corynebacterium*, *Enterococcus faecium*.
5GCB;82V >@30=V7<8
@0<=530B82=V 05@>18: 2848 *Acinetobacter*, *Citrobacter freundii*, 2848 *Enterobacter*, *Hafnia alvei*, *Legionella pneumophila*, *Morganella morganii*, 2848 *Providencia*, 2848 *Pseudomonas*, 2848 *Serratia*, *Stenotrophomas maltophilia*, *Yesinia enterolitica*
=HV: *Chlamydia pneumonia*, *Chlamydia psittaci*, 2848 *Chlamydia*, *Coxiella burnetti*, 2848 *Mycoplasma*.
\$0@<0:>:V=5B8:0.
A<>:BC20==O: 0<>:A8F8;V= V ::02C;0=>20 :8A;>B0 ?>2=VABN @>7G8==V C 2>4=8E @>7G8=0E ?@8 DV7V>;>3VG=8E 7=0G5==OE @. 18420 :>=5=B8 H284:> V 4>1@5 2A<>:BCNBLAO ?@8 ?5@>@0;L=> 70AB>AC20==V. A<>:BC20==O 0<>:A8F8;V=C/:;02C;0=>2>W :8A;>B8 ?>:@0ICTBLAO ?@8 9>3> 70AB>AC20==V =0 ?>G0B:C ?@89> VA;O ?5@>@0;L=>3> ?@89>1>E :>=5=BV2 ?@5?0@0BC >4=0:>2V V G0A ?V:>2>W :>=F5=B@0FVW 2 ?;07_{max}) 2 :>6=>28BL ?@81;87=> 1 3>48=C.
57C;LB0B8 D0@<0:>:V=5B8G=8E 4>A;V465=L ?@8 ?@89>

"01;8FO 2

!5@54=V (±SD) D0@<0:>:V=5B8G=V ?0@<5B@8

:B82=0 @5G>28=0	>70 <3	! _{max} <3/<;	T _{max} [*] 3>4	AUC _(0-24 3>4) <3.3>4/<;	T _{1/2} 3>4
<>:A8F8;V=					
AMX/CA 500<3/125 <3	500	7,19±2,26	1,5 (1,0-2,5)	53,5±8,87	1,15±0,20
;02C;0=>20 :8A;>B0					
AMX/CA 500 <3/125 <3	125	2,4±0,83	1,5 (1,0-2,0)	15,72±3,86	0,98±0,12
AMX 0<>:A8F8;V=, CA ::02C;0=>20 :8A;>B0 *<54V0=0 (<56V)					

>=F5=B@0FVO 2 ?;072V 0<>:A8F8;V=C B0 ::02C;0=>2>W :8A;>B8 B0:V 6, O: V ?@8 ?5@>@0;L=>:@5 <8E 5:2V20;5=B=8E 4>7 0<>:A8F8;V=C 01> ::02C;0=>2>W :8A;>B8.
>7?>4V;.
@81;87=> 25 % ::02C;0=>2>W :8A;>B8 V 18 % 0<>:A8F8;V=C 72 07CNBLAO 7 1V;:0<8 :@>2V. 1T< @>7?>4V;C 0,3-0,4 ;/:3 4;O 0<>:A8F8;V=C B0 0,2 ;/:3 4;O ::02C;0=>2>W :8A;>B8.
V>B@0=AD>@<0FVO.
<>:A8F8;V= G0AB:>2> 282>48BLAO =8@:0<8 C 283;O4V =50:B82=>W ?5=VF8;>W4=>W :8A;>B8 2 :V;L:>ABOE, 5:2V20;5=B=8E 10-25 % ?@89=OB>W 4>78. ;02C;0=>20 :8A;>B0<5B01>;V7CTBLAO V 284V;OTBLAO A5G5N V :0;×, 0 B0:>6 ?>2VB@O<, I> 2848E0TBLAO, C 283;O4V 2C3;5:8A;>3> 307C. 82545==O.
<>:A8F8;V= 282>48BLAO 2 >A=>2=> V V=H8<8 H;OE0<8.
!5@54=V9 ?5@>V>4 =0?V2282545==O 0<>:A8F8;V=C/:;02C;0=>2>W :8A;>B8 AB0=>28BL ?@81;87=> 1 3>48=C, A5@54=V9 ::V@5=A ?@81;87=> 25 ;/3>4 C 74>@>28E 4>1@>2>;LFV2. @81;87=> 60-70 % 0 <>:A8F8;V=C B0 40-65 % ::02C;0=>2>W :8A;>B8 282>4OBLAO 7 A5G5N 2 =57BO3× ?5@H8E 6 3>48= ?VA;O ?@89>2>W 4>78 250 <3/125 <3 500 <3/125 <3. V7=V 4>A;V465==O ?>:07CNBL 282545==O 7 A5G5N 50-85 % 0<>:A8F8;V=C V 27-60 % ::02C;0=>2>W :8A;>B8 ?@>BO3× 24 3>48=. 5;8:0 :V;L:VABL ::02C;0=>2>W :8A;>B8 284V;OTBLAO ?@>BO3× ?5@H8E 42>E 3>48= ?VA;O ?@89> 4=>G0A=89 ?@89>< ?@>15=5F84C 70B@82>W :8A;>B8 =8@:0<8, (482. @>74V; «70T<>4VO 7 V=H8<8 ;V:0@AL:8<8 70A>10<8 B0 V=HV 2848 270T<>4V9»)).
V:.
5@>V>4 =0?V2282545==O 0<>:A8F8;V=C >4=0:>289 4;O 4VB59 2V:× 2V4 3 2 @>:V2, 0 B0:>6 4;O 4VB59 AB0@H>3> 2V:C B0 4>@>A;8E. # ?0FVT=BV2 AB0@H>3> 2V:C G0ABVH5 7CAB@VG0NBLAO ?>@CH5==O DC=:FVW =8@>:, =0 I> A;V4 725@=CB8 C203C ?@8 281>@>V 4>78 ?@5?0@0BC V ?@8 ?@>2545==V <=>VB>@8=3C DC=:FVW =8@>:..
!B0BL.
\$0@<0:>:V=5B8:0 0<>:A8F8;V=C/:;02C;0=>2>W :8A;>B8 =5 70;568BL 2V4 AB0BV.
8@:>20 =54>AB0B=VABL.

;V@5=A 0<:A8F8;V=C/:;02C;0=>2>W :8A;>B8 7<5=HCTBLAO ?@>?>@FV9=>=8@:>2V9
=54>AB0B=>ABV.

<5=H5==O :;V@5=AC 1V;LH E0@0:B5@=> 4;O 0<:A8F8;V=C, =V6 4;O :;02C;0=>2>W :8A;>B8,
>A:V;L:8 0<:A8F8;V= 2 >A=>2=> 0<:A8F8;V=C, 0;5 ?V4B@82>W :8A;>B8 (482. @>74V; «!>AV1
70AB>AC20==O B0 4>78»).

5GV=:>20 =54>AB0B=VABL.

>15@56=VABN ?@87=0G0B8 ?0FVT=B0< 7 ?>@CH5==O< DC=:FVW ?5GV=:8 V ?5@V>48G=>
:>=B@>;N20B8 DC=:FVN ?5GV=:8 C B0:8E ?0FVT=BV2.

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

>:070==O.

V:C20==O 10:B5@V0;L=8E V=D5:FV9, A?@8G8=5=8E GCB;828<8 >@30=V7<0<8, B0:8E O::

- ?V4B25@465=89 3>AB@89 10:B5@V0;L=89 A8=CA8B;
- 3>AB@89 A5@54=V9 >B8B;
- ?V4B25@465=5 703>AB@5==O E@>=VG=>3> 1@>=EVBC;
- =53>A?VB0;L=0 ?=52<=>=VO;
- F8AB8B8;
- ?VT;>=5D@8B8;
- V=D5:FVW H:V@8 B0 <O:8E B:0=8=, C B.G. F5;N;VB8, C:CA8 B20@8=, BO6:V
45=B>0;L25>;O@=V 01AF5A8 7 ?>H8@5=8< F5;N;VB><;
- V=D5:FVW :VAB>: B0 AC3;>1V2, C B.G. >AB5>

@>B8?>:070==O.

V428I5=0 GCB;82VABL 4> 1C4L-O:8E :>5=BV2 ?@5?0@0BC, 4> 1C4L-O:8E 0=B810:B5@V;L=8E
70A>1V2 3@C?8 ?5=VF8;V=V2.

0O2=VABL 2 0=0<=57V BO6:8E @50:FV9 3V?5@GCB;82>ABV (2 B.G. 0=0DV;0:AVW), ?>2O70=8E V7
70AB>AC20==O< V=H8E 15B0-;0:B0<=8E 035=BV2 (C B.G. F5D0;>A?>@8=V2, :0@10?5=5 <=>10:B0
0O2=VABL 2 0=0<=57V 6>2BO=8FV 01> 48ADC=:FVW ?5GV=:8, ?>2O70=8E V7 70AB>AC20==O< 0
<:A8F8;V=C/:;02C;0=0BC (482.@>74V; «>1VG=V @50:FVW»).

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

5@>@0;L=V 0=B8:>03C;O=B8.

?@0:B8G=V9 <548F8=V >4=>G0A=> 70AB>A>2CNBL ?5@>@0;L=V 0=B8:>03C;O=B8 B0 ?5=VF8;V=8,
=5 ?>2V4><;O;>AO ?@> WE 270T<>4VW.

?8A0=> >:@54=>3>=>@<0;V7>20=>3> 2V4=>H5==O () C ?0FVT=BV2, O:V >4=>G0A=> ?@89<0;8 0
<:A8F8;V= B0 0F5=>:C<0@>; 01> 20@D0@8=. /:I> B0:5 70AB>AC20==O =5>1EV4=5, A;V4 @5B5;L=>
:>=B@>;N20B8 ?@>B@><1V=>289 G0A 01> 7 4>4020==O< 01> ?@8?8=5==O< ;V:C20==O 0<:A8F8;V=>
5B>B@5:A0B.

5=VF8;V=8 <6CBL 7<5=HC20B8 282545==O <5B>B@5:A0BC, I> <65 A?@8G8=8B8 7@>AB0==O
B>:A8G=>ABV >AB0==L>3>.

@>15=5F84.

4=>G0A=5 70AB>AC20==O ?@>15=5F84C =5 @5:><5=4CTBLAO. @>15=5F84 7=86CT =8@:>2C
:0=0;LF52C A5:@5FVN 0<:A8F8;V=C. 4=>G0A=5 70AB>AC20==O ?@>15=5F84C 7 0<:A8F8;V=><
<>65 ?@8725AB8 4> ?V428I5==O @V2=O B0 1V;LH B@820;>465==N 0<:A8F8;V=C 2 :@>2V, ?@>B5 =5
2?;820T =0 @V25=L :;02C;0=>2>W :8A;>B8.

4=>G0A=5 70AB>AC20==O 0;>?C@8=>;C ?V4 G0A ;V:C20==O 0<:A8F8;V=>< <>65 71V;LH8B8 V
<>2V@=VABL 0;5@3VG=8E H:V@=8E @50:FV9.

/: V V=HV 0=B81V>B8:8, <>65 <0B8 2?;82 =0 D;>@C :8H5G=8:C, I> ?@872>48BL 4> 7<5=H5==O
@501A>@1FVW 5AB@>35=V2 B0 7<5=H5==O 5D5:B82=>ABV :><1V=>20=8E ?5@>@0;L=8E
:>=B@0F5?B82=8E 70A>1V2.

E2>@8E, O:V ;V:CNBLAO D5=>;0B>< <>D5BV;>, ?VA;O ?>G0B:C 70AB>AC20==O ?5@>@0;L=>3> 0
<:A8F8;V=C 7 :;02C;0=>2>N :8A;>B>N <>65 7<5=H8B8AL ?@54>7>20 :>=F5=B@0FVO 0:B82=>3>
<5B01>;VBC D5=>;L=>W :8A;>B8 ?@81;87=> =0 50 %. &O 77>2>3> @V2=O <>65 =5 B>G=>
2V4?>2V40B8 7W 5:A?>78FVW D5=>;L=>W :8A;>B8.

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

5@54 ?>G0B:<< ;V:C20==O 0<<:A8F8;V=>2>N :8A;>B>N =5>1EV4=> B>G=> 287=0G8B8 =0O2=VABL 2
0=0<=57V @50:FV9 3V?5@GCB;82>ABV 4> ?5=VF8;V=V2, F5D0;>A?>@8=V2 01> V=H8E 0;5@35=V2
(482. @>74V;8 «@>B8?>:070==O», «>1VG=V @50:FVW»).

!5@9>7=V, 0 G0A< =02VBL ;5B0;L=V 28?04:8 3V?5@GCB;82>ABV (0=0DV;0:B>W4=V @50:FVW)
A?>AB5@V30NBLAO C ?0FVT=BV2 ?V4 G0A B5@0?VW ?5=VF8;V=>3V4=VH5 28=8:0NBL C E2>@8E
7 =0O2=VABN 3V?5@GCB;82>ABV 4> ?5=VF8;V=V2 2 0=0<=57V B0 2 ?0FVT=BV2 7 0B>?VTN. # @07V
28=8:=5==O 0;5@3VG=>W @50:FVW B5@0?VN 0<<:A8F8;V=>< A;V4 ?@8?8=8B8 B0 ?@87=0G8B8
2V4?>2V4=5 ;V:C20==O.

@07V O:I> 4>2545=>, I> V=D5:FVO 7C<>2;5=0 >@30=V7<0<8, GCB;828<8 4> 0<<:A8F8;V=C,
=5>1EV4=> 72068B8 <>6;82VABL ?5@5E>4C 7 :<1V=0FVW 0<<:A8F8;V=/:;02C;0=>20 :8A;>B0 =0 0
<<:A8F8;V= 2V4?>2V4=> 4> >DV FV9=8E @5:><5=40FV9.

0AB>AC20==O 0<<:A8F8;V=C/:;02C;0=>2>W :8A;>B8 =5 ?>:070=> C @07V 28A>:>3> @878:C 7=865=>W
GCB;82>ABV 01> @578AB5=B=>ABV >@30=V7 15B0-;0:B0<=8E 0=B81V>B8:V2, O:V =5GCB;82V 4>
?@83=VG5==O 15B0-;0:B0<07 :;02C;0=>2>N :8A;>B>N.

<<:A8F8;V=/:;02C;0=>2C :8A;>BC =5 A;V4 70AB>AC20B8 4;O ;V:C20==O ?5=VF8;V=-@578AB5=B=>3>S
.pneumoniae.

?0FVT=BV2 7 ?>@CH5==O< DC=:FVW =8@>: 01> ?@8 ?@89>:8E 4>7 <>6CBL 28=8:0B8 AC4<8 (482.
@>74V; «>1VG=V @50:FVW»).

\$;5<<:;02 !>;NB01® =5 A;V4 ?@87=0G0B8 ?@8 ?V4>7@V =0 V=D5:FV9=89 <>=>=C:;5>7, >A:V;L:8 ?@8
70AB>AC20==V 0<<:A8F8;V=C ?@8 40=V9 ?0B>;>3VW A?>AB5@V30;8AO 28?04:8 :>@5?>4V1=8E
28A8?0=L.

"@820;5 70AB>AC20==O ?@5?0@0BC V=>4V <>65 A?@8G8=OB8 =04W 4> ?@5?0@0BC \$;5<<:;02
!>;NB01® D;>@8.

>O20 =0 ?>G0B:C ;V:C20==O 35=5@0;V7>20=>W 5@8B5<8 7 30@OG:>N, 0A>FV9>20=> 7 ?CABC;0<8,
<>65 1CB8 A8<< 3>AB@>3> 35=5@0;V7>20=>3> 5:70=B5<0B>7=>3> ?CABC;L>7C (482. @>74V;
«>1VG=V @50:FVW»).

B0:>1EV4=> ?@8?8=8B8 ;V:C20==O V 2 ?>40;LH>B8?>:070=> 70AB>A>2C20B8
0<<:A8F8;V=.

>15@56=VABN A;V4 70AB>A>2C20B8 ?0FVT=B0< 7 ?>@CH5==O< DC=:FVW ?5GV=:8 (482. @>74V;8
«!>AV1 70AB>AC20==O B0 4>78», «@>B8?>:070==O», «>1VG=V @50:FVW»).

:C ?5GV=:8, ?@> O:V ?>2V4><;O;>AO ?5@5206=> C G>;>2V:V2 B0 ?0FVT=BV2 ;VB=L>3> 2V:C,
<>6CBL 1CB8 ?>2O70=V 7 ;V:C20==O< ?@>BO3<< B@820;>3> G0AC. &V 7 A?>AB5@V30;8AL C
4VB59. # 2AVE ?>?C;OFVOE ?@>O28 728G09=> 28=8:0;8 ?V4 G0A 01> 2V4@07C 6 ?VA;O ;V:C20==O
?@5?0@0B<, ?@>B5 2 45O:8E 28?04:0E <>6CBL 28=8:0B8 ?@>BO3<< 45;V;L:>E B86=V2 ?VA;O
;V:C20==O. &V O28I0 728G09=> >1>@>B=V.:C ?5GV=:8 <>6CBL 1CB8 A5@9>7=V, 0 2 4C65 @V4:8E
28?04:0E ?>2V4><;O;>AO ?@> ;5B0;L=V 28?04:8. 0965 702648 7:C ?5GV=:8 28=8:0;8 C ?0FVT=BV2 7
A5@9>7=8<8 >A=>2=8<8 70E2>@N20==O<8 B0 C ?0FVT=BV2, O:V >4=>G0A=> ?@89<0NBL
;V:0@AL:V 70A>18 7 ?>B5=FV9=8< 2?;82<< =0 ?5GV=:C (482. @>74V; «>1VG=V @50:FVW»).

@8 70AB>AC20==V ?@0:B8G=> 2AVE 0=B810:B5@V0;L=8E ?@5?0@0BV2 ?>2V4<;O;>AO ?@>
@>728B>: 0=B81V>B8:>0A>FV9>20=>3> :>;VBC 2V4 ;53:>3> ABC?5=O 4> B0:>3>, I> AB0=>28BL
703@>7C 68BBN (482. @>74V; «>1VG=V @50:FVW»).

"0:8< G8=><, A;V4 702648 ?0<OB0B8 ?@>
0=B81V>B8:>0A>FV9>20=89 :>;VB C ?0FVT=BV2, C O:8E 2V4 ?VA;O ?@89>1V2. @8 28=8:=5==V
0=B81V>B8:>0A>FV9>20=>3> :>;VBC, A;V4 =5309=> ?@8?8=8B8 ?@89<< 0<<:A8F8;V=C/:;02C;0=>2>W
:8A;>B8, ?@>:>=AC;LBC20B8AO 7 ;V:0@5< V 268B8 2V4?>2V4=8E 70E>4V2. # FV9 A8BC0FVW
?@>B8?>:070=V 0=B8?5@8AB0;LB8G=V ;V:0@AL:V 70A>18.

@8 ;V:C20==V ?@>BO3<< B@820;>3> G0AC @5:><5=4>20=> ?5@V>48G=> >FV=N20B8 DC=:FVN
A8AB5< >@30=V72C, ?5GV=:>2C B0 35<<?>5B8G=C A8AB5
@V4:0 C ?0FVT=BV2, O:V ?@89<0NBL 0<<:A8F8;V=/:;02C;0=>2C :8A;>BC B0 ?5@>@0;L=V
0=B8:>03C;O=B8, <>65 A?>AB5@V30B8AO ?>=04=>@<>20=5 ?>4>265==O ?@>B@<<1V=>2>3> G0AC.
@8 >4=>G0A=>03C;O=V2 =5>1EV4=89 2V4?>2V4=89 <>=VB>@8=3. >65 1CB8 ?>B@V1=0 :>@5:FVO
4>78 ?5@>@0;L=8E 0=B8:>03C;O=V2 4;O ?V4B@81EV4=>3> @V2=O 0=B8:>03C;OFVW (482.
@>74V;8 «70T<>4VO 7 V=H8<8 ;V:0@AL:8<8 70A>10<8 B0 V=HV 2848 270T<>4V9» «>1VG=V
@50:FVW»).

;O ?0FVT=BV2 7 ?>@CH5==O< DC=:FVW =8@>: =5>1EV4=> :>@83C20B8 4>7C 2V4?>2V4=> 4>
ABC?5=O ?>@CH5==O DC=:FVW =8@>: (482. @>74V; «!>AV1 70AB>AC20==O B0 4>78»).

?0FVT=BV2 7V 7=865=>N 5:A:@5FVTN A5GV 4C65 @V4:><65 A?>AB5@V30B8AO :@8AB0;C@VO,
3>;>2=8< G8=>< ?@8 ?0@5=B5@0;L=>:8<8 4>70<8 0<:A8F8;V=C 4;O 7<5=H5==O @878:C 28=8:=5==O
:@8AB0;C@VW @5:><5=4CTBLAO ?V4B@8N @V48=>N B0 282545=>N A5G5N (482. @>74V;
«5@54>7C20==O»). # ?0FVT=BV2 7 :0B5B5@>< C A5G>2>1EV4=> ?5@V>48G=> A2>TG0A=> 7
@8 ;V:C20==V 0<:A8F8;V=>< 4;O 287=0G5==O @V2=O 3;N:>78 2 A5GV A;V4 28:>@8AB>2C20B8
=5D5@<5=B0B82=V @50:FVW 7 3;N:>7>:A8407>N, >A;V;L:8 =5 D5@<5=B=V <5B>48 <6CBL 4020B8
E81=>?>78B82=V @57C;LB0B8.

@8ACB=VABL ;:02C;0=>2>W :8A;>B8<>65 A?@8G8=OB8 =5A?5F8DVG=5 72 O7C20==O IgG V 0;L1C;,
<>6;8289 E81=>?>78B82=89 @57C;LB0B ?@8 ?@>2545==V B5ABC C<1A0.

?>2V4><;5==O ?@> E81=>?>78B82=V @57C;LB0B8 B5ABV2 =0 =0O2=VABL *Aspergillus* C ?0FVT=BV2,
O:V >B@8Bio-Rad Laboratories Platelis *Aspergillus* EIA B5ABC). ">78B82=V @57C;LB0B8 C ?0FVT=BV2,
O:V ;V:CNBLAO 0<:A8F8;V=>2>N :8A;>B>N, A;V4 V=B5@?@5BC20B8 7 >15@56=VABN B0
?V4B25@46C20B8 V=H8<8 4V03=>AB8G=8<8 <5B>40<8.

@5?0@0B \$;5<:;02 !>;NB01® 125/31,25

@5?0@0B \$;5<:;02 !>;NB01® 250/62,5

@5?0@0B \$;5<:;02 !>;NB01® 500/125

?0FVT=BV2 7V 7=865=>N DC=:FVTN =8@>: 01> C ?0FVT=BV2, O:V :>=B@>;NNBL @V25=L :0;VN
4VTB>N, A;V4 ?0<OB0B8 ?@> :V;L:VABL :0;VN 1V;LH5 =V61 <<:;L =0 4>1C.

5 70AB>A>2C20B8 ?@5?0@0B ?VA;O 70:V=G5==O 40B8 B5@ABV, 2:070=>3> =0 C?0:>2FV!

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

03VB=VABL

>A;V465==O =0 B20@8=0E =5 ?>:07CNBL ?@O<8E G8 =5?@O<8E H:V4;828E 4V9 =0 203VB=VABL,

@>728B>: 5<1@V>=0/?>;>40 G8 ?>AB=0B0;L=89 @>728B>:. 1<565=V 40=V 70AB>AC20==O 0

<>:A8F8;V=C/:;02C;0=>2>W :8A;>B8 ?V4 G0A 203VB=>ABV =5 28O2;O;8 ?V428I5=>3> @878:C

28=8:=5==O 2@>465=8E 204 @>728B:C. E>4V >4=>3> 4>A;V465==O 70 CG0ABN 6V=>: 7 ?5@54G0A=8

< @>7@82><>1>;>=: ?;>40 ?>2V4><;O;>AO, I> ?@>DV;0:B8G=5 70AB>AC20==O 0<:A8F8;V=C

/:;02C;0=>2>W :8A;>B8<>65 1CB8 ?>2O70=5 7 ?V428I5==O< @878:C =5:@>B87CNG>3> 5=B5@>:;VBC

C=>2>=0@>465=8E. !;V4 C=8:0B8 70AB>AC20==O ?@5?0@0BC ?V4 G0A 203VB=>ABV, 70 28=OB:>

=5>1EV4=>ABV 70AB>AC20==O C 28?04:0E, O:V >FV=NT ;V:0@.

5@V>4 3>4C20==O 3@C44N

18420 0:B82=V :>=5=B8 ?@5?0@0BC 5:A:@5BCNBLAO C 3@C4=5 <>;>: (=5<0T V=D>@<0FVW

AB>A>2=> 2?;82C ;:02C;0=>2>W :8A;>B8 =0 =5<>2;O, O:5 7=0E>48BLAO =0 3@C4=>4>2C20==V).

V4?>2V4=>, C =5<>2;OB8, O:5 7=0E>48BLAO =0 3@C4=>4>2C20==V, <>6;820 ?>O20 4V0@5W B0

3@81:>2>W V=D5:FVW A;87>28E >1>;>=:, B>4C20==O 3@C44N A;V4 ?@8?8=8B8.

@5?0@0B C ?5@V>4 3>4C20==O 3@C44N <>6=0 70AB>A>2C20B8 ;8H5 B>4V, :>;8, =0 4C@8ABL 2V4

70AB>AC20==O 1C45 ?5@52060B8 @878:.

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.

5 ?@>2>48;8AL 4>A;V465==O 2?;82C =0 740B=VABL :5@C20B8 02B>>1V;5< B0 V=H8<8 <5E0=V7<0

<8. @>B5 <>6CBL 28=8:0B8 ?>1VG=V @50:FVW (=0?@8:;04 0;5@3VG=V @50:FVW, 70?0<>@>G5==O,

AC4><8), O:V <>6CBL 2?;820B8 =0 740B=VABL :5@C20B8 02B>>1V;5< 01> V=H8<8 <5E0=V7<0<8

(482. @>74V; <>1VG=V 5D5:B8»).

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

>7C 2:070=> 2V4?>2V4=> 4> 2

@8 281>@V 4>78 0<:A8F8;V=C/:;02C;0=>2>W :8A;>B8 4;O ;V:C20==O ?52=8E V=D5:FV9 A;V4 1@0B8

4> C2038 >GV:C20=V ?0B>35=8 V <>6;82C GCB;82VABL 4> 0=B810:B5@V0;L=8E ;V:0@AL:8E 70A>1V2

(482. @>74V; «A>1;82>ABV 70AB>AC20==O»); ABC?V=L B06:>ABV B0 ;>:0;V70FVN V=D5:FV9=>3>

?@>F5AC; 2V;,<0AC BV;0 B0 DC=:FVN =8@>;, O: 707=0G5=> =86G5.

/:I> 4;O ;V:C20==O ?>B@V1=> ?@87=0G0B8 1V;LHV 4>78 0<:A8F8;V=C, A;V4 70AB>A>2C20B8 V=HV

D>@<8 0<:A8F8;V=C/:;02C;0=>2>W :8A;>B8, I>1 C=8:=CB8 ?@87=0G5==O 70928E 28A>:8E 4>7

;:02C;0=>2>W :8A;>B8 (482. @>74V; «A>1;82>ABV 70AB>AC20==O», «\$0@<0:>48=0ABV»).

;O 4>@>A;8E B0 4VB59 7 <0A>N BV;0 ≥ 40 :3 \$;5<>;02 !>;NB01® 500/125 70157?5GCT 4>1>2C 4>7C, O:0 AB0=>28BL 1500 <3 0<>:A8F8;V=C/375 <3 ::02C;0=>2>W :8A;>B8.
;O 4VB59 7 <0A>N BV;0 <40 :3 \$;5<>;02 !>;NB01® 125/31,25 V 250 <3/62,5 <3 70157?5GCNBL <0:A8 <0;L=C 4>1>2C 4>7C 2400 <3 0<>:A8F8;V=C/600 <3 ::02C;0=>2>W :8A;>B8 ?@8 70AB>AC20==V, O: 2:070=>=86G5.
"@820;VABL ;V:C20==O 287=0G0TBLAO 2V4?>2V44N ?0FVT=B0 =0 ;V:C20==O. 5O:V V=D5:FVW, (=0?@8::04 >AB5>B@51CNBL ;V:C20==O ?@>BO3< B@820;>3> G0AC. V:C20==O =5 A;V4 ?@>4>26C20B8 1V;LH5 14 4V1 157 >FV=:8 AB0=C E2>@>3> (482. @>74V; «A>1;82>ABV 70AB>AC20==O» I>4> B@820;>3> 70AB>AC20==O ?@5?0@0BC).
>@>A;V B0 4VB8 7 <0A>N BV;0 ≥ 40 :3
1 B01;5B:0 500/125 3 @078 =0 4>1C
VB8 7 <0A>N BV;0 <40 :3
V4 20 <3/5 <3/:3/4>1C 4> 60 <3/15 <3/:3/4>1C, @>74V;82H8 =0 3 ?@89<8. ;V=VG=V 40=V 70AB>AC20==O 0<>:A8F8;V=C/:;02C;0=>2>W :8A;>B8 V7 A?V22V4=>H5==O< 4:1 C 4VB59 2V:< 4> 2 @>:V2 C 4>7V ?>=04 40 <3/10 <3/:3 <0A8 BV;0 =0 4>1C 2V4ACB=V.
0FVT=B8 ;VB=L>3> 2V:C
V4ACB=O =5>1EV4=VABL :>@5:FVW 4>78.
8@.:>20 =54>AB0B=VABL
>70 287=0G0TBLAO 2V4?>2V4=> 4> @V2=O 0<>:A8F8;V=C
5<0T =5>1EV4=>ABV 77C ?0FVT=BC ?@8 ::V@5=AV :@50B8=V=C > 30<:/E2.

"01;8FO 3

>@>A;V B0 4VB8 7 <0A>N BV;0 ≥ 40 :3

;V@5=A :@50B8=V=C 10-30 <:/E2	500 <3/125 <3 2 @078 =0 4>1C
;V@5=A :@50B8=V=C < 10 <:/E2	500 <3/125 <3 1 @07 =0 4>1C
5<>4V0;V7	500 <3/125 <3 :>6=V 24 3>4 ?;NA 500 <3/125 <3 ?V4 G0A V ?>2B>@=> 2 :V=FV 4V0;V7C (:>=F5=B@0FVO 0<>:A8F8;V=C B0 ::02C;0=>2>W :8A;>B8 7=86CTBLAO)

"01;8FO 4

>@>A;V B0 4VB8 7 <0A>N BV;0 < 40 :3

;V@5=A :@50B8=V=C: 10-30 <:/E2	15 <3/3,75 <3/:3 2 @078 =0 4>1C (<0:A. 500 <3/125 <3 2 @078 =0 4>1C)
;V@5=A :@50B8=V=C < 10 <:/E2	15<3/3,75 <3/:3 1 @07 =0 4>1C (<0:A. 500 <3/125 <3)
5<>4V0;V7	15 <3/3,75 <3/:3 1 @07 =0 4>1C 5@54 35<>4V0;V7>< - 15 <3/3,75 <3/:3. ;O 2V4=>2;5==O F8@:C;OFVW ?@5?0@0BC 2 :@>2V - 15 <3/3,75 <3/:3 ?VA;O ?@>2545=>3> 35<>4V0;V7C.

5GV=:>20 =54>AB0B=VABL
0AB>A>2C20B8 7 >15@56=VABN V ?5@V>48G=> :>=B@>;N20B8 DC=:FVN ?5GV=:8 (482. @>74V;8 «@>B8?>:070==O», «A>1;82>ABV 70AB>AC20==O»).

!>>AV1 70AB>AC20==O.
\$;5<>;02 !>;NB01® ?@89<0NBL 2A5@548=C.
\$;5<>;02 !>;NB01□ ?@87=0G0NBL =0 ?>G0B:C ?@89>1 7<5=H8B8 48A?5?A8G=V A8<8 B0 ?>:@0I8B8 2A<>:BC20==O ?@5?0@0BC.
V:C20==O <>6CBL ?>G8=0B8 7 ?0@5=B5@0;L=>3> 70AB>AC20==O 0<>:A8F8;V=C/:;02C;0=>2>W :8A;>B8 73V4=> 7 V=AB@C:FVTN 4;O <548G=>3> 70AB>AC20==O 7 ?>40;LH8< ?5@5E>4>< =0 ?5@>@0;L=89 ?@89>
"01;5B:C :>2B0NBL FV;>N, 70?820NG8 AB0:0=< 2>48, 01> @>7G8=ONBL 2 =525;8:V9 :V;L:>ABV 2>48.
;O 4VB59 7 <0A>N BV;0 < 40 :3 @5:<5=4>20=> @>7G8=8B8 2 =525;8:V9 :V;L:>ABV 2>48.

VB8. V:0@AL:89 70AV1 C 40=V9 ;V:0@AL:V9 D>@

5B0;L=C V=D>@<0FVN I>4> 4>7C20==O C 4VB59 482. C @>74V;V «!>AV1 70AB>AC20==O B0 4>78».

5@54>7C20==O.

5@54>7C20==O <>65 AC?@>2>46C20B8AO A8<0<8 7 1>:C B@02=>3> B@0:BC B0 ?>@CH5==O< 2>4=>-5;5:B@>;VB=>3> 10;0=AC. >2V4><;O;>AO ?@> 28?04:8 :@8AB0;C@VW 2=0A;V4>: ?@89># ?0FVT=BV2 7 ?>@CH5==O< DC=:FVW =8@>: 01> ?@8 ?@89>:8E 4>7 <>6CBL 28=8:0B8 AC4<8. # ?0FVT=BV2 7 :0B5B5@>< 2 A5G>2>1EV4=> ?5@V>48G=> A2>TG0A=> 7 (482. @>74V; «A>1;82>ABV 70AB>AC20==O»).

V:C20==O. (;C=>2>-:8H:>2V A8<8 ;V:CNBL A8<0B8G=>, ?@84V;ONG8 C203C :>@5:FVW 2>4=>- 5;5:B@>;VB=>3> 10;0=AC. <>:A8F8;V=/:;02C;0=>2C :8A;>BC <>6=0 2840;8B8 7 :@>2>B>:C H;OE<< 35 <>4V0;V7C.

>1VG=V @50:FVW.

09G0ABVH5 ?>2V4><;O;>AL ?@> B0:V ?>1VG=V @50:FVW: 4V0@5O, =C4>B0 B0 1;N20==O. >1VG=V @50:FVW, I> A?>AB5@V30;8AO ?V4 G0A ?@>2545==O ;V=VG=8E 4>A;V465=L 0 <>:A8F8;V=C/;:02C;0=>2>W :8A;>B8 B0 ?VA;O@5TAB@0FV9=>3> =03;04C, 73@C?>20=> 2V4?>2V4=> 4> ;:0A8DV:0FVW MEDDRA. >1VG=V @50:FVW ;:0A8DV:>20=> 70 >@30=0<8 V A8AB5<0<8 B0 70 G0AB>B>N WE 28=8:=5==O. 0 G0AB>B>N 28=8:=5==O 287=0G0NBL B0:V :0B53>@VW: 4C65 G0AB> ≥1/10, G0AB> ≥1/100 B0 <1/10, =5G0AB> ≥1/1000 B0 <1/100, @V4:> ≥1/10 000 B0 <1/1 000, 4C65 @V4:> <1/10 000, =52V4><> (=5<>6;82> >FV=8B8 ?@8 =002=>ABV 4>ABC?=8E 40=8E).

=D5:FVW B0 V=207VW

'0AB>: :0=484>7 H:V@8 B0 A;87>28E >1>;>=>:.

52V4><>: =04>@30=V7

@>2>=>A=0 B0 ;V

V4>: >1>@>B=0 ;59:>?5=VO (2;;NG0NG8 =59B@>?5=VN) B0 B@><1>F8B>?5=VO.

52V4><>: >1>@>B=89 03@0=C;>F8B>7 B0 35<>;VB8G=0 0=52>B5GV B0 ?@>B@><1V=>2>3> V=45:AC (482. @>74V; «A>1;82>ABV 70AB>AC20==O»).

52V4><>: 0=3V>=52@>B8G=89 =01@O:, 0=0DV;0:AVO, A8@>20B:>?>4V1=89 A8=4@×, 0;5@3VG=89 20A:C;VB.

5@2>20 A8AB5<0

5G0AB>: 70?0<>@>G5==O, 3>;>2=89 1V;L.

52V4><>: >1>@>B=0 3V?5@0:B82=VABL V AC4<8. !C4><8 <>6CBL 28=8:0B8 C ?0FVT=BV2 7 ?>@CH5=>N DC=:FVTN =8@>: 01> C B8E, EB> >B@8:V 4>78 ?@5?0@0BC.

"@02=89 B@0:B

C65 G0AB>: 4V0@5O.

'0AB>: =C4>B0, 1;N20==O.

C4>B0 G0ABVH5 0A>FVNTBLAO 7 28A>:8<8 4>70<8 ?@5?0@0BC. 8I5707=0G5=V A8<8 7 1>:C B@02=>3> B@0:BC <>6=0 7<5=H8B8, O:I> 70AB>A>2C20B8 ?@5?0@0B =0 ?>G0B:C ?@89>

5G0AB>: ?>@CH5==O B@02;5==O.

52V4><>: 0=B81V>B8:0A>FV9>20=89 :>;VB (2;;NG0NG8 ?A524><5<1@0=>7=89 :>;VB B0 35

<>@03VG=89 :>;VB), G>@=89 2>;>A0B89 078:.

5?0B>1V;V0@=V @50:FVW

5G0AB>: ?> " 2V47=0G0;>AL C E2>@8E, O:V ;V:C20;8AL 0=B81V>B8:0<8 3@C?8 15B0-;0:B04=0: ;:V=VG=5 7=0G5==O FL>3> =5 2AB0=>2;5=>.

52V4><>: 35?0B8B8 B0 E>;5AB0B8G=0 6>2BO=8FO. &V O28I0 28=8:0;8 ?@8 70AB>AC20==V V=H8E ?5=VF8;V=V2 B0 F5D0;>A?>@8=V2 (482. @>74V; «A>1;82>ABV 70AB>AC20==O»).

(:V@0 B0 ?V4H:V@=V B:0=8=8

5G0AB>: H:V@=V 28A8?0==O, A25@1V6, :@>?82O=:0.

V4>: ?>;V<>@D=0 5@8B5<0.

52V4><>: A8=4@× !BV25=A06>=A>=0, B>:A8G=89 5?V45@<0;L=89 =5:@>;V7, ?CE8@G0AB89 5:AD>;V0B82=89 45@<0B8B, 3>AB@89 35=5@0;V7>20=89 5:70=B5<0B>7=89 ?CABC;L>7 (482. @>74V; «@>B8?>:070==O»).

@07V ?>O28 1C4L-O:>3> 0;5@3VG=>3> 45@<0B8BC ;V:C20==O A;V4 ?@8?8=8B8 (482. @>74V; «A>1;82>ABV 70AB>AC20==O»).

8@:8 B0 A5G>284V;L=0 A8AB5<0
52V4><: V=B5@AB8FV0;L=89 =5D@8B, :@8AB0;C@VO (482. @>74V; «5@54>7C20==O»).

"5@ABV.3 @>: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. > 4 B01;5B:8 C 1;VAB5@V; ?> 5 1;VAB5@V2 C :0@B>==V9 :>@>1FV.

0B53>@VO 2V4?CA:C. □0 @5F5?B>

8@>1=8:. AB5;;0A \$0@<0 .@>? ..

VAF57=0E>465==O 28@>1=8:0 B0 04@5A0 20465==O 9>3> 4VO;L=>ABV.%>35<0B 2, 7942 5??5;,
V45@;0=48.