CLAIMS

1. An antibacterial complex comprising a nucleic acid sequence and at least one delivery moiety, wherein the delivery moiety is selected from quaternary amine compounds; bis-aminoalkanes and unsaturated derivatives thereof, wherein the amino component of the aminoalkane is an amino group forming part of a heterocyclic ring; and an antibacterial peptide.

2. An antibacterial complex according to Claim 1 wherein the delivery moiety is selected from a quaternary derivative of quinoline or acridine and an antibacterial peptide.

3. A complex according to Claim 2, wherein the delivery moiety is a bis-quinolinium.

4. A complex according to Claim 3, wherein the delivery moiety is dequalinium or an analogue thereof.

5. A complex according to Claim 4, wherein the alkyl chain of the dequalinium analogue has between 8 and 14 methyl groups.

6. A complex according to Claim 5, wherein the alkyl chain has 10 or 12 methyl groups.

7. A complex according to Claim 1, wherein the quaternary amine compound is 10,10'-(decane-1,10-diyl) bis (9-amino-1,2,3,4-tetrahydroacridinium) dichloride.

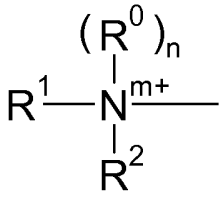
8. A complex according to Claim 1, wherein the quaternary amine compound is 10,10'-(dodecane-1,12-diyl) bis (9-amino-1,2,3,4-tetrahydroacridinium) dichloride.

9. A complex according to Claim 1 wherein the quaternary amine compounds and bis-aminoalkanes and unsaturated derivatives thereof are selected from compounds of the formula (I):

$$Q-(CH_2)_p-A-(CH_2)_q-R^3 \quad (I)$$

wherein Q is selected from:

(a) a group $Q^1$ having the formula:



and

(b) a group $Q^2$, $Q^2$-NH-, $Q^2$-O-, or $Q^2$-S- wherein $Q^2$ is selected from monocyclic, bicyclic and tricyclic heteroaromatic groups of 5 to 14 ring members, of which 1, 2 or 3 are heteroatom ring members selected from N, O and S provided that at least one nitrogen ring member is present, wherein the heteroaromatic groups are optionally substituted by one or two substituents $R^{4a}$ and wherein the said one nitrogen ring member may form an N-oxide or may be substituted with $C_{1-4}$ alkyl, phenyl-$C_{1-4}$ alkyl or di-phenyl-$C_{1-4}$ alkyl to form a quaternary group, wherein the phenyl moieties in each case are optionally substituted with one or two halogen, methyl or methoxy groups;

m is 0 or 1;

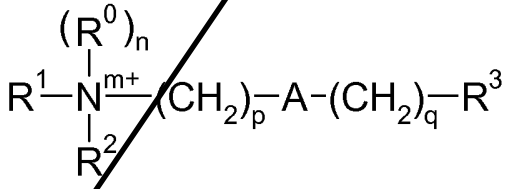
n is 0 or 1;

p and q are the same or different and each is an integer from 1 to 12;

A is a bond or is selected from a naphthalene, biphenyl, terphenyl, phenanthrene, fluorene, stilbene, a group $C_6H_4(CH_2)_rC_6H_4$, a group $C_6H_4$-C≡C-$C_6H_4$, a pyridine-2,6-diyl-bis(benzene-1,4-diyl) group, a group CH=CH-$(CH_2)_s$-$(CH=CH)_t$-; and a group C≡C-$(CH_2)_u$-$(C≡C)_v$-; wherein r is 0-4, s is 0 to 4, t is 0 or 1; u is 0-4 and v is 0 or 1;

when n is 1, $R^0$, $R^1$ and $R^2$ are each selected from $C_{1-4}$ alkyl; and when n is 0, then N, $R^1$ and $R^2$ together form a monocyclic, bicyclic or tricyclic heteroaromatic group of 5 to 14 ring members, of which one is the nitrogen atom N and 0, 1 or 2 are further heteroatom ring members selected from N, O and S, and wherein the heteroaromatic group is optionally substituted by one or two substituents $R^{4b}$; and $R^3$ is selected from hydrogen, $C_{1-4}$ alkyl, halogen, monocyclic carbocyclic groups of 3 to 7 ring members each optionally substituted by one or two substituents $R^{4c}$, a group Q; a group – NH-$Q^2$, a group –O-$Q^2$ and a group –S-$Q^2$; and $R^{4a}$, $R^{4b}$ and $R^{4c}$ are the same or different and each is selected from $C_{1-4}$ alkyl optionally substituted with one or more fluorine atoms: $C_{1-4}$ alkoxy optionally substituted with one or more fluorine atoms; nitro; amino; mono- and di-$C_{1-4}$ alkylamino; halogen; phenyl-$C_{1-2}$ alkyl wherein the phenyl moiety is optionally substituted with one or two methoxy, methyl or halogen substituents; ureido and guanidinyl.

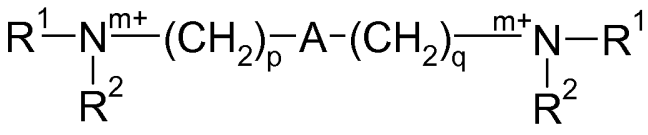
10. A complex according to Claim 9 wherein the compound of formula (I) is represented by formula (II):



(II)

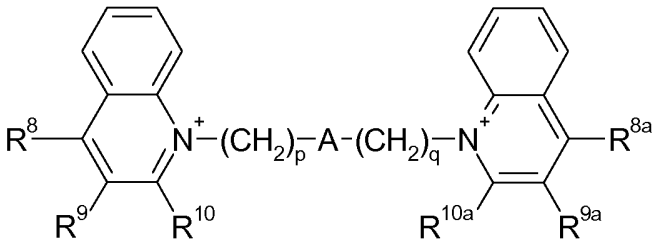
wherein $R^1$, $R^2$, m, p, A, q and $R^3$ are as defined in claim 9.

11. A complex according to Claim 10 wherein $R^3$ is $Q^1$ and n in each instance is 0, and wherein the compound of formula (II) is represented by formula (III):



(III)

12. A complex according to Claim 9 wherein the compound of formula (I) is represented by formula (IV):



(IV)

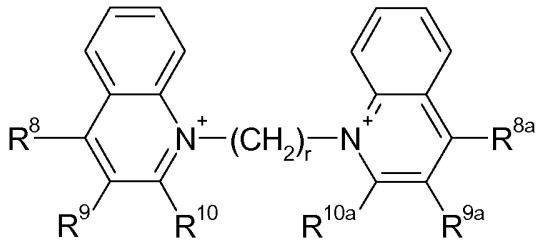
wherein:

p and q are the same or different and each is an integer from 1 to 12;

A is a bond or is selected from naphthalene, biphenyl, terphenyl, phenanthrene, fluorene, stilbene, a group $C_6H_4(CH_2)_rC_6H_4$, a group $C_6H_4$-C≡C-$C_6H_4$, a pyridine-2,6-diyl-bis(benzene-1,4-diyl) group, a group CH=CH-$(CH_2)_s$-$(CH=CH)_t$-; and a group C≡C-$(CH_2)_u$-$(C≡C)_v$-; wherein r is 0-4, s is 0 to 4, t is 0 or 1; u is 0-4 and v is 0 or 1;

$R^8$, $R^9$ and $R^{10}$ are the same or different and are each selected from hydrogen; $C_{1-4}$ alkyl optionally substituted with one or more fluorine atoms: $C_{1-4}$ alkoxy optionally substituted with one or more fluorine atoms; nitro; amino; mono- and di-$C_{1-4}$ alkylamino; halogen, phenyl-$C_{1-2}$ alkyl wherein the phenyl moiety is optionally substituted with one or two methoxy, methyl or halogen substituents; ureido and guanidinyl; or $R^9$ and $R^{10}$ link together to form an alkylene chain $(CH_2)_w$ wherein w is 3 to 5; and$R^{8a}$, $R^{9a}$ and $R^{10a}$ are the same or different and are each selected from hydrogen; $C_{1-4}$ alkyl optionally substituted with one or more fluorine atoms: $C_{1-4}$ alkoxy optionally substituted with one or more fluorine atoms; nitro; amino; mono- and di-$C_{1-4}$ alkylamino; halogen, phenyl-$C_{1-2}$ alkyl wherein the phenyl moiety is optionally substituted with one or two methoxy, methyl or halogen substituents; ureido and guanidinyl; or $R^{9a}$ and $R^{10a}$ link together to form an alkylene chain $(CH_2)_w$ wherein w is 3 to 5.

13. A complex according to Claim 12 wherein the compound of formula (IV) is represented by formula (V):



(V)

wherein:

r is an integer from 2 to 24;

$R^8$, $R^9$ and $R^{10}$ are the same or different and are each selected from hydrogen; $C_{1-4}$ alkyl optionally substituted with one or more fluorine atoms: $C_{1-4}$ alkoxy optionally substituted with one or more fluorine atoms; nitro; amino; mono- and di-$C_{1-4}$ alkylamino; halogen, phenyl-$C_{1-2}$ alkyl wherein the phenyl moiety is optionally substituted with one or two methoxy, methyl or halogen substituents; ureido and guanidinyl; or $R^9$ and $R^{10}$ link together to form an alkylene chain $(CH_2)_w$ wherein w is 3 to 5; and$R^{8a}$, $R^{9a}$ and $R^{10a}$ are the same or different and are each selected from hydrogen; $C_{1-4}$ alkyl optionally substituted with one or more fluorine atoms: $C_{1-4}$ alkoxy optionally substituted with one or more fluorine atoms; nitro; amino; mono- and di-$C_{1-4}$ alkylamino; halogen, phenyl-$C_{1-2}$ alkyl wherein the phenyl moiety is optionally substituted with one or two methoxy, methyl or halogen substituents; ureido and guanidinyl; or $R^{9a}$ and $R^{10a}$ link together to form an alkylene chain $(CH_2)_w$ wherein w is 3 to 5;

provided that:

(i) when $R^{10}$ and $R^{10a}$ are both hydrogen or are both methyl, and $R^9$ and $R^{9a}$ are both hydrogen, then at least one of $R^8$ and $R^{8a}$ is other than hydrogen, amino or dimethylamino; and

(ii) when $R^9$ and $R^{10}$ link together to form an alkylene chain $(CH_2)_w$ wherein w is 4 and $R^{9a}$ and $R^{10a}$ link together to form an alkylene chain $(CH_2)_w$ wherein w is 4, then at least one of $R^8$ and $R^{8a}$ is other than amino.

14. A complex according to any one of Claims 1 to 13, wherein the antibacterial peptide is a naturally occurring peptide.

15. A complex according to any one of Claims 1 to 13, wherein the antibacterial peptide is a peptidomimetic or synthetic variant of a naturally occurring peptide.

16. A complex according to any one of Claims 1 to 15, wherein the antibacterial peptide permeabilises bacterial cell membrane.

17. A complex according to Claim 15, wherein the antibacterial peptide is selected from the group comprising defensins, pleuricidins, magainins, dermaseptins, apidaecins, cecropins, microcins and pediocins.

18. A complex according to Claim 17, wherein the antibacterial peptide is selected from the group comprising Gramicidin and Polymyxin.

19. A complex according to any one of Claims 1 to 15, wherein the antibacterial peptide has an intracellular target.

20. A complex according to Claim 19, wherein the complex further comprises a linker.

21. A complex according to Claim 20, wherein the linker is a carboxyl-group-to-primary-amine cross-linker.

22. A complex according to Claim 21 or Claim 22, wherein the linker is EDC.

23. A complex according to any one of Claims 19 to 22, wherein the antibacterial peptide is selected from the group comprising antibiotics, glycopeptide antibiotics, cationic, polypeptides such as polylysine and polyarginine

24. A complex according to Claim 23, wherein the antibacterial peptide is Buforin or a derivative thereof.

25. A complex according to any one of Claims 1 to 24, wherein the nucleic acid sequence comprises the sequence of a native cellular binding site for a transcription factor.

26. A complex according to Claim 25, wherein the native cellular binding site comprises the sequence of a bacterial Sig binding site.

27. A complex according to Claim 26, wherein the nucleic acid sequence has the sequence set out in SEQ ID NOs:9, 10, 30 and 31, 39, 40 or 41.

28. A complex according to Claim 25, wherein the native cellular binding site comprises the sequence of a bacterial Fur binding site.

29. A complex according to Claim 28, wherein the nucleic acid sequence has the sequence set out in SEQ ID NOs:11, 12 or 13.

30. An antibacterial complex comprising:
a) a nucleic acid sequence comprising the sequence of a native cellular binding site for a transcription factor,
b) 10,10'-( dodecane-1,12-diyl ) bis ( 9-amino-1,2,3,4-tetrahydroacridinium ) dichloride; and optionally
c) an antibacterial peptide.

31. A complex according to Claim 30, wherein the nucleic acid sequence has the sequence set out in SEQ ID NOs:30 and 31.

32. Use of the complex according to any one of Claims 1 to 31 for the treatment of bacterial infection.

33. A pharmaceutical composition or medicament comprising a complex according to any one of Claims 1 to 32 and a physiologically acceptable carrier or excipient.

34. A pharmaceutical composition or medicament as claimed in Claim 33, for use in the treatment of bacterial infection.

**CLAIMS**

1. An antibacterial complex comprising a nucleic acid sequence and at least one delivery moiety, wherein the delivery moiety is selected from quaternary amine compounds; bis-aminoalkanes and unsaturated derivatives thereof, wherein the amino component of the aminoalkane is an amino group forming part of a heterocyclic ring; and an antibacterial peptide.

2. An antibacterial complex according to Claim 1 wherein the delivery moiety is selected from a quaternary derivative of quinoline or acridine and an antibacterial peptide.

3. A complex according to Claim 2, wherein the delivery moiety is a bis-quinolinium.

4. A complex according to Claim 3, wherein the delivery moiety is dequalinium or an analogue thereof.

5. A complex according to Claim 4, wherein the alkyl chain of the dequalinium analogue has between 8 and 14 methyl groups.

6. A complex according to Claim 5, wherein the alkyl chain has 10 or 12 methyl groups.

7. A complex according to Claim 1, wherein the quaternary amine compound is 10,10'-(decane-1,10-diyl) bis (9-amino-1,2,3,4-tetrahydroacridinium) dichloride.

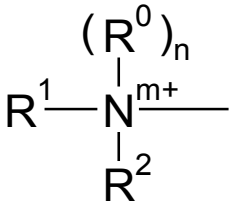
8. A complex according to Claim 1, wherein the quaternary amine compound is 10,10'-(dodecane-1,12-diyl) bis (9-amino-1,2,3,4-tetrahydroacridinium) dichloride.

9. A complex according to Claim 1 wherein the quaternary amine compounds and bis-aminoalkanes and unsaturated derivatives thereof are selected from compounds of the formula (I):

$$Q-(CH_2)_p-A^{-}-(CH_2)_q-R^3 \quad (I)$$

wherein Q is selected from:

(a) a group $Q^1$ having the formula:



and

(b) a group $Q^2$, $Q^2$-NH-, $Q^2$-O-, or $Q^2$-S- wherein $Q^2$ is selected from monocyclic, bicyclic and tricyclic heteroaromatic groups of 5 to 14 ring members, of which 1, 2 or 3 are heteroatom ring members selected from N, O and S provided that at least one nitrogen ring member is present, wherein the heteroaromatic groups are optionally substituted by one or two substituents $R^{4a}$ and wherein the said one nitrogen ring member may form an N-oxide or may be substituted with $C_{1-4}$ alkyl, phenyl-$C_{1-4}$ alkyl or di-phenyl-$C_{1-4}$ alkyl to form a quaternary group, wherein the phenyl moieties in each case are optionally substituted with one or two halogen, methyl or methoxy groups;

m is 0 or 1;

n is 0 or 1;

p and q are the same or different and each is an integer from 1 to 12;

A is a bond or is selected from a naphthalene, biphenyl, terphenyl, phenanthrene, fluorene, stilbene, a group $C_6H_4(CH_2)_rC_6H_4$, a group $C_6H_4$-C≡C-$C_6H_4$, a pyridine-2,6-diyl-bis(benzene-1,4-diyl) group, a group CH=CH-$(CH_2)_s$-$(CH=CH)_t$-; and a group C≡C-$(CH_2)_u$-$(C≡C)_v$-; wherein r is 0-4, s is 0 to 4, t is 0 or 1; u is 0-4 and v is 0 or 1;

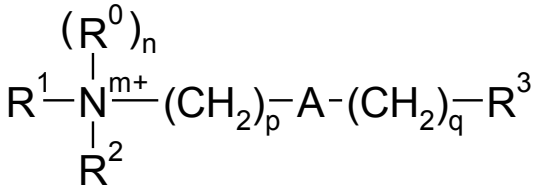
when n is 1, $R^0$, $R^1$ and $R^2$ are each selected from $C_{1-4}$ alkyl; and when n is 0, then N, $R^1$ and $R^2$ together form a monocyclic, bicyclic or tricyclic heteroaromatic group of 5 to 14 ring members, of which one is the nitrogen atom N and 0, 1 or 2 are further heteroatom ring members selected from N, O and S, and wherein the heteroaromatic group is optionally substituted by one or two substituents $R^{4b}$; and

$R^3$ is selected from hydrogen, $C_{1-4}$ alkyl, halogen, monocyclic carbocyclic groups of 3 to 7 ring members each optionally substituted by one or two substituents $R^{4c}$, a group Q; a group – NH-$Q^2$, a group –O-$Q^2$ and a group –S-$Q^2$; and

$R^{4a}$, $R^{4b}$ and $R^{4c}$ are the same or different and each is selected from $C_{1-4}$ alkyl optionally substituted with one or more fluorine atoms: $C_{1-4}$ alkoxy optionally

substituted with one or more fluorine atoms; nitro; amino; mono- and di-$C_{1-4}$ alkylamino; halogen; phenyl-$C_{1-2}$ alkyl wherein the phenyl moiety is optionally substituted with one or two methoxy, methyl or halogen substituents; ureido and guanidinyl.

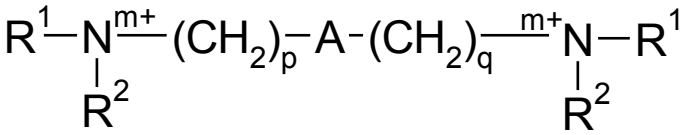
10. A complex according to Claim 9 wherein the compound of formula (I) is represented by formula (II):



(II)

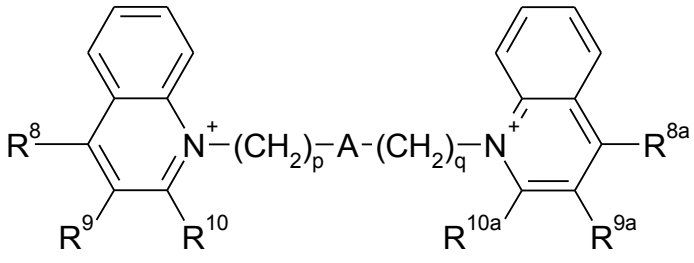
wherein $R^1$, $R^2$, m, p, A, q and $R^3$ are as defined in claim 9.

11. A complex according to Claim 10 wherein $R^3$ is $Q^1$ and n in each instance is 0, and wherein the compound of formula (II) is represented by formula (III):



(III)

12. A complex according to Claim 9 wherein the compound of formula (I) is represented by formula (IV):



(IV)

wherein:

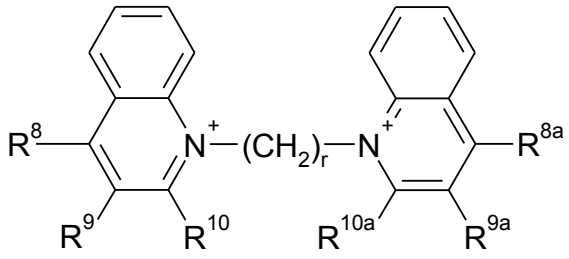
p and q are the same or different and each is an integer from 1 to 12;

A is a bond or is selected from naphthalene, biphenyl, terphenyl, phenanthrene, fluorene, stilbene, a group $C_6H_4(CH_2)_rC_6H_4$, a group $C_6H_4$-C≡C-$C_6H_4$, a pyridine-2,6-

diyl-bis(benzene-1,4-diyl) group, a group CH=CH-$(CH_2)_s$-$(CH=CH)_t$-; and a group C≡C-$(CH_2)_u$-$(C≡C)_v$-; wherein r is 0-4, s is 0 to 4, t is 0 or 1; u is 0-4 and v is 0 or 1;

$R^8$, $R^9$ and $R^{10}$ are the same or different and are each selected from hydrogen; $C_{1-4}$ alkyl optionally substituted with one or more fluorine atoms: $C_{1-4}$ alkoxy optionally substituted with one or more fluorine atoms; nitro; amino; mono- and di-$C_{1-4}$ alkylamino; halogen, phenyl-$C_{1-2}$ alkyl wherein the phenyl moiety is optionally substituted with one or two methoxy, methyl or halogen substituents; ureido and guanidinyl; or $R^9$ and $R^{10}$ link together to form an alkylene chain $(CH_2)_w$ wherein w is 3 to 5; and$R^{8a}$, $R^{9a}$ and $R^{10a}$ are the same or different and are each selected from hydrogen; $C_{1-4}$ alkyl optionally substituted with one or more fluorine atoms: $C_{1-4}$ alkoxy optionally substituted with one or more fluorine atoms; nitro; amino; mono- and di-$C_{1-4}$ alkylamino; halogen, phenyl-$C_{1-2}$ alkyl wherein the phenyl moiety is optionally substituted with one or two methoxy, methyl or halogen substituents; ureido and guanidinyl; or $R^{9a}$ and $R^{10a}$ link together to form an alkylene chain $(CH_2)_w$ wherein w is 3 to 5.

13. A complex according to Claim 12 wherein the compound of formula (IV) is represented by formula (V):




(V)

wherein:

r is an integer from 2 to 24;

$R^8$, $R^9$ and $R^{10}$ are the same or different and are each selected from hydrogen; $C_{1-4}$ alkyl optionally substituted with one or more fluorine atoms: $C_{1-4}$ alkoxy optionally substituted with one or more fluorine atoms; nitro; amino; mono- and di-$C_{1-4}$ alkylamino; halogen, phenyl-$C_{1-2}$ alkyl wherein the phenyl moiety is optionally substituted with one or two methoxy, methyl or halogen substituents; ureido and guanidinyl; or $R^9$ and $R^{10}$ link together to form an alkylene chain $(CH_2)_w$ wherein w is

3 to 5; and$R^{8a}$, $R^{9a}$ and $R^{10a}$ are the same or different and are each selected from hydrogen; $C_{1-4}$ alkyl optionally substituted with one or more fluorine atoms: $C_{1-4}$ alkoxy optionally substituted with one or more fluorine atoms; nitro; amino; mono- and di-$C_{1-4}$ alkylamino; halogen, phenyl-$C_{1-2}$ alkyl wherein the phenyl moiety is optionally substituted with one or two methoxy, methyl or halogen substituents; ureido and guanidinyl; or $R^{9a}$ and $R^{10a}$ link together to form an alkylene chain $(CH_2)_w$ wherein w is 3 to 5;

provided that:

(i) when $R^{10}$ and $R^{10a}$ are both hydrogen or are both methyl, and $R^9$ and $R^{9a}$ are both hydrogen, then at least one of $R^8$ and $R^{8a}$ is other than hydrogen, amino or dimethylamino; and

(ii) when $R^9$ and $R^{10}$ link together to form an alkylene chain $(CH_2)_w$ wherein w is 4 and $R^{9a}$ and $R^{10a}$ link together to form an alkylene chain $(CH_2)_w$ wherein w is 4, then at least one of $R^8$ and $R^{8a}$ is other than amino.

14. A complex according to any one of Claims 1 to 13, wherein the antibacterial peptide is a naturally occurring peptide.

15. A complex according to any one of Claims 1 to 13, wherein the antibacterial peptide is a peptidomimetic or synthetic variant of a naturally occurring peptide.

16. A complex according to any one of Claims 1 to 15, wherein the antibacterial peptide permeabilises bacterial cell membrane.

17. A complex according to Claim 15, wherein the antibacterial peptide is selected from the group comprising defensins, pleuricidins, magainins, dermaseptins, apidaecins, cecropins, microcins and pediocins.

18. A complex according to Claim 17, wherein the antibacterial peptide is selected from the group comprising Gramicidin and Polymyxin.

19. A complex according to any one of Claims 1 to 15, wherein the antibacterial peptide has an intracellular target.

20. A complex according to Claim 19, wherein the complex further comprises a linker.

21. A complex according to Claim 20, wherein the linker is a carboxyl-group-to-primary-amine cross-linker.

22. A complex according to Claim 21 or Claim 22, wherein the linker is EDC.

23. A complex according to any one of Claims 19 to 22, wherein the antibacterial peptide is selected from the group comprising antibiotics, glycopeptide antibiotics, cationic, polypeptides such as polylysine and polyarginine

24. A complex according to Claim 23, wherein the antibacterial peptide is Buforin or a derivative thereof.

25. A complex according to any one of Claims 1 to 24, wherein the nucleic acid sequence comprises the sequence of a native cellular binding site for a transcription factor.

26. A complex according to Claim 25, wherein the native cellular binding site comprises the sequence of a bacterial Sig binding site.

27. A complex according to Claim 26, wherein the nucleic acid sequence has the sequence set out in SEQ ID NOs:9, 10, 30 and 31, 39, 40 or 41.

28. A complex according to Claim 25, wherein the native cellular binding site comprises the sequence of a bacterial Fur binding site.

29. A complex according to Claim 28, wherein the nucleic acid sequence has the sequence set out in SEQ ID NOs:11, 12 or 13.

30. An antibacterial complex comprising:

(a) a nucleic acid sequence comprising the sequence of a native cellular binding site for a transcription factor,

(b) 10,10'-( dodecane-1,12-diyl ) bis ( 9-amino-1,2,3,4-tetrahydroacridinium ) dichloride; and optionally

(c) an antibacterial peptide.

31. A complex according to Claim 30, wherein the nucleic acid sequence has the sequence set out in SEQ ID NOs:30 and 31.

32. Use of the complex according to any one of Claims 1 to 31 for the manufacture of a medicament for the treatment of bacterial infection.

33. A pharmaceutical composition or medicament comprising a complex according to any one of Claims 1 to 32 and a physiologically acceptable carrier or excipient.

34. A pharmaceutical composition or medicament as claimed in Claim 33, for use in the manufacture of a medicament for the treatment of bacterial infection.