Abstract:
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(54) Title: COMPOSITIONS FOR IMMUNISING AGAINST STAPHYLOCOCCUS AERUS

(57) Abstract: An effective Staphylococcus aureus vaccine may require several antigenic components, and so various combinations of S. aureus antigens are identified for use in immunisation. These polypeptides may optionally be used in combination with S. aureus saccharides.
COMPOSITIONS FOR IMMUNISING AGAINST STAPHYLOCOCCUS AUREUS

TECHNICAL FIELD

This invention relates to antigens derived from S. aureus and to their use in immunisation.

BACKGROUND ART

5 Staphylococcus aureus is a Gram-positive spherical bacterium. Annual US mortality exceeds that of any other infectious disease, including HIV/AIDS, and S. aureus is the leading cause of bloodstream, lower respiratory tract, skin & soft tissue infections. There is currently no authorised vaccine. A vaccine based on a mixture of surface polysaccharides from bacterial types 5 and 8, StaphVAX™, failed to reduce infections when compared to the placebo group in a phase III clinical trial in 2005.

Reference 1 reports that the "V710" vaccine from Merck and Intercell is undergoing a phase 2/3 trial on patients undergoing cardiothoracic surgery. The V710 vaccine is based on a single antigen, IsdB [2], a conserved iron-sequestering cell-surface protein.

S. aureus causes a range of illnesses from minor skin infections to life-threatening diseases such as pneumonia, meningitis, osteomyelitis, bacteremia, endocarditis, toxic shock syndrome, organ abscesses and septicemia. The bacterium has multiple virulence factors which are differentially expressed during different phases of its life cycle, and so a vaccine which can prevent one disease might not prevent another. For instance, the V710 vaccine may be effective against hematic spread of the S. aureus, but may be ineffective against pneumonia and may not elicit any opsonic activity. One aim of the invention is to provide vaccines which can protect against hematic spread and pneumonia, and which may also elicit an opsonic response.

Thus there remains a need to identify further and improved antigens for use in S. aureus vaccines, and in particular for vaccines which are useful against multiple S. aureus pathologies.

DISCLOSURE OF THE INVENTION

The inventors have identified various S. aureus polypeptides that are useful for immunisation, either alone or in combination. These polypeptides may be combined with S. aureus saccharides or other S. aureus polypeptides. The antigens are useful in S. aureus vaccines but may also be used as components in vaccines for immunising against multiple pathogens.

The inventors have identified the following 36 polypeptides: clfA, clfB, coA, cap, ebhA, ebpS, efb, emp, esaC, exxA, exxB, FnBA, FnBB, Hla, hlgB, hlgC, isdA, isdB, isdC, isdG, isdH, isdl, lukD, lukE, lukF, lukS, nuc, sasA, sasB, sasC, sasD, sasF, sdrC, sdrD, spa, and sdrE2. This set of antigens is referred to herein as 'the first antigen group'. Thus the invention provides an immunogenic composition comprising a combination of antigens, said combination comprising two or more (i.e. 2, 3, 4, 5, 6 or more) antigens selected from the group consisting of: (1) a clfA antigen; (2) a clfB antigen; (3) a coA antigen; (4) a cap antigen; (5) a ebhA antigen; (6) a ebpS antigen; (7) a efb
antigen; (8) a emp antigen; (9) a esaC antigen; (10) a esxA antigen; (11) a esxB antigen; (12) a FnBA antigen; (13) a FnBB antigen; (14) a Hla antigen; (15) a hlgB antigen; (16) a hlgC antigen; (17) a isdA antigen; (18) a isdB antigen; (19) a isdC antigen; (20) a isdG antigen; (21) a isdH antigen; (22) a isdl antigen; (23) a lukD antigen; (24) a lukE antigen; (25) a lukF antigen; (26) a lukS antigen; (27) a nuc antigen; (28) a sasA antigen; (29) a sasB antigen; (30) a sasC antigen; (31) a sasD antigen; (32) a sasF antigen; (33) a sdrC antigen; (34) a sdrD antigen; (35) a spa antigen; (36) a sdrE2 antigen.

Within the first antigen group, antigens are preferably selected from a subset of 16 of the 36 polypeptides, namely: clfA, clfB, emp, esaC, esxA, esxB, hla, isdA, isdB, isdC, sasD, sasF, sdrC, sdrD, spa, and sdrE2. Thus the invention provides an immunogenic composition comprising a combination of antigens, said combination comprising two or more (i.e. 2, 3, 4, 5, 6 or more) antigens selected from the group consisting of these sixteen antigens.

The inventors have also identified the following 128 polypeptides: staO01, staO02, staO03, staO04, staO05, staO06, staO07, staO08, staO09, staO10, staO11, staO12, staO13, staO14, staO15, staO16, staO17, staO18, staO19, staO20, staO21, staO22, staO23, staO24, staO25, staO26, staO27, staO28, staO29, staO30, staO31, staO32, staO33, staO34, staO35, staO36, staO37, staO38, staO39, staO40, staO41, staO42, staO43, staO44, staO45, staO46, staO47, staO48, staO49, staO50, staO51, staO52, staO53, staO54, staO55, staO56, staO57, staO58, staO59, staO60, staO61, staO62, staO63, staO64, staO65, staO66, staO67, staO68, staO69, staO70, staO71, staO72, staO73, staO74, staO75, staO76, staO77, staO78, staO79, staO80, staO81, staO82, staO83, staO84, staO85, staO86, staO87, staO88, staO89, staO90, staO91, staO92, staO93, staO94, staO95, staO96, staO97, staO98, staO99, staO100, staO101, staO102, staO103, staO104, staO105, staO106, staO107, staO108, staO109, staO110, staO111, staO112, staO113, staO114, staO115, staO116, staO117, staO118, staO119, staO120, staO121, staO122, staO123, staO124, staO125, staO126, staO127, staO128.

This set of antigens is referred to herein as 'the second antigen group'. Thus the invention provides an immunogenic composition comprising a combination of antigens, said combination comprising two or more (i.e. 2, 3, 4, 5, 6 or more) antigens selected from the group consisting of: (1) a staO01 antigen; (2) a staO02 antigen; (3) a staO03 antigen; (4) a staO04 antigen; (5) a staO05 antigen; (6) a staO06 antigen; (7) a staO07 antigen; (8) a staO08 antigen; (9) a staO09 antigen; (10) a staO10 antigen; (11) a staO11 antigen; (12) a staO12 antigen; (13) a staO13 antigen; (14) a staO14 antigen; (15) a staO15 antigen; (16) a staO16 antigen; (17) a staO17 antigen; (18) a staO18 antigen; (19) a staO19 antigen; (20) a staO20 antigen; (21) a staO21 antigen; (22) a staO22 antigen; (23) a staO23 antigen; (24) a staO24 antigen; (25) a staO25 antigen; (26) a staO26 antigen; (27) a staO27 antigen; (28) a staO28 antigen; (29) a staO29 antigen; (30) a staO30 antigen; (31) a staO31 antigen; (32) a staO32 antigen; (33) a staO33 antigen; (34) a staO34 antigen; (35) a staO35 antigen; (36) a staO36 antigen; (37) a staO37 antigen; (38) a staO38 antigen; (39) a staO39 antigen; (40) a staO40 antigen; (41) a staO41 antigen; (42) a staO42 antigen; (43) a staO43 antigen; (44) a staO44 antigen; (45) a staO45 antigen; (46) a staO46 antigen; (47) a staO47 antigen; (48) a staO48 antigen; (49) a staO49 antigen; (50) a staO50 antigen; (51) a staO51 antigen; (52) a staO52 antigen; (53) a staO53 antigen; (54) a staO54 antigen; (55) a staO55 antigen; (56) a staO56 antigen; (57) a staO57 antigen; (58) a staO58 antigen; (59) a staO59 antigen; (60) a
Within the second antigen group of 128 antigens, a preferred subset of 113 antigens omits (81) and (107) to (120) from this list.

Within the second antigen group, a subset of 27 of the 128 polypeptides is referred to herein as 'the third antigen group', namely: staO01, staO02, staO03, staO04, staO05, staO06, staO07, staO08, staO09, staO10, staO19, staO28, staO40, staO49, staO57, staO64, staO73, staO95, staO98, staO10, staO5, NW_1, NW_6, NWJ, NWJ, NW_9 and NW_10. The invention provides an immunogenic composition comprising a combination of antigens, said combination comprising two or more (i.e. 2, 3, 4, 5, 6 or more) antigens selected from the third antigen group.

The 101 antigens that are in the second antigen group but not in the third antigen group are referred to herein as 'the fourth antigen group'. Within the fourth antigen group of 101 antigens, a preferred subset of 86 antigens omits (81) and (107) to (120) from the above list. The second antigen group thus consists of a combination of the third and fourth antigen groups.

Within the second antigen group, a subset of 8 of the 128 polypeptides is referred to herein as 'the fifth antigen group', namely: staO04, staO06, staO07, staO11, staO28, staO60, staO98 and stal2. The invention provides an immunogenic composition comprising a combination of antigens, said combination comprising two or more (i.e. 2, 3, 4, 5, 6 or more) antigens selected from the fifth antigen group.
Within the 36 antigens of the first antigen group there are 630 possible pairs of different antigens. All such pairs are disclosed herein and are part of the invention. Thus the invention provides an immunogenic composition comprising a pair of antigens, wherein said pair is one of said 630 pairs.

Within the 128 antigens of the second antigen group there are 8128 possible pairs of different antigens. All such pairs are disclosed herein and are part of the invention. Thus the invention provides an immunogenic composition comprising a pair of antigens, wherein said pair is one of said 8128 pairs.

Within the preferred 113 antigens of the second antigen group there are 6328 possible pairs of different antigens. All such pairs are disclosed herein and are part of the invention. Thus the invention provides an immunogenic composition comprising a pair of antigens, wherein said pair is one of said 6328 pairs.

Within the preferred 27 antigens of the third antigen group there are 351 possible pairs of different antigens. All such pairs are disclosed herein and are part of the invention. Thus the invention provides an immunogenic composition comprising a pair of antigens, wherein said pair is one of said 351 pairs.

Within the 101 antigens of the fourth antigen group there are 5050 possible pairs of different antigens. All such pairs are disclosed herein and are part of the invention. Thus the invention provides an immunogenic composition comprising a pair of antigens, wherein said pair is one of said 5050 pairs.

Within the preferred 86 antigens of the fourth antigen group there are 3655 possible pairs of different antigens. All such pairs are disclosed herein and are part of the invention. Thus the invention provides an immunogenic composition comprising a pair of antigens, wherein said pair is one of said 3655 pairs.

In one embodiment, a composition includes at least one antigen (i.e. 1, 2, 3, 4, 5, 6 or more) selected from the first antigen group and at least one antigen (i.e. 1, 2, 3, 4, 5, 6 or more) selected from the second antigen group. Antigens from the first antigen group may be selected from the preferred subset of 16 antigens, and antigens from the second antigen group may be selected from the third antigen group or the fifth antigen group.

The invention also provides an immunogenic composition comprising a combination of antigens, said combination comprising two or more (i.e. 2, 3, 4, 5, 6 or more) antigens selected from the group consisting of: (1) a clfA antigen; (2) a clfB antigen; (3) a sdrE2 antigen; (4) a sdrC antigen; (5) a SasF antigen; (6) a emp antigen; (7) a sdrD antigen; (8) a spa antigen; (9) a esaC antigen; (10) a esxA antigen; (11) a esxB antigen; (12) a sta006 antigen; (13) a isdC antigen; (14) a hla antigen; (15) a staOl 1 antigen; (16) isdA antigen; (17) a isdB antigen; (18) a sasF antigen. This group of 18 antigens is sometimes referred to herein as the 'sixth antigen group'.
The invention also provides an immunogenic composition comprising a combination of antigens, said combination comprising two or more (i.e. 2, 3, 4 or 5) antigens selected from the group consisting of: (1) a esxA antigen; (2) a esxB antigen; (3) a staO0O antigen; (4) a hla antigen; and/or (5) a staO1 I antigen. The composition may also include an adjuvant e.g. an aluminium hydroxide adjuvant.

Advantageous combinations of the invention are those in which two or more antigens act synergistically. Thus the protection against S. aureus disease achieved by their combined administration exceeds that expected by mere addition of their individual protective efficacy.

Specific combinations of interest include, but are not limited to:

1. An immunogenic composition comprising a sdrD antigen, a sdrE2 antigen and a isdC antigen. The sdrD and sdrE2 antigens can usefully be combined as a hybrid polypeptide, as discussed below, e.g. an SdrDE hybrid with an sdrE2 antigen downstream of a sdrD antigen.

2. An immunogenic composition comprising a sasD antigen, a clfB antigen and a sdrC antigen.

3. An immunogenic composition comprising a sasD antigen, a clfB antigen, a sdrC antigen and a clfA antigen.

4. An immunogenic composition comprising a sdrD antigen, a sdrE2 antigen, a isdC antigen and a staO1 I antigen. The sdrD and sdrE2 antigens can usefully be combined as a hybrid polypeptide, as discussed below, e.g. a SdrDE hybrid with an sdrE2 antigen downstream of a sdrD antigen.

5. An immunogenic composition comprising a sasD antigen, a clfB antigen, a sdrC antigen and a staO0O antigen.

6. An immunogenic composition comprising a sdrD antigen, a sdrE2 antigen, a isdC antigen and a hla antigen. The sdrD and sdrE2 antigens can usefully be combined as a hybrid polypeptide, as discussed below, e.g. a SdrDE hybrid with a sdrE2 antigen downstream of a sdrD antigen. The Hla antigen may be a detoxified mutant e.g. including a H35L mutation.

7. An immunogenic composition comprising a sasD antigen, a clfB antigen, a sdrC antigen and an esxA antigen.

8. An immunogenic composition comprising a esxA antigen, a esxB antigen, a staO0O antigen and a hla antigen. The esxA and esxB antigens can usefully be combined as a hybrid polypeptide, as discussed below, e.g. a EsxAB hybrid with a esxB antigen downstream of an esxA antigen. The Hla antigen may be a detoxified mutant e.g. including a H35L mutation.

9. An immunogenic composition comprising a sdrD antigen, a sdrE2 antigen, a isdC antigen and an esxA antigen. The sdrD and sdrE2 antigens can usefully be combined as a hybrid polypeptide, as discussed below, e.g. a SdrDE hybrid with a sdrE2 antigen downstream of a sdrD antigen.
(10) An immunogenic composition comprising a esxA antigen, a esxB antigen, a staO06 antigen and a staO1l antigen. The esxA and esxB antigens may be combined as a hybrid polypeptide, as discussed below, e.g. an EsxAB hybrid.

(11) An immunogenic composition comprising a esxA antigen, a esxB antigen and a staO1l antigen. The esxA and esxB antigens can usefully be combined as a hybrid polypeptide, as discussed below, e.g. a EsxAB hybrid with a esxB antigen downstream of a esxA antigen.

(12) An immunogenic composition comprising a sasD antigen, a clfB antigen, a sdrC antigen and a spa antigen.

(13) An immunogenic composition comprising a esxA antigen, a esxB antigen, a isdA antigen, a staO06 antigen, a staO1l antigen and a spa antigen. The esxA and esxB antigens may be combined as a hybrid polypeptide, as discussed below, e.g. an EsxAB hybrid. The isdA antigen may be a fragment of a full-length isdA antigen e.g. SEQ ID NO: 157. The spa antigen may be a fragment of a full-length spa antigen, such as a Spa(D) domain mutated to disrupt or decrease binding to IgG Fc.

(14) An immunogenic composition comprising a esxA antigen, a esxB antigen, a Hla antigen, a staO06 antigen and a staO1l antigen. The esxA and esxB antigens may be combined as a hybrid polypeptide, as discussed below, e.g. an EsxAB hybrid. The Hla antigen may be a detoxified mutant e.g. including a H35L mutation.

(15) An immunogenic composition comprising a sdrD antigen, a sdrE2 antigen, a isdC antigen and a sdrE2 antigen. The sdrD and sdrE2 antigens can usefully be combined as a hybrid polypeptide, as discussed below, e.g. a SdrDE hybrid with a sdrE2 antigen downstream of a sdrD antigen.

(16) An immunogenic composition comprising a esxA antigen, a esxB antigen and a hla antigen. The esxA and esxB antigens can usefully be combined as a hybrid polypeptide, as discussed below, e.g. a EsxAB hybrid with a esxB antigen downstream of a esxA antigen. The Hla antigen may be a detoxified mutant e.g. including a H35L mutation.

(17) An immunogenic composition comprising a hla antigen, a isdA antigen, a staO06 antigen and a staO1l antigen. The isdA antigen may be a fragment of a full-length isdA antigen e.g. SEQ ID NO: 157. The Hla antigen may be a detoxified mutant e.g. including a H35L mutation.

(18) An immunogenic composition comprising a esxA antigen, a esxB antigen, a staO06 antigen and a isdA antigen. The esxA and esxB antigens can usefully be combined as a hybrid polypeptide, as discussed below, e.g. a EsxAB hybrid with a esxB antigen downstream of a esxA antigen. The isdA antigen may be a fragment of a full-length isdA antigen e.g. SEQ ID NO: 157.

(19) An immunogenic composition comprising a sasD antigen, a clfB antigen, a sdrC antigen and a hla antigen. The Hla antigen may be a detoxified mutant e.g. including a H35L mutation.
(20) An immunogenic composition comprising a HIa antigen, a staOOΩ antigen and a staOll antigen. The HIa antigen may be a detoxified mutant *e.g.* including a H35L mutation.

(21) An immunogenic composition comprising a esxA antigen and a esxB antigen. The esxA and esxB antigens can usefully be combined as a hybrid polypeptide, as discussed below, *e.g.* an EsxAB hybrid with an esxB antigen downstream of an esxA antigen.

(22) An immunogenic composition comprising a esxA antigen, a esxB antigen and a staOOΩ antigen. The esxA and esxB antigens can usefully be combined as a hybrid polypeptide, as discussed below, *e.g.* a EsxAB hybrid with a esxB antigen downstream of a esxA antigen.

(23) An immunogenic composition comprising a spa antigen, a staOOΩ antigen and a staOll antigen. The spa antigen may be a fragment of a full-length spa antigen, such as a Spa(D) domain mutated to disrupt or decrease binding to IgG Fc.

(24) An immunogenic composition comprising a esxA antigen, a esxB antigen, a isdA antigen, a staOOΩ antigen and a staOll antigen. The esxA and esxB antigens may be combined as a hybrid polypeptide, as discussed below, *e.g.* an EsxAB hybrid. The isdA antigen may be a fragment of a full-length isdA antigen *e.g.* SEQ ID NO: 157. The clfB antigen may be a fragment of a full-length clfB antigen *e.g.* SEQ ID NO: 163.

(25) An immunogenic composition comprising a staOOΩ antigen and a staOl1 antigen.

(26) An immunogenic composition comprising a esxA antigen, a esxB antigen, a staOOΩ antigen, a isdA antigen and a clfB antigen. The esxA and esxB antigens can usefully be combined as a hybrid polypeptide, as discussed below, *e.g.* a EsxAB hybrid with a esxB antigen downstream of a esxA antigen. The isdA antigen may be a fragment of a full-length isdA antigen *e.g.* SEQ ID NO: 157. The clfB antigen may be a fragment of a full-length clfB antigen *e.g.* SEQ ID NO: 163.

(27) An immunogenic composition comprising a staOOΩ antigen, a staOl1 antigen and a staO19 antigen.

(28) An immunogenic composition comprising a esxA antigen, a esxB antigen, a staOOΩ antigen, a hla antigen and a clfB antigen. The esxA and esxB antigens can usefully be combined as a hybrid polypeptide, as discussed below, *e.g.* a EsxAB hybrid with a esxB antigen downstream of a esxA antigen. The clfB antigen may be a fragment of a full-length clfB antigen *e.g.* SEQ ID NO: 163. The HIa antigen may be a detoxified mutant *e.g.* including a H35L mutation.

(29) An immunogenic composition comprising a staOOΩ antigen, a staOl1 antigen, a staO19 antigen, and a hla antigen. The HIa antigen may be a detoxified mutant *e.g.* including a H35L mutation.

(30) An immunogenic composition comprising a esxA antigen, a esxB antigen, a staOOΩ antigen, a staOl1 antigen and a clfB antigen. The esxA and esxB antigens can usefully be combined as a hybrid
polypeptide, as discussed below, e.g. a EsxAB hybrid with a esxB antigen downstream of a esxA antigen. The clfB antigen may be a fragment of a full-length clfB antigen e.g. SEQ ID NO: 163.

(31) An immunogenic composition comprising a spa antigen, a esxA antigen, a esxB antigen, a staO06 antigen and a staO1 antigen. The spa antigen may be a fragment of a full-length spa antigen, such as a Spa(D) domain mutated to disrupt or decrease binding to IgG Fc. The esxA and esxB antigens may be combined as a hybrid polypeptide, as discussed below, e.g. an EsxAB hybrid.

(32) An immunogenic composition comprising a sdrD antigen, a sdrE2 antigen, a isdC antigen and a esxB antigen. The sdrD and sdrE2 antigens can usefully be combined as a hybrid polypeptide, as discussed below, e.g. a SdrDE hybrid with a sdrE2 antigen downstream of a sdrD antigen.

(33) An immunogenic composition comprising a esxA antigen, a esxB antigen, a staO06 antigen, a staO11 antigen and a staO19 antigen. The esxA and esxB antigens can usefully be combined as a hybrid polypeptide, as discussed below, e.g. a EsxAB hybrid with a esxB antigen downstream of a esxA antigen.

(34) An immunogenic composition comprising a esxA antigen, a esxB antigen, a staO06 antigen, a isdA antigen and a sdrD antigen. The esxA and esxB antigens can usefully be combined as a hybrid polypeptide, as discussed below, e.g. a EsxAB hybrid with a esxB antigen downstream of a esxA antigen. The isdA antigen may be a fragment of a full-length isdA antigen e.g. SEQ ID NO: 157. The sdrD antigen may be a fragment of a full-length sdrD antigen e.g. SEQ ID NO: 156.

(35) An immunogenic composition comprising a esxA antigen, a esxB antigen, and a isdA antigen. The esxA and esxB antigens can usefully be combined as a hybrid polypeptide, as discussed below, e.g. a EsxAB hybrid with a esxB antigen downstream of an esxA antigen. The isdA antigen may be a fragment of a full-length isdA antigen e.g. SEQ ID NO: 157.

(36) An immunogenic composition comprising a sasD antigen, a clfB antigen, a sdrC antigen, a esxA antigen and a esxB antigen. The esxA and esxB antigens can usefully be combined as a hybrid polypeptide, as discussed below, e.g. an EsxAB hybrid with an esxB antigen downstream of an esxA antigen.

(37) An immunogenic composition comprising a H1a antigen, a spa antigen, a staO06 antigen and a staO1 antigen. The H1a antigen may be a detoxified mutant e.g. including a H35L mutation. The spa antigen may be a fragment of a full-length spa antigen, such as a Spa(D) domain mutated to disrupt or decrease binding to IgG Fc.

In some embodiments, any of these 37 compositions may include additional staphylococcal antigens, and these further antigens can be polypeptides and/or saccharides. For example, they can usefully also include one or more S. aureus capsular saccharide conjugate(s) e.g. against a serotype 5 and/or a serotype 8 strain. The inclusion of one or both such conjugates is particularly useful for combinations (8), (10), (20), and (31) and (37).
In other embodiments, these 37 compositions include no additional staphylococcal polypeptide antigens, but in other embodiments, these 37 compositions include no additional staphylococcal antigens, other than those listed in SEQ ID NOs 1-217. The invention also provides a polypeptide comprising amino acid sequence (a) having 80% or more identity (e.g. 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 151; and/or (b) comprising a fragment of at least 'n' consecutive amino acids from amino acids 1-97 of SEQ ID NO: 151 and at least 'n' consecutive amino acids from amino acids 104-207 of SEQ ID NO: 151, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). The invention also provides a polypeptide comprising amino acid sequence (a) having 80% or more identity (e.g. 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 152; and/or (b) comprising a fragment of at least 'n' consecutive amino acids from amino acids 1-104 of SEQ ID NO: 152 and at least 'n' consecutive amino acids from amino acids 111-207 of SEQ ID NO: 152, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These polypeptides can elicit antibodies (e.g. when administered to a human) which recognise both the wild-type staphylococcal protein comprising SEQ ID NO: 10 and the wild-type staphylococcal protein comprising SEQ ID NO: 11. Thus the immune response will recognise both of antigens esxA and esxB. Preferred fragments of (b) provide an epitope from SEQ ID NO: 10 and an epitope from SEQ ID NO: 11. The invention also provides an immunogenic composition comprising a combination of such a protein and an adjuvant, such as an aluminium hydroxide adjuvant.

The invention also provides a polypeptide comprising amino acid sequence (a) having 80% or more identity (e.g. 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 241; and/or (b) comprising both a fragment of at least 'n' consecutive amino acids from amino acids 1-96 of SEQ ID NO: 241 and a fragment of at least 'n' consecutive amino acids from amino acids 103-205 of SEQ ID NO: 241, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These polypeptides (e.g. SEQ ID NO: 250) can elicit antibodies (e.g. when administered to a human) which recognise both the wild-type staphylococcal protein comprising SEQ ID NO: 10 and the wild-type staphylococcal protein comprising SEQ ID NO: 11. Thus the immune response will recognise both of antigens esxA and esxB. Preferred fragments of (b) provide an epitope from SEQ ID NO: 10 and an epitope from SEQ ID NO: 11. The invention also provides an immunogenic composition comprising a combination of such a protein and an adjuvant, such as an aluminium hydroxide adjuvant.

The invention also provides a polypeptide comprising a staphylococcal hemolysin sequence, wherein the sequence does not include a sequence having at least 90% identity to SEQ ID NO: 217 but can elicit antibodies which can kill staphylococci. The polypeptide may have a first sequence having 80% or more identity (e.g. 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 218 and a second sequence having 80% or more identity (e.g. 80%,
85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 219,
wherein the first and second sequences are either directly joined or are joined by an intervening
amino acid sequence having fewer than 40 amino acids (e.g. ≤35 amino acids, ≤30 amino acids, ≤25
amino acids, ≤20 amino acids, ≤15 amino acids, ≤10 amino acids, ≤5 amino acids). SEQ ID NOs:
189 and 216 are examples of such polypeptides, in which the first and second sequences are joined
by a tetrapeptide PSGS sequence (SEQ ID NO: 225).

The invention also provides an immunogenic composition comprising a StaOl1 antigen and a Ca++
ion. The antigen and Ca++ ion may form a complex e.g. atoms in the antigen may coordinate the Ca++
ion. The immunogenic composition may also include an adjuvant.

The invention also provides a oligomer of a StaOl1 antigen, and also immunogenic compositions
comprising such oligomers. The oligomer can be a dimer, trimer, tetramer, pentamer, hexamer,
heptamer, octamer or higher. An oligomer may comprise a Ca++ ion, and a composition comprising
StaOl1 oligomers may comprise 5-500mM Ca++ ions.

**Further polypeptide antigens**

In additions to antigens from the various antigen groups of the invention, immunogenic compositions
may include one or more of the following *S.aureus* antigens (or antigens comprising immunogenic
fragment(s) thereof) to enhance the efficacy against *S.aureus* of an immune response elicited by the
composition [e.g. see references 3-10]:

- AhpC
- AhpF
- Autolysin amidase
- Autolysin glucosaminidase
- Collagen binding protein CAN
- EbhB
- GehD lipase
- Heparin binding protein HBP (17kDa)
- Laminin receptor
- MAP
- MntC (also known as SitC)
- MRPII
- Npase
- ORF0594
- ORF0657n
- ORF0826
- PBP4
- RAP (RNA III activating protein)
The individual antigens identified in the antigen groups of the invention may be used in combination with conjugated saccharide antigens. Thus the invention provides an immunogenic composition comprising a combination of:

(1) one or more antigen(s) selected from the first, second, third or fourth antigen groups (as defined above); and

(2) one or more conjugates of a *S. aureus* exopolysaccharide and a carrier protein.

A conjugate used in component (2) of this combination includes a saccharide moiety and a carrier moiety. The saccharide moiety is from the exopolysaccharide of *S. aureus*, which is a poly-N-acetylglucosamine (PNAG). The saccharide may be a polysaccharide having the size that arises during purification of the exopolysaccharide from bacteria, or it may be an oligosaccharide achieved by fragmentation of such a polysaccharide e.g. size can vary from over 400kDa to between 75 and 40OkDa, or between 10 and 75kDa, or up to 30 repeat units. The saccharide moiety can have various degrees of N-acetylation and, as described in reference 11, the PNAG may be less than 40% N-acetylated (e.g. less than 35, 30, 20, 15, 10 or 5% N-acetylated; deacetylated PNAG is also known as dPNAG). Deacetylated epitopes of PNAG can elicit antibodies that are capable of mediating opsonic killing. The PNAG may or may not be O-succinylated e.g. it may be O-succinylated on fewer less than 25, 20, 15, 10, 5, 2, 1 or 0.1% of residues.

The invention also provides an immunogenic composition comprising a combination of:

(1) one or more antigen(s) selected from the first, second, third or fourth antigen groups; and

(2) one or more conjugates of a *S. aureus* capsular saccharide and a carrier protein.

A conjugate used in component (2) of this combination includes a saccharide moiety and a carrier moiety. The saccharide moiety is from the capsular saccharide of a *S. aureus*. The saccharide may be a polysaccharide having the size that arises during purification of capsular polysaccharide from bacteria, or it may be an oligosaccharide achieved by fragmentation of such a polysaccharide. Capsular saccharides may be obtained from any suitable strain of *S. aureus* (or any bacterium having a similar or identical saccharide), such as from a type 5 and/or a type 8 *S. aureus* strain and/or a type 336 *S. aureus* strain. Most strains of infectious *S. aureus* contain either Type 5 or Type 8 capsular
saccharides. Both have FucNAcp in their repeat unit as well as ManNAcA which can be used to introduce a sulfhydryl group for linkage. The repeating unit of the Type 5 saccharide is $\alphaL\text{-FucNAc}(3\text{OAc})-(1\rightarrow4)$-$\betaD\text{-ManNAcA}$, whereas the repeating unit of the Type 8 saccharide is $\alphaL\text{-FucNAc}(3\text{OAc})-(1\rightarrow3)$-$\betaD\text{-ManNAcA}$.

The type 336 saccharide is a $\beta$-linked hexosamine with no O-acetylation [12,13] and is cross-reactive with antibodies raised against the 336 strain (ATCC 55804). A combination of a type 5 and a type 8 saccharide is typical, and a type 336 saccharide may be added to this pairing [14].

The invention also provides an immunogenic composition comprising a combination of:

1. one or more antigen(s) selected from the first, second, third or fourth antigen groups;
2. one or more conjugates of a S.aureus exopolysaccharide and a carrier protein; and
3. one or more conjugates of a S.aureus capsular saccharide and a carrier protein.

The carrier moiety in these conjugates will usually be a protein, but usually not one of the antigens of (1). Typical carrier proteins are bacterial toxins, such as diphtheria or tetanus toxins, or toxoids or mutants or fragments thereof. The CRM197 diphtheria toxin mutant [15] is useful. Other suitable carrier proteins include the N.meningitidis outer membrane protein complex [16], synthetic peptides [17,18], heat shock proteins [19,20], pertussis proteins [21,22], cytokines [23], lymphokines [23], hormones [23], growth factors [23], artificial proteins comprising multiple human CD4+ T cell epitopes from various pathogen-derived antigens [24] such as N19 [25], protein D from H.influenzae [26-28], pneumolysin [29] or its non-toxic derivatives [30], pneumococcal surface protein PspA [31], iron-uptake proteins [32], toxin A or B from C.difficile [33], recombinant P.aeruginosa exoprotein A (rEPA) [34], etc. In some embodiments the carrier protein is a S.aureus protein, such as an antigen selected from the first, second, third or fourth antigen groups.

Where a composition includes more than one conjugate, each conjugate may use the same carrier protein or a different carrier protein.

Conjugates may have excess carrier (w/w) or excess saccharide (w/w). In some embodiments, a conjugate may include substantially equal weights of each.

The carrier molecule may be covalently conjugated to the carrier directly or via a linker. Direct linkages to the protein may be achieved by, for instance, reductive animation between the saccharide and the carrier, as described in, for example, references 35 and 36. The saccharide may first need to be activated e.g. by oxidation. Linkages via a linker group may be made using any known procedure, for example, the procedures described in references 37 and 38. A preferred type of linkage is an adipic acid linker, which may be formed by coupling a free $-\text{NH}_2$ group (e.g. introduced to a glucan by amination) with adipic acid (using, for example, diimide activation), and then coupling a protein to the resulting saccharide-adipic acid intermediate [39,40]. Another preferred type of linkage is a carbonyl linker, which may be formed by reaction of a free hydroxyl group of a saccharide CDI [41, 42] followed by reaction with a protein to form a carbamate linkage. Other linkers include $\beta$-
propionamido [43], nitrophenyl-ethylamine [44], haloacyl halides [45], glycosidic linkages [46], 6-
aminoacaproic acid [47], ADH [48], C₄ to C₂ moieties [49], etc. Carbodiimide condensation can also
be used [50].

PNAG conjugates may be prepared in various ways e.g. by a process comprising: a) activating the
PNAG by adding a linker comprising a maleimide group to form an activated PNAG; b) activating
the carrier protein by adding a linker comprising a sulphydryl group to form an activated carrier
protein; and c) reacting the activated PNAG and the activated carrier protein to form a PNAG-carrier
protein conjugate; or by a process comprising a) activating the PNAG by adding a linker comprising
a sulphydryl group to form an activated PNAG; b) activating the carrier protein by adding a linker
comprising a maleimide group to form an activated carrier protein; and c) reacting the activated
PNAG and the activated carrier protein to form a PNAG-carrier protein conjugate; or by a process
comprising a) activating the PNAG by adding a linker comprising a sulphydryl group to form an
activated PNAG; b) activating the carrier protein by adding a linker comprising a sulphydryl group to
form an activated carrier protein; and c) reacting the activated PNAG and the activated carrier
protein to form a PNAG-carrier protein conjugate.

The individual antigens identified in the antigen groups of the invention may be used as carrier
proteins for exopolysaccharides, to form a covalent conjugate. Thus the invention provides an
immunogenic composition comprising a conjugate of (1) an antigen selected from the first, second,
third and fourth antigen groups and (2) a S. aureus exopolysaccharide. The invention also provides an
immunogenic composition comprising a conjugate of (1) an antigen selected from the first, second,
third and fourth antigen groups and (2) a S. aureus capsular saccharide. Further characteristics of such
conjugates are described above. These conjugates may be combined with any of the antigens
disclosed herein.

**Combinations with non-staphylococcal antigens**

The individual antigens identified in the antigen groups of the invention may be used in combination
with non-staphylococcal antigens, and in particular with antigens from bacteria associated with
nosocomial infections. Thus the invention provides an immunogenic composition comprising a
combination of:

(1) one or more antigen(s) selected from the first, second, third and fourth antigen groups (as
defined above); and

(2) one or more antigen(s) selected from the group consisting of: Clostridium difficile;
Pseudomonas aeruginosa; Candida albicans; and extraintestinal pathogenic Escherichia coli.

Further suitable antigens for use in combination with staphylococcal antigens of the invention are
listed on pages 33-46 of reference 51.
First antigen group

clfA

The 'clfA' antigen is annotated as 'clumping factor A'. In the NCTC 8325 strain clfA is SAOUHSC_00812 and has amino acid sequence SEQ ID NO: 1 (GI:88194572). In the Newman strain it is nwmn_0756 (GI: 151220968).

Useful clfA antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 1 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 1; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 1, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These clfA proteins include variants of SEQ ID NO: 1. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 1. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 1 while retaining at least one epitope of SEQ ID NO: 1. The final 368 C-terminal amino acids of SEQ ID NO: 1 can usefully be omitted. The first 39 N-terminal amino acids of SEQ ID NO: 1 can usefully be omitted. Other fragments omit one or more protein domains.

SEQ ID NO: 224 is a useful fragment of SEQ ID NO: 1 ('ClfA_{40-559}')- This fragments omits the long repetitive region towards the C-terminal of SEQ ID NO: 1.

clfB

The 'clfB' antigen is annotated as 'clumping factor B'. hi the NCTC 8325 strain clfB is SAOUHSC_02963 and has amino acid sequence SEQ ID NO: 2 (GI:88196585). In the Newman strain it is nwmn_2529 (GI: 151222741).

Useful clfB antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 2 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 2; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 2, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These clfB proteins include variants of SEQ ID NO: 2. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 2. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 2 while retaining at least one epitope of SEQ ID NO: 2. The final 40 C-terminal amino acids of SEQ ID NO: 2 can usefully be omitted. The first 44 N-terminal amino acids of SEQ ID NO: 2 can usefully be omitted. Other fragments omit one or more protein domains. ClfB is naturally a long protein and so the use of fragments is helpful e.g. for purification, handling, fusion, expression, etc.
SEQ ID NO: 163 is a useful fragment of SEQ ID NO: 2 ('CIfB_{45-552}'). This fragment includes the most exposed domain of CIfB and is more easily used at an industrial scale. It also reduces the antigen's similarity with human proteins. Other useful fragments, based on a 3-domain model of CIfB, include: CIfB_{45-360} (also known as CIfB-N12; SEQ ID NO: 196); CIfB_{212-542} (also known as CIfB-N23; SEQ ID NO: 197); and CIfB_{360-542} (also known as CIfB-N3; SEQ ID NO: 198).

**coA**
The 'coA' antigen is annotated as 'coagulate Coa'. In the NCTC 8325 strain coA is SAOUHSC_00192 and has amino acid sequence SEQ ID NO: 3 (GI:88194002). In the Newman strain it is nwmn_0166 (GI:151220378).

Useful coA antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 3 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 3; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 3, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These coA proteins include variants of SEQ ID NO: 3. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 3. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 3 while retaining at least one epitope of SEQ ID NO: 3. The first 14 N-terminal amino acids of SEQ ID NO: 3 can usefully be omitted. Other fragments omit one or more protein domains.

**eap**
The 'eap' antigen is annotated as 'MHC class II analog protein', the NCTC 8325 strain eap is SAOUHSC_02161 and has amino acid sequence SEQ ID NO: 4 (GI:88195840). In the Newman strain it is nwmn_1872 (GI:151220284).

Useful eap antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 4 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 4; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 4, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These eap proteins include variants of SEQ ID NO: 4. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 4. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 4 while retaining at least one epitope of SEQ ID NO: 4. The first 17 N-terminal amino acids of SEQ ID NO: 4 can usefully be omitted. Other fragments omit one or more protein domains.
"ebhA"

The 'ebhA' antigen is annotated as 'EbhA'. In the NCTC 8325 strain ebhA is SAOUHSC_O1447 and has amino acid sequence SEQ ID NO: 5 (GI:88195168).

Useful ebhA antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 5 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 5; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 5, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These ebhA proteins include variants of SEQ ID NO: 5.

Preferred fragments of (b) comprise an epitope from SEQ ID NO: 5. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 5 while retaining at least one epitope of SEQ ID NO: 5. The first 39 N-terminal amino acids of SEQ ID NO: 5 can usefully be omitted. Other fragments omit one or more protein domains.

"ebpS"

The 'ebpS' antigen is annotated as 'elastin binding protein EbpS'. In the NCTC 8325 strain ebpS is SAOUHSC_01501 and has amino acid sequence SEQ ID NO: 6 (GI:88195217). In the Newman strain it is nwmn_1389 (GI:151221601).

Useful ebpS antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 6 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 6; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 6, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These ebpS proteins include variants of SEQ ID NO: 6. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 6. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 6 while retaining at least one epitope of SEQ ID NO: 6. Other fragments omit one or more protein domains.

SEQ ID NO: 165 is a useful fragment of SEQ ID NO: 6 (EbpSi.i\textsubscript{89}). This fragment includes the most exposed domain of EbpS and is more easily used at an industrial scale. It also reduces the antigen's similarity with human proteins.
The 'efb' antigen is annotated as 'fibrinogen-binding protein truncated'. In the NCTC 8325 strain efb is SAOUHSC_Ot 114 and has amino acid sequence SEQ ID NO: 7 (GI:88194860). In the Newman strain it is nwmn_1069 (GI:151221281).

Useful efb antigens can elicit an antibody \(\text(e.g. \text{when administered to a human})\) that recognises SEQ ID NO: 7 and/or may comprise an amino acid sequence: (a) having 50% or more identity \(\text(e.g. 60\%, 65\%, 70\%, 75\%, 80\%, 85\%, 90\%, 91\%, 92\%, 93\%, 94\%, 95\%, 96\%, 97\%, 98\%, 99\%, 99.5\% \text{or more})\) to SEQ ID NO: 7; and/or (b) comprising a fragment of at least W consecutive amino acids of SEQ ID NO: 7, wherein 'n' is 7 or more \(\text(e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150 \text{or more})\). These efb proteins include variants of SEQ ID NO: 7. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 7. Other preferred fragments lack one or more amino acids \(\text(e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 \text{or more})\) from the C-terminus and/or one or more amino acids \(\text(e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 \text{or more})\) from the N-terminus of SEQ ID NO: 7 while retaining at least one epitope of SEQ ID NO: 7. The first 14 N-terminal amino acids of SEQ BD NO: 7 can usefully be omitted. Other fragments omit one or more protein domains.

The 'emp' antigen is annotated as 'extracellular matrix and plasma binding protein'. In the NCTC 8325 strain emp is SAOUHSC_00816 and has amino acid sequence SEQ ID NO: 8 (GI:88194575). In the Newman strain it is nwmn_0758 (GI:151220970).

Useful emp antigens can elicit an antibody \(\text(e.g. \text{when administered to a human})\) that recognises SEQ ID NO: 8 and/or may comprise an amino acid sequence: (a) having 50% or more identity \(\text(e.g. 60\%, 65\%, 70\%, 75\%, 80\%, 85\%, 90\%, 91\%, 92\%, 93\%, 94\%, 95\%, 96\%, 97\%, 98\%, 99\%, 99.5\% \text{or more})\) to SEQ ID NO: 8; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 8, wherein 'n' is 7 or more \(\text(e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 \text{or more})\). These emp proteins include variants of SEQ ID NO: 8. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 8. Other preferred fragments lack one or more amino acids \(\text(e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 \text{or more})\) from the C-terminus and/or one or more amino acids \(\text(e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 \text{or more})\) from the N-terminus of SEQ ID NO: 8 while retaining at least one epitope of SEQ ID NO: 8. The first 26 N-terminal amino acids of SEQ ID NO: 8 can usefully be omitted. Other fragments omit one or more protein domains.

SEQ ID NOs: 190, 191, 192 and 193 are useful fragments of SEQ ID NO: 8 \(\text(E\text{mp}_{35-348} \text{E}\text{mp}_{27-334}\text{'Emp}_{35-333}' \text{and 'Emp}_{27-147}', \text{respectively})\).

The 'esaC' antigen is annotated as 'esaC'. In the NCTC 8325 strain esaC is SAOUHSC_00264 and has amino acid sequence SEQ ID NO: 9 (GI:88194069).
Useful esaC antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 9 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 9; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 9, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100 or more). These esaC proteins include variants of SEQ ID NO: 9. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 9. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 9 while retaining at least one epitope of SEQ ID NO: 9. Other fragments omit one or more protein domains.

esxA

The 'esxA' antigen is annotated as 'protein'. In the NCTC 8325 strain esxA is SAOUHSC_00257 and has amino acid sequence SEQ ID NO: 10 (GI:88194063).

Useful esxA antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 10 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 10; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 10, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100 or more). These esxA proteins include variants of SEQ ID NO: 10. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 10. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 10 while retaining at least one epitope of SEQ ID NO: 10. Other fragments omit one or more protein domains.

esxB

The 'esxB' antigen is annotated as 'esxB'. In the NCTC 8325 strain esxB is SAOUHSC_00265 and has amino acid sequence SEQ ID NO: 11 (GI:88194070).

Useful esxB antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 11 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 11; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 11, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100 or more). These esxB proteins include variants of SEQ ID NO: 11. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 11. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 11.
while retaining at least one epitope of SEQ ID NO: 11. Other fragments omit one or more protein domains.

**FnBA**

The ‘FnBA’ antigen is annotated as ‘fibronectin-binding protein A precursor FnBPA’. In the NCTC 8325 strain FnBA is SAOUHSC_02803 and has amino acid sequence SEQ ID NO: 12 (GL88196438). In the Newman strain it is nwmn_2399 (GI:151222611). Proteomic analysis has revealed that this protein is secreted or surface-exposed.

Useful FnBA antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 12 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 12; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 12, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These FnBA proteins include variants of SEQ ID NO: 12.

Preferred fragments of (b) comprise an epitope from SEQ ID NO: 12. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 12 while retaining at least one epitope of SEQ ID NO: 12. The final 37 C-terminal amino acids of SEQ ID NO: 12 can usefully be omitted. Other fragments omit one or more protein domains. FnBA is naturally a long protein and so the use of fragments is helpful e.g. for purification, handling, fusion, expression, etc.

SEQ ID NOs: 166 (‘FnBA15311’) and 167 (‘FnBA162933’) are useful fragments of SEQ ID NO: 12. These fragments are more easily used at an industrial scale.

**FnBB**

The 'FnBB' antigen is annotated as 'fibronectin binding protein B FnBPB'. In the NCTC 8325 strain FnBB is SAOUHSC_02802 and has amino acid sequence SEQ ID NO: 13 (GI:88196437). In the Newman strain it is nwmn_2397 (GI:151222609).

Useful FnBB antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 13 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%; 99.5% or more) to SEQ ID NO: 13; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 13, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These FnBB proteins include variants of SEQ ID NO: 13. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 13. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 13 while retaining at least one epitope of SEQ ID NO: 13. The final 37 C-
terminal amino acids of SEQ ID NO: 13 can usefully be omitted. Other fragments omit one or more protein domains.

**Hla**

The 'Hla' antigen is the 'alpha-hemolysin precursor' also known as 'alpha toxin' or simply 'hemolysin'. The NCTC 8325 strain Hla is SAOUHSC_Ol 121 and has amino acid sequence SEQ ID NO: 14 (GI:88194865). In the Newman strain it is nwmn_1073 (GI:151221285). Hla is an important virulence determinant produced by most strains of *S.aureus*, having pore-forming and haemolytic activity. Anti-Hla antibodies can neutralise the detrimental effects of the toxin in animal models, and Hla is particularly useful for protecting against pneumonia.

Useful Hla antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 14 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 14; and/or (b) comprising a fragment of at least V consecutive amino acids of SEQ ID NO: 14, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These Hla proteins include variants of SEQ ID NO: 14. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 14. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 14 while retaining at least one epitope of SEQ ID NO: 14. The first 26 N-terminal amino acids of SEQ ID NO: 14 can usefully be omitted (e.g. to give SEQ ID NO: 231). Truncation at the C-terminus can also be used e.g. leaving only 50 amino acids (residues 27-76 of SEQ ID NO: 14) [52]. Other fragments omit one or more protein domains.

Hla's toxicity can be avoided in compositions of the invention by chemical inactivation (e.g. using formaldehyde, glutaraldehyde or other cross-linking reagents). Instead, however, it is preferred to use mutant forms of Hla which remove its toxic activity while retaining its immunogenicity. Such detoxified mutants are already known in the art. One useful Hla antigen has a mutation at residue 61 of SEQ ID NO: 14, which is residue 35 of the mature antigen (*i.e. after omitting the first 26 N-terminal amino acids = residue 35 of SEQ ID NO: 231*). Thus residue 61 may not be histidine, and may instead be *e.g.* He, Val or preferably Leu. A His-Arg mutation at this position can also be used.

For example, SEQ ID NO: 150 is the mature mutant Hla-H35L sequence (*i.e. SEQ ID NO: 231 with a H35L mutation*) and a useful Hla antigen comprises SEQ ID NO: 150. Another useful mutation replaces a long loop with a short sequence *e.g.* to replace the 39mer at residues 136-174 of SEQ ID NO: 14 with a tetramer such as PSGS (SEQ ID NO: 225), as in SEQ ID NO: 189 (which also includes the H35L mutation) and SEQ ID NO: 216 (which does not include the H35L mutation).

Another useful mutation replaces residue Y101 *e.g.* with a leucine (SEQ ID NO: 242). Another useful mutation replaces residue D152 *e.g.* with a leucine (SEQ ID NO: 243). Another useful mutant
replaces residues H35 and Y1Ol e.g. with a leucine (SEQ ID NO: 244). Another useful mutant replaces residues H35 and D152 e.g. with a leucine (SEQ ID NO: 245).

Further useful Hla antigens are disclosed in references 53 and 54.

SEQ ID NOs: 160, 161 & 194 are three useful fragments of SEQ ID NO: 14 ('Hla_{27-76}', 'Hla_{27-89}' and 'Hla_{27-76}', respectively). SEQ ID NOs: 158, 159 and 195 are the corresponding fragments from SEQ ID NO: 150.

One useful Hla sequence is SEQ ID NO: 232, which was used in the examples. It has a N-terminal Met, then an Ala-Ser dipeptide from the expression vector, then SEQ ID NO: 150 (from NCTC8325 strain). It is encoded by SEQ ID NO: 233.

MgB

The 'hlgB' antigen is annotated as 'leukocidin f subunit precursor HlgB'. In the NCTC 8325 strain hlgB is SAOUHSC_02710 and has amino acid sequence SEQ ID NO: 15 (GI:88196350).

Useful hlgB antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 15 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 15; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 15, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These hlgB proteins include variants of SEQ ID NO: 15. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 15. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 15 while retaining at least one epitope of SEQ ID NO: 15. The first 26 N-terminal amino acids of SEQ ID NO: 15 can usefully be omitted. Other fragments omit one or more protein domains.

MgC

The 'hlgC' antigen is annotated as 'leukocidin s subunit precursor HlgC'. In the NCTC 8325 strain hlgC is SAOUHSC_02709 and has amino acid sequence SEQ ID NO: 16 (GI:88196349).

Useful hlgC antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 16 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 16; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 16, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These hlgC proteins include variants of SEQ ID NO: 16. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 16. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ
ID NO: 16 while retaining at least one epitope of SEQ ID NO: 16. The first 29 N-terminal amino acids of SEQ ID NO: 16 can usefully be omitted. Other fragments omit one or more protein domains.

_isdA_

The 'isdA' antigen is annotated as 'IsdA protein'. In the NCTC 8325 strain isdA is SAOUHSC_O1081 and has amino acid sequence SEQ ID NO: 17 (GI:88194829). In the Newman strain it is nwmn_1041 (GI: 151221253).

Useful isdA antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 17 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 17; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 17, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These isdA proteins include variants of SEQ ID NO: 17. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 17. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 17 while retaining at least one epitope of SEQ ID NO: 17. The final 38 C-terminal amino acids of SEQ ID NO: 17 can usefully be omitted. The first 46 N-terminal amino acids of SEQ ID NO: 17 can usefully be omitted. Truncation to exclude the C-terminal 38mer of SEQ ID NO: 17 (beginning with the LPK TG motif) is also useful. Other fragments omit one or more protein domains.

SEQ ID NO: 157 is a useful fragment of SEQ ID NO: 17 (amino acids 40-184 of SEQ ID NO: 17; 'IsdA<sub>40-184</sub>') which includes the natural protein's heme binding site and includes the antigen's most exposed domain. It also reduces the antigen's similarity with human proteins. Other useful fragments are disclosed in references 55 and 56.

IsdA does not adsorb well to aluminium hydroxide adjuvants, so IsdA present in a composition may be unadsorbed or may be adsorbed to an alternative adjuvant e.g. to an aluminium phosphate.

Anti-IsdA antibodies protect mice against _S.aureus_ abscess formation and lethal challenge [57].

_isdB_

The 'isdB' antigen is annotated as 'neurofilament protein isdB'. In the NCTC 8325 strain isdB is SAOUHSC_01079 and has amino acid sequence SEQ ID NO: 18 (GL88194828). IsdB has been proposed for use as a vaccine antigen on its own [2], but this may not prevent pneumonia.

Useful isdB antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 18 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 18; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of...
SEQ ID NO: 18, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These isdB proteins include variants of SEQ ID NO: 18. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 18. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 18 while retaining at least one epitope of SEQ ID NO: 18. The final 36 C-terminal amino acids of SEQ ID NO: 18 can usefully be omitted. The first 40 N-terminal amino acids of SEQ ID NO: 18 can usefully be omitted. Other fragments omit one or more protein domains. Useful fragments of IsdB are disclosed in references 56 and 58 e.g. lacking 37 internal amino acids of SEQ ID 18.

Anti-IsdB antibodies protect mice against *S.aureus* abscess formation and lethal challenge [57].

In some embodiments, compositions of the invention do not include an isdB antigen.

**isdC**

The 'isdC' antigen is annotated as 'protein'. In the NCTC 8325 strain isdB is SAOUHSC_O1082 and has amino acid sequence SEQ ID NO: 19 (GI:88194830).

Useful isdC antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 19 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 19; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 19, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These isdC proteins include variants of SEQ ID NO: 19. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 19. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 19 while retaining at least one epitope of SEQ ID NO: 19. The final 39 C-terminal amino acids of SEQ ID NO: 19 can usefully be omitted. The first 28 N-terminal amino acids of SEQ ID NO: 19 can usefully be omitted. Other fragments omit one or more protein domains. Useful fragments of IsdB are disclosed in reference 56.

Reference 59 discloses antigens which usefully include epitopes from both IsdB and IsdH.

**isdG**

The 'isdG' antigen is annotated as 'heme-degrading monooxygenase IsdG'. In the NCTC 8325 strain isdG is SAOUHSC_01089 and has amino acid sequence SEQ ID NO: 20 (GI:88194836).

Useful isdG antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 20 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or
more) to SEQ ID NO: 20; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 20, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100 or more). These isdG proteins include variants of SEQ ID NO: 20. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 20. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 20 while retaining at least one epitope of SEQ ID NO: 20. Other fragments omit one or more protein domains.

isdH

The 'isdH' antigen is annotated as 'isdH'. In the NCTC 8325 strain isdH is SAOUHSC_Oi 843 and has amino acid sequence SEQ ID NO: 21 (GI:88195542). In the Newman strain it is nwmn_1624 (GI: 151221836). It has also been known as HarA.

Useful isdH antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 21 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 21; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 21, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These isdH proteins include variants of SEQ ID NO: 21. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 21. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 21 while retaining at least one epitope of SEQ ID NO: 21. The final 35 C-terminal amino acids of SEQ ID NO: 21 can usefully be omitted. The first 40 N-terminal amino acids of SEQ ID NO: 21 can usefully be omitted. Other fragments omit one or more protein domains.

Reference 59 discloses antigens which usefully include epitopes from both IsdB and IsdH.

isdI

The 'isdI' antigen is annotated as 'heme-degrading monooxygenase Isdl'. In the NCTC 8325 strain isdl is SAOUHSC_oo 130 and has amino acid sequence SEQ ID NO: 22 (GI:88193943).

Useful isdI antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 22 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 22; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 22, wherein V is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100 or more). These isdl proteins include variants of SEQ ID NO: 22. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 22. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino
acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 22 while retaining at least one epitope of SEQ ID NO: 22. Other fragments omit one or more protein domains.

*lukD*

The 'lukD' antigen is annotated as 'leukotoxin LukD'. In the NCTC 8325 strain lukD is SAOUHSC_01954 and has amino acid sequence SEQ ID NO: 23 (GI:88195647). hi the Newman strain it is nwmm_1718 (GI:151221930).

Useful lukD antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 23 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 23; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 23, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These lukD proteins include variants of SEQ ID NO: 23. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 23. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 23 while retaining at least one epitope of SEQ ID NO: 23. The final 43 C-terminal amino acids of SEQ ID NO: 23 can usefully be omitted. The first 26 N-terminal amino acids of SEQ ID NO: 23 can usefully be omitted. Other fragments omit one or more protein domains.

*lukE*

The 'lukE' antigen is annotated as 'leukotoxin LukE'. In the NCTC 8325 strain lukE is SAOUHSCJ 1955 and has amino acid sequence SEQ ID NO: 24 (GI:88195648).

Useful lukE antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 24 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 24; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 24, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These lukE proteins include variants of SEQ ID NO: 24. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 24. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 24 while retaining at least one epitope of SEQ ID NO: 24. Other fragments omit one or more protein domains.

*lukF*

The 'lukF' antigen is annotated as 'Leukocidin/Hemolysin toxin family LukF'. In the NCTC 8325 strain lukF is SAOUHSC_02241 and has amino acid sequence SEQ ID NO: 25 (GI:88195914).
Useful lukF antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 25 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 25; and/or (b) comprising a fragment of at least V consecutive amino acids of SEQ ID NO: 25, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These lukF proteins include variants of SEQ ID NO: 25. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 25. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 25 while retaining at least one epitope of SEQ ID NO: 25. Other fragments omit one or more protein domains.

lukS

The 'lukS' antigen is annotated as 'probable leukocidin S subunit LukS'. In the NCTC 8325 strain lukS is SAOUHSC_02243 and has amino acid sequence SEQ ID NO: 26 (GI:88195915). In the Newman strain it is nwmn_1928 (GI:151222140).

Useful lukS antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 26 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 26; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 26, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These lukS proteins include variants of SEQ ID NO: 26. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 26. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 26 while retaining at least one epitope of SEQ ID NO: 26. The first 22 N-terminal amino acids of SEQ ID NO: 26 can usefully be omitted. Other fragments omit one or more protein domains.

nuc

The 'nuc' antigen is annotated as 'thermonuclease precursor'. In the NCTC 8325 strain nuc is SAOUHSC_01316 and has amino acid sequence SEQ ID NO: 27 (GI:88195046).

Useful nuc antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 27 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 27; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 27, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150 or more). These nuc proteins include variants of SEQ ID NO: 27. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 27. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more...
amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 27 while retaining at least one epitope of SEQ ID NO: 27. The final 39 C-terminal amino acids of SEQ ID NO: 27 can usefully be omitted. The first 19 N-terminal amino acids of SEQ ID NO: 27 can usefully be omitted. Other fragments omit one or more protein domains.

5 sasA

The 'sasA' antigen is annotated as 'SasA'. In the NCTC 8325 strain sasA is SAOUHSC_02990 and has amino acid sequence SEQ ID NO: 28 (GI:88196609).

Useful sasA antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 28 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 28; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 28, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sasA proteins include variants of SEQ ID NO: 28. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 28. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 28 while retaining at least one epitope of SEQ ID NO: 28. The final 43 C-terminal amino acids of SEQ ID NO: 28 can usefully be omitted. The first 90 N-terminal amino acids of SEQ ID NO: 28 can usefully be omitted. Other fragments omit one or more protein domains.

10 sasB

The 'sasB' antigen is annotated as 'frmtB protein; SasB'. In the NCTC 8325 strain sasB is SAOUHSC_02404 and has amino acid sequence SEQ ID NO: 29 (GI:88196065).

Useful sasB antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 29 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 29; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 29, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sasB proteins include variants of SEQ ID NO: 29. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 29. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 29 while retaining at least one epitope of SEQ ID NO: 29. The final 39 C-terminal amino acids of SEQ ID NO: 29 can usefully be omitted. The first 38 N-terminal amino acids of SEQ ID NO: 29 can usefully be omitted. Other fragments omit one or more protein domains.
sasC

The 'sasC antigen is annotated as 'Mrp protein; SasC. In the NCTC 8325 strain sasC is SAOUHSC_01873 and has amino acid sequence SEQ ID NO: 30 (GI:88195570).

Useful sasC antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 30 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 30; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 30, wherein V is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sasC proteins include variants of SEQ ID NO: 30. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 30. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 30 while retaining at least one epitope of SEQ ID NO: 30. The final 36 C-terminal amino acids of SEQ ID NO: 30 can usefully be omitted. The first 37 N-terminal amino acids of SEQ ID NO: 30 can usefully be omitted. Other fragments omit one or more protein domains.

sasD

The 'sasD' antigen is annotated as 'SasD protein'. In the NCTC 8325 strain sasD is SAOUHSC_00094 and has amino acid sequence SEQ ID NO: 31 (GL88193909).

Useful sasD antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 31 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 31; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 31, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150 or more). These sasD proteins include variants of SEQ ID NO: 31. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 31. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 31 while retaining at least one epitope of SEQ ID NO: 31. The first 28 N-terminal amino acids of SEQ ID NO: 31 can usefully be omitted. Other fragments omit one or more protein domains.

sasF

The 'sasF antigen is annotated as 'sasF protein'. In the NCTC 8325 strain sasF is SAOUHSC_02982 and has amino acid sequence SEQ ID NO: 32 (GI:88196601).

Useful sasF antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 32 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 32; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of
The 'sdrC' antigen is annotated as 'sdrC protein'. In the NCTC 8325 strain sdrC is SAOUHSC_00544 and has amino acid sequence SEQ ID NO: 33 (GI:88194324).

Useful sdrC antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 33 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 33; and/or (b) comprising a fragment of at least V consecutive amino acids of SEQ ID NO: 33, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sdrC proteins include variants of SEQ ID NO: 33. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 33. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 33 while retaining at least one epitope of SEQ ID NO: 33. The final 39 C-terminal amino acids of SEQ ID NO: 33 can usefully be omitted. The first 37 N-terminal amino acids of SEQ ID NO: 33 can usefully be omitted. Other fragments omit one or more protein domains. SdrC is naturally a long protein and so the use of fragments is helpful e.g. for purification, handling, fusion, expression, etc.

SEQ ID NO: 164 is a useful fragment of SEQ ID NO: 33 ('SdrC518'). This fragment includes the most exposed domain of SdrC and is more easily used at an industrial scale. It also reduces the antigen's similarity with human proteins.

The 'sdrD' antigen is annotated as 'sdrD protein'. In the NCTC 8325 strain sdrD is SAOUHSC_00545 and has amino acid sequence SEQ ID NO: 34 (GI:88194325).

Useful sdrD antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 34 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 34; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 34, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80,
90, 100, 150, 200, 250 or more). These sdrD proteins include variants of SEQ ID NO: 34. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 34. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 34 while retaining at least one epitope of SEQ ID NO: 34. The final 38 C-terminal amino acids of SEQ ID NO: 34 can usefully be omitted. The first 52 N-terminal amino acids of SEQ ID NO: 34 can usefully be omitted. Other fragments omit one or more protein domains. SdrD is naturally a long protein and so the use of fragments is very helpful e.g. for purification, handling, fusion, expression, etc.

SEQ ID NO: 156 is a useful fragment of SEQ ID NO: 34 (‘SdT\textsubscript{D3-592}’). This fragment includes the most exposed domain of SdrD and is more easily used at an industrial scale. It also reduces the antigen’s similarity with human proteins. Another useful fragment, with the same C-terminus residue, is SdT\textsubscript{D394-592} (also known as SdrD-N3; SEQ ID NO: 199). Another useful fragment is SEQ ID NO: 236 (amino acids 593-1123 of SEQ ID NO: 34), referred to herein as ‘SdrD\textsubscript{C\textsubscript{na}B’}. sdrE2

The 'sdrE2' antigen is annotated as 'Ser-Asp rich fibrinogen/bone sialoprotein-binding protein SdrE'. In the Newman strain sdrE2 is NWMM\textsubscript{0}525 and has amino acid sequence SEQ ID NO: 35 (GL151220737).

Useful sdrE2 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 35 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 35; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 35, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sdrE2 proteins include variants of SEQ ID NO: 35. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 35. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 35 while retaining at least one epitope of SEQ ID NO: 35. The final 38 C-terminal amino acids of SEQ ID NO: 35 can usefully be omitted. The first 52 N-terminal amino acids of SEQ ID NO: 35 can usefully be omitted. Other fragments omit one or more protein domains. SdrE2 is naturally a long protein and so the use of fragments is very helpful e.g. for purification, handling, fusion, expression, etc.

SEQ ID NO: 155 is a useful fragment of SEQ ID NO: 35 (‘SdrE\textsubscript{53-632}’). This fragment includes the most exposed domain of SdrE2 and is more easily used at an industrial scale. It also reduces the antigen’s similarity with human proteins.
The 'spa' antigen is annotated as 'protein A' or 'SpA'. In the NCTC 8325 strain spa is SAOUHSC_00069 and has amino acid sequence SEQ ID NO: 36 (GI:88193885). In the Newman strain it is nwmn_0055 (GI:151220267). All S.aureus strains express the structural gene for spa, a well characterized virulence factor whose cell wall-anchored surface protein product has five highly homologous immunoglobulin binding domains designated E, D, A, B, and C [60]. These domains display -80% identity at the amino acid level, are 56 to 61 residues in length, and are organized as tandem repeats [61]. SpA is synthesized as a precursor protein with an N-terminal signal peptide and a C-terminal sorting signal [62,63]. Cell wall-anchored spa is displayed in great abundance on the staphylococcal surface [64,65]. Each of its immunoglobulin binding domains is composed of anti-parallel α-helices that assemble into a three helix bundle and can bind the Fc domain of immunoglobulin G (IgG) [66,67], the VH3 heavy chain (Fab) of IgM [i.e. the B cell receptor] [68], the von Willebrand factor at its A1 domain [69] and/or the TNF-α receptor I (TNFRI) [70], which is displayed on surfaces of airway epithelia.

Useful spa antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 36 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 36; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 36, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These spa proteins include variants of SEQ ID NO: 36. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 36. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 36 while retaining at least one epitope of SEQ ID NO: 36. The final 35 C-terminal amino acids of SEQ ID NO: 36 can usefully be omitted. The first 36 N-terminal amino acids of SEQ ID NO: 36 can usefully be omitted. Other fragments omit one or more protein domains. Reference 71 suggests that individual IgG-binding domains might be useful immunogens, alone or in combination.

SEQ ID NO: 162 is a useful fragment of SEQ ID NO: 36 ('Spa_{37-325}'). This fragment contains all the five SpA Ig-binding domains (which are naturally arranged from N- to C-terminus in the order E, D, A, B, C) and includes the most exposed domain of SpA. It also reduces the antigen's similarity with human proteins. Other useful fragments may omit 1, 2, 3 or 4 of the natural A, B, C, D and/or E domains to prevent the excessive B cell expansion and then apoptosis which might occur if spa functions as a B cell superantigen. As reported in reference 71, other useful fragments may include only 1, 2, 3 or 4 of the natural A, B, C, D and/or E domains e.g. comprise only the SpA(A) domain but not B to E, or comprise only the SpA(D) domain but not A, B, C or E, etc. Thus a spa antigen useful with the invention may include 1, 2, 3, 4 or 5 IgG-binding domains, but ideally has 4 or fewer
If an antigen includes only one type of spa domain (e.g. only the Spa(A) or SpA(D) domain), it may include more than one copy of this domain e.g. multiple SpA(D) domains in a single polypeptide chain.

An individual domain within the antigen may be mutated at 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more amino acids relative to SEQ ID NO: 36 (e.g. see ref. 71, disclosing mutations at residues 3 and/or 24 of domain D, at residue 46 and/or 53 of domain A, etc.). Such mutants should not remove the antigen's ability to elicit an antibody that recognises SEQ ID NO: 36, but may remove the antigen's binding to IgG and/or other human proteins (such as human blood proteins).

In certain aspects a spa antigen includes a substitution at (a) one or more amino acid substitution in an IgG Fc binding sub-domain of SpA domain A, B, C, D and/or E that disrupts or decreases binding to IgG Fc, and (b) one or more amino acid substitution in a Vβ3 binding sub-domain of SpA domain A, B, C, D, and/or E that disrupts or decreases binding to Vβ3. In certain embodiments, a variant SpA comprises at least or at most 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more variant SpA domain D peptides.

**Second antigen group**

**sta001**

The 'sta001' antigen is annotated as '5'-nucleotidase family protein', hi the NCTC 8325 strain sta001 is SAOUHSC_00025 and has amino acid sequence SEQ ID NO: 37 (GI:88193846). hi the Newman strain it is nwmn_0022 (GI:151220234). It has also been referred to as AdsA and SasH and SA0024.

Useful sta001 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 37 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 37; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 37, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta001 proteins include variants of SEQ ID NO: 37.

Preferred fragments of (b) comprise an epitope from SEQ ID NO: 37. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 37 while retaining at least one epitope of SEQ ID NO: 37. The final 34 C-terminal amino acids of SEQ ID NO: 37 can usefully be omitted. The first 38 N-terminal amino acids of SEQ ID NO: 37 can usefully be omitted. Other fragments omit one or more protein domains.

**sta002**

The 'sta002' antigen is annotated as 'lipoprotein', hi the NCTC 8325 strain sta002 is SAOUHSC_00356 and has amino acid sequence SEQ ID NO: 38 (GL88194155). hi the Newman strain it is nwmn_0364 (GI:151220576).

Useful sta002 antigens can elicit an antibody (e.g. when administered to a human) that recognizes SEQ ID NO: 38 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g.
60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 38; and/or (b) comprising a fragment of at least \( n \) consecutive amino acids of SEQ ID NO: 38, wherein \( n \) is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150 or more). These sta002 proteins include variants of SEQ ID NO: 38. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 38. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 38 while retaining at least one epitope of SEQ ID NO: 38. The first 18 N-terminal amino acids of SEQ ID NO: 38 can usefully be omitted. Other fragments omit one or more protein domains.

SEQ ID NOs: 153 ('sta002i _9_{i87}^i') and 154 ('sta002i _9_{i124}^i') are two useful fragments of SEQ ID NO: 38 which reduce the antigen's similarity with human proteins.

**sta003**

The 'sta003' antigen is annotated as 'surface protein', hi the NCTC 8325 strain sta003 is SAOUHSC_00400 and has amino acid sequence SEQ ID NO: 39 (GI:88194195). In the Newman strain it is nwmn_0401 (GI:151220613).

Useful sta003 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 39 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 39; and/or (b) comprising a fragment of at least \( n \) consecutive amino acids of SEQ ID NO: 39, wherein \( n \) is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta003 proteins include variants of SEQ ID NO: 39. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 39. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 39 while retaining at least one epitope of SEQ ID NO: 39. The first 32 N-terminal amino acids of SEQ ID NO: 39 can usefully be omitted. Other fragments omit one or more protein domains.

**sta004**

The 'sta004' antigen is annotated as 'Siderophore binding protein FatB'. In the NCTC 8325 strain sta004 is SAOUHSC_00749 and has amino acid sequence SEQ ID NO: 40 (GI:88194514). In the Newman strain it is nwmn_0705 (GI:151220917).

Useful sta004 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 40 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 40; and/or (b) comprising a fragment of at least \( V \) consecutive amino acids of SEQ ID NO: 40, wherein \( n \) is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70,
80, 90, 100, 150, 200, 250 or more). These sta004 proteins include variants of SEQ ID NO: 40. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 40. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 40 while retaining at least one epitope of SEQ ID NO: 40. The first 18 N-terminal amino acids of SEQ ID NO: 40 can usefully be omitted. Other fragments omit one or more protein domains.

**sta005**

The ‘sta005’ antigen is annotated as ‘superantigen-like protein’. In the NCTC 8325 strain sta005 is SAOUHSC_Ol 127 and has amino acid sequence SEQ ID NO: 41 (GI: 88194870). In the Newman strain it is nwmn_1077 (GI: 151221289).

Useful sta005 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 41 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 41; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 41, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These sta005 proteins include variants of SEQ ID NO: 41. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 41. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 41 while retaining at least one epitope of SEQ ID NO: 41. The first 18 N-terminal amino acids of SEQ ID NO: 41 can usefully be omitted. Other fragments omit one or more protein domains.

**sta006**

The ‘sta006’ antigen is annotated as ‘ferrichrome-binding protein’, and has also been referred to as ‘FhuD2’ in the literature [72]. In the NCTC 8325 strain sta006 is SAOUHSC_02554 and has amino acid sequence SEQ ID NO: 42 (GL88196199). In the Newman strain it is nwmn_2185 (GI: 151222397).

Useful sta006 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 42 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 42; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 42, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta006 proteins include variants of SEQ ID NO: 42. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 42. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 42 while retaining at least one epitope of SEQ ID NO: 42. The first 17
N-terminal amino acids of SEQ ID NO: 42 can usefully be omitted (to provide SEQ ID NO: 246). Other fragments omit one or more protein domains. Mutant forms of sta006 are reported in reference 73. A sta006 antigen may be lipitated e.g. with an acylated N-terminus cysteine. One useful sta006 sequence is SEQ ID NO: 248, which has a Met-Ala-Ser- sequence at the N-terminus.

sta007

The 'sta007' antigen is annotated as 'secretory antigen precursor', hi the NCTC 8325 strain sta007 is SAOUHSC_02571 and has amino acid sequence SEQ ID NO: 43 (GI:88196215). hi the Newman strain it is nwmn_2199 (GI:151222411). Proteomic analysis has revealed that this protein is secreted or surface-exposed.

Useful sta007 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 43 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 43; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 43, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta007 proteins include variants of SEQ ID NO: 43. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 43. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 43 while retaining at least one epitope of SEQ ID NO: 43. The first 27 N-terminal amino acids of SEQ ID NO: 43 can usefully be omitted. Other fragments omit one or more protein domains.

sta008

The 'sta008' antigen is annotated as 'lipoprotein', hi the NCTC 8325 strain sta008 is SAOUHSC_02650 and has amino acid sequence SEQ ID NO: 44 (GI:88196290). hi the Newman strain it is nwmn_2270 (GI:151222482).

Useful sta008 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 44 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 44; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 44, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These sta008 proteins include variants of SEQ ID NO: 44. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 44. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 44 while retaining at least one epitope of SEQ ID NO: 44. The first 17 N-terminal amino acids of SEQ ID NO: 44 can usefully be omitted. Other fragments omit one or more protein domains.
The 'sta009' antigen is annotated as 'immunoglobulin G-binding protein Sbi'. In the NCTC 8325 strain sta009 is SAOUHSC_02706 and has amino acid sequence SEQ ID NO: 45 (GI:88196346). In the Newman strain it is nwmn_2317 (GI: 151222529).

Useful sta009 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 45 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 45; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 45, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta009 proteins include variants of SEQ ID NO: 45. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 45. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 45 while retaining at least one epitope of SEQ ID NO: 45. The first 29 N-terminal amino acids of SEQ ID NO: 45 can usefully be omitted. Other fragments omit one or more protein domains.

The 'staO1O' antigen is annotated as 'immunodominant antigen A'. In the NCTC 8325 strain staO1O is SAOUHSC_02887 and has amino acid sequence SEQ ID NO: 46 (GI:88196515). In the Newman strain it is nwmn_2469 (GI: 151222681). Proteomic analysis has revealed that this protein is secreted or surface-exposed.

Useful staO1O antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 46 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 46; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 46, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These staO1O proteins include variants of SEQ ID NO: 46. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 46. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 46 while retaining at least one epitope of SEQ ID NO: 46. The first 29 N-terminal amino acids of SEQ ID NO: 46 can usefully be omitted. Other fragments omit one or more protein domains.

The 'staOl1' antigen is annotated as 'lipoprotein'. In the NCTC 8325 strain staOl1 is SAOUHSC_00052 and has amino acid sequence SEQ ID NO: 47 (GL88193872).
Useful staOl antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 47 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 47; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 47, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staOl proteins include variants of SEQ ID NO: 47. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 47. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 47 while retaining at least one epitope of SEQ ID NO: 47. The first 23 N-terminal amino acids of SEQ ID NO: 47 can usefully be omitted (to provide SEQ ID NO: 247). Other fragments omit one or more protein domains. A staOl antigen may be lipidated e.g. with an acylated N-terminus cysteine. One useful staOl sequence is SEQ ID NO: 249, which has a N-terminus methionine.

Variant forms of SEQ ID NO: 47 which may be used as or for preparing staOl l antigens include, but are not limited to, SEQ ID NOs: 213, 214 and 215 with various Ile/Val/Leu substitutions.

StaOl1 can exist as a monomer or an oligomer, with Ca\(^{++}\) ions favouring oligomerisation. The invention can use monomers and/or oligomers of StaOl 1.

*staOl2*

The ‘staOl2’ antigen is annotated as ‘protein with leader’. In the NCTC 8325 strain staOl2 is SAOUHSC_00106 and has amino acid sequence SEQ ID NO: 48 (GI:88193919).

Useful staOl2 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 48 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 48; and/or (b) comprising a fragment of at least V consecutive amino acids of SEQ ID NO: 48, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staOl2 proteins include variants of SEQ ID NO: 48. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 48. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 48 while retaining at least one epitope of SEQ ID NO: 48. The first 21 N-terminal amino acids of SEQ ID NO: 48 can usefully be omitted. Other fragments omit one or more protein domains.
The staO13 antigen is annotated as 'poly-gamnia-glutamate capsule biosynthesis protein', the NCTC 8325 strain staO13 is SAOUHSC_00107 and has amino acid sequence SEQ ID NO: 49 (GI:88193920).

Useful staO13 antigens can elicit an antibody \( \text{e.g.} \) when administered to a human) that recognises SEQ ID NO: 49 and/or may comprise an amino acid sequence: (a) having 50% or more identity \( \text{e.g.} \) 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 49; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 49, wherein 'n' is 7 or more \( \text{e.g.} \) 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO13 proteins include variants of SEQ ID NO: 49. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 49. Other preferred fragments lack one or more amino acids \( \text{e.g.} \) 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids \( \text{e.g.} \) 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 49 while retaining at least one epitope of SEQ ID NO: 49. Other fragments omit one or more protein domains.

The staO14 antigen is annotated as 'lipoprotein'. In the NCTC 8325 strain staO14 is SAOUHSC_00137 and has amino acid sequence SEQ ED NO: 50 (GI:88193950).

Useful staO14 antigens can elicit an antibody \( \text{e.g.} \) when administered to a human) that recognises SEQ ID NO: 50 and/or may comprise an amino acid sequence: (a) having 50% or more identity \( \text{e.g.} \) 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 50; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 50, wherein 'n' is 7 or more \( \text{e.g.} \) 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO14 proteins include variants of SEQ ID NO: 50.

Preferred fragments of (b) comprise an epitope from SEQ ID NO: 50. Other preferred fragments lack one or more amino acids \( \text{e.g.} \) 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids \( \text{e.g.} \) 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 50 while retaining at least one epitope of SEQ ID NO: 50. The first 17 N-terminal amino acids of SEQ ID NO: 50 can usefully be omitted. Other fragments omit one or more protein domains.

The staO15 antigen is annotated as 'extracellular solute-binding protein; RGD containing lipoprotein'. In the NCTC 8325 strain staO15 is SAOUHSC_00170 and has amino acid sequence SEQ ID NO: 51 (GI:88193980).

Useful staO15 antigens can elicit an antibody \( \text{e.g.} \) when administered to a human) that recognises SEQ ID NO: 51 and/or may comprise an amino acid sequence: (a) having 50% or more identity \( \text{e.g.}
60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 51; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 51, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO15 proteins include variants of SEQ ID NO: 51.

Preferred fragments of (b) comprise an epitope from SEQ ID NO: 51. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 51 while retaining at least one epitope of SEQ ID NO: 51. The first 18 N-terminal amino acids of SEQ ID NO: 51 can usefully be omitted. Other fragments omit one or more protein domains.

staOlô

The 'staOl6' antigen is annotated as 'gamma-glutamyltranspeptidase'. In the NCTC 8325 strain staOlô is SAOUHSC_00171 and has amino acid sequence SEQ ID NO: 52 (GI:88193981).

Useful staOlô antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 52 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 52; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 52, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staOlô proteins include variants of SEQ ID NO: 52.

Preferred fragments of (b) comprise an epitope from SEQ ID NO: 52. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 52 while retaining at least one epitope of SEQ ID NO: 52. Other fragments omit one or more protein domains.

staO17

The 'staO17' antigen is annotated as 'lipoprotein'. In the NCTC 8325 strain staO17 is SAOUHSC_00186 and has amino acid sequence SEQ ID NO: 53 (GI:88193996).

Useful staO17 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 53 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 53; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 53, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO17 proteins include variants of SEQ ID NO: 53. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 53. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 53 while retaining at least one epitope of SEQ ID NO: 53. The first 17 N-
The terminal amino acids of SEQ ID NO: 53 can usefully be omitted. Other fragments omit one or more protein domains.

**staO18**

The 'staO18' antigen is annotated as 'extracellular solute-binding protein'. In the NCTC 8325 strain staO18 is SAOUHSC_00201 and has amino acid sequence SEQ ID NO: 54 (GL8819401 1).

Useful staO18 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 54 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 54; and/or (b) comprising a fragment of at least ‘n’ consecutive amino acids of SEQ ID NO: 54, wherein ‘n’ is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO18 proteins include variants of SEQ ID NO: 54. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 54. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 54 while retaining at least one epitope of SEQ ID NO: 54. Other fragments omit one or more protein domains.

**staO19**

The 'staO19' antigen is annotated as 'peptidoglycan hydrolase'. In the NCTC 8325 strain staO19 is SAOUHSC_00248 and has amino acid sequence SEQ ID NO: 55 (GI:88194055). In the Newman strain it is nwmn_02 10 (GI:151220422).

Useful staO19 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 55 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 55; and/or (b) comprising a fragment of at least ‘n’ consecutive amino acids of SEQ ID NO: 55, wherein ‘n’ is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO19 proteins include variants of SEQ ID NO: 55. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 55. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 55 while retaining at least one epitope of SEQ ID NO: 55. The first 25 N-terminal amino acids of SEQ ID NO: 55 can usefully be omitted. Other fragments omit one or more protein domains. Useful fragments are SEQ ID NOs: 228 and 229.

StaO19 does not adsorb well to aluminium hydroxide adjuvants, so StaO19 present in a composition may be unadsorbed or may be adsorbed to an alternative adjuvant e.g. to an aluminium phosphate.
The 'sta020' antigen is annotated as 'exported protein'. In the NCTC 8325 strain sta020 is SAOUHSC_00253 and has amino acid sequence SEQ ID NO: 56 (GI:88 194059).

Useful sta020 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 56 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 56; and/or (b) comprising a fragment of at least V consecutive amino acids of SEQ ID NO: 56, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta020 proteins include variants of SEQ ID NO: 56.

Preferred fragments of (b) comprise an epitope from SEQ ID NO: 56. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 56 while retaining at least one epitope of SEQ ID NO: 56. The first 30 N-terminal amino acids of SEQ ID NO: 56 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta021' antigen is annotated as 'secretory antigen SsaA-like protein'. In the NCTC 8325 strain sta021 is SAOUHSC_00256 and has amino acid sequence SEQ ID NO: 57 (GI:88 194062).

Useful sta021 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 57 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 57; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 57, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta021 proteins include variants of SEQ ID NO: 57.

Preferred fragments of (b) comprise an epitope from SEQ ID NO: 57. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 57 while retaining at least one epitope of SEQ ID NO: 57. The first 24 N-terminal amino acids of SEQ ID NO: 57 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta022' antigen is annotated as 'lipoprotein'. In the NCTC 8325 strain sta022 is SAOUHSC_00279 and has amino acid sequence SEQ ID NO: 58 (GI:88194083).

Useful sta022 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 58 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5%...
or more) to SEQ ID NO: 58; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 58, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100 or more). These staO22 proteins include variants of SEQ ID NO: 58. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 58. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 58 while retaining at least one epitope of SEQ ID NO: 58. The first 17 N-terminal amino acids of SEQ ID NO: 58 can usefully be omitted. Other fragments omit one or more protein domains.

**staO23**

The 'staO23' antigen is annotated as '^-nucleotidase; lipoprotein e(P4) family'. In the NCTC 8325 strain staO23 is SAOUHSC_00284 and has amino acid sequence SEQ ID NO: 59 (GI:88194087).

Useful staO23 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 59 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 59; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 59, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO23 proteins include variants of SEQ ID NO: 59. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 59. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 59 while retaining at least one epitope of SEQ ID NO: 59. The first 31 N-terminal amino acids of SEQ ID NO: 59 can usefully be omitted. Other fragments omit one or more protein domains.

**staO24**

The 'staO24' antigen is annotated as 'lipase precursor'. In the NCTC 8325 strain staO24 is SAOUHSC_00300 and has amino acid sequence SEQ ID NO: 60 (GI:88194101).

Useful staO24 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 60 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 60; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 60, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO24 proteins include variants of SEQ ID NO: 60. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 60. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 60 while retaining at least one epitope of SEQ ID NO: 60. The first 37 N-
terminal amino acids of SEQ ID NO: 60 can usefully be omitted. Other fragments omit one or more protein domains.

**staO25**

The 'staO25' antigen is annotated as 'lipoprotein'. In the NCTC 8325 strain staO25 is SAOUHSC_00362 and has amino acid sequence SEQ ID NO: 61 (GI:88194160).

Useful staO25 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ED NO: 61 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 61; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 61, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These staO25 proteins include variants of SEQ ID NO: 61. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 61. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 61 while retaining at least one epitope of SEQ ED NO: 61. The first 19 N-terminal amino acids of SEQ ID NO: 61 can usefully be omitted. Other fragments omit one or more protein domains.

**staO26**

The 'staO26' antigen is annotated as 'lipoprotein'. In the NCTC 8325 strain staO26 is SAOUHSC_00404 and has amino acid sequence SEQ ID NO: 62 (GI:88194198).

Useful staO26 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ED NO: 62 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ED NO: 62; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 62, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO26 proteins include variants of SEQ ID NO: 62. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 62. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 62 while retaining at least one epitope of SEQ ID NO: 62. The first 22 N-terminal amino acids of SEQ ED NO: 62 can usefully be omitted. Other fragments omit one or more protein domains.

**staO27**

The 'staO27' antigen is annotated as 'probable lipase'. In the NCTC 8325 strain staO27 is SAOUHSC_00661 and has amino acid sequence SEQ ID NO: 63 (GL88 194426).

Useful staO27 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 63 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g.
60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 63; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 63, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO27 proteins include variants of SEQ ID NO: 63. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 63. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 63 while retaining at least one epitope of SEQ ID NO: 63. The first 23 N-terminal amino acids of SEQ ID NO: 63 can usefully be omitted. Other fragments omit one or more protein domains.

staO28

The 'staO28' antigen is annotated as 'secretory antigen SsaA-like protein'. In the NCTC 8325 strain staO28 is SAOUHSC_00671 and has amino acid sequence SEQ ID NO: 64 (GI:88194436). In the Newman strain it is nwmn_0634 (GI: 151220846).

Useful staO28 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 64 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 64; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 64, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO28 proteins include variants of SEQ ID NO: 64. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 64. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 64 while retaining at least one epitope of SEQ ID NO: 64. The first 25 N-terminal amino acids of SEQ ID NO: 64 can usefully be omitted. Other fragments omit one or more protein domains.

staO29

The 'staO29' antigen is annotated as 'ferrichrome binding protein'. In the NCTC 8325 strain staO29 is SAOUHSC_00754 and has amino acid sequence SEQ ID NO: 65 (GI: 88194518).

Useful staO29 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 65 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 65; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 65, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO29 proteins include variants of SEQ ID NO: 65. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 65. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus
and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 65 while retaining at least one epitope of SEQ ID NO: 65. The final 25 C-terminal amino acids of SEQ ID NO: 65 can usefully be omitted. The first 19 N-terminal amino acids of SEQ ID NO: 65 can usefully be omitted. Other fragments omit one or more protein domains.

5 staO30

The ‘staO30’ antigen is annotated as 'lipoprotein'. In the NCTC 8325 strain staO30 is SAOUHSC_00808 and has amino acid sequence SEQ ID NO: 66 (GI:88194568).

Useful staO30 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 66 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 66; and/or (b) comprising a fragment of at least ‘n’ consecutive amino acids of SEQ ID NO: 66, wherein ‘n’ is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These staO30 proteins include variants of SEQ ID NO: 66. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 66. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 66 while retaining at least one epitope of SEQ ID NO: 66. The first 17 N-terminal amino acids of SEQ ID NO: 66 can usefully be omitted. Other fragments omit one or more protein domains.

staO31

The ‘staO31’ antigen is annotated as '5-nucleotidase family protein'. In the NCTC 8325 strain staO31 is SAOUHSC_00860 and has amino acid sequence SEQ ID NO: 67 (GI:88194617).

Useful staO31 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 67 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 67; and/or (b) comprising a fragment of at least ‘n’ consecutive amino acids of SEQ ID NO: 67, wherein ‘n’ is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO31 proteins include variants of SEQ ID NO: 67. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 67. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 67 while retaining at least one epitope of SEQ ID NO: 67. Other fragments omit one or more protein domains.

staO32

The ‘staO32’ antigen is annotated as 'serine protease HtrA'. In the NCTC 8325 strain staO32 is SAOUHSC_00958 and has amino acid sequence SEQ ID NO: 68 (GI:88194715).
Useful staO32 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 68 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 68; and/or (b) comprising a fragment of at least V consecutive amino acids of SEQ ID NO: 68, wherein V is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO32 proteins include variants of SEQ ID NO: 68. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 68. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 68 while retaining at least one epitope of SEQ ID NO: 68. Other fragments omit one or more protein domains.

*staO33*

The 'staO33' antigen is annotated as 'cysteine protease precursor'. In the NCTC 8325 strain staO33 is SAOUHSC_00987 and has amino acid sequence SEQ ID NO: 69 (GI:88194744).

Useful staO33 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 69 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 69; and/or (b) comprising a fragment of at least n' consecutive amino acids of SEQ ID NO: 69, wherein n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO33 proteins include variants of SEQ ID NO: 69. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 69. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 69 while retaining at least one epitope of SEQ ID NO: 69. The first 29 N-terminal amino acids of SEQ ID NO: 69 can usefully be omitted. Other fragments omit one or more protein domains.

*staO34*

The 'staO34' antigen is annotated as 'glutamyl endopeptidase precursor'. In the NCTC 8325 strain staO34 is SAOUHSC_00988 and has amino acid sequence SEQ ID NO: 70 (GI:88194745).

Useful staO34 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 70 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 70; and/or (b) comprising a fragment of at least n' consecutive amino acids of SEQ ID NO: 70, wherein n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO34 proteins include variants of SEQ ID NO: 70. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 70. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus
and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 70 while retaining at least one epitope of SEQ ID NO: 70. The first 29 N-terminal amino acids of SEQ ID NO: 70 can usefully be omitted. Other fragments omit one or more protein domains.

staO35

The 'staO35' antigen is annotated as 'frnt protein'. In the NCTC 8325 strain staO35 is SAOUHSC_00998 and has amino acid sequence SEQ ID NO: 71 (GI:88194754).

Useful staO35 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 71 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 71; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 71, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO35 proteins include variants of SEQ ID NO: 71.

Preferred fragments of (b) comprise an epitope from SEQ ID NO: 71. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 71 while retaining at least one epitope of SEQ ID NO: 71. The first 25 N-terminal amino acids of SEQ ID NO: 71 can usefully be omitted. Other fragments omit one or more protein domains.

staO36

The 'staO36' antigen is annotated as 'iron-regulated protein with leader'. In the NCTC 8325 strain staO36 is SAOUHSC_01084 and has amino acid sequence SEQ ID NO: 72 (GI:88194831).

Useful staO36 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 72 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 72; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 72, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO36 proteins include variants of SEQ ID NO: 72.

Preferred fragments of (b) comprise an epitope from SEQ ID NO: 72. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 72 while retaining at least one epitope of SEQ ID NO: 72. The final 27 C-terminal amino acids of SEQ ID NO: 72 can usefully be omitted. The first 32 N-terminal amino acids of SEQ ID NO: 72 can usefully be omitted. Other fragments omit one or more protein domains.
The 'staO37' antigen is annotated as 'iron ABC transporter; iron-binding protein IsdE'. In the NCTC 8325 strain staO37 is SAOUHSC_01085 and has amino acid sequence SEQ ID NO: 73 (GI:88194832).

Useful staO37 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 73 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 73; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 73, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO37 proteins include variants of SEQ ID NO: 73. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 73. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 73 while retaining at least one epitope of SEQ ID NO: 73. The first 9 N-terminal amino acids of SEQ ID NO: 73 can usefully be omitted. Other fragments omit one or more protein domains.

The 'staO38' antigen is annotated as NPQTN specific sortase B'. In the NCTC 8325 strain staO38 is SAOUHSC_01088 and has amino acid sequence SEQ ID NO: 74 (GI:88194835).

Useful staO38 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 74 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 74; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 74, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These staO38 proteins include variants of SEQ ID NO: 74. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 74. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 74 while retaining at least one epitope of SEQ ID NO: 74. The first 21 N-terminal amino acids of SEQ ID NO: 74 can usefully be omitted. Other fragments omit one or more protein domains.

The 'staO39' antigen is annotated as 'superantigen-like protein'. In the NCTC 8325 strain staO39 is SAOUHSC_Ol 124 and has amino acid sequence SEQ ID NO: 75 (GL88194868).

Useful staO39 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 75 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5%
or more) to SEQ ID NO: 75; and/or (b) comprising a fragment of at least V consecutive amino acids of SEQ ID NO: 75, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These staO39 proteins include variants of SEQ ID NO: 75. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 75. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 75 while retaining at least one epitope of SEQ ID NO: 75. The first 22 N-terminal amino acids of SEQ ID NO: 75 can usefully be omitted. Other fragments omit one or more protein domains.

staO40

The ‘staO40’ antigen is annotated as ‘superantigen-like protein 1’. In the NCTC 8325 strain staO40 is SAOUHSCJ1 125 and has amino acid sequence SEQ ID NO: 76 (GI:88194869). In the Newman strain it is nwmn_1076 (GI:151221288).

Useful staO40 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 76 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 76; and/or (b) comprising a fragment of at least V consecutive amino acids of SEQ ID NO: 76, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These staO40 proteins include variants of SEQ ID NO: 76. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 76. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 76 while retaining at least one epitope of SEQ ID NO: 76. The first 21 N-terminal amino acids of SEQ ID NO: 76 can usefully be omitted. Other fragments omit one or more protein domains.

staO41

The ‘staO41’ antigen is annotated as ‘fibronectin-binding protein A-related’. In the NCTC 8325 strain staO41 is SAOUHSC_01 175 and has amino acid sequence SEQ ID NO: 77 (GI:88194914).

Useful staO41 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 77 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 77; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 77, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO41 proteins include variants of SEQ ID NO: 77. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 77. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 77 while retaining at least one epitope of SEQ ID NO: 77. Other fragments omit one or more protein domains.
staO42

The 'staO42' antigen is annotated as 'lipoprotein'. In the NCTC 8325 strain staO42 is SAOUHSC_0180 and has amino acid sequence SEQ ID NO: 78 (GI:88194919).

Useful staO42 antigens can elicit an antibody (e.g. when administered to a human) that recognises

SEQ ID NO: 78 and/or may comprise an amino acid sequence: (a) having 50% or more identity {e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more} to SEQ ID NO: 78; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 78, wherein 'n' is 7 or more {e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more}. These staO42 proteins include variants of SEQ ID NO: 78.

Preferred fragments of (b) comprise an epitope from SEQ ID NO: 78. Other preferred fragments lack one or more amino acids {e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more} from the C-terminus and/or one or more amino acids {e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more} from the N-terminus of SEQ ID NO: 78 while retaining at least one epitope of SEQ ID NO: 78. The first 18 N-terminal amino acids of SEQ ID NO: 78 can usefully be omitted. Other fragments omit one or more protein domains.

staO43

The 'staO43' antigen is annotated as 'cell wall hydrolase'. hi the NCTC 8325 strain staO43 is SAOUHSC_01219 and has amino acid sequence SEQ ID NO: 79 (GI:88194955).

Useful staO43 antigens can elicit an antibody (e.g. when administered to a human) that recognises

SEQ ID NO: 79 and/or may comprise an amino acid sequence: (a) having 50% or more identity {e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more} to SEQ ID NO: 79; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 79, wherein 'n' is 7 or more {e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more}. These staO43 proteins include variants of SEQ ID NO: 79.

Preferred fragments of (b) comprise an epitope from SEQ ID NO: 79. Other preferred fragments lack one or more amino acids {e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more} from the C-terminus and/or one or more amino acids {e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more} from the N-terminus of SEQ ID NO: 79 while retaining at least one epitope of SEQ ID NO: 79. The first 38 N-terminal amino acids of SEQ ID NO: 79 can usefully be omitted. Other fragments omit one or more protein domains.

staO44

The 'staO44' antigen is annotated as 'lipoprotein'. In the NCTC 8325 strain staO44 is SAOUHSC_01508 and has amino acid sequence SEQ ID NO: 80 (GI:88195223).

Useful staO44 antigens can elicit an antibody (e.g. when administered to a human) that recognises

SEQ ID NO: 80 and/or may comprise an amino acid sequence: (a) having 50% or more identity {e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5%}
or more) to SEQ ID NO: 80; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 80, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO44 proteins include variants of SEQ ID NO: 80. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 80. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 80 while retaining at least one epitope of SEQ ID NO: 80. The first 17 N-terminal amino acids of SEQ ID NO: 80 can usefully be omitted. Other fragments omit one or more protein domains.

staO45

The 'staO45' antigen is annotated as 'lipoprotein'. In the NCTC 8325 strain staO45 is SAOUHSC_01627 and has amino acid sequence SEQ ID NO: 81 (GL88195337).

Useful staO45 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 81 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 81; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 81, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150 or more). These staO45 proteins include variants of SEQ ID NO: 81. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 81. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 81 while retaining at least one epitope of SEQ ID NO: 81. The first 16 N-terminal amino acids of SEQ ID NO: 81 can usefully be omitted. Other fragments omit one or more protein domains.

staO46

The 'staO46' antigen is annotated as 'Excalibur protein'. In the NCTC 8325 strain staO46 is SAOUHSC_01918 and has amino acid sequence SEQ ID NO: 82 (GI:88195613).

Useful staO46 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 82 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 82; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 82, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These staO46 proteins include variants of SEQ ID NO: 82. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 82. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 82 while retaining at least one epitope of SEQ ID NO: 82. The first 53 N-terminal amino acids of SEQ ID NO: 82 can usefully be omitted. Other fragments omit one or more protein domains.
staO47

The 'staO47' antigen is annotated as 'lipoprotein'. In the NCTC 8325 strain staO47 is SAOUHSC_01920 and has amino acid sequence SEQ ID NO: 83 (GI:88195615).

Useful staO47 antigens can elicit an antibody (e.g. when administered to a human) that recognises

SEQ ID NO: 83 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 83; and/or (b) comprising a fragment of at least 5 consecutive amino acids of SEQ ID NO: 83, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These staO47 proteins include variants of SEQ ID NO: 83. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 83. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 83 while retaining at least one epitope of SEQ ID NO: 83. The first 18 N-terminal amino acids of SEQ ID NO: 83 can usefully be omitted. Other fragments omit one or more protein domains.

staO48

The 'staO48' antigen is annotated as 'intracellular serine protease'. In the NCTC 8325 strain staO48 is SAOUHSC_01949 and has amino acid sequence SEQ ID NO: 84 (GI:88195642).

Useful staO48 antigens can elicit an antibody (e.g. when administered to a human) that recognises

SEQ ID NO: 84 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 84; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 84, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO48 proteins include variants of SEQ ID NO: 84. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 84. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 84 while retaining at least one epitope of SEQ ID NO: 84. The first 27 N-terminal amino acids of SEQ ID NO: 84 can usefully be omitted. Other fragments omit one or more protein domains.

staO49

The 'staO49' antigen is annotated as 'protein export protein PrsA'. In the NCTC 8325 strain staO49 is SAOUHSCJ) 1972 and has amino acid sequence SEQ ID NO: 85 (GI:88195663). In the Newman strain it is nwmn_1733 (GL151221945).

Useful staO49 antigens can elicit an antibody (e.g. when administered to a human) that recognises

SEQ ID NO: 85 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5%
or more) to SEQ ID NO: 85; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 85, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO49 proteins include variants of SEQ ID NO: 85. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 85. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 85 while retaining at least one epitope of SEQ ID NO: 85. The first 25 N-terminal amino acids of SEQ ID NO: 85 can usefully be omitted. Other fragments omit one or more protein domains.

staO50

The 'staO50' antigen is annotated as 'staphopain thiol proteinase'. In the NCTC 8325 strain staO50 is SAOUHSC _02127 and has amino acid sequence SEQ ID NO: 86 (GI:88 195808).

Useful staO50 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 86 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 86; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 86, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO50 proteins include variants of SEQ ID NO: 86. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 86. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 86 while retaining at least one epitope of SEQ ID NO: 86. The first 25 N-terminal amino acids of SEQ ID NO: 86 can usefully be omitted. Other fragments omit one or more protein domains.

staO51

The 'staO51' antigen is annotated as 'protein with leader'. In the NCTC 8325 strain staO51 is SAOUHSC _02147 and has amino acid sequence SEQ ID NO: 87 (GI:88 195827).

Useful staO51 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 87 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 87; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 87, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO51 proteins include variants of SEQ ID NO: 87. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 87. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 87 while retaining at least one epitope of SEQ ID NO: 87. The first 24 N-
terminal amino acids of SEQ ID NO: 87 can usefully be omitted. Other fragments omit one or more protein domains.

**staO52**
The 'staO52' antigen is annotated as 'ferric hydroxamate receptor 1'. In the NCTC 8325 strain staO52 is SAOUHSC_02246 and has amino acid sequence SEQ ID NO: 88 (GL88195918).

Useful staO52 antigens can elicit an antibody \(\text{\textit{e.g.} when administered to a human}\) that recognises SEQ ID NO: 88 and/or may comprise an amino acid sequence: (a) having 50% or more identity \(\text{\textit{e.g.} 60\%, 65\%, 70\%, 75\%, 80\%, 85\%, 90\%, 91\%, 92\%, 93\%, 94\%, 95\%, 96\%, 97\%, 98\%, 99\%, 99.5\% and/or more}\) to SEQ ID NO: 88; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 88, wherein 'n' is 7 or more \(\text{\textit{e.g.} 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more}\). These staO52 proteins include variants of SEQ ID NO: 88. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 88. Other preferred fragments lack one or more amino acids \(\text{\textit{e.g.} 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more}\) from the C-terminus and/or one or more amino acids \(\text{\textit{e.g.} 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more}\) from the N-terminus of SEQ ID NO: 88 while retaining at least one epitope of SEQ ID NO: 88. The first 17 N-terminal amino acids of SEQ ID NO: 88 can usefully be omitted. Other fragments omit one or more protein domains.

**staO53**
The 'staO53' antigen is annotated as 'srdH family protein 1'. In the NCTC 8325 strain staO53 is SAOUHSC_02257 and has amino acid sequence SEQ ID NO: 89 (GI: 88195928).

Useful staO53 antigens can elicit an antibody \(\text{\textit{e.g.} when administered to a human}\) that recognises SEQ ID NO: 89 and/or may comprise an amino acid sequence: (a) having 50% or more identity \(\text{\textit{e.g.} 60\%, 65\%, 70\%, 75\%, 80\%, 85\%, 90\%, 91\%, 92\%, 93\%, 94\%, 95\%, 96\%, 97\%, 98\%, 99\%, 99.5\% and/or more}\) to SEQ ID NO: 89; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 89, wherein 'n' is 7 or more \(\text{\textit{e.g.} 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more}\). These staO53 proteins include variants of SEQ ID NO: 89. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 89. Other preferred fragments lack one or more amino acids \(\text{\textit{e.g.} 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more}\) from the C-terminus and/or one or more amino acids \(\text{\textit{e.g.} 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more}\) from the N-terminus of SEQ ID NO: 89 while retaining at least one epitope of SEQ ID NO: 89. The first 26 N-terminal amino acids of SEQ ID NO: 89 can usefully be omitted. Other fragments omit one or more protein domains.

**staO54**
The 'staO54' antigen is annotated as 'Probable transglycosylase isA precursor'. In the NCTC 8325 strain staO54 is SAOUHSC_02333 and has amino acid sequence SEQ ID NO: 90 (GI:88195999).
Useful staO54 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 90 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 90; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 90, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These staO54 proteins include variants of SEQ ID NO: 90. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 90. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 90 while retaining at least one epitope of SEQ ID NO: 90. The first 27 N-terminal amino acids of SEQ ID NO: 90 can usefully be omitted. Other fragments omit one or more protein domains.

staO55

The 'staO55' antigen is annotated as 'surface hydrolase'. In the NCTC 8325 strain staO55 is SAOUHSC_02448 and has amino acid sequence SEQ ID NO: 91 (GL88196100).

Useful staO55 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 91 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 91; and/or (b) comprising a fragment of at least V consecutive amino acids of SEQ ID NO: 91, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO55 proteins include variants of SEQ ID NO: 91. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 91. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 91 while retaining at least one epitope of SEQ ID NO: 91. The first 31 N-terminal amino acids of SEQ ID NO: 91 can usefully be omitted. Other fragments omit one or more protein domains.

staO56

The 'staO56' antigen is annotated as 'hyaluronate lyase'. In the NCTC 8325 strain staO56 is SAOUHSC_02463 and has amino acid sequence SEQ ID NO: 92 (GI:88196115).

Useful staO56 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 92 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 92; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 92, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO56 proteins include variants of SEQ ID NO: 92. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 92. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus
and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminal of SEQ ID NO: 92 while retaining at least one epitope of SEQ ID NO: 92. The first 24 N-terminal amino acids of SEQ ID NO: 92 can usefully be omitted. Other fragments omit one or more protein domains.

5 staO57
The 'staO57' antigen is annotated as 'secretory antigen precursor SsaA'. In the NCTC 8325 strain staO57 is SAOUHSC_02576 and has amino acid sequence SEQ ID NO: 93 (GI:88196220). In the Newman strain it is nwmn_2203 (GI:151222415).

Useful staO57 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 93 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 93; and/or (b) comprising a fragment of at least V consecutive amino acids of SEQ ID NO: 93, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150 or more). These staO57 proteins include variants of SEQ ID NO: 93. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 93. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 93 while retaining at least one epitope of SEQ ID NO: 93. The first 27 N-terminal amino acids of SEQ ID NO: 93 can usefully be omitted. Other fragments omit one or more protein domains.

10 staO58
The 'staO58' antigen is annotated as 'Zn-binding lipoprotein adcA-like'. In the NCTC 8325 strain staO58 is SAOUHSC_02690 and has amino acid sequence SEQ ID NO: 94 (GL88196330).

Useful staO58 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 94 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 94; and/or (b) comprising a fragment of at least W consecutive amino acids of SEQ ID NO: 94, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO58 proteins include variants of SEQ ID NO: 94. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 94. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 94 while retaining at least one epitope of SEQ ID NO: 94. The first 20 N-terminal amino acids of SEQ ID NO: 94 can usefully be omitted. Other fragments omit one or more protein domains.
The 'staO59' antigen is annotated as 'gamma-hemolysin h-gamma-ii subunit'. In the NCTC 8325 strain staO59 is SAOUHSC_02708 and has amino acid sequence SEQ ID NO: 95 (GI:88196348).

Useful staO59 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 95 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 95; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 95, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO59 proteins include variants of SEQ ID NO: 95.

Preferred fragments of (b) comprise an epitope from SEQ ID NO: 95. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 95 while retaining at least one epitope of SEQ ID NO: 95. The first 20 N-terminal amino acids of SEQ ID NO: 95 can usefully be omitted. Other fragments omit one or more protein domains.

The 'sta060' antigen is annotated as 'peptide ABC transporter; peptide-binding protein'. In the NCTC 8325 strain sta060 is SAOUHSC_02767 and has amino acid sequence SEQ ID NO: 96 (GI:88196403).

Useful sta060 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 96 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 96; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 96, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta060 proteins include variants of SEQ ID NO: 96.

Preferred fragments of (b) comprise an epitope from SEQ ID NO: 96. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 96 while retaining at least one epitope of SEQ ID NO: 96. The first 20 N-terminal amino acids of SEQ ID NO: 96 can usefully be omitted. Other fragments omit one or more protein domains.

The 'staO61' antigen is annotated as 'protein with leader'. In the NCTC 8325 strain staO61 is SAOUHSC_02783 and has amino acid sequence SEQ ID NO: 97 (GL88196419).

Useful staO61 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 97 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g.
Preferred fragments of (b) comprise an epitope from SEQ ID NO: 97. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 97 while retaining at least one epitope of SEQ ID NO: 97. The first 21 N-terminal amino acids of SEQ ID NO: 97 can usefully be omitted. Other fragments omit one or more protein domains.

staO62

The ‘staO62’ antigen is annotated as ‘protein with leader’. In the NCTC 8325 strain staO62 is SAOUHSC_02788 and has amino acid sequence SEQ ID NO: 98 (GI: 88196424).

Useful staO62 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 98 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 98; and/or (b) comprising a fragment of at least ‘n’ consecutive amino acids of SEQ ID NO: 98, wherein ‘n’ is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO62 proteins include variants of SEQ ID NO: 98.

Preferred fragments of (b) comprise an epitope from SEQ ID NO: 98. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 98 while retaining at least one epitope of SEQ ID NO: 98. The first 22 N-terminal amino acids of SEQ ID NO: 98 can usefully be omitted. Other fragments omit one or more protein domains.

staO63

The ‘staO63’ antigen is annotated as 'aureolysin'. In the NCTC 8325 strain staO63 is SAOUHSC_02971 and has amino acid sequence SEQ ID NO: 99 (GL88196592).

Useful staO63 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 99 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 99; and/or (b) comprising a fragment of at least ‘n’ consecutive amino acids of SEQ ID NO: 99, wherein ‘n’ is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO63 proteins include variants of SEQ ID NO: 99.

Preferred fragments of (b) comprise an epitope from SEQ ID NO: 99. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-
terminus of SEQ ID NO: 99 while retaining at least one epitope of SEQ ID NO: 99. The first 16 N-terminal amino acids of SEQ ID NO: 99 can usefully be omitted. Other fragments omit one or more protein domains.

staO64

The 'staO64' antigen is annotated as 'lipase'; the NCTC 8325 strain staO64 is SAOUHSC_03006 and has amino acid sequence SEQ ID NO: 100 (GI:88196625). The Newman strain it is nwmn_2569 (GI: 151222781).

Useful staO64 antigens can elicit an antibody {e.g. when administered to a human} that recognises SEQ ID NO: 100 and/or may comprise an amino acid sequence: (a) having 50% or more identity {e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more} to SEQ ID NO: 100; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 100, wherein 'n' is 7 or more {e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more}. These staO64 proteins include variants of SEQ ID NO: 100. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 100. Other preferred fragments lack one or more amino acids {e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more} from the C-terminus and/or one or more amino acids {e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more} from the N-terminus of SEQ ID NO: 100 while retaining at least one epitope of SEQ ID NO: 100. The first 34 N-terminal amino acids of SEQ ID NO: 100 can usefully be omitted. Other fragments omit one or more protein domains.

staO65

The 'staO65' antigen is annotated as '1-phosphatidylinositol phosphodiesterase precursor'. In the NCTC 8325 strain staO65 is SAOUHSC_00051 and has amino acid sequence SEQ ID NO: 101 (GI:88193871).

Useful staO65 antigens can elicit an antibody {e.g. when administered to a human} that recognises SEQ ID NO: 101 and/or may comprise an amino acid sequence: (a) having 50% or more identity {e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more} to SEQ ID NO: 101; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 101, wherein 'n' is 7 or more {e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more}. These staO65 proteins include variants of SEQ ID NO: 101. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 101. Other preferred fragments lack one or more amino acids {e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more} from the C-terminus and/or one or more amino acids {e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more} from the N-terminus of SEQ ID NO: 101 while retaining at least one epitope of SEQ ID NO: 101. The first 26 N-terminal amino acids of SEQ ID NO: 101 can usefully be omitted. Other fragments omit one or more protein domains.
staO66

The 'staO66' antigen is annotated as 'protein'. In the NCTC 8325 strain staO66 is SAOUHSC_00172 and has amino acid sequence SEQ ID NO: 102 (GI:88 193982).

Useful staO66 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 102 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 102; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 102, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO66 proteins include variants of SEQ ID NO: 102. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 102. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 102 while retaining at least one epitope of SEQ ID NO: 102. The first 21 N-terminal amino acids of SEQ ID NO: 102 can usefully be omitted. Other fragments omit one or more protein domains.

staO67

The 'staO67' antigen is annotated as 'bacterial extracellular solute-binding protein'. In the NCTC 8325 strain staO67 is SAOUHSC_00176 and has amino acid sequence SEQ ID NO: 103 (GL88 193986).

Useful staO67 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 103 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 103; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 103, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO67 proteins include variants of SEQ ID NO: 103. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 103. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 103 while retaining at least one epitope of SEQ ID NO: 103. The first 20 N-terminal amino acids of SEQ ID NO: 103 can usefully be omitted. Other fragments omit one or more protein domains.

staO68

The 'staO68' antigen is annotated as 'iron permease FTR1'. In the NCTC 8325 strain staO68 is SAOUHSC_00327 and has amino acid sequence SEQ ID NO: 104 (GL88194127).

Useful staO68 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 104 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 104; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 104, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO68 proteins include variants of SEQ ID NO: 104. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 104. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 104 while retaining at least one epitope of SEQ ID NO: 104. The first 20 N-terminal amino acids of SEQ ID NO: 104 can usefully be omitted. Other fragments omit one or more protein domains.
99.5% or more) to SEQ ID NO: 104; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 104, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO68 proteins include variants of SEQ ID NO: 104. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 104. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 104 while retaining at least one epitope of SEQ ID NO: 104. The final 20 C-terminal amino acids of SEQ ID NO: 104 can usefully be omitted. The first 14 N-terminal amino acids of SEQ ID NO: 104 can usefully be omitted. Other fragments omit one or more protein domains.

**staO69**

The 'staO69' antigen is annotated as 'autolysin precursor'. In the NCTC 8325 strain staO69 is SAOUHSC_00427 and has amino acid sequence SEQ ID NO: 105 (GL88194219).

Useful staO69 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 105 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% 99.5% or more) to SEQ ID NO: 105; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 105, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO69 proteins include variants of SEQ ID NO: 105. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 105. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 105 while retaining at least one epitope of SEQ ID NO: 105. The first 25 N-terminal amino acids of SEQ ID NO: 105 can usefully be omitted. Other fragments omit one or more protein domains.

**staO70**

The 'staO70' antigen is annotated as 'immunogenic secreted precursor-like protein (truncated)'. In the NCTC 8325 strain staO70 is SAOUHSC_00773 and has amino acid sequence SEQ ID NO: 106 (GL88194535).

Useful staO70 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 106 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% 99.5% or more) to SEQ ID NO: 106; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 106, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO70 proteins include variants of SEQ ID NO: 106. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 106. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the
C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 106 while retaining at least one epitope of SEQ ID NO: 106. The first 24 N-terminal amino acids of SEQ ID NO: 106 can usefully be omitted. Other fragments omit one or more protein domains.

5 staO71
The 'staO71' antigen is annotated as 'hemolysin'. In the NCTC 8325 strain staO71 is SAOUHSC_00854 and has amino acid sequence SEQ ID NO: 107 (GL88194612).

Useful staO71 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 107 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 107; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 107, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO71 proteins include variants of SEQ ID NO: 107. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 107. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 107 while retaining at least one epitope of SEQ ID NO: 107. The first 24 N-terminal amino acids of SEQ ID NO: 107 can usefully be omitted. Other fragments omit one or more protein domains.

10 staO72
The 'staO72' antigen is annotated as 'extramembranal protein'. In the NCTC 8325 strain staO72 is SAOUHSC_00872 and has amino acid sequence SEQ ID NO: 108 (GI:88194629).

Useful staO72 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 108 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 108; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 108, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO72 proteins include variants of SEQ ID NO: 108. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 108. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 108 while retaining at least one epitope of SEQ ID NO: 108. The first 24 N-terminal amino acids of SEQ ID NO: 108 can usefully be omitted. Other fragments omit one or more protein domains.
The 'staO73' antigen is annotated as 'bifunctional autolysin precursor'. In the NCTC 8325 strain staO73 is SAOUHSC_00994 and has amino acid sequence SEQ ID NO: 109 (GL:88194750). In the Newman strain it is nwmn_0922 (GI:151221134). Proteomic analysis has revealed that this protein is secreted or surface-exposed.

Useful staO73 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 109 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 109; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 109, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO73 proteins include variants of SEQ ID NO: 109. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 109. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 109 while retaining at least one epitope of SEQ ID NO: 109. The first 24 N-terminal amino acids of SEQ ID NO: 109 can usefully be omitted. Other fragments omit one or more protein domains.

A StaO73 antigen can usefully be included in a composition in combination with a Stal 12 [74].

StaO73 does not adsorb well to aluminium hydroxide adjuvants, so StaO73 present in a composition may be unadsorbed or may be adsorbed to an alternative adjuvant e.g. to an aluminium phosphate.

The 'staO74' antigen is annotated as 'factor essential for methicillin resistance'. In the NCTC 8325 strain staO74 is SAOUHSC_01220 and has amino acid sequence SEQ ID NO: 110 (GL:88194956).

Useful staO74 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 110 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 110; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 110, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO74 proteins include variants of SEQ ID NO: 110. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 110. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 110 while retaining at least one epitope of SEQ ID NO: 110. Other fragments omit one or more protein domains.
staO75

The 'staO75' antigen is annotated as 'insulysin; peptidase family M16'. In the NCTC 8325 strain, staO75 is SAOUHSC_01256 and has amino acid sequence SEQ ID NO: 111 (GI:88194989).

Useful staO75 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 111 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 111; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 111, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO75 proteins include variants of SEQ ID NO: 111. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 111. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 111 while retaining at least one epitope of SEQ ID NO: 111. Other fragments omit one or more protein domains.

staO76

The 'staO76' antigen is annotated as 'hydrolase'. In the NCTC 8325 strain staO76 is SAOUHSC_01263 and has amino acid sequence SEQ ID NO: 112 (GI:88194996).

Useful staO76 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 112 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 112; and/or (b) comprising a fragment of at least V consecutive amino acids of SEQ ID NO: 112, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO76 proteins include variants of SEQ ID NO: 112. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 112. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 112 while retaining at least one epitope of SEQ ID NO: 112. The first 24 N-terminal amino acids of SEQ ID NO: 112 can usefully be omitted. Other fragments omit one or more protein domains.

staO77

The 'staO77' antigen is annotated as 'protein'. In the NCTC 8325 strain staO77 is SAOUHSC_01317 and has amino acid sequence SEQ ID NO: 113 (GI:88195047). Proteomic analysis has revealed that this protein is secreted or surface-exposed.

Useful staO77 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 113 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 113; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 113, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO77 proteins include variants of SEQ ID NO: 113. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 113. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 113 while retaining at least one epitope of SEQ ID NO: 113. The first 24 N-terminal amino acids of SEQ ID NO: 113 can usefully be omitted. Other fragments omit one or more protein domains.
99.5% or more) to SEQ ID NO: 113; and/or (b) comprising a fragment, of at least 'n' consecutive amino acids of SEQ ID NO: 113, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO77 proteins include variants of SEQ ID NO: 113. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 113. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 113 while retaining at least one epitope of SEQ ID NO: 113. The first 20 N-terminal amino acids of SEQ ID NO: 113 can usefully be omitted. Other fragments omit one or more protein domains.

staO78

The 'staO78' antigen is annotated as 'FtsK/SpoIIIE family protein'. In the NCTC 8325 strain staO78 is SAOUHSC_01857 and has amino acid sequence SEQ ID NO: 114 (GI:88195555).

Useful staO78 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 114 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 114; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 114, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO78 proteins include variants of SEQ ID NO: 114. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 114. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 114 while retaining at least one epitope of SEQ ID NO: 114. Other fragments omit one or more protein domains.

staO79

The 'staO79' antigen is annotated as 'serine protease SpIF'. In the NCTC 8325 strain staO79 is SAOUHSC_01935 and has amino acid sequence SEQ ID NO: 115 (GI:88195630).

Useful staO79 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 115 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 115; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 115, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO79 proteins include variants of SEQ ID NO: 115. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 115. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 115 while retaining at least one epitope of SEQ ID NO: 115. The first
36 N-terminal amino acids of SEQ ID NO: 115 can usefully be omitted. Other fragments omit one or more protein domains.

*sta*O80

The 'staO80' antigen is annotated as 'serine protease SpIE'. In the NCTC 8325 strain staO80 is SAOUHSC_01936 and has amino acid sequence SEQ ID NO: 116 (GI:88195631).

Useful staO80 antigens can elicit an antibody *(e.g. when administered to a human)* that recognises SEQ ID NO: 116 and/or may comprise an amino acid sequence: (a) having 50% or more identity *(e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more)* to SEQ ID NO: 116; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 116, wherein 'n' is 7 or more *(e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more)*. These staO80 proteins include variants of SEQ ID NO: 116. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 116. Other preferred fragments lack one or more amino acids *(e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more)* from the C-terminus and/or one or more amino acids *(e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more)* from the N-terminus of SEQ ID NO: 116 while retaining at least one epitope of SEQ ID NO: 116. The first 36 N-terminal amino acids of SEQ ID NO: 116 can usefully be omitted. Other fragments omit one or more protein domains.

*sta*O81

The 'staO81' antigen is annotated as 'serine protease SpI(D EC:3.4.21.19)'. In the NCTC 8325 strain staO81 is SAOUHSC_01938 and has amino acid sequence SEQ ID NO: 170 (GI:88195633).

Useful staO81 antigens can elicit an antibody *(e.g. when administered to a human)* that recognises SEQ ID NO: 170 and/or may comprise an amino acid sequence: (a) having 50% or more identity *(e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more)* to SEQ ID NO: 170; and/or (b) comprising a fragment of at least V consecutive amino acids of SEQ ID NO: 170, wherein 'n' is 7 or more *(e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more)*. These staO81 proteins include variants of SEQ ID NO: 170. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 170. Other preferred fragments lack one or more amino acids *(e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more)* from the C-terminus and/or one or more amino acids *(e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more)* from the N-terminus of SEQ ID NO: 170 while retaining at least one epitope of SEQ ID NO: 170. The first 36 N-terminal amino acids of SEQ ID NO: 170 can usefully be omitted. Other fragments omit one or more protein domains.

*sta*O82

The 'staO82' antigen is annotated as 'serine protease SpIC'. In the NCTC 8325 strain staO82 is SAOUHSC_01939 and has amino acid sequence SEQ ID NO: 117 (GI:88195634).
Useful staO82 antigens can elicit an antibody (e.g. when administered to a human) that recognises
SEQ ID NO: 117 and/or may comprise an amino acid sequence: (a) having 50% or more identity
(e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%,
99.5% or more) to SEQ ID NO: 117; and/or (b) comprising a fragment of at least 'n' consecutive
amino acids of SEQ ID NO: 117, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35,
40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These staO82 proteins include variants of SEQ ID NO:
117. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 117. Other preferred
fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the
C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from
the N-terminus of SEQ ID NO: 117 while retaining at least one epitope of SEQ ID NO: 117. The first
36 N-terminal amino acids of SEQ ID NO: 117 can usefully be omitted. Other fragments omit one or
more protein domains.

staO83
The 'staO83' antigen is annotated as 'serine protease SpIB'. In the NCTC 8325 strain staO83 is
SAOUHSC_01941 and has amino acid sequence SEQ ID NO: 118 (GI:88195635).

Useful staO83 antigens can elicit an antibody (e.g. when administered to a human) that recognises
SEQ ID NO: 118 and/or may comprise an amino acid sequence: (a) having 50% or more identity
(e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%,
99.5% or more) to SEQ ID NO: 118; and/or (b) comprising a fragment of at least 'n' consecutive
amino acids of SEQ ID NO: 118, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35,
40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These staO83 proteins include variants of SEQ ID NO:
118. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 118. Other preferred
fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the
C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from
the N-terminus of SEQ ID NO: 118 while retaining at least one epitope of SEQ ID NO: 118. The first
36 N-terminal amino acids of SEQ ID NO: 118 can usefully be omitted. Other fragments omit one or
more protein domains.

staO84
The 'staO84' antigen is annotated as 'serine protease SpIA'. In the NCTC 8325 strain staO84 is
SAOUHSC_01942 and has amino acid sequence SEQ ID NO: 119 (GI:88195636).

Useful staO84 antigens can elicit an antibody (e.g. when administered to a human) that recognises
SEQ ID NO: 119 and/or may comprise an amino acid sequence: (a) having 50% or more identity
(e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%,
99.5% or more) to SEQ ID NO: 119; and/or (b) comprising a fragment of at least 'n' consecutive
amino acids of SEQ ID NO: 119, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35,
40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These staO84 proteins include variants of SEQ ID NO:
119. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 119. Other preferred
fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 119 while retaining at least one epitope of SEQ ID NO: 119. The first 35 N-terminal amino acids of SEQ ID NO: 119 can usefully be omitted. Other fragments omit one or more protein domains.

\textit{staO85}

The 'sta085' antigen is annotated as 'staphylokinase precursor'. In the NCTC 8325 strain staO85 is SAOUHSC_02171 and has amino acid sequence SEQ ID NO: 120 (GI:88195848).

Useful staO85 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 120 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 120; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 120, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150 or more). These staO85 proteins include variants of SEQ ID NO: 120.

Preferred fragments of (b) comprise an epitope from SEQ ID NO: 120. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 120 while retaining at least one epitope of SEQ ID NO: 120. The first 27 N-terminal amino acids of SEQ ID NO: 120 can usefully be omitted. Other fragments omit one or more protein domains.

\textit{staO86}

The 'sta086' antigen is annotated as 'OxaA-like protein'. In the NCTC 8325 strain staO86 is SAOUHSC_02327 and has amino acid sequence SEQ ID NO: 121 (GI:88195993).

Useful staO86 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 121 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 121; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 121, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO86 proteins include variants of SEQ ID NO: 121. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 121. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 121 while retaining at least one epitope of SEQ ID NO: 121. The first 19 N-terminal amino acids of SEQ ID NO: 121 can usefully be omitted. Other fragments omit one or more protein domains.
staO87

The 'staO87' antigen is annotated as 'teicoplanin resistance protein TcaA'. In the NCTC 8325 strain staO87 is SAOUHSC_02635 and has amino acid sequence SEQ ID NO: 122 (GI:88196276).

Useful staO87 antigens can elicit an antibody (e.g. when administered to a human) that recognises
SEQ ID NO: 122 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 122; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 122, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO87 proteins include variants of SEQ ID NO: 122. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 122. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 122 while retaining at least one epitope of SEQ ID NO: 122. Other fragments omit one or more protein domains.

staO88

The 'staO88' antigen is annotated as 'esterase', hi the NCTC 8325 strain staO88 is SAOUHSC_02844 and has amino acid sequence SEQ ID NO: 123 (GI:88196477).

Useful staO88 antigens can elicit an antibody (e.g. when administered to a human) that recognises
SEQ ID NO: 123 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 123; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 123, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO88 proteins include variants of SEQ ID NO: 123. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 123. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 123 while retaining at least one epitope of SEQ ID NO: 123. The first 18 N-terminal amino acids of SEQ ID NO: 123 can usefully be omitted. Other fragments omit one or more protein domains.

staO89

The 'staO89' antigen is annotated as 'LysM domain protein'. In the NCTC 8325 strain staO89 is SAOUHSC_02855 and has amino acid sequence SEQ ID NO: 124 (GI:88196486).

Useful staO89 antigens can elicit an antibody (e.g. when administered to a human) that recognises
SEQ ID NO: 124 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 124; and/or (b) comprising a fragment of at least 'n' consecutive
amino acids of SEQ ID NO: 124, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100 or more). These sta089 proteins include variants of SEQ ID NO: 124. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 124. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 124 while retaining at least one epitope of SEQ ID NO: 124. The first 20 N-terminal amino acids of SEQ ID NO: 124 can usefully be omitted. Other fragments omit one or more protein domains.

sta090

The 'sta090' antigen is annotated as 'LysM domain protein'. In the NCTC 8325 strain sta090 is SAOUHSC_02883 and has amino acid sequence SEQ ID NO: 125 (GI:88196512).

Useful sta090 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 125 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 125; and/or (b) comprising a fragment of at least V consecutive amino acids of SEQ ID NO: 125, wherein V is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These sta090 proteins include variants of SEQ ID NO: 125. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 125. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 125 while retaining at least one epitope of SEQ ID NO: 125. The first 26 N-terminal amino acids of SEQ ID NO: 125 can usefully be omitted. Other fragments omit one or more protein domains.

sta091

The 'sta091' antigen is annotated as 'lipoprotein'. In the NCTC 8325 strain sta091 is SAOUHSC_00685 and has amino acid sequence SEQ ID NO: 126 (GI:88194450).

Useful sta091 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 126 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 126; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 126, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100 or more). These sta091 proteins include variants of SEQ ID NO: 126. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 126. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 126 while retaining at least one epitope of SEQ ID NO: 126. The first 15
N-terminal amino acids of SEQ ID NO: 126 can usefully be omitted. Other fragments omit one or more protein domains.

**staO92**

The 'staO92' antigen is annotated as 'M23/M37 peptidase domain protein'. In the NCTC 8325 strain staO92 is SAOUHSC_00174 and has amino acid sequence SEQ ID NO: 127 (GI:88193984).

Useful staO92 antigens can elicit an antibody (*e.g.* when administered to a human) that recognises SEQ ID NO: 127 and/or may comprise an amino acid sequence: (a) having 50% or more identity (*e.g.* 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 127; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 127, wherein 'n' is 7 or more (*e.g.* 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150 or more). These staO92 proteins include variants of SEQ ID NO: 127. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 127. Other preferred fragments lack one or more amino acids (*e.g.* 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (*e.g.* 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 127 while retaining at least one epitope of SEQ ID NO: 127. The first 25 N-terminal amino acids of SEQ ID NO: 127 can usefully be omitted. Other fragments omit one or more protein domains.

**staO93**

The 'staO93' antigen is annotated as 'protein'. In the NCTC 8325 strain staO93 is SAOUHSC_O1854 and has amino acid sequence SEQ ID NO: 128 (GI:88195552).

Useful staO93 antigens can elicit an antibody (*e.g.* when administered to a human) that recognises SEQ ID NO: 128 and/or may comprise an amino acid sequence: (a) having 50% or more identity (*e.g.* 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 128; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 128, wherein 'n' is 7 or more (*e.g.* 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO93 proteins include variants of SEQ ID NO: 128. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 128. Other preferred fragments lack one or more amino acids (*e.g.* 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (*e.g.* 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 128 while retaining at least one epitope of SEQ ID NO: 128. Other fragments omit one or more protein domains.

**staO94**

The 'staO94' antigen is annotated as 'protein'. In the NCTC 8325 strain staO94 is SAOUHSC_O15512 and has amino acid sequence SEQ ID NO: 129 (GI:88195226).

Useful staO94 antigens can elicit an antibody (*e.g.* when administered to a human) that recognises SEQ ID NO: 129 and/or may comprise an amino acid sequence: (a) having 50% or more identity...
(e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 129; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 129, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO94 proteins include variants of SEQ ID NO: 129. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 129. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 129 while retaining at least one epitope of SEQ ID NO: 129. The first 17 N-terminal amino acids of SEQ ID NO: 129 can usefully be omitted. Other fragments omit one or more protein domains.

staO95

The 'staO95' antigen is annotated as 'superantigen-like protein'. In the NCTC 8325 strain staO95 is SAOUHSC_00383 and has amino acid sequence SEQ ID NO: 130 (GI:88194180). In the Newman strain it is nwmn_0388 (GI: 15 1220600).

Useful staO95 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 130 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 130; and/or (b) comprising a fragment of at least W consecutive amino acids of SEQ ID NO: 130, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These staO95 proteins include variants of SEQ ID NO: 130. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 130. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 130 while retaining at least one epitope of SEQ ID NO: 130. The first 32 N-terminal amino acids of SEQ ID NO: 130 can usefully be omitted. Other fragments omit one or more protein domains.

staO96

The 'staO96' antigen is annotated as 'superantigen-like protein'. In the NCTC 8325 strain staO96 is SAOUHSC_00384 and has amino acid sequence SEQ ID NO: 131 (GI:88194181).

Useful staO96 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 131 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 131; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 131, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These staO96 proteins include variants of SEQ ID NO: 131. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 131. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the
C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 131 while retaining at least one epitope of SEQ ID NO: 131. The first 30 N-terminal amino acids of SEQ ID NO: 131 can usefully be omitted. Other fragments omit one or more protein domains.

staO97
The 'staO97' antigen is annotated as 'superantigen-like protein'. In the NCTC 8325 strain staO97 is SAOUHSC_00386 and has amino acid sequence SEQ ID NO: 132 (GI:88194182).

Useful staO97 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 132 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 132; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 132, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO97 proteins include variants of SEQ ID NO: 132. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 132. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 132 while retaining at least one epitope of SEQ ID NO: 132. The first 30 N-terminal amino acids of SEQ ID NO: 132 can usefully be omitted. Other fragments omit one or more protein domains.

staO98
The 'staO98' antigen is annotated as 'superantigen-like protein'. In the NCTC 8325 strain staO98 is SAOUHSC_00389 and has amino acid sequence SEQ ID NO: 133 (GL88194184). In the Newman strain it is nwmn_0391 (GI: 151220603).

Useful staO98 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 133 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 133; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 133, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These staO98 proteins include variants of SEQ ID NO: 133. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 133. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 133 while retaining at least one epitope of SEQ ID NO: 133. The first 30 N-terminal amino acids of SEQ ID NO: 133 can usefully be omitted. Other fragments omit one or more protein domains.
The 'sta099' antigen is annotated as 'superantigen-like protein 5'. In the NCTC 8325 strain staO99 is SAOUHSC_00390 and has amino acid sequence SEQ ID NO: 134 (GL88194185).

Useful staO99 antigens can elicit an antibody (*e.g.* when administered to a human) that recognises SEQ ID NO: 134 and/or may comprise an amino acid sequence: (a) having 50% or more identity (*e.g.* 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 134; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 134, wherein 'n' is 7 or more (*e.g.* 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These staO99 proteins include variants of SEQ ID NO: 134. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 134. Other preferred fragments lack one or more amino acids (*e.g.* 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (*e.g.* 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 134 while retaining at least one epitope of SEQ ID NO: 134. The first 30 N-terminal amino acids of SEQ ID NO: 134 can usefully be omitted. Other fragments omit one or more protein domains.

The 'stalOO' antigen is annotated as 'superantigen-like protein'. In the NCTC 8325 strain stalOO is SAOUHSC_00391 and has amino acid sequence SEQ ID NO: 135 (GI:88194186).

Useful stalOO antigens can elicit an antibody (*e.g.* when administered to a human) that recognises SEQ ID NO: 135 and/or may comprise an amino acid sequence: (a) having 50% or more identity (*e.g.* 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 135; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 135, wherein 'n' is 7 or more (*e.g.* 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These stalOO proteins include variants of SEQ ID NO: 135. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 135. Other preferred fragments lack one or more amino acids (*e.g.* 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (*e.g.* 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 135 while retaining at least one epitope of SEQ ID NO: 135. The first 30 N-terminal amino acids of SEQ ID NO: 135 can usefully be omitted. Other fragments omit one or more protein domains.

The 'stalOl' antigen is annotated as 'superantigen-like protein 7'. In the NCTC 8325 strain stalOl is SAOUHSC_00392 and has amino acid sequence SEQ ID NO: 136 (GL88194187). In the Newman strain it is nwmn_0394 (GI:151220606).

Useful stalOl antigens can elicit an antibody (*e.g.* when administered to a human) that recognises SEQ ID NO: 136 and/or may comprise an amino acid sequence: (a) having 50% or more identity
(e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 136; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 136, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These stalO1 proteins include variants of SEQ ID NO: 136. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 136. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 136 while retaining at least one epitope of SEQ ID NO: 136. The first 30 N-terminal amino acids of SEQ ID NO: 136 can usefully be omitted. Other fragments omit one or more protein domains.

**stalO2**

The 'stalO2' antigen is annotated as 'superantigen-like protein', hi the NCTC 8325 strain stalO2 is SAOUHSC_00393 and has amino acid sequence SEQ ID NO: 137 (GI:88194188).

Useful stalO2 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 137 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 137; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 137, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These stalO2 proteins include variants of SEQ ID NO: 137. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 137. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 137 while retaining at least one epitope of SEQ ID NO: 137. The first 17 N-terminal amino acids of SEQ ID NO: 137 can usefully be omitted. Other fragments omit one or more protein domains.

**stalO3**

The 'stalO3' antigen is annotated as 'superantigen-like protein', hi the NCTC 8325 strain stalO3 is SAOUHSC_00394 and has amino acid sequence SEQ ID NO: 138 (GI:88194189).

Useful stalO3 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 138 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 138; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 138, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These stalO3 proteins include variants of SEQ ID NO: 138. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 138. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from
the N-terminus of SEQ ID NO: 138 while retaining at least one epitope of SEQ ID NO: 138. The first 23 N-terminal amino acids of SEQ ID NO: 138 can usefully be omitted. Other fragments omit one or more protein domains.

stalO4

The ‘stalO4’ antigen is annotated as ‘superantigen-like protein’. In the NCTC 8325 strain stalO4 is SAOUHSC_00395 and has amino acid sequence SEQ ID NO: 139 (GI:88194190).

Useful stalO4 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 139 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 139; and/or (b) comprising a fragment of at least ‘n’ consecutive amino acids of SEQ ID NO: 139, wherein ‘n’ is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These stalO4 proteins include variants of SEQ ID NO: 139. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 139. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 139 while retaining at least one epitope of SEQ ID NO: 139. Other fragments omit one or more protein domains.

stalO5

The ‘stalO5’ antigen is annotated as ‘superantigen-like protein’. In the NCTC 8325 strain stalO5 is SAOUHSC_00399 and has amino acid sequence SEQ ID NO: 140 (GI:88194194). In the Newman strain it is nwmn_0400 (GI:151220612).

Useful stalO5 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 140 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 140; and/or (b) comprising a fragment of at least ‘n’ consecutive amino acids of SEQ ID NO: 140, wherein ‘n’ is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These stalO5 proteins include variants of SEQ ID NO: 140. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 140. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 140 while retaining at least one epitope of SEQ ID NO: 140. The first 30 N-terminal amino acids of SEQ ID NO: 140 can usefully be omitted. Other fragments omit one or more protein domains.

stalOô

The ‘stalOô’ antigen is annotated as ‘hypoethetical protein’. In the NCTC 8325 strain stalOô is SAOUHSC_0115 and has amino acid sequence SEQ ID NO: 141 (GI:88194861).
Useful stalO6 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 141 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 141; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 141, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100 or more). These stalO6 proteins include variants of SEQ ID NO: 141. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 141. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 141 while retaining at least one epitope of SEQ ID NO: 141. The first 16 N-terminal amino acids of SEQ ID NO: 141 can usefully be omitted. Other fragments omit one or more protein domains.

stalO7

The 'stalO7' antigen is annotated as 'hypothetical protein'. In the NCTC 8325 strain stalO7 is SAOUHSC_00354 and has amino acid sequence SEQ ID NO: 177 (GI:88194153).

Useful stalO7 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 177 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 177; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 177, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These stalO7 proteins include variants of SEQ ID NO: 177. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 177. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 177 while retaining at least one epitope of SEQ ID NO: 177. The first 35 N-terminal amino acids of SEQ ID NO: 177 can usefully be omitted. Other fragments omit one or more protein domains.

stalO8

The 'stalO8' antigen is annotated as 'hypothetical protein'. In the NCTC 8325 strain stalO8 is SAOUHSC_00717 and has amino acid sequence SEQ ID NO: 178 (GI:88194482).

Useful stalO8 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 178 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 178; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 178, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100 or more). These stalO8 proteins include variants of SEQ ID NO: 178. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 178. Other preferred fragments
lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 178 while retaining at least one epitope of SEQ ID NO: 178. The first 20 N-terminal amino acids of SEQ ID NO: 178 can usefully be omitted. Other fragments omit one or more protein domains.

stalO9

The 'stalO9' antigen is annotated as "N-acetylmuramoyl-L-alanine amidase '. In the NCTC 8325 strain stalO9 is SAOUHSC_02979 and has amino acid sequence SEQ ID NO: 179 (GI:88196599).

Useful stalO9 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 179 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 179; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 179, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These stalO9 proteins include variants of SEQ ID NO: 179. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 179. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 179 while retaining at least one epitope of SEQ ID NO: 179. The first 27 N-terminal amino acids of SEQ ID NO: 179 can usefully be omitted. Other fragments omit one or more protein domains.

stalO

The 'stalO' antigen is annotated as 'hypothetical protein'. In the NCTC 8325 strain stalO is SAOUHSC_01039 and has amino acid sequence SEQ ID NO: 180 (GI:88194791).

Useful stalO antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 180 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 180; and/or (b) comprising a fragment of at least V consecutive amino acids of SEQ ID NO: 180, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These stalO proteins include variants of SEQ ID NO: 180. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 180. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 180 while retaining at least one epitope of SEQ ID NO: 180. The first 19 N-terminal amino acids of SEQ ID NO: 180 can usefully be omitted. Other fragments omit one or more protein domains.
The 'stall I' antigen is annotated as 'hypothetical protein'. In the NCTC 8325 strain stalll is SAOUHSC_01005 and has amino acid sequence SEQ ID NO: 181 (GI:88194760).

Useful stall1 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 181 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 181; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 181, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100 or more). These stall 1 proteins include variants of SEQ ID NO: 181.

Preferred fragments of (b) comprise an epitope from SEQ ID NO: 181. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 181 while retaining at least one epitope of SEQ ID NO: 181. The first 20 N-terminal amino acids of SEQ ID NO: 181 can usefully be omitted. Other fragments omit one or more protein domains.

The 'stall I2' antigen is annotated as a putative 'ABC transporter, substrate-binding protein'. In the NCTC 8325 strain stall2 is SAOUHSC_00634 and has amino acid sequence SEQ ID NO: 182 (GI:88194402).

Useful stall2 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 182 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 182; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 182, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These stall 2 proteins include variants of SEQ ID NO: 182. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 182. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 182 while retaining at least one epitope of SEQ ID NO: 182. The first 17 N-terminal amino acids of SEQ ID NO: 182 can usefully be omitted. Other fragments omit one or more protein domains.

A Stal 12 antigen can usefully be included in a composition in combination with a StaO73 [74].

The 'stal I3' antigen is annotated as 'hypothetical protein'. In the NCTC 8325 strain stal 13 is SAOUHSC_00728 and has amino acid sequence SEQ ID NO: 183 (GL88194493).
Useful stal 13 antigens can elicit an antibody (e.g. when administered to a human) that recognises SI NO: 183 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 183; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 183, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These stal 13 proteins include variants of SEQ ID NO: 183. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 183. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 183 while retaining at least one epitope of SEQ ID NO: 183. The first 173 N-terminal amino acids of SEQ ID NO: 183 can usefully be omitted. Other fragments omit one or more protein domains.

stalkH

The 'stalk 14' antigen is annotated as 'hypothetical protein'. In the NCTC 8325 strain stalk 14 is SAOUHSC_00810 and has amino acid sequence SEQ ID NO: 184 (GL88194570).

Useful stalk 14 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 184 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 184; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 184, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150 or more). These stalk 14 proteins include variants of SEQ ID NO: 184. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 184. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 184 while retaining at least one epitope of SEQ ID NO: 184. Other fragments omit one or more protein domains.

stalks

The 'stalk 15' antigen is annotated as 'hypothetical protein'. In the NCTC 8325 strain stalk 15 is SAOUHSC_00817 and has amino acid sequence SEQ ID NO: 185 (GI:88194576).

Useful stalk 15 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 185 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 185; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 185, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150 or more). These stalk 15 proteins include variants of SEQ IDNO: 185. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 185. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-
terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 185 while retaining at least one epitope of SEQ ID NO: 185. The first 18 N-terminal amino acids of SEQ ID NO: 185 can usefully be omitted. Other fragments omit one or more protein domains.

5 **stalló**
The 'stal 16' antigen is annotated as 'formyl peptide receptor-like 1 inhibitory protein'. In the NCTC 8325 strain stalló is SAOUHSCJ112 and has amino acid sequence SEQ ID NO: 186 (GI:88194858).

Useful stalló antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 186 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 186; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 186, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100 or more). These stalló proteins include variants of SEQ ID NO: 186.

Preferred fragments of (b) comprise an epitope from SEQ ID NO: 186. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 186 while retaining at least one epitope of SEQ ID NO: 186. The first 20 N-terminal amino acids of SEQ ID NO: 186 can usefully be omitted. Other fragments omit one or more protein domains.

**stall7**
The 'stal 17' antigen is annotated as 'truncated beta-hemolysin'. In the NCTC 8325 strain stall 17 is SAOUHSC_02240 and has amino acid sequence SEQ ID NO: 187 (GI:88195913).

Useful stall 17 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 187 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 187; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 187, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These stall 17 proteins include variants of SEQ ID NO: 187. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 187. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 187 while retaining at least one epitope of SEQ ID NO: 187. Other fragments omit one or more protein domains.
The 'stal 18' antigen is annotated as 'cell division protein FtsZ'. In the NCTC 8325 strain stall is SAOUHSCJ1 150 and has amino acid sequence SEQ ID NO: 188 (GI:88194892).

Useful stall 8 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 188 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 188; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 188, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These stall 18 proteins include variants of SEQ ID NO: 188. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 188. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 188 while retaining at least one epitope of SEQ ID NO: 188. Other fragments omit one or more protein domains.

The 'stal 19' antigen is annotated as 'thioredoxin'. In the NCTC 8325 strain stal 19 is SAOUHSCJ1 100 and has amino acid sequence SEQ ID NO: 200 (GI:88194846).

Useful stal 19 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 200 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 200; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 200, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100 or more). These stal 19 proteins include variants of SEQ ID NO: 200. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 200. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 200 while retaining at least one epitope of SEQ ID NO: 200. Other fragments omit one or more protein domains.

The 'stal 20' antigen is annotated as 'alkyl hydroperoxide reductase subunit C'. In the NCTC 8325 strain stal20 is SAOUHSCC_00365 and has amino acid sequence SEQ ID NO: 201 (GI:88194163).

Useful stal 20 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 201 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 201; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 201, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35,
40, 50, 60, 70, 80, 90, 100, 150 or more). These stal20 proteins include variants of SEQ ID NO: 201. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 201. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 201 while retaining at least one epitope of SEQ ID NO: 201. Other fragments omit one or more protein domains.

NW_6
The NW_6 antigen is annotated as 'secreted von Willebrand factor-binding protein precursor'. In the Newman strain NW_6 is NWMN_0757 and has amino acid sequence SEQ ID NO: 142 (GI: 151220969).

Useful NW_6 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 142 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 142; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 142, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These NW_6 proteins include variants of SEQ ID NO: 142. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 142. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 142 while retaining at least one epitope of SEQ ID NO: 142. The first 13 N-terminal amino acids of SEQ ID NO: 142 can usefully be omitted. Other fragments omit one or more protein domains.

NW_9
The "NW_9" antigen is annotated as 'lipoprotein'. In the Newman strain NW_9 is NWMN_0958 and has amino acid sequence SEQ ID NO: 143 (GI: 151221170).

Useful NW_9 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 143 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 143; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 143, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). These NW_9 proteins include variants of SEQ ID NO: 143. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 143. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 143 while retaining at least one epitope of SEQ ID NO: 143. The first 19 N-terminal amino acids of SEQ ID NO: 143 can usefully be omitted. Other fragments omit one or more protein domains.
The NW_10 antigen is annotated as 'fibrinogen binding-related protein'. In the Newman strain NW_10 is NWMN_1066 and has amino acid sequence SEQ ID NO: 144 (GI:151221278).

Useful NW_10 antigens can elicit an antibody (e.g. when administered to a human) that recognises

SEQ ID NO: 144 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 144; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 144, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100 or more). These NW_10 proteins include variants of SEQ ID NO: 144.

Preferred fragments of (b) comprise an epitope from SEQ ID NO: 144. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 144 while retaining at least one epitope of SEQ ID NO: 144. The first 20 N-terminal amino acids of SEQ ID NO: 144 can usefully be omitted. Other fragments omit one or more protein domains.

NW_7

The NW_7' antigen is annotated as 'staphylococcal complement inhibitor SCIN'. In the Newman strain NW_7 is NWMN_1876 and has amino acid sequence SEQ ID NO: 145 (GI: 15122088).

Useful NW_7 antigens can elicit an antibody (e.g. when administered to a human) that recognises

SEQ ID NO: 145 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 145; and/or (b) comprising a fragment of at least V consecutive amino acids of SEQ ID NO: 145, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100 or more). These NW_7 proteins include variants of SEQ ID NO: 145.

Preferred fragments of (b) comprise an epitope from SEQ ID NO: 145. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 145 while retaining at least one epitope of SEQ ID NO: 145. The first 17 N-terminal amino acids of SEQ ID NO: 145 can usefully be omitted. Other fragments omit one or more protein domains.

NW_8

The NW_8' antigen is annotated as 'chemotaxis-inhibiting protein CHIPS'. In the Newman strain NWJ is NWMN_1877 and has amino acid sequence SEQ IDNO: 146 (GI: 15122089).

Useful NWJ antigens can elicit an antibody (e.g. when administered to a human) that recognises

SEQ ID NO: 146 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%,
99.5% or more) to SEQ ID NO: 146; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 146, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100 or more). These NWJ proteins include variants of SEQ ID NO: 146. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 146. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 146 while retaining at least one epitope of SEQ ID NO: 146. The first 19 N-terminal amino acids of SEQ ID NO: 146 can usefully be omitted. Other fragments omit one or more protein domains.

NWJ

The NWJ antigen is annotated as 'enterotoxin type A precursor'. In the Newman strain NWJ is NWMNJ 883 and has amino acid sequence SEQ ID NO: 147 (GI: 151222095).

Useful NWJ antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 147 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 147; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 147, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These NWJ proteins include variants of SEQ ID NO: 147. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 147. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 147 while retaining at least one epitope of SEQ ID NO: 147. The first 16 N-terminal amino acids of SEQ ID NO: 147 can usefully be omitted. Other fragments omit one or more protein domains.

NWJ

The TsTWJ' antigen is annotated as 'lipoprotein'. In the Newman strain NWJ is NWMN_1924 and has amino acid sequence SEQ ID NO: 148 (GI: 151222136).

Useful NWJ antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 148 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 148; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 148, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150 or more). These NWJ proteins include variants of SEQ ID NO: 148. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 148. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 148 while retaining at least one epitope of SEQ ID NO: 148. The first 17
N-terminal amino acids of SEQ ID NO: 148 can usefully be omitted. Other fragments omit one or more protein domains.

**NWJ**

The 'NW_5' antigen is annotated as 'cell wall surface anchor family protein'. In the Newman strain NWJ is NWMN_2392 and has amino acid sequence SEQ ID NO: 149 (GI: 151222604).

Useful NW_5 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 149 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 149; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 149, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These NWJ proteins include variants of SEQ ID NO: 149. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 149. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 149 while retaining at least one epitope of SEQ ID NO: 149. The first 52 N-terminal amino acids of SEQ ID NO: 149 can usefully be omitted. Other fragments omit one or more protein domains.

**Hybrid polypeptides**

Antigens used in the invention may be present in the composition as individual separate polypeptides. Where more than one antigen is used, however, they do not have to be present as separate polypeptides. Instead, at least two (e.g. 2, 3, 4, 5, or more) antigens can be expressed as a single polypeptide chain (a 'hybrid' polypeptide). Hybrid polypeptides offer two main advantages: first, a polypeptide that may be unstable or poorly expressed on its own can be assisted by adding a suitable hybrid partner that overcomes the problem; second, commercial manufacture is simplified as only one expression and purification need be employed in order to produce two polypeptides which are both antigenically useful.

The hybrid polypeptide may comprise two or more polypeptide sequences from the first antigen group. The hybrid polypeptide may comprise one or more polypeptide sequences from the first antigen group and one or more polypeptide sequences from the second antigen group. Moreover, the hybrid polypeptide may comprise two or more polypeptide sequences from each of the antigens listed above, or two or more variants of the same antigen in the cases in which the sequence has partial variability across strains.

Hybrids consisting of amino acid sequences from two, three, four, five, six, seven, eight, nine, or ten antigens are useful, in particular, hybrids consisting of amino acid sequences from two, three, four, or five antigens are preferred, such as two or three antigens.
Different hybrid polypeptides may be mixed together in a single formulation. Hybrids may be combined with non-hybrid antigens selected from the first, second or third antigen groups. Within such combinations, an antigen may be present in more than one hybrid polypeptide and/or as a non-hybrid polypeptide. It is preferred, however, that an antigen is present either as a hybrid or as a non-hybrid, but not as both.

The hybrid polypeptides can also be combined with conjugates or non-*S. aureus* antigens as described above.

Hybrid polypeptides can be represented by the formula NH₂-A-(-X-L-J-B-COOH, wherein: X is an amino acid sequence of a *S. aureus* antigen, as described above; L is an optional linker amino acid sequence; A is an optional N-terminal amino acid sequence; B is an optional C-terminal amino acid sequence; n is an integer of 2 or more (*e.g.* 2, 3, 4, 5, 6, *etc.*). Usually n is 2 or 3.

If a -X- moiety has a leader peptide sequence in its wild-type form, this may be included or omitted in the hybrid protein. In some embodiments, the leader peptides will be deleted except for that of the -X- moiety located at the N-terminus of the hybrid protein *i.e.* the leader peptide of X₁ will be retained, but the leader peptides of X₂ ... Xₙ will be omitted. This is equivalent to deleting all leader peptides and using the leader peptide of X₁ as moiety -A-.

For each n instances of {-X-L-}, linker amino acid sequence -L- may be present or absent. For instance, when n =2 the hybrid may be NH₂-X₁-L₁-X₂-L₂-COOH, NH₂-X₁-L₁-X₂-COOH, NH₂-X₁-L₁-X₂-COOH, NH₂-X₁-L₁-X₂-COOH, etc. Linker amino acid sequence(s) -L- will typically be short (*e.g.* 20 or fewer amino acids *i.e.* 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, 2, 1). Examples comprise short peptide sequences which facilitate cloning, poly-glycine linkers (*i.e.* comprising Glyₙ where n = 2, 3, 4, 5, 6, 7, 8, 9, 10 or more), and histidine tags (*i.e.* Hisₙ where n = 3, 4, 5, 6, 7, 8, 9, 10 or more). Other suitable linker amino acid sequences will be apparent to those skilled in the art. A useful linker is GSGGGG (SEQ ID NO: 171) or GSGSGGGG (SEQ ID NO: 172), with the Gly-Ser dipeptide being formed from a *BamH* restriction site (or two of them, to form the SEQ ID NO: 230 tetrapeptide), thus aiding cloning and manipulation, and the (Gly)₄ tetrapeptide (SEQ ID NO: 227) being a typical poly-glycine linker. Other suitable linkers, particularly for use as the final Lₙ are ASGGGS (SEQ ID NO: 173 *e.g.* encoded by SEQ ID NO: 174) or a Leu-Glu dipeptide.

-A- is an optional N-terminal amino acid sequence. This will typically be short (*e.g.* 40 or fewer amino acids *i.e.* 40, 39, 38, 37, 36, 35, 34, 33, 32, 31, 30, 29, 28, 27, 26, 25, 24, 23, 22, 21, 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, 2, 1). Examples include leader sequences to direct protein trafficking, or short peptide sequences which facilitate cloning or purification (*e.g.* histidine tags *i.e.* Hisₙ where n = 3, 4, 5, 6, 7, 8, 9, 10 or more). Other suitable N-terminal amino acid sequences will be apparent to those skilled in the art. *If* lacks its own N-terminus methionine, -A- is preferably an oligopeptide (*e.g.* with 1, 2, 3, 4, 5, 6, 7 or 8 amino acids) which provides a N-terminus methionine *e.g.* Met-Ala-Ser, or a single Met residue.
-B- is an optional C-terminal amino acid sequence. This will typically be short (e.g. 40 or fewer amino acids \( i.e. 39, 38, 37, 36, 35, 34, 33, 32, 31, 30, 29, 28, 27, 26, 25, 24, 23, 22, 21, 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, 2, 1 \)). Examples include sequences to direct protein trafficking, short peptide sequences which facilitate cloning or purification (e.g. comprising histidine tags \( i.e. \text{His}_n \), where \( n = 3, 4, 5, 6, 7, 8, 9, 10 \) or more, such as SEQ ID NO: 226), or sequences which enhance protein stability. Other suitable C-terminal amino acid sequences will be apparent to those skilled in the art.

One hybrid polypeptide of the invention may include both EsxA and EsxB antigens. These may be in either order, N- to C- terminus. SEQ ID NOs: 151 (‘EsxAB’; encoded by SEQ ID NO: 169) and 152 (‘EsxBA’) are examples of such hybrids, both having hexapeptide linkers ASGGGS (SEQ ID NO: 173). Another ‘EsxAB’ hybrid comprises SEQ ID NO: 241, which may be provided with a N-terminus methionine (e.g. SEQ ID NO: 250).

Another hybrid polypeptide of the invention may include both SdrD and SdrE antigens. These may be in either order, N- to C- terminus. SEQ ID NO: 168 (‘SdrED’ is an example of such a hybrid, having a hexapeptide linker ASGGGS (SEQ ID NO: 173).

Another hybrid polypeptide of the invention may include both CIfB and SdrD antigens. These may be in either order, N- to C- terminus. SEQ ID NO: 202 (‘CIfB-SdrD’) is an example of such a hybrid, having a hexapeptide linker ASGGGS (SEQ ID NO: 173). SEQ ID NO: 203 (‘SdrD-CIfB’) is another example of such a hybrid, having a hexapeptide linker ASGGGS (SEQ ID NO: 173). SEQ ID NO: 211 (‘CIfB-N3-sdrD-N3’) is another example of such a hybrid, where the N3 fragments of CIfB and SdrD are joined by hexapeptide linker ASGGGS (SEQ ID NO: 173).

Another hybrid polypeptide of the invention may include both IsdA and EsxA antigens. These may be in either order, N- to C- terminus. SEQ ID NO: 204 (‘IsdA-EsxA’) is an example of such a hybrid, having a hexapeptide linker ASGGGS (SEQ ID NO: 173). SEQ ID NO: 209 (‘IsdA40-184-esxA’) is another example of such a hybrid, in which ISdA\(_{40-184}\) is joined to EsxA via linker ASGGGS (SEQ ID NO: 173).

Another hybrid polypeptide of the invention may include both IsdA and sta006 antigens. These may be in either order, N- to C- terminus. SEQ ID NO: 221 (‘IsdA40-184-sta006’) is an example of such a hybrid, in which ISdA\(_{40-184}\) is joined to Sta006 via hexapeptide linker ASGGGS (SEQ ID NO: 173).

Another hybrid polypeptide of the invention may include both H1a and sta006 antigens. These may be in either order, N- to C- terminus. SEQ ID NO: 222 (H1aH35L-sta006) is an example of such a hybrid, in which a H35L mutant of H1a is joined to Sta006 via hexapeptide linker ASGGGS (SEQ ID NO: 173).

Another hybrid polypeptide of the invention may include both H1a and Emp antigens. These may be in either order, N- to C- terminus. SEQ ID NO: 205 (H1aH35L-Emp) is an example of such a
hybrid, in which a H35L mutant HIa is joined to Emp via linker ASGGGS (SEQ ID NO: 173). SEQ ID NO: 206 ('Hla27-76-Emp') is another example of such a hybrid, in which a HIa fragment is joined to Emp via linker ASGGGS (SEQ ID NO: 173); SEQ ID NO: 207 is a H35L mutant of SEQ ID NO: 206. SEQ ID NO: 208 ('HlaPSGS-Emp') is another example of such a hybrid, in which a HIa mutant is joined to Emp via linker ASGGGS (SEQ ID NO: 173).

Another hybrid polypeptide of the invention may include IsdA and EsxA and EsxB antigens. These may be in any order, N- to C- terminus. SEQ ID NO: 210 ('IsdA40-184-esxAB') is an example of such a triple hybrid, in which IsdA40-184 is joined to EsxAB via linker ASGGGS (SEQ ID NO: 173). The EsxAB already includes the same linker, so SEQ ID NO: 210 includes two of these linkers. SEQ ID NO: 212 ('IsdA-esxAB') is another example of such a triple hybrid, in which IsdA is joined to EsxAB via linker ASGGGS (SEQ ID NO: 173).

Another hybrid polypeptide of the invention may include HIa and EsxA and EsxB antigens. These may be in any order, N- to C- terminus. SEQ ID NO: 220 ('HlaH35L-esxAB') is an example of such a triple hybrid, in which a H35L mutant of HIa is joined to EsxAB via linker ASGGGS (SEQ ID NO: 173). The EsxAB already includes the same linker, so SEQ ID NO: 220 includes two of these linkers. Another example of a hybrid polypeptide including HIa and EsxA and EsxB antigens is SEQ ID NO: 237 ('HlaH35L-esxAB' as used in the examples), in which a H35L mutant of HIa is joined to EsxA via linker APTARG (SEQ ID NO: 239) to replace its N-terminus, then to EsxB via linker ASGGGS (SEQ ID NO: 173) to replace its N-terminus. This hybrid can be provided with a suitable N-terminal sequence such as SEQ ID NO: 240.

Another hybrid polypeptide of the invention may include sta006 and EsxA and EsxB antigens. These may be in any order, N- to C- terminus. SEQ ID NO: 223 ('sta006-esxAB') is an example of such a triple hybrid, in which sta006 is joined to EsxAB via linker ASGGGS (SEQ ID NO: 173). The EsxAB already includes the same linker, so SEQ ID NO: 223 includes two of these linkers. Another example of a hybrid polypeptide including sta006 and EsxA and EsxB antigens is SEQ ID NO: 238 ('sta006-esxAB' as used in the examples), in which a sta006 is joined to EsxA via linker APTARG (SEQ ID NO: 239) to replace its N-terminus, then to EsxB via linker ASGGGS (SEQ ID NO: 173) to replace its N-terminus. This hybrid can be provided with a suitable N-terminal sequence such as SEQ ID NO: 240.

Usefully, these hybrid polypeptides can elicit an antibody (e.g. when administered to a human) that recognise each of the wild-type staphylococcal proteins (e.g. as shown in the sequence listing) represented in the hybrid e.g. which recognise both wild-type EsxA and wild-type EsxB, or which recognise both wild-type SdrD and wild-type SdrE, or which recognise both wild-type SdrD and wild-type CIIIB, or which recognise both wild-type IsdA and wild-type EsxA, or which recognise both wild-type IsdA and wild-type sta006, or which recognise both wild-type HIa and wild-type Emp, or which recognise wild-type...
IsdA and wild-type EsxA and wild-type EsxB, or which recognise wild-type Hla and wild-type EsxA and wild-type EsxB, or which recognise wild-type sta006 and wild-type EsxA and wild-type EsxB.

**Polypeptides used with the invention**

Polypeptides used with the invention can take various forms (e.g. native, fusions, glycosylated, non-glycosylated, lipiddated, non-lipiddated, phosphorylated, non-phosphorylated, myristoylated, non-myristoylated, monomeric, multimeric, particulate, denatured, etc.).

Polypeptides used with the invention can be prepared by various means (e.g. recombinant expression, purification from cell culture, chemical synthesis, etc.). Recombinantly-expressed proteins are preferred, particularly for hybrid polypeptides.

Polypeptides used with the invention are preferably provided in purified or substantially purified form i.e. substantially free from other polypeptides (e.g. free from naturally-occurring polypeptides), particularly from other staphylococcal or host cell polypeptides, and are generally at least about 50% pure (by weight), and usually at least about 90% pure i.e. less than about 50%, and more preferably less than about 10% (e.g. 5%) of a composition is made up of other expressed polypeptides. Thus the antigens in the compositions are separated from the whole organism with which the molecule is expressed.

Polypeptides used with the invention are preferably staphylococcal polypeptides.

The term "polypeptide" refers to amino acid polymers of any length. The polymer may be linear or branched, it may comprise modified amino acids, and it may be interrupted by non-amino acids. The terms also encompass an amino acid polymer that has been modified naturally or by intervention; for example, disulfide bond formation, glycosylation, lipiddation, acetylation, phosphorylation, or any other manipulation or modification, such as conjugation with a labeling component. Also included are, for example, polypeptides containing one or more analogs of an amino acid (including, for example, unnatural amino acids, etc.), as well as other modifications known in the art. Polypeptides can occur as single chains or associated chains.

The invention provides polypeptides comprising a sequence -P-Q- or -Q-P-, wherein: -P- is an amino acid sequence as defined above and -Q- is not a sequence as defined above i.e. the invention provides fusion proteins. Where the N-terminus codon of -P- is not ATG, but this codon is not present at the N-terminus of a polypeptide, it will be translated as the standard amino acid for that codon rather than as a Met. Where this codon is at the N-terminus of a polypeptide, however, it will be translated as Met. Examples of -Q- moieties include, but are not limited to, histidine tags (i.e. His<sub>n</sub> where n = 3, 4, 5, 6, 7, 8, 9, 10 or more), maltose-binding protein, or glutathione-S-transferase (GST).

The invention also provides a process for producing a polypeptide of the invention, comprising the step of culturing a host cell transformed with nucleic acid of the invention under conditions which induce polypeptide expression.
Although expression of the polypeptides of the invention may take place in a *Staphylococcus*, the invention will usually use a heterologous host for expression (recombinant expression). The heterologous host may be prokaryotic (e.g. a bacterium) or eukaryotic. It may be *E.coli*, but other suitable hosts include *Bacillus subtilis*, *Vibrio cholerae*, *Salmonella typhi*, *Salmonella typhimurium*, *Neisseria lactamica*, *Neisseria cinerea*, *Mycobacteria* (e.g. *M.tuberculosis*), yeasts, etc. Compared to the wild-type *S.aureus* genes encoding polypeptides of the invention, it is helpful to change codons to optimise expression efficiency in such hosts without affecting the encoded amino acids.

The invention provides a process for producing a polypeptide of the invention, comprising the step of synthesising at least part of the polypeptide by chemical means.

**Nucleic acids**

The invention also provides nucleic acid encoding polypeptides and hybrid polypeptides of the invention. It also provides nucleic acid comprising a nucleotide sequence that encodes one or more polypeptides or hybrid polypeptides of the invention.

The invention also provides nucleic acid comprising nucleotide sequences having sequence identity to such nucleotide sequences. Identity between sequences is preferably determined by the Smith-Waterman homology search algorithm as described above. Such nucleic acids include those using alternative codons to encode the same amino acid.

The invention also provides nucleic acid which can hybridize to these nucleic acids. Hybridization reactions can be performed under conditions of different "stringency". Conditions that increase stringency of a hybridization reaction of widely known and published in the art (e.g. page 7.52 of reference 276). Examples of relevant conditions include (in order of increasing stringency): incubation temperatures of 25°C, 37°C, 50°C, 55°C and 68°C; buffer concentrations of 10 x SSC, 6 x SSC, 1 x SSC, 0.1 x SSC (where SSC is 0.15 M NaCl and 15 mM citrate buffer) and their equivalents using other buffer systems; formamide concentrations of 0%, 25%, 50%, and 75%; incubation times from 5 minutes to 24 hours; 1, 2, or more washing steps; wash incubation times of 1, 2, or 15 minutes; and wash solutions of 6 x SSC, 1 x SSC, 0.1 x SSC, or de-ionized water. Hybridization techniques and their optimization are well known in the art (e.g. see refs 75, 76, 276, 278, etc.).

In some embodiments, nucleic acid of the invention hybridizes to a target under low stringency conditions; in other embodiments it hybridizes under intermediate stringency conditions; in preferred embodiments, it hybridizes under high stringency conditions. An exemplary set of low stringency hybridization conditions is 50°C and 10 x SSC. An exemplary set of intermediate stringency hybridization conditions is 55°C and 1 x SSC. An exemplary set of high stringency hybridization conditions is 68°C and 0.1 x SSC.

The invention includes nucleic acid comprising sequences complementary to these sequences (e.g. for antisense or probing, or for use as primers).
Nucleic acids of the invention can be used in hybridisation reactions (e.g. Northern or Southern blots, or in nucleic acid microarrays or 'gene chips') and amplification reactions (e.g. PCR, SDA, SSSR, LCR, TMA, NASBA, etc.) and other nucleic acid techniques.

Nucleic acid according to the invention can take various forms (e.g. single-stranded, double-stranded, vectors, primers, probes, labelled etc.). Nucleic acids of the invention may be circular or branched, but will generally be linear. Unless otherwise specified or required, any embodiment of the invention that utilizes a nucleic acid may utilize both the double-stranded form and each of two complementary single-stranded forms which make up the double-stranded form. Primers and probes are generally single-stranded, as are antisense nucleic acids.

Nucleic acids of the invention are preferably provided in purified or substantially purified form i.e. substantially free from other nucleic acids (e.g. free from naturally-occurring nucleic acids), particularly from other staphylococcal or host cell nucleic acids, generally being at least about 50% pure (by weight), and usually at least about 90% pure. Nucleic acids of the invention are preferably staphylococcal nucleic acids.

Nucleic acids of the invention may be prepared in many ways e.g. by chemical synthesis (e.g. phosphoramidite synthesis of DNA) in whole or in part, by digesting longer nucleic acids using nucleases (e.g. restriction enzymes), by joining shorter nucleic acids or nucleotides (e.g. using ligases or polymerases), from genomic or cDNA libraries, etc.

Nucleic acid of the invention may be attached to a solid support (e.g. a bead, plate, filter, film, slide, microarray support, resin, etc.). Nucleic acid of the invention may be labelled e.g. with a radioactive or fluorescent label, or a biotin label. This is particularly useful where the nucleic acid is to be used in detection techniques e.g. where the nucleic acid is a primer or as a probe.

The term "nucleic acid" includes in general means a polymeric form of nucleotides of any length, which contain deoxyribonucleotides, ribonucleotides, and/or their analogs. It includes DNA, RNA, DNA/RNA hybrids. It also includes DNA or RNA analogs, such as those containing modified backbones (e.g. peptide nucleic acids (PNAs) or phosphorothioates) or modified bases. Thus the invention includes mRNA, tRNA, rRNA, ribozymes, DNA, cDNA, recombinant nucleic acids, branched nucleic acids, plasmids, vectors, probes, primers, etc. Where nucleic acid of the invention takes the form of RNA, it may or may not have a 5' cap.

Nucleic acids of the invention may be part of a vector i.e. part of a nucleic acid construct designed for transduction/transfection of one or more cell types. Vectors may be, for example, "cloning vectors" which are designed for isolation, propagation and replication of inserted nucleotides, "expression vectors" which are designed for expression of a nucleotide sequence in a host cell, "viral vectors" which is designed to result in the production of a recombinant virus or virus-like particle, or "shuttle vectors", which comprise the attributes of more than one type of vector. Preferred vectors are plasmids. A "host cell" includes an individual cell or cell culture which can be or has been a
recipient of exogenous nucleic acid. Host cells include progeny of a single host cell, and the progeny may not necessarily be completely identical (in morphology or in total DNA complement) to the original parent cell due to natural, accidental, or deliberate mutation and/or change. Host cells include cells transfected or infected in vivo or in vitro with nucleic acid of the invention.

Where a nucleic acid is DNA, it will be appreciated that "U" in a RNA sequence will be replaced by "T" in the DNA. Similarly, where a nucleic acid is RNA, it will be appreciated that "T" in a DNA sequence will be replaced by "U" in the RNA.

The term "complement" or "complementary" when used in relation to nucleic acids refers to Watson-Crick base pairing. Thus the complement of C is G, the complement of G is C, the complement of A is T (or U), and the complement of T (or U) is A. It is also possible to use bases such as I (the purine inosine) e.g. to complement pyrimidines (C or T).

Nucleic acids of the invention can be used, for example: to produce polypeptides; as hybridization probes for the detection of nucleic acid in biological samples; to generate additional copies of the nucleic acids; to generate ribozymes or antisense oligonucleotides; as single-stranded DNA primers or probes; or as triple-strand forming oligonucleotides.

The invention provides a process for producing nucleic acid of the invention, wherein the nucleic acid is synthesised in part or in whole using chemical means.

The invention provides vectors comprising nucleotide sequences of the invention (e.g. cloning or expression vectors) and host cells transformed with such vectors.

Nucleic acid amplification according to the invention may be quantitative and/or real-time.

For certain embodiments of the invention, nucleic acids are preferably at least 7 nucleotides in length (e.g. 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 45, 50, 55, 60, 65, 70, 75, 80, 90, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200, 225, 250, 275, 300 nucleotides or longer).

For certain embodiments of the invention, nucleic acids are preferably at most 500 nucleotides in length (e.g. 450, 400, 350, 300, 250, 200, 150, 140, 130, 120, 110, 100, 90, 80, 75, 70, 65, 60, 55, 50, 45, 40, 39, 38, 37, 36, 35, 34, 33, 32, 31, 30, 29, 28, 27, 26, 25, 24, 23, 22, 21, 20, 19, 18, 17, 16, 15 nucleotides or shorter).

Primers and probes of the invention, and other nucleic acids used for hybridization, are preferably between 10 and 30 nucleotides in length (e.g. 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 nucleotides).

Strains and variants
Antigens are defined above by reference to existing nomenclature (e.g. "CIfA"), to "sta" numbers or to "NW_" numbers. Table 1 herein relates these three naming/numbering systems to existing
SAOUHSC numbering and/or NWMN numbering. SAOUHSC numbering refers to the genome of \textit{S.aureus} strain NCTC 8325 (sequenced by Oklahoma University Health Sciences Center and disclosed in GenBank as CP000253.1; GL87201381), and individual SAOUHSC numbers are given as "locus\_tag" entries in the genome sequence's "features" section. Similarly, NWMN numbering refers to the genome of \textit{S.aureus} strain Newman (isolated in 1952 from a human infection, and having robust virulence phenotype) disclosed in GenBank as AP009351.1 (GI:150373012) and individual NWMN numbers are given as "locus\_tag" entries in the genome sequence's "features" section. Functional annotations for each antigen are also given in the databases.

Table 1 also includes the GI number for each antigen of the invention. Thus an exemplary amino acid and nucleotide sequence for any of these antigens can easily be found in public sequence databases from the NCTC 8325 and/or Newman strain, but the invention is not limited to sequences from the NCTC 8325 and Newman strains. Genome sequences of several other strains of \textit{S.aureus} are available, including those of MRSA strains N315 and Mu50 [77], MW2, N315, COL, MRSA252, MSSA476, RF122, USA300 (very virulent), JHI and JH9. Standard search and alignment techniques can be used to identify in any of these (or other) further genome sequences the homolog of any particular sequence from the Newman or NCTC 8325 strain. Moreover, the available sequences from the Newman and NCTC 8325 strains can be used to design primers for amplification of homologous sequences from other strains. Thus the invention is not limited to these two strains, but rather encompasses such variants and homologs from other strains of \textit{S.aureus}, as well as non-natural variants. In general, suitable variants of a particular SEQ ID NO include its allelic variants, its polymorphic forms, its homologs, its orthologs, its paralogs, its mutants, \textit{etc.}

Thus, for instance, polypeptides used with the invention may, compared to the SEQ ID NO herein, include one or more (\textit{e.g.} 1, 2, 3, 4, 5, 6, 7, 8, 9, \textit{etc.}) amino acid substitutions, such as conservative substitutions \textit{(i.e.} substitutions of one amino acid with another which has a related side chain). Genetically-encoded amino acids are generally divided into four families: (1) acidic \textit{i.e.} aspartate, glutamate; (2) basic \textit{i.e.} lysine, arginine, histidine; (3) non-polar \textit{i.e.} alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan; and (4) uncharged polar \textit{i.e.} glycine, asparagine, glutamine, cysteine, serine, threonine, tyrosine. Phenylalanine, tryptophan, and tyrosine are sometimes classified jointly as aromatic amino acids. In general, substitution of single amino acids within these families does not have a major effect on the biological activity. The polypeptides may also include one or more (\textit{e.g.} 1, 2, 3, 4, 5, 6, 7, 8, 9, \textit{etc.}) single amino acid deletions relative to the SEQ ID NO sequences. The polypeptides may also include one or more (\textit{e.g.} 1, 2, 3, 4, 5, 6, 7, 8, 9, \textit{etc.}) insertions (\textit{e.g.} each of 1, 2, 3, 4 or 5 amino acids) relative to the SEQ ID NO sequences.

Similarly, a polypeptide used with the invention may comprise an amino acid sequence that:

is identical \textit{(i.e.} 100% identical) to a sequence disclosed in the sequence listing;
shares sequence identity \textit{(e.g.} 80\%, 85\%, 90\%, 91\%, 92\%, 93\%, 94\%, 95\%, 96\%, 97\%, 98\%, 99\%, 99.5\% or more) with a sequence disclosed in the sequence listing;
has 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 (or more) single amino acid alterations (deletions, insertions, substitutions), which may be at separate locations or may be contiguous, as compared to the sequences of (a) or (b); and

when aligned with a particular sequence from the sequence listing using a pairwise alignment algorithm, each moving window of \(x\) amino acids from N-terminus to C-terminus (such that for an alignment that extends to \(p\) amino acids, where \(p > x\), there are \(p-x+1\) such windows) has at least \(xy\) identical aligned amino acids, where: \(x\) is selected from 20, 25, 30, 35, 40, 45, 50, 60, 70, 80, 90, 100, 150, 200; \(y\) is selected from 0.50, 0.60, 0.70, 0.75, 0.80, 0.85, 0.90, 0.91, 0.92, 0.93, 0.94, 0.95, 0.96, 0.97, 0.98, 0.99; and \(nxy\) is not an integer then it is rounded up to the nearest integer. The preferred pairwise alignment algorithm is the Needleman-Wunsch global alignment algorithm [78], using default parameters (e.g. with Gap opening penalty = 10.0, and with Gap extension penalty = 0.5, using the EBLOSUM62 scoring matrix). This algorithm is conveniently implemented in the \textit{needle} tool in the EMBOSS package [79].

Where hybrid polypeptides are used, the individual antigens within the hybrid (i.e. individual \(-\text{X-moieties}\)) may be from one or more strains. Where \(n=2\), for instance, \(X_2\) may be from the same strain as \(X_1\) or from a different strain. Where \(n=3\), the strains might be (i) \(X_1=X_2=X_3\) (ii) \(X_1=X_2\neq X_3\) (iii) \(X_1\neq X_2=X_3\) (iv) \(X_1\neq X_2\neq X_3\) or (v) \(X_i\neq X_j\neq X_k\), etc.

Within group (c), deletions or substitutions may be at the N-terminus and/or C-terminus, or may be between the two termini. Thus a truncation is an example of a deletion. Truncations may involve deletion of up to 40 (or more) amino acids at the N-terminus and/or C-terminus. N-terminus truncation can remove leader peptides e.g. to facilitate recombinant expression in a heterologous host. C-terminus truncation can remove anchor sequences e.g. to facilitate recombinant expression in a heterologous host.

In general, when an antigen comprises a sequence that is not identical to a complete \textit{S. aureus} sequence from the sequence listing (e.g. when it comprises a sequence listing with <100% sequence identity thereto, or when it comprises a fragment thereof) it is preferred in each individual instance that the antigen can elicit an antibody which recognises the respective complete \textit{S. aureus} sequence.

\textit{Mutant bacteria}

The invention also provides a \textit{S. aureus} bacterium in which one or more of the antigens from the various antigen groups of the invention has/have been knocked out. Techniques for producing knockout bacteria are well known, and knockout \textit{S. aureus} strains have been reported. A knockout mutation may be situated in the coding region of the gene or may lie within its transcriptional control regions (e.g. within its promoter). A knockout mutation will reduce the level of mRNA encoding the antigen to <1% of that produced by the wild-type bacterium, preferably <0.5%, more preferably <0.1%, and most preferably to 0%.

-95-
The invention also provides a \textit{S.aureus} in which one or more of the antigens from the various antigen groups of the invention has a mutation which inhibits its activity. The gene encoding the antigen will have a mutation that changes the encoded amino acid sequence. Mutation may involve deletion, substitution, and/or insertion, any of which may involve one or more amino acids.

The invention also provides a bacterium, such as a \textit{S.aureus} bacterium, which hyper-expresses an antigen of the invention.

The invention also provides a bacterium, such as a \textit{S.aureus} bacterium, that constitutively expresses an antigen of the invention. The invention also provides a meningococcus comprising a gene encoding an antigen of the invention, wherein the gene is under the control of an inducible promoter.

\textit{Immunogenic compositions and medicaments}

Immunogenic compositions of the invention may be useful as vaccines. Vaccines according to the invention may either be prophylactic (\textit{i.e.} to prevent infection) or therapeutic (\textit{i.e.} to treat infection), but will typically be prophylactic.

Compositions may thus be pharmaceutically acceptable. They will usually include components in addition to the antigens \textit{e.g.} they typically include one or more pharmaceutical carrier(s) and/or excipient(s). A thorough discussion of such components is available in reference 273.

Compositions will generally be administered to a mammal in aqueous form. Prior to administration, however, the composition may have been in a non-aqueous form. For instance, although some vaccines are manufactured in aqueous form, then filled and distributed and administered also in aqueous form, other vaccines are lyophilised during manufacture and are reconstituted into an aqueous form at the time of use. Thus a composition of the invention may be dried, such as a lyophilised formulation.

The composition may include preservatives such as thiomersal or 2-phenoxyethanol. It is preferred, however, that the vaccine should be substantially free from (\textit{i.e.} less than 5\(\mu\)g/ml) mercurial material \textit{e.g.} thiomersal-free. Vaccines containing no mercury are more preferred. Preservative-free vaccines are particularly preferred.

To improve thermal stability, a composition may include a temperature protective agent. Further details of such agents are provided below.

To control tonicity, it is preferred to include a physiological salt, such as a sodium salt. Sodium chloride (NaCl) is preferred, which may be present at between 1 and 20 mg/ml \textit{e.g.} about 10±2 mg/ml NaCl. Other salts that may be present include potassium chloride, potassium dihydrogen phosphate, disodium phosphate dehydrate, magnesium chloride, calcium chloride, \textit{etc.}
Compositions will generally have an osmolality of between 200 mOsm/kg and 400 mθ sm/kg, preferably between 240-360 m θ sm/kg, and will more preferably fall within the range of 290-310 mOsm/kg.

Compositions may include one or more buffers. Typical buffers include: a phosphate buffer; a Tris buffer; a borate buffer; a succinate buffer; a histidine buffer (particularly with an aluminum hydroxide adjuvant); or a citrate buffer. Buffers will typically be included in the 5-20mM range.

The pH of a composition will generally be between 5.0 and 8.1, and more typically between 6.0 and 8.0 e.g. 6.5 and 7.5, or between 7.0 and 7.8.

The composition is preferably sterile. The composition is preferably non-pyrogenic e.g. containing <1 EU (endotoxin unit, a standard measure) per dose, and preferably <0.1 EU per dose. The composition is preferably gluten free.

The composition may include material for a single immunisation, or may include material for multiple immunisations (i.e. a 'multidose' kit). The inclusion of a preservative is preferred in multidose arrangements. As an alternative (or in addition) to including a preservative in multidose compositions, the compositions may be contained in a container having an aseptic adaptor for removal of material.

Human vaccines are typically administered in a dosage volume of about 0.5ml, although a half dose (i.e. about 0.25ml) may be administered to children.

Immunogenic compositions of the invention may also comprise one or more immunoregulatory agents. Preferably, one or more of the immunoregulatory agents include one or more adjuvants. The adjuvants may include a TH1 adjuvant and/or a TH2 adjuvant, further discussed below.

Thus the invention provides an immunogenic composition comprising a combination of:

(1) one or more antigen(s) selected from the first, second, third and fourth antigen groups (as defined above); and

(2) an adjuvant, such as an aluminium hydroxide adjuvant (for example, one or more antigens may be adsorbed to aluminium hydroxide).

For instance, the invention provides an immunogenic composition comprising a combination of a sta006 antigen and an adjuvant, such as an aluminium hydroxide adjuvant. Similarly, the invention provides an immunogenic composition comprising a combination of a staOll antigen and an adjuvant, such as an aluminium hydroxide adjuvant. These compositions are ideally buffered e.g. with a histidine buffer.

Adjuvants which may be used in compositions of the invention include, but are not limited to:
A. Mineral-containing compositions

Mineral-containing compositions suitable for use as adjuvants in the invention include mineral salts, such as aluminium salts and calcium salts (or mixtures thereof). Calcium salts include calcium phosphate (e.g. the "CAP" particles disclosed in ref. 80). Aluminum salts include hydroxides, phosphates, sulfates, etc., with the salts taking any suitable form (e.g. gel, crystalline, amorphous, etc.). Adsorption to these salts is preferred (e.g. all antigens may be adsorbed). The mineral containing compositions may also be formulated as a particle of metal salt [81].

The adjuvants known as aluminum hydroxide and aluminum phosphate may be used. These names are conventional, but are used for convenience only, as neither is a precise description of the actual chemical compound which is present (e.g. see chapter 9 of reference 82)). The invention can use any of the "hydroxide" or "phosphate" adjuvants that are in general use as adjuvants. The adjuvants known as "aluminium hydroxide" are typically aluminium oxyhydroxide salts, which are usually at least partially crystalline. The adjuvants known as "aluminium phosphate" are typically aluminium hydroxyphosphates, often also containing a small amount of sulfate (i.e. aluminium hydroxyphosphate sulfate). They may be obtained by precipitation, and the reaction conditions and concentrations during precipitation influence the degree of substitution of phosphate for hydroxyl in the salt.

A fibrous morphology (e.g. as seen in transmission electron micrographs) is typical for aluminium hydroxide adjuvants. The π of aluminium hydroxide adjuvants is typically about 11 i.e. the adjuvant itself has a positive surface charge at physiological pH. Adsorptive capacities of between 1.8-2.6 mg protein per mg Al^{+++} at pH 7.4 have been reported for aluminium hydroxide adjuvants.

Aluminium phosphate adjuvants generally have a PO_4/Al molar ratio between 0.3 and 1.2, preferably between 0.8 and 1.2, and more preferably 0.95±0.1. The aluminium phosphate will generally be amorphous, particularly for hydroxyphosphate salts. A typical adjuvant is amorphous aluminium hydroxyphosphate with POVAl molar ratio between 0.84 and 0.92, included at 0.6mg Al^{+++}/ml. The aluminium phosphate will generally be particulate (e.g. plate-like morphology as seen in transmission electron micrographs). Typical diameters of the particles are in the range 0.5-20μm (e.g. about 5-10μm) after any antigen adsorption. Adsorptive capacities of between 0.7-1.5 mg protein per mg Al^{+++} at pH 7.4 have been reported for aluminium phosphate adjuvants.

The point of zero charge (PZC) of aluminium phosphate is inversely related to the degree of substitution of phosphate for hydroxyl, and this degree of substitution can vary depending on reaction conditions and concentration of reactants used for preparing the salt by precipitation. PZC is also altered by changing the concentration of free phosphate ions in solution (more phosphate = more acidic PZC) or by adding a buffer such as a histidine buffer (makes PZC more basic). Aluminium phosphates used according to the invention will generally have a PZC of between 4.0 and 7.0, more preferably between 5.0 and 6.5 e.g. about 5.7.
As shown below, adsorption of *S. aureus* protein antigens (except IsdA, StaO19 and StaO73) to an aluminium hydroxide adjuvant is advantageous, particularly in a multi-protein combination (in which all antigens may be adsorbed). A histidine buffer can usefully be included in such adjuvanted compositions.

Suspensions of aluminium salts used to prepare compositions of the invention may contain a buffer *(e.g. a phosphate or a histidine or a Tris buffer)*, but this is not always necessary. The suspensions are preferably sterile and pyrogen-free. A suspension may include free aqueous phosphate ions *(e.g. present at a concentration between 1.0 and 2.0 mM, preferably between 5 and 15 mM, and more preferably about 10 mM.)* The suspensions may also comprise sodium chloride.

The invention can use a mixture of both an aluminium hydroxide and an aluminium phosphate. In this case there may be more aluminium phosphate than hydroxide *(e.g. a weight ratio of at least 2:1 *(e.g. >5:1, >6:1, >7:1, >8:1, >9:1, etc.*).

The concentration of Al**+** in a composition for administration to a patient is preferably less than 10mg/ml *(e.g. <5 mg/ml, <4 mg/ml, <3 mg/ml, <2 mg/ml, <1 mg/ml, etc.*. A preferred range is between 0.3 and 1mg/ml. A maximum of 0.85mg/dose is preferred.

**B. Oil Emulsions**

Oil emulsion compositions suitable for use as adjuvants in the invention include squalene-water emulsions, such as MF59 [Chapter 10 of ref. 82; see also ref. 83] *(5% Squalene, 0.5% Tween 80, and 0.5% Span 85, formulated into submicron particles using a microfluidizer). Complete Freund's adjuvant (CFA) and incomplete Freund's adjuvant (IFA) may also be used.

Various oil-in-water emulsion adjuvants are known, and they typically include at least one oil and at least one surfactant, with the oil(s) and surfactant(s) being biodegradable *(metabolisable)* and biocompatible. The oil droplets in the emulsion are generally less than 5µm in diameter, and ideally have a sub-micron diameter, with these small sizes being achieved with a microfluidiser to provide stable emulsions. Droplets with a size less than 220nm are preferred as they can be subjected to filter sterilization.

The emulsion can comprise oils such as those from an animal *(such as fish)* or vegetable source. Sources for vegetable oils include nuts, seeds and grains. Peanut oil, soybean oil, coconut oil, and olive oil, the most commonly available, exemplify the nut oils. Jojoba oil can be used *(e.g. obtained from the jojoba bean). Seed oils include safflower oil, cottonseed oil, sunflower seed oil, sesame seed oil and the like. In the grain group, corn oil is the most readily available, but the oil of other cereal grains such as wheat, oats, rye, rice, teff, triticale and the like may also be used. 6-10 carbon fatty acid esters of glycerol and 1,2-propanediol, while not occurring naturally in seed oils, may be prepared by hydrolysis, separation and esterification of the appropriate materials starting from the nut and seed oils. Fats and oils from mammalian milk are metabolizable and may therefore be used in the practice of this invention. The procedures for separation, purification, saponification and other means.
necessary for obtaining pure oils from animal sources are well known in the art. Most fish contain metabolizable oils which may be readily recovered. For example, cod liver oil, shark liver oils, and whale oil such as spermaceti exemplify several of the fish oils which may be used herein. A number of branched chain oils are synthesized biochemically in 5-carbon isoprene units and are generally referred to as terpenoids. Shark liver oil contains a branched, unsaturated terpenoids known as squalene, 2,6,10,15,19,23-hexamethyl-2,6,10,14,18,22-tetracosahexaene, which is particularly preferred herein. Squalane, the saturated analog to squalene, is also a preferred oil. Fish oils, including squalene and squalane, are readily available from commercial sources or may be obtained by methods known in the art. Other preferred oils are the tocopherols (see below). Mixtures of oils can be used.

Surfactants can be classified by their 'HLB' (hydrophilic/lipophilic balance). Preferred surfactants of the invention have a HLB of at least 10, preferably at least 15, and more preferably at least 16. The invention can be used with surfactants including, but not limited to: the polyoxyethylene sorbitan esters surfactants (commonly referred to as the Tweens), especially polysorbate 20 and polysorbate 80; copolymers of ethylene oxide (EO), propylene oxide (PO), and/or butylene oxide (BO), sold under the DOWFAX™ tradename, such as linear EO/PO block copolymers; octoxynols, which can vary in the number of repeating ethoxy (oxy-1,2-ethanediyl) groups, with octoxynol-9 (Triton X-100, or t-octylphenoxypropyethoxylanol) being of particular interest; (octylphenoxy)polyethoxyethanol (IGEPAL CA-630/NP-40); phospholipids such as phosphatidylcholine (lecithin); nonylphenol ethoxylates, such as the Tergitol™ NP series; polyoxyethylene fatty ethers derived from lauril, cetyl, stearyl and oleyl alcohols (known as Brij surfactants), such as triethyleneglycol monolauryl ether (Brij 30); and sorbitan esters (commonly known as the SPANS), such as sorbitan trioleate (Span 85) and sorbitan monolaurate. Non-ionic surfactants are preferred. Preferred surfactants for including in the emulsion are Tween 80 (polyoxyethylene sorbitan monooleate), Span 85 (sorbitan trioleate), lecithin and Triton X-100.

Mixtures of surfactants can be used e.g. Tween 80/Span 85 mixtures. A combination of a polyoxyethylene sorbitan ester such as polyoxyethylene sorbitan monooleate (Tween 80) and an octoxynol such as t-octylphenoxypropyethoxylanol (Triton X-100) is also suitable. Another useful combination comprises laureth 9 plus a polyoxyethylene sorbitan ester and/or an octoxynol.

Preferred amounts of surfactants (% by weight) are: polyoxyethylene sorbitan esters (such as Tween 80) 0.01 to 1%, in particular about 0.1%; octyl- or nonylphenoxy polyoxyethanols (such as Triton X-100, or other detergents in the Triton series) 0.001 to 0.1%, in particular 0.005 to 0.02%; polyoxyethylene ethers (such as laureth 9) 0.1 to 20%, preferably 0.1 to 10% and in particular 0.1 to 1% or about 0.5%.

Preferred emulsion adjuvants have an average droplets size of <1µm e.g. <750nm, <500nm, <400nm, <300nm, <250nm, <220nm, <200nm, or smaller. These droplet sizes can conveniently be achieved by techniques such as microfluidisation.
Specific oil-in-water emulsion adjuvants useful with the invention include, but are not limited to:

- A submicron emulsion of squalene, Tween 80, and Span 85. The composition of the emulsion by volume can be about 5% squalene, about 0.5% polysorbate 80 and about 0.5% Span 85. In weight terms, these ratios become 4.3% squalene, 0.5% polysorbate 80 and 0.48% Span 85. This adjuvant is known as 'MF59' [84-86], as described in more detail in Chapter 10 of ref. 87 and chapter 12 of ref. 88. The MF59 emulsion advantageously includes citrate ions e.g. 10mM sodium citrate buffer.

- An emulsion of squalene, a tocopherol, and polysorbate 80 (Tween 80). The emulsion may include phosphate buffered saline. It may also include Span 85 (e.g. at 1%) and/or lecithin. These emulsions may have from 2 to 10% squalene, from 2 to 10% tocopherol and from 0.3 to 3% Tween 80, and the weight ratio of squalene:tocopherol is preferably ≤ 1 as this provides a more stable emulsion. Squalene and Tween 80 may be present volume ratio of about 5:2 or at a weight ratio of about 11:5. One such emulsion can be made by dissolving Tween 80 in PBS to give a 2% solution, then mixing 90ml of this solution with a mixture of (5g of DL-α-tocopherol and 5ml squalene), then microfluidising the mixture. The resulting emulsion may have submicron oil droplets e.g. with an average diameter of between 100 and 250nm, preferably about 180nm. The emulsion may also include a 3-de-O-acylated monophosphoryl lipid A (3d-MPL). Another useful emulsion of this type may comprise, per human dose, 0.5-10 mg squalene, 0.5-1 mg tocopherol, and 0.1-4 mg polysorbate 80 [89].

- An emulsion of squalene, a tocopherol, and a Triton detergent (e.g. Triton X-100). The emulsion may also include a 3d-MPL (see below). The emulsion may contain a phosphate buffer.

- An emulsion comprising a polysorbate (e.g. polysorbate 80), a Triton detergent (e.g. Triton X-100) and a tocopherol (e.g. an α-tocopherol succinate). The emulsion may include these three components at a mass ratio of about 75:1:10 (e.g. 750µg/ml polysorbate 80, 100µg/ml Triton X-100 and 100µg/ml α-tocopherol succinate), and these concentrations should include any contribution of these components from antigens. The emulsion may also include squalene. The emulsion may also include a 3d-MPL (see below). The aqueous phase may contain a phosphate buffer.

- An emulsion of squalane, polysorbate 80 and poloxamer 401 ("Pluronic™ L121"). The emulsion can be formulated in phosphate buffered saline, pH 7.4. This emulsion is a useful delivery vehicle for muramyl dipeptides, and has been used with threonyl-MDP in the "SAF-I" adjuvant [90] (0.05-1% Thr-MDP, 5% squalane, 2.5% Pluronic L121 and 0.2% polysorbate 80). It can also be used without the Thr-MDP, as in the "AF" adjuvant [91] (5% squalane, 1.25% Pluronic L121 and 0.2% polysorbate 80). Microfluidisation is preferred.

- An emulsion comprising squalene, an aqueous solvent, a polyoxyethylene alkyl ether hydrophilic nonionic surfactant (e.g. polyoxyethylene (12) cetostearyl ether) and a
hydrophobic nonionic surfactant (e.g. a sorbitan ester or mannide ester, such as sorbitan monoleate or 'Span 80'). The emulsion is preferably thermoreversible and/or has at least 90% of the oil droplets (by volume) with a size less than 200 nm [92]. The emulsion may also include one or more of: alditol; a cryoprotective agent (e.g. a sugar, such as dodecylmaltoside and/or sucrose); and/or an alkylpolyglycoside. The emulsion may include a TLR4 agonist [93]. Such emulsions may be lyophilized.

- An emulsion of squalene, poloxamer 105 and Abil-Care [94]. The final concentration (weight) of these components in adjuvanted vaccines are 5% squalene, 4% poloxamer 105 (pluronic polyol) and 2% Abil-Care 85 (Bis-PEG/PPG-16/16 PEG/PPG-16/16 dimethicone; caprylic/capric triglyceride).

- An emulsion having from 0.5-50% of an oil, 0.1-10% of a phospholipid, and 0.05-5% of a non-ionic surfactant. As described in reference 95, preferred phospholipid components are phosphatidylcholine, phosphatidylethanolamine, phosphatidyserine, phosphatidylinositol, phosphatidylglycerol, phosphatic acid, sphingomyelin and cardiolipin. Submicron droplet sizes are advantageous.

- A submicron oil-in-water emulsion of a non-metabolisable oil (such as light mineral oil) and at least one surfactant (such as lecithin, Tween 80 or Span 80). Additives may be included, such as QuilA saponin, cholesterol, a saponin-lipophile conjugate (such as GPI-0100, described in reference 96, produced by addition of aliphatic amine to desacylsaponin via the carboxyl group of glucuronic acid), dimethyldioctadecylammonium bromide and/or N,N-dioctadecyl-N,N-bis (2-hydroxyethyl)propanediamine.

- An emulsion in which a saponin (e.g. QuilA or QS21) and a sterol (e.g. a cholesterol) are associated as helical micelles [97].

- An emulsion comprising a mineral oil, a non-ionic lipophilic ethoxylated fatty alcohol, and a non-ionic hydrophilic surfactant (e.g. an ethoxylated fatty alcohol and/or polyoxyethylene-polyoxypropylene block copolymer) [98].

- An emulsion comprising a mineral oil, a non-ionic hydrophilic ethoxylated fatty alcohol, and a non-ionic lipophilic surfactant (e.g. an ethoxylated fatty alcohol and/or polyoxyethylene-polyoxypropylene block copolymer) [98].

In some embodiments an emulsion may be mixed with antigen extemporaneously, at the time of delivery, and thus the adjuvant and antigen may be kept separately in a packaged or distributed vaccine, ready for final formulation at the time of use. In other embodiments an emulsion is mixed with antigen during manufacture, and thus the composition is packaged in a liquid adjuvanted form. The antigen will generally be in an aqueous form, such that the vaccine is finally prepared by mixing two liquids. The volume ratio of the two liquids for mixing can vary (e.g. between 5:1 and 1:5) but is generally about 1:1. Where concentrations of components are given in the above descriptions of
specific emulsions, these concentrations are typically for an undiluted composition, and the concentration after mixing with an antigen solution will thus decrease.

Where a composition includes a tocopherol, any of the α, β, γ, δ, ε or ξ tocopherols can be used, but α-tocopherol is preferred. The tocopherol can take several forms e.g. different salts and/or isomers.

Salts include organic salts, such as succinate, acetate, nicotinate, etc. D-α-tocopherol and DL-α-tocopherol can both be used. Tocopherols are advantageously included in vaccines for use in elderly patients (e.g. aged 60 years or older) because vitamin E has been reported to have a positive effect on the immune response in this patient group [99]. They also have antioxidant properties that may help to stabilize the emulsions [100]. A preferred α-tocopherol is DL-α-tocopherol, and the preferred salt of this tocopherol is the succinate. The succinate salt has been found to cooperate with TNF-related ligands in vivo.

C. Saponin formulations [chapter 22 of ref. 82]

Saponin formulations may also be used as adjuvants in the invention. Saponins are a heterogeneous group of sterol glycosides and triterpenoid glycosides that are found in the bark, leaves, stems, roots and even flowers of a wide range of plant species. Saponin from the bark of the Quillaja saponaria Molina tree have been widely studied as adjuvants. Saponin can also be commercially obtained from Smilax ornata (sarsaparilla), Gypsophilla paniculata (bridges veil), and Saponaria officinalis (soap root). Saponin adjuvant formulations include purified formulations, such as QS21, as well as lipid formulations, such as ISCOMs. QS21 is marketed as Stimulon™.

Saponin compositions have been purified using HPLC and RP-HPLC. Specific purified fractions using these techniques have been identified, including QS7, QS17, QS18, QS21, QH-A, QH-B and QH-C. Preferably, the saponin is QS21. A method of production of QS21 is disclosed in ref. 101. Saponin formulations may also comprise a sterol, such as cholesterol [102].

Combinations of saponins and sterols can be used to form unique particles called immunostimulating complexes (ISCOMs) [chapter 23 of ref. 82]. ISCOMs typically also include a phospholipid such as phosphatidylethanolamine or phosphatidylycholine. Any known saponin can be used in ISCOMs. Preferably, the ISCOM includes one or more of QuilA, QHA & QHC. ISCOMs are further described in refs. 102-104. Optionally, the ISCOMS may be devoid of additional detergent [105].

A review of the development of saponin based adjuvants can be found in refs. 106 & 107.

D. Virosomes and virus-like particles

Virosomes and virus-like particles (VLPs) can also be used as adjuvants in the invention. These structures generally contain one or more proteins from a virus optionally combined or formulated with a phospholipid. They are generally non-pathogenic, non-replicating and generally do not contain any of the native viral genome. The viral proteins may be recombinantly produced or isolated from whole viruses. These viral proteins suitable for use in virosomes or VLPs include proteins derived
from influenza virus (such as HA or NA), Hepatitis B virus (such as core or capsid proteins), Hepatitis E virus, measles virus, Sindbis virus, Rotavirus, Foot-and-Mouth Disease virus, Retrovirus, Norwalk virus, human Papilloma virus, HIV, RNA-phages, Qβ-phage (such as coat proteins), GA-phage, fr-phage, AP205 phage, and Ty (such as retrotransposon Ty protein pi). VLPs are discussed further in refs. 108-113. Virosomes are discussed further in, for example, ref. 114

E. Bacterial or microbial derivatives

Adjuvants suitable for use in the invention include bacterial or microbial derivatives such as non-toxic derivatives of enterobacterial lipopolysaccharide (LPS). Lipid A derivatives, immunostimulatory oligonucleotides and ADP-ribosylating toxins and detoxified derivatives thereof.

Non-toxic derivatives of LPS include monophosphoryl lipid A (MPL) and 3-O-deacylated MPL (3dMPL). 3dMPL is a mixture of 3 de-O-acylated monophosphoryl lipid A with 4, 5 or 6 acylated chains. A preferred "small particle" form of 3 De-O-acetylated monophosphoryl lipid A is disclosed in ref. 115. Such "small particles" of 3dMPL are small enough to be sterile filtered through a 0.22µm membrane [115]. Other non-toxic LPS derivatives include monophosphoryl lipid A mimics, such as aminoalkyl glucosaminide phosphate derivatives e.g. RC-529 [116,117].

Lipid A derivatives include derivatives of lipid A from Escherichia coli such as OM-174. OM-174 is described for example in refs. 118 & 119.

Immunostimulatory oligonucleotides suitable for use as adjuvants in the invention include nucleotide sequences containing a CpG motif (a dinucleotide sequence containing an unmethylated cytosine linked by a phosphate bond to a guanosine). Double-stranded RNAs and oligonucleotides containing palindromic or poly(dG) sequences have also been shown to be immunostimulatory.

The CpG’s can include nucleotide modifications/analogs such as phosphorothioate modifications and can be double-stranded or single-stranded. References 120, 121 and 122 disclose possible analog substitutions e.g. replacement of guanosine with 2’-deoxy-7-deazaguanosine. The adjuvant effect of CpG oligonucleotides is further discussed in refs. 123-128.

The CpG sequence may be directed to TLR9, such as the motif GTCGTT or TTCGTT [129]. The CpG sequence may be specific for inducing a ThI immune response, such as a CpG-A ODN, or it may be more specific for inducing a B cell response, such a CpG-B ODN. CpG-A and CpG-B ODNs are discussed in refs. 130-132. Preferably, the CpG is a CpG-A ODN.

Preferably, the CpG oligonucleotide is constructed so that the 5’ end is accessible for receptor recognition. Optionally, two CpG oligonucleotide sequences may be attached at their 3’ ends to form “immunomers”. See, for example, refs. 129 & 133-135.

A useful CpG adjuvant is CpG7909, also known as ProMune™ (Coley Pharmaceutical Group, Inc.). Another is CpGl 826. As an alternative, or in addition, to using CpG sequences, TpG sequences can be used [136], and these oligonucleotides may be free from unmethylated CpG motifs. The
immunostimulatory oligonucleotide may be pyrimidine-rich. For example, it may comprise more
than one consecutive thymidine nucleotide (e.g. TTTT, as disclosed in ref. 136), and/or it may have a
nucleotide composition with >25% thymidine (e.g. >35%, >40%, >50%, >60%, >80%, etc.). For
example, it may comprise more than one consecutive cytosine nucleotide (e.g. CCCC, as disclosed in
ref. 136), and/or it may have a nucleotide composition with >25% cytosine (e.g. >35%, >40%,
>50%, >60%, >80%, etc.). These oligonucleotides may be free from unmethylated CpG motifs.
Immunostimulatory oligonucleotides will typically comprise at least 20 nucleotides. They may
comprise fewer than 100 nucleotides.

A particularly useful adjuvant based around immunostimulatory oligonucleotides is known as
IC-31™ [137]. Thus an adjuvant used with the invention may comprise a mixture of (i) an
oligonucleotide (e.g. between 15-40 nucleotides) including at least one (and preferably multiple) Cpo
motifs (i.e. a cytosine linked to an inosine to form a dinucleotide), and (ii) a polycationic polymer,
such as an oligopeptide (e.g. between 5-20 amino acids) including at least one (and preferably
multiple) Lys-Arg-Lys tripeptide sequence(s). The oligonucleotide may be a deoxynucleotide
comprising 26-mer sequence 5’-(IC)5-3’ (SEQ ID NO: 175). The polycationic polymer may be a
peptide comprising 11-mer amino acid sequence KLKLLLLLKLK (SEQ ID NO: 176). The
oligonucleotide and polymer can form complexes e.g. as disclosed in references 138 & 139.

Bacterial ADP-ribosylating toxins and detoxified derivatives thereof may be used as adjuvants in the
invention. Preferably, the protein is derived from E.coli (E.coli heat labile enterotoxin "LT"), cholera
("CT"), or pertussis ("PT"). The use of detoxified ADP-ribosylating toxins as mucosal adjuvants is
described in ref. 140 and as parenteral adjuvants in ref. 141. The toxin or toxoid is preferably in the
form of a holotoxin, comprising both A and B subunits. Preferably, the A subunit contains a
detoxifying mutation; preferably the B subunit is not mutated. Preferably, the adjuvant is a detoxified
LT mutant such as LT-K63, LT-R72, and LT-Gl 92. The use of ADP-ribosylating toxins and
detoxified derivatives thereof, particularly LT-K63 and LT-R72, as adjuvants can be found in refs.
142-149. A useful CT mutant is or CT-E29H [150]. Numerical reference for amino acid substitutions
is preferably based on the alignments of the A and B subunits of ADP-ribosylating toxins set forth in
ref. 151, specifically incorporated herein by reference in its entirety.

F. Human immunomodulators

Human immunomodulators suitable for use as adjuvants in the invention include cytokines, such as
interleukins (e.g. IL-1, IL-2, IL-4, IL-5, IL-6, IL-7, IL-12 [152], etc.) [153], interferons (e.g.
interferon-γ), macrophage colony stimulating factor, and tumor necrosis factor. A preferred
immunomodulator is IL-12.

G. Bioadhesives and Mucoadhesives

Bioadhesives and mucoadhesives may also be used as adjuvants in the invention. Suitable
bioadhesives include esterified hyaluronic acid microspheres [154] or mucoadhesives such as
cross-linked derivatives of poly(acrylic acid), polyvinyl alcohol, polyvinyl pyrolidone,
polysaccharides and carboxymethylcellulose. Chitosan and derivatives thereof may also be used as adjuvants in the invention [155].

H. Microparticles

Microparticles may also be used as adjuvants in the invention. Microparticles (i.e. a particle of ~100nm to ~150μm in diameter, more preferably ~200nm to ~30μm in diameter, and most preferably ~500nm to ~10μm in diameter) formed from materials that are biodegradable and non-toxic (e.g. a poly(α-hydroxy acid), a polyhydroxybutyric acid, a polyorthoester, a polyanhydride, a polycaprolactone, etc.), with poly(lactide-co-glycolide) are preferred, optionally treated to have a negatively-charged surface (e.g. with SDS) or a positively-charged surface (e.g. with a cationic detergent, such as CTAB).

I. Liposomes (Chapters 13 & 14 of ref. 82)

Examples of liposome formulations suitable for use as adjuvants are described in refs. 156-158.

J. Polyoxyethylene ether and polyoxyethylene ester formulations

Adjuvants suitable for use in the invention include polyoxyethylene ethers and polyoxyethylene esters [159]. Such formulations further include polyoxyethylene sorbitan ester surfactants in combination with an octoxynol [160] as well as polyoxyethylene alkyl ethers or ester surfactants in combination with at least one additional non-ionic surfactant such as an octoxynol [161]. Preferred polyoxyethylene ethers are selected from the following group: polyoxyethylene-9-lauryl ether (laureth 9), polyoxyethylene-9-steoryl ether, polyoxythylene-8-steoryl ether, polyoxyethylene-4-lauryl ether, polyoxyethylene-35-lauryl ether, and polyoxyethylene-23-lauryl ether.

K. Phosphazenes

A phosphazene, such as poly[di(carboxylatophenoxy)phosphazene] ("PCPP") as described, for example, in references 162 and 163, may be used.

L. Muramyl peptides

Examples of muramyl peptides suitable for use as adjuvants in the invention include N-acetyl-muramyl-L-threonyl-D-isoglutamine (thr-MDP), N-acetyl-normuramyl-L-alanyl-D-isoglutamine (nor-MDP), and N-acetyl-muramyl-L-alanyl-D-isoglutaminyl-L-alanine-2-(r-2'-dipahntoyl-glycero-3-hydroxyphosphoryloxy)-ethylamine MTP-PE).

M. Imidazoquinoline Compounds.

Examples of imidazoquinoline compounds suitable for use adjuvants in the invention include Imiquimod ("R-837") [164,165], Resiquimod ("R-848") [166], and their analogs; and salts thereof (e.g. the hydrochloride salts). Further details about immunostimulatory imidazoquinolines can be found in references 167 to 171.

N. Substituted ureas

Substituted ureas useful as adjuvants include compounds of formula I, II or III, or salts thereof:
as defined in reference 172, such as 'ER 803058', 'ER 803732', 'ER 804053', ER 804058', 'ER 804059', 'ER 804442', 'ER 804680', 'ER 804764', ER 803022 or 'ER 804057' e.g.:

Further adjuvants that may be used with the invention include:

- An aminoalkyl glucosaminide phosphate derivative, such as RC-529 [173, 174].

Cyclic diguanylate ('c-di-GMP'), which has been reported as a useful adjuvant for *S.aureus* vaccines [175].

A thiosemicarbazone compound, such as those disclosed in reference 176. Methods of formulating, manufacturing, and screening for active compounds are also described in reference 176. The
thiosemicarbazones are particularly effective in the stimulation of human peripheral blood
mononuclear cells for the production of cytokines, such as TNF-α.

A tryptanthrin compound, such as those disclosed in reference 177. Methods of formulating,
manufacturing, and screening for active compounds are also described in reference 177. The
thiosemicarbazones are particularly effective in the stimulation of human peripheral blood
mononuclear cells for the production of cytokines, such as TNF-α.

- A nucleoside analog, such as: (a) Isatorabine (ANA-245; 7-thia-8-oxoguanosine):

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and prodrugs thereof; (b) ANA975; (c) ANA-025-1; (d) ANA380; (e) the compounds
disclosed in references 178 to 180loxoribine (7-allyl-8-oxoguanosine) [181].

- Compounds disclosed in reference 182, including: Acylpiperazine compounds, Indoledione
compounds, Tetrahydraisquinoline (THIQ) compounds, Benzocyclodione compounds,
Aminoazavinyl compounds, Aminobenzimidazole quinolinone (ABIQ) compounds
[183,184], Hydraphalamic acid compounds, Benzophenone compounds, Isoxazole compounds,
Sterol compounds, Quinazilinone compounds, Pyrrole compounds [185], Anthraquinone
compounds, Quinoxaline compounds, Triazine compounds, Pyrazalopyrimidine compounds,
and Benzazole compounds [186].

- Compounds containing lipids linked to a phosphate-containing acyclic backbone, such as the
TLR4 antagonist E5564 [187,188]:

- A polyoxidonium polymer [189,190] or other N-oxidized polyethylene-piperazine derivative.
- Methyl inosine 5'-monophosphate ("MIMP") [191].
- A polyhydroxlated pyrrolizidine compound [192], such as one having formula:

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RO
HO
N
HO
CH₂OH
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where R is selected from the group comprising hydrogen, straight or branched, unsubstituted
or substituted, saturated or unsaturated acyl, alkyl (e.g. cycloalkyl), alkenyl, alkynyl and aryl
groups, or a pharmaceutically acceptable salt or derivative thereof. Examples include, but are
not limited to: casuarine, casuarine-6-α-D-glucopyranose, 3-epi-casuarine, 7-epi/-casuarine,
3,7-diep/-casuarine, etc.
• A CDId ligand, such as an α-glycosylceramide [193-200] (e.g. α-galactosylceramide), phytosphingosine-containing α-glycosylceramides, OCH, KRN7000 [(2S,3S,4R)-1-O-(α-D-galactopyranosyl)-2-(N-hexacosanoylamino)-1,3,4-octadecanetriol], CRONY- 101, 3”-O-sulfo-galactosylceramide, etc.

• A gamma inulin [201] or derivative thereof, such as algamulin.

Adjuvant combinations
The invention may also comprise combinations of one or more of the adjuvants identified above. For example, the following adjuvant compositions may be used in the invention: (1) a saponin and an oil-in-water emulsion [202]; (2) a saponin (e.g. QS21) + a non-toxic LPS derivative (e.g. 3dMPL) [203]; (3) a saponin (e.g. QS21) + a non-toxic LPS derivative (e.g. 3dMPL) + a cholesterol; (4) a saponin (e.g. QS21) + 3dMPL + IL-12 (optionally + a sterol) [204]; (5) combinations of 3dMPL with, for example, QS21 and/or oil-in-water emulsions [205]; (6) SAF, containing 10% squalane, 0.4% Tween 80™, 5% pluronic-block polymer L121, and thr-MDP, either microfluidized into a submicron emulsion or vortexed to generate a larger particle size emulsion. (7) Ribi™ adjuvant system (RAS), (Ribi Immunochem) containing 2% squalene, 0.2% Tween 80, and one or more bacterial cell wall components from the group consisting of monophosphoryl lipid A (MPL), trehalose dimycolate (TDM), and cell wall skeleton (CWS), preferably MPL + CWS (Detox™); and (8) one or more mineral salts (such as an aluminum salt) + a non-toxic derivative of LPS (such as 3dMPL).

Other substances that act as immunostimulating agents are disclosed in chapter 7 of ref. 82.

The use of an aluminium hydroxide and/or aluminium phosphate adjuvant is particularly preferred, and antigens are generally adsorbed to these salts. Calcium phosphate is another preferred adjuvant. Other preferred adjuvant combinations include combinations of ThI and Th2 adjuvants such as CpG & alum or resiquimod & alum. A combination of aluminium phosphate and 3dMPL may be used.

The compositions of the invention may elicit both a cell mediated immune response as well as a humoral immune response. This immune response will preferably induce long lasting (e.g. neutralising) antibodies and a cell mediated immunity that can quickly respond upon exposure to pnuemococcus.
Two types of T cells, CD4 and CD8 cells, are generally thought necessary to initiate and/or enhance cell mediated immunity and humoral immunity. CD8 T cells can express a CD8 co-receptor and are commonly referred to as Cytotoxic T lymphocytes (CTLs). CD8 T cells are able to recognized or interact with antigens displayed on MHC Class I molecules.

CD4 T cells can express a CD4 co-receptor and are commonly referred to as T helper cells. CD4 T cells are able to recognize antigenic peptides bound to MHC class II molecules. Upon interaction with a MHC class II molecule, the CD4 cells can secrete factors such as cytokines. These secreted cytokines can activate B cells, cytotoxic T cells, macrophages, and other cells that participate in an immune response. Helper T cells or CD4+ cells can be further divided into two functionally distinct subsets: TH1 phenotype and TH2 phenotypes which differ in their cytokine and effector function.

Activated TH1 cells enhance cellular immunity (including an increase in antigen-specific CTL production) and are therefore of particular value in responding to intracellular infections. Activated TH1 cells may secrete one or more of IL-2, IFN-γ, and TNF-β. A TH1 immune response may result in local inflammatory reactions by activating macrophages, NK (natural killer) cells, and CD8 cytotoxic T cells (CTLs). A TH1 immune response may also act to expand the immune response by stimulating growth of B and T cells with IL-12. TH1 stimulated B cells may secrete IgG2a.

Activated TH2 cells enhance antibody production and are therefore of value in responding to extracellular infections. Activated TH2 cells may secrete one or more of IL-4, IL-5, IL-6, and IL-10. A TH2 immune response may result in the production of IgG1, IgE, IgA and memory B cells for future protection.

An enhanced immune response may include one or more of an enhanced TH1 immune response and a TH2 immune response.

A TH1 immune response may include one or more of an increase in CTLs, an increase in one or more of the cytokines associated with a TH1 immune response (such as IL-2, IFN-γ, and TNF-β), an increase in activated macrophages, an increase in NK activity, or an increase in the production of IgG2a. Preferably, the enhanced TH1 immune response will include an increase in IgG2a production.

A TH1 immune response may be elicited using a TH1 adjuvant. A TH1 adjuvant will generally elicit increased levels of IgG2a production relative to immunization of the antigen without adjuvant. TH1 adjuvants suitable for use in the invention may include for example saponin formulations, virosomes and virus like particles, non-toxic derivatives of enterobacterial lipopolysaccharide (LPS), immunostimulatory oligonucleotides. Immunostimulatory oligonucleotides, such as oligonucleotides containing a CpG motif, are preferred TH1 adjuvants for use in the invention.

A TH2 immune response may include one or more of an increase in one or more of the cytokines associated with a TH2 immune response (such as IL-4, IL-5, IL-6 and IL-10), or an increase in the
production of IgG1, IgE, IgA and memory B cells. Preferably, the enhanced TH2 immune response will include an increase in IgG1 production.

A TH2 immune response may be elicited using a TH2 adjuvant. A TH2 adjuvant will generally elicit increased levels of IgG1 production relative to immunization of the antigen without adjuvant. TH2 adjuvants suitable for use in the invention include, for example, mineral containing compositions, oil-emulsions, and ADP-ribosylating toxins and detoxified derivatives thereof. Mineral containing compositions, such as aluminium salts are preferred TH2 adjuvants for use in the invention.

Preferably, the invention includes a composition comprising a combination of a TH1 adjuvant and a TH2 adjuvant. Preferably, such a composition elicits an enhanced TH1 and an enhanced TH2 response, i.e., an increase in the production of both IgG1 and IgG2a production relative to immunization without an adjuvant. Still more preferably, the composition comprising a combination of a TH1 and a TH2 adjuvant elicits an increased TH1 and/or an increased TH2 immune response relative to immunization with a single adjuvant (i.e., relative to immunization with a TH1 adjuvant alone or immunization with a TH2 adjuvant alone).

The immune response may be one or both of a TH1 immune response and a TH2 response. Preferably, immune response provides for one or both of an enhanced TH1 response and an enhanced TH2 response.

The enhanced immune response may be one or both of a systemic and a mucosal immune response. Preferably, the immune response provides for one or both of an enhanced systemic and an enhanced mucosal immune response. Preferably the mucosal immune response is a TH2 immune response. Preferably, the mucosal immune response includes an increase in the production of IgA.

*S. aureus* infections can affect various areas of the body and so the compositions of the invention may be prepared in various forms. For example, the compositions may be prepared as injectables, either as liquid solutions or suspensions. Solid forms suitable for solution in, or suspension in, liquid vehicles prior to injection can also be prepared (e.g. a lyophilised composition or a spray-freeze dried composition). The composition may be prepared for topical administration e.g. as an ointment, cream or powder. The composition may be prepared for oral administration e.g. as a tablet or capsule, as a spray, or as a syrup (optionally flavoured). The composition may be prepared for pulmonary administration e.g. as an inhaler, using a fine powder or a spray. The composition may be prepared as a suppository or pessary. The composition may be prepared for nasal, aural or ocular administration e.g. as drops. The composition may be in kit form, designed such that a combined composition is reconstituted just prior to administration to a patient. Such kits may comprise one or more antigens in liquid form and one or more lyophilised antigens.

Where a composition is to be prepared extemporaneously prior to use (e.g. where a component is presented in lyophilised form) and is presented as a kit, the kit may comprise two vials, or it may
comprise one ready-filled syringe and one vial, with the contents of the syringe being used to reactivate the contents of the vial prior to injection.

Immunogenic compositions used as vaccines comprise an immunologically effective amount of antigen(s), as well as any other components, as needed. By 'immunologically effective amount', it is meant that the administration of that amount to an individual, either in a single dose or as part of a series, is effective for treatment or prevention. This amount varies depending upon the health and physical condition of the individual to be treated, age, the taxonomic group of individual to be treated (e.g. non-human primate, primate, etc.), the capacity of the individual's immune system to synthesise antibodies, the degree of protection desired, the formulation of the vaccine, the treating doctor's assessment of the medical situation, and other relevant factors. It is expected that the amount will fall in a relatively broad range that can be determined through routine trials. Where more than one antigen is included in a composition then two antigens may be present at the same dose as each other or at different doses.

As mentioned above, a composition may include a temperature protective agent, and this component may be particularly useful in adjuvanted compositions (particularly those containing a mineral adjuvant, such as an aluminium salt). As described in reference 206, a liquid temperature protective agent may be added to an aqueous vaccine composition to lower its freezing point e.g. to reduce the freezing point to below 0°C. Thus the composition can be stored below 0°C, but above its freezing point, to inhibit thermal breakdown. The temperature protective agent also permits freezing of the composition while protecting mineral salt adjuvants against agglomeration or sedimentation after freezing and thawing, and may also protect the composition at elevated temperatures e.g. above 40°C. A starting aqueous vaccine and the liquid temperature protective agent may be mixed such that the liquid temperature protective agent forms 1-80% by volume of the final mixture. Suitable temperature protective agents should be safe for human administration, readily miscible/soluble in water, and should not damage other components (e.g. antigen and adjuvant) in the composition. Examples include glycerin, propylene glycol, and/or polyethylene glycol (PEG). Suitable PEGs may have an average molecular weight ranging from 200-20,000 Da. In a preferred embodiment, the polyethylene glycol can have an average molecular weight of about 300 Da ('PEG-300').

The invention provides an immunogenic composition comprising: (i) one or more antigen(s) selected from the first, second, third or fourth antigen groups; and (ii) a temperature protective agent. This composition may be formed by mixing (i) an aqueous composition comprising one or more antigen(s) selected from the first, second, third or fourth antigen groups, with (ii) a temperature protective agent. The mixture may then be stored e.g. below 0°C, from 0-20°C, from 20-35°C, from 35-55°C, or higher. It may be stored in liquid or frozen form. The mixture may be lyophilised. The composition may alternatively be formed by mixing (i) a dried composition comprising one or more antigen(s) selected from the first, second, third or fourth antigen groups, with (ii) a liquid
composition comprising the temperature protective agent. Thus component (ii) can be used to reconstitute component (i).

Methods of treatment, and administration of the vaccine

The invention also provides a method for raising an immune response in a mammal comprising the step of administering an effective amount of a composition of the invention. The immune response is preferably protective and preferably involves antibodies and/or cell-mediated immunity. The method may raise a booster response.

The invention also provides at least two antigens of the invention for combined use as a medicament e.g. for use in raising an immune response in a mammal.

The invention also provides the use of at least two antigens of the invention in the manufacture of a medicament for raising an immune response in a mammal.

By raising an immune response in the mammal by these uses and methods, the mammal can be protected against *S.aureus* infection, including a nosocomial infection. More particularly, the mammal may be protected against a skin infection, pneumonia, meningitis, osteomyelitis endocarditis, toxic shock syndrome, and/or sepsicaemia.

The invention also provides a kit comprising a first component and a second component wherein neither the first component nor the second component is a composition of the invention as described above, but wherein the first component and the second component can be combined to provide a composition of the invention as described above. The kit may further include a third component comprising one or more of the following: instructions, syringe or other delivery device, adjuvant, or pharmaceutically acceptable formulating solution.

The invention also provides a delivery device pre-filled with an immunogenic composition of the invention.

The mammal is preferably a human. Where the vaccine is for prophylactic use, the human is preferably a child (e.g. a toddler or infant) or a teenager; where the vaccine is for therapeutic use, the human is preferably a teenager or an adult. A vaccine intended for children may also be administered to adults e.g. to assess safety, dosage, immunogenicity, etc. Other mammals which can usefully be immunised according to the invention are cows, dogs, horses, and pigs.

One way of checking efficacy of therapeutic treatment involves monitoring *S.aureus* infection after administration of the compositions of the invention. One way of checking efficacy of prophylactic treatment involves monitoring immune responses, systemically (such as monitoring the level of IgGl and IgG2a production) and/or mucosally (such as monitoring the level of IgA production), against the antigens in the compositions of the invention after administration of the composition. Typically, antigen-specific serum antibody responses are determined post-immunisation but pre-challenge
whereas antigen-specific mucosal antibody responses are determined post-immunisation and post-
challenge.

Another way of assessing the immunogenicity of the compositions of the present invention is to
express the proteins recombinantly for screening patient sera or mucosal secretions by immunoblot
and/or microarrays. A positive reaction between the protein and the patient sample indicates that the
patient has mounted an immune response to the protein in question. This method may also be used to
identify immunodominant antigens and/or epitopes within antigens.

The efficacy of vaccine compositions can also be determined in vivo by challenging animal models
of S.aureus infection, e.g., guinea pigs or mice, with the vaccine compositions. In particular, there
are three useful animal models for the study of S.aureus infectious disease, namely: (i) the murine
abscess model [207], (ii) the murine lethal infection model [207] and (iii) the murine pneumonia
model [208]. The abscess model looks at abscesses in mouse kidneys after intravenous challenge.
The lethal infection model looks at the number of mice which survive after being infected by a
normally-lethal dose of S.aureus by the intravenous or intraperitoneal route. The pneumonia model
also looks at the survival rate, but uses intranasal infection. A useful vaccine may be effective in one
or more of these models. For instance, for some clinical situations it may be desirable to protect
against pneumonia, without needing to prevent hematic spread or to promote opsonisation; in other
situations the main desire may be to prevent hematic spread. Different antigens, and different antigen
combinations, may contribute to different aspects of an effective vaccine.

Compositions of the invention will generally be administered directly to a patient. Direct delivery
may be accomplished by parenteral injection (e.g. subcutaneously, intraperitoneally, intravenously,
intramuscularly, or to the interstitial space of a tissue), or mucosally, such as by rectal, oral (e.g.
tablet, spray), vaginal, topical, transdermal or transcutaneous, intranasal, ocular, aural, pulmonary or
other mucosal administration.

The invention may be used to elicit systemic and/or mucosal immunity, preferably to elicit an
enhanced systemic and/or mucosal immunity.

Preferably the enhanced systemic and/or mucosal immunity is reflected in an enhanced TH1 and/or
TH2 immune response. Preferably, the enhanced immune response includes an increase in the
production of IgG1 and/or IgG2a and/or IgA.

Dosage can be by a single dose schedule or a multiple dose schedule. Multiple doses may be used in
a primary immunisation schedule and/or in a booster immunisation schedule, hi a multiple dose
schedule the various doses may be given by the same or different routes e.g. a parenteral prime and
mucosal boost, a mucosal prime and parenteral boost, etc. Multiple doses will typically be
administered at least 1 week apart (e.g. about 2 weeks, about 3 weeks, about 4 weeks, about 6 weeks,
about 8 weeks, about 10 weeks, about 12 weeks, about 16 weeks, etc.).
Vaccines prepared according to the invention may be used to treat both children and adults. Thus a human patient may be less than 1 year old, 1-5 years old, 5-15 years old, 15-55 years old, or at least 55 years old. Preferred patients for receiving the vaccines are the elderly (e.g. ≥50 years old, ≥60 years old, and preferably ≥65 years), the young (e.g. ≤5 years old), hospitalised patients, healthcare workers, armed service and military personnel, pregnant women, the chronically ill, or immunodeficient patients. The vaccines are not suitable solely for these groups, however, and may be used more generally in a population.

Vaccines produced by the invention may be administered to patients at substantially the same time as other vaccines e.g. at substantially the same time as an influenza vaccine, a measles vaccine, a mumps vaccine, a rubella vaccine, a MMR vaccine, a varicella vaccine, a MMRV vaccine, a diphtheria vaccine, a tetanus vaccine, a pertussis vaccine, a DTP vaccine, a conjugated *H.influenzae* type b vaccine, an inactivated poliovirus vaccine, a hepatitis B virus vaccine, a meningococcal conjugate vaccine (such as a tetravalent A-C-W1 35-Y vaccine), a respiratory syncytial virus vaccine, etc. Further non-staphylococcal vaccines suitable for co-administration may include one or more antigens listed on pages 33-46 of reference 51.

**Nucleic acid immunisation**

The immunogenic compositions described above include polypeptide antigens from *S.aureus*. In all cases, however, the polypeptide antigens can be replaced by nucleic acids (typically DNA) encoding those polypeptides, to give compositions, methods and uses based on nucleic acid immunisation. Nucleic acid immunisation is now a developed field (e.g. see references 209 to 216 etc.).

The nucleic acid encoding the immunogen is expressed *in vivo* after delivery to a patient and the expressed immunogen then stimulates the immune system. The active ingredient will typically take the form of a nucleic acid vector comprising: (i) a promoter; (ii) a sequence encoding the immunogen, operably linked to the promoter; and optionally (iii) a selectable marker. Preferred vectors may further comprise (iv) an origin of replication; and (v) a transcription terminator downstream of and operably linked to (ii). In general, (i) & (v) will be eukaryotic and (iii) & (iv) will be prokaryotic.

Preferred promoters are viral promoters e.g. from cytomegalovirus (CMV). The vector may also include transcriptional regulatory sequences (e.g. enhancers) in addition to the promoter and which interact functionally with the promoter. Preferred vectors include the immediate-early CMV enhancer/promoter, and more preferred vectors also include CMV intron A. The promoter is operably linked to a downstream sequence encoding an immunogen, such that expression of the immunogen-encoding sequence is under the promoter's control.
Where a marker is used, it preferably functions in a microbial host (e.g. in a prokaryote, in a bacteria, in a yeast). The marker is preferably a prokaryotic selectable marker (e.g. transcribed under the control of a prokaryotic promoter). For convenience, typical markers are antibiotic resistance genes.

The vector of the invention is preferably an autonomously replicating episomal or extrachromosomal vector, such as a plasmid.

The vector of the invention preferably comprises an origin of replication. It is preferred that the origin of replication is active in prokaryotes but not in eukaryotes.

Preferred vectors thus include a prokaryotic marker for selection of the vector, a prokaryotic origin of replication, but a eukaryotic promoter for driving transcription of the immunogen-encoding sequence. The vectors will therefore (a) be amplified and selected in prokaryotic hosts without polypeptide expression, but (b) be expressed in eukaryotic hosts without being amplified. This arrangement is ideal for nucleic acid immunization vectors.

The vector of the invention may comprise a eukaryotic transcriptional terminator sequence downstream of the coding sequence. This can enhance transcription levels. Where the coding sequence does not have its own, the vector of the invention preferably comprises a polyadenylation sequence. A preferred polyadenylation sequence is from bovine growth hormone.

The vector of the invention may comprise a multiple cloning site

In addition to sequences encoding the immunogen and a marker, the vector may comprise a second eukaryotic coding sequence. The vector may also comprise an IRES upstream of said second sequence in order to permit translation of a second eukaryotic polypeptide from the same transcript as the immunogen. Alternatively, the immunogen-coding sequence may be downstream of an IRES.

The vector of the invention may comprise unmethylated CpG motifs e.g. unmethylated DNA sequences which have in common a cytosine preceding a guanosine, flanked by two 5' purines and two 3' pyrimidines. In their unmethylated form these DNA motifs have been demonstrated to be potent stimulators of several types of immune cell.

Vectors may be delivered in a targeted way. Receptor-mediated DNA delivery techniques are described in, for example, references 217 to 222. Therapeutic compositions containing a nucleic acid are administered in a range of about 100µg to about 200µg of DNA for local administration in a gene therapy protocol. Concentration ranges of about 500 ng to about 50 mg, about 1µg to about 2 mg, about 5µg to about 500µg, and about 20µg to about 100µg of DNA can also be used during a gene therapy protocol. Factors such as method of action (e.g. for enhancing or inhibiting levels of the encoded gene product) and efficacy of transformation and expression are considerations which will affect the dosage required for ultimate efficacy. Where greater expression is desired over a larger area of tissue, larger amounts of vector or the same amounts re-administered in a successive protocol of administrations, or several administrations to different adjacent or close tissue portions may be
required to effect a positive therapeutic outcome. In all cases, routine experimentation in clinical trials will determine specific ranges for optimal therapeutic effect.

Vectors can be delivered using gene delivery vehicles. The gene delivery vehicle can be of viral or non-viral origin (see generally references 223 to 226).

Viral-based vectors for delivery of a desired nucleic acid and expression in a desired cell are well known in the art. Exemplary viral-based vehicles include, but are not limited to, recombinant retroviruses (e.g. references 227 to 237), alphavirus-based vectors (e.g. Sindbis virus vectors, Semliki forest virus (ATCC VR-67; ATCC VR-1247), Ross River virus (ATCC VR-373; ATCC VR-1246) and Venezuelan equine encephalitis virus (ATCC VR-923; ATCC VR-1250; ATCC VR 1249; ATCC VR-532); hybrids or chimeras of these viruses may also be used), poxvirus vectors (e.g. vaccinia, fowlpox, canarypox, modified vaccinia Ankara, etc.), adenovirus vectors, and adeno-associated virus (AAV) vectors (e.g. see refs. 238 to 243). Administration of DNA linked to killed adenovirus [244] can also be employed.

Non-viral delivery vehicles and methods can also be employed, including, but not limited to, polycationic condensed DNA linked or unlinked to killed adenovirus alone [e.g. 244], ligand-linked DNA [245], eukaryotic cell delivery vehicles cells [e.g. refs. 246 to 250] and nucleic charge neutralization or fusion with cell membranes. Naked DNA can also be employed. Exemplary naked DNA introduction methods are described in refs. 251 and 252. Liposomes (e.g. immunoliposomes) that can act as gene delivery vehicles are described in refs. 253 to 257. Additional approaches are described in references 258 & 259.

Further non-viral delivery suitable for use includes mechanical delivery systems such as the approach described in ref. 259. Moreover, the coding sequence and the product of expression of such can be delivered through deposition of photopolymerized hydrogel materials or use of ionizing radiation [e.g. refs. 260 & 261]. Other conventional methods for gene delivery that can be used for delivery of the coding sequence include, for example, use of hand-held gene transfer particle gun [262] or use of ionizing radiation for activating transferred genes [260 & 261].

Delivery DNA using PLG (poly(lactide-co-glycolide)} microparticles is a particularly preferred method e.g. by adsorption to the microparticles, which are optionally treated to have a negatively-charged surface (e.g. treated with SDS) or a positively-charged surface (e.g. treated with a cationic detergent, such as CTAB).

S.epidermidis

Although the invention focuses on S.aureus, the inventors also realise that the sta006 and sta011 antigens have homologs in S.epidermidis. For example, SEQ ID NO: 234 is the 'iron (Fe+3) ABC superfamily ATP binding cassette transporter, binding protein' from S.epidermidis strain M23864:W1, with 73% identity to SEQ ID NO: 42 (sta006), and SEQ ID NO: 235 is the 'putative lipoprotein' from S.epidermidis strain RP62A, with 67% identity to SEQ ID NO: 47 (staOl 1).
S.epidermidis is commonly present on human skin and can sometimes cause illness. Infection is usually associated with medical devices, such as catheters, and is a cause of nosocomial infections. The results disclosed herein for sta006 and sta011 against S.aureus suggest that the homologous proteins in S.epidermidis could be useful for immunising against this pathogen.

The invention provides an immunogenic composition comprising:

(i) a polypeptide comprising an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 234; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 234, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more);

and/or

(ii) a polypeptide comprising an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 235; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 235, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more).

The composition may also include an adjuvant. These compositions are particularly useful for immunising a mammal (including a human) against S.epidermidis infection.

Preferred fragments of (b) comprise an epitope from SEQ ID NO: 234 or 235, respectively. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 234/235 while retaining at least one epitope of SEQ ID NO: 234/235.

More generally, the invention provides the use of the sta006 and/or sta011 homolog from any Staphylococcus species for immunising a mammal against that species.

**Antibodies**

Antibodies against S.aureus antigens can be used for passive immunisation. Thus the invention provides an antibody which is specific for an antigen in the first, second, third or fourth antigen groups. The invention also provides the use of such antibodies in therapy. The invention also provides the use of such antibodies in the manufacture of a medicament. The invention also provides a method for treating a mammal comprising the step of administering an effective amount of an antibody of the invention. As described above for immunogenic compositions, these methods and uses allow a mammal to be protected against S.aureus infection.
The term "antibody" includes intact immunoglobulin molecules, as well as fragments thereof which are capable of binding an antigen. These include hybrid (chimeric) antibody molecules [263, 264]; F(ab')2 and F(ab) fragments and Fv molecules; non-covalent heterodimers [265, 266]; single-chain Fv molecules (sFv) [267]; dimeric and trimeric antibody fragment constructs; minibodies [268, 269]; humanized antibody molecules [270-272]; and any functional fragments obtained from such molecules, as well as antibodies obtained through non-conventional processes such as phage display. Preferably, the antibodies are monoclonal antibodies. Methods of obtaining monoclonal antibodies are well known in the art. Humanised or fully-human antibodies are preferred.

General

The practice of the present invention will employ, unless otherwise indicated, conventional methods of chemistry, biochemistry, molecular biology, immunology and pharmacology, within the skill of the art. Such techniques are explained fully in the literature. See, e.g., references 273-280, etc.

"GI" numbering is used above. A GI number, or "GenInfo Identifier", is a series of digits assigned consecutively to each sequence record processed by NCBI when sequences are added to its databases. The GI number bears no resemblance to the accession number of the sequence record. When a sequence is updated (e.g. for correction, or to add more annotation or information) then it receives a new GI number. Thus the sequence associated with a given GI number is never changed.

Where the invention concerns an "epitope", this epitope may be a B-cell epitope and/or a T-cell epitope. Such epitopes can be identified empirically (e.g. using PEPSCAN [281,282] or similar methods), or they can be predicted (e.g. using the Jameson- Wolf antigenic index [283], matrix-based approaches [284], MAPITOPE [285], TEPITOPE [286,287], neural networks [288], OptiMer & EpiMer [289, 290], ADEPT [291], Tsites [292], hydrophilicity [293], antigenic index [294] or the methods disclosed in references 295-299, etc.). Epitopes are the parts of an antigen that are recognised by and bind to the antigen binding sites of antibodies or T-cell receptors, and they may also be referred to as "antigenic determinants".

Where an antigen "domain" is omitted, this may involve omission of a signal peptide, of a cytoplasmic domain, of a transmembrane domain, of an extracellular domain, etc.

The term "comprising" encompasses "including" as well as "consisting" e.g. a composition "comprising" X may consist exclusively of X or may include something additional e.g. X + Y.

The term "about" in relation to a numerical value is optional and means, for example, ±10%.

References to a percentage sequence identity between two amino acid sequences means that, when aligned, that percentage of amino acids are the same in comparing the two sequences. This alignment and the percent homology or sequence identity can be determined using software programs known in the art, for example those described in section 7.7.18 of ref. 300. A preferred alignment is determined by the Smith-Waterman homology search algorithm using an affine gap search with a gap open
penalty of 12 and a gap extension penalty of 2, BLOSUM matrix of 62. The Smith-Waterman homology search algorithm is disclosed in ref. 301.

BRIEF DESCRIPTION OF DRAWINGS

Figure 1 shows bacterial counts (Log cfu/ml) after challenge of mice previously immunised with the indicated antigens.

Figures 2 to 4 show survival (%) after challenge of mice previously immunised with various mixtures of antigens over 14 days. In Figure 2, the six groups from SA-10-a are, from top to bottom at day 14, groups (i), (iii) & (iv) together, (ii), IsdB, then the negative control. In Figure 3, the six groups from SA-10-a are, from top to bottom at day 14, groups (i), (iii) & (iv) together, (ii), IsdB, then the negative control. In Figure 3, the six groups from SA-10-b are, from top to bottom at day 14, groups (iii), (i), (iv), (ii) and IsdB together, then the negative control. In Figure 4, the six groups from SA-14 are, from top to bottom at day 14, groups (iv), (ii), (i), (iii), negative control, and IsdB.

Figure 5 shows collected data on mouse survival from four different experiments after challenge of mice previously immunised with various compositions (PBS negative control; IsdB antigen; and "Combo- 1" and "Combo-2" antigen combinations of the invention). Individual symbols show the survival duration of individual mice; the horizontal bar for each group shows the median survival duration; the percentage figures are survival 14 days after challenge; and the p values at the top are t-Test values for comparison of median survival durations between groups.

Figure 6 shows the number of colony forming units (cfu) in mouse kidneys after infection with 9x10^6 cfu of Newman strain in the abscess model. Horizontal bars are averages per group, and the figure beneath each group is the log reduction relative to the PBS control group.

Figure 7 shows bacterial count (log CFU/ml) in kidneys of mice in an abscess model experiment. Mice were challenged with the following strains: (A) MW2; (B) LAC; (C) Staph9; or (D) MU50. Each point is an individual animal and the bar shows the median count per group. Mice had been immunised as shown on the x-axis label.

Figure 8 shows the formation of StaOll oligomers in the presence of increasing concentrations of Ca^+ ions. Numbers indicate mM concentrations, and a * indicates the presence of 50mM EDTA.

Figure 9 shows IgG titers against (A) EsxAB (B) Sta006 (C) Hla-H35L (D) StaOl l. Each graph has three groups, with a pair of bars per group. The right-hand bar in a pair shows pre-immune IgG and the left-hand bar shows post-immune IgG. The three groups are the compositions used for immunising and, from left to right, are: negative control of adjuvant alone; the Combo l combination; and the relevant antigen alone.

Figure 10 shows bacterial counts values (log CFU/ml) in mice after challenge with the indicated strains. Each point is an individual animal and the bar shows the median CFU. The P value beneath the IsdB and Combo columns is a comparison against the adjuvant-only control.
Figure 11 shows the area of abscesses (mm²) in mice after challenge with Newman strain.

Figure 12 shows days of survival of mice after challenge with four different strains: Newman (o), ST-80 (d), USA300-FPR3757 (∆) or USA300-Lac (x) strains. Each point is an individual animal, the bar shows the median survival, and the heading number shows the % of animals surviving after 15 days. Mice received aluminium hydroxide adjuvant alone, IsdB or Combo 1.

Figure 13 shows the median survival (days) of mice after challenge. The mice had been immunised with the antigens indicated on the X-axis. Each point is an individual animal and the bar shows the median survival. The heading numbers show the % of animals surviving after 15 days.

MODES FOR CARRYING OUT THE INVENTION

10 Antigen selection

*S.aureus* proteins have been selected for use as vaccine components based on various criteria.

IsdA is a surface protein involved in iron uptake. It is detectable with a high molecular weight (>250kDa) in immunoblots of whole cell lysates and cell wall fractions of *S. aureus*. Furthermore, labelled anti-IsdA antibodies revealed extracellular structures. These structures were seen in a variety of growth and infection conditions, including iron positive conditions (in which IsdA expression is reported to be suppressed). The structures have a tail up to 4μm long, with a typical orientation parallel to the mammalian cell surface. Detached IsdA-positive structures were observed to adhere on the surface of epithelial cells, but lose cell junction localization. Epithelia/bacteria interaction may stimulate expression of the structures. In addition, the inventors have found that IsdA is well conserved between different strains (present in 36/36 strains tested; see below), thus offering protection across a broad population of circulating strains. Iron uptake is important for virulence, so the protein is likely to be available for immune attack at pathological stages of the bacterial life cycle. The inventors have found that the protein is not cytotoxic to human cells (see below). The protein can also adsorb reasonably well to aluminium hydroxide (see below), which is useful for stable formulation for delivery to humans. It is useful for providing an immune response to prevent hematic spread of the bacterium.

EsxA and EsxB are small acidic dimeric secreted proteins. The inventors have found that EsxA is highly conserved between different strains (present in 36/36 strains tested; see below), while EsxB is present in 25/36 strains. The proteins are involved in persisting an infection and so are likely to be available for immune attack at pathological stages of the bacterial life cycle. The inventors have found that a fusion of EsxA and EsxB ('EsxAB') is not cytotoxic to human cells (see below). It can also adsorb well to aluminium hydroxide (see below), which is useful for stable formulation for delivery to humans. Thus the antigens are useful for providing an immune response to prevent hematic spread of the bacterium.
HIa is a pore-forming secreted toxin. This protein is well conserved between different strains (present in 36/36 strains tested; see below), thus offering protection across a broad population of circulating strains. It is an important virulence factor so is likely to be available for immune attack at pathological stages of the bacterial life cycle. It is not cytotoxic to human cells (see below). The protein can adsorb reasonably well to aluminium hydroxide (see below), which is useful for stable formulation for delivery to humans. It is useful for providing an immune response to prevent pneumonia.

Spa is a surface protein involved in Fc binding. The inventors have found that this protein is well conserved between different strains (present in 36/36 strains tested), thus offering protection across a broad population of circulating strains. It is important for virulence so is likely to be available for immune attack at pathological stages of the bacterial life cycle. The protein can also adsorb reasonably well to aluminium hydroxide (see below), which is useful for stable formulation for delivery to humans. It is useful for providing an immune response to prevent hematic spread of the bacterium.

StaO06 (also known as FhuD2) is a surface protein involved in iron uptake. The inventors have found that this protein is well conserved between different strains (present in 36/36 strains tested; see below), thus offering protection across a broad population of circulating strains. The inventors have found that the protein is not cytotoxic to human cells (see below). The protein can also adsorb well to aluminium hydroxide (see below), which is useful for stable formulation for delivery to humans. It is useful for providing an immune response to prevent hematic spread of the bacterium.

StaOl I is a surface lipoprotein. The inventors have found that this protein is well conserved between different strains (present in 36/36 strains tested; see below), thus offering protection across a broad population of circulating strains. The inventors have found that the protein is not cytotoxic to human cells (see below). The protein can also adsorb reasonably well to aluminium hydroxide (see below), which is useful for stable formulation for delivery to humans. It is useful for providing an immune response to prevent hematic spread of the bacterium. This protein has been shown to assemble into oligomers in the presence of Ca^{2+} ions, but not Mg^{2+} ions (see Figure 8). These experiments used 5μg recombinant tag-free StaOll, incubated at 37°C for 25 minutes with increasing CaCl₂ concentrations from 0.5-50mM, then analysed by gel electrophoresis on a clear native gel. A mobility shift (indicating oligomerisation) was evident from 2mM Ca^{2+}, and particularly >5mM. These levels compare to blood Ca^{2+} concentrations of about 1.2mM, serum concentrations of about 1mM, and milk concentrations of about 32mM. EDTA reversed the shift.

Surface digestion [302] and/or analysis of secreted proteins revealed peptide fragments from CIfA, CIfB, coA, eap, ebhA, ebpS, efb, emp, FnBA, FnBB, hla, IsdA, IsdB, IsdH, ukD, lukS, sdrD, sdrE, sasB, sasD, sasF, spa, staO01, staO02, staO03, staO04, staO05, staO06, staO07, staO08, staO09, staO10, staO11, staO19, staO23, staO24, staO28, staO36, staO40, staO49, staO50, staO54, staO57, staO64, staO65, staO73, staO95, staO96, staO98, staO10, staO12, staO13, staO15, staO17, staO8, staO9, stal II.
stal l2, stal l3, stall5, stal 16, stal 17, stal 18, stal20, NW_06, NW_07, NW_08, NW_09 and NW_10 e.g. SEQ ID NOs: 228 and 229 were identified as fragments of staO19.

Conjugated capsular saccharides are useful for providing opsonic immunity. Serotypes 5 and 8 cover about 85% of clinical isolates.

5 Strain coverage
A panel of 36 clinical isolates was used to represent circulating strains, including strains belonging to the five clonal lineages representing the vast majority of worldwide circulating CA-MRSA (community-associated methicillin-resistant *S.aureus*). HA-MRSA (hospital-associated MRSA) and non-MRSA strains were also included. Overall the panel included 9 HA-MRSA strains, 7 CA-MRSA strains, 2 MRSA strains, and 18 other strains.

Genes encoding IsdA, Hla, EsxA, StaO06, StaOll, Spa, and CIfB were present in all 36 strains. The gene for EsxB was absent from 11/36 strains, and the gene for SdrD was absent from 6/36 strains.

The encoded IsdA sequences were 95-100% identical across the panel, and the protein was expressed in iron-limited conditions in the stationary growth phase. The encoded SdrD sequences were 95-100% identical in the 30/36 SdrD+ve panel members. The encoded EsxA sequences were 100% identical across the panel; the encoded EsxB sequences were 95-100% identical in the 25 EsxB+ve strains. The encoded CIfB sequences were 93-100% identical across the panel, and this protein was also found to be highly surface-exposed in the early exponential growth phase.

Conservation in the encoded amino acid sequences were as follows (% identity):

<table>
<thead>
<tr>
<th>Antigen</th>
<th>IsdA</th>
<th>CIfB</th>
<th>SdrD</th>
<th>Spa</th>
<th>Hla</th>
<th>EsxA</th>
<th>EsxB</th>
<th>Sta006</th>
</tr>
</thead>
<tbody>
<tr>
<td>%</td>
<td>95-100</td>
<td>97-100</td>
<td>88-100</td>
<td>98-100</td>
<td>97-100</td>
<td>100</td>
<td>95-100</td>
<td>99.7-100</td>
</tr>
</tbody>
</table>

A larger panel of 61 strains was screened for the presence of genes encoding Hla and StaO06, as well as for their expression. This panel covered both MRSA and MSSA strains, a variety of geographical origins, and a variety of ST and clonal complex types. 9/61 strains did not express Hla, whereas all but one strain expressed StaO06 (data for the 61st strain were inconclusive). Thus a vaccine based on Hla alone is unlikely to give adequate coverage for a universal vaccine, but this problem could be overcome by addition of StaO06.

Cytotoxicity and cell binding studies
The analysis of the potential cellular cytotoxicity by *S.aureus* recombinant antigens Hla, Hla-H35L, IsdA, IsdB, staO06, staOll and EsxB was conducted on HBMECs and A549 cells. Annexin V and propidium iodide staining were used to measure the percentage of early and late apoptotic cells by flow cytometry. Endothelial cells were grown in 24 well plates up to fully confluent. Cells were then incubated for 24 hours with three different concentration of recombinant antigens (10 µg/ml, 1µg/ml, 0.1 µg/ml). The combination of TNF-α and cycloheximide (CHX), which has been reported to induce
apoptosis in endothelial cells, was used as a positive control. Incubation with PBS buffer alone was a negative control. Analysis was then performed by FACS.

None of the antigens induced a cytotoxic effect on HBMECs or A549 cells. Indeed, the percentage of live cell population compared to control cells remained essentially constant up to 24 hours of incubation. In contrast, the combination of TNF-α and CHX induced a 25% increase in the number of apoptotic cells.

HBMECs were also used as an in vitro model for testing the binding of S. aureus recombinant antigens to human endothelial cells. HBMECs were grown up to confluence at 37°C in humidified atmosphere in RPMI 1640 medium supplemented with 10% heat-inactivated fetal calf serum, 10% NuSerum, 2mM glutamine, 1 mM pyruvate, 1% non-essential amino acids, 1% MEM vitamins, 100 units/ml penicillin, and 100 μg/ml streptomycin. Binding of recombinant antigens to the cells was tested by indirect immunofluorescence and analyzed by FACS. The cells positive for binding were measured as net mean intensity of fluorescence respect to negative controls, identified as unspecific antibody recognition. Binding experiments were performed at 4°C. Mouse polyclonal antibodies specific for each of the recombinant antigens were used as primary antibodies and binding was detected by R-Phycoerythrin-conjugated goat anti-mouse IgG secondary antibody. As negative control, HBMECs were incubated with primary polyclonal antibodies detected by fluorescence-labeled secondary antibody or fluorescence-labeled secondary antibody alone. Binding of a known surfaced-exposed GBS antigen was used as positive control.

Hla and Hla-H35L were the only antigens able to strongly bind to endothelial cells. The haemolytic activity of these two antigens was also tested.

De-fibrinated sheep and rabbit blood were used to measure their haemolytic activity by spectrophotometric assay. The blood was incubated at 37°C for 30 minutes with serial dilution 1:4 of the two proteins. Incubation with water, to cause osmotic lysis, and incubation with a S. pyogenes protein, were positive controls; as negative control, the blood was incubated with PBS+ BSA 0.5%.

Recombinant native Hla, but not its H35L mutant form, showed haemolytic activity on rabbit erythrocytes. The mutant was at least 150-fold less haemolytic than wild-type. Both proteins had no haemolytic activity on sheep blood.

Thus the S. aureus recombinant vaccine candidates do not show any cytotoxicity both on A549 epithelial cell line and HBMEC endothelial cell line. Importantly, Hla, a secreted toxin known to form pores into the plasma membrane of host cells, could bind A549 cells but did not induce cytotoxicity on them; it was also able to induce haemolysis of rabbit erythrocytes. In contrast, recombinant Hla-H35L, a variant toxin with a single amino acid substitution that cannot form cytolytic pores, did not induce cellular damage in both human cell lines and rabbit erythrocytes. These findings indicate that this mutant form of Hla may be more safely used in a vaccine composition. None of the other antigens showed the capacity to bind to host cells.
Adjuvant formulation

Selected *S. aureus* protein antigen candidates have been formulated with aluminium hydroxide, either individually or as a combination of proteins, with or without capsular polysaccharide conjugate(s). The formulations have been optimized for pH and osmolality.

The antigens were EsxA-B, StaOO6, StaOl1, Hla-H35L, SdrD, IsdA, ISdA₄₀₋₁₈₄, StaO19, StaO21, StaO73, ClfB₄₅₋₅₅₂, SdrD₅₃₋₅₉₂, SasF, and IsdB. These are formulated as monovalent antigens at 100µg/ml, or as combinations at 50µg/ml each. Capsular saccharide conjugates from type 5 or type 8 strains are added at 5µg/ml, 10µg/ml or 25µg/ml. Aluminium hydroxide was used at 2mg/ml, in a 10mM histidine buffer (pH 6.5) and with 9mg/ml NaCl.

All monovalent and combination formulations, with or without conjugates, could be adjusted with respect to a desired pH and osmolality. The formulations had pH in the range 6.2-7.3, and osmolality in the range 248-360 mOsm/kg. Glycerol was excluded from formulations as it had a negative impact on osmolality.

All proteins tested, in various monovalent and combination formulations, adsorbed well to the aluminium hydroxide adjuvant, except for IsdA, ISdA₄₀₋₁₈₄, StaO19, and StaO73.

The individual StaOO6, StaOl1, EsxA-B and Hla-H35L proteins were completely adsorbed, and could be desorbed without altering their pre-adsorption electrophoretic profile.

Each antigen in a combination of StaOO6, StaOl1, EsxA-B and Hla-H35L was completely adsorbed, with no inter-antigen competition for the adjuvant. The antigens in a combination of StaOO6, StaOl1, EsxA-B and ISdA₄₀₋₁₈₄ were also completely adsorbed, except for ISdA₄₀₋₁₈₄, which behaved in the same way as the monovalent protein. For both combinations, the antigens could be desorbed without altering their pre-adsorption electrophoretic profile.

The additional presence of type 5 and/or type 8 conjugates also did not change the adsorption or desorption characteristics of the antigens e.g. in combination with StaOO6+StaOl1+EsxA-B.

A short stability study (2 weeks at 4°C) was performed to evaluate the stability of monovalent formulations and to evaluate antigen integrity. All tested formulations were stable for their pH and osmolality. All antigens remained completely adsorbed to the adjuvant. All antigens maintained their desorption characteristics. There was no evidence of increased degradation or aggregation of antigens after desorption.

Efficacy testing

Individual antigens staOO6, staOll, staO12, staO17, staO19, staO21 and staO28 were tested for their ability to protect against IV challenge by 1.2x10⁷ cfu of Newman strain (type 5). Results are shown in Figure 1. All antigens reduced bacterial numbers compared with the control, and the best results were seen with staOO6, staO1l and staO19.
Further individual antigens were tested: (i) NW_10; (ii) ISdA_{40-184}; (iii) Sta002; (iv) Sta003; (v) Sta073; (vi) StaOl; (vii) StaO14; (viii) Hla-PSGS; (ix) SdrD_{CnA}. The increase in survival, compared to the negative control group, 15 days after challenge was: (i) 50%; (ii) 19%; (iii) 37%; (iv) 43%; (v) 25%; (vi) 12%; (vii) 25%; (viii) 56%; (ix) 39%.

Two hybrid polypeptides were also tested: (i) HlaH35L-EsxAB; (ii) Sta006-EsxAB. The increase in survival after challenge, compared to the negative control group, was: (i) 25%; (ii) 25%.

Table 2 gives a summary of results obtained with various antigens in the abscess model.

Experiment SA-10-a tested the efficacy of antigen combinations. Six groups of twelve CD1 mice received a negative control (PBS), IsdB, or one of the following combinations, adjuvanted with aluminium hydroxide: (i) EsxAB + Hla-H35L; (ii) StaO06 + StaOl 1 + EsxAB; (iii) StaO06 + StaOl 1 + EsxAB + Hla-H35L; or (iv) StaO06 + StaOl 1 + ISdA_{40-184} + EsxAB. Two administrations were given, at days 0 and 14. At day 24 mice received 3x10^8 cfu of Newman strain staphylococcus and survival in each group was assessed every 24 hours for two weeks. Results are shown in Figure 2. After 14 days, 25% of animals in the positive control group had survived, but 50% of animals in group (ii) had survived, as had 58% of animals in groups (iii) & (iv), and 75% in group (i).

Experiment SA-10-b used the same methods to test: (i) CIfB_{45,552} + Hla-H35L + StaO06 + EsxAB; (ii) CIfB_{45,552} + StaOl 1 + StaO06 + EsxAB; (iii) CIfB_{45,552} + ISdA_{40-184} + StaO06 + EsxAB; or (iv) SdrD_{53,592} + ISdA_{40-184} + StaO06 + EsxAB. Results are shown in Figure 3. After 14 days, 25% of animals in the positive control group and in group (ii) had survived, but 33% of animals in group (iv) had survived, 75% of animals in group (i), and 83% of animals in group (iii).

Further combinations were also used to immunise mice. The combinations were typically adjuvanted with aluminium hydroxide (see above) and were administered on days 0 and 14. The immunisations were in CD1 mice, 12 per group. On day 24 the mice were challenged with a lethal dose of live bacteria and survival was then followed for 14 further days. For comparison, PBS was used as a negative control and IsdB as a positive control [2].

Experiment SA-11 tested: (i) a type 5 conjugate combined with EsxAB + StaO06 + StaOl 1; (ii) EsxAB + StaOl 9 + StaO06 + StaOl 1; (iii) a type 5 conjugate + Hla-H35L + StaO06 + StaOl 1; (iv) EsxAB + Hla-H35L + StaO06 + StaOl 1; or (v) EsxAB + ISdA_{40-184} + StaO06 + StaOl 1. 14 days after challenge all of the negative control animals had died, but 42% of positive control animals had survived. Survival results in the test groups were as follows: (i) 67%; (ii) 42%; (iii) 75%; (iv) 33%; and (v) 25%.

Experiment SA-12 tested: (i) Hla-H35L + ISdA_{40-184} + StaO06 + StaOl 1; (ii) Hla-H35L + EsxAB + StaO06 + StaOl 1; (iii) EsxAB + ISdA_{40-184} + StaO06 + StaOl 1; (iv) EsxAB + ISdA + StaO06 + StaOl 1. 14 days after challenge 8% of the negative control animals and 17% of positive control animals had survived. Survival results in the test groups were as follows: (i) 50%; (ii) 50%; (iii) 25%; (iv) 33%.
Experiment SA-14 tested: (i) EsxAB + Hla-H35L + StaOOØ + StaOl1; (ii) EsxAB + ISdA40-184 + StaOOØ + StaOl1; (iii) StaOOØ + StaOl1 + StaO19 + EsxAB; (iv) StaOOØ + StaOl1 + StaO19 + Hla-H35L. 14 days after challenge with 5x10^8 CFU of Newman strain, 18% of the negative control animals and 9% of positive control animals had survived; survival results in the test groups were as follows: (i) 58%; (ii) 67%; (iii) 42%; (iv) 83%. Survival numbers over 14 days are shown in Figure 4, showing that all combinations performed better than the two controls on every post-challenge day.

Experiment SA-17a tested: (i) EsxAB + StaOOØ + StaOl1 + serotype 5 conjugate + serotype 8 conjugate; (ii) EsxAB + StaO73 + StaOl1 + serotype 5 conjugate + serotype 8 conjugate; (iii) EsxAB + Hla-H35L + StaOll + StaO73. Compared to the negative control, the increase in survival 15 days after challenge with Newman strain was: (i) 17%; (ii) 42%; (iii) 34%. The median survival in groups (ii) and (iii) was the full 15 days, and was 12 days in group (i).

Further antigen combination experiments tested: (a) serotype 5 conjugate + serotype 8 conjugate + EsxAB + StaOOØ + StaOll; (b) Sta002+Sta003+Sta021+NW-10; (c) EsxAB+ HlaH35L + StaOOØ + StaO19; and (d) EsxAB + Sta006+Sta019. Compared to the negative control, the increase in survival after challenge with Newman strain was: (a) 37%; (b) 36%; (c) 13%. ; and (d) 0%.

Survival data from studies SA-10, SA-11, SA-12 and SA-14 were combined to assess the efficacy of two combinations when compared to PBS or IsdB. "Combo- 1" was EsxAB+Hla-H35L+Sta006+Sta011 (with polypeptides comprising SEQ ID NOs: 241, 150, 246 & 247). "Combo-2" was EsxAB+IsdA_501g+StaOO6+StaOll. The median survival times for each group of 48 mice after 14 days were compared. Whereas the PBS and IsdB groups had a median survival time of 1 day, mice in the "Combo- 1" and "Combo-2" groups had a median survival time of 14 days. The differences in median survival duration were compared by a t-test: survival in the "Combo- 1" group was statistically superior to both the PBS group (p<0.0001) and the IsdB group (p<0.0001); survival in the "Combo-2" group was statistically superior to both the PBS group (p<0.0001) and the IsdB group (p=0.0049). These data are shown in Figure 5.

Figure 6 shows data with Combo- 1 and Combo-2 in the abscess model. Kidneys of mice are isolated after challenge and are then homogenised and plated. The cfu count indicates the level of abscess formation. Figure 6 shows data from a single experiment. The numbers beneath the data show the log reduction relative to the PBS group. The reduction is bigger in the two combination groups than with IsdB alone, with U-test (one tail) values of 0.0001 for Combo- 1 and 0.0005 for Combo-2. The same effect was seen in the two combination groups in a second experiment in which an IsdB group was not included.

Further experiments compared protection achieved with Combo- 1, IsdB or PBS against challenge with three different strains: Staph-19, FPR3757(USA300) and Lac(USA300). There were 44 mice per group and results were as follows (see also Figure 12), including one-tailed p-values for the
survival proportion, where: \( P_1 \) compares Combo-1 with PBS; \( P_2 \) compares Combo-1 with IsdB; and \( P_3 \) compared PBS with IsdB:

<table>
<thead>
<tr>
<th></th>
<th>Staph-19</th>
<th></th>
<th></th>
<th>Lac</th>
</tr>
</thead>
<tbody>
<tr>
<td>Survival</td>
<td>%</td>
<td>Days</td>
<td>%</td>
<td>Days</td>
</tr>
<tr>
<td>PBS</td>
<td>20</td>
<td>1</td>
<td>45</td>
<td>8</td>
</tr>
<tr>
<td>IsdB</td>
<td>32</td>
<td>1</td>
<td>52</td>
<td>15</td>
</tr>
<tr>
<td>Combo-1</td>
<td>80</td>
<td>15</td>
<td>91</td>
<td>15</td>
</tr>
<tr>
<td>( P_1 )</td>
<td>&lt;0.0001</td>
<td>-</td>
<td>&lt;0.0001</td>
<td>-</td>
</tr>
<tr>
<td>( P_2 )</td>
<td>&lt;0.0001</td>
<td>-</td>
<td>&lt;0.0004</td>
<td>-</td>
</tr>
<tr>
<td>( P_3 )</td>
<td>0.1715</td>
<td>-</td>
<td>0.2137</td>
<td>-</td>
</tr>
</tbody>
</table>

Further experiments showed that immunisation with adjuvanted Combo 1 reduced CFU counts after challenge with Newman, USA100, CC30 and USA300 strains, when compared to immunisation with adjuvant alone (aluminium hydroxide) or IsdB. Figure 10 shows CFU values (log/ml) for the four challenge strains. The lowest count, with \( p<0.015 \) in each case, was achieved with Combo 1. The area of abscess was also assessed and was also lower in the Combo 1-immunised mice (e.g. Figure 11).

Further experiments showed that Combo 1 is highly protective against clinically relevant strains in the sepsis model, and always achieved a higher survival % than IsdB. Figure 12 shows that the median survival in Combo 1-immunised mice (40 per group, 3 experiments) was the full 15 days when challenged with Newman, ST-80, FPR3757 or Lac strains, and that the proportion of mice surviving was \( \geq 75\% \). In contrast, the median survival in IsdB-immunised mice was only 1 day with Newman and ST-80 challenge, with \( <65\% \) survival for all four challenge strains.

*Comparison of Combo 1 to its individual polypeptides*

Various tests were performed to compare Combo 1 to its four individual polypeptides (*i.e.* EsxAB, Hla-H35L, Sta006, Sta011), as well as to IsdB or to an antigen-free negative control.

The opsonophagocytic activity of sera from immunised animals was tested. Sera were obtained using (i) the four individual polypeptides, (ii) all pairs of the polypeptides, (iii) all triplets, or (iv) the full Combo 1 combination. For comparison, anti-IsdB serum was used. Pre-immune and negative control sera showed no killing of Newman strain in this assay. In a first experiment: anti-IsdB serum showed 27% killing; sera against each of the four individual polypeptides showed between 26-34% killing; all multi-polypeptide combinations showed at least 34% killing; and sera raised with Combo-1 showed 39% killing. In a second experiment sera with Combo-1 showed 43% killing but anti-IsdB serum performed slightly better; all single or multi-polypeptide sera using the Combo-1 polypeptides showed at least 26% killing.

Further experiments looked at passive protection achieved by transferring into mice (20 per group, 8 week old CD1 mice) antiserum from immunised rabbits. Four groups received 200µl of sera from
rabbits immunised with one of EsxAB, Hla-H35L, Sta006, StaOl1; a fifth group received 50µl of each serum (200µl in total). Two other groups received serum from IsdB-immunised rabbits or serum from rabbits immunised with saline+adjuvant. 15 minutes later the mice were challenged intraperitoneally (10^8 CFU of Newman strain) and then mortality was assessed after 14 days. Results were as follows:

<table>
<thead>
<tr>
<th></th>
<th>EsxA-B</th>
<th>Sta006</th>
<th>Sta011</th>
<th>HlaH35L</th>
<th>Combo1</th>
<th>IsdB</th>
<th>-ve ctrl</th>
</tr>
</thead>
<tbody>
<tr>
<td>Survival</td>
<td>5%</td>
<td>26%</td>
<td>0%</td>
<td>15%</td>
<td>25%</td>
<td>10%</td>
<td>5%</td>
</tr>
</tbody>
</table>

In further experiments the level of specific antibodies induced in CD1 mice were examined to assess the immunogenicity of the four polypeptides in Combol. Compositions included either 20µg of each of the four single polypeptides, or 4x10µg in the combination. The compositions included an aluminium hydroxide adjuvant. Serum levels of antigen-specific IgG were determined by Luminex 4Plex assay. As shown in Figure 9, all four polypeptides were highly immunogenic in CD1 mice on their own and in combination. In each case the titer against a polypeptide was higher when it was administered in the combination than when administered alone (compare middle and right pairs).

Further experiments compared protection achieved either with Combo-1 or with its four individual polypeptides. IsdB was also included for comparison. The proportions of animals surviving (40 animals per group) 15 days after challenge with Newman strain, and the average (median) survival in days, were as follows, including a one-tailed p-value of the surviving proportion in comparison with a PBS+adjuvant negative control:

<table>
<thead>
<tr>
<th></th>
<th>EsxA-B</th>
<th>Sta006</th>
<th>Sta011</th>
<th>HlaH35L</th>
<th>Combo1</th>
<th>IsdB</th>
<th>PBS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Survival</td>
<td>34%</td>
<td>28%</td>
<td>16%</td>
<td>39%</td>
<td>59%</td>
<td>22%</td>
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</tr>
<tr>
<td>p</td>
<td>0.0017</td>
<td>0.0003</td>
<td>0.0064</td>
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<td>&lt;0.0001</td>
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<td>-</td>
</tr>
<tr>
<td>Days</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>10</td>
<td>15</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

The murine abscess model was used to compare the four individual polypeptides with the Combol combination. In some experiments mice were immunised with IsdB for comparison. Antigens were adjuvanted with aluminium hydroxide, and adjuvant alone was used as a negative control. Figure 7 shows the numbers of bacteria in animals' kidneys after challenge with four different strains. The lowest average counts were seen for the Combol combination.

Challenge experiments were performed following immunisation with (i) the four individual polypeptides, (ii) all pairs, (iii) all triplets, or (iv) the full Combol combination. IsdB or buffer alone were used for comparison. Survival results from 24 mice per group (3 experiments) after challenge with 5x10^8 CFU of Newman strain are shown in Figure 13. The median survival for IsdB was only 2 days. The median survival for the individual Combol polypeptides ranged from 1-6 days. Pairs of the polypeptides gave median survival of 2-11 days. Triplets gave median survival of 8-15 days. The
full Combo 1 combination gave a median survival of the full 15 days, with 59% of mice surviving this long (c/ only 35% with IsdB).

It will be understood that the invention has been described by way of example only and modifications may be made whilst remaining within the scope and spirit of the invention.

5 **TABLE 1: NOMENCLATURE CROSS-REFERENCE**

<table>
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** Log reduction in kidney CFU

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[272] GB 2,276,169.
[280] PCR (Introduction to Biotechniques Series), 2nd ed. (Newton & Graham eds., 1997, Springer Verlag)
1. An immunogenic composition comprising a combination of antigens, said combination comprising two or more antigens selected from the group consisting of: (1) a staO06 antigen; (2) a staO1 antigen; (3) a exsA antigen; (4) a exsB antigen; (5) a hla antigen; (6) a ebpS antigen; (7) a efb antigen; (8) a emp antigen; (9) a esaC antigen; (10) a coA antigen; (11) a eap antigen; (12) a FnBA antigen; (13) a FnBB antigen; (14) a ebhA antigen; (15) a hlgB antigen; (16) a hlgC antigen; (17) a isaD antigen; (18) a isdB antigen; (19) a isdC antigen; (20) a isdG antigen; (21) a isdH antigen; (22) a isdL antigen; (23) a lukD antigen; (24) a lukE antigen; (25) a lukF antigen; (26) a lukS antigen; (27) a nuc antigen; (28) a sasA antigen; (29) a sasB antigen; (30) a sasC antigen; (31) a sasD antigen; (32) a sasF antigen; (33) a sdrC antigen; (34) a sdrD antigen; (35) a sdrE2 antigen; (36) a spa antigen; (37) a clfA antigen; (38) a clfB antigen; (39) a staO01 antigen; (40) a staO02 antigen; (41) a staO03 antigen; (42) a staO04 antigen; (43) a staO05 antigen; (44) a staO07 antigen; (45) a staO08 antigen; (46) a staO09 antigen; (47) a staO10 antigen; (48) a staO12 antigen; (49) a staO13 antigen; (50) a staO14 antigen; (51) a staO15 antigen; (52) a staO16 antigen; (53) a staO17 antigen; (54) a staO18 antigen; (55) a staO19 antigen; (56) a staO20 antigen; (57) a staO21 antigen; (58) a staO22 antigen; (59) a staO23 antigen; (60) a staO24 antigen; (61) a staO25 antigen; (62) a staO26 antigen; (63) a staO27 antigen; (64) a staO28 antigen; (65) a staO29 antigen; (66) a staO30 antigen; (67) a staO31 antigen; (68) a staO32 antigen; (69) a staO33 antigen; (70) a staO34 antigen; (71) a staO35 antigen; (72) a staO36 antigen; (73) a staO37 antigen; (74) a staO38 antigen; (75) a staO39 antigen; (76) a staO40 antigen; (77) a staO41 antigen; (78) a staO42 antigen; (79) a staO43 antigen; (80) a staO44 antigen; (81) a staO45 antigen; (82) a staO46 antigen; (83) a staO47 antigen; (84) a staO48 antigen; (85) a staO49 antigen; (86) a staO50 antigen; (87) a staO51 antigen; (88) a staO52 antigen; (89) a staO53 antigen; (90) a staO54 antigen; (91) a staO55 antigen; (92) a staO56 antigen; (93) a staO57 antigen; (94) a staO58 antigen; (95) a staO59 antigen; (96) a staO60 antigen; (97) a staO61 antigen; (98) a staO62 antigen; (99) a staO63 antigen; (100) a staO64 antigen; (101) a staO65 antigen; (102) a staO66 antigen; (103) a staO67 antigen; (104) a staO68 antigen; (105) a staO69 antigen; (106) a staO70 antigen; (107) a staO71 antigen; (108) a staO72 antigen; (109) a staO73 antigen; (110) a staO74 antigen; (111) a staO75 antigen; (112) a staO76 antigen; (113) a staO77 antigen; (114) a staO78 antigen; (115) a staO79 antigen; (116) a staO80 antigen; (117) a staO82 antigen; (118) a staO83 antigen; (119) a staO84 antigen; (120) a staO85 antigen; (121) a staO86 antigen; (122) a staO87 antigen; (123) a staO88 antigen; (124) a staO89 antigen; (125) a staO90 antigen; (126) a staO91 antigen; (127) a staO92 antigen; (128) a staO93 antigen; (129) a staO94 antigen; (130) a staO95 antigen; (131) a staO96 antigen; (132) a staO97 antigen; (133) a staO98 antigen; (134) a staO99 antigen; (135) a stalO0 antigen; (136) a stalO1 antigen; (137) a stalO2 antigen; (138) a stalO3 antigen; (139) a stalO4 antigen; (140) a stalO5 antigen; (141) a stalO6 antigen; (142) a stalO7 antigen; (143) a stalO8 antigen; (144) a stalO9 antigen; (145) a stallO antigen; (146) a stall 1 antigen; (147) a stall 2 antigen; (148) a stall3 antigen; (149) a stall 14 antigen; (150) a stall5 antigen; (151) a stall 16 antigen; (152) a stall 17 antigen; (153) a stall 18 antigen; (154) a stall9 antigen; (155) a stall20 antigen; (156) a NW_6 antigen; (157) a NW_9 antigen; (158) a NW_10 antigen; (159) a NW_7 antigen; (160) a NWJ
antigen; (161) a NW_2 antigen; (162) a NW_1 antigen; (163) a staO81 antigen; and (164) a NW_5 antigen.

2. The composition of claim 1, comprising at least one antigen selected from numbers (3) to (38) and at least one antigen selected from numbers (1), (2) and (37) to (149).

3. The composition of claim 2, comprising:
   at least one antigen selected from numbers (37), (38), (8), (9), (3), (4), (5), (17), (18), (19), (31), (32), (33), (34), (35) and (36);
   and at least one antigen selected from (40), (1), (43), (2), (64), (96), (133) and (147).

4. The composition of claim 1, comprising two or more antigens selected from the group consisting of: (1) a clfA antigen; (2) a clfB antigen; (3) a sdrE2 antigen; (4) a sdrC antigen; (5) a SasF antigen; (6) a emp antigen; (7) a sdrD antigen; (8) a spa antigen; (9) a esaC antigen; (10) a esaA antigen; (11) a exsB antigen; (12) a sta006 antigen; (13) a isdC antigen; (14) a hla antigen; (15) a staOl l antigen; (16) isdA antigen; (17) a isdB antigen; (18) a sasF antigen.

5. The composition of claim 1, two or more antigens selected from the group consisting of: (1) a exsA antigen; (2) a exsB antigen; (3) a sta006 antigen; (4) a hla antigen; (5) a staOl l antigen.

6. The composition of any preceding claim, wherein one or more of said antigens is adsorbed to an aluminium hydroxide adjuvant, and optionally wherein the composition includes a histidine buffer.

7. The composition of any preceding claim, further comprising: one or more conjugates of (i) a S. aureus exopolysaccharide and (ii) a carrier protein.

8. The composition of any preceding claim, further comprising: one or more conjugates of (i) a S. aureus capsular polysaccharide and (ii) a carrier protein.

9. A polypeptide of formula NH₂₆₋[-X-L-]π-B-COOH, wherein:
   X is an amino acid sequence of a staphylococcal antigen, selected from the group consisting of S. aureus antigens sta006, staOl 1, esaA, exsB, hla, clfA, clfB, coA, eap, ebhA, ebpS, efb, emp, esaC, FnBA, FnBB, hlgB, hlgC, isdA, isdB, isdC, isdG, isdH, isdL, lukD, lukE, lukF, lukS, nuc, sasA, sasB, sasC, sasD, sasF, sdrC, sdrD, sdrE2, spa, staO01, sta002, sta003, sta004, sta005, sta007, sta008, sta009, staO10, staO12, staO13, staO14, staO15, staO16, staO17, staO18, staO19, staO20, staO21, staO22, staO23, staO24, staO25, staO26, staO27, staO28, staO29, staO30, staO31, staO32, staO33, staO34, staO35, staO36, staO37, staO38, staO39, staO40, staO41, staO42, staO43, staO44, staO45, staO46, staO47, staO48, staO49, staO50, staO51, staO52, staO53, staO54, staO55, staO56, staO57, staO58, staO59, staO60, staO61, staO62, staO63, staO64, staO65, staO66, staO67, staO68, staO69, staO70, staO71, staO72, staO73, staO74, staO75, staO76, staO77, staO78, staO79, staO80, staO81, staO82, staO83, staO84, staO85, staO86, staO87, staO88, staO89, staO90, staO91, staO92, staO93, staO94, staO95, staO96, staO97, staO98, staO99, stao0, stao10, stao1, stao12, stao13, stao14, stao15, stao16, stao17, stao18, stao19, stao20, stao21, stao22, stao23, stao24, stao25, stao26, stao27, stao28, stao29, stao30, stao31, stao32, stao33, stao34, stao35, stao36, stao37, stao38, stao39, stao40, stao41, stao42, stao43, stao44, stao45, stao46, stao47, stao48, stao49, stao50, stao51, stao52, stao53, stao54, stao55, stao56, stao57, stao58, stao59, stao60, stao61, stao62, stao63, stao64, stao65, stao66, stao67, stao68, stao69, stao70, stao71, stao72, stao73, stao74, stao75, stao76, stao77, stao78, stao79, stao80, stao81, stao82, stao83, stao84, stao85, stao86, stao87, stao88, stao89, stao90, stao91, stao92, stao93, stao94, stao95, stao96, stao97, stao98, stao99, stao0, stao10, stao1, stao2, stao3, stao4, stao5, stao6, stao7, stao8, stao9, stalo, stal1, stal2, stal3, stal4, stal5, stal6, stal7, stal8, stalo1, stalo2, stalo3, stalo4, stalo5, stalo6, stalo7, stalo8, stalo9, stal0, stal1, stal2, stal3, stal4, stal5, stal6, stal7, stal8, stalo1, stalo2, stalo3, stalo4, stalo5, stalo6, stalo7, stalo8, stalo9, stal0, stal1, stal2, stal3, stal4, stal5, stal6, stal7, stal8, stalo1, stalo2, stalo3, stalo4, stalo5, stalo6, stalo7, stalo8, stalo9, stal0, stal1, stal2, stal3, stal4, stal5, stal6, stal7, stal8, stalo1, stalo2, stalo3, stalo4, stalo5, stalo6, stalo7, stalo8, stalo9, stal0, stal1, stal2, stal3, stal4, stal5, stal6, stal7, stal8, stalo1, stalo2, stalo3, stalo4, stalo5, stalo6, stalo7, stalo8, stalo9, stal0, stal1, and stal2;
L is an optional linker amino acid sequence;
A is an optional N-terminal amino acid sequence;
B is an optional C-terminal amino acid sequence; and
n is an integer of 2 or more.

10. An immunogenic composition comprising the polypeptide of claim 9 and further comprising:
(A) one or more conjugates of (i) a \textit{S.aureus} exopolysaccharide and (ii) a carrier protein; and/or
(B) one or more conjugates of (i) a \textit{S.aureus} capsular polysaccharide and (ii) a carrier protein.

11. The composition or polypeptide of any preceding claim, wherein the clfA antigen can elicit an
antibody which recognises SEQ ID NO: 1 and comprises an amino acid sequence: (a) having
80\% or more identity to SEQ ID NO: 1; and/or (b) comprising a fragment of at least 7
consecutive amino acids of SEQ ID NO: 1, wherein the fragment comprises an epitope from SEQ
ID NO: 1.

12. A polypeptide comprising amino acid sequence (a) having 80\% or more identity to SEQ ID NO:
151; and/or (b) comprising a fragment of at least 7 consecutive amino acids from amino acids
1-97 of SEQ ID NO: 151 and at least 7 consecutive amino acids from amino acids 104-207 of
SEQ ID NO: 151, wherein the polypeptide can elicit antibodies which recognise both the wild-
type staphylococcal protein comprising SEQ ID NO: 10 and the wild-type staphylococcal protein
comprising SEQ ID NO: 11.

13. An immunogenic composition comprising the polypeptide of claim 12 and one or more of (i) a
\textit{S.aOO6} antigen; (ii) a hla antigen; and/or (iii) a staOl 1 antigen.

14. The composition of claim 13, including an adjuvant.

15. A polypeptide comprising amino acid sequence having 80\% or more identity to an amino acid
sequence selected from SEQ ID NOs: 151, 152, 168, 202, 203, 204, 205, 206, 207, 208, 209,
210, 211, 212, 220, 221, 222, 223, 224, 237, 238, 241.

16. A polypeptide comprising an amino acid sequence selected from SEQ ID NOs: 151, 152, 168,
202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 220, 221, 222, 223, 224, 237, 238, 241,
242, 243, 244, 245.

17. A polypeptide comprising: (a) a first sequence having 90\% or more identity to SEQ ID NO: 218;
and (b) a second sequence having 90\% or more identity to SEQ ID NO: 219, wherein the first
and second sequences are either directly joined or are joined by an intervening amino acid
sequence having fewer than 10 amino acids.

18. A pharmaceutical composition comprising the polypeptide of any one of claims 12, 15, 16 or 17.

19. A method for raising an immune response in a mammal comprising the step of administering to
the mammal an effective amount of the polypeptide or composition of any preceding claim.

20. Nucleic acid encoding the polypeptide of claim 9, 12, 15, 16 or 17.
**FIGURE 7C**

![Figure 7C](image)

**FIGURE 7D**

![Figure 7D](image)
FIGURE 13

- PBS
- lsdB
- Sta006
- Hla H35L
- Hla H35L + EsxA-B
- Hla H35L + Sta006
- EsxA-B + Sta006
- Sta006 + Sta011
- Hla H35L + EsxA-B + Sta006 + Sta011
- Combo 1

Legend:
- 8%
- 35%
- 13%
- 42%
- 42%
- 29%
- 50%
- 37%
- 42%
- 29%
- 42%
- 37%
- 71%
- 50%
- 58%
- 46%
- 59%