CLAIMS

1. ~~A~~ An in vitro method of eliminating or reducing a bacterial biofilm comprising

a) providing a fusion protein comprising an endolysin or bacteriocin to which a peptide ~~with membrane or LPS disrupting activity~~ is fused, wherein said peptide fused to the endolysin or bacteriocin is a synthetic cationic, a synthetic polycationic, a synthetic hydrophobic, a synthetic amphiphatic or a naturally occurring antimicrobial peptide; and

b) contacting a material, liquid, surface or biological material with said fusion protein.

2. The method according to claim 1, wherein said peptide fused to the endolysin, or bacteriocin is a synthetic or naturally occurring peptide having a length of 6 to 39 amino acid residues.

~~3. The method according to claim 1 or 2, wherein said peptide fused to the endolysin or bacteriocin is a synthetic cationic, a synthetic polycationic, a synthetic hydrophobic, a synthetic amphiphatic or a naturally occurring antimicrobial peptide.~~

~~4.~~3. The method according to any one of the preceding claims, wherein said peptide is fused to the N- and/or the C-terminus of the endolysin.

~~5.~~4. The method according to any one of the preceding claims, wherein said endolysin or bacteriocin has the activity of degrading the cell wall of Gram-negative and/or Gram-positive bacteria.

~~6.~~5. The method according to claim ~~5~~4, wherein the cell wall of the Gram-negative bacteria is selected from the group consisting of *Enterobacteriaceae* (*Escherichia*, especially *E. coli, Salmonella, Shigella, Citrobacter, Edwardsiella, Enterobacter, Hafnia, Klebsiella, especially K. pneumoniae, Morganella, Proteus, Providencia, Serratia, Yersinia*), *Pseudomonadaceae* (*Pseudomonas,* especially *P. aeruginosa, Burkholderia, Stenotrophomonas, Shewanella, Sphingomonas, Comamonas*), *Neisseria, Moraxella, Vibrio, Aeromonas, Brucella, Francisella, Bordetella,*

Legionella, Bartonella, Coxiella, Haemophilus, Pasteurella, Mannheimia, Actinobacillus, Gardnerella, Spirochaetaceae (*Treponema and Borrelia*), *Leptospiraceae, Campylobacter, Helicobacter, Spirillum, Streptobacillus, Bacteroidaceae* (*Bacteroides, Fusobacterium, Prevotella, Porphyromonas*), *Acinetobacter*, especially *A. baumannii* and wherein the Gram-positive bacteria are selected from the group consisting of *Listeria monocytogenes, Staphylococcus aureus, Enterococcus faecalis, Enterococcus faecium, Streptococcus pneumoniae, Streptococcus pyogenes, Streptococcus mutans, Streptococcus equi, Clostridium difficile, Clostridium botulinum, Clostridium tetani, Clostridium perfringens, Bacillus anthracis, Bacillus cereus, Propionibacterium acnes, Mycobacterium avium, Mycobacterium tuberculosis, Corynebacterium diphteriae, Mycoplasma pneumoniae, Actinomyces.*

~~7.~~6. The method according to any one of the preceding claims, wherein said endolysin is selected from the group consisting of phiKZgp144 according to SEQ ID NO: 1, ELgp188 according to SEQ ID NO: 2, *Salmonella endolysin* according to SEQ ID NO: 3, *Enterobacteria phage T4 endolysin* according to SEQ ID NO: 4, *Acinetobacter baumannii endolysin* according to SEQ ID NO: 5, *E.coli* Phage K1F endolysin according to SEQ ID NO: 6, OBPgpLys according to SEQ ID NO: 7, PSP3 salmonella endolysin according to SEQ ID NO: 8, E.coli Phage P2 endolysin according to SEQ ID NO: 9, Ply511 according to SEQ ID NO: 85, Ply2638 according to SEQ ID NO: 92 or wherein said bacteriocin is according to SEQ ID NO: 87.

~~8.~~7. The method according to any one of the preceding claims, wherein the cationic/ polycationic peptide exhibits an amino acid sequence according to SEQ ID NO: 10 to 30 and 32 to 34, or wherein the antimicrobial peptide exhibits an amino acid sequence according to SEQ ID NO: 93 to 133, or wherein the hydrophobic peptide exhibits an amino acid sequence according to SEQ ID NO: 134 and 135; or wherein the amphiphatic peptide exhibits an amino acid sequence according to SEQ ID NO: 136 to 138.

~~9.~~8. The method according to any one of the preceding claims, wherein said endolysin variant or bacteriocin variant comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 35 to 49, 53, 57, 62 to 64, 66 to 78 and 139 to 142.

~~10.~~9. The method according to any one of the preceding claims, wherein the material contacted with the fusion protein is a stone, rocks, soil, sediments, food, feed or cosmetics.

~~11.~~10. The method according to any one of the preceding claims, wherein the liquid contacted with the fusion protein is water.

~~12.~~11. The method according to claim ~~11~~10, wherein water is drinking water, ground water or waste water, hot spring, sea, lake, river, any kind of aqueous system, cleaning and storage solutions of contact lenses, dentures, implants, prothesis or braces.

~~13.~~12. The method according to any one of the preceding claims, wherein the liquid contacted with the fusion protein is any substance derived or obtained from a living organism.

~~14.~~13. The method according to any one of the preceding claims, wherein the liquid contacted with the fusion protein is surface of medical devices, of industrial or potable water system piping and of natural aquatic systems.

~~15.~~14. The method according to any one of the preceding claims, wherein in combination or in addition to the fusion protein antibiotics can be added.

~~16.~~15. ~~An~~ The use of an endolysin variant or a bacteriocin variant comprising an endolysin or bacteriocin to which a peptide ~~with membrane or LPS disrupting activity~~ is fused ~~for use as~~in the preparation of a medicament for the treatment of Gram-negative and/or Gram-positive bacterial infections associated with bacterial biofilm, wherein said peptide fused to the endolysin or bacteriocin is a synthetic cationic, a synthetic polycationic, a synthetic hydrophobic, a synthetic amphiphatic or a naturally occurring antimicrobial peptide.

~~17.~~16. ~~An~~ The use of an endolysin variant or a bacteriocin variant ~~for use~~ according to claim ~~16~~15, wherein the endolysin variant or bacteriocin variant is used in combination or in addition to antibiotics.

~~18.~~17. The use of an endolysin variant or a bacteriocin variant comprising an endolysin or bacteriocin to which a peptide ~~with membrane or LPS disrupting activity~~ is fused for the removal and/or reduction of Gram-negative and/or Gram-positive bacterial contamination associated with bacterial biofilm of foodstuff, of food processing equipment, of food processing plants, of surfaces coming into contact with foodstuff, of medical devices, of surfaces in hospitals or surgeries, wherein said peptide fused to the endolysin or bacteriocin is a synthetic cationic, a synthetic polycationic, a synthetic hydrophobic, a synthetic amphiphatic or a naturally occurring antimicrobial peptide.

~~19.~~18. The use of an endolysin variant or a bacteriocin variant comprising an endolysin or bacteriocin to which a peptide ~~with membrane or LPS disrupting activity~~ is fused as a diagnostic means in medicinal, food or feed or environmental diagnostics of bacteria infection associated with bacterial biofilm, as disinfectant or cosmetic substance, wherein said peptide fused to the endolysin or bacteriocin is a synthetic cationic, a synthetic polycationic, a synthetic hydrophobic, a synthetic amphiphatic or a naturally occurring antimicrobial peptide.

~~20.~~19. The use according to claims ~~18~~ 17 and ~~19~~18, wherein the endolysin variant or bacteriocin variant is used in combination or in addition to antibiotics.