CLAIMS:

1. Use of a nucleic acid vector comprising a~~A~~ host modifying (HM) CRISPR array~~/Cas system,~~ in the manufacture of a medicament for ~~use in~~ treating or preventing, in a human or animal subject, a condition or disease mediated by bacterial host cells~~,~~ by altering the relative ratio of sub-populations of first and second bacteria in a mixed population of bacteria, the second bacteria comprising host cells, wherein the mixed population is comprised by the subject~~-~~,
wherein the second sub-population consists of a different bacterial species to that of the first sub-population,
wherein each host cell has a host target sequence and at least one nucleic acid sequence encoding a Cas nuclease endogenous to the host cell,
wherein the ~~system comprising (a) host cells of the second bacterial population and (b) for each host cell of (a) at least one nucleic acid vector and components according to (i) to (ii):~~
~~(i) at least one nucleic acid sequence encoding a Cas nuclease;~~
~~(ii) a host cell target sequence and an~~ engineered host modifying (HM) CRISPR array comprises~~ing~~ a spacer sequence (HM-spacer) and repeats encoding a HM-crRNA, the HM-crRNA comprising a sequence that is capable of hybridising to the host target sequence ~~to guide said Cas to the target in the host cell to modify the target sequence~~;
~~-~~wherein the ~~said components (i) and (ii) of the system are split between the host cell and the at least one nucleic acid~~ vector ~~that~~ can transform the host cell,
~~wherein the at least one nucleic acid sequence encoding a Cas nuclease is endogenous to the host cell or is in the at least one vector, the host cell target sequence is in the host cell, and the engineered host modifying (HM) CRISPR array is in the at least one vector,~~ wherein~~by~~ the HM-crRNA guides the Cas nuclease to the target to modify the target sequence in the host cell, whereby the host cell is killed or host cell growth is reduced,~~;~~ ~~and~~

wherein the nucleic acid vector is a plasmid vector comprised by a carrier bacterium, or the vector is a phage vector, or the vector is a phagemid vector~~first sub-population consists of *E coli* cells; and~~
~~wherein the second sub-population consists of a different bacterial species to that of the first sub-population~~.

2. Use of a nucleic acid vector comprising ~~A~~a host modifying (HM) CRISPR~~/Cas system~~ array and a nucleic acid sequence encoding a Cas nuclease~~,~~ in the manufacture of a medicament for ~~use in~~ treating or preventing, in a human or animal subject, a condition or disease mediated by

bacterial host cells~~,~~ by altering the relative ratio of sub-populations of first and second bacteria in a mixed population of bacteria, the second bacteria comprising host cells, ~~-~~wherein the mixed population is comprised by the subject,

wherein the second sub-population consists of a different bacterial species to that of the first sub-population,

wherein each host cell has a host target sequence,

wherein the ~~system comprising (a) host cells of the second bacterial population and (b) for each host cell of (a) at least one nucleic acid vector and components according to (i) to (ii):-~~

~~(i) at least one nucleic acid sequence encoding a Cas nuclease;~~

~~(ii) a host cell target sequence and an~~ engineered host modifying (HM) CRISPR array compris~~es~~~~ing~~ a spacer sequence (HM-spacer) and repeats encoding a HM-crRNA, the HM-crRNA comprising a sequence that is capable of hybridising to the host target sequence ~~to guide said Cas to the target in the host cell to modify the target sequence~~;

wherein the ~~said components (i) and (ii) are split between the host cell and the at least one nucleic acid~~ vector ~~that~~ can transform the host cell, ~~wherein the at least one nucleic acid sequence encoding a Cas nuclease is in the at least one vector, the host cell target sequence is in the host cell, and the engineered host modifying (HM) CRISPR array is in the at least one vector,~~

where~~in~~~~by~~ the HM-crRNA guides the Cas nuclease to the target to modify the target sequence in the host cell, whereby the host cell is killed or host cell growth is reduced~~,~~~~;~~

wherein the nucleic acid vector is a plasmid vector comprised by a carrier bacterium, or the vector is a phage vector, or the vector is a phagemid vector ~~first sub-population consists of *E coli* cells; and~~

~~wherein the second sub-population consists of a different bacterial species to that of the first sub-population~~.

3. Use of a nucleic acid vector comprising an engineered host modifying (HM) CRISPR~~/Cas system~~ array for altering the relative ratio of sub-populations of first and second bacteria in an *ex vivo* mixed population of bacteria, the second bacteria comprising host cells,

wherein the second sub-population consists of a different bacterial species to that of the first sub-population,

wherein each host cell has a host target sequence and at least one nucleic acid sequence encoding a Cas nuclease endogenous to the host cell,

wherein the engineered host modifying (HM) CRISPR array comprises a spacer sequence (HM-spacer) and repeats encoding a HM-crRNA, the HM-crRNA comprising a sequence that is capable of hybridising to the host target sequence;

wherein the vector can transform the host cell,

wherein the HM-crRNA guides the Cas nuclease to the target to modify the target sequence in the host cell, whereby the host cell is killed or host cell growth is reduced,

wherein the nucleic acid vector is a plasmid vector comprised by a carrier bacterium, or the vector is a phage vector, or the vector is a phagemid vector.

~~the system comprising (a) host cells of the second bacterial population and (b) for each host cell of (a) at least one nucleic acid vector and components according to (i) to (ii):~~

~~(i) at least one nucleic acid sequence encoding a Cas nuclease;~~

~~(ii) a host cell target sequence and an engineered host modifying (HM) CRISPR array comprising a spacer sequence (HM-spacer) and repeats encoding a HM-crRNA, the HM-crRNA comprising a sequence that hybridises to the host cell target sequence to guide said Cas to the target in the host cell to modify the target sequence;~~

~~wherein said components (i) and (ii) are split between the host cell and the at least one nucleic acid vector that transforms the host cell, wherein the at least one nucleic acid sequence encoding a Cas nuclease is endogenous to the host cell or is in the at least one vector, the host cell target sequence is in the host cell, and the engineered host modifying (HM) CRISPR array is in the at least one vector, whereby the HM-crRNA guides Cas to the target to modify the target sequence in the host cell;~~

~~wherein the target sequence is modified by the Cas whereby the host cell is killed or host cell growth is reduced;~~

~~wherein the first sub-population consists of *E coli* cells; and~~

~~wherein the second sub-population consists of a different bacterial species to that of the first sub-population.~~

4. Use of a nucleic acid vector comprising an engineered host modifying (HM) CRISPR~~/Cas system~~ array and a nucleic acid sequence encoding a Cas nuclease for altering the relative ratio of sub-populations of first and second bacteria in an *ex vivo* mixed population of bacteria, the second bacteria comprising host cells,

wherein the second sub-population consists of a different bacterial species to that of the first sub-population,

wherein each host cell has a host target sequence,

wherein the engineered host modifying (HM) CRISPR array comprises a spacer sequence (HM-spacer) and repeats encoding a HM-crRNA, the HM-crRNA comprising a sequence that is capable of hybridising to the host target sequence,

wherein the vector can transform the host cell,

wherein the HM-crRNA guides the Cas nuclease to the target to modify the target sequence in the host cell, whereby the host cell is killed or host cell growth is reduced,

wherein the nucleic acid vector is a plasmid vector comprised by a carrier bacterium, or the vector is a phage vector, or the vector is a phagemid vector.

~~the system comprising (a) host cells of the second bacterial population and (b) for each host cell of (a) at least one nucleic acid vector and components according to (i) to (ii):-~~

~~(i) at least one nucleic acid sequence encoding a Cas nuclease;~~

~~(ii) a host cell target sequence and an engineered host modifying (HM) CRISPR array comprising a spacer sequence (HM-spacer) and repeats encoding a HM-crRNA, the HM-crRNA comprising a sequence that hybridises to the host cell target sequence to guide said Cas to the target in the host cell to modify the target sequence;~~

~~wherein said components (i) and (ii) are split between the host cell and the at least one nucleic acid vector that transforms the host cell, wherein the at least one nucleic acid sequence encoding a Cas nuclease is in the at least one vector, the host cell target sequence is in the host cell, and the engineered host modifying (HM) CRISPR array is in the at least one vector,~~

~~whereby the HM-crRNA guides Cas to the target to modify the target sequence in the host cell;~~

~~wherein the target sequence is modified by the Cas whereby the host cell is killed or host cell growth is reduced;~~

~~wherein the first sub-population consists of *E coli* cells; and~~

~~wherein the second sub-population consists of a different bacterial species to that of the first sub-population.~~

5. The use of claims 3 or 4 for treating an industrial or an *ex vivo* medical fluid, surface, apparatus or container; or for treating a waterway, water, a beverage, a foodstuff or a cosmetic, wherein the host cell(s) are comprised by or on the fluid, surface, apparatus, container, waterway, water, beverage, foodstuff or cosmetic.

~~6. The use of claims 3 or 4, wherein the mixed population is a gut microbiota population *ex vivo*; optionally wherein the host cells are *Firmicutes* or *Clostridium difficile* cells.~~

~~7. The use or system for use according to any preceding claim, wherein~~

~~(a) each host cell is of a strain or species found in human microbiota;~~

~~(b) each host cell is a *Staphylococcus, Streptococcus, Pseudomonas, Salmonella, Listeria, Desulfovibrio,* or *Clostridium* host cell;~~

~~(c) the first bacteria are probiotic, commensal or symbiotic with humans (eg, in the human gut); or~~

~~(d) the first bacteria are *Enterobacteriaceae* and the second bacteria are *Firmicutes*.~~

~~8.~~6. The use ~~or system for use~~ according to any preceding claim, wherein ~~alternatively~~ the HM-crRNA and a tracrRNA are comprised by a single guide RNA (gRNA).

~~9.~~7. The use ~~or system for use~~ according to any preceding claim, wherein host cell population growth is reduced by of at least 5-fold compared to the growth of a population of said host cells not transformed with said HM-CRISPR array or a nucleotide sequence encoding said gRNA.

~~10.~~8. The use ~~or system for use~~ according to ~~any preceding~~ claim 3 or 4, or any one of claims 5 to 7 when dependent on claim 3 or 4, wherein host cell population growth on a surface is inhibited.

~~11.~~9. The use ~~or system for use~~ according to ~~any~~ claim 1 or 3, or any one of claims 5 to 8 when dependent on claim 1 or 3~~preceding claim~~, wherein each vector lacks a Cas nuclease encoding sequence.

~~12. The use or system for use or vector according to any preceding claim, wherein each vector is a phage vector.~~

~~13.~~10. The use ~~or system for use~~ according to any preceding claim, wherein ~~for each host cell the system further comprises a tracrRNA sequence or~~ the vector comprises a DNA sequence for expressing a tracrRNA sequence.

~~14.~~11. The ~~system for~~ use according to any ~~one of claims 1, 2 and 7 to 13 when dependent on claim 1 or 2~~preceding claim, wherein the mixed population is comprise~~sd by a gut microbiota of the subject~~ *S. thermophilus*, *L. lactis* and *E. coli*.

~~15.~~12. The use ~~or system for use~~ according to ~~claims 2, 4 and 7 to 14 when dependent on claim 2 or 4~~any preceding claim, wherein the ~~at least one nucleic acid sequence encoding a Cas nuclease and the engineered host modifying (HM) CRISPR array are in different vectors~~Cas nuclease is a type I cas nuclease, a type II Cas nuclease or a type III Cas nuclease.

~~16.~~13. The use according to any preceding claim, ~~An engineered nucleic acid vector for use in treating or preventing in a human or animal subject, a condition or disease mediated by pathogenic bacterial host cells, by altering the relative ratio of sub-populations of first and second bacteria in a mixed population of bacteria, the second bacteria comprising host cells, wherein the mixed population is comprised by the subject, wherein the first sub-population consists of *E coli* cells and the second sub-population consists of a different bacterial species to that of the first sub-population, ,~~ the vector comprising nucleic acid sequences for expressing a plurality of different crRNAs (eg, comprised by gRNAs), ~~for use in a CRISPR/Cas system or use according to any preceding claim; and~~

wherein a first of said crRNAs is capable of hybridising to a first nucleic acid sequence in said host cell; and a second of said crRNAs is capable of hybridising to a second nucleic acid sequence in said host cell, wherein said second sequence is different from said first sequence; and

(a) the first sequence is comprised by an antibiotic resistance gene ~~(~~or RNA thereof~~)~~ and the second sequence is comprised by an antibiotic resistance gene ~~(~~or RNA thereof~~)~~; optionally wherein the genes are different;

(b) the first sequence is comprised by an antibiotic resistance gene ~~(~~or RNA thereof~~)~~ and the second sequence is comprised by an essential or virulence gene ~~(~~or RNA thereof~~)~~;

(c) the first sequence is comprised by an essential gene ~~(~~or RNA thereof~~)~~ and the second sequence is comprised by an essential or virulence gene ~~(~~or RNA thereof~~)~~; or

(d) the first sequence is comprised by a virulence gene ~~(~~or RNA thereof~~)~~ and the second sequence is comprised by an essential or virulence gene ~~(~~or RNA thereof~~)~~.

~~17.~~14. The use according to any one of claims 1 or 3, and 6 to 12 when dependent on claims 1 or 3, ~~A nucleic acid vector for use in treating or preventing in a human or animal subject, a condition or disease mediated by pathogenic bacterial host cells, by altering the relative ratio of sub-populations of first and second bacteria in a mixed population of bacteria, the second bacteria comprising host cells, wherein the mixed population is comprised by the subject, the first sub-population consists of *E coli* cells and the second sub-population consists of a different bacterial species to that of the first sub-population, wherein either i) the vector is for use in the use or system of claim 1 or 3 or any one of claims 5 to 16 when dependent on claim 1 or 3,~~ the vector comprising more than 1.4kb of exogenous DNA sequence, wherein the exogenous DNA encodes one or more components of the CRISPR/Cas system and comprises the engineered array for expressing HM-crRNAs or gRNAs in host cells, ~~wherein the exogenous sequence is devoid of a nucleotide sequence encoding a Cas nuclease that is cognate to the cRNA(s) or gRNA(s);~~ wherein

at least 2 different crRNAs or gRNAs are encoded by the exogenous DNA (eg, by at least 2 HM-CRISPR arrays)~~, or ii) wherein the vector is for use in a system according to claim 1 or 2 or any one of claims 7 to 16 when dependent on claim 1 or 2, wherein the vector comprises the engineered host modifying (HM) CRISPR array comprising a spacer sequence (HM-spacer) and repeats encoding a HM-crRNA, the HM-crRNA comprising a sequence that is capable of hybridising to the host target sequence to guide the Cas to the target in the host cells to modify the target sequence, wherein the vector is capable of being administered to the human or animal subject, and said HM-crRNA is expressed in the subject~~.

~~18.~~15. The ~~nucleic acid vector~~ use according to any one of claims 1, 3 and 6 to 14 when dependent on claim 1 or 3~~ 16 or 17~~, wherein the vector is devoid of a nucleotide sequence encoding a Cas nuclease that is cognate to the crRNA(s) or gRNA(s).

~~A host modifying CRISPR RNA (HM-crRNA) for use in treating or preventing in a human or animal subject, a condition or disease mediated by pathogenic bacterial host cells, by altering the relative ratio of sub-populations of first and second bacteria in a mixed population of bacteria, the second bacteria comprising host cells, wherein the mixed population is comprised by the subject, and wherein the first sub-population consists of *E coli* cells, wherein the HM-crRNA is encoded by an engineered host modifying (HM) CRISPR array as recited in claim 1 or 2 or any one of claims 7 to 16 when dependent on claim 1 or 2, wherein the vectors of the system as recited in claim 1 or 2 or any one of claims 7 to 16 when dependent on claim 1 or 2, are capable of being administered to the human or animal subject, and said HM-crRNA is expressed in the subject.~~