IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	:	David Bikard et al.
U.S. Serial No.	:	15/159,929
U.S. Filing Date	:	May 20, 2016
Title	:	SEQUENCE SPECIFIC ANTIMICROBIALS
Examiner	:	Nancy J. Leith
Art Unit	:	1636
Confirmation No.	:	1125
Attorney Docket No.	:	076091.00023

AMENDMENT AND REQUEST FOR INTERFERENCE

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In response to the Office Action mailed January 24, 2020, Applicant submits the following amendments and remarks. Please amend this application as follows:

Amendments to the Claims are reflected in the listing of claims in this paper.

Remarks begin after the amendment section of this paper.

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions and listings of claims in the application:

Listing of Claims:

1-19. (Cancelled).

20. (Currently amended) A method for killing targeted bacteria in a mixed bacterial population comprising:

providing a pharmaceutical composition comprising a pharmaceutically acceptable carrier and packaged, recombinant phagemids that are packaged in phage capsids,

wherein the packaged phagemids comprise a clustered regularly interspaced short palindromic repeats (CRISPR) system,

wherein the CRISPR system comprises DNA encoding: i) a type II CRISPR-associated enzyme; and ii) a targeting RNA that targets at least one bacterial chromosome at a target site; and

contacting the bacterial population with the pharmaceutical composition,

wherein the contacting with the pharmaceutical composition introduces at least some of the phagemids into at least some of the bacteria in the bacterial population,

wherein subsequent to the introduction of the phagemids, the bacteria into which the phagemid is introduced expresses the targeting RNA and the type II CRISPR-associated enzyme,

wherein the expressed type II CRISPR-associated enzyme cleaves the bacterial chromosome at the target site of the targeting RNA, and

wherein the cleavage of the bacterial chromosome at the target site kills the bacteria.

21. (Currently amended) The method of claim 20, wherein the type II CRISPR-associated enzyme is a Cas9 enzyme.

22. (Previously presented) The method of claim 21, wherein the Cas9 enzyme is a *Streptococcus pyogenes* Cas9.

23. (Previously presented) The method of claim 20, further comprising detecting the killing of bacteria by the pharmaceutical composition.

24. (Previously presented). The method of claim 20, wherein the mixed bacterial population comprises one or a combination of bacterial species selected from the group consisting of *Staphylococcus, Clostridium, Bacillus, Salmonella, Helicobacter pylori, Neisseria gonorrhoeae, Neisseria meningitidis,* and *Escherichia coli*.

25. (Previously presented) The method of claim 24, wherein the bacteria is *Staphylococcus aureus*.

26. (Previously presented) The method of claim 25, wherein the bacteria is a methicillin-resistant *Staphylococcus aureus*.

27. (Currently amended) A method for killing targeted bacteria in a mixed bacterial population, wherein the mixed bacterial population comprises at least two different bacterial species, comprising:

providing a pharmaceutical composition comprising a pharmaceutically acceptable carrier and packaged, recombinant phagemids that are packaged in phage capsids,

wherein the packaged phagemids comprise a clustered regularly interspaced short palindromic repeats (CRISPR) system,

wherein the CRISPR system comprises DNA encoding: i) a type II CRISPR-associated enzyme; and ii) multiple targeting RNAs, one of which targets a virulence gene on a chromosome or on a plasmid at a target site within the chromosome or within the plasmid and one of which targets an antibiotic resistance gene on a plasmid at a target site within the plasmid; and

contacting the bacterial population with the pharmaceutical composition,

wherein the contacting with the pharmaceutical composition introduces at least some of the phagemids into at least some of the bacteria in the bacterial population that contain the virulence gene on a chromosome or on a plasmid and the antibiotic resistance gene on a plasmid,

wherein subsequent to the introduction of the phagemids, the bacteria into which the phagemid is introduced expresses the targeting RNAs and the type II CRISPR-associated enzyme,

wherein the expressed type II CRISPR-associated enzyme cleaves the virulence gene on a chromosome or on a plasmid at the target site within the chromosome or within the plasmid and the antibiotic resistance gene on a plasmid at the target site within the plasmid, and

wherein the cleavage of the bacterial plasmid at the target site of the antibiotic resistance gene within the plasmid kills the bacteria in the presence of the antibiotic.

28. (Currently amended) The method of claim 27, wherein the type II CRISPR-associated enzyme is a Cas9 enzyme.

29. (Previously presented) The method of claim 28, wherein the Cas9 enzyme is a *Streptococcus pyogenes* Cas9.

30. (Previously presented) The method of claim 27, further comprising detecting the killing of bacteria by the pharmaceutical composition.

31. (Previously presented) The method of claim 27, wherein the bacteria that contains the antibiotic resistance gene on a plasmid is selected from the group consisting of *Staphylococcus, Clostridium, Bacillus, Salmonella, Helicobacter pylori, Neisseria gonorrhoeae, Neisseria meningitidis,* and *Escherichia coli*.

32. (Previously presented) The method of claim 31, wherein the bacteria that contains the antibiotic resistance gene on a plasmid is *Staphylococcus aureus*.

33. (Previously presented) The method of claim 32, wherein the bacteria is a methicillin-resistant *Staphylococcus aureus*.

REMARKS

Claims 20 and 27 have been amended as suggested by the Examiner to place the claims in condition for allowance. The Amendment adds no new matter.

SUGGESTION OF INTERFERENCE UNDER 37 C.F.R. § 41.202(a)

Applicant hereby requests an interference between the claims in the present application and the claims in U.S. Patents 10,463,049; 10,506,812; 10,561,148; and 10,524,477 and allowed U.S. Appln. 15/460,962.

(1) U.S. Patent 10,463,049 issued on November 5, 2019, to Clube et al. and includes 27 claims (1 independent claim and 26 dependent claims). U.S. Patent 10,506,812 issued on December 17, 2019, to Clube et al. and includes 23 claims (1 independent claim and 22 dependent claims). U.S. Patent 10,524,477 issued on January 7, 2020, to Clube et al. and includes 25 claims (1 independent claim and 24 dependent claims). U.S. Patent 10,561,148 issued on February 18, 2020, to Clube et al. and includes 16 claims (4 independent claims and 12 dependent claims). In U.S. Appln. 15/460,962, a Notice of Allowance was mailed on January 24, 2020, and the Issue Fee was paid on January 27, 2020. An Issue Notification in Appln. 15/460,962 indicates that this application will issue as U.S. Patent 10,582,712 on March 10, 2020.

(2) Applicant believes all of claims 20-33 in the present application interfere with all of claims in U.S. Patents 10,463,049; 10,506,812; 10,561,148; and 10,524,477 and allowed U.S. Appln. 15/460,962. Applicant proposes the following count: "Claim 1 of U.S. Appln. 15/460,962 or Claim 24 of U.S. Appln. 15/159,929."

According to 37 CFR 41.207 (b)(2), a claim corresponds to a count if the subject matter of the count, treated as prior art to the claim, would have anticipated or rendered obvious the subject matter of the claim. Applicant's claims 21-23 and 25-26 depend from claim 20 and are directed to the same invention as claim 24. Applicant's claims 28-33 depend from claim 27 and are directed to the same invention as claim 24. The subject matter of the count, treated as prior art to these claims, would have anticipated or rendered obvious the subject matter of the claims. Similarly, all of claims in U.S. Patents 10,463,049, 10,506,812, 10,524,477, and 10,561,148 are directed to the same invention as claim 1 of allowed U.S. Appln. 15/460,962. For example, during prosecution, the Examiner rejected all of the claims of U.S. Patents 10,463,049, 10,506,812, 10,524,477, and 10,561,148 for double patenting over the claims of allowed U.S. Appln. 15/460,962. Terminal Disclaimers over U.S. Appln.

15/460,962 were submitted by the patentee to gain allowance of each of these patents. The subject matter of the count, treated as prior art to these claims, would have anticipated or rendered obvious the subject matter of the claims.

(3) According to 37 CFR 41.203(a), an interference exists if the subject matter of a claim of one party *would, if prior art, have anticipated or rendered obvious the subject matter of a claim of the opposing party and vice versa.*

Claim 1 of U.S. Appln. 15/460,962 and Applicant's claim 24 are virtually identical. Despite the minor differences that will be discussed below, Applicant's Claim 24, if prior art, anticipates or rendered obvious the subject matter of claim 1 of U.S. Appln. 15/460,962, and *vice versa*. A claim chart comparing these two claims is provided:

U.S. Appln. 15/460,962	**U.S. Appln. 15/159,929**
1. A method of modifying a mixed population of bacteria,	20. A method for killing targeted bacteria in a mixed bacterial population,
wherein the mixed population comprises a first bacterial sub-population and a second bacterial sub-population, wherein the first bacterial sub-population comprises a first bacterial species and the second bacterial sub-population comprises host cells of a second bacterial species, wherein the second bacterial species is a different species than the first bacterial species, the method comprising	(Claim 24.) wherein the mixed bacterial population comprises one or a combination of bacterial species selected from the group consisting of *Staphylococcus, Clostridium, Bacillus, Salmonella, Helicobacter pylori, Neisseria gonorrhoeae, Neisseria meningitidis,* and *Escherichia coli*.
a. contacting the mixed population of an engineered nucleic acid sequence for producing a host modifying crRNA (HM-crRNA), and	providing a pharmaceutical composition comprising a pharmaceutically acceptable carrier and packaged, recombinant phagemids that are packaged in phage capsids, wherein the packaged phagemids comprise a clustered regularly interspaced short palindromic repeats (CRISPR) system, wherein the CRISPR system comprises DNA encoding: i) a type II CRISPR-associated enzyme; and ii) a targeting RNA that targets at least one bacterial chromosome at a target site; and contacting the bacterial population with the pharmaceutical composition

b. producing the HM-crRNA in the host cells,	wherein the contacting with the pharmaceutical composition introduces at least some of the phagemids into at least some of the bacteria in the bacterial population, wherein subsequent to the introduction of the phagemids, the bacteria into which the phagemid is introduced expresses the targeting RNA and the CRISPR-associated enzyme
wherein the HM-crRNA is operable with a Cas nuclease in the host cells,	wherein the expressed type II CRISPR-associated enzyme cleaves the bacterial chromosome at the target site of the targeting RNA
wherein the engineered nucleic acid sequence and the Cas nuclease are comprised by an HM-CRISPR/Cas system, and	wherein the CRISPR system comprises DNA encoding: i) a type II CRISPR-associated enzyme; and ii) a targeting RNA that targets at least one bacterial chromosome at a target site
wherein the HM-crRNA comprises a nucleic acid sequence that is capable of hybridizing to a target sequence in the host cells to guide the Cas nuclease to modify the target sequence in the host cells;	wherein the CRISPR system comprises DNA encoding: i) a type II CRISPR-associated enzyme; and ii) a targeting RNA that targets at least one bacterial chromosome at a target site
whereby the host cells are killed or growth of the host cells is reduced, thereby reducing the proportion of the host cells and altering the relative ratio of the first and second bacterial sub-populations in the mixed population of bacteria; and	wherein the cleavage of the bacterial chromosome at the target site kills the bacteria.
wherein the mixed population of bacteria comprises *E. coli*.	(Claim 24.) wherein the mixed bacterial population comprises one or a combination of bacterial species selected from the group consisting of *Staphylococcus, Clostridium, Bacillus, Salmonella, Helicobacter pylori, Neisseria gonorrhoeae, Neisseria meningitidis,* and *Escherichia coli.*

Claim 1 of U.S. Appln. 15/460,962 is directed to a method of modifying a mixed population of bacteria. As a consequence of this method, the bacteria cells are killed or growth of the host cells is reduced. Although Applicant's claim 24 uses somewhat different wording, Applicant is claiming essentially the same method. As made clear in claim 62 of U.S. Appln. 15/460,962, the method can use a phagemid. This is explicit in Applicant's claim 24. Applicant's claim 24 recites that the CRISPR-associated enzyme is type II; whereas, claim 1 of U.S. Appln. 15/460,962 simply designates "Cas nuclease." Applicant's claimed type II CRISPR-associated enzyme is encompassed within the "Cas nuclease" of claim 1 of U.S. Appln. 15/460,962. In addition, Applicant's

claimed type II CRISPR-associated enzyme was a well-known type of Cas nuclease at the time that U.S. Appln. 15/460,962 was filed, as demonstrated in the publication of WO 2014/124226A1 on August 14, 2014. Consequently, Applicant's claim 24 is directed to essentially the same method as claim 1 of U.S. Appln. 15/460,962. Consequently, Applicant's claim 24, if prior art, anticipates or rendered obvious the subject matter of Claim 1 of U.S. Appln. 15/460,962, and *vice versa*.

Moreover, claim 1 of U.S. Patent 10,463,049 and Applicant's claim 27 are virtually identical. Despite the minor differences that will be discussed below, Applicant's Claim 27, if prior art, anticipates or rendered obvious the subject matter of Claim 1 of U.S. Patent 10,463,049, and *vice versa*. A claim chart comparing these two claims is provided:

U.S. Patent 10,463,049	**U.S. Appln. 15/159,929**
1. A method of modifying a mixed population of bacteria,	27. A method for killing targeted bacteria in a mixed bacterial population,
wherein the mixed population of bacteria comprises a first bacterial sub-population and a second bacterial sub-population, wherein the first bacterial sub-population comprises a first bacterial species and the second bacterial sub-population comprises a population of host cells of a second bacterial species, wherein the second bacterial species is a different species than the first bacterial species, the method comprising:	wherein the mixed bacterial population comprises at least two bacterial species, comprising
(a) contacting the mixed population of bacteria with an engineered nucleic acid for producing a plurality of different host modifying crRNAs (HM-crRNAs), and	providing a pharmaceutical composition comprising a pharmaceutically acceptable carrier and packaged, recombinant phagemids that are packaged in phage capsids, wherein the packaged phagemids comprise a clustered regularly interspaced short palindromic repeats (CRISPR) system, wherein the CRISPR system comprises DNA encoding: i) a type II CRISPR-associated enzyme; and ii) multiple targeting RNAs, one of which targets a virulence gene on a chromosome or on a plasmid at a target site within the chromosome or within the plasmid and one of which targets an antibiotic resistance gene on a plasmid at a target site within the plasmid; and contacting the bacterial population with the pharmaceutical composition

(b) producing the plurality of different HM-crRNAs in the host cells	wherein the contacting with the pharmaceutical composition introduces at least some of the phagemids into at least some of the bacteria in the bacterial population that contain the virulence gene on a chromosome or on a plasmid and the antibiotic resistance gene on a plasmid, wherein subsequent to the introduction of the phagemids, the bacteria into which the phagemid is introduced expresses the targeting RNAs and the type II CRISPR-associated enzyme
wherein the plurality of different HM-crRNAs comprises a first nucleotide sequence that hybridizes to a first target sequence in the host cells; and a second nucleotide sequence that hybridizes to a second target sequence in the host cells, wherein the second target sequence is different from the first target sequence; and	ii) multiple targeting RNAs, one of which targets a virulence gene on a chromosome or on a plasmid at a target site within the chromosome or within the plasmid and one of which targets an antibiotic resistance gene on a plasmid at a target site within the plasmid
wherein: 1) the first target sequence is comprised by a first antibiotic resistance gene or RNA thereof and the second target sequence is comprised by a second antibiotic resistance gene or RNA thereof; 2) the first target sequence is comprised by an antibiotic resistance gene or RNA thereof and the second target sequence is comprised by an essential gene or a virulence gene or RNA thereof; 3) the first target sequence is comprised by a first essential gene or RNA thereof and the second target sequence is comprised by a second essential gene or a virulence gene or RNA thereof; or 4) the first target sequence is comprised by a first virulence gene or RNA thereof and the second target sequence is comprised by an essential gene or a second virulence gene or RNA thereof;	one of which targets a virulence gene on a chromosome or on a plasmid at a target site within the chromosome or within the plasmid and one of which targets an antibiotic resistance gene on a plasmid at a target site within the plasmid
wherein: (i) the plurality of HM-crRNAs is operable with a Type II Cas in the host cells, wherein the engineered nucleic acid and the Type II Cas are comprised by a Type II HM-CRISPR/Cas system in the host cells; and	wherein the CRISPR system comprises DNA encoding: i) a type II CRISPR-associated enzyme; and ii) multiple targeting RNAs, one of which targets a virulence gene on a chromosome or on a plasmid at a target site within the chromosome or within the plasmid and one of which targets an antibiotic resistance gene on a plasmid at a target site within the plasmid

(ii) the plurality of HM-crRNAs guide the Type II Cas to modify the target sequences in the host cells,	wherein subsequent to the introduction of the phagemids, the bacteria into which the phagemid is introduced expresses the targeting RNAs and the type II CRISPR-associated enzyme,
wherein the host cells are modified by the Type II HM-CRISPR/Cas system.	wherein the expressed type II CRISPR-associated enzyme cleaves the virulence gene on a chromosome or on a plasmid at the target site within the chromosome or within the plasmid and the plasmid encoding antibiotic resistance at the target site within the plasmid, and wherein the cleavage of the bacterial plasmid at the target site of the antibiotic resistance gene within the plasmid kills the bacteria in the presence of the antibiotic.

Claim 1 of U.S. Patent 10,463,049 is directed to a method of modifying a mixed population of bacteria. As a consequence of this method, the bacteria cells are modified by a Type II HM-CRISPR/Cas system using a plurality of different HM-crRNAs Although Applicant's claim 27 uses somewhat different wording, Applicant is claiming essentially the same method. As made clear in claim 2 of U.S. Patent 10,463,049 ("wherein the host cells are killed or growth of the host cells is reduced"), the method can kill the bacterial cells. This is explicit in Applicant's claim 27. As made clear in claim 6 of U.S. Patent 10,463,049 ("wherein the engineered nucleic acid for producing the plurality of HM-crRNAs is present in a phage, phagemid or plasmid"), the method can use a phagemid for producing the crRNAs. This is explicit in Applicant's claim 27. As made clear in claim 7 of U.S. Patent 10,463,049 ("wherein the engineered nucleic acid encoding the Type II Cas is present in a phage, phagemid or plasmid"), the method can use a phagemid for producing the Cas. This is explicit in Applicant's claim 27. Subparts 1)-4) of claim 1 of U.S. Patent 10,463,049 limit the targets in the second bacterial species to a combination of any two of an antibiotic resistance gene, an essential gene, or a virulence gene or RNAs thereof. Applicant's claim 27 makes explicit that one of the targets is a virulence gene and one the targets is an antibiotic resistance gene. Consequently, Applicant's claim 27 is directed to essentially the same method as claim 1 of U.S. Patent 10,463,049. Consequently, Applicant's claim 27, if prior art, anticipates or rendered obvious the subject matter of Claim 1 of U.S. Patent 10,463,049, and *vice versa*.

(4) Applicant will prevail on priority because Applicant has the earliest constructive reduction, both in the present application (a Div. of U.S. Appln. 14/766675, which is the U.S. National Stage of International Application PCT/US14/15252 filed February 7, 2014) and in Applicant's priority application U.S. 61/761,971 filed February 7, 2013). All of these dates are more than a year before the filing date of the earliest application to which U.S. Patents 10,463,049, 10,506,812, 10,524,477, and 10,561,148 and allowed U.S. Appln. 15/460,962 claim benefit (various GB applications filed on May 6, 2015).

(5) Applicant's claims are fully supported in Applicant's specification as follows:

Claims in U.S. Appln. 15/159,929	**Support in Appln. 15/159,929 (Published U.S. Patent Publ. 2016/0324938)**
20. A method for killing targeted bacteria in a mixed bacterial population,	Original claim 8, Abstract, paragraph [0006], and paragraph [0044].
providing a pharmaceutical composition comprising a pharmaceutically acceptable carrier and packaged, recombinant phagemids that are packaged in phage capsids, wherein the packaged phagemids comprise a clustered regularly interspaced short palindromic repeats (CRISPR) system, wherein the CRISPR system comprises DNA encoding: i) a type II CRISPR-associated enzyme; and ii) a targeting RNA that targets at least one bacterial chromosome at a target site; and contacting the bacterial population with the pharmaceutical composition	Original claims 1 and 8, paragraph [0006], paragraph [0041], and paragraph [0044].
wherein the contacting with the pharmaceutical composition introduces at least some of the phagemids into at least some of the bacteria in the bacterial population, wherein subsequent to the introduction of the phagemids, the bacteria into which the phagemid is introduced expresses the targeting RNA and the type II CRISPR-associated enzyme	Original claim 8, paragraph [0006], and paragraph [0044].
wherein the expressed type II CRISPR-associated enzyme cleaves the bacterial chromosome at the target site of the targeting RNA	Paragraph [0041]
wherein the cleavage of the bacterial chromosome at the target site kills the bacteria.	Paragraph [0002], paragraph [0009], paragraph [0018], and paragraph [0052]
21. The method of claim 20, wherein the type II CRISPR-associated enzyme is a Cas9 enzyme.	Original claim 11.

22. The method of claim 21, wherein the Cas9 enzyme is a *Streptococcus pyogenes* Cas9.	Original claim 12.
23. The method of claim 20, further comprising detecting the killing of bacteria by the pharmaceutical composition.	Paragraphs [0053]-[0054].
24. The method of claim 20, wherein the mixed bacterial population comprises one or a combination of bacterial species selected from the group consisting of *Staphylococcus, Clostridium, Bacillus, Salmonella, Helicobacter pylori, Neisseria gonorrhoeae, Neisseria meningitidis,* and *Escherichia coli*.	Original claim 14, paragraph [0033], and paragraph [0047].
25. The method of claim 24, wherein the bacteria is *Staphylococcus aureus*.	Original claim 14, paragraph [0033], paragraphs [0053]-[0054].
26. The method of claim 25, wherein the bacteria is a methicillin-resistant *Staphylococcus aureus*.	Paragraphs [0039]-[0040], and paragraph [0053].
27. A method for killing targeted bacteria in a mixed bacterial population,	Original claim 8, Abstract, paragraph [0006], and paragraph [0044].
wherein the mixed bacterial population comprises at least two bacterial species, comprising	Original claim 1, paragraph [0036].
providing a pharmaceutical composition comprising a pharmaceutically acceptable carrier and packaged, recombinant phagemids that are packaged in phage capsids, wherein the packaged phagemids comprise a clustered regularly interspaced short palindromic repeats (CRISPR) system, wherein the CRISPR system comprises DNA encoding: i) a CRISPR-associated enzyme; and ii) multiple targeting RNAs, one of which targets a virulence gene on a chromosome or on a plasmid at a target site within the chromosome or within the plasmid and one of which-targets an antibiotic resistance gene on a plasmid at a target site within the plasmid; and contacting the bacterial population with the pharmaceutical composition	Original claims 1 and 8, original claim 9, paragraph [0006], paragraph [0041], and paragraph [0044].
wherein the contacting with the pharmaceutical composition introduces at least some of the phagemids into at least some of the bacteria in the bacterial population that contain the virulence gene on a chromosome or on a plasmid and the antibiotic resistance gene on a plasmid, wherein subsequent to the introduction of the phagemids, the bacteria into which the phagemid is introduced expresses the targeting RNAs and the CRISPR-associated enzyme	Original claim 8, paragraph [0006], and paragraph [0044].
one of which targets a virulence gene on a chromosome or on a plasmid at a target site within the	Original claim 8.

chromosome or within the plasmid and one of which targets an antibiotic resistance gene on a plasmid at a target site within the plasmid	
wherein subsequent to the introduction of the phagemids, the bacteria into which the phagemid is introduced expresses the targeting RNAs and the CRISPR-associated enzyme,	Paragraph [0041] and paragraph [0056].
wherein the expressed CRISPR-associated enzyme cleaves the virulence gene on a chromosome or on a plasmid at the target site within the chromosome or within the plasmid and the plasmid encoding antibiotic resistance at the target site within the plasmid, and wherein the cleavage of the bacterial plasmid at the target site of the antibiotic resistance gene within the plasmid kills the bacteria in the presence of the antibiotic.	Paragraph [0041] and paragraphs [0054]-[0056].
28. The method of claim 27, wherein the CRISPR-associated enzyme is a Cas9 enzyme.	Original claim 11.
29. The method of claim 28, wherein the Cas9 enzyme is a *Streptococcus pyogenes* Cas9.	Original claim 12.
30. The method of claim 27, further comprising detecting the killing of bacteria by the pharmaceutical composition.	Paragraphs [0053]-[0054].
31. The method of claim 27, wherein the bacteria that contains the antibiotic resistance gene on a plasmid is selected from the group consisting of *Staphylococcus, Clostridium, Bacillus, Salmonella, Helicobacter pylori, Neisseria gonorrhoeae, Neisseria meningitidis,* and *Escherichia coli*.	Original claim 14, paragraph [0033], and paragraph [0047].
32. The method of claim 31, wherein the bacteria that contains the antibiotic resistance gene on a plasmid is *Staphylococcus aureus*.	Original claim 14, paragraph [0033], paragraphs [0053]-[0054].
33. The method of claim 32, wherein the bacteria is a methicillin-resistant *Staphylococcus aureus*.	Paragraphs [0039]-[0040], and paragraph [0053].

(6) U.S. Appln. 15/159,929 is a Div. of U.S. Appln. 14/766675, which is the U.S. National Stage of International Application PCT/US14/15252 filed February 7, 2014. Thus, all have the same specification and Applicant should be accorded the benefit of PCT/US14/15252 filed February 7, 2014.

Applicant's priority application U.S. 61/761,971 filed February 7, 2013, also provides a constructive reduction to practice within the scope of the interfering subject matter as follows:

COUNT – Claim 24 of Appln. 15/159,929	**Support in U.S. Appln. 61/761,971**
20. A method for killing targeted bacteria in a mixed bacterial population,	Original claims 7-12, paragraph bridging pages 15-16, Examples 1-6 on pages 18-20.
providing a pharmaceutical composition comprising a pharmaceutically acceptable carrier and packaged, recombinant phagemids that are packaged in phage capsids, wherein the packaged phagemids comprise a clustered regularly interspaced short palindromic repeats (CRISPR) system, wherein the CRISPR system comprises DNA encoding: i) a type II CRISPR-associated enzyme; and ii) a targeting RNA that targets at least one bacterial chromosome at a target site; and contacting the bacterial population with the pharmaceutical composition	Original claims 7-12, paragraph bridging pages 15-16, Examples 1-6 on pages 18-20.
wherein the contacting with the pharmaceutical composition introduces at least some of the phagemids into at least some of the bacteria in the bacterial population, wherein subsequent to the introduction of the phagemids, the bacteria into which the phagemid is introduced expresses the targeting RNA and the type II CRISPR-associated enzyme	Original claims 7-12, paragraph bridging pages 15-16, Examples 1-6 on pages 18-20.
wherein the expressed type II CRISPR-associated enzyme cleaves the bacterial chromosome at the target site of the targeting RNA	Original claims 7-12, paragraph bridging pages 15-16, Examples 1-6 on pages 18-20.
wherein the cleavage of the bacterial chromosome at the target site kills the bacteria.	Original claims 7-12, paragraph bridging pages 15-16, Examples 1-6 on pages 18-20.
24. The method of claim 20, wherein the mixed bacterial population comprises one or a combination of bacterial species selected from the group consisting of *Staphylococcus, Clostridium, Bacillus, Salmonella, Helicobacter pylori, Neisseria gonorrhoeae, Neisseria meningitidis,* and *Escherichia coli*.	Original claims 7-12, paragraph bridging pages 14-15, page 15, second full paragraph, paragraph bridging pages 15-16, Examples 1-6 on pages 18-20.

Applicant further notes the following patent and pending applications related to the above-referenced applications and patents: 9,701,964, 15/478,912, 15/817,142, 15/817,144, 15/862,527, 16/364,002, 16/588,754, 16/588,842, 16/682,889, and 16/737,793.

Applicant submits that this application is in condition for allowance. If the Examiner believes that issues remain to be addressed before a Notice of Allowance, Applicant respectfully requests that the Examiner contact the undersigned to discuss any outstanding issues.

It is believed no extension of time is required to submit this response. If any fees are due, the USPTO is authorized to charge any such fees to Deposit Account No. 08-2442 of the undersigned.

Respectfully submitted,
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