

Figure 1 a

MTTASTSQVRQNYHQDSEAAINRQINLELYAGYVYLSMSYYFDRDDVALKNFAKYFL
HQSHEEREHAELMKLQNRQGRIFLODIKKPDCDDWESGLNAMECALHLEKNVNS
LLELHKLATDKNDPHLCDFIETHYLNEQVKAIKELGDHVTNLRKMGAPESGLAEYLF
DKHTLGDSDNES

Figure 1 b

ATGGCTGATATC
GGATCCATACATATGACGACCGCGTCCACCTCGCAGGTGCGCCAGAACTACCACCAG
GACTCAGAGGCCCGCCATCAACCGCCAGATCAACCTGGAGCTCTACGCCTCCTACGTT
TACCTGTCCATGTCTTACTACTTTGACCGCGATGATGTGGCTTTGAAGAACTTTGCC
AAATACTTTCTTCACCAATCTCATGAGGAGAGGGAACATGCTGAGAACTGATGAAG
CTGCAGAACCAACGAGGTGGCCGAATCTTCCTTCAGGATATCAAGAAACCAACTGT
GATGACTGGGAGAGCGGGCTGAATGCAATGGAGTGTGCATTACATTTGGAAAAAAT
GTGAATCAGTCACCTACTGGAACCTGCACAACTGGCCACTGACAAAAATGACCCCCAT
TTGTGTGACTTCATTGAGACACATTACCTGAATGAGCAGGTGAAAGCCATCAAAGAA
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GAATATCTCTTTGACAAGCACACCCTGGGAGACAGTGATAATGAAAGCTAACCTAGG
CACCTCGAG

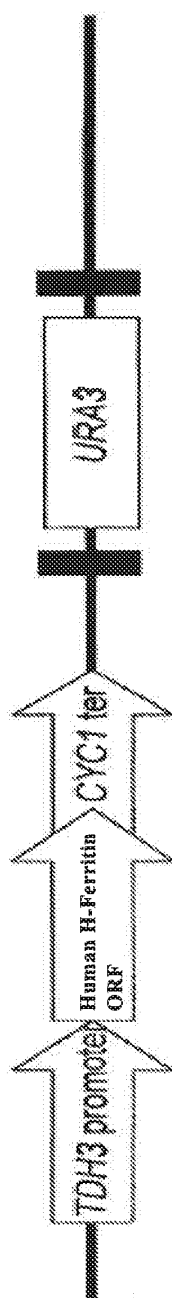


FIG. 2

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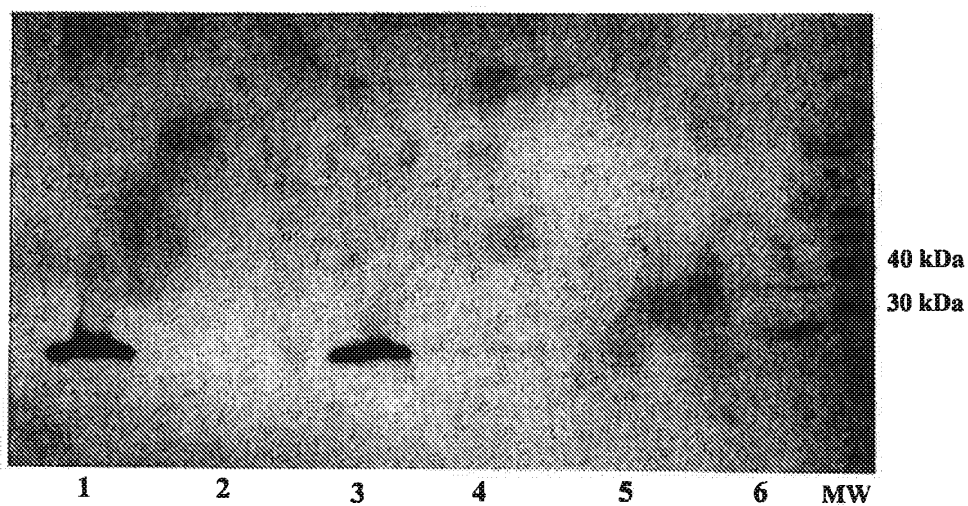


FIG. 3

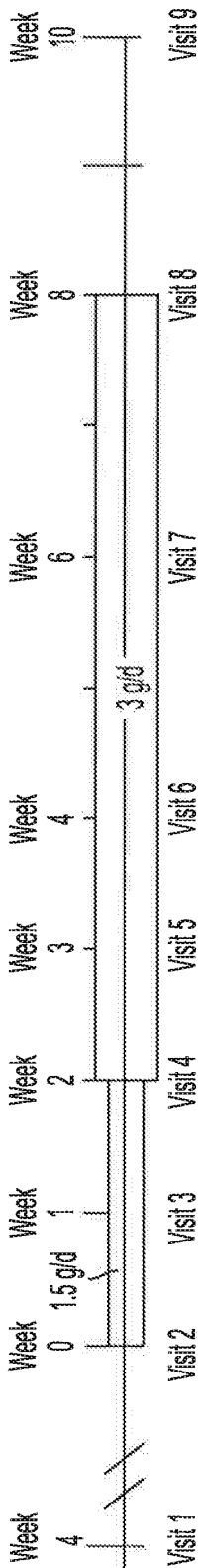


FIG. 4

Study Calendar

	Visit 1 Week -4	Visit 2 Week 0	Visit 3 Week 1	Visit 4 Week 2	Visit 5 Week 3	Visit 6 Week 4	Visit 7 Week 6	Visit 8 Week 8	Visit 9 Week 10
	Screen ¹	Enroll	Follow-up	Increase Intake	Follow-up	Follow-up	Follow-up	Follow-up	End of Study
Intake Level		Start 1.5 g/d	1.5 g/d	Start 3.0 g/d	3.0 g/d	3.0 g/d	3.0 g/d	Stop 3.0 g/d	
Medical History	X								
Limited Physical ²	X								
Pregnancy Testing ³	X								
Adverse Events ⁴		X	X	X	X	X	X	X	X
Concomitant Medications ⁵	X	X	X	X	X	X	X	X	X
Diet/Menses Review ⁶	X	X	X	X	X	X	X	X	X
Vital Signs & Weight ⁷	X	X	X	X	X	X	X	X	X
Local Labs ⁸	X	X	X	X	X	X	X	X	X
Health Surveys ⁹	X	X	X	X	X	X	X	X	X
Stool Sampling ¹⁰	X			X		X		X	X

FIG. 5

Footnotes

- 1) Consumption of iron supplements was stopped, or iron containing multivitamins were switched to vitamins not containing iron, for at least four weeks before screening. Screening took place up to four weeks prior to enrollment. The time between screening and enrollment was minimal as practical.
- 2) Limited physical exam by a licensed physician or advanced practice nurse targeting the circulatory and digestive systems
- 3) Urine was collected from all female participants for pregnancy testing.
- 4) AE review began at the time of enrollment and continued until Week 10/Visit 9 and was completed by clinical personnel at every visit.
- 5) Current concomitant medication and dose capture, including compliance with Composition A, began at the time of screening (30 days prior) and continued until Week 10/Visit 9 and was completed by clinical personnel at every visit.
- 6) General questioning about dietary changes and menses status and regularity since last contact was completed by clinical personnel at every visit.
- 7) Vital signs included blood pressure, heart rate, temperature and weight.
- 8) Local labs included serum iron, TIBC, serum ferritin, C-reactive protein, CBC with differential, and CMP
- 9) Health Survey questionnaires were reviewed for completeness, unreported AEs or discrepancies in the subject's health record, and collected by clinical personnel at every visit.
- 10) Screening stool sample was collected as close to the enrollment visit as possible. Week 8 stool sample was collected just prior to discontinuation of Composition A. All other stool samples were collected just prior to the coinciding visit.

FIG. 5 Continued

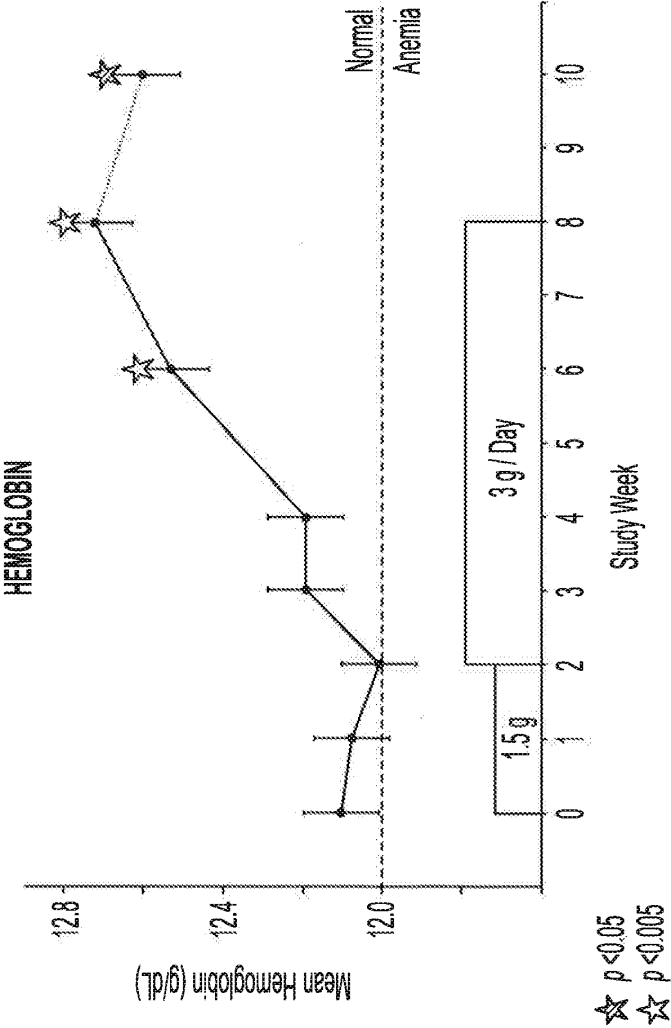


FIG. 6

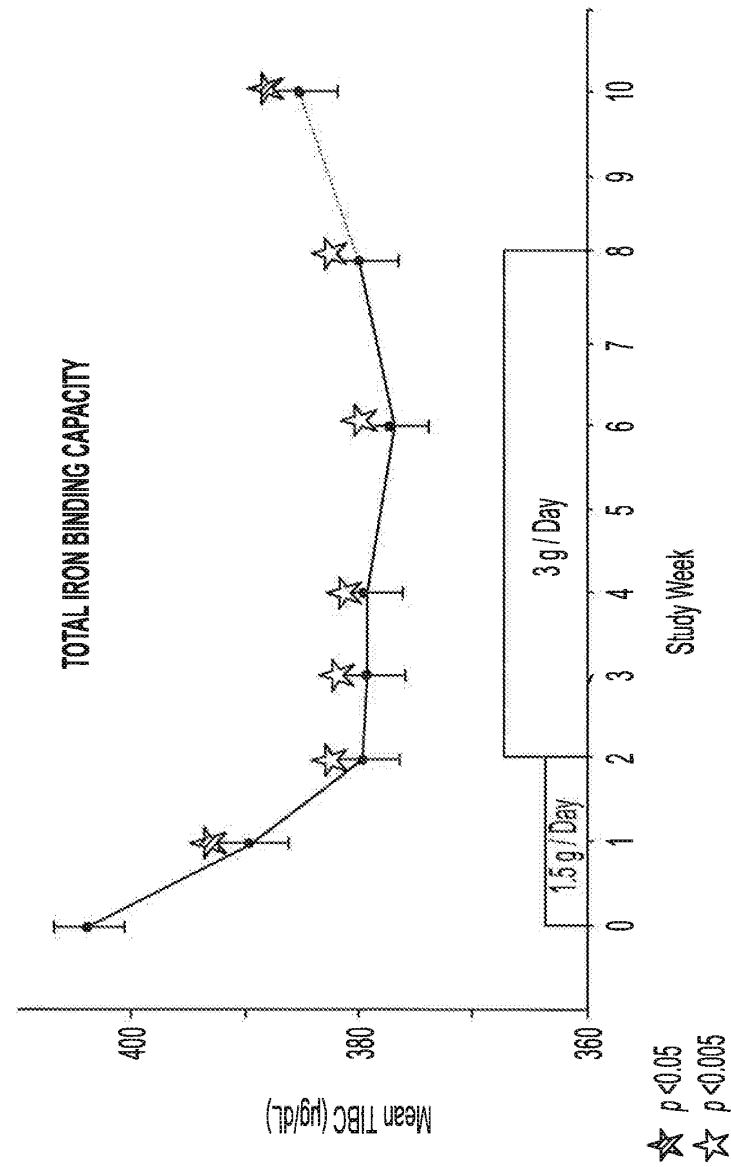


FIG. 7

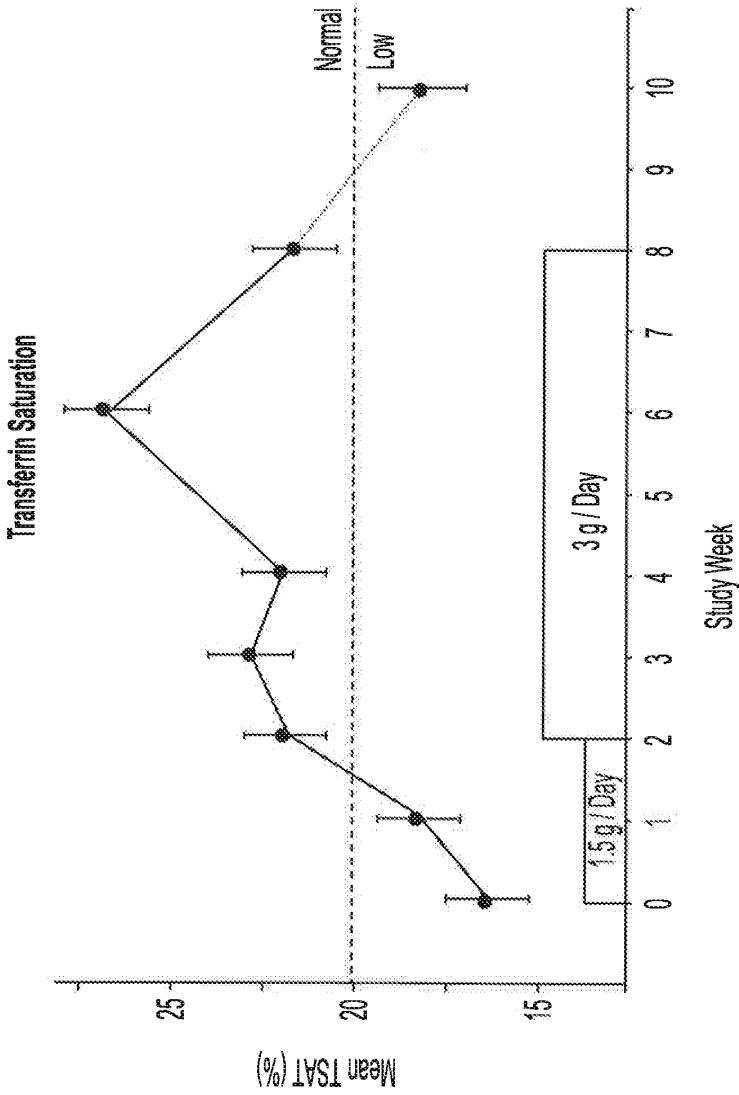


FIG. 8

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FACIT Fatigue Scale (Version 4)

Please circle or mark one number per line to indicate your response as it applies to the past 7 days.

	Not at all	A little bit	Some- what	Quite a bit	Very much
I feel fatigued	0	1	2	3	4
I feel weak all over	0	1	2	3	4
I feel listless ("washed out")	0	1	2	3	4
I feel tired	0	1	2	3	4
I have trouble <u>starting</u> things because I am tired	0	1	2	3	4
I have trouble <u>finishing</u> things because I am tired	0	1	2	3	4
I have energy	0	1	2	3	4
I am able to do my usual activities	0	1	2	3	4
I need to sleep during the day	0	1	2	3	4
I am too tired to eat	0	1	2	3	4
I need help doing my usual activities	0	1	2	3	4
I am frustrated by being too tired to do the things I want to do	0	1	2	3	4
I have to limit my social activity because I am tired	0	1	2	3	4

FIG. 9

SUBSTITUTE SHEET (RULE 26)

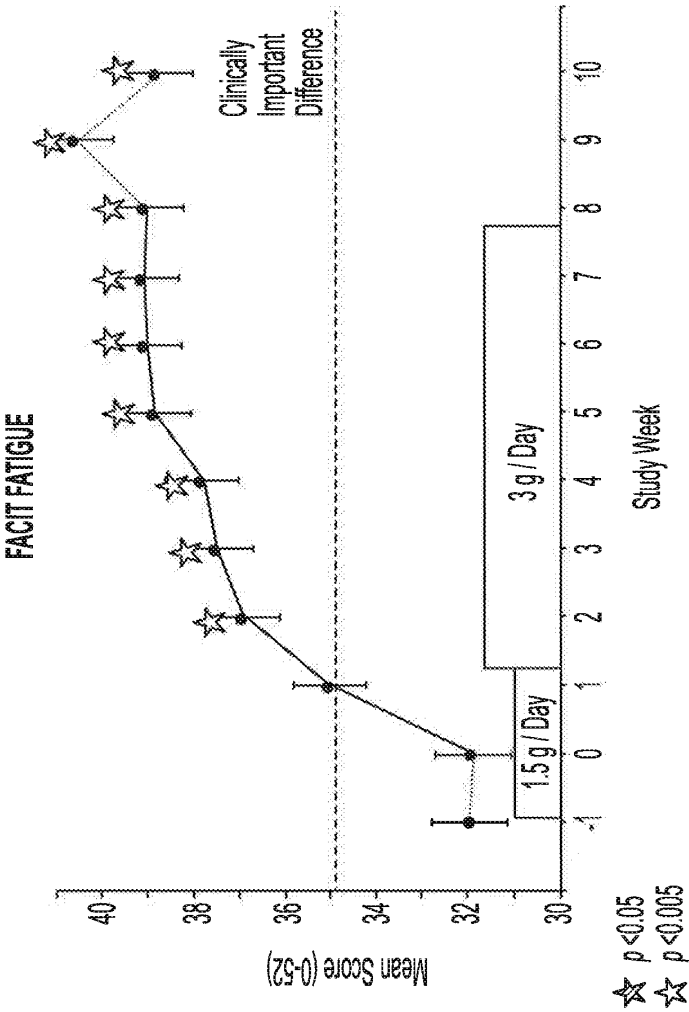


FIG. 10



HEALTH



RAND > RAND Health Care > Surveys > RAND Medical Outcomes Study > 36-Item Short Form Survey (SF-36) >

36-Item Short Form Survey Instrument (SF-36)

RAND 36-Item Health Survey 1.0 Questionnaire Items

Choose one option for each questionnaire item.

1. In general, would you say your health is:

- ☐ 1 - Excellent
- ☐ 2 - Very good
- ☐ 3 - Good
- ☐ 4 - Fair
- ☐ 5 - Poor

2. Compared to one year ago, how would you rate your health in general now?

- ☐ 1 - Much better now than one year ago
- ☐ 2 - Somewhat better now than one year ago
- ☐ 3 - About the same
- ☐ 4 - Somewhat worse now than one year ago
- ☐ 5 - Much worse now than one year ago

FIG. 11A

The following items are about activities you might do during a typical day. Does **your health now limit you** in these activities? If so, how much?

	Yes, limited a lot	Yes, limited a little	No, not limited at all
3. Vigorous activities , such as running, lifting heavy objects, participating in strenuous sports	☐ 1	☐ 2	☐ 3
4. Moderate activities , such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	☐ 1	☒ 2	☐ 3
5. Lifting or carrying groceries	☐ 1	☐ 2	☐ 3
6. Climbing several flights of stairs	☐ 1	☐ 2	☐ 3
7. Climbing one flight of stairs	☐ 1	☐ 2	☐ 3
8. Bending, kneeling, or stooping	☐ 1	☐ 2	☐ 3
9. Walking more than a mile	☐ 1	☐ 2	☐ 3
10. Walking several blocks	☐ 1	☐ 2	☐ 3
11. Walking one block	☐ 1	☐ 2	☐ 3
12. Bathing or dressing yourself	☐ 1	☐ 2	☐ 3

FIG. 11B

During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities **as a result of your physical health?**

- | | Yes | No |
|---|-------------------------|-------------------------|
| 13. Cut down the amount of time you spent on work or other activities | ☐ 1 | ☐ 2 |
| 14. Accomplished less than you would like | ☐ 1 | ☐ 2 |
| 15. Were limited in the kind of work or other activities | ☐ 1 | ☐ 2 |
| 16. Had difficulty performing the work or other activities (for example, it took extra effort) | ☐ 1 | ☐ 2 |

During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities **as a result of any emotional problems** (such as feeling depressed or anxious)?

- | | Yes | No |
|--|-------------------------|-------------------------|
| 17. Cut down the amount of time you spent on work or other activities | ☐ 1 | ☐ 2 |
| 18. Accomplished less than you would like | ☐ 1 | ☐ 2 |
| 19. Didn't do work or other activities as carefully as usual | ☐ 1 | ☐ 2 |

20. During the **past 4 weeks**, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?

- ☐ 1 - Not at all
- ☐ 2 - Slightly
- ☐ 3 - Moderately
- ☐ 4 - Quite a bit
- ☐ 5 - Extremely

FIG. 11C

21. How much **bodily** pain have you had during the **past 4 weeks**?

- ☐ 1 - None
- ☐ 2 - Very mild
- ☐ 3 - Mild
- ☐ 4 - Moderate
- ☐ 5 - Severe
- ☐ 6 - Very severe

22. During the **past 4 weeks**, how much did **pain** interfere with your normal work (including both work outside the home and housework)?

- ☐ 1 - Not at all
- ☐ 2 - A little bit
- ☐ 3 - Moderately
- ☐ 4 - Quite a bit
- ☐ 5 - Extremely

FIG. 11D

These questions are about how you feel and how things have been with you **during the past 4 weeks**. For each question, please give the one answer that comes closest to the way you have been feeling.

How much of the time during the **past 4 weeks**...

	All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
23. Did you feel full of pep?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
24. Have you been a very nervous person?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
25. Have you felt so down in the dumps that nothing could cheer you up?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
26. Have you felt calm and peaceful?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
27. Did you have a lot of energy?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
28. Have you felt downhearted and blue?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
29. Did you feel worn out?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
30. Have you been a happy person?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
31. Did you feel tired?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6

32. During the **past 4 weeks**, how much of the time has **your physical health or emotional problems** interfered with your social activities (like visiting with friends, relatives, etc.)?

- ☐ 1 - All of the time
- ☐ 2 - Most of the time
- ☐ 3 - Some of the time
- ☐ 4 - A little of the time
- ☐ 5 - None of the time

FIG. 11E

SUBSTITUTE SHEET (RULE 26)

How TRUE or FALSE is each of the following statements for you.

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
33. I seem to get sick a little easier than other people	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
34. I am as healthy as anybody I know	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
35. I expect my health to get worse	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
36. My health is excellent	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

ABOUT

The RAND Corporation is a research organization that develops solutions to public policy challenges to help make communities throughout the world safer and more secure, healthier and more prosperous. RAND is nonprofit, nonpartisan, and committed to the public interest.



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FIG. 11F

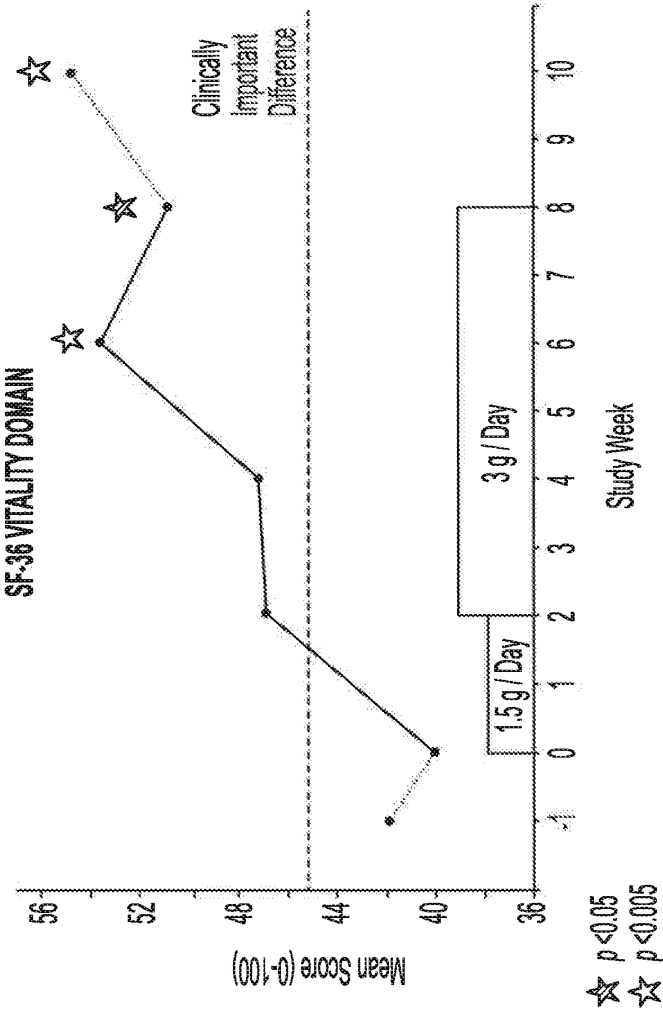


FIG. 12

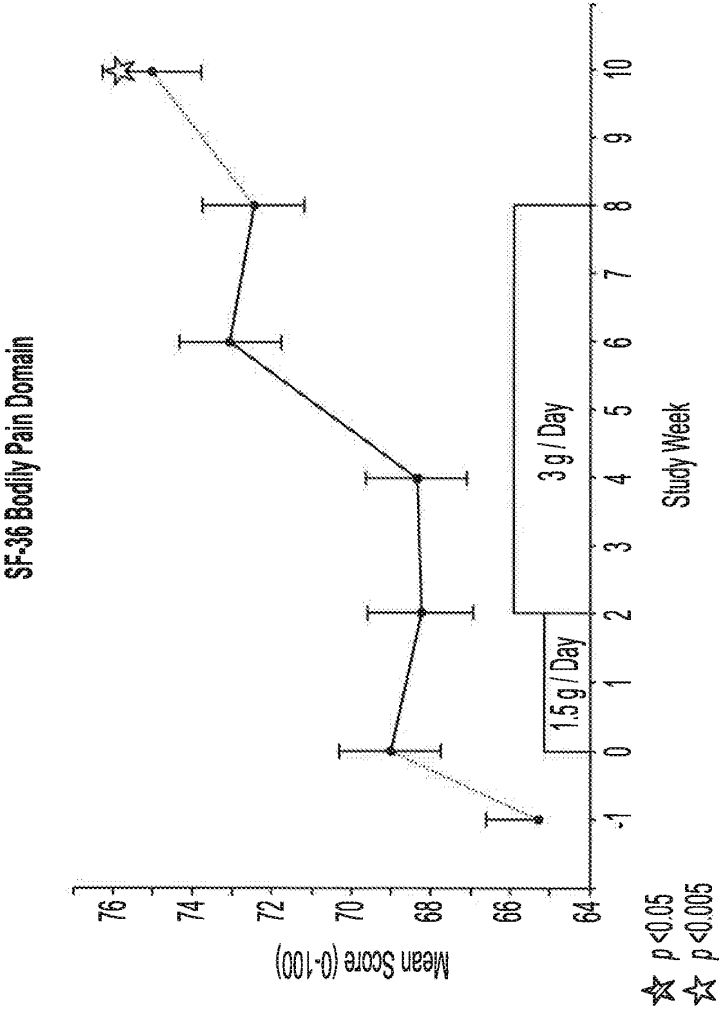


FIG. 13

Please record any symptoms you may have had today (tick one box for each symptom experienced)

Absent *I did not have this symptom at all*
Mild *I had this symptom occasionally, but it did not really bother me*
Moderate *I had this symptom often, it bothered me quite a bit*
Severe *I had this symptom very often, it bothered me a great deal*

	Absent	Mild	Moderate	Severe
Have you felt any nausea (wanting to vomit) today?	☐	☐	☐	☐
Have you actually vomited today?	☐	☐	☐	☐
Have you had heartburn (burning in chest) today?	☐	☐	☐	☐
Have you had abdominal pain today?	☐	☐	☐	☐
Have you had a headache today?	☐	☐	☐	☐
Have you been breathless today?	☐	☐	☐	☐
Have you had diarrhoea today?	☐	☐	☐	☐
Have you had constipation today?	☐	☐	☐	☐

How many bowel movements have you had today? (Specify) ☐☐

Is this normal for you? Yes ☐ No ☐

How many of your bowel movements were black? (Specify) ☐☐

Did you take your tablets today? (If yes, please tick box)

Morning ☐ Evening ☐

If you did not take either of your tablets, please explain why?

FIG. 14

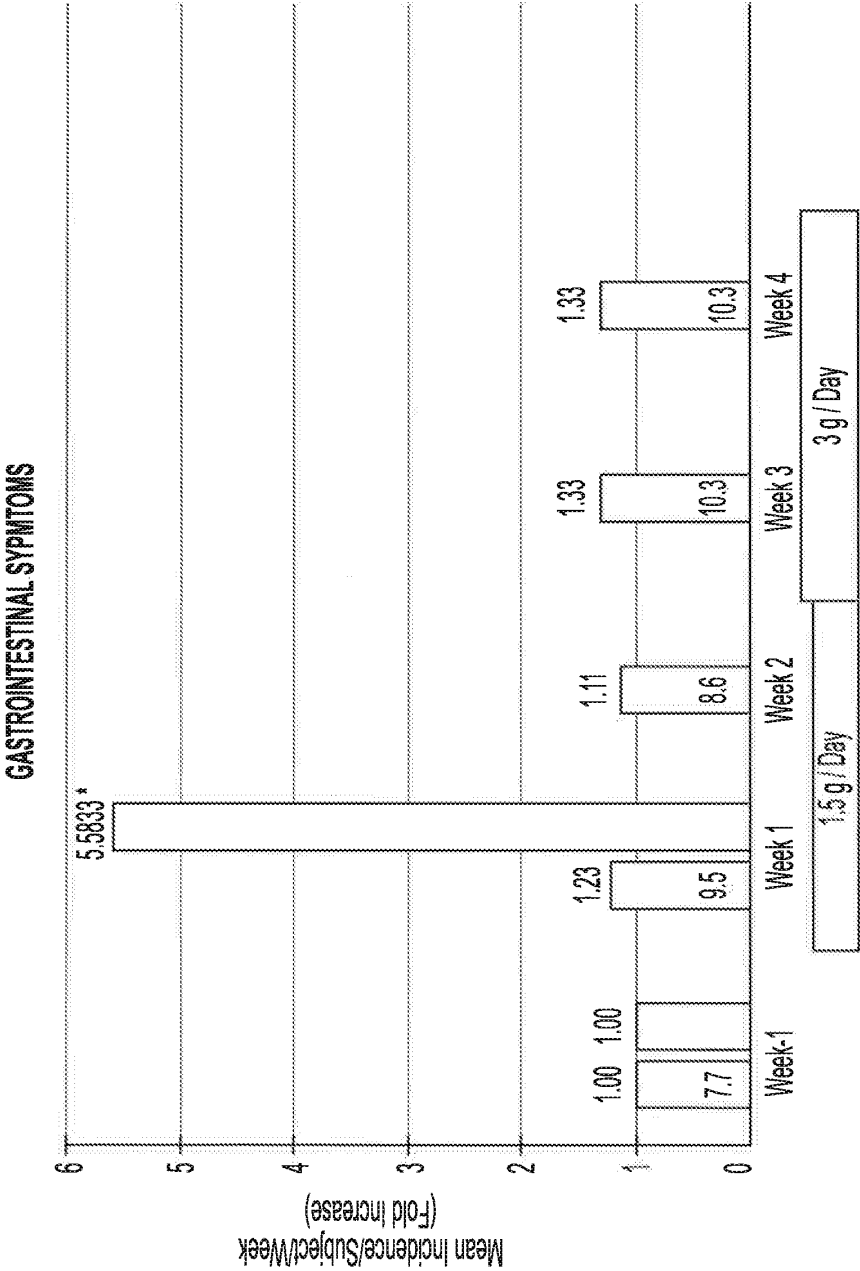


FIG. 15

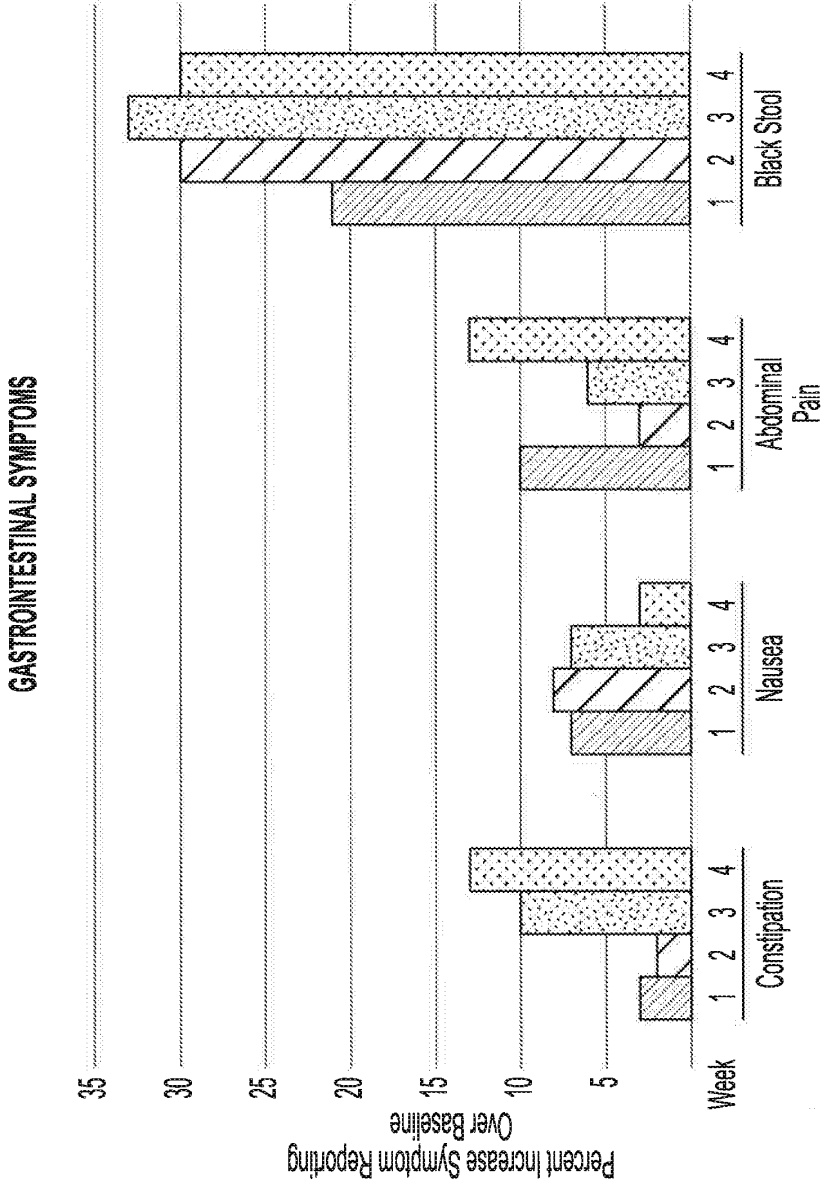
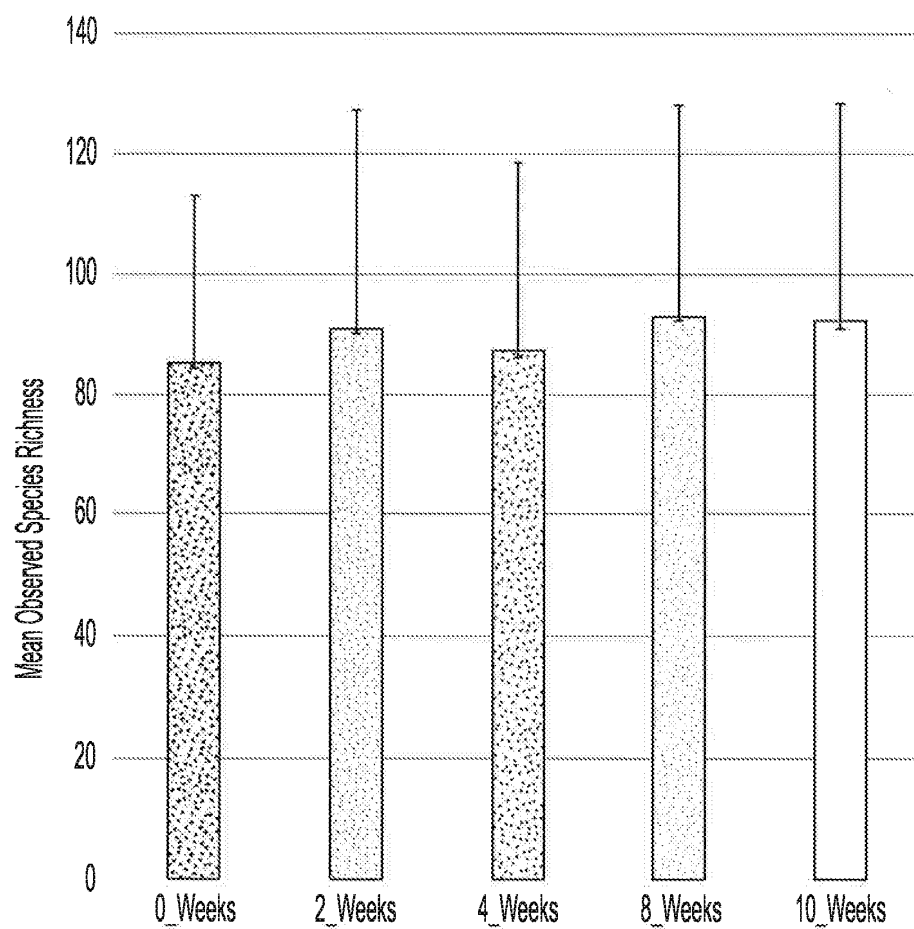


FIG. 16

FIG. 17



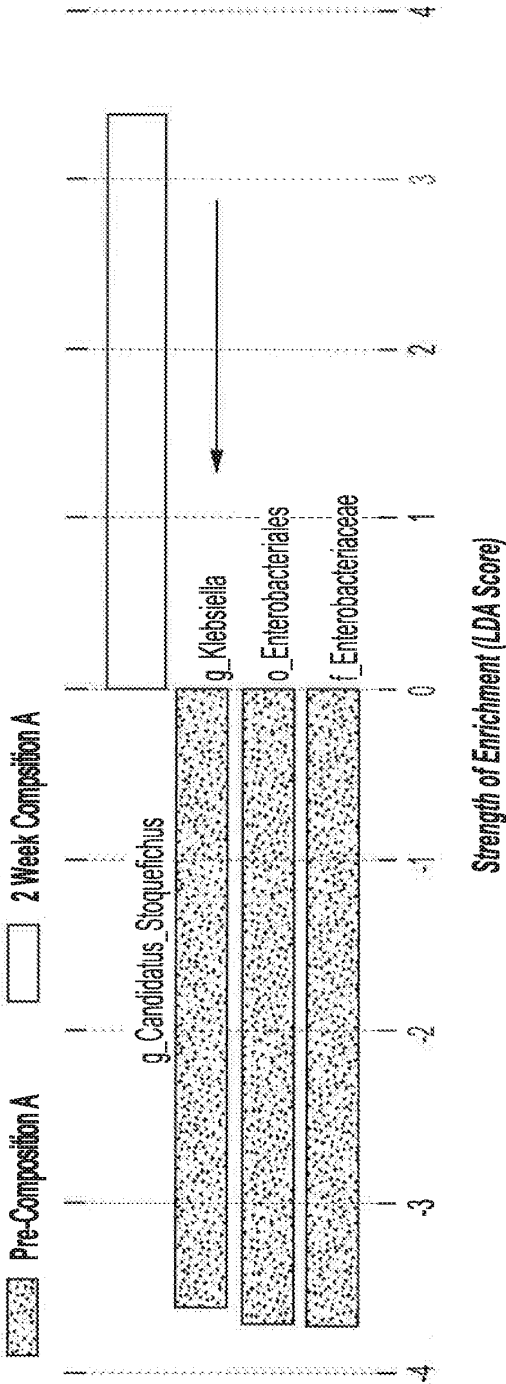


FIG. 18

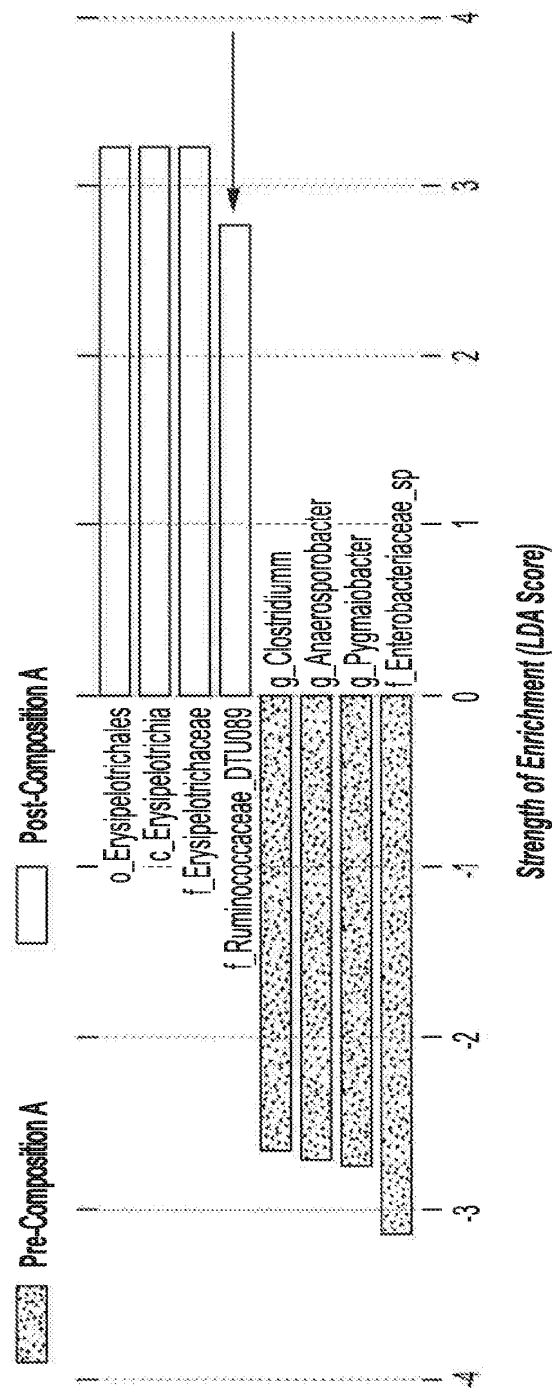


FIG. 19

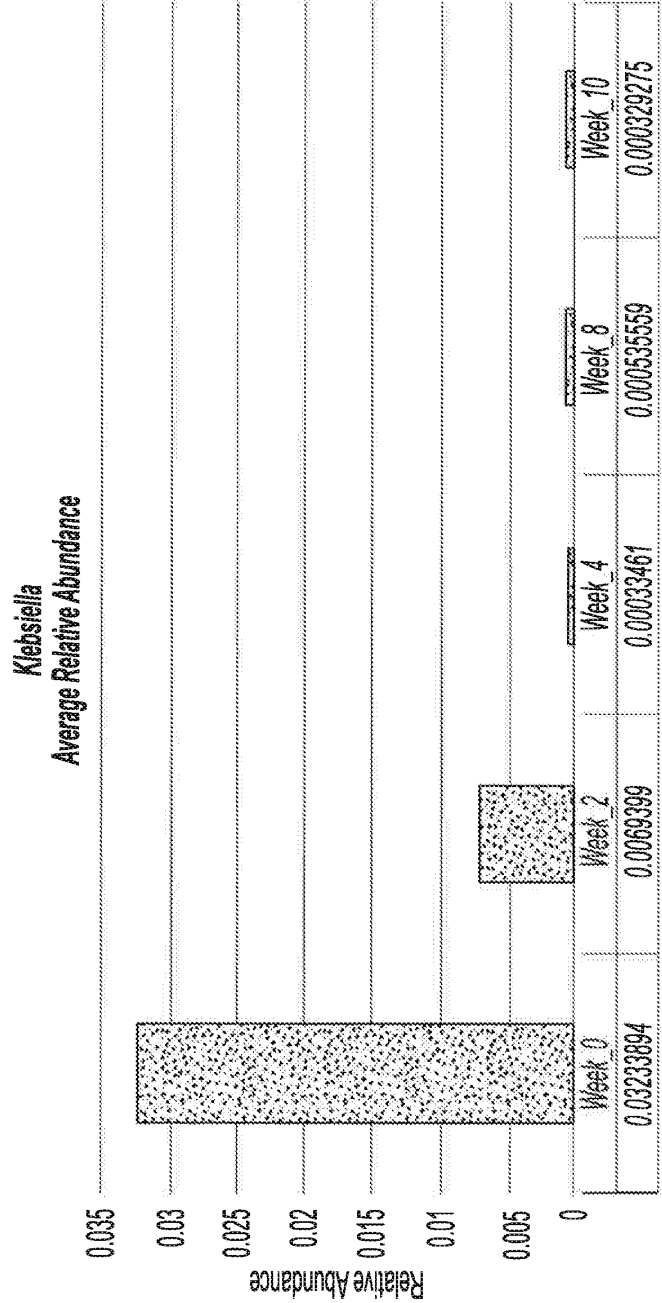


FIG. 20

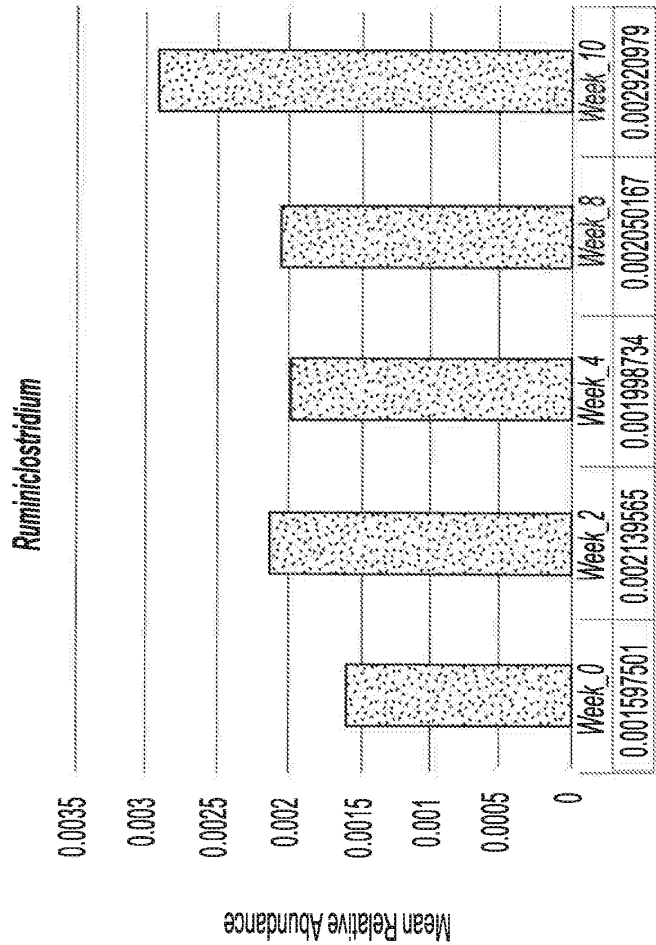


FIG. 21

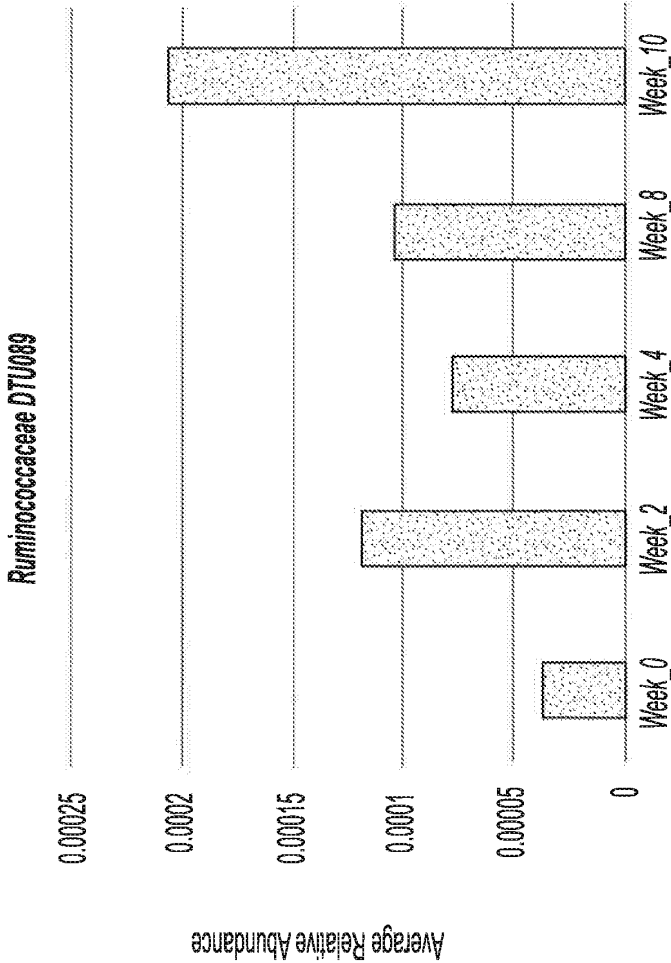


FIG. 22

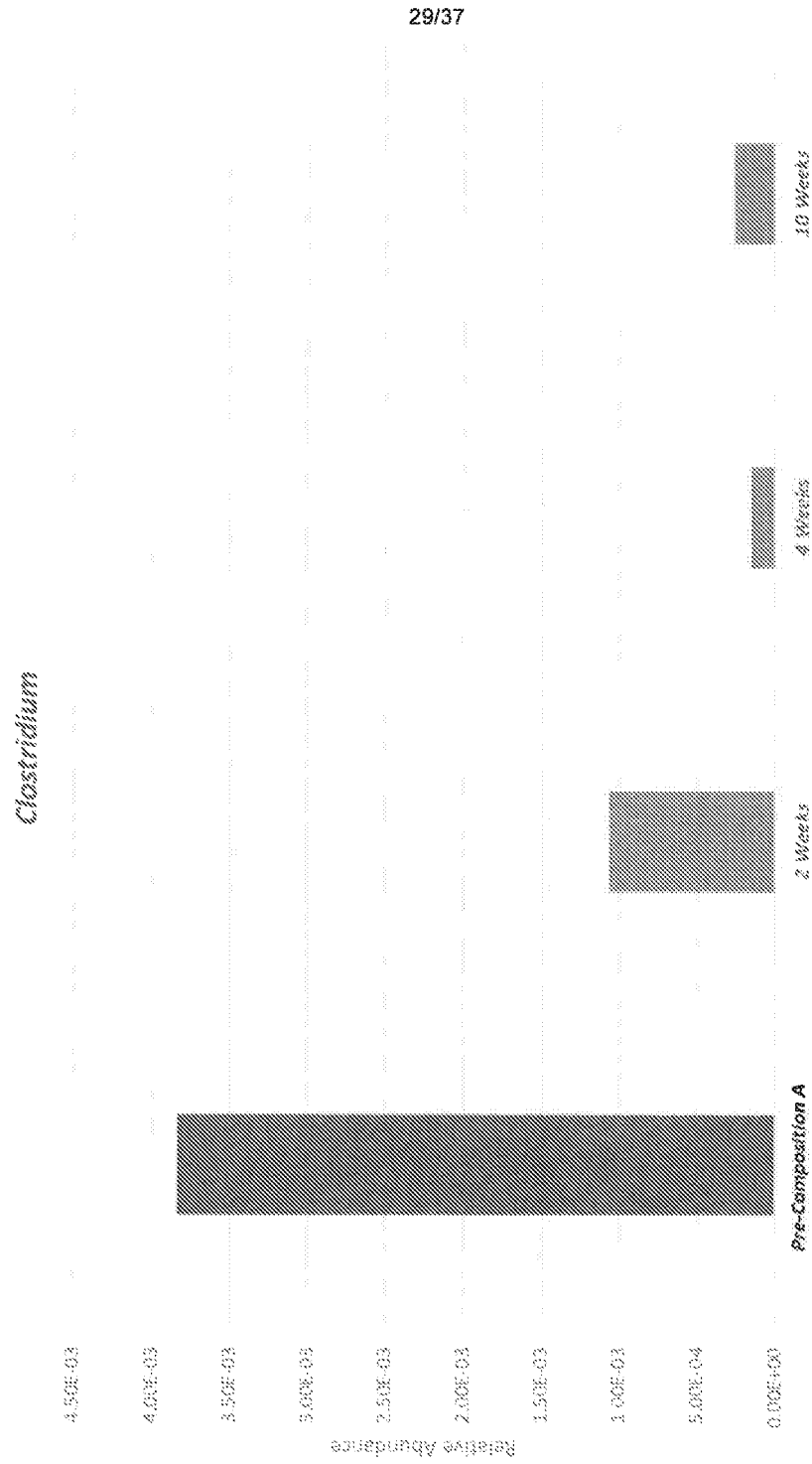


FIG. 23

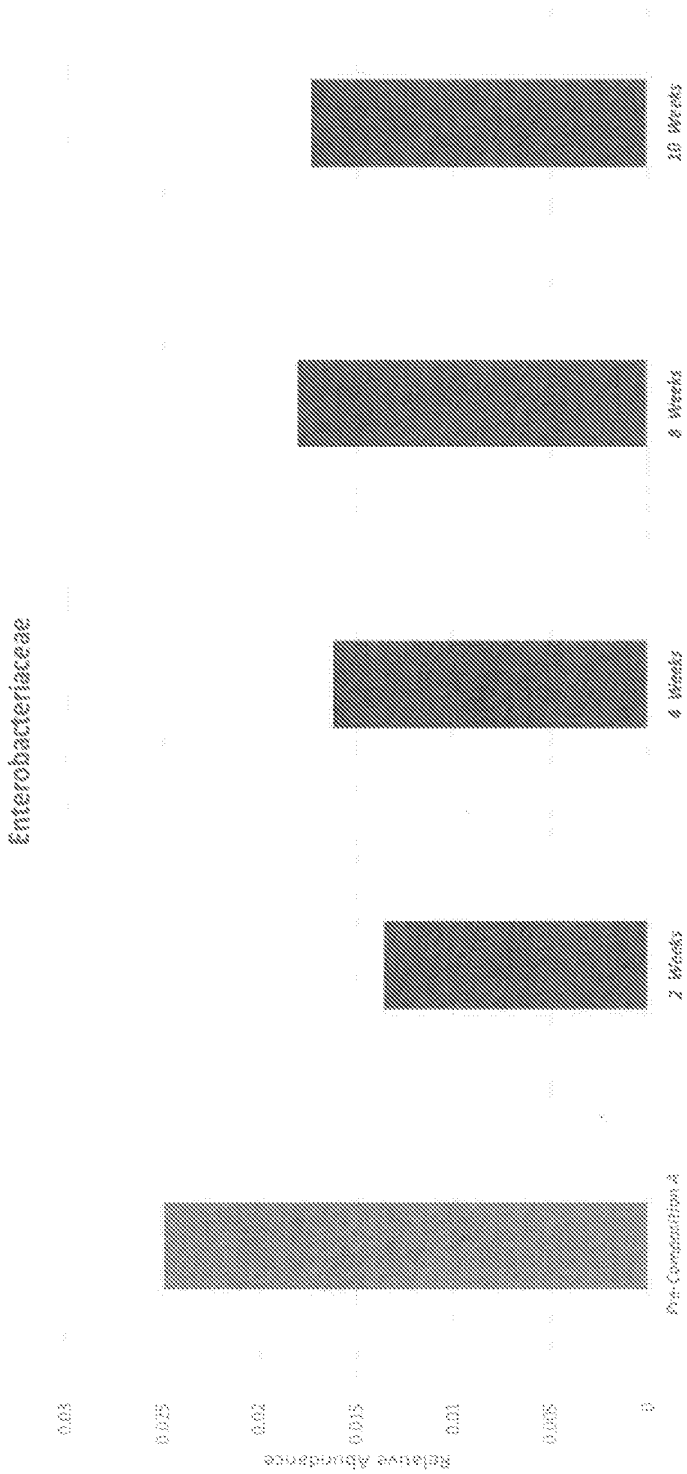


FIG. 24

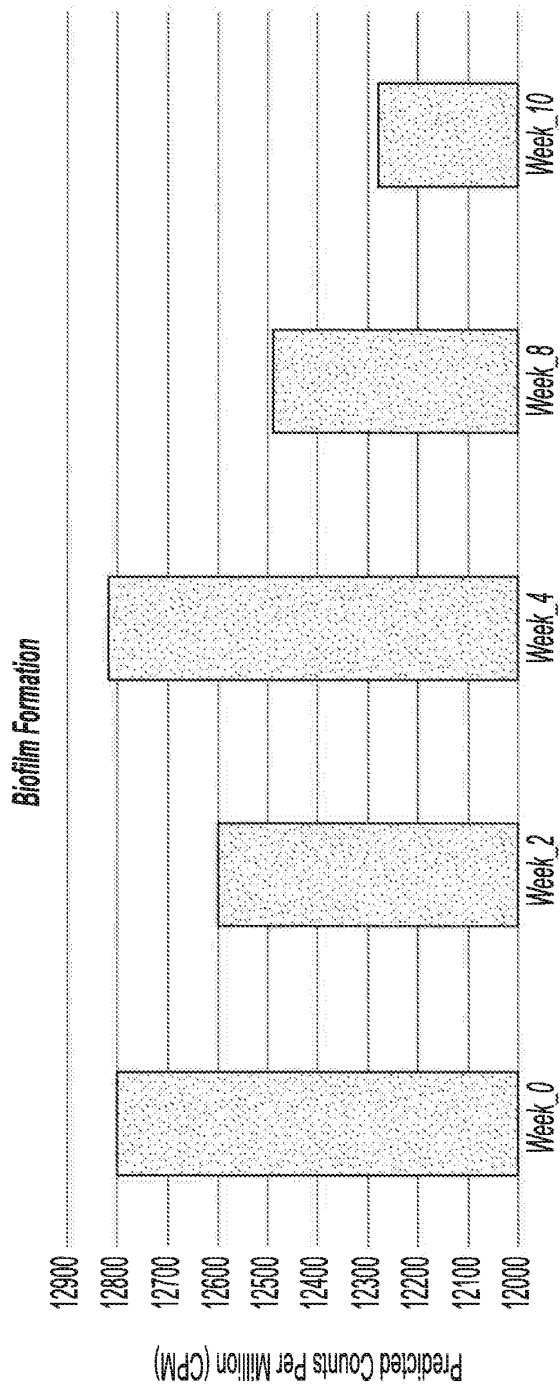


FIG. 25

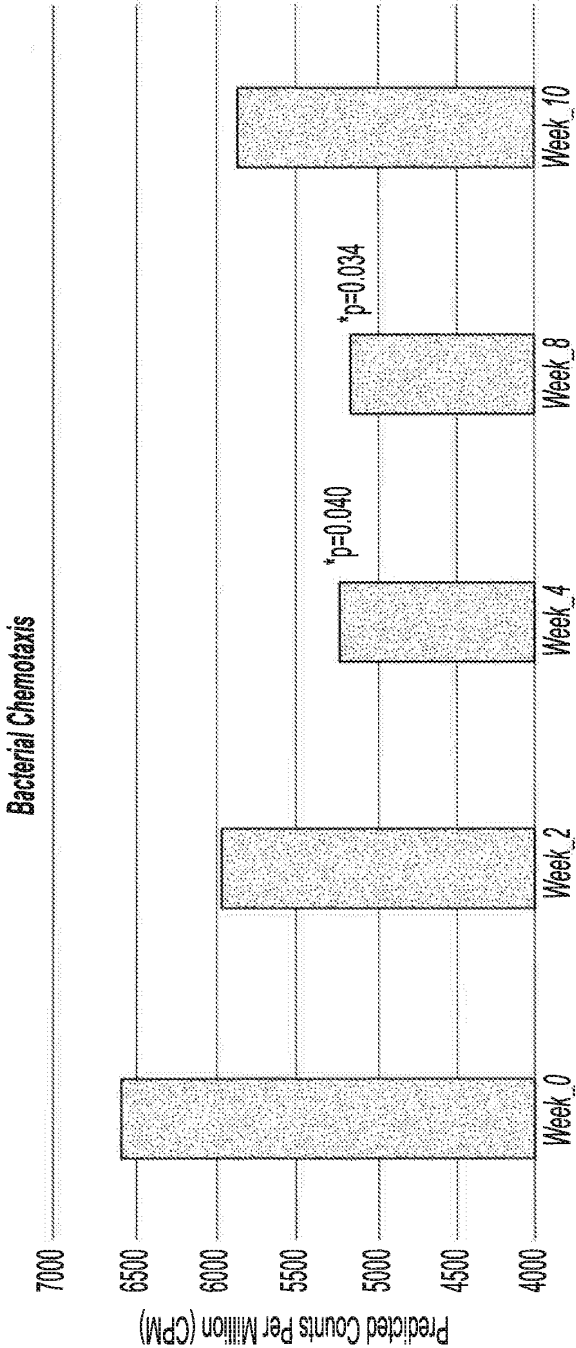


FIG. 26

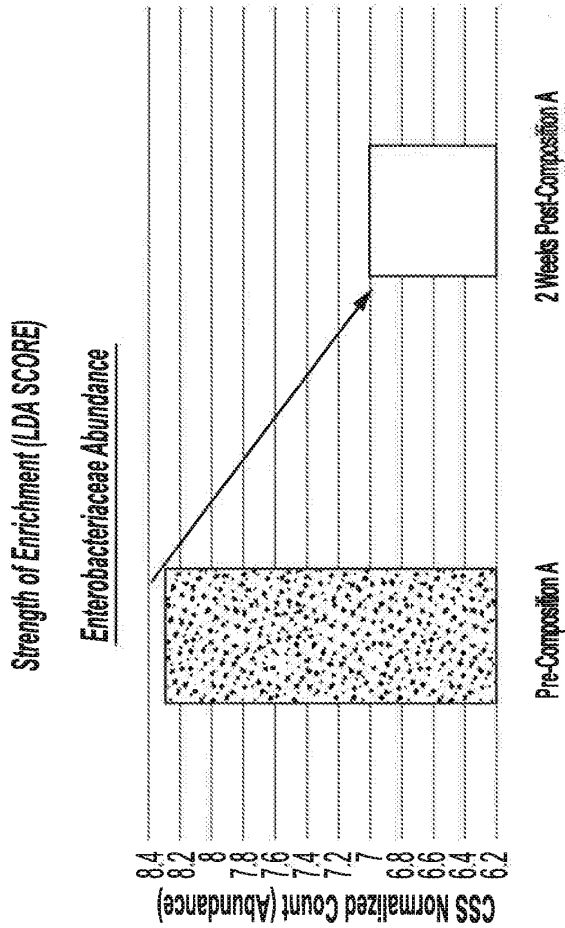


FIG. 27B

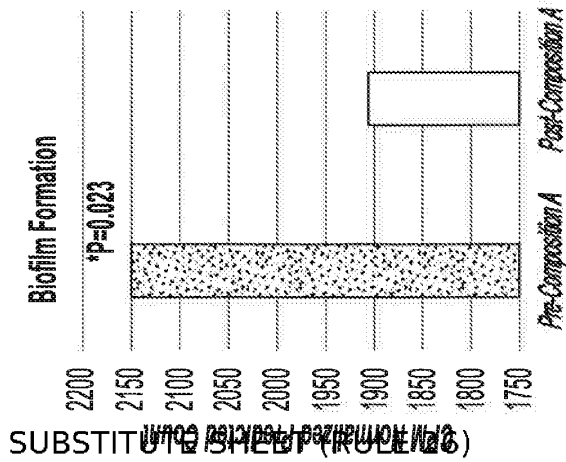


FIG. 27A

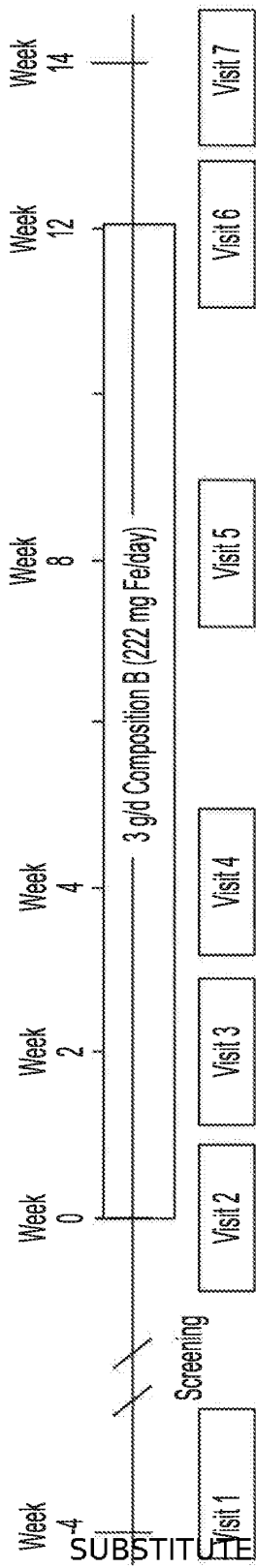


FIG. 28

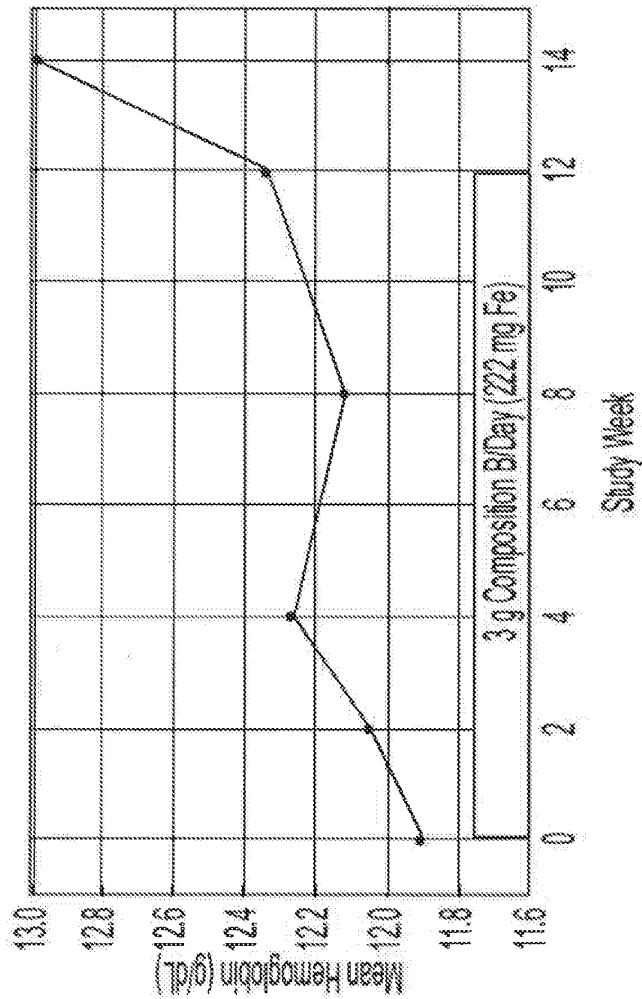


FIG. 29

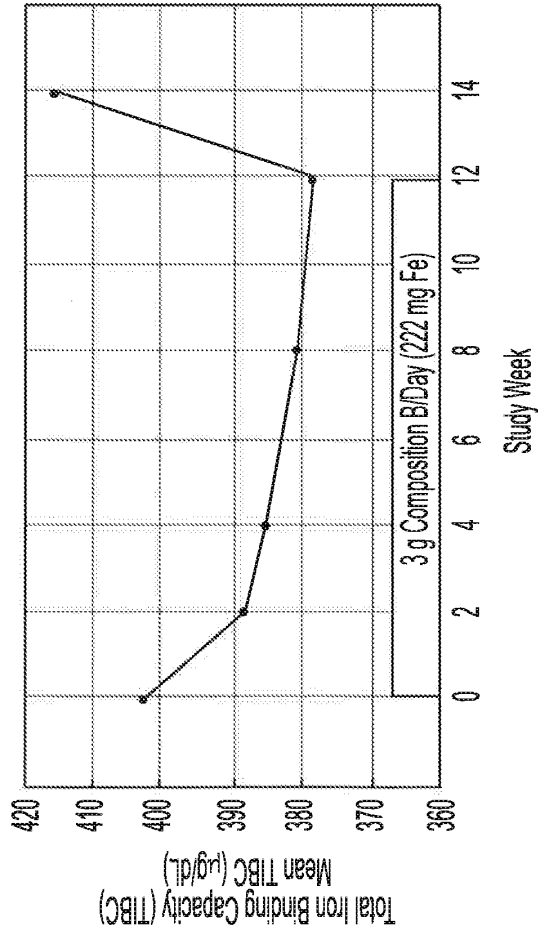


FIG. 30

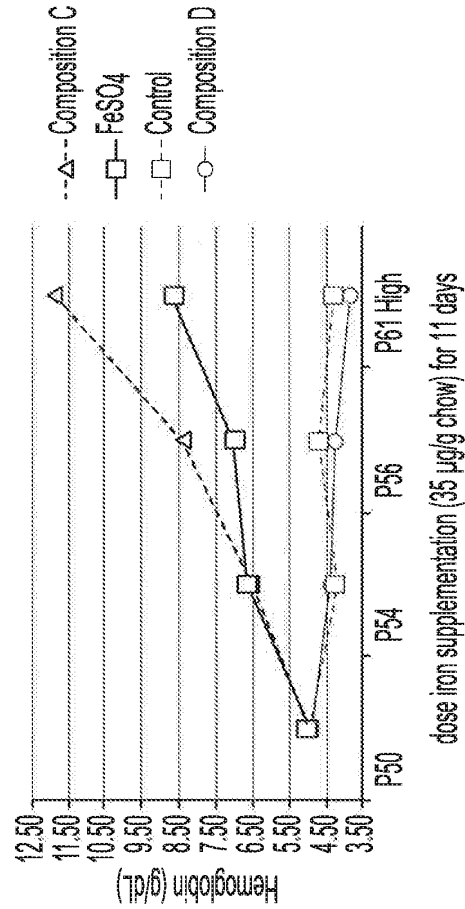


FIG. 31